

ENDOSCOPY HANDBOOK

2011 EDITION

Edited by
Michael Bourke and Ian Norton

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SECTION 1

BACKGROUND AND PREPARATION FOR ENDOSCOPY

- How Endoscopes Work *(Ian Norton)*
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How Endoscopes Work

Ian Norton

It is important for endoscopists to have a general idea of how an endoscope works, primarily so that they can attempt to trouble-shoot equipment malfunction. From a practical point of view, when using accessory instruments it is important to know that an accessory is compatible with a particular endoscope (i.e. length and channel diameter) as well as having an idea where on the visual field the accessory will appear.

This summary will outline the fundamental workings of an endoscope with some reference at the end to specialist scopes such as EUS instruments. Reference to specific proprietary aspects of one company's instrument versus another has been avoided as much as possible.

A Bit of History

Phillip Bozini is credited with the earliest known attempt to visualise the interior of a body cavity in 1805. He devised a tin tube illuminated by a candle which was used with limited success to investigate the genitourinary tract. Adolf Kussmaul is credited as being the first to perform gastroscopy in 1868 using a rigid tube and a cooperative sword-swallower! Illumination and negotiating curves were insoluble problems and he abandoned further development. In 1886 Josef Leiter was the first to use the electric light bulb in a cystoscope and subsequent rigid instruments with distal bulbs were used by ENT surgeons until the 1960s to examine the oesophagus.

A semiflexible instrument with a rigid proximal portion utilising glass prisms in a semi-flexible portion was launched by Wolf and Schindler in 1932. In 1950 Olympus Corp. introduced the gastrocamera which took photographs of the stomach using microfilm and a synchronised flash.

Basil Hirschowitz introduced a flexible instrument utilising fibreoptics in 1958. The "panendoscope" was introduced by ACMI in 1971. Techniques rapidly advanced. ERCP was demonstrated with a side-viewing instrument in 1970 and endoscopic sphincterotomy was reported by Kawai in Japan and Classen in Germany. Colonoscopy was performed in 1970 and polypectomy in 1973. Videoendoscopes were introduced in 1984 and subsequent improvements have dramatically improved the quality of imaging as well as improving the comfort and ease of performing the procedure.

Basic Components

Most endoscopes are very similar in construction.

1. **Insertion Tube.** The insertion tube characteristics (stiffness, etc) is the main determinant of a proceduralists preference for one scope over another. The distal part of the insertion tube is made of articulated metal rings. The shaft is made of a series of metal bands spiralling in different directions. These give the scope its stiffness and torque characteristics. Variable stiffness instruments have a series of wires running most of the length which, when tightened, increase the rigidity of the instrument. Note that these wires do not go to the tip of the instrument, so the final 30cm or so does not stiffen. Most instruments have 4-way tip deflection, with left, right and down deflection about 90 degrees and up about 210 degrees, (depending on the instrument).
2. **Air, Water and Suction channels.** Standard instruments have these channels. In addition some colonoscopes have an added water jet channel, EUS instruments have an extra channel for balloon water insufflation and some therapeutic scopes have 2 channels for suction/appliances. When planning a procedure you must know the location of the accessory channel relative to the image (e.g. 5 o'clock versus 7 o'clock). It is also essential to know the diameter of the accessory channel relative to therapeutic devices planned (e.g. a colonic stent will not pass through a gastroscope or paediatric colonoscope, etc).

Water to clean the lens is provided by a water bottle. This system is pressurised by a small pump. Air is always circulating across the top of the water bottle, up the umbilical cord and effluxing from the air water valve (that's why you can always feel air at this valve). Covering this efflux vent with your finger forces the air instead down the air/water channel and into the lumen. Depressing your finger on this valve cuts off this air flow and instead opens a channel from the water in the bottle to the air/water channel. Due to the increased pressure in the water bottle, water is forced through this system, washing the lens.

The suction channel is connected by a valve (shut in the neutral position) to another channel in the umbilical cord to the wall suction connector. Depressing this valve opens this channel to the suction system. For most of its path this channel uses the same channel as the biopsy/accessory channel. A rubber cap prevents air escaping from the biopsy channel.

Light is supplied by a high intensity light source in the endoscope tower. The light is conveyed by bundles of glass fibres via the umbilical cord and instrument shaft to the instrument tip. Thus, this system removes the light bulb from the instrument tip, preventing heat build up at the instrument tip. The light source has an automated iris which adjusts light output to the lumen being examined. In some systems the light output can be manipulated to select specific wavelengths (Narrow Band Imaging (Olympus). In other systems post- capture processing of the image is performed to display specific wavelengths (e.g. FICE (Fuji) and i-Scan (Pentax).

3. **Video imaging.** This is a complex field beyond the scope of this paper and only a short summary will be presented here. At the tip of the instrument is a charge-coupled device (CCD) silicon chip. A photon of light hitting a particular point of the surface generates an electrical charge which can then be reconstructed into a point of light on an image. Two CCD systems are in common usage, R-G-B sequential scopes and colour-chip scopes.

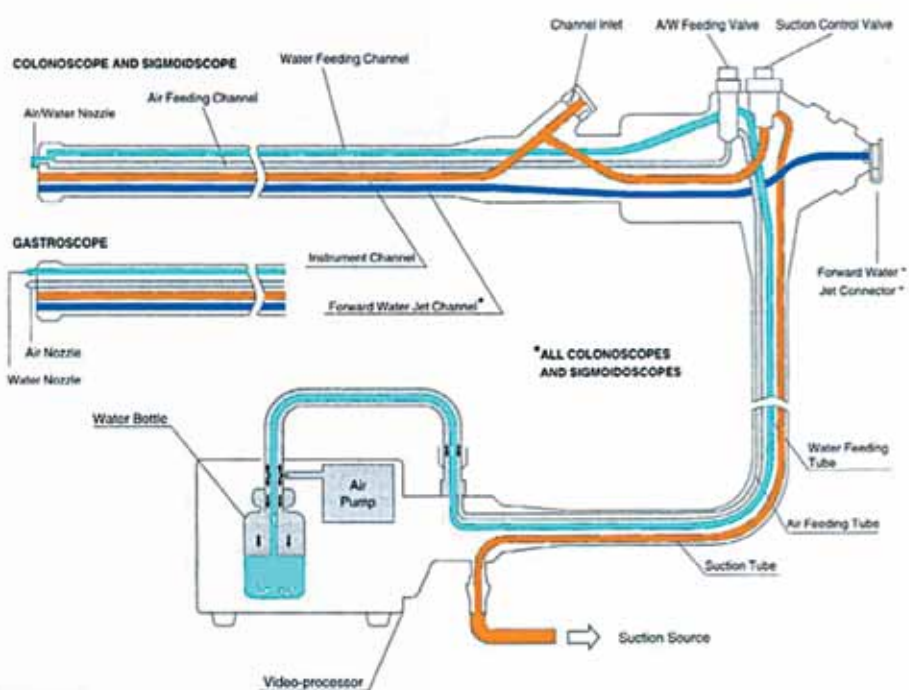
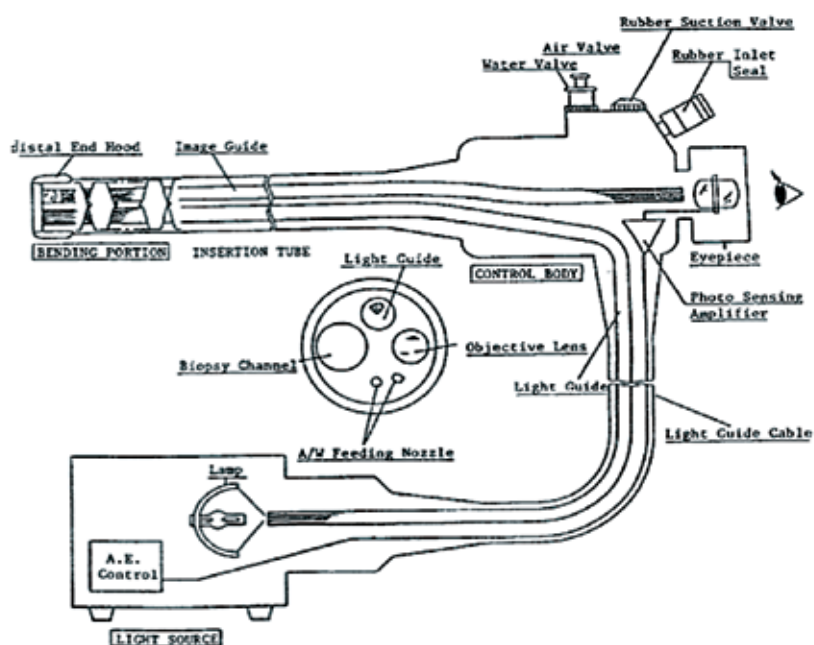
- i. **RGB Sequential Imaging.** All colours seen by the human eye can be generated by a combination of red (R), green (G) and blue (B). These instruments have a black and white chip at the tip. The light used to illuminate the image is not continuous, but pulsed or strobed. Before entering the patient the light is passed through a rotating wheel with red, green and blue filters. Because it is rotating too fast for the eye to see (20-30 revs/sec) these red, blue and green images coalesce to form a replication of the original image. A disadvantage of this system is that during movement there can appear to be a strobing effect which can be annoying for the viewer. An advantage of this system is that all CCD images are used for each capture, leading to a high-resolution image.
- ii. **Colour Chip Imaging.** This uses a multicoloured microfilter at the chip surface to instantly generate a colour representation of the image. Thus, there is no strobing effect (no mechanical colour wheel). Furthermore, since image capture is faster there is less blurring during movement. A disadvantage is that since each pixel in the chip is colour-specific (yellow, magenta, cyan and green), the resolution of the image is less than that possible with RGB sequential imaging. Complementary colours are used rather than primary colours in order to increase image brightness.

Endoscopic Ultrasound

Endoscopic ultrasound is made possible by the presence of an ultrasound transducer at the tip of the instrument. An extra channel and more complicated valve system is required in order to insufflate and deflate a balloon with water. This balloon helps to facilitate acoustic coupling with the mucosal surface.

There are two basic designs, radial and linear. The linear instrument has a curvilinear array distal to, and in alignment with, the instrument channel. This ensures that a needle projecting from the channel will pass through the length of the ultrasound beam, permitting real time imaging during biopsy. The radial instrument scans at 90-degrees to the long axis of the instrument shaft (the Pentax unit has the transducer proximal to an end-viewing scope whereas the Olympus instrument has the transducer distal to an oblique-viewing instrument). Previously the radial instrument was the scope of choice for diagnostic work due to its easier image to orientate and assess. In recent times sonographers have become more comfortable using the linear configuration for diagnostic work also. Virtually all dedicated EUS instruments now use solid-state technology rather than a mechanical rotating transducer.

Nomenclature of Fibrescope



The illustration above shows the actual routes taken by air, water, suction and forward water jet through Pentax video GASTROSCOPE, COLONOSCOPE and SIGMOIDOSCOPE. Please note that all delivery systems have separate independent channels all of which must first be cleaned with an enzymatic detergent and then exposed to a high-level disinfectant or sterilant.

Endoscope Reprocessing

Robyn Brown & Di Jones

Introduction

Since the first clinical report of flexible fibreoptic endoscopy in 1961 endoscopy procedures have become a commonly performed investigation. In the early years endoscopy was often performed by physicians working in ward side rooms or other available space. Scant regard was given to the processes which were applied to ready the instrument to be used on the next patient. Indeed, the overarching concern was the delicacy of the endoscope and potential for damage should anything other than a careful swabbing of the exterior of the instrument be undertaken. As technological developments produced more robust equipment and allowed more invasive procedures to be performed, the need for attention to infection control principles became paramount. Modern endoscopy demands high quality in all aspects of the procedure, including safety from transmission of infection during the procedure. Compliance with endoscope reprocessing guidelines is the key factor underpinning that safety.

Relevant literature

In 1968 Earle Spaulding devised a rational approach to disinfection and sterilisation of reusable medical devices. Spaulding proposed that instruments and equipment should be cleaned and reprocessed according to the level of risk associated with their intended use. The three categories he described were critical, semicritical and noncritical, based upon whether a device contacted intact skin, mucous membranes, or was introduced into a sterile cavity of the body (Fig 1). In that schema, endoscopes are classed as semi-critical. Equipment reprocessing guidelines have subsequently been framed within that categorisation and take into account the scientific knowledge of a microorganism's resistance to disinfection. There is a hierarchy of susceptibility to the cidal effects of disinfectants (Fig 2) and a disinfectant's strength must match the decontamination requirements of a medical device. The biocide also needs to be in contact with all external and internal surfaces. Thus, given 100% surfaces in contact, the critical process parameters of biocides used in endoscope reprocessing are time, temperature and concentration of the chemical.

Figure 1: Spaulding Classification.

Website: http://www.health.qld.gov.au/EndoscopeReprocessing/module_2/2_1.asp

Level of risk	Application	Process
Critical	Entry or penetration into sterile tissue, cavity or bloodstream	Sterility required
Semi-critical	Contact with intact non sterile mucosa or non intact skin	Sterilisation preferred where possible. If sterilisation not possible then high-level chemical disinfection required.
Non-critical	Contact with intact skin	Clean as necessary with detergent and water

The level of bioburden on endoscopes is also a crucial determinant of the effectiveness of disinfection or sterilisation processes. Alfa et al identified the composition of the residual soil on endoscopes both before and after cleaning. These values are used to determine the efficacy of cleaning and reprocessing practices.

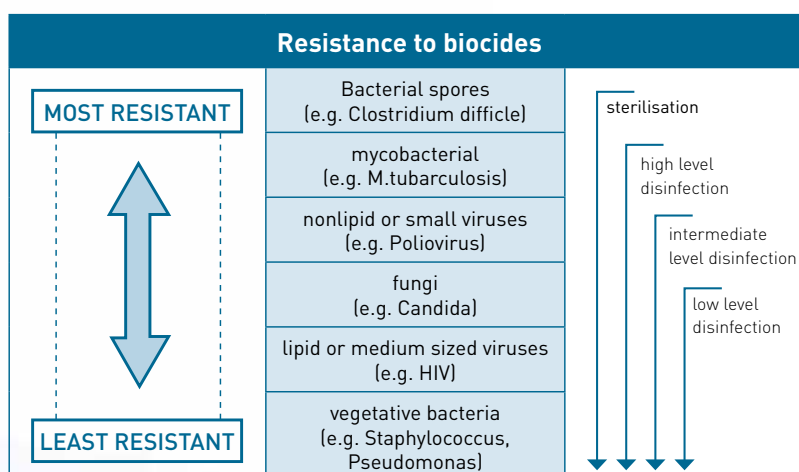
Infections associated with endoscopic procedures arise from endogenous and exogenous sources. The use of antibiotics to prevent transmigration of organisms during procedures e.g. oral flora to skin during PEG insertion, is directed at preventing infection from endogenous sources whilst compliance with accepted reprocessing guidelines is believed to provide virtually no risk of transmission of patient-borne or environmental organisms via the endoscope.

The accumulation of a layer of cells and extracellular materials or biofilms can protect microorganisms from the cidal action of biocides. A biocide must saturate or penetrate the biofilm matrix before it can kill the microorganisms within it. Biofilms can form on surfaces of endoscopy equipment and in the tubing of automated washer/disinfectors as well as on water filters, housings and pipes thus protecting the embedded organisms from exposure to biocides and serving as a reservoir for continuous contamination. Scrupulous cleaning can help to remove biofilms on endoscopes and thus eliminate this problem. The use of an antibiofilm agent reduces the biofilm build up inside the reprocessing machines.

The quality of the rinse water used is a key determinant of the success of an endoscope reprocessing procedure. Delivery of bacteria-free water for endoscope rinsing, either in manual systems or via reprocessing machine, is a complex and expensive undertaking. Given the difficulty in maintaining rinse water quality, emphasis is placed on drying the endoscope to remove any water-borne organisms, preventing disease transmission.

Figure 2: Hierarchy of Microbial Susceptibility to Biocides.

Website: http://www.health.qld.gov.au/EndoscopeReprocessing/module_2/2_2.asp



Potential Complications and Adverse Events

Infection transmission arising from endoscopy has been estimated to have occurred during the last decade at a rate of 1 in ten million procedures. During the period 1974-2004, gastrointestinal endoscopy (including ERCP) procedures accounted for 47.5% of the endoscopy related infections in the USA and 75% in other countries. Endemic transmission may go unrecognised as a result of asymptomatic infection, low frequency and the lack of disease surveillance, and infections are often only recognised if clusters occur. These limitations make it likely that the number of infections reported in the literature represent only a small fraction of the events.

The review by Spach identified that the most common causative agents of infection in endoscopy were salmonella and pseudomonas. The clinical spectrum of infection ranged from colonisation to death. The recent reviews by Seoane-Vazquez et al and Nelson identified some changes in the organisms involved, with no case of Salmonella transmission reported since 1987. However, the root causes of the infection transmissions remain unchanged: they are:

- **Inadequate cleaning – failing to clean all channels;**
- **Inappropriate/ineffective disinfection – incorrect exposure time, failure to perfuse some channels, not testing concentration of the biocide, using an ineffective or inappropriate disinfectant;**
- **Failure to follow recommended disinfection practices – using tapwater for rinsing;**
- **Flaws in the design of endoscopes or reprocessing machines**

With the exception of the design problems of either machine or endoscope, all other causes arise from non-compliance with the guidelines.

Principles of Endoscope Reprocessing

The most important step in the process of endoscope decontamination is scrupulous cleaning prior to disinfection.

Even minor deviations from cleaning protocols result in persistent microbiological contamination after disinfection.

Endoscopy should not be performed in centres where adequate facilities for cleaning and disinfection are not available. These facilities include:

Personal protective equipment (PPE) required to safely perform reprocessing should include:

- Gloves
- Protective impervious gown
- Face/eye protection

Cleaning equipment required:

- Cleaning adaptors
- Cloths
- Syringes

Chemicals required:

- Enzymatic or biofilm removal detergents
- Biocide
- Alcohol 70%

Brushes required:

- Toothbrush
- Short stubby brush
- Brush for each channel, select for correct size.

In order for cleaning to be effective it must:

- Be performed by a person conversant with the structure of the endoscope and trained in cleaning techniques:
- Be undertaken immediately after the endoscope is used so that secretions do not dry and harden:
- Follow a protocol which, using appropriate detergents and cleaning equipment, allows all surfaces of the endoscope, internal and external, to be cleaned:
- Be followed by thorough rinsing to ensure all debris and detergents are removed prior to disinfection.

Practitioners undertaking endoscope decontamination should be familiar with the particular features of the endoscope being decontaminated. It is important to ensure manufacturers' endoscope cleaning instructions for each individual endoscope are available and all members of staff responsible for decontamination have been fully trained.

Documentation

Clear and detailed quality management systems should be in place to ensure full compliance with all aspects of cleaning, disinfection and sterilisation protocols. Microbiological testing of the endoscopes should be undertaken at the recommended interval.

Records should be maintained to document the endoscope reprocessing steps and allow patient tracking if required.

They should include:

- Date
- Instrument serial number / other identification
- Patient details

- Identification of the person who:
 - Cleaned the endoscope and connected it to the automated flexible endoscope reprocessor (AFER) or placed it in the biocide
 - Removed the endoscope from the AFER or biocide, rinsed it if using a manual process, and released it as safe to be used or completed the pre-storage procedures
- Records of the biocide used: batch number, date decanted, date changed or topped up. The minimum effective concentration (MEC) of the biocide should be recorded as per product instructions. In addition, critical parameters for biocidal activity should be recorded (can be by exception)
 - Temperature of the biocide
 - Immersion time in biocide

Water quality

Water quality available for endoscope reprocessing should be validated by quality control measures.

The final rinse water for duodenoscopes should be bacteria free. The final rinse water for other endoscopes should be of high quality and free of bacteria known to cause invasive clinical disease including pseudomonas species.

Technique

A standardised technique is important to ensure all steps are completed. Instructions will differ slightly depending on the brand of endoscope.

Pre Cleaning

- IMMEDIATELY after the procedure wipe the insertion tube from control head to distal tip with a disposable cloth dampened in an detergent solution.
- Aspirate detergent solution through suction/biopsy channels. Continue until the expelled solution is visibly clean. Alternate suctioning of the fluid and of air to enhance cleaning effectiveness of the aspirated solution.
- Depress and release air/water button several times.
- Follow manufacturer's instructions to complete flushing of air / water channel with brand specific equipment if required.
- Disconnect from processor taking care not to contaminate water bottle.
- Attach protective video cap
- Transport endoscope to the cleaning area in a manner that does not cause contamination of the environment.

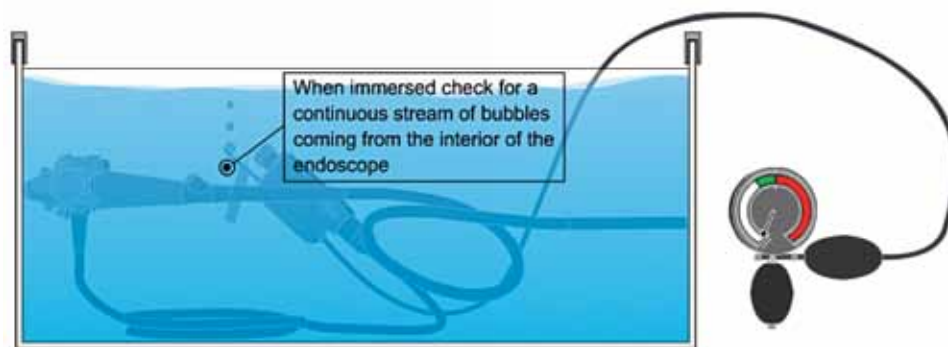
Leak Testing

Leak testing is the process by which the external surface and the internal channels of the endoscope are placed under pressure to identify structural defects, identified by bubbles appearing from the external surface or from any of the channel openings. Perforated channels of endoscopes pose an infection control risk and damage may also occur to parts of the endoscope not designed for fluid exposure.

- All valves and buttons should be removed prior to leak testing. Leak test according to manufacturer's instructions.
- Leak tester should be attached and the endoscope pressurised before immersing in water
- Careful inspection should be followed including bending the distal portion of the endoscope in all directions whilst observing for a continuous stream of bubbles.

Figure 3: Leak testing.

Website: http://www.health.qld.gov.au/EndoscopeReprocessing/module_5/5_3.asp



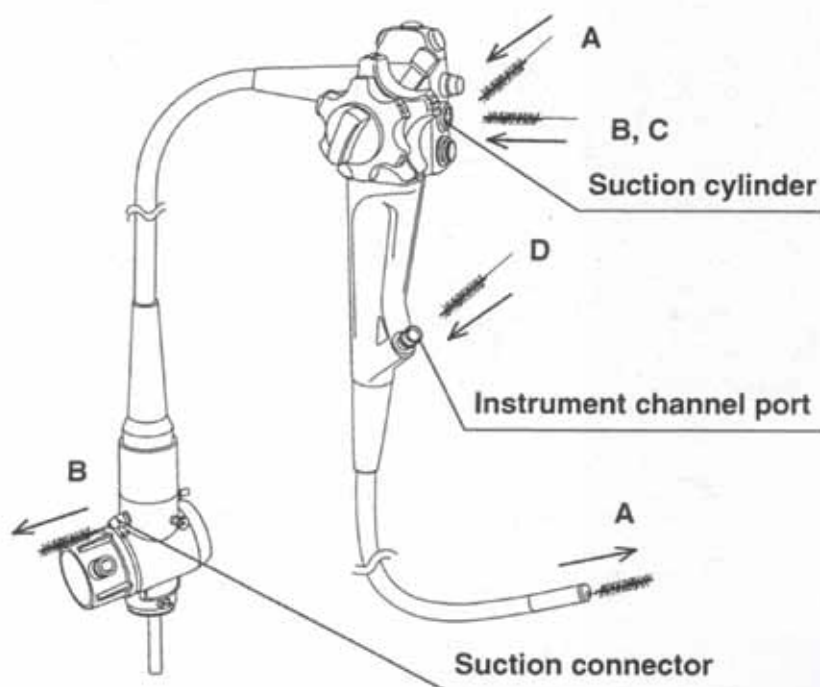
Cleaning

1. Fill sink to cover endoscope and add detergent (accurately measure quantity as per manufacturer's instructions)
2. Brush buttons, (ensuring all shelves/orifices are accessed) soak, rinse, and place in ultrasonic cleaner for required time
3. Remove accessories from ultrasonic, rinse in water and prepare for further processing by steam sterilisation.
4. Brush all channels, using a long brush. Clean end of brush when exited from endoscope (channel access may differ with different brands of endoscope)

NOTE: three channels:

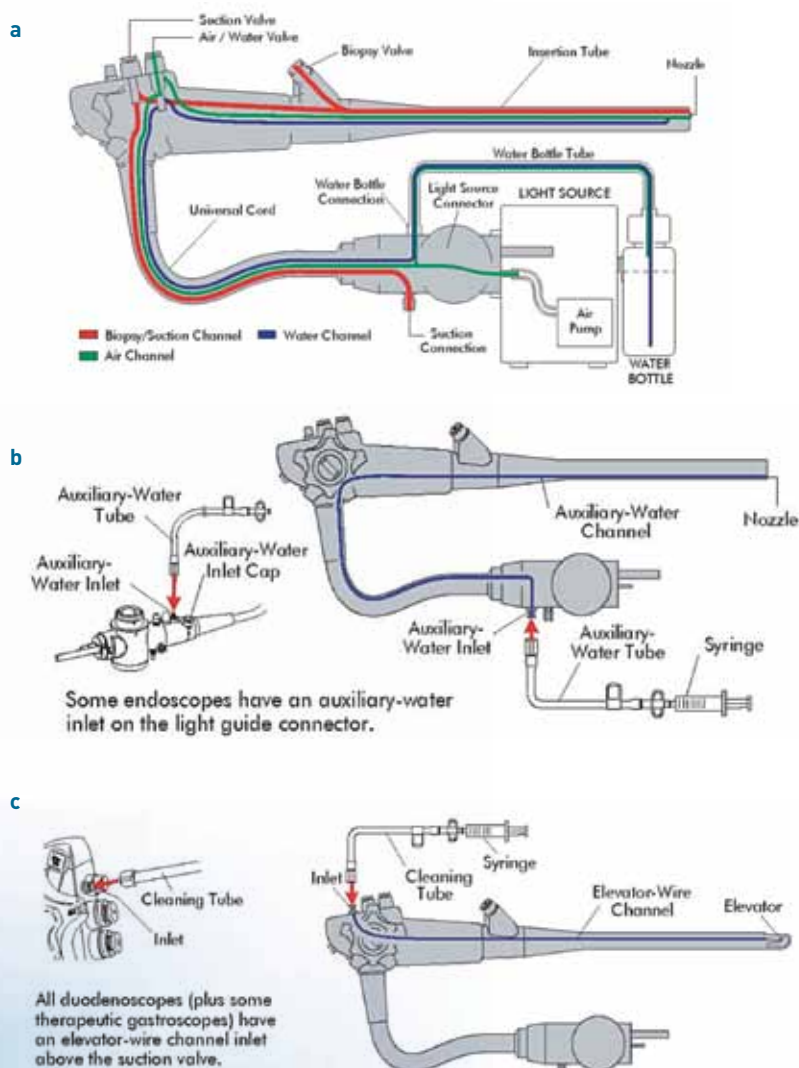
1. Control head to suction connector 90°
 2. Control head to distal tip 45°
 3. Biopsy port to distal tip (Figure 4)
5. Brush valve/button seats (using a stubby brush):
1. Air water
 2. Suction
 3. Biopsy port
 4. Suction connector
6. Brush control head using a toothbrush. Clean all grooves and recesses as grossly contaminated.
7. Brush distal tip (using a toothbrush)
- Caution - clean lens gently
- NOTE: Duodenoscope distal cap – brush, flush 30mls
8. Brush light guide plug (using a toothbrush). Pay particular attention to under the auxiliary wash channel connector.
9. Wipe all surfaces using a disposable cloth to remove contaminants

Figure 4: Channel Brushing (Diagram courtesy of Olympus Australia).



10. Secure cleaning attachments to endoscope channels. Flush detergent through channels using a syringe or automatic pump (Figure 5A)
 - i. NOTE: syringe until bubbles cease to exit endoscope to ensure channels flushed
 - ii. ENSURE: detergent remains in contact for product specified time
11. All accessory channels (auxiliary water / forceps elevator) MUST be flushed (Figures 5B & 5C)
12. Empty sink, purge detergent solution from the channels, rinse channels, rinse exterior of endoscope under running water, dry, (using lint free cloth)
13. Place endoscope in Automatic Flexible Endoscope Reprocessor (AFER) or container of biocide for further processing. When cycle / immersion time completed, remove instrument, paying particular attention to observe that all channel connections have remained attached during the cycle / immersion. If using AFER, check cycle print out for compliance with critical parameters.

Figure 5 a, b, c: (Diagrams courtesy of Olympus Australia).



Endoscope Storage

The following steps are recommended to store the endoscope safely and enhance the drying process.

- Flush all channels with 70% alcohol (this may be completed in the AFER)
- Dry instrument channels with pressurised air (this may be completed in the AFER)
- Remove the cleaning adaptors.
- Dry exterior surfaces with a soft lint free cloth
- Check for sheath or lens damage.
- Store in a well ventilated storage cupboard hanging full length on safe support structures.

Conclusion

Reprocessing practices have evolved and current guidelines appear to be adequate for the protection of patients so that where appropriate guidelines are followed, endoscopes pose minimal risk of transmission of infection. Such reassurance to patients can only be made if there is total compliance with the guidelines.

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Reporting, Documentation and Risk Management

Ian Norton

Introduction

Procedural activities carry specific risks to the patient and expose the gastroenterologist to more potential for litigation than many other physicians. This is particularly the case since most procedures are performed on “the walking well,” patients often without a defined major illness who therefore have little expectation of a poor outcome (compared, for example, with cardiologists performing infarct angioplasty). In spite of this, a recent review of medical claims in the US ranked gastroenterologists 23rd of 28 specialties in number of claims.

It is a reality of practice for endoscopists that malpractice litigation is a real possibility (or even probability) during their career. Nothing can eliminate this risk, but sound medical practice, good documentation and appropriate informed consent processes will reduce the chance of both poor outcomes and litigation when adverse events occur. It is important to bear in mind that an adverse outcome is not the same as malpractice. Pancreatitis following an ERCP is not malpractice, it is a statistical certainty. The issue is whether the patient had proper informed consent.

Relationship of Practitioner Behaviour to Litigation

In the Harvard Medical Practice Study less than 2% of patients with an iatrogenic injury filed a claim. Clearly other factors determine whether a claim is filed. Several studies have addressed this issue and found that a major determinant of a patient’s decision whether to sue is patient dissatisfaction and the physician’s communicative and interpersonal skills. The clear message here is that **communication with the patient and family is of utmost importance, particularly when mishaps occur**. Patients suffering a significant complication will often have their care transferred to the appropriate specialist for correction of the problem (e.g. intensivist or surgeon). It is an important risk management strategy to be available to the patient and family even if no longer participating in the direct care of the patient. This will demonstrate empathy and prevent anger arising from the perception of being “abandoned” by the physician.

Claims Against Gastroenterologists

The Physician Insurers Association of America pools information from 20 member insurers and periodically publish their data. The claims fall into the following groups:

1. **Iatrogenic Injury:** Nearly 30% of claims related to improper endoscopic practice causing injury. Ninety five percent of these cases were perforation or laceration of the gut and its sequelae. Other injuries such as pancreatitis, haemorrhage, dental injury and falling from the bed whilst sedated, also constituted claims.
2. **Errors in Diagnosis:** About 25% of claims related to errors in diagnosis, two-thirds of which were missed malignancies, particularly of the right colon and stomach. Missed colon cancer constituted over 50% of colonoscopic claims and over 75% of claims relating to sigmoidoscopy. Another relatively frequent scenario was delay in diagnosis of malignancy through failure to perform endoscopic examinations. Another frequent scenario was delayed diagnosis of non-gastrointestinal tract neoplasia, especially gynecological and pulmonary. The message here is that gastroenterologists must be clear where their duty of care to the patient ends, such as, thinking whether extra-GI conditions might account for the symptom and investigate or refer appropriately. For example, a 50yr old female with pelvic pain and a normal colonoscopy should not just be reassured, but referred on for appropriate further investigation (such as gynaecological).
3. **Medication Error:** This was relatively uncommon, accounting for less than 10% of gastroenterology claims. However, two notable areas are endoscopist supervised sedation and prescription of corticosteroids and immunosuppressive agents.

Overall, approximately two thirds of claims against gastroenterologists could be considered “cognitive” and one-third “procedural mishap”. **Problems with informed consent were present in about half the cases.**

Legal Principles in Medical Practice

Principles of Tort Law

Claims for medical negligence fall under the principles of tort law. Torts are “civil wrongs” where one private citizen has brought legal proceedings against another (in this case, the physician). It does not involve criminal behaviour and is usually settled with financial compensation to the injured party (the award of “damages”).

Tort law (with respect to medical negligence) involves four steps:

1. **A duty.** The physician’s responsibility to the patient to comply with professional standards of practice
2. **A breach of duty.** The physician didn’t fulfil that responsibility
3. **Causation.** The physician’s failure was a cause of the patient’s suffering.
4. **Injury.** The patient suffered a definable injury (physical or psychological)

Standards of Care

This is a legal concept which attempts to determine the duty which physicians must fulfil in their care of the patient. Failure to practice to this standard constitutes a breach of duty. The court usually determines this standard by hearing expert testimony as well as reliance upon published data such as peer reviewed journal articles and practice guidelines. Thus, the standard is tailored to the specific case under review and should reflect current practice at the time of the injury.

The standard of care is best described as good patient care. It is not defined as best medical practice (for example, that provided by a world-leader in a field), but rather on what would be expected from a peer under the same circumstances.

Defining Responsibility

Joint Liability and Comparative Fault: This concept recognises that many health care workers may be involved in the circumstances leading to an adverse outcome. Therefore, the blame may be appropriately shared over many doctors, nurses, institutions, etc. For example, a colonic perforation is not necessarily negligent. However, if occurring with inadequate consent or poorly recognised by the nurse in recovery, the doctors caring for the patient on the ward or mismanaged by the surgeon, there may be shared blame amongst many individuals.

Respondeat Superior and Vicarious Liability: Respondeat Superior is a legal term referring to the concept that a master is responsible for the mistakes of his servant. Vicarious liability means a corporation is responsible for the acts of its employees and agents. In this sense, a consultant supervising a Fellow doing an ERCP may be liable for a proportion of the damages arising from a duodenal perforation. The degree of liability will vary depending upon the factors such as whether the patient had consented that the procedure would be performed by a trainee, the degree of seniority/supervision of the trainee and whether the trainee was performing appropriately. Similarly, a physician could be responsible for a secretarial mishap leading to a poor patient outcome.

Informed Consent

It is a basic legal principle that a competent individual has the right to determine what shall happen to their body. Thus, the physician must obtain the consent of the patient (or his or her legal guardian) prior to performing any procedure, with certain exceptions (see below).

It is crucial to understand that informed consent is a process, not a signed piece of paper. Though most institutions use a signed consent form, it is usually a generic document and therefore may not reflect that the patient was aware of all the elements necessary for informed consent for that particular procedure in that particular patient. Nonetheless, a signed consent form is very useful evidence in court as tangible evidence that a defendant did go through some process of consent and provided the opportunity to ask questions.

Several elements constitute informed consent:

1. **Risks.** All procedures have some risk and patients must be made aware of any risk which, in the view of a reasonable person, might have played a role in that specific patient's decision to proceed. This typically includes the most severe complications (for example, death, haemorrhage, disability), as well as common side effects. You must make some attempt to frame discussion of risk in the context of the patient – losing a finger means different things to a 90yr old in a nursing home compared with a concert pianist!
2. **Benefits.** The patient must understand why they are undergoing the procedure.
3. **Alternatives.** The patient must understand the relative risks and benefits of alternative investigations. The patient should also understand the alternative of not performing any procedure. This aspect of informed consent is often the most poorly performed.
4. **The opportunity to ask questions**

You should avoid coercion of any sort and should avoid being emotionally invested in getting the patient to consent to what you believe to be the best course of management. The physician should not be judgmental or emotive.

It is often stated that obtaining informed consent in the endoscopy room immediately prior to the procedure could be perceived as being coercive in that the patient, being prepared, gowned, having taken time off work and possibly with an IV in situ is unlikely to back out of the procedure. Also, the endoscopy suite environment is unlikely to provide the patient with an adequate opportunity to ask questions. These issues are especially important in the open access endoscopy setting.

Obviously, informed consent must be obtained in the language suitable to the patient's comprehension. If the patient has difficulty understanding English, consent should be obtained through a health professional or interpreter service. The patient's friends or relatives should not be used for interpreting, this may constitute a breach of confidentiality and the patient may be misled by the friend/relative's own biases about what they wish the patient to hear.

Exceptions to Informed Consent

1. **Emergency.**
2. **Waiver.** A patient may occasionally assign his or her right to determination to the physician for the management of a specific condition. This must be well documented.
3. **Therapeutic Privilege.** This is an unusual situation where the physician believes that fully informing the patient would be a detriment to the patient. This usually refers to emotional issues. Clearly, there is a danger here that mental health patients could be denied a basic right of self-determination.

4. **Legal Mandate.** In some circumstances the court may order that a patient undergo a medical procedure without requiring the patient's consent. Obtaining concealed contraband and forensic pathology specimens are examples.
5. **Incompetency.** If the patient is incompetent to make decisions the responsibility of providing informed consent defers to the patient's legal guardian.

Informed Refusal

The inverse of informed consent is informed refusal. If a patient refuses specific medical treatment, there is a duty of care for the physician to ensure that the refusal is informed. For example, it is negligent to allow a patient to leave hospital against medical advice without informing them of the risks of doing so.

Documentation

Sound documentation is an important risk management tool as well as a component of good medical practice. Nothing in a patient's management plan should be left to the memory of the physician. A case may come to trial years after the event and in a case of conflicting memory of a conversation between a patient and a physician (years down the track), the patient will often be the more convincing witness.

Medical record retention laws vary and the physician should be acquainted with how long records of adults and minors need to be retained. The physician owns the record, but the patient has the right to control access to the information. The patient has a right to see the medical record and copy it.

Documents should be concise, logical and legible. All entries must be dated. Never make demeaning or insulting comments about the patient (it will look bad in court!). If an error occurs, it should be struck through once (still legible) and a correction made, signed and dated. **Notations must never be altered.** Forensic techniques are available to determine whether numbers, etc have been changed subsequently. Notations can be corrected or supplemented if the changes are clearly identified and dated.

Electronic Media

The substance of telephone conversations should be recorded in the notes. E-mail is increasingly used to communicate with other health professionals and patients. There are issues of confidentiality regarding email. Its use is generally not to be encouraged, but if you do use email, print out a copy and keep it in your medical record.

Procedure Documentation

Procedures may be documented by dictated, hand written or generated by databases. Irrespective of the method of documentation all endoscopic reports should contain the following information:

• Patient name
• Unique patient identification number
• Date of procedure
• Instrument used
• Name of procedurelist and assistants
• Drugs used (and their doses)
• A comment regarding obtained consent
• Indication for the procedure
• Findings
• Procedures undertaken
• Whether pathological specimens were obtained
• Post procedure instructions
• Follow-up

It is wise to include post-procedure documentation since many patients will have persistent amnesia attributable to the effects of sedation at the time of discussion prior to leaving the endoscopy unit (in spite of appearing to be alert). This documentation should include advice regarding driving, important decision making or dangerous activities following sedation, follow-up arrangements and a plan in case of emergency following the procedure. Depending upon the findings of the procedure and the level of relationship between the endoscopist and the patient, it may or may not be appropriate to include a summary of the findings of the procedure. There are several software reporting systems which incorporate many of the necessary elements of the report. This may also include embedding of photographs which may be used both to document pathology as well as the adequacy of the examination (e.g. documentation of visualisation of the ileocecal valve).

Risk Management

Many of the issues already discussed comprise important aspects of risk management.

- a. **Sound Medical Practice.** The best defence against poor outcomes and possible litigation is good medical practice. An important aspect of this is efforts on the part of the individual and the institution to remain current with the medical literature and practice in line with government statutes and societal guidelines. It is important to note that courts have been reluctant to accept financial constraint as a mitigating factor when assessing a poor outcome (though, of course, this may shift some blame from the individual to the institution).

- b. **Good Documentation.** This is obvious, both in terms of being able to appropriately manage multiple episodes of care and communication as well as a defensive tool in court.
- c. **Informed Consent.** See previously
- d. **Peer Review.** This is a vital mechanism to identify endemic problems and to recognise and discuss problems in order to prevent their recurrence. This must always be done in a non-threatening manner so as to maintain a true reflection of the unit's complication profile. It should be a formal process, usually involving a meeting of all senior staff on a regular basis with recording of minutes.

The physician should be aware of their own complication profile and where they stand relative to their peers. Some very experienced proceduralists may have high complication rates due to the complexity of work they perform, and in this circumstance, should have some way of illustrating their work-mix. Patients have a right to know, in general terms, your complication and outcome profile.

- e. **Adequate Indemnity Insurance.** Some large institutions may self-insure their employees, but it is the responsibility of every physician to ensure that he or she has adequate indemnity cover both for claims occurring now, as well as claims which may occur years into the future (though many states have a statute of limitation on medical malpractice claims).

Management of Anti-Platelet and Anti-Coagulant Agents for Endoscopic Procedures

J P Bate & M N Schoeman

1. Introduction

Endoscopic procedures are being performed more frequently in patients who are receiving anti-platelet and/or anti-coagulant therapy. Management of these patients and their medications in the peri-procedural period requires clinical judgement and an understanding of risks involved; the latter includes both the risks of haemorrhage when performing endoscopic procedures on anti-platelet or anti-coagulant therapy and the risks of thromboembolism and other adverse events when ceasing these medications. Patients will need individual assessment and it is not possible to give guidance to cover all situations.

All endoscopic procedures have an inherent risk of bleeding. Minor bleeding is common but clinically relevant bleeding, defined as bleeding requiring specific intervention, unplanned admission to hospital or blood transfusion, should be rare. Traditionally procedures have been divided into those at low and high risk for haemorrhage (see Table 1). Similarly, there are low and high risk situations with regards to ceasing anti-platelet or anti-coagulant medications (see Tables 2 & 3). Both these aspects need to be considered before a decision is made to cease anti-platelet or anti-coagulant medication. In some high risk situations, these medications cannot be ceased without very significant consequences.

The recommendations made in this chapter are consistent with guidelines from the American Society for Gastrointestinal Endoscopy and the British Society of Gastroenterology.

Acute gastrointestinal bleeding in patients taking anti-platelet or anti-coagulant therapy will not be discussed here. A decision regarding cessation or reversal of such therapy should be individualised, carefully weighing risks of thromboembolism against those of continued bleeding.

2. Risk Stratification

2.1 Bleeding

Aspirin does not increase the risk of clinically significant bleeding following either low or high risk endoscopic procedures. This includes procedures such as colonic polypectomy and biliary sphincterotomy.

There are no good data regarding the bleeding risk during endoscopic procedures when patients are on **clopidogrel**. However, there are recent data in a small number of patients showing an excessive bleeding risk when trans-bronchial lung biopsies are taken whilst patients are on clopidogrel (3.4 vs 89%). The risk of bleeding after trans-bronchial biopsy is not increased in patients taking aspirin. The latter finding is similar to the endoscopic data and by extrapolation clopidogrel should be used with great caution in patients undergoing high risk procedures.

There are no data regarding bleeding risk in patients on **low molecular weight heparin** (LMWH).

A significant risk of haemorrhage exists when high risk endoscopic procedures are performed on patients taking **warfarin**. Few studies have been published since anti-coagulation is generally avoided when high risk procedures are performed, but one study did show a high rate of bleeding when colonic polypectomy was performed with patients on warfarin (0.8 vs 10.8%; OR 13.37). There are also data showing a high risk (10 to 15%) of significant bleeding when performing an ERCP with sphincterotomy in patients where warfarin is restarted within 72 hours.

2.2 Thromboembolism

A significant risk of coronary stent thrombosis exists when anti-platelet therapy is prematurely discontinued. This includes both bare metal and drug eluting stents, but the period for which most risk is present differs. Clopidogrel should preferably not be stopped for at least one month after insertion of a bare metal stent. When clopidogrel is prescribed following placement of a drug eluting stent, cessation of therapy should be discussed with the patient's cardiologist. Premature discontinuation of the drug results in rates of stent thrombosis of up to 29%. Stent thrombosis results in acute closure of a major coronary vessel, resulting in myocardial infarction with a significant risk of death. If therapy does need to be ceased then the duration that the therapy is stopped should be less than 5 days.

Cessation of warfarin results in varying risks of thromboembolism, depending on the underlying condition (see Table 3). The highest risk exists for conditions such as prosthetic heart valves and atrial fibrillation (AF) with high risk features and there is a risk of thromboembolism (3.6%) in these situations despite bridging therapy with LMWH. The risk in patients undergoing endoscopy, who have their anti-coagulation adjusted for the procedure, ranges from 0.31 to 2.93%. The risk of thromboembolism in AF without anti-coagulation ranges from 1.9 to 18.2% depending on concomitant risk factors. The risk of discontinuing warfarin in the setting of treatment for venous thromboembolism is probably low, particularly if more than three months have passed since the event.

3. Anti-Platelet Agents

3.1. Aspirin

Aspirin can be continued for all low and high risk endoscopic procedures as the bleeding risk is minimal.

3.2. Clopidogrel

Clopidogrel should be continued in patients who are undergoing low risk endoscopic procedures. Expert opinion suggests that mucosal biopsies can be safely taken whilst patients are on clopidogrel.

There is a significant bleeding risk when high risk procedures are performed in patients taking clopidogrel. Ideally, clopidogrel should be stopped at least 7 days prior to a procedure, but cessation of this medication can cause significant morbidity and mortality in certain situations as discussed above (see Table 2).

If patients are on clopidogrel for a low risk condition, an assessment must be made as to whether or not it can be ceased temporarily; aspirin therapy for the peri-procedure period may be a reasonable alternative.

In high risk situations when clopidogrel is prescribed for recently inserted coronary stents, ceasing the clopidogrel can result in stent thrombosis, which may be fatal. It is important to know if a bare metal or a drug eluting stent is in situ. For bare metal stents, a one month period on dual anti-platelet therapy is recommended. High risk endoscopic procedures (especially elective procedures) should be avoided in this period if possible. Following the initial one month period, a single anti-platelet agent is usually sufficient. If a high risk endoscopic procedure needs to be performed at this stage, the clopidogrel should be ceased and aspirin continued or commenced.

The above principles also apply for drug eluting stents, but the recommended period for dual anti-platelet therapy is up to twelve months.

Clopidogrel can generally be restarted the day following the procedure, but this decision should be made on a case by case basis. Consultation with the patient's cardiologist is always recommended prior to ceasing clopidogrel.

4. Anti-Coagulant Agents

4.1. Low molecular weight heparin

Patients often receive LMWH in the setting of deep vein thrombosis, pulmonary embolism or as a bridging therapy to endoscopic procedures for those on chronic warfarin therapy. Patients can stay on LMWH up until the day before the procedure; the anti-coagulation is then held for at least 8 hours prior to the procedure, including on the day of the procedure.

The decision regarding when to restart anticoagulation should again be made on a case by case basis.

4.2. Warfarin

Warfarin may be continued when a low risk endoscopic procedure is performed. This includes when mucosal biopsies are taken (expert opinion). However, it should be ensured that the INR is not above the therapeutic range.

Management of warfarin and anti-coagulation prior to a high risk endoscopic procedure is more difficult. An assessment must be made as to whether or not the patient requires anti-coagulant therapy in the peri-procedural period. If the risk of thromboembolism is low and anti-coagulation is not required, then the warfarin should be ceased 5 days prior to the procedure. The INR should be less than 1.5 prior to the procedure, although studies have not defined a definite safe level of coagulopathy for which high risk procedures can be undertaken.

If anti-coagulation therapy is required in the peri-procedural period, guidelines recommend that warfarin be ceased and LMWH commenced as a bridging therapy; this option may also be cost effective. The warfarin should be ceased 5 days prior to the procedure, with LMWH (at a therapeutic dose) commenced two days later. Management of the LMWH is then the same as described above.

Warfarin generally can then be restarted on the night of the procedure and the LMWH continued from the following day until a therapeutic INR has been achieved; overlap for 2 days is recommended. The timing of restarting anti-coagulation should be individualised.

5. Summary

In summary, management of anti-platelet and anti-coagulant medications for endoscopic procedures requires risk stratification of both the risk of bleeding from the procedure (see Table 1) balanced against the risk to the patient of ceasing anticoagulation (see Tables 2 and 3). These permutations are summarised in Figures 1 and 2.

6. Risk Stratification

Figure 1. Low risk endoscopic procedure.

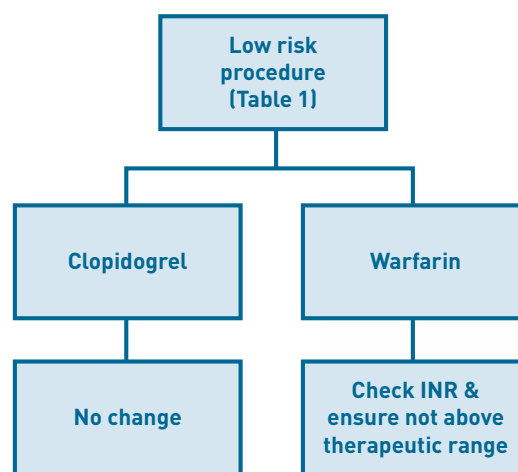
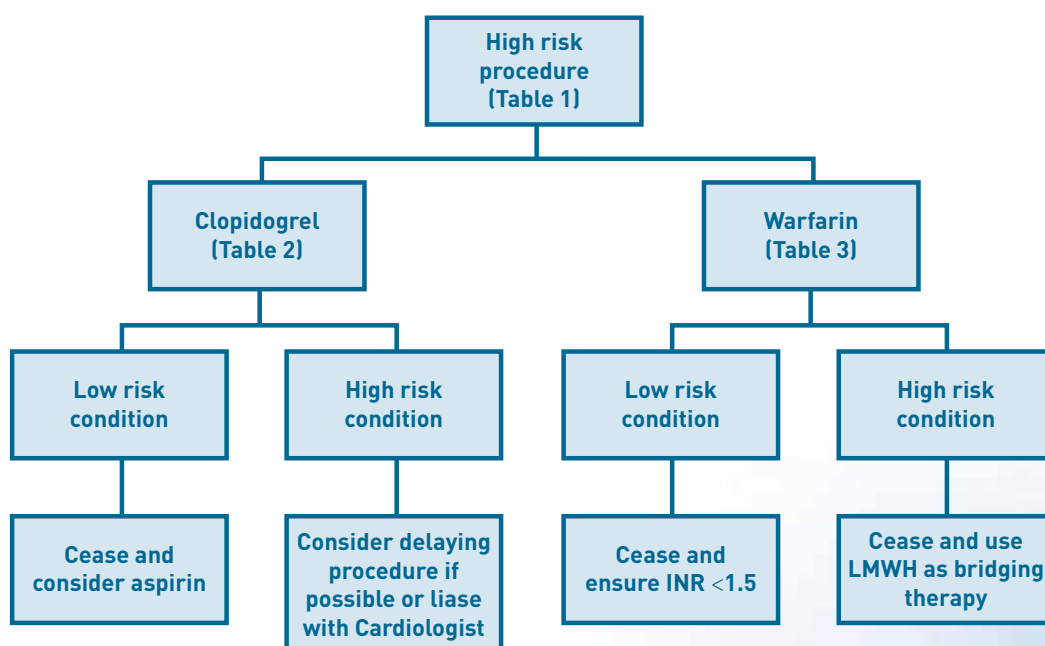


Figure 2. High risk endoscopic procedure with low or high risk condition.



7. Tables

Table 1. Low and high risk endoscopic procedures.

Low risk	High risk
Diagnostic procedures ± biopsy	Polypectomy
ERCP without sphincterotomy	ERCP with sphincterotomy
Biliary or pancreatic stenting	Dilatation of strictures
Diagnostic EUS	Therapy of varices
Enteroscopy	PEG insertion
	EMR
	EUS with FNA

ERCP = endoscopic retrograde cholangiopancreatography

EUS = endoscopic ultrasound

PEG = percutaneous endoscopic gastrostomy

EMR = endoscopic mucosal resection

FNA = fine needle aspiration

Table 2. Low and high risk conditions for ceasing clopidogrel.

Low risk	High risk
Ischaemic heart disease without stent	Bare metal stent (within 1 month)
Cerebrovascular disease	Drug eluting stent (within 12 months)
Peripheral vascular disease	

Table 3. Low and high risk conditions for ceasing warfarin.

Low risk	High risk
Prosthetic (metal) aortic valve	Prosthetic (metal) mitral valve
Prosthetic (xenograft) valve	Prosthetic (metal) valve and AF or prior thromboembolic event
AF without valvular heart disease	AF and valvular heart disease (especially mitral stenosis)
Over 3 months since VTE	Under three months since VTE
	Thrombophilia syndromes

AF = atrial fibrillation

VTE = venous thromboembolism

Further Reading

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Sedation and Patient Monitoring for Gastrointestinal Endoscopy

D. Brian Jones

Introduction

Gastrointestinal endoscopy (GIE) has become one of the most common interventional medical procedures. Approximately 700,000 endoscopic procedures are billed annually to Medicare, a figure which does not include non billable inpatients in Australian public hospitals. With the exception of flexible sigmoidoscopy, over 95% of GIE is performed under some sort of sedation, ranging from intravenous midazolam plus or minus opiate through to full general anaesthesia administered by an anaesthetist. GIE is remarkably safe. Death directly attributable to sedation for GIE or its sequelae is quoted at a rate of 3/33,854. Sedation is intended primarily to reduce patient anxiety and discomfort, consequently improving tolerability and satisfaction for both patient and endoscopist. Despite its benefits, its use remains problematic in that sedation delays patient discharge, adds to the costs and is potentially associated with cardiopulmonary complications.

Aims of Sedation

Sedation may be defined as a drug-induced depression in the level of consciousness. It needs to be appreciated that sedation is a continuum from minimal sedation to general anaesthesia. This is summarised in Table 1:

Table 1: Modified from American Society of Anaesthesiologists.

	Minimal sedation	Moderate sedation	Deep sedation	General anaesthesia
Responsiveness	Normal to verbal stimulation	Purposeful responsiveness to verbal or tactile stimulation	Purposeful responsiveness to repeated or painful tactile stimulus	Unrousable even to painful stimulus
	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

It must be appreciated that patients may move from one level of sedation to another quite precipitously depending on age, co-morbidities, concurrent medications such as sedatives and opiate analgesics, and dose and rapidity of administration of intravenous sedatives.

Facilities and Equipment

Safe sedation for GIE is only possible in a location which is adequate in size, suitably staffed by experienced medical and nursing staff, and equipped to deal with cardiopulmonary emergency. The reader is directed to professional guidelines produced by the Australian and New Zealand College of Anaesthetists and available on its website <http://www.anzca.edu.au/resources/professional-documents/ps9.html>

Pre-procedure Assessment

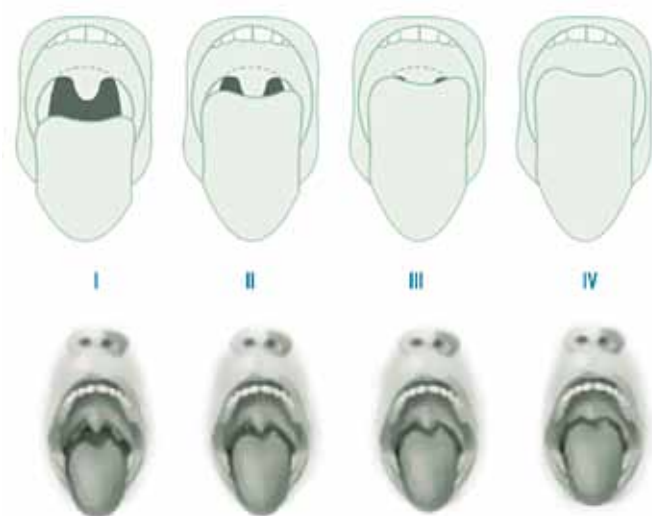
Pre-procedure assessment is essential and patient selection can go a long way to preventing sedation related complications. History should include significant cardiopulmonary disease, neurologic or seizure disorder, snoring or sleep apnoea, previous adverse reactions to anaesthetics or sedation, current medications and allergies, alcohol and smoking history, and duration of fasting. Although not perfect, using classifications such as the ASA classification (Table 2) may assist with patient selection, particularly as a guide to which patients require anaesthetist support.

Table 2: ASA classification. © American Society of Anaesthesiologists.

Class	Description
I	Normal and healthy patient
II	Mild and systemic disease not limiting activities (e.g. controlled hypertension)
III	Moderate or systemic disease (e.g. stable angina)
IV	Severe systemic disease that is potentially life threatening (e.g. CCF)
V	Patient is morbid and is at risk of death within 24 hours
E	Emergency status i.e. underlying emergency procedure in addition to ASA I-V

Physical examination should include vital signs, weight and body mass index, baseline level of consciousness and assessment of airway. This last issue is especially important in patients with obesity, short thick neck, and structural abnormalities of mouth jaw and palate. In this setting use of the Mallampati score for predicting problem airways may be useful (Figure 1).

Figure 1: Mallampati score for prediction of difficult intubation.



Pharmacology of Sedation

The most commonly used drugs for sedation in Australia are opiates, benzodiazepines and propofol, often in combination.

Opioids

The principle effects of opioids are analgesia and sedation. They exert their pharmacologic effects by binding to specific opioid receptors present in central nervous system and peripheral tissue. The most commonly used opioids in Australia are *pethidine* and *fentanyl*. The induction dose of pethidine is 25 to 50mg given intravenously over two minutes. Its onset of action is three to six minutes with a duration of action of up to three hours. Fentanyl is a synthetic opioid narcotic which is highly lipid soluble with a rapid onset of action. It is usually given in doses commencing at 25ug up to 100ug.

The major adverse effect with opioids is respiratory depression and concomitant use of benzodiazepine has a synergistic effect. Opioid induced nausea and vomiting is also a potential side effect. *Naloxone* is an *opioid antagonist* which is structurally related to oxymorphone. It antagonises all of the central nervous effects of opioids. The onset of action of naloxone is one to two minutes and it has a half life of 30 to 45 minutes. For reversal of opioid respiratory depression it is recommended that such patients receive a dose of 0.2 to 0.4mg intravenously every 2-3 minutes until reversal is obtained. Supplemental doses may be necessary in some patients after 20 to 30 minutes.

Benzodiazepines

The pharmacologic effects of benzodiazepines include anxiolysis, amnesia, sedation, muscle relaxation and in larger doses anaesthesia. Benzodiazepines enhance activity of the inhibitory neurotransmitter gamma amino butyric acid (GABA) by binding to the GABA-a receptor on the post synaptic nerve membrane in the cerebral cortex. Although *diazepam* is still widely used worldwide the most common benzodiazepine used in Australia for GIE sedation is *midazolam*. It has a more rapid onset of action and shorter duration of action. After intravenous administration midazolam has an onset of action within 1-2 minutes with a peak effect in 3-4 minutes. Its duration of action is up to 80 minutes. The initial intravenous dose should be of the order of 1-2mg with increments of 1mg. Most patients can be sedated with doses of up to 5-6mg particularly if used in conjunction with fentanyl in small doses. As for opiates the major potential issue is oversedation (or in effect inadvertent general anaesthesia) with respiratory depression. *Flumazenil* is structurally related to midazolam and is a specific benzodiazepine antagonist. It reverses midazolam induced sedation and psychomotor impairment. Flumazenil has a half life of up to 1.3 hours and the average duration of antagonism is one hour. Because the effects of midazolam may persist for more than 80 minutes resedation may occur. Incremental intravenous doses of flumazenil of 0.1 to 0.3mg are effective in reversal of benzodiazepine over sedation. It can also be given as an infusion (0.3 to 0.5mg/hr).

Propofol

Propofol (2,6-diisopropofol) is a hypnotic with minimal analgesic effect. At subhypnotic doses it produces sedation and amnesia. It acts via the GABA system. Propofol is highly lipid soluble and has a rapid onset of action of between 30 and 45 seconds (one arm-brain circulation). It is metabolised rapidly in the liver and its metabolites excreted in the kidney. Despite this its pharmacokinetic profile is not significantly altered in cirrhosis or renal failure. Its duration of action is short, of the order of only 4-8 minutes and is delivered either in multiple small boluses or by infusion. The current formulation of propofol contains 1% propofol in soybean oil, glycerol and purified egg phosphatide, and should be avoided in patients with soy or egg allergies. Pain on injection occurs in 30% of patients and other adverse effects include a decrease in cardiac output and hypotension. There is no reversal agent for propofol but its relatively rapid metabolism allows rapid recovery if oversedated.

Nonetheless, anyone using this agent must be prepared to provide mask ventilation if required.

Other agents

Most GIE in Australia is performed with midazolam and an opiate, plus or minus propofol where available. Other agents used include alfentanil, ketamine, remifentanil, and sevoflurane. In the USA droperidol is occasionally used.

Monitoring during sedation

Patient monitoring during sedation for GIE is an essential element, and at least one staff member should exclusively be responsible for monitoring the sedated patient, using both visual assessment as well as electronic devices (figure 2) from the time of induction of sedation through to safe delivery to the recovery area. This individual should have an understanding of the pharmacology of drugs used, the stages of sedation which can be achieved, interpretation of changes in physiologic parameters, skills to “rescue” the patient if complications arise, and current certification in basic and advanced life support. Many professional bodies have produced guidelines on safe sedation, and a tripartite working group comprising the Australian and New Zealand College of Anaesthetists (ANZCA), Gastroenterological Society of Australia (GESA) and the Royal Australasian College of Surgeons (RACS) have published guidelines known as PS9 and available on the ANZCA website. The minimum equipment requirements for safe administration of endoscopy with sedation are summarised in table 3.

Figure 2: Example of monitor data measured during sedation and anaesthesia.



The level of monitoring will vary depending upon many factors including patient comorbidities, level of sedation and the type of procedure.

Table 3: Minimal Monitoring and Emergency Resuscitative Equipment.

Basic airway management equipment
Supplemental oxygen
Suction
Nasal cannulae and face masks
Bag mask ventilation device
Oral and nasal airways (all sizes)
Advanced airway management equipment
Laryngoscope handles and blades
Endotracheal tubes and stylets
Laryngeal masks
Cardiorespiratory equipment and monitoring devices
Pulse oximetry
Capnography (desirable if not essential)
Close access to defibrillator and crash trolley
Emergency drugs
Atropine
Antihistamines such as diphenhydramine
Adrenaline
Flumazenil
Naloxone
Glucose 50%
Hydrocortisone
Lignocaine

Who should administer sedation for GI Endoscopy?

The types of sedation used in Australia varies according to institutions and whether GIE is being performed in public or private hospitals or day surgery type units. In private institutions sedation is mostly provided by a medical practitioner trained in the use of sedative agents including propofol. These sedationists may be either specialist anaesthetists or non anaesthetist medical practitioners. A survey of 200 Australian anaesthetists involved in administration of sedation for GIE, was published in 2008. Almost 100% used propofol as the main drug, usually co-administered with either midazolam alone (14%), fentanyl alone (6%) or more commonly midazolam plus fentanyl (61%). The depth of sedation aimed for by anaesthetists equates to a full general anaesthetic according to ASA criteria (table 1).

In public hospitals there are at least three models of sedation delivery:

1. Full propofol based anaesthetic, with or without midazolam and/or fentanyl, administered by a specialist anaesthetist as in the private system
2. Sedation with midazolam plus or minus opioid such as fentanyl or pethidine, administered by one of two endoscopy nurses in the procedure room, under the direction and guidance of the endoscopist. Typical doses would be between 3.5 and 7.5mg of midazolam and between 50 and 100ug of fentanyl.
3. Sedation with midazolam plus or minus an opioid in smaller doses than outlined above, with small increments of propofol given as frequent “top ups” according to patient discomfort. The multiple bolus technique should follow the 20:20 rule (no more than 20mg of propofol at a time with at least 20 seconds between each bolus). In other countries propofol may be administered by a nurse (so called NAPS or nurse administered propofol system) trained in its use. This approach has gained widespread use in the USA and Switzerland. The alternative model is to have the propofol administered by a non-anaesthetist medical practitioner trained in its use. This system has been used very successfully in Canberra and elsewhere. What has been striking about each of these non-anaesthetist administered propofol systems is the incredible safety profile with no deaths in over 220,000 cases and only one case of endotracheal intubation. Most episodes of hypoxaemia are transient and can be managed with bag mask ventilation for a few minutes until the propofol is metabolised.

The future of GIE sedation in Australia

The issue of what constitutes optimal sedation, which drugs to use, and who should administer the drugs is still somewhat controversial and is still evolving. Great strides have been made with the Tripartite Committee (representing gastroenterologists, surgeons and anaesthetists) and document PS9 will continue to evolve. The professional bodies are still developing suitable training programmes for non anaesthetist administered sedation utilising the use of simulators and hands on delivery of propofol and other agents at individual hospital level under the auspices of the departments of anaesthetics. The current recommendations of PS9 in terms of who should administer sedation is summarised in the appendix.

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Appendix (adapted from Document PS9)

Personnel for Procedural Sedation and Analgesia

Scenario 1: Three practitioners – Sedation by Proceduralist

- Medical practitioner proceduralist with airway and resuscitation skills, and training in sedation
- Practitioner with training in monitoring sedation
- Assistant to assist both
- Conscious sedation in ASA P 1-2 patients
- Propofol, thiopentone and other intravenous anaesthetic agents must not be used

Scenario 2: Three practitioners – Sedation by Medical Practitioner

- Proceduralist
- Medical practitioner with airway and resuscitation skills, and training in sedation
- Assistant to assist both
- Conscious sedation in ASA P 1-2 patients
- Propofol, thiopentone and other intravenous anaesthetic agents may only be used by a medical practitioner trained in their use

Scenario 3: Four practitioners – Sedation by Medical Practitioner

- Proceduralist
- Medical practitioner with airway and resuscitation skills, and training in sedation
- Assistant to assist **each***
- Conscious sedation in ASA P 1-3 patients #
- Propofol, thiopentone and other intravenous anaesthetic agents may only be used by a medical practitioner trained in their use

Scenario 4: Three practitioners – Sedation by Anaesthetist

- Proceduralist
- Anaesthetist
- Assistant to assist both
- Conscious, deep sedation or general anaesthesia in all patients
- All approved anaesthetic drugs may be used

Scenario 5: Four practitioners – Sedation by Anaesthetist

- Proceduralist
- Anaesthetist
- Assistant to assist **each***
- Conscious sedation, deep sedation or general anaesthesia in all patients
- All approved anaesthetic drugs may be used

*Recommended if assistance is likely to be required for the majority of the case (e.g. complex or emergency patients)

Antibiotic Use in Endoscopy

Sarah Cho

Introduction

Bacteraemia may occur with diagnostic endoscopy and may be more common following some forms of therapeutic endoscopy because of mucosal trauma arising during the procedure. An endoscopy may also result in local infections in which a typical sterile space or tissue is breached and contaminated by an endoscopic accessory or by contrast injection. The traditional guidance has been that patients at high risk of endocarditis, such as those with a prosthetic (i.e. tissue or mechanical) valve and/or a past history of endocarditis should receive antibiotics for all endoscopic procedures, and patients at moderate risk of endocarditis, such as those with acquired valvular heart disease should receive antibiotics for therapeutic endoscopic procedures. However, complications resulting from bacteraemia are uncommon and infective endocarditis appears to be extremely rare following any form of endoscopy. Moreover, there is scant evidence that antibiotic prophylaxis reduce the incidence of infective endocarditis. Recent American Society for Gastrointestinal Endoscopy (ASGE) and British Society of Gastroenterology (BSG) guidelines have made substantial changes to reflect these findings.

Bacteraemia and risk of endocarditis

The incidences of bacteraemia during upper and lower endoscopies have been well established in numerous series (Table 1). However, transient bacteraemia during routine daily activity has been shown to occur at higher rates than those associated with gastrointestinal endoscopy. It may be present at rates of 20-68% with brushing and flossing of teeth and 7-51% with simply chewing food. Furthermore, in most cases, endoscopy related bacteraemia does not appear to be associated with any infection-related complications, and infective endocarditis is indeed a very rare clinical sequelae. In the United States, an estimated 14.2 million colonoscopies and 2.8million flexible sigmoidoscopies, and perhaps as many upper endoscopies are performed each year, and only 15 cases of infective endocarditis have been reported with a temporal association with an endoscopic procedure. Furthermore there are no data that demonstrate a conclusive causal link between gastrointestinal endoscopy and infective endocarditis in these cases, or that antibiotic prophylaxis prevents infective endocarditis after gastrointestinal endoscopy.

The American Heart Association (AHA), ASGE and BSG have recently revised their respective guidelines for prophylaxis of infective endocarditis, which represents significant change from their previous guidelines and international consensus and now advise **against** endocarditis prophylaxis for most circumstances.

Recommendations on endocarditis prophylaxis during endoscopy

Antibiotic prophylaxis solely to prevent infective endocarditis is no longer recommended in patients with cardiac risk factors who undergo diagnostic or therapeutic endoscopy. Nonetheless, the possibility of infective endocarditis should be considered in patients who develop symptoms and signs of infection during weeks following an endoscopic procedure, and should be investigated and treated appropriately.

For patients with established gastrointestinal infections, the antibiotics should have been commenced as a part of routine care for these patients prior to endoscopy, not specifically in preparation for endoscopy. If enterococci are suspected to be part of the infecting bacterial flora (such as cholangitis) in patients with cardiac conditions associated with the high risk of adverse outcome from endocarditis, amoxicillin, or ampicillin should be included in the antibiotic regimen for enterococcal coverage. Vancomycin may be substituted for patients allergic to or unable to tolerate amoxicillin or ampicillin.

Prevention of infection other than infective endocarditis

Endoscopic Retrograde Cholangiopancreatography (ERCP)

Cholangitis occurs after 0.5-3% of ERCP. Antibiotic prophylaxis has been shown to reduce the incidence of bacteraemia associated with an ERCP, but clear benefit in prevention of cholangitis has not been demonstrated. Therefore routine antibiotic prophylaxis for ERCP is not recommended.

Antibiotic prophylaxis for ERCP should be given in the following settings:

1. Patients with known or suspected biliary obstruction, in which there is a possibility that complete biliary drainage may not be achieved e.g. hilar cholangiocarcinoma, primary sclerosing cholangitis;
2. Patients with communicating pancreatic pseudocyst;
3. Patients with severe neutropenia ($<0.5 \times 10^9/L$) and/or advanced haematological malignancy;
4. Patients with a history of liver transplantation.

Incomplete biliary drainage is a chief predictor of post-ERCP cholangitis. Therefore antibiotic therapy is indicated if biliary drainage achieved at an ERCP is incomplete or is achieved with difficulty, such as in cases of hilar cholangiocarcinoma and primary sclerosing cholangitis. One dose of peri-procedural antibiotic is unlikely to prevent cholangitis in patients with incomplete biliary drainage. Antibiotics should be continued until complete drainage is obtained. Antibiotic that cover gram-negative organisms and enterococci should be used. Patients with previous liver transplantation are at significantly greater risk of developing post ERCP cholangitis, therefore continuation of antibiotics may be beneficial in these patients even when complete biliary drainage is achieved.

Percutaneous Endoscopic Gastrostomy

Antibiotic prophylaxis is effective in reducing the incidence of peristomal infection. A single dose intravenous antibiotic that provides optimal coverage of cutaneous organisms, such as second- or third-generation cephalosporin should be administered 30 minutes before the procedure.

A significant proportion of peristomal infections are MRSA related, and MRSA decolonisation using oral or nasally delivered preparations appear to be effective in reducing the risk of MRSA-related peristomal infection in the patients with nasopharyngeal colonisation.

Variceal bleeding

Patients with suspected variceal bleeding (or patients with decompensated liver disease who develop acute gastrointestinal bleeding) should have already been established on intravenous antibiotics before undergoing endoscopy. A meta-analysis of 8 trials indicated that antibiotic therapy reduced the incidence of bacterial infections and mortality in patients with cirrhosis who develop acute gastrointestinal bleeding. Intravenous ceftriaxone has been shown to be superior to oral norfloxacin in preventing infections in patients with suspected variceal bleeding in a recent study.

Endoscopic Ultrasound (EUS)

Clinical infection following EUS guided fine needle aspiration is uncommon. It appears to occur more commonly in patients with cysts than solid lesions. A subgroup analysis of patients with cysts who were undergoing a EUS guided FNA indicated a 14% risk of infectious complications in a retrospective series. Infections of mediastinal cysts after an EUS-FNA have also been reported. Although benefit of prophylactic antibiotic has not been validated by prospective randomised studies, most expert opinion currently favors administration of intravenous antibiotics before and often oral antibiotics for 3-5 days after an EUS-FNA of cystic lesions. Antibiotic prophylaxis for diagnostic EUS or EUS-FNA of solid lesions are not recommended.

Orthopedic Prosthesis / Vascular Grafts / Non-vascular cardiovascular implanted material

The same rationale for not administering prophylactic antibiotics for infective endocarditis applies here. There are no reported cases in the literature of a vascular graft infection after an endoscopy, and there are only two case reports that describe pyogenic arthritis in patients with orthopedic prosthesis after an endoscopy. Antibiotic prophylaxis before gastrointestinal endoscopy is not recommended for patients with orthopedic prosthesis, synthetic vascular grafts, pacemakers, defibrillators, coronary artery stents, and vena cava filters.

Table 1. Approximate incidence of bacteraemia in immunocompetent individuals undergoing gastrointestinal endoscopy.

Bacteraemia	BSC review (%)
Diagnostic endoscopy +/- biopsy	4
Colonoscopy	2-4
ERCP (no duct occlusion)	6
ERCP (duct occluded)	11
EUS +/- FNA	0-6
Variceal band ligation	6
Oesophageal dilatation/prosthesis	34-54

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Approach to the Patient with Non-Variceal Upper Gastrointestinal Bleeding (NVUGIB)

Paul Edwards

Overview

The management of non-variceal upper gastrointestinal bleeding (NVUGIB (bleeding proximal to the ligament of Trietz) has changed profoundly over the last 25 years. The endoscopist's role has "morphed" from localising the source of bleeding for the surgeon, to being the leader of a multidisciplinary team, where the expected clinical norm is to:

- effectively resuscitate the patient
- accurately predict the patient's prognosis using well validated risk stratification tools
- endoscopically identify the source of bleeding
- arrest bleeding by using multiple therapeutic modalities all delivered via the channel of the endoscope, in the endoscopy suite or the operating theatre.

Epidemiology/Pathology

The US data for NVUGIB are roughly applicable for an Australian setting. There are 160-180 hospital admissions per 100,000 population. Greater than two thirds of patients are over 60 years, 25% are greater than 80 years. A dramatic trend is that an increasing proportion of bleeding admissions (especially moderate to severe bleeding) are associated with the use of aspirin, NSAID's, platelet inhibitors and other anti-coagulants. Gastro-duodenal peptic ulceration accounts for the majority of lesions causing NVUGIB. (See table 1 for a comprehensive list of aetiologies). The mortality rate ranges between 5-10%, although experts in the field believe that we may now be witnessing better outcomes in terms of mortality and morbidity as management guidelines are both standardised and improved.

Table 1: Causes of Upper Gastrointestinal Bleeding.

Peptic ulcer disease	35 to 50%: (25% duodenal ulcer, 20% gastric ulcer)
Gastro duodenal erosions	8 to 15%
Oesophagitis	5 to 15%
Oesophageal varices	5 to 10%
'Mallory-Weiss' tears	15%
Upper gastrointestinal malignancy	1%
Vascular malformations	5%
Rare causes	less than 5%: These include: Dieulafoy lesion; Angiodysplasia; Haemobilia; Pancreatic pseudocyst and pseudo aneurysm; aorto-enteric fistula; Bleeding diathesis, EhlersDanlos syndrome; Pseudoxanthoma syndrome; Gastric antral vascular ectasia (GAVE); OslerWeber-Rendu syndrome

Clinical Assessment / Risk Stratification

The most frequent presenting signs of acute upper gastrointestinal tract hemorrhage are haematemesis and melaena (see Table 2 for frequency of presenting symptoms). Elderly or frail patients, with tachycardia (PR >100), hypotension (BP <90 systolic), or a haemoglobin level less than 10g/dL require urgent and vigorous resuscitation using supplemental oxygen, airway management, transfusion of plasma expanders with or without the use of packed red blood cells, correction of coagulopathy and intravascular monitoring. In patients who are less seriously compromised volume replacement with crystalloid intravenous fluids will usually restore haemodynamic stability.

There is overwhelming evidence that the uses of clinical and endoscopic criteria are powerful predictors of subsequent mortality and rebleeding, hence early risk stratification is both useful and effective.

The Rockall score, see Table 3, is the most widely accepted risk-stratification tool for all upper-gastrointestinal hemorrhage and has been well validated. It accurately predicts risk of both rebleeding and death. The Rockall score uses both clinical and endoscopic data with scores ranging from 0 to 11 points (higher scores indicating higher risk). Numerous other scoring algorithms are "variations on a theme", however they all effectively stratify the risk for patients with NVUGIB.

Table 2: Frequency of Presenting Symptoms for NVUGIB.

Haematemesis; including coffee-ground emesis	40 to 50%
Melaena	70 to 80%
Haematochezia (red or maroon stool)	15 to 20%
Syncope	14%
Presyncope	43%
Dyspepsia	18%
Epigastric pain	41%

Table 3: Rockall Classification.

Variable	Score 0	Score 1	Score 2	Score 3
Age	<60	60- 79	>80	
Shock	No shock	Pulse >100	SBP <100	
Co morbidity	Nil major		CCF, IHD, major morbidity	Renal failure, liver failure, metastatic cancer
Diagnosis	Mallory-Weiss	All other diagnoses	GI malignancy	
Evidence of bleeding	None		Blood, adherent clot, spurting vessel	

More recent data from a large Asian centre, reported 7.1% mortality in over 3000 high risk patients. In this study significant predictors of death were; age (>70 y), the presence of more than one listed co morbidity, haematemesis at presentation, systolic blood pressure lower than 100mm Hg, in-hospital bleeding, rebleeding, and a need for surgery. Interestingly an *H pylori*-related ulcer was significantly associated with a lower risk of mortality.

In terms of non- patient related prognostic factors there is recent data from two Canadian studies suggesting that weekend admission of patients with NVUGIB is associated with excess mortality. (Odds ratios of 1.21 [95% confidence interval [CI], 1.09-1.35] and 1.08 [95% CI, 1.02-1.15]. These publications illustrate that logistic issues i.e. the difficulty in providing after hours endoscopy services (cf “classical” after hours urgent surgery) may also be significant determinants of patient outcome.

Pharmacotherapy

The goal of pharmacotherapy for NVUGIB is to achieve profound acid suppression using proton pump inhibitors (PPI's), as increasing and maintaining the intragastric pH to 6 or more probably promotes clot stability. The use of Histamine H₂-receptor antagonists has not significantly improved outcomes in patients with NVUGIB.

Studies have shown that PPI's significantly reduce the risk for ulcer rebleeding, the need for urgent surgery, and the risk of death. However, in high-risk patients with severe bleeding, mortality rate is lower only in patients who have first undergone endoscopic therapy. Hence the use of an intravenous PPI bolus followed by a continuous infusion for up to 72 hours after endoscopic haemostasis is now an accepted cornerstone of therapy. There is emerging evidence to suggest that use of high-dose IV PPI, while the patient is awaiting endoscopy, may be associated with a beneficial "down staging" of endoscopic lesions.

The use of prokinetic agents such as erythromycin prior to endoscopy has been shown to improve visualisation of the upper GI tract.

Role of Endoscopy

Staff/Training

There are no standardised guidelines dictating "who" actually performs therapeutic endoscopy for NVUGIB in Australian hospitals.

Most cases of NVUGIB in city /large regional teaching hospitals are managed by endoscopists with Conjoint Committee for Recognition of Training of Gastrointestinal Endoscopy (CCRTGE) recognition in gastroscopy (mostly physicians). At smaller city hospitals and country hospitals general/GI surgeons may do the bulk of this urgent endoscopic work.

Performing endoscopy for patients with NVUGIB requires the endoscopist to discern between the different causative pathologies and then to decide which therapeutic modalities are most appropriate (e.g. injection/ heater/gold probes/clips/rubber bands/ glue). This requires specialised training to gain the required skills and competence levels. Endoscopic training guidelines in Australia for physicians and surgeons require that 20 supervised therapeutic endoscopies (not necessarily for GI bleeding) be successfully completed before accreditation to perform endoscopic therapy for NVUGIB is granted.

Skilled endoscopy nurse assistants play a crucial role in the successful delivery of therapeutic modalities for NVUGIB. In many instances after hours urgent endoscopy, usually in the OR, is performed by the endoscopist without the help of specialist nursing assistants that are available during normal working hours. Some units have programs where general nurses gain proficiency in endoscopic procedures, or other hospitals have specialist endoscopy nurses on 24 hr call. My personal experience/perspective is that having trained endoscopy nurses attend urgent cases enhances the outcomes.

Timing of Endoscopy

Patients who are actively bleeding, and/or high risk with poor predicted outcomes should be hospitalised, commenced on appropriate pharmacotherapy and receive urgent endoscopic therapy, and then triaged to a monitored setting or intensive care unit within the first 24 hours. Given that the risk of rebleeding for this group is greatest in the first 72 hours minimum predicted hospital stay would be at least 3 days.

Those patients who need urgent/ immediate endoscopy and therapy are usually obvious. The exact meaning of “urgent” is loosely defined, however most urgent cases of NVUGIB can be triaged using surgical systems i.e. (1) life threatening problem which needs immediate surgery and must be in theatre within an hour, or (2) “organ” threatening disease, but relatively stable and can wait up to 4 hours. There is a sub group of patients who become stable with resuscitation and can wait (in a monitored setting such as ICU on a high dose PPI infusion) for 6-8 hours and have a “daylight/working hours” endoscopy often when trained staff is readily available. Most units would endoscope stable/ low risk patients with NVUGIB on the same day list or the next working day.

Endoscopy performed within 24 hours after presentation has been shown to improve outcomes such as the number of units of blood transfused and the length of the hospital stay for selected high-risk patients. Endoscopic haemostasis has been shown to decrease rebleeding rates, the need for urgent surgery, and mortality rates. Endoscopic treatments may include injection therapy with saline, vasoconstrictors, sclerosing agents, and/or tissue adhesives; thermal therapy with contact or noncontact methods; and mechanical therapy, usually with endoscopic clips or rubber band ligation.

Risk Stratification Using Endoscopic Criteria

The Forrest classification uses the endoscopic appearance of a bleeding ulcer to predict the likelihood of recurrent bleeding. High-risk lesions are those with active blood spurting (grade IA) or oozing (grade IB), a nonbleeding “visible vessel” (actually a fibrin plug) appearing as a pigmented protuberance (grade IIA), and an adherent clot that cannot be dislodged by suction or forceful irrigation (grade IIB). Low-risk lesions are flat, pigmented spots (grade IIC) and clean-base ulcers (grade III). See Table 4.

Table 4; Forrest classification and risk of rebleeding.

Forrest class	Type of lesion	Risk of rebleeding if untreated
IA	Arterial spurting bleeding	100%
IB	Arterial oozing bleeding	55% (17 - 100%)
IIA	Visible vessel	43% (8-81%)
IIB	Sentinel clot	22% (14 - 36%)
IIC	Hematin covered flat spot	10% (0 - 13%)
III	No stigmata of hemorrhage	5% (0 - 10%)

Therapeutic Modalities

Each method of endoscopic haemostasis has been proven superior to no endoscopic intervention at all, but adding a second haemostatic approach further decreases rebleeding rates, the need for surgery, and mortality rates. Hence most experts agree that adrenaline injection alone should be avoided.

Although a recent consensus statement recommends combination therapy with injection, volume tamponade, and obtaining a clear view of the bleeding vessel (which may require clot removal by suction and/ or snare), followed by targeted contact thermal therapy, this may be no better than contact thermal therapy alone. Endoscopic therapy in high-risk patients with an adherent clot remains controversial. Endoscopic clips alone may give similar outcomes to those seen with thermal therapy alone, a combination of injection and contact thermal therapy, and clips followed by injection. In Australia most units would use injection/volume tamponade employing adrenaline, followed by contact thermal therapy, then a consideration of metal clips.

Planned, second-look endoscopy within 24 hours after initial endoscopic therapy is not routinely recommended, but a second endoscopy may be considered on a case-by-case basis for clinical signs of recurrent bleeding or uncertainty regarding the effectiveness of initial haemostasis.

Patients with minor acute NVUGIB and endoscopic low risk lesions i.e. flat-pigmented spots and clean base ulcers can safely undergo early discharge from hospital on medical therapy, provided they have support at home and are not geographically isolated.

Approach To Re-bleeding And Endoscopic Failure

Despite the huge advances in endoscopic management surgical rates for management of a bleeding peptic ulcer are approximately 5% to 7% over most series. This reflects the dictum that “if a bleeding vessel is big enough to have its own name, then endoscopic therapy is unlikely to be effective”. The surgical approach has also changed significantly in the past two decades, given our new understanding of the causation of peptic ulcer disease. The aim of emergency surgery is no longer to cure the disease (by oversew, resection and/ or vagotomy), but rather to stop the haemorrhage when endoscopic therapy has failed or is unavailable.

As a consequence of this the use of angiography with transcatheter embolisation has become a much more viable option to treat rebleeding and endoscopic failures. Such radiological services are usually only available at large tertiary care hospitals. The provision of these services to this sub group of “endoscopic failures” may also pose significant logistic difficulties as radiology suites may be much more “anaesthetic/ resuscitation unfriendly” compared to endoscopy suites.

At our institution 70% of rebleeding and endoscopic treatment failures are successfully treated by percutaneous transcatheter embolisation (PTE) and 30% would have surgery. Often the consultant surgeon makes the request for PTE. In an interesting parallel to the endoscopic literature a recent study from Loffroy et al. concluded that angiographic embolisation should be performed early in the course of re bleeding and that multiple modalities of embolisation should be applied i.e. coils, gelatin sponge, particles or glue to obtain the best outcomes.

Summary

In patients with NVUGIB various clinical and endoscopic determinants are powerful predictors of subsequent mortality, underpinning the importance of early risk stratification. Major outcomes including; mortality, rebleeding and the need for surgery have improved dramatically due to enhanced resuscitative and supportive measures, multiple modality endoscopic therapy and profound acid suppression. The optimal timing of the diagnostic/therapeutic endoscopy requires further study, however, at the very least, early endoscopy i.e. within 24 hrs of admission results in shorter and cheaper hospital stays. Logistic and staffing issues are also important. The gastroenterologist now effectively leads a multidisciplinary team (ER physicians, intensivists, surgeons, radiologists) in the management of NVUGIB.

Table 5: Practical Tips.

(1)	Use clinical and endoscopic data to determine early risk stratification, and base clinical decisions on this.
(2)	Give high dose bolus and then start PPI infusion.
(3)	Consider giving a prokinetic agent such as erythromycin 30 minutes before the procedure
(4)	Develop adequate logistical plans to manage NVUGIB at your hospital. Endoscopy should be performed in a safe environment for the patient and a familiar working environment for the endoscopist and the anaesthetic/resuscitation staff.
(5)	At endoscopy use further risk stratification based on Forrest classification (see above). Arrest bleeding using multiple therapies; usually starts with volume tamponade using adrenaline, followed by thermal coagulation e.g. Gold probe and then consider endoscopic clips as further therapy if required.
(6)	In the presence of rebleeding consider further endoscopic therapy or PTE or surgical options.

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Illustration 1: Spurting Vessel (Forrest 1a lesion)

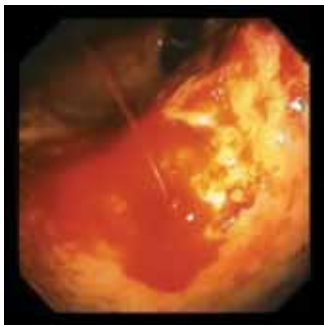


Illustration 2: Visible Vessel (Forrest 2a) Before and after Thermal Therapy.



Illustration 3: Visible Vessel (Forrest 2a) Before and after Clipping.



Chromoendoscopy and Other Advanced Imaging Methods

William Tam

Introduction

The tools and technologies used for imaging of the gastrointestinal tract have undergone significant transformation over the last decade. Not only have there been vigorous efforts to produce better endoscopes with superior optics, but increasing emphasis has been placed on developing novel technology for image processing during real-time endoscopy. In this review, conventional chromoendoscopy will be discussed along with digital chromoendoscopy, magnification endoscopy and other emerging methods of endoscopic imaging.

Conventional chromoendoscopy

Chromoendoscopy, or dye staining, involves the topical application of various stains during endoscopy to improve visualisation of mucosal surfaces in the gastrointestinal tract (Table 1). The stains can be divided into three classes – absorptive, contrast and reactive. Absorptive stains (for example, Lugol's iodine, methylene blue, crystal violet) are absorbed into components of cellular structures in the mucosa. Differences in the mucosal uptake of the absorptive stain can therefore be used to define different types of mucosa. Contrast stains, on the other hand, pool in the mucosal crevices, thereby accentuating its surface topography. Indigo carmine, for instance, is used to define mucosal irregularities in colonic polyps. Reactive stains such as Congo red and phenol red are pH-dependent stains that change colour in response to changes in pH. Congo red turns dark blue or black in acidic conditions, while phenol red turns red in the presence of alkali.

Technique of conventional chromoendoscopy

Chromoendoscopy involves three basic steps – removal of mucus, dye application and water irrigation (Figure 1). It is generally accepted that because the gastrointestinal tract is covered with a variable amount of mucus, optimal staining can only be obtained after topical application of a mucolytic agent prior to dye spraying. The most commonly used mucolytic agent is 10% N-acetylcysteine, although one study has shown the proteolytic enzyme pronase to be useful.

Dye spraying is generally carried out using a spray catheter inserted through the working channel of a standard endoscope. The volume of stain, its optimal concentration and dye contact time have varied considerably amongst different investigators. Some investigators argue that the amount of dye used should depend on the extent of mucosa to be stained. In the case of Barrett's oesophagus, for instance, the length of the metaplastic mucosa would determine the volume of stain used. At present, there are no randomised data to provide an authoritative guide.

Table 1. Stains commonly used in chromoendoscopy.

Stain	Type of Stain	Clinical Use
Lugol's iodine	Absorptive	Squamous cell oesophageal cancer, Barrett's (delineates squamous from columnar)
Toluidine blue	Absorptive	Squamous cell oesophageal cancer, Barrett's (stains both gastric and intestinal metaplasia)
Methylene blue	Absorptive	Gastric intestinal metaplasia, Barrett's (stains specialised columnar epithelium, not gastric type)
Crystal violet	Absorptive	Colonic polyps (taken up by Lieberkuhn gland openings (crypts))
Indigo carmine	Contrast	Highlights mucosal irregularities in the oesophagus (Barrett's) or colon (flat colon tumours)
Congo red	Reactive	Early gastric carcinoma, heterotopic gastric mucosa (reacts with acid-secreting gastric cells)
Phenol red	Reactive	<i>H. pylori</i> infection in the stomach

Figure 1. Technique of chromoendoscopy



Digital chromoendoscopy

Digital or electronic chromoendoscopy refers to imaging techniques used to enhance images of the gastrointestinal tract. Enhanced images are obtained during real-time endoscopy by activating the specific function on the endoscope processor. In this way, white-light images can be switched to enhanced imaging on-demand during endoscopy. There are three commercially available methods of digital chromoendoscopy:

Narrow band imaging (Olympus)

Narrow band imaging utilises a special filter which restricts the incident white light into two narrow bands of different wavelengths (blue at 415nm and green at 540nm). Narrow band blue light displays the superficial capillary networks, while green light displays the subepithelial vessels.

FICE (Fujinon)

The FICE system utilises a computer algorithm incorporated into the endoscope processor. FICE uses spectral image processing technology which enables the selection of a large number of wavelength combinations for different gastrointestinal tract mucosa to produce optimal image quality.

i-scan (Pentax)

The *i-scan* system utilises computer-based enhancement filters to produce enhanced images during real-time endoscopy. Three modes of enhancement are possible – surface, contrast and tone enhancement.

Magnification endoscopy

Technique of magnification endoscopy

Recent refinements in endoscopic technology have produced high-magnification endoscopes with movable lenses that allow real-time image assessment across a range of magnifications, up to 150-fold. Improvement in the design of charged-couple devices, the electronic light-sensing device located at the tip of video endoscopes, has also given rise to less bulky high-resolution instruments. High-resolution and high-magnification endoscopes have the potential to significantly enhance image quality, and is often used in conjunction with the technique of chromoendoscopy. In addition, there is a growing trend for fully digital transmission of high-resolution images - from the endoscope to the processor and the high-definition monitor, so that there is no attenuation of image quality at any stage.

Magnification endoscopy has been used for the assessment of a wide variety of lesions in the upper and lower digestive tract. In the small intestine, villi can be observed clearly to allow an assessment for Coeliac disease and rejection after intestinal transplantation (though this does not replace need for biopsy confirmation). Blood vessel morphology under magnification and Lugol's iodine staining of squamous epithelium in the oesophagus can be used to detect oesophageal squamous cell carcinoma.

Emerging imaging technology – Autofluorescence imaging (AFI)

Video autofluorescence endoscopy is a novel imaging technique which may assist with the detection of early cancer. When a xenon light source is directed at gastrointestinal mucosa, endogenous fluorophores emit a certain amount of fluorescence, while the remaining incident light is reflected, absorbed and scattered. The autofluorescence light can be captured and made to pass through a barrier filter and a black/white filter and is then digitally altered to produce a composite image. The fluorescence characteristics of normal mucosa are different to that of inflamed or dysplastic mucosa, and it is this feature which is used in autofluorescence imaging.

Clinical utility of chromoendoscopy and other imaging techniques

Almost every region of the gastrointestinal tract has been evaluated using chromoendoscopy, from Cameron's erosions to intestinal metaplasia and Coeliac disease. For the purpose of this review, discussion will be restricted to the most widely evaluated and clinically relevant areas.

Detection of oesophageal squamous cell carcinoma

Numerous studies have led to the general opinion that chromoendoscopy is useful in the detection of oesophageal squamous cell carcinoma (SCC). Lugol's iodine stains the glycogen component of normal squamous mucosa brown; the absence of staining (i.e. 'negative' staining) is therefore indicative of mucosal abnormality. This technique is also useful to delineate the margins of the tumour, and therefore assists in facilitation of biopsies and for making clinical decisions relating to treatment, e.g. endoscopic mucosal resection versus surgery.

The use of Lugol's iodine vital staining is used in clinical practice to screen for oesophageal SCC in high risk patients, for instance those with head and neck cancer. There are now several studies which have used narrow band imaging, in isolation and in conjunction with magnification endoscopy and Lugol's iodine chromoendoscopy, to detect oesophageal SCC, with encouraging results. The blood vessel morphology (intra-papillary capillary loops) under ultra-high magnification has been used in combination with Lugol's iodine staining of squamous epithelium in the oesophagus to facilitate the detection of squamous cell carcinoma.

Barrett's oesophagus

Despite the profusion of clinical studies in the 1990s into the usefulness of methylene blue vital staining in Barrett's oesophagus, chromoendoscopy has not emerged as a helpful tool in the routine clinical assessment of Barrett's oesophagus. This is probably related, in part, to the discrepant results and the failure of other centres to replicate results produced by expert institutions. Methylene blue is now rarely used in Barrett's oesophagus evaluation.

Chromoendoscopy using Lugol's iodine, as well as digital chromoendoscopy (NBI, FICE and *i-scan*) have been shown to be helpful in defining the squamo-columnar junction and therefore the extent of Barrett's oesophagus.

There is ongoing active research into the clinical utility of narrow band imaging in the assessment of Barrett's oesophagus. The pit pattern of Barrett's oesophagus has been classified by different investigators, which may predict the presence or absence of specialised intestinal metaplasia. NBI is often used in surveillance of Barrett's oesophagus to help target biopsy of irregular areas of mucosa.

Detection of dysplasia and carcinoma in Barrett's oesophagus

Several studies have evaluated the role of high-resolution magnification chromoendoscopy in the detection of dysplasia and carcinoma in Barrett's oesophagus. Although more studies are needed to determine applicability to general gastroenterological practice, the presence of irregular pit patterns seen under high-magnification and chromoendoscopy suggest the presence of high-grade dysplasia and cancer. Similar conclusions have resulted from studies using narrow band imaging. The vascular patterns can be better appreciated with NBI and are irregular in high-grade dysplasia and carcinoma.

Two multi-centre studies from expert centres suggested that the combination of magnification endoscopy, narrow band imaging and auto-fluorescence endoscopy is useful to evaluate Barrett's oesophagus and dysplasia. Autofluorescence imaging is generally used after white light endoscopy and serves as a 'red flag' method to draw the endoscopist's attention to areas of interest. After identification of suspicious areas using AFI, detailed examination can be performed using chromoendoscopy and/or magnification endoscopy.

This is an area of active research and more data are expected.

***Helicobacter pylori* gastritis**

Although the clinical usefulness of an endoscopic diagnosis of *Helicobacter pylori* gastritis is not determined, there are several studies which have documented the ability for accurate diagnosis using chromoendoscopy, magnification endoscopy and FICE.

Colonic polyps

In the colon, magnification endoscopy, with or without high-resolution endoscopy, has been used to assess colonic polyps, aberrant crypt foci and colon cancer. Conventional chromoendoscopy with and without magnification have been reported to reliably differentiate between hyperplastic (dot pattern) and adenomatous (cerebiform pattern) polyps. Similar conclusions have been reached using narrow band imaging. A recent paper assessed NBI in combination with magnification endoscopy and concluded that in expert hands, the histologic type and depth of invasion of polyps could be reliably predicted using these techniques.

Detection of dysplasia within inflammatory bowel disease

The role of chromoendoscopy to detect dysplasia in patients with long-standing inflammatory bowel disease undergoing endoscopic surveillance has not been defined. Using magnification endoscopy and chromoendoscopy, the extent of mucosal abnormality, including DALM lesions, could be assessed, but biopsy is still essential to obtain histological confirmation. Limited studies using narrow band imaging appear to show discrepant results; more studies are needed to make an authoritative comment. There are no studies involving FICE or the Pentax EPKI system in this field of research.

Limitations of chromoendoscopy

The lack of standardisation of technique is one major reason for the poor uptake of chromoendoscopy, particularly in Australia. Other reasons include the paucity of well conducted studies that determine its clinical utility and cost efficacy. Patient acceptance and tolerability of chromoendoscopy has been variably reported in the literature. In one study, the procedure was prolonged by up to 12 minutes as a direct consequence of staining, and is associated with increased patient discomfort. Vomiting and risk of aspiration have been identified as specific risks of this procedure.

Limitations of digital chromoendoscopy, magnification endoscopy and other imaging methods

It is important to bear in mind that the bulk of data relating to digital chromoendoscopy and other novel imaging methods have been derived from specialist tertiary centres with interest in these techniques. Whether the conclusions reached in these studies are applicable to general gastroenterological practice is unclear. Cost and expertise should also be considered. Inter- and intra-observer agreement is a significant concern and the data from the small number of studies which have evaluated this are modest at best. Several studies have confirmed that AFI is associated with a high false positive rate. Further studies are needed to clarify the shortcomings of these novel techniques.

Conclusions

While conventional chromoendoscopy has been embraced by a few enthusiastic endoscopists, there is no doubt that digital chromoendoscopy has much wider appeal, resulting in rapid uptake into routine general gastroenterological practice. It is expected that a large amount of clinical data will become available in the coming years which will, in turn, help define the role of chromoendoscopy in gastrointestinal imaging.

SECTION 2

UPPER ENDOSCOPY

- Barrett's Oesophagus: Diagnosis and Management *(Darren Pavey)*
- Endoscopic Treatment of Barrett's High Grade Dysplasia and Mucosal Cancer *(Luke Hourigan)*
- Endoscopic Management of Non-Variceal Upper GI Bleeding *(Brad Kendall)*
- Endoscopic Management of Varices and Variceal Haemorrhage *(David Koorey & Crispin Corte)*

Barrett's Oesophagus: Diagnosis and Management

Darren Pavey

Barrett's oesophagus (BE) is a metaplastic change in the oesophageal epithelium thought to result from injury due to chronic exposure of reflux gastric acid. Normal oesophageal squamous epithelium is replaced by specialised intestinal epithelium also known as intestinal metaplasia. Progression of non dysplastic intestinal metaplasia to low grade dysplasia (LGD), high grade dysplasia (HGD) and oesophageal adenocarcinoma is well described, and the incidence of oesophageal adenocarcinoma (OAC) continues to rise particularly amongst the elderly population.

Definition of Barrett's Oesophagus

Barrett's oesophagus is a change in the distal oesophageal epithelium of any length that can be recognised as columnar type mucosa at endoscopy and is confirmed to have intestinal metaplasia by biopsy of the oesophagus. The presence of goblet cells or intestinal metaplasia on the biopsies is vital to make the histological diagnosis.

The endoscopic assessment of Barrett's oesophagus should be performed utilising the Prague Classification whereby the circumferential (C) and maximal extent of tongue-like protrusious (M) are reported, e.g. [C₃M₄].

General Principles

Approximately 10% of the population with chronic reflux have Barrett's oesophagus, and the prevalence of the condition in a recent population study was 1.6%. The significance of the Barrett's oesophagus is its association with an increased risk of oesophageal adenocarcinoma. Importantly the incidence of oesophageal adenocarcinoma is progressively increasing. Oesophageal adenocarcinoma also remains highly lethal with a 5 year survival rate of less than 15%.

Barrett's oesophagus with no evidence of cellular atypia is classified as non dysplastic Barrett's. Intestinal metaplasia may develop with progressively more abnormal features including LGD and finally HGD. The natural history of Barrett's oesophagus is still being determined. The largest study that had examined the natural history of non dysplastic Barrett's oesophagus identified 1376 subjects with a first ever diagnosis of Barrett's. Of these, 618 subjects had long term follow up available at a mean of 4.12 years. Oesophageal adenocarcinoma developed in 12/618 (2%) subjects, high grade dysplasia developed in 22/618 (3.6%), and low grade dysplasia developed in 100/618 (16.1%). There was no progression to dysplasia in 484/618 subjects. Overall, 21.7% of subjects with non dysplastic Barrett's progressed to dysplasia or adenocarcinoma during the follow up period of a mean of 4.1 years.

Screening

Screening for Barrett's oesophagus remains controversial because of the lack of documented impact on mortality from oesophageal adenocarcinoma. The large number of patients that lack reflux symptoms but have Barrett's oesophagus provides a diagnostic challenge. The highest yield for Barrett's oesophagus is in older (aged 50 or more) Caucasian males with long standing heartburn.

The challenges to screening for Barrett's oesophagus include the inability to predict who has BE prior to endoscopy, the lack of evidence based on criteria, the invasiveness and the expense of an endoscopy, and the increasing documentation of a sub group of subjects with BE who lack reflux symptoms.

More recently, body mass index (BMI) has also been correlated with Barrett's oesophagus. The increasing proportion of the population with a high BMI suggests that a greater number of the population are at risk from chronic reflux disease including Barrett's and may partly explain the increasing prevalence of oesophageal adenocarcinoma in recent years.

Management of Barrett's Oesophagus

The grade of dysplasia determines the most appropriate surveillance intervals. Any grade of dysplasia by histology should be confirmed by an expert pathologist.

Surveillance endoscopy remains controversial because of the lack of randomised trials supporting its value. Multiple retrospective studies have been published which indicate that survival is statistically enhanced if oesophageal adenocarcinoma is detected by endoscopic surveillance rather than presenting with symptoms (Table 1).

Following the diagnosis of Barrett's oesophagus the patient should be assessed as to whether they are a suitable candidate to enter a surveillance program. It is recommended that the patients are advised of the benefits and risks of surveillance endoscopy. Consideration for commencing a surveillance program should include the age, likelihood of survival over the next 5 years, the patient's understanding of the process and its limitation for the detection of cancer, and the willingness of the patient to adhere to the recommendation.

Reflux symptoms should be adequately controlled with a proton pump inhibitor prior to entering a surveillance program. The goal is to heal the oesophagitis to reduce the likelihood of the inflammatory process interfering with the visual recognition of Barrett's oesophagus and contributing to cellular changes which can confuse the interpretation of dysplasia.

Table 1. Retrospective Surgical Series of Survival for EAC Based on Surveillance Status.

Author	Surveillance (N)	No surveillance (N)	P Value
Streitz, et al [81]	62% (19)	20% (58)	0.007
Peters, et al [82]	90% (17)	20% (35)	0.09
vanSandick, et al [83]	86% (16)	43% (54)	0.0029
Incarbone, et al [84]	100% (12)	25% (85)	0.01
Ferguson [85]	84% (12)	19% (68)	0.001
Corley [28]	73% (15)	13% (8)	0.001
Fountoulakis [86]	80% (17)	31% (74)	0.008

Challenges in the Management of Barrett's Oesophagus

Current challenges include identifying which patients will progress to higher levels of dysplasia and subsequently oesophageal adenocarcinoma. Patients with nodularity are at increased risk of progressing to OAC, however, other markers are still being developed. There are also issues with biopsy sampling errors with subjects on surveillance programs. There is also a high level of inter observer variability for the interpretation of dysplasia. Surveillance programs have not been shown to be cost effective.

Once high grade dysplasia develops studies have suggested that spacing of four quadrant biopsies every 1cm leads to a lower false negative rate for detecting cancer. In addition nodular areas within the segment of Barrett's should undergo endoscopic resection for histological evaluation. The use of large capacity (jumbo forceps) has also been advocated in the setting of high grade dysplasia although direct comparison to standard biopsy forceps has not been conducted. The suggested endoscopic technique to be used to maximise tissue yield is a "turn and suck" technique which should bring the mucosa in direct position to the biopsy forceps. Endoscopic brush cytology has also been used in Barrett's surveillance, however, studies are conflicting as to how much additional information this provides. Recent studies examining the use of fluorescent insitu hybridisation may be promising in increasing the pick-up rate of brush cytology.

Non-dysplastic Barrett's Oesophagus

Four quadrant biopsies every 2cm of the Barrett's mucosa (Seattle protocol) samples a small fraction of the lining but offers the possibility of recognising dysplasia. Ideally the biopsies from a given segment of Barrett's oesophagus should be submitted to pathology in a separate container to enable the identification of subsequent biopsies on the area if dysplasia is identified. Cost effective studies are needed to evaluate this approach.

Initially two endoscopies within 1 year are suggested (Table 2). If biopsies show no evidence of dysplasia then a follow up interval of 3 years for surveillance is recommended by the American College of Gastroenterology. Of concern, a recent combined cohort of Barrett's patients documented that half of the patients who subsequently develop high grade dysplasia or oesophageal adenocarcinoma had no dysplasia on their first 2 endoscopies.

Table 2. Dysplasia Grade and Surveillance Interval.

Dysplasia	Documentation	Follow-Up
None	Two EGDs with biopsy within 1 year	Endoscopy every 3 years
Low Grade	<ul style="list-style-type: none">• Highest grade on repeat EGD* with biopsies within 6 months• Expert pathologist confirmation	1 year interval until no dysplasia x 2
High Grade	<ul style="list-style-type: none">• Mucosal irregularity• Repeat EGD with biopsies to rule out OAC* within 3 months• Expert pathologist confirmation	ER* Continued 3 month surveillance or intervention based on results and patient

*EGD – esophagogastroduodenoscopy; ER – endoscopic resection; OAC – Oesophageal adenocarcinoma

Low grade dysplasia

The finding of low grade dysplasia (LGD) warrants a follow up endoscopy within 6 months to ensure that no higher grade of dysplasia is present in the oesophagus. If none is found then yearly endoscopy is warranted until no dysplasia is present on two consecutive annual biopsies.

LGD should be confirmed by an expert GI pathologist because of the problem of reading variabilities. When two pathologists agree on the diagnosis of LGD the patient has a greater likelihood of neoplastic progression. Forty percent of biopsies following the recognition of LGD will be negative. In 156 patients with LGD, regression to no dysplasia occurred in 66%, persistent LGD in 21%, and progression to HGD/cancer in 13%, after a mean follow up of 4 years.

High grade dysplasia

The finding of high grade dysplasia (HGD) in flat mucosa should lead to confirmation by an expert GI pathologist and a subsequent endoscopy within 3 months. Although the natural history of HGD is variable, there is a 5 year risk of oesophageal adenocarcinoma exceeding 30% (not excluding prevalent cases in the first year). It is because of the high risk of prevalent cancers that these patients were often evaluated as if cancer is present. Staging procedures with endoscopic ultrasonography, CT scan and PET scan have been studied, although there is not sufficient evidence to warrant their routine application. Subjects with confirmed high grade dysplasia should be counselled regarding their therapeutic options which include: intensive endoscopic surveillance program every 3 months, oesophagectomy or endoscopic therapies. Most experts use HGD as a threshold for therapeutic intervention or more intensive surveillance.

Patients who appear to have lost their dysplasia on surveillance should be treated according to the highest degree of dysplasia previously found. This recommendation is based on the problem of sampling error on subsequent biopsies.

Endoscopic Techniques for Management of Barrett's Oesophagus

Current endoscopic techniques include mechanical techniques such as endoscopic mucosal resection (EMR), thermal techniques such as radiofrequency ablation (RFA), argon plasma coagulation (APC), multipolar coagulation, bipolar energy, laser and cryotherapy. Photochemical therapies such as photodynamic therapy (PDT) have also been well studied.

Endoscopic mucosal resection is particularly suited for the management of nodular areas within Barrett's oesophagus. Several techniques have been used, the most widespread technique is the use of a band ligator device. The advantage of endoscopic mucosal resection is that it provides a deep tissue sample for histological evaluation of the depth of invasions. This provides more accurate staging for high grade dysplasia and early oesophageal adenocarcinoma. The disadvantages of the technique include the risk of

bleeding and stricture rate and the risk of perforation. A staged mucosal resection for circumferential Barrett's utilising a band ligator device for semi circumferential resection followed by a second stage to complete the circumferential resection may reduce the stricture rate. This technique is usually limited to Barrett's segments <4-5cm in length.

Photodynamic therapy has been shown in a randomised prospective controlled trial to significantly decrease cancer risks in Barrett's oesophagus. In this study, 208 patients were randomised to photodynamic therapy plus PPI or PPI alone. PDT was shown to reduce the risk of progression to cancer to 15% of the subjects in the PDT arm compared to 29% of subjects in the control arm. PDT was also associated with the resolution of high grade dysplasia in 77% of subjects in the PDT arm versus 39% of subjects in the control arm.

Surgical resection (oesophagectomy) has been a standard of care for Barrett's oesophagus with high grade dysplasia for some time based upon concerns that endoscopic surveillance protocols may not detect early cancers in up to 40% of subjects. More recently the frequency of OAC at resection in patients with HGD at biopsy has been as low as 17%. Also recent studies have indicated that the risk of metastatic cancer in the setting of intra mucosal carcinoma is as low as 4%, especially if there is no evidence of mucosal lesions. This has led to changes in the way of oesophagectomies are performed in these patients. Oesophagectomy can now be performed with minimally invasive techniques that involve the use of laparoscopy and thoracoscopy. However, despite the decreased invasiveness, one large series of 206 patients reported the overall major complication rates (32%), the mean time in hospital (7 days) and time of procedures (4 hours) to be similar to that reported for transhiatal esophagectomy. Patients requiring oesophagectomy should be referred to centres that perform a high volume of procedures for the best results. A recent analysis of the literature has suggested that there needs to be at least 20 oesophagectomies performed per year at an institution to decrease the operative mortality rate to 5% or less. Despite advances the morbidity rate remains high with up to 30% of patients suffering major complications such as oesophageal strictures or leaks.

Radiofrequency ablation (RFA) is the application of electrical energy to an electrode to provide a superficial burn in the oesophageal mucosa. Currently two devices are available including a balloon based device which is capable of producing a circumferential ablation and an endoscope mounted device which is able to perform focal ablations. RFA was recently evaluated in a randomised controlled trial that was stratified by the degree of dysplasia and length of segments. All histopathology was reviewed by the Cleveland Clinic to confirm eligibility. All subjects there treated with high dose acid suppression for the duration of the trial (esomeprazole 40mg BID). Subjects randomised to RFA had complete eradication of all intestinal metaplasia in 77.4% of subjects compared to 2.3% of controls. Of subjects with low grade dysplasia, 90.5% of subjects randomised to RFA had complete eradication of dysplasia compared to 22.7% of controls. Of subjects with high grade dysplasia, 81% randomised to RFA had complete eradication of dysplasia compared to 19% of controls. Subjects randomised to RFA were also less likely to have progression of disease and progression to cancer. Of subjects with high grade dysplasia, 19% in the control arm progressed to cancer compared to 2.4% of those randomised to RFA. Of subjects with low grade dysplasia, 13.6% in the control arm progressed to high grade dysplasia compared to 4.8% of those randomised to RFA. The overall stricture

occurrence in the study was 6%. All of these subjects achieved complete eradication of intestinal metaplasia and dysplasia. The presence of subsquamous intestinal metaplasia following radiofrequency ablation was 5.1% at 12 months compared to 40% of subjects randomised to the control arm. The durability of the response was also subsequently evaluated at the 2 year follow up mark for subjects in the initial study. 96% of subject's maintained complete eradication of all intestinal metaplasia at the 2 year outcome follow up point.

Studies have evaluated the properties of the neosquamous epithelium following radiofrequency ablation. These studies have shown normalisation of immuno histochemistry and genetic markers that are associated with progression to adenocarcinoma. A recent cost utility analysis has also shown that RFA may be the preferred strategy for the management of patients with Barrett's oesophagus with high grade dysplasia.

Future Directions

Barrett's oesophagus has been the subject of several new imaging modalities. These new imaging modalities include NBI and FICE. In recent studies the use of NBI may reduce the number of biopsies required for surveillance however the significance of this result is yet to be determined. Auto fluorescent imaging has also been used in the evaluation of Barrett's oesophagus. This technology uses blue light illumination to detect fluorescence from cellular components in the oesophagus. Chromo endoscopy has also been used to help to identify areas of Barrett's with high grade dysplasia for targeted biopsies. The role of these and other new technologies including optical tomography (OCT) and confocal endomicroscopy are yet to be determined.

Biomarkers in Barrett's Oesophagus

Biomarkers have been proposed but very few have actually been adequately studied prospectively. There is promise in the use of nuclear DNA, content abnormalities such as aneuploidy and tetraploidy in biopsy specimens in predicting cancer risks as well as loss of heterozygosity of specific genes such as P16 and P53. In addition recent studies demonstrate that methylation of P16, RUNX3 and HPPI as well as demographic characteristics of the patients and the BE length are indicators of cancer risks. No biomarkers are currently ready for routine clinical use.

Chemoprevention in Barrett's Oesophagus

Chemoprevention represents a promising future strategy. The best evidence for any chemoprevention agent lies with non steroidal anti inflammatory drugs that have been shown in epidemiological studies to be associated with a significant reduced risk of cancer.

Large scale trials are being conducted to investigate the use of aspirin and low and high dose of proton pump inhibitor (PPI) therapy in Barrett's oesophagus, but these will take several years to complete. Data from two retrospective cohort studies suggest that PPI therapy significantly reduces the likelihood of developing dysplasia. This provides a rationale to treat even asymptomatic BE patients with PPI, however the benefit of acid suppressive therapy as a means of preventing cancer has not been documented prospectively.

Reflux Control in Patients with Barrett's Oesophagus

For patients with Barrett's oesophagus the goal of pharmacologic acid suppression with agents such as proton pump inhibitors is to control reflux symptoms. Retrospective studies have shown a decrease in development in dysplasia in patients treated with prescribed proton pump inhibitors. Studies have suggested that normalisation of oesophageal acid suppression may decrease markers of proliferation. However, there is currently no data that directly supports the use of high dose anti secretory therapy to delay or prevent the development of oesophageal carcinoma. Subjects who are candidates for surgery may elect a fundoplication especially if reflux symptoms are not controlled despite proton pump inhibitor therapy.

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Fig.1: Photomicrograph, hematoxylin and eosin, x200 of biopsies showing intestinal metaplasia with features of low grade dysplasia.

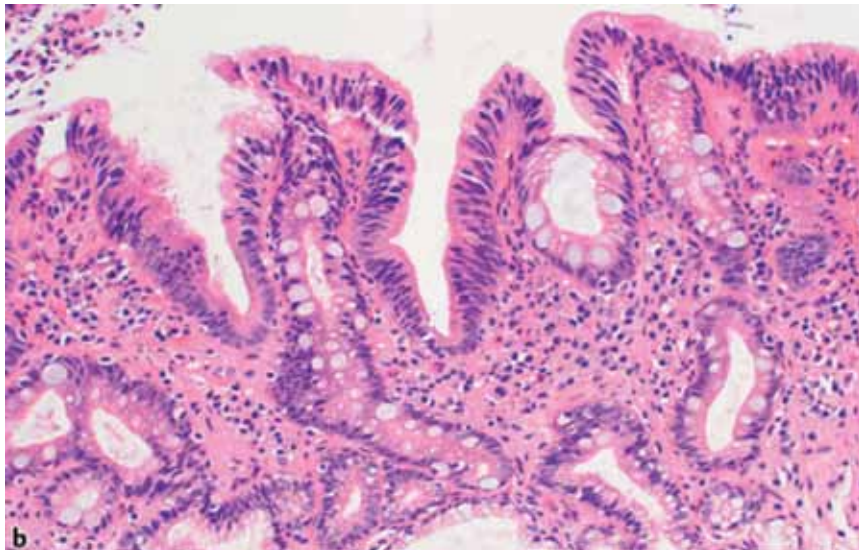


Fig. 2: Endoscopic appearance of a circumferential ablation procedure using the HALO360 system.
 a) C4M4 Barrett's esophagus with high grade dysplasia;
 b) HALO360 ablation balloon positioned 1cm above the maximum extent of the Barrett's esophagus;
 c) HALO360 ablation balloon after being inflated;
 d) ablation effect immediately after deflation of the balloon;
 e) ablation effect after ablation of the whole Barrett's esophagus;
 f) ablation effect after cleaning off the coagulum.

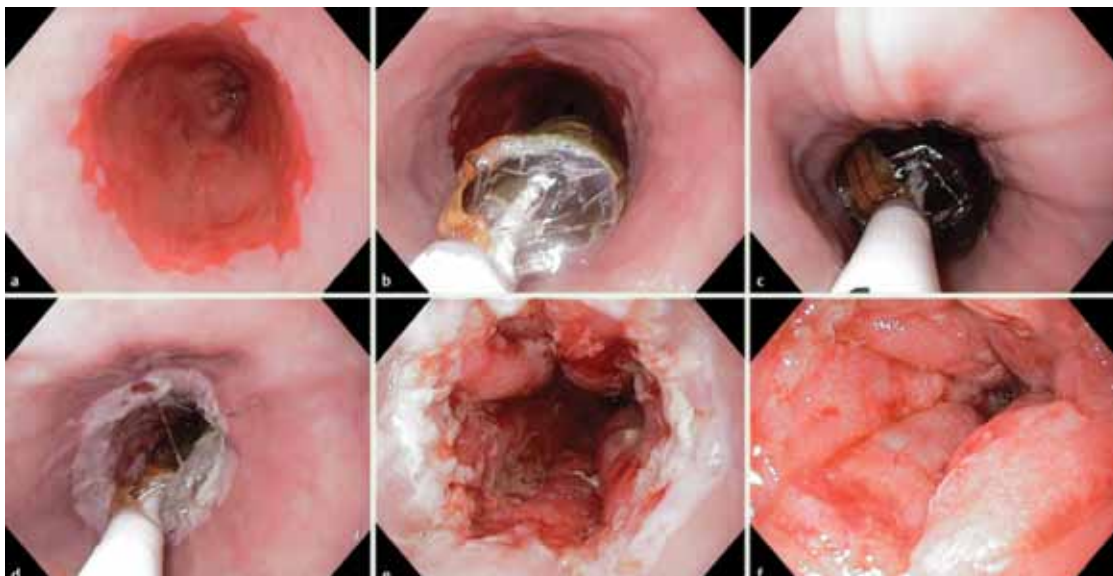
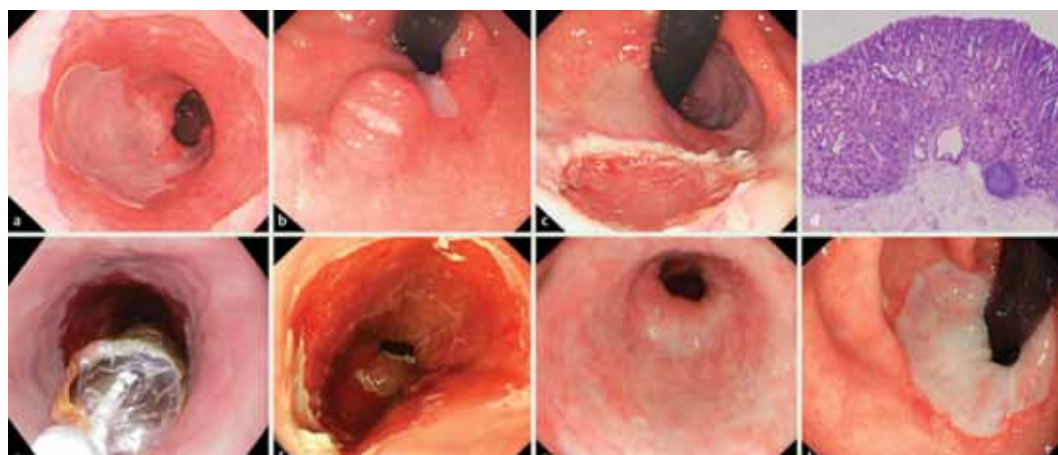


Fig. 3: Endoscopic treatment of a C4M5 Barrett's oesophagus with high-grade dysplasia (HGD) and a visible lesion at the lower end of the Barrett's segment (a,b), with a combination of endoscopic resection and ablation therapy. The visible abnormality was first focally removed with endoscopic resection (c). The resection specimen showed a radically resected well-differentiated mucosal cancer (d), biopsies from the remaining Barrett's oesophagus showed HGD. The Barrett's oesophagus was subsequently ablated using the HALO360 system supplemented with focal ablation with the HALO90 (e) system (not shown) for a complete endoscopic and histological removal of all dysplasia and all Barrett's oesophagus without any stenosis (f±h). IMC, intramucosal cancer; LGD, low-grade dysplasia; RFA, radiofrequency ablation.



Acknowledgements

Table 1. and 2. courtesy of Wang KK, Sampliner RE. Practice Parameters Committee of the American College of Gastroenterology. Updated guidelines 2008 for the diagnosis, surveillance and therapy of Barrett's esophagus. *Am J Gastroenterol.* 2008 Mar;103(3): 788-97.

Fig. 1. courtesy of Sharma VK, Kim HJ, Das A, Dean P, DePetrìs G, Fleischer DE. A prospective pilot trial of ablation of Barrett's esophagus with low-grade dysplasia using stepwise circumferential and focal ablation (HALO system). *Endoscopy.* 2008 May;40(5):380-7

Fig 2. and 3. courtesy of Gondrie JJ, Pouw RE, Sondermeijer CM, Peters FP, Curvers WL, Rosmolen WD, Krishnadath KK, Ten Kate F, Fockens P, Bergman JJ.

Stepwise circumferential and focal ablation of Barrett's esophagus with high grade dysplasia: results of the first prospective series of 11 patients. *Endoscopy.* 2008 May;40(5):359-69.

Endoscopic Treatment of Barrett's High Grade Dysplasia and Mucosal Cancer

Luke Hourigan

Introduction

The endoscopic approach to Barrett's high grade dysplasia (HGD) and early mucosal cancer has undergone significant change over the past few years. Strong evidence is accumulating that the endoscopic management of Barrett's oesophagus HGD and related early malignant lesions is safe and effective and may eventually be preferred over oesophagectomy. The most widely accepted new endoscopic methods include transparent cap endoscopic mucosal resection and radio frequency ablation. These recent changes in endoscopic technology have radically changed the approach to high grade dysplastic Barrett's and early oesophageal cancers. The previous approach was based on endoscopic surveillance of Barrett's mucosa with eventual surgery for those with high grade dysplasia or malignancy. The more modern approach is to survey all lesions, select those which can be endoscopically treated and reserve surgery only for patients with cancers involving the sub mucosa.

General Principles

Endoscopic detection and the proper staging of patients with Barrett's oesophagus neoplasia prior to therapy are essential.

Endoscopic resection is the corner stone for endoscopic management of Barrett's oesophagus related neoplasia as it allows histological correlation and enables optimal patient selection. Patients with submucosal invasion should be referred for surgery as they have a 15-30% risk of positive local lymph node involvement. The risk is minimal in patients with intramucosal cancer or high grade dysplasia.

The compromise for patients undergoing endoscopic management is the need to accept an intense regimen of initial endoscopic staging, treatment and then continued surveillance.

Endoscopic mucosal resection is complimented by radio frequency ablation which appears to have many of the features of an ideal ablation technique. Radio frequency ablation has an impressive efficacy and safety profile in several studies. Also, the neosquamous mucosa that develops after the ablation has been shown to be free of genetic abnormalities. There is also a very low occurrence of residual areas of columnar mucosa underneath the neosquamous mucosa (buried glands). Potential management of non dysplastic Barrett's oesophagus will prove to be a controversial issue. It is therefore too early to embrace radio frequency ablation for the treatment of non dysplastic Barrett's oesophagus.

Successful endoscopic management of high grade dysplastic Barrett's and early oesophageal malignancy is dependent on good patient selection, accurate grading and staging of the Barrett's segment and access to expertise in pathological assessment and endoscopic skills.

Techniques

Endoscopic workup of early Barrett's neoplasia

The goal of endoscopic surveillance of patients with Barrett's oesophagus is the detection of early neoplastic lesions. There are three useful basic rules. Firstly use the best endoscope you have available. The second rule is that "you do not detect what you see but you detect what you recognise". The third rule is to perform a systematic endoscopic inspection.

Some of the advanced endoscopic imaging modalities for detection of early neoplasia and Barrett's oesophagus include high definition endoscopy, chromoendoscopy and more recently narrow band imaging. Other technologies include auto florescence and confocal microscopy.

The importance of endoscopic work up and staging of patients with suspected early Barrett's oesophageal neoplasia is to identify patients who are eligible for endoscopic therapy and to select those patients who require surgical management as curative treatment. The endoscopic work up should focus on identifying the most suspicious areas in the Barrett's segment which subsequently needs to be removed by a diagnostic endoscopic resection. Endoscopic resection allows for optimal diagnosis and staging, is potentially curative and guides the selection of patients for endoscopic therapy. Patients who are eligible for endoscopic therapy have high grade dysplasia or well or moderately differentiated cancers limited to the mucosa without lympho-vascular invasion.

Endoscopic ultrasound has a limited role in the T & N staging of early neoplasia in Barrett's oesophagus. Differentiation of intramucosal and submucosal lesions is much more difficult in Barrett's oesophagus compared to squamous cell lesions. Ultimately, the best method for assessment of the risk of lymph node involvement may not be EUS but a diagnostic endoscopic resection with assessment of the infiltration

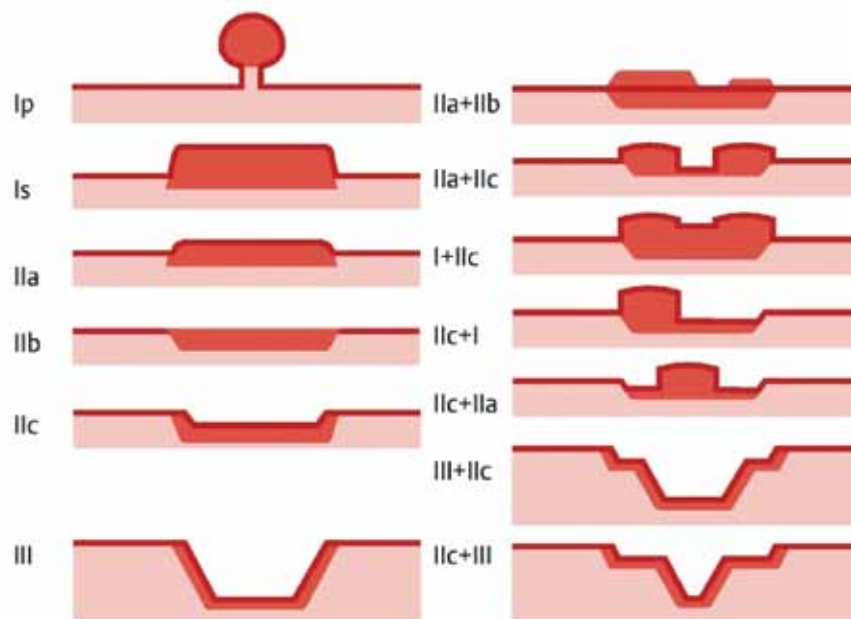
CT and PET scanning have minimal value in loco-regional staging of early neoplasia in Barrett's oesophagus.

Macroscopic appearances of early neoplasia in Barrett's oesophagus

Visible lesions in Barrett's oesophagus may be classified according to the Paris classification (adopted from the Japanese gastric classification of gastric carcinoma).

Repressed lesions carry a higher risk of submucosal invasion than flat or elevated lesions. Type 0-III lesions always have deep submucosive invasion and are usually accompanied by a dense desmoplastic reaction. These are therefore not suitable for endoscopic treatment.

Paris Classification



Is lesion

Ila lesion

same Ila lesion (outlined)



(Luke Hourigan 2009)

Staging

Depth of infiltration

The most important risk factor predicting lymph node metastasis in early neoplasia of Barrett's oesophagus is the depth of infiltration of the lesion. Mucosal lesions (T1A) are sub divided into three categories: T1m1 which is limited to the epithelial layer, T1m2 with infiltration into the lamina propria, T1m3 with infiltration into the muscularis mucosae. Submucosal lesions (T1B) are divided into T1sm1 which is infiltration into the superficial one third, T1sm2 infiltration into the intermediate one third, T1sm3 infiltration into the deepest third.

Patients with mucosal carcinoma are considered to have a negligible risk of lymph node metastases and therefore eligible for endoscopic treatment. Patients with deep submucosal invasion are generally considered to be at risk of lymphatic dissemination and should therefore be considered for surgical treatment. Recent studies suggest that T1sm1 tumours show a much lower risk (0-8%) of lymph node involvement than T1sm2-3 tumours (26-67%). Given the risks of oesophagectomy and relatively poor outcome when there are positive lymph nodes, this suggests that endoscopic treatment may also be a valid treatment option for patients with superficial submucosal invasion in their endoscopic resection specimens.

Barrett's Histology

The presence of a double muscularis in Barrett's oesophagus makes interpretation of dysplasia and adenocarcinoma difficult, particularly in biopsy specimens.

Determination of the precise location of neoplastic involvement in Barrett's oesophagus is important since several studies have shown that tumours that infiltrate into and even through the new muscularis mucosa have a very low risk of metastasis compared with tumours which penetrate the deeper (original) muscularis mucosa into the true submucosal layer.

Endoscopic Mucosal Resection (EMR)

The two most commonly used devices include the original Inoue device (Olympus) and the Duette multiband mucosectomy device (Cook). It is possible to achieve good overlapping of margins during piecemeal endoscopic mucosal resection with both devices.

Submucosal preinjection is not essential with the multiband mucosectomy device but can be helpful, especially at the cardio-oesophageal junction.

Total endoscopic resection of Barrett's can be performed in a single session or as a staged procedure with a hemi circumferential resection of the first session, dependent on the length of the Barrett's oesophagus. Although circumferential EMR in one single session is associated with stricture formation, the circumstances for obtaining complete resection are optimal in the first EMR session. Fibrosis with scar formation makes EMR more difficult at subsequent endoscopic resections. For a staged procedure, repeat endoscopy and EMR are performed at 4-6 week intervals until complete resection is achieved. Patients are treated with high dose proton pump inhibitors during this period.

Single Duette resection of Type IIa early oesophageal adenocarcinoma.



(Luke Hourigan 2009)

Two Duette resections required to remove a larger Type IIa oesophageal adenocarcinoma.



(Luke Hourigan 2009)

Results of total endoscopic resection

With localised EMR, the reported rates of recurrence or metachronous carcinomas at 34 months follow up were as high as 23-30%. The higher recurrence rate is due to the presence of multifocal synchronous lesions overlooked by biopsy prior to EMR as well as metachronous development of new foci of dysplasia. Technical success rates range from 70-100% and recurrence rates for high grade dysplasia or intramucosal cancer range from 0-12%.

The problem of recurrent disease despite total endoscopic resection is due to incomplete resection of the Barrett's mucosa and the issue of remnant ridges of diseased mucosa is very pertinent with regard to piecemeal resection. Using the multiband mucosectomy device to carry out sequential overlapping resections and if necessary, the subsequent additional removal of the remaining ridges using a small monofilament snare, this risk can be minimised and the results of resection can be comparable to those of ESD.

Fortunately the frequency of complications associated with EMR is modest. Significant bleeding is observed in up to 14% of cases. However, most patients with bleeding are managed endoscopically in an outpatients setting. Perforation is observed in 1.8% of procedures and may even be treated effectively with medical therapy (i.e. clips) in some circumstances. There have been no reports of deaths due to EMR.

Stricture formation is a common complication of extensive mucosal resection with reported rates ranging from 0-70% and can be a major problem for both total endoscopic resection and ESD. Strictures can be treated endoscopically with balloon dilatation. To reduce the risks of stricture formation, total endoscopic resection may be carried out in multiple sessions. The use of total endoscopic resection should be limited to Barrett's oesophagus of less than 5cm in length as application to longer Barrett's oesophagus segments can result in the long strictures that are often difficult to dilate after total endoscopic resection.

En bloc resection with ESD

Only preliminary attempts have been made to achieve total endoscopic resection with ESD for Barrett's oesophagus. It potentially permits en bloc resection of lesions larger than 15mm that otherwise would require piecemeal resection with cap based techniques. However ESD has generally not been used for total endoscopic resection and is technically more demanding and time consuming.

Ablation Techniques

Photodynamic therapy for Barrett's oesophagus

Photodynamic therapy was the first treatment to have shown to significantly decrease high grade dysplasia and cancer in patients with Barrett's oesophagus. However its use has been limited primarily because of the side effects which include oesophageal strictures, cutaneous photosensitivity, chest pain and nausea and vomiting.

Argon plasma coagulation

Most experts do not recommend APC as a primary ablation method for dysplastic Barrett's oesophagus.

Radio frequency ablation

Current data suggests that radio frequency ablation is a very encouraging modality for eradication of Barrett's oesophagus with many appealing features. RFA has been proven to be highly effective in eradicating intestinal metaplasia and its associated dysplasia. It has a low complication rate, preserves the functional integrity of the oesophagus and is relatively easy to apply. The regenerating neosquamous epithelium is free of the pre existing oncogenetic alterations. For patients with intramucosal cancer (IMC) and HGD, radio frequency ablation appears to be a valid and less invasive alternative to PDT, APC or oesophagectomy, albeit after thorough endoscopic work up and endoscopic resection of IMC and visible lesions. The role of RFA treatment in patients with LGD or non dysplastic Barrett's oesophagus requires more study.

The HALO 360 and HALO 90 ablation procedures

Step-wise circumferential and focal ablation of a Barrett's oesophagus generally starts with a circumferential ablation procedure using the HALO 360 system. Initially the oesophageal landmarks are recorded. After spraying the oesophageal all with acetylcysteine (1%) and flushing it with plan water to remove excess mucus, the top of the gastric folds and the furthest proximal extent of the Barrett's oesophagus are recorded for reference during the sizing and ablation procedures. A stiff guide wire or Savary metal wire is then introduced and the endoscope is removed. The next step is sizing the inner oesophageal diameter. This is generally performed as a blind procedure using the 1cm scale on the catheter shaft for reference. The measurement cycle is started with the catheter positioned at least 12cm above the gastro-oesophageal junction with measurements taken every 1cm.

The Halo 360 ablation catheter size is selected on the basis of the balloon measurements. In patients who have undergone prior endoscopic resection, the ablation catheter is selected conservatively.



The first circumferential ablation pass

The HALO 360 catheter is introduced followed by the endoscope. Under endoscopic visualisation, the proximal margin of the electrode is placed 1cm above the furthest proximal extent of the Barrett's oesophagus. The balloon is inflated and the electrode is then activated via a foot switch. Moving from proximal to distal, the balloon is repositioned, allowing a small overlap of about 10mm with the previous ablation zone, until the entire Barrett's oesophagus has been ablated.

The cleaning procedure between ablation cycles

After the first ablation pass, the ablation catheter is removed and the electrode surface is cleaned. A transparent cap is fitted on the tip of the endoscope to slough off the coagulum from the ablation zone. Although the extensive cleaning procedure requires extra procedure time, it has been proven to increase the efficacy of the first ablation session from 90% surface regression to 95%. There is a second ablation pass after the cleaning procedure. The entire Barrett's oesophagus is ablated the second time.

A minimum of eight weeks after the first circumferential ablation treatment, patients are rescheduled to undergo a second ablation. Patients with residual circumferential Barrett's oesophagus >2cm in size and or multiple isles or tongues are treated with a second circumferential ablation. Patients with an irregular Z-line, small tongues and circumferential extent below 2cm or diffuse isles are treated with focal ablation using the HALO 90 system.

The HALO 90 system allows direct application of radio frequency ablation. The electrode is brought into close contact with the mucosa and kept in place. It is immediately activated resulting in a double application of energy. Ablation of the entire Z-line with the HALO 90 device is recommended to ensure eradication of intestinal metaplasia at the gastro oesophageal junction. After all residual Barrett's oesophagus has been ablated, the coagulum is carefully pushed off the oesophageal wall with the leading edge of the electrode or with a transparent cap, followed by cleaning of the electrode outside the patient and cleaning of the ablation zone with the forceful spraying of water. A second ablation pass is performed. Ablation can be repeated every two to three months until all Barrett's oesophagus have been eradicated visually and the eradication is confirmed histologically. Most patients will need one circumferential ablation session and one or two focal ablation sessions for all dysplasia and intestinal metaplasia to be eradicated.



(Luke Hourigan 2009)

Neosquamous epithelium after radio frequency ablation

After radio frequency ablation, Barrett's oesophagus is re-epithelialised by newly developed squamous epithelium referred to as neosquamous epithelium (NSE).

Conclusion

There have been significant advancements in the endoscopic approach to Barrett's HGD and early mucosal cancer. Whereas previously endoscopy was essentially purely for diagnosis and surveillance, it now offers intervention with staging and/or cure in well selected cases. The revolution in endoscopic intervention centres around the advent of effective endoscopic mucosal resection complemented by radio frequency ablation. At the very least, endoscopic mucosal resection of early oesophageal malignant lesions provides histological staging to assist with the decision between ongoing endoscopic management or surgery. The future will see the development of consensus on the application of the endoscopic approach and the requirement for ongoing surveillance.

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Endoscopic Management of Non-Variceal Upper GI Bleeding

Brad Kendall

Introduction

Upper gastrointestinal bleeding (UGB) is the most common gastrointestinal emergency managed by gastroenterologists. There are a wide variety of causes of UGB, with the majority due to peptic ulcer bleeding (PUB) (Figure 1). The annual population incidence of PUB is 60 per 100,000 population. In recent times there have been significant advances in the pharmacological and endoscopic treatment of PUB but it remains a life threatening condition with 5% mortality. Mortality is greatest in the elderly and in those with concurrent medical conditions. The aim of this chapter is to review the current evidence based management of UGB with particular emphasis on PUB. The chapter will be divided into three sections a) pre-endoscopy b) endoscopy and c) post-endoscopy management.

Fig 1. Causes of upper gastrointestinal bleeding. From ref 1.

Diagnosis	Frequency (%)
Duodenal ulcer	24.3
Gastric erosions	23.4
Gastric ulcer	21.3
Varices	10.3
Mallory – Weiss tear	7.2
Oesophagitis	6.3
Erosive duodenitis	5.8
Neoplasm	2.9
Miscellaneous	10.3

Pre-Endoscopy

Resuscitation

An immediate evaluation of haemodynamic stability should be made in all patients who present with UGB. Pulse rate and blood pressure should be measured in both the supine and erect position as significant degrees of intravascular depletion may only become apparent with these orthostatic measures. Baseline measures of biochemistry, full blood count and coagulation profile should be performed. It should be noted that even in large volume gastrointestinal bleeding, the haemoglobin may remain normal for a number of hours until haemodilution has occurred. Blood should be at least grouped and held in all patients and cross-matched where transfusion is anticipated. Large-bore intravenous access should be obtained on presentation. The threshold to transfuse a patient with

UGB varies from patient to patient depending on factors such as age, concurrent medical conditions, amount of blood loss and haemodynamic instability. The method of reversal of any coagulopathy will be dependent on the underlying aetiology and the degree of ongoing bleeding.

History and examination

The history in a patient with UGB is important in generating a provisional diagnosis for the cause of the bleeding. For example, a history of vomiting prior to the UGB suggests a Mallory-Weiss tear, a history of aspirin and non-steroidal anti-inflammatory drug (NSAID) use or previous peptic ulceration are suggestive of underlying peptic ulceration. A history of an abdominal aortic aneurysm repair should always be sort as an aorto-enteric fistula may present with a less severe herald bleed. A history or examination that suggests underlying portal hypertension warrants the use of intravenous Octreotide pending an upper endoscopy. In addition, as outlined above, the examination is vital in assessing haemodynamic stability in the patient with UGB.

Risk-stratification

A number of validated scoring tools have been developed to provide an objective measure of the need for urgent endoscopy in patients with UGB and their risk of an adverse outcome (Figure 2). Some of these scoring systems include the results of an endoscopic assessment (complete Rockall score) and others are based on pre-endoscopy clinical and laboratory evaluation (clinical Rockall score and Blatchford score). Whether formalised by a scoring system or not, the clinical and laboratory measures used in these tools are what the clinician uses in determining the timing of upper endoscopy in UGB. In those patients with a high-score and therefore at high risk, the endoscopy needs to be performed on an urgent basis and often require anaesthetic or intensive care support. In patients with a low score and therefore low risk of adverse outcome (complete Rockall score ≤ 2 or clinical Rockall or Blatchford score of 0), endoscopy may be deferred to a semi-urgent setting. Although validated in well-conducted studies, the use of these scores has yet to become universal.

Pre-Endoscopy PPI

Gastric acid leads to lysis of clots, impaired clot formation and inhibition of platelet function. Prevention of these effects by maintaining the intragastric pH >6 is the principle behind the use of high dose IV infusions (80mg bolus and then 8mg/hr infusion) of proton pump inhibitors (PPI) in PUB. A number of studies have shown that the pre-endoscopy use of high dose IV infusions of PPI in patients with UGB leads to down staging of the endoscopic stigmata of PUB and lessens the requirements for endoscopic therapy of PUB. There are no effects on need for surgery or mortality. Economic modelling studies of this intervention have given variable results and therefore the use of pre-endoscopy PPI is still somewhat controversial.

Use of an intravenous prokinetic agent such as erythromycin may help to empty the stomach of blood, leading to improved endoscopic visualisation.

Figure 2: Blatchford and Rockall scores for risk-stratification in UGB. From ref 4.

A Blatchford Score		
At Presentation		Points
Systolic blood pressure		
100-109 mm Hg		1
90-99 mm Hg		2
<90 mm Hg		3
Blood urea nitrogen		
6.5-7.9 mmol/litre		2
8.0-9.9 mmol/litre		3
10.0-24.9 mmol/litre		4
≥25 mmol/litre		6
Hemoglobin for men		
12.0-12.9 g/dl		1
10.0-11.9 g/dl		3
<10.0 g/dl		6
Hemoglobin for women		
10.0-11.9 g/dl		1
<10.0 g/dl		6
Other variables at presentation		
Pulse ≥100		1
Melena		1
Syncope		2
Hepatic disease		2
Cardiac failure		2
B Rockall Score		
Variable		Points
Complete Rockall Score	Clinical Rockall Score	Age
		<60 yr
		60-79 yr
		≥80 yr
		Shock
		Heart rate >100 beats/min
		Systolic blood pressure <100 mm Hg
		Coexisting illness
		Ischemic heart disease, congestive heart failure, other major illness
		Renal failure, hepatic failure, metastatic cancer
		Endoscopic diagnosis
		No lesion observed, Mallory-Weiss tear
		Peptic ulcer, erosive disease, esophagitis
		Cancer of upper GI tract
		Endoscopic stigmata of recent hemorrhage
		Clean base ulcer, flat pigmented spot
		Blood in upper GI tract, active bleeding, visible vessel, clot

Communication

A patient with a significant UGB is a medical emergency and like all medical emergencies, effective communication is vital to a successful outcome. Decisions need to be made when, where and by whom, the endoscopy is to be performed as early endoscopic assessment and treatment is required in high-risk patients. In addition, anaesthetic, intensive care, radiological and surgical support may be required. All these factors become more challenging in the after-hours setting. It is vital that trainees are orientated concerning these factors and the systems in place to optimise the coordinated management of patients with UGB.

Endoscopy

The aim of endoscopy in the UGB is to ascertain the cause of the bleeding, determine prognosis and undertake endoscopic therapy if indicated.

Staff and equipment

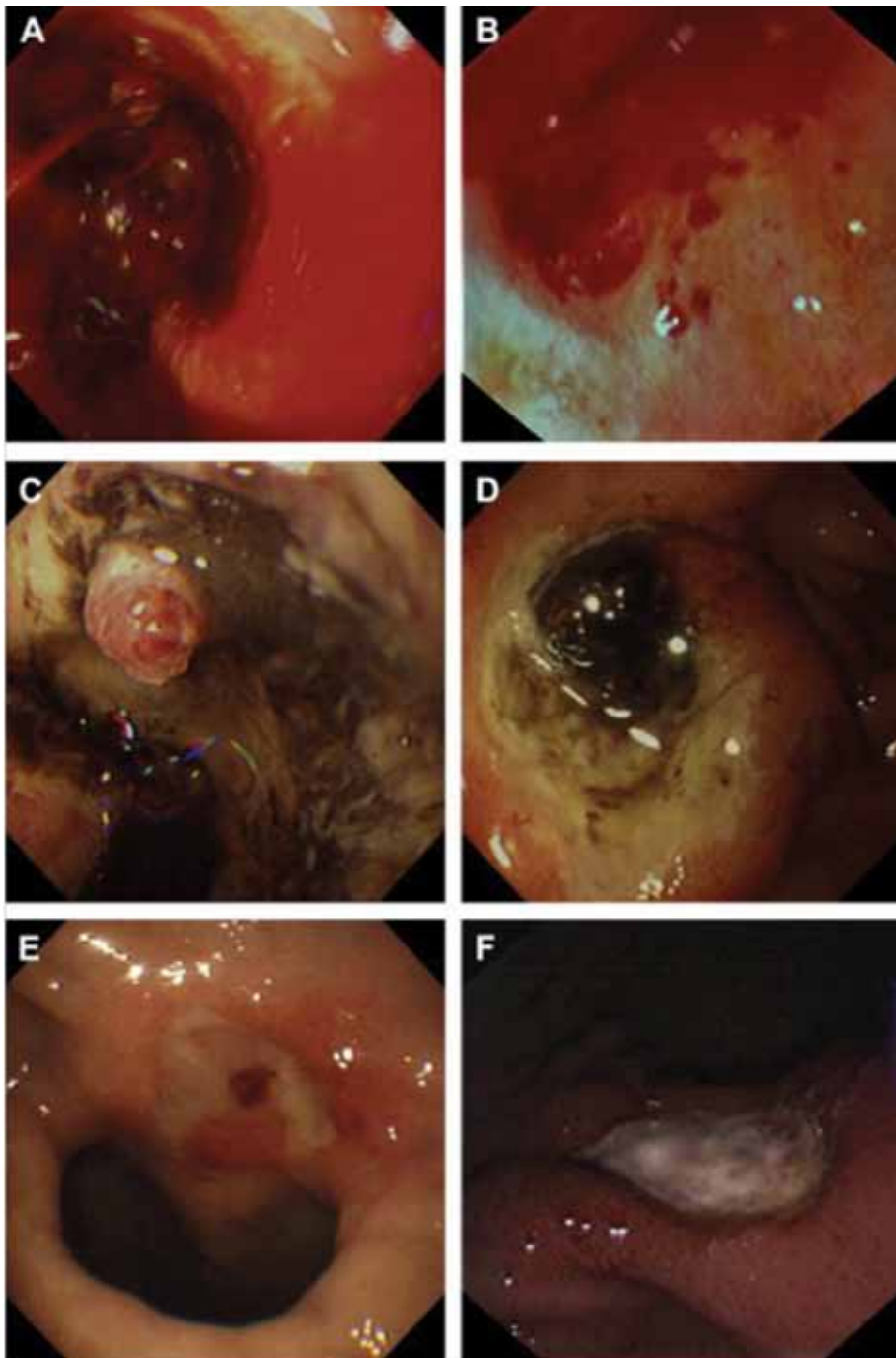
A trained endoscopist, with trained endoscopy assistants, should perform the upper endoscopy in patients with UGB. The endoscopy should be undertaken in a setting where all potentially required equipment is immediately available. Anaesthetic support should be available if required. Whether all this can be achieved both in and out of hours in the endoscopy unit or requires transfer to the operating theatre varies from centre to centre.

Ideally a centre that manages patients with UGB should have either a large channel (>3.8mm) or double-channel endoscope available. The benefit of these instruments are that they provide better suction and flushing capabilities and allow the passage of 10F contact thermal probes. In addition needles for endoscopic injection, contact thermal probes (bipolar or heater probe, ideally 10F), band ligators, adrenaline, histoacryl glue with lipoidal and endoscopic clips should be immediately available at the time of endoscopy for UGB. Rarely a side-viewing endoscope may be required to assess and effectively treat patients with PUB.

Endoscopic assessment

In patients who are found to have PUB at the time of endoscopy, the appearance of the ulcer base can be categorised according to the Forrest classification, which ranges from IA to III (see Figure 3). This classification is used to predict the risk of ulcer rebleeding. Lesions with a high-risk (22-55%) of rebleeding if left untreated endoscopically are those with active spurting of blood (grade IA), oozing blood (IB), nonbleeding visible vessel (IIA) or an adherent clot which cannot be dislodged by suction or vigorous irrigation (IIB). These high-risk stigmata are seen in 30-50% of patients with PUB. Lesions with a low-risk of rebleeding are flat, pigmented spots (grade IIC) and clean-based ulcers (III).

Figure 3. Forrest classification of ulcer bleeding. (a) Ia, spurt bleeding; (b) Ib, oozing bleeding; (c) IIa, visible vessel; (d) IIb, adherent clot; (e) IIc, flat spot; and (f) III, clean ulcer base. From ref 1.



Endoscopic treatment in PUB

Patients with high-risk endoscopic stigmata should undergo endoscopic haemostasis. This has been shown to decrease rates of rebleeding, need for urgent surgery and mortality in these patients. Endoscopic haemostasis can be classified as injection therapy (adrenaline – most studies using 1:10,000 dilution), contact thermal therapy (bipolar or heater probe – most studies using 10F probes) and mechanical therapy (endoscopic clips) (Figure 4). Often combination therapy with adrenaline and one of the other modalities is used. All endoscopic therapies have been shown to be superior to no therapy, but injection therapy alone is inferior to contact therapy either alone or combined with injection therapy. Therefore, injection therapy alone should not be used. The results for mechanical therapy are promising but incompletely defined. The ideal endoscopic therapy does vary from case to case. For example where there is brisk active bleeding, initial injection therapy often helps improve the endoscopic view to allow subsequent thermal or mechanical therapy (Figure 5). In other cases, the lesion may only be accessible tangentially thereby precluding mechanical haemostasis but allowing contact thermal therapy. Contact thermal therapy exerts its effects by a process called coaptation in which both the mechanical force of the probe plus the thermal energy lead to coagulation of the underlying bleeding vessel. In other cases, for example an easily accessible acute bleeding ulcer without fibrosis of the base, mechanical haemostasis with endoscopic clips may be preferable (Figure 6).

The management of the patient with an adherent clot, where the clot cannot be removed with vigorous washing, is controversial. Previously some had advocated aggressive removal of the clot with instruments such as a snare and treatment of any underlying high-risk stigmata. In recent times, there has been a trend towards not disturbing adherent clots and treating patients with high-dose IV infusions of a PPI for the 72 hours post endoscopy.

Figure 4. Contact thermal probes used in the treatment of high risk lesions in PUB. Bipolar probe with injection needle (left) and heater probe (right).

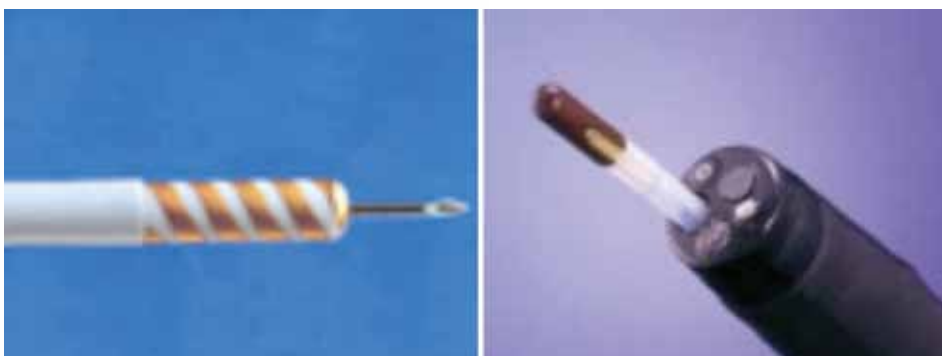


Figure 5. Use of a bipolar contact thermal probe for initial injection with 1:10,000 adrenaline and subsequent coaptation of a visible vessel (Forrest classification IIA) in the base of a peptic ulcer.
From http://www.gastro.org/userassets/html/DDSEP5_Demo/site/Syllabus/chap5.htm

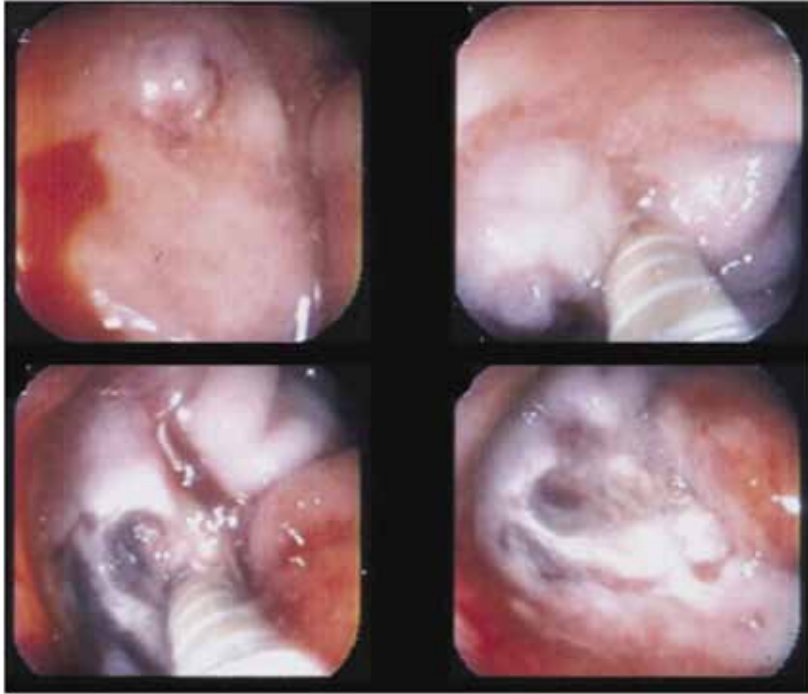
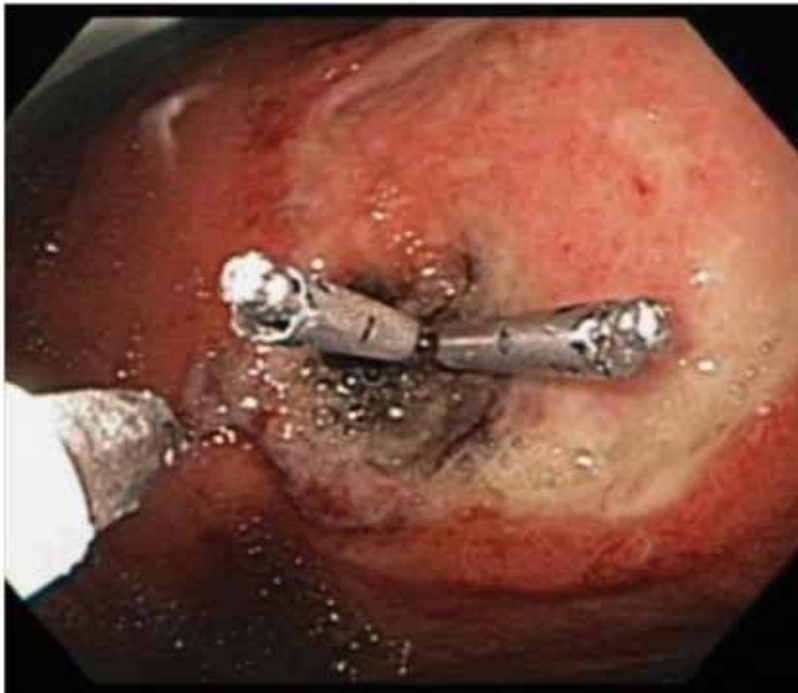


Figure 6. Mechanical haemostasis of a bleeding peptic ulcer using endoscopic clips.
From <http://bestpractice.bmj.com/best-practice/monograph/456/resources/image/bp/4.html>



Endoscopic treatment of non peptic ulcer UGB

The most common cause of non-peptic ulcer, non-variceal UGB is a Mallory-Weiss tear. In addition to the techniques used in PUB, band ligation has also been used successfully in this condition. Upper gastrointestinal neoplasia can occasionally present with UGB. The techniques used in PUB can also be used in the treatment of neoplastic UGB, but adequate haemostasis may be more difficult to achieve because of the underlying neoplastic process. In these circumstances, radiological or surgical treatment may be required to stop the bleeding.

Post-Endoscopy

Monitoring

Patients who have undergone endoscopic haemostasis for high-risk endoscopic stigmata of PUB should be closely monitored in the first 24 hours after the endoscopy and should remain in hospital for at least 72 hours post endoscopy.

Post-Endoscopic treatment PPI

Studies of high-dose PPI infusion (80mg bolus and 8mg/hr infusion) for 72 hours post endoscopic treatment of high-risk endoscopic stigma of PUB have shown that they significantly decrease the risk of ulcer rebleeding, need for urgent surgery and risk of death. These benefits have been shown in both Asian and predominately Caucasian patients and therefore this regimen should be routinely used in patients who have had endoscopic therapy of high-risk stigmata of PUB.

Second look endoscopy

Routine early second-look endoscopy following endoscopic treatment of PUB is not recommended. In some circumstances, such as uncertainty as to the adequacy of initial endoscopic therapy, a repeat upper endoscopy within 24 hours may be indicated.

In those with a gastric ulcer, a repeat endoscopy should be performed in approximately 2 months to ensure ulcer healing and exclude a malignant ulcer. If there is a high endoscopic suspicion of an underlying malignancy, early repeat endoscopy with biopsy should be performed when the patient has recovered from the acute bleeding episode. There are some that advocate a two month follow up endoscopy to ensure ulcer healing in those with PUB due to a duodenal ulcer. There is no evidence that this affects outcomes.

Rebleeding

Rebleeding will occur in 10-20% of patients who undergo endoscopic haemostasis of PUB. Risk factors for rebleeding include a previous history of peptic ulcer or PUB, shock at presentation, active bleeding at the time of endoscopy, a large (>2cm) ulcer or large (>2mm) underlying vessel or ulcers located on the lesser curve of the stomach or posterior duodenal bulb.

If rebleeding occurs, the patient's haemodynamic stability should be closely reassessed and resuscitation undertaken if required. For most patients with rebleeding, a repeat endoscopy and endoscopic treatment is successful. Care should be taken with retreatment with contact thermal probes to areas that were treated with this modality at the initial endoscopy. If repeat endoscopic treatment is unsuccessful, then the patient will require radiological embolisation or surgery of the PUB. In some circumstances such as failure of primary endoscopic treatment or rebleeding that is massive or from a very large or difficult to treat ulcer, direct referral for radiological or surgical treatment rather than repeat endoscopic treatment may be indicated.

Risk factor modification and need for long term PPI

All patients with PUB, *H.pylori* should be thoroughly excluded. *H.pylori* positive patients should undergo a course of *H.pylori* treatment once medically stable. *H.pylori* eradication should be confirmed by follow-up testing. In those patients with PUB and a negative *H.pylori* test, a repeat test using a second, different method should be performed to confirm the negative status.

In patients who are on anti-platelets (aspirin or clopidogrel) at the time of PUB, management of the medication depends on their indication. If there is no medical indication for them, they can be ceased permanently. If there is a medical indication for them, then any decision about ceasing the medications should only be made after discussion with the physician who initiated the anti-platelet therapy. If anti-platelets need to be continued then concurrent PPI treatment is required. A randomised controlled trial has shown that in patients with PUB who require anti-platelet therapy, aspirin and concurrent PPI results in less 12 month rebleeding rates than treatment with clopidogrel alone.

In patients on NSAID, these can be ceased in the acute setting. If patients with a previous peptic ulcer or PUB absolutely require a NSAID in the long-term, they should always receive a concurrent PPI.

In patients where the underlying risk factor for PUB has been treated (*H.pylori*) or permanently removed (anti-platelets or NSAID), a two-month course of standard dose PPI should be given. Whether PPI treatment beyond that period is needed is uncertain. In patients where there were no identifiable risk factors for PUB, the PPI should be continued long term.

Summary

Although the management of UGB is one of the more challenging aspects of endoscopy, it is also one of the most rewarding. In PUB, there are number of widely available endoscopic and medical treatment options which have been shown, in well conducted trials, to be effective in altering the natural history of this condition including mortality. Like all emergencies, streamlined systems and effective communication in a team setting are vital in ensuring a successful outcome for the patient.

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Endoscopic Management of Varices and Variceal Haemorrhage

David Koorey & Crispin Corte

Introduction

Up to 30% of well-compensated cirrhotics and 60% of those with decompensated disease will have varices. The mortality of a first episode of variceal bleeding is approximately 15-30% and 1 year survival figures ranging from 30 to 80% have been reported in the literature. Variceal bleeding is therefore a common and important complication of chronic liver disease. Gastroenterologists need to be able to identify those at risk of bleeding, reduce that risk (primary prophylaxis), manage acute varical bleeding and prevent rebleeding (secondary prophylaxis). This chapter will provide an overview of management focussing on endoscopic intervention.

General Principles of Management

Primary Prophylaxis: Guidelines vary as to who should be screened for varices. Some recommend that all patients with cirrhosis undergo upper endoscopy while others restrict screening to those with clues to the presence of portal hypertension such as splenomegaly or thrombocytopaenia. If the initial examination reveals no varices, follow-up endoscopy after two years has been recommended. If varices are found, the risk of bleeding should be assessed. Key factors predicting an increased risk include severity of the liver disease, size of the varices and presence of red markings – red wale markings, cherry red spots and haematocystic spots (Figure 1). Patients with small, low risk varices can be followed with annual endoscopy or commenced on a non-selective beta blocker (e.g. propranolol) aiming for a 25% reduction in resting heart rate. Some units measure wedged hepatic venous pressure gradients to assess response to beta blockers. In patients with high risk varices, options for primary prophylaxis include non-selective beta blockade and variceal band ligation. Both reduce first bleeding episodes and bleeding related mortality. Variceal band ligation reduces the risk of first bleeding compared to beta blockade in those with high risk varices but a mortality benefit over beta blockade has not been established. Any benefit needs to be balanced against the inconvenience, discomfort and possible complications associated with banding. Band ligation is the clear choice in those with high risk varices if there are contraindications to beta blockers or they are poorly tolerated.

Figure 1:

- i) Varices with red wale markings: longitudinal dilated venules that resemble whip marks.**
- ii) Varices with cherry red spots: small red spots up to about 2mm in diameter.**
- iii) Varices with a haematocystic spot: a large (>3mm), round, crimson projection resembling a blood blister.**



Acute Variceal Haemorrhage

Acute variceal haemorrhage is a medical emergency and should be suspected in any patient with upper gastrointestinal bleeding in the context of chronic liver disease or portal hypertension. Initial management should focus on adequate resuscitation, pharmacologic intervention and early endoscopic treatment. Venous access sufficient to allow rapid transfusion is essential. At least four units of packed cells or whole blood should be cross-matched initially depending on the patient's condition. Coagulopathy and thrombocytopenia may need correction either on presentation or with ongoing transfusion. The safety of the airway should be evaluated given the risk of aspiration in patients with reduced consciousness due to encephalopathy and ongoing haematemesis. Intravenous octreotide or terlipresin should be commenced: these agents reduce portal pressures and improve early haemostasis. Prophylactic antibiotics (for example intravenous ceftriaxone) should be given routinely. They reduce infections and rebleeding and improve survival in acute variceal haemorrhage.

Only 50% of variceal bleeding will cease spontaneously (compared to about 90% of non-variceal upper gastrointestinal bleeding) and early endoscopy is therefore a priority. Rarely, massive blood loss will be immediately life threatening and balloon tamponade for suspected varices will be necessary without preceding endoscopy. In most cases, however, resuscitation and pharmacologic intervention will allow early endoscopy. Whenever possible this should be performed with an anaesthetist present and the patient intubated to protect the airway. It is important to ensure that all equipment likely to be required is available: a banding device and an endoscope of suitable size for the device (larger, dual channel scopes may not readily accept a standard banding device); glue, lipiodol and an appropriate injector; a Linton tube, Sengstaken tube or similar for uncontrollable variceal bleeding; and, injectors, heater probe, clips etc should a non-variceal source be found.

Band ligation will control bleeding from oesophageal varices in 80-90% of cases with fewer complications and lower mortality than sclerotherapy. When bleeding from gastric varices is identified injection of glue is the treatment of choice. When bleeding cannot be controlled at initial endoscopy, balloon tamponade should be considered with a view to a second attempt at endoscopic management the following day (endoscopists should familiarise themselves with the protocols for balloon tamponade before the need arises). If endoscopic

therapy again fails, salvage TIPS may be an option but outcomes are likely to be poor in the setting of advanced liver disease, multi-organ failure and ongoing bleeding.

Secondary prophylaxis In patients who survive a first episode of variceal haemorrhage, 40-60% will rebleed by 6 weeks and 60-80% by one year. Rebleeding is predicted by the severity of the initial bleed, the severity of the liver disease and portal hypertension, active bleeding at the initial endoscopy and large varices with high risk stigmata. Variceal band ligation should be repeated at intervals of 2-4 weeks until varices have been obliterated. Non-selective beta blockade reduces rebleeding and bleeding related mortality in secondary prophylaxis. The combination of variceal band ligation with beta blockade appears to provide the best reduction in rebleeding rates. Nevertheless 5-20% of patients will rebleed despite secondary prophylaxis and in these patients TIPS should be considered.

Endoscopic Oesophageal Band Ligation

Technique: In the elective setting of primary or secondary prophylaxis, the goal is obliteration of the varices whilst minimising the risk of complications. More than one treatment session is usually required. Correction of mild to moderate thrombocytopaenia or coagulopathy is generally not needed. In patients with ascites prophylactic antibiotics may reduce the risk of spontaneous bacterial peritonitis post banding.

Elective band ligation can generally be performed under conscious sedation in day patients. The endoscope is first passed without the banding device to assess the varices. Note should be made of the lowest level that the varices appear as this is where banding should commence. Generally it is at or just below the cardio-oesophageal junction. Retroflexion in the stomach is important to check for emerging gastric varices (Figure 2). The endoscope is then reintroduced with the banding device attached. Various multi-band ligators are available and the endoscopist should be familiar with those used in their institution. The first band is generally deployed at the lowest point of the largest varix. The varix should be sucked into the ligator until the view is obliterated ('red-out') and the band then deployed. Slight, gentle alternating clockwise and anti-clockwise twisting of the endoscope can facilitate suction of the varix. Occasionally a varix will rupture during suction often at a point of wall thinness such as a haematocystic spot. It is important in this situation to maintain suction and deploy the band without delay. The second and subsequent bands are deployed on the remaining varices initially targeting the largest varices and those with high risk stigmata. The endoscope should be withdrawn slightly as banding proceeds. Although banding will generally be concentrated in the distal oesophagus, multiple bands should not be deployed at exactly the same level and some intervening mucosa should be left between adjacent bandings (Figure 3). This helps to reduce the risk of confluent post-banding ulceration. It is best to avoid passing the endoscope beyond bands that have been applied as occasionally this will dislodge the band and cause bleeding. Once recovered from their sedation patients should take fluids only for the remainder of the day and soft food the subsequent day. They should be warned to expect some chest pain and difficulty swallowing for a few days. A proton pump inhibitor may facilitate healing of post-banding ulcers.

In the setting of acute upper gastrointestinal bleeding endoscopy should be performed in theatres with the patient intubated to protect the airway. Initial endoscopy will help to exclude other sources of bleeding such as peptic ulcer disease and to differentiate oesophageal from gastric variceal bleeding. If significant oesophageal varices are found and there is no other source of bleeding it is reasonable to assume that the varices have bled and proceed to band ligation. Active bleeding points or visible fibrin plugs should be targeted if apparent. If brisk haemorrhage prevents identification of the bleeding point, bands should be applied to the largest varices commencing distally. If there is no active bleeding at endoscopy and a specific bleeding point cannot be identified, the procedure is similar to that used in elective band ligation. If bleeding cannot be controlled balloon tamponade is required.

Recent data suggests that following successful band ligation to treat active bleeding, consideration for early elective TIPS (within 72 hrs) may be appropriate.

Complications: Many patients will experience chest discomfort and some difficulty swallowing for a few days following band ligation. Pain is generally mild to moderate in severity and can be managed with simple analgaesics such as paracetamol syrup. Occasionally patients with more severe pain will require admission to hospital for analgesia and to exclude a more serious complication such as oesophageal perforation. Fortunately complications such as perforation or major bleeding are unusual though minor bleeding is not uncommon when bands are deployed. Post –banding ulceration is the most common significant complication and can present with delayed bleeding (usually within a few weeks of banding) or pain. Repeated banding occasionally causes dysphagia due to oesophageal scarring with loss of oesophageal compliance or overt stricture formation.

Glue Injection of Gastric Varices

Technique: When gastric varices bleed they often bleed massively. The upper stomach may be obscured by blood and clot. Rolling the patient to the right lateral position and slightly feet down (if the blood pressure is stable) should provide better visualisation. Prolonged washing and aspiration may still be necessary. In some cases, if the bleeding point cannot be visualised, balloon tamponade will be needed with continued pharmacologic therapy and repeat endoscopy after 12 to 24 hours.

Injection of glue remains the prime endoscopic therapy for gastric variceal haemorrhage. The endoscopist and assistant need to be familiar with the procedure and follow protocols carefully to optimise results and minimise the risk of equipment damage. Only needles suitable for use with glue should be used. The injecting needle is first primed with lipiodol and then partly primed with a histoacryl/lipiodol mix to about 10cm from the needle tip (the histoacryl is purple and should be visible in the injector). It is important not to fully prime with histoacryl/lipiodol to avoid glue contaminating the channel as the injector is introduced through the endoscope. After obtaining a satisfactory view and good position, the injector is passed down the channel. The bleeding varix or the largest varix, if a bleeding point cannot be identified, is injected with histoacryl/lipiodol followed by lipiodol alone to push the remainder of the glue into the varix. The procedure can be repeated for additional injections but at no stage should the injector be withdrawn into the endoscope. After the last injection, the injector is flushed with water. The needle is retracted into the injector but the injector is NOT retracted into the endoscope. The endoscope is removed

from the patient with the injector still protruding. The injector is then again flushed with water and wiped with a water moistened gauze before it is removed from the endoscope. The biopsy channel is then immediately flushed with water.

Complications: Bleeding may occur at the time of the procedure related to injection or weeks after injection related to sloughing of the glue cast and resulting ulceration. Glue embolism, both pulmonary and paradoxical can occur.

Figure 2: Gastric varices seen on retroflexion.



Figure 3: Bands have been applied in the distal oesophagus at slightly different levels leaving some intervening mucosa to reduce the risk of confluent ulceration.



Figure 4: Post banding ulceration of the oesophagus.



Conclusion

The identification and management of patients at risk for variceal haemorrhage, the resuscitation, medical management and endoscopic control of active variceal bleeding and the prevention of rebleeding are all essential skills for practising gastroenterologists. Primary and secondary prophylaxis allow endoscopists to hone their ligation skills for more testing cases of active bleeding. Injection of glue, on the other hand, is relatively uncommon on elective lists and trainee endoscopists need to take every opportunity to practise this skill so that they are ready for the next case of massive gastric variceal haemorrhage they encounter.

Further Reading

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SECTION 3

COLONOSCOPY

- Colonoscopy: Insertion and Withdrawal Technique (*Michael Bourke*)
- Polypectomy (*Michael Bourke*)
- Colorectal Cancer Screening and Surveillance (*Lennart Choo & Ian Norton*)
- Colonoscopic Stenting (*Michael K.L. Suen & Christopher J. Young*)
- Acute Colonic Bleeding (*Simon Zanati*)

Colonoscopy: Insertion and Withdrawal Technique

Michael Bourke

Successful colonoscopy, like all high quality endoscopy, starts with careful preparation. This may seem obvious, but it is often overlooked and cannot be over emphasised. Nothing should be taken for granted or assumed. One must be familiar and comfortable with the equipment, the colonoscope of choice, the nursing staff, sedationists and other assistants and the environment in which the procedure will be completed. A useful analogy is to envisage every colonoscopic procedure unfolding like a Mozart clarinet concerto, with the endoscopist as the conductor. Each professional has a role to fulfil and the endoscopist and their co-workers should be continuously cognisant of the music of the procedure room as the procedure evolves. When endoscopy units and procedural teams are able to generate this level of awareness, rhythm and harmony then it becomes immediately obvious to all involved when something or someone is out of tune. In such situations a major complication or problem may well be imminent and this can be avoided by early recognition by any member of the group with remedial action taken by the appropriate member of the team.

The endoscopist must know the patient well. Important features include a history of previous abdomino-pelvic surgery/pathology such as previous hysterectomy or pelvic radiotherapy. A thorough understanding of the cardio-respiratory status and physiological reserve of all patients scheduled for endoscopy is essential. Some patients will tolerate a prolonged or difficult procedure very poorly due to poor general medical health.

8 key points for safe and effective colonoscopy

- Know and check your instruments and processor before your colonoscopy list commences. For most colonoscopy procedures the air setting should be on low. Carbon dioxide is proven to be superior to air for insufflation during colonoscopy with advantages of reduced post procedural pain and swifter patient recovery. At present in 2010 it is not commonly available for routine procedures.
- Check the compliance or degree of tension of the patients abdominal wall (whilst they are relaxed in the left lateral position) just before starting and monitor this periodically during the procedure.
- Be a gentle perfectionist. Each instrument manipulation should be completed precisely as well as it possibly can be on every occasion.
- Keep the scope as short and straight as possible and withdraw and straighten after completing the insertion for each segment of colon and all major corners.

- Try and maintain continuous awareness of your anatomical location and the three dimensional position of the scope.
- Never try and push through fixed resistance, force does not work in endoscopy.
- If you are not making progress, change your strategy. Doing the same thing over and over is unlikely to be successful.
- Master the left colon, this holds the key to maximising caecal intubation success and minimising insertion time.

It is possible to learn from almost every colonoscopy that one performs, whether that is 5 or 50 per week. Challenging cases create the opportunity to reflect on technique and how this might be generally improved or specifically adapted to particular challenges.

Basic Technique

Caecal intubation should be as efficient as reasonably possible as this is the most uncomfortable phase of colonoscopy. Much of the colon is a mobile elastic tube, particularly the sigmoid, and thus a hurried forceful intubation results in looping, patient discomfort and a potentially failed complete examination. The great paradox of colonoscopy is “slower is faster”. Purposeful and controlled movements will result in a more complete examination than a flurry of exuberant actions.

Endoscope handling

- The predominant technique is that of torque steering. This implies that the right hand remains on the insertion tube (IT) of the instrument with the fingers and wrist of that hand in coordination with the left thumb on the large wheel (or up down control) of the endoscope. Most changes of direction in colonoscopy are a coordinated movement between the right wrist and the left thumb. Torque steering involves first gently angulating up (most frequent) or down with the thumb on the large wheel whilst rotating the shaft (most frequently clockwise on insertion through sigmoid and descending colon) (Fig 1). Angulation, even slight, confers lateral deviation of the tip of the instrument as the twist on the shaft is applied, without tip angulation no lateral deviation will occur, and hence no ability to steer through a corner. Hold the IT with your fingers as if it were a pencil (not like a tennis racquet) (Fig 2). This will maximise sensory feedback informing the proceduralist on the amount of tension within the IT. When the scope is straight, the IT at the level of the anus will feel relatively “floppy” and it seemingly falls onto the bed as it exits the anus. In contrast when the scope is severely angulated or looped the IT will feel stiff and it does not fall on the bed.
- For major corners, rotate the IT so that the axis of the corner is in the 6-12 o'clock orientation which is the most powerful bending direction of the instrument (especially upwards). Resist the temptation to move the right hand off the IT up to the left/right control (small wheel). This interrupts the fluidity of the insertion technique and adds very little to the overall angulation that one can obtain at the tip if a torque steering technique is being utilised.

- With optimal technique, the right hand is almost exclusively responsible for rotation of the IT while the left hand may adjust the position of the scope head and with the thumb move the up/down control and occasionally smaller left right wheel. Disciplined coordination between the two hands is the foundation of good technique.
- If at any point you lose your view (red out) simply pull the instrument back gently and insufflate.
- Most movements are small as they are being effected on a long lever, that being the endoscope and thus the net result at the tip can be significant.
- Minimise air insufflation on insertion and suction air frequently. The colon is a readily distensible mobile elastic tube which when over inflated becomes long and tortuous, enhancing the difficulty of the insertion procedure.
- When advancing through straight segments, use suction liberally as one progresses forward. This makes such segments easier to traverse and concertina's the colon on the scope, ultimately making the insertion less difficult.
- When aspirating fluid use a 2 finger technique with the index finger over the air button and the middle finger on suction. This avoids unnecessary suction of the bowel wall which if it occurs, impedes the view and mandates gentle withdrawal of the instrument and a time delay with re-orientation of the scope tip before insertion can recommence.
- When suctioning fluid, perform a submarine periscope technique to maintain a luminal view. The working channel (and suction channel) of the colonoscope is in the 5 to 6 o'clock position. The relationship between the lens, light source and working channel is fixed and thus this orientation is constant. Position your view just above the fluid and thus the suction port will be beneath the surface.

Figure 1: Torque steering: Coordinated movements between the right wrist and the left thumb comfortably negotiate most corners.



Figure 2: Hold the insertion tube like a pencil. The fingertips sense tension in the insertion tube and inform on the degree of resistance at the scope tip.



Looping, pressure and non progression

In ideal insertion conditions, the length of instrument inserted at the anus results in an equal (or greater if the colon is being shortened onto the IT) distance of endoscope tip progression in the colon. This is termed one to one progress. During insertion, loss of one to one progress indicates that the scope is bowing (consider the situation in gastroscopy when advancing to the pylorus. The flexible endoscope will bow for a variable distance on the greater curve of the stomach and then as it is splinted by the fixed gastric wall, progress towards the pylorus will resume) or a loop may be developing. This is a frequent occurrence in the left colon and is acceptable if after 5-8cm of insertion, with marginally increased resistance, progress resumes. This should be relatively painless and should not require a substantial increase in force. After the next corner, the scope can be "straightened" by gentle withdrawal, suction and torque. If however, there is a seemingly, long straight segment of resistance free insertion then a loop is probably being formed. This should be relatively painless and tension in the IT should be only marginally increased. At the end of the loop where all the "slack" of the redundant loop (and loose mesentery) has been taken up, progress will steadily halt, tension in the IT will gradually increase and the patient may experience pain. The loop can then be resolved by simultaneous usually clockwise torque, suction and gentle withdrawal of the IT. The IT may rotate more than 180 degrees in the endoscopist's hand. If the loop is being resolved correctly, the scope tip will not fall back more than a few centimetres and will often advance proximally in the colon and tension in the IT will rapidly decrease.

Abdominal pressure is a very effective technique when used strategically. Knowledge of the endoscope's location allows logical application. It is most useful when the scope is straight and the tip is beyond the sigmoid. After 5-6cm of non-progression, apply pressure to where bowing of the IT is most likely occurring. (See later sections)

Segment Specific Technique

There are aspects of core technique that are particular to each segment of the colon and it is not uncommon that subtle manoeuvres adopted early when difficulty is encountered will easily overcome what may at first appear a major obstacle to complete examination. Key amongst these is the concept of mastering the left colon. Approximately two-thirds of your total insertion time should be spent in the left colon. All loops should be reduced and the scope straight before you move beyond the splenic flexure. All people are created approximately equal in length between the anus and the splenic flexure as at this point insertion length should be between 45-50cms.

Use suction liberally during insertion to encourage the colon to concertina onto the colonoscope especially when advancing easily through straight segments. Use pressure for short periods of time and try and be specific and algorithmic in its application. In best practice colonoscopy, caecal intubation is achieved expeditiously with a short straight scope, limited use of the insertion length of the instrument and minimal patient discomfort. Insertion length at the caecal pole is ideally between 65-90 centimetres. When difficulty on insertion arises, there are generally three potential areas for remediation or problem avoidance.

1. endoscope handling and insertion technique
2. abdominal pressure
3. change in position

In order from 1-3 they represent the relative ease with which each of these interventions can be completed with change of position being the most difficult, particularly in large heavily sedated patients. Still at times this is vitally important. The underlying principle is to do the simple things first and to change strategy promptly and sequentially if successive techniques fail to resolve the problem. In addition in specific situations a change of instrument is necessary, e.g. stenosing diverticular disease.

Rectum and rectosigmoid

After digital rectal examination, the instrument with its distal 5cms well lubricated is inserted beyond the anus into the rectum. Hold the endoscope between one and two hand's breadths from the buttocks. It is useful to pause at the anorectal junction and carefully inspect the rectum in front of you. The anorectal junction is best examined in retroflexion. Retroflexion in the rectum is relatively contra-indicated particularly with an adult colonoscope in individuals with poorly distensible rectums such as those with chronic colitis or previous radiotherapy. If necessary it may be safely performed in these patients with a gastroscope. Passing from the rectum into the sigmoid is accomplished by torque steering. This angle may be very acute, particularly in:

- elderly patients with stenosing diverticular disease
- patients with a history of previous low abdominal or pelvic surgery such as previous abdominal hysterectomy
- young women

Even when this angle is easily overcome, it is best not to push forcefully through elongating the sigmoid colon on the instrument, but rather keep a short scope and use torque steering and rotation of the IT (particularly clockwise) to reach the descending colon. The scope may tend to form a loop on the bed exterior to the patient. This can be resolved upon reaching the descending colon or splenic flexure.

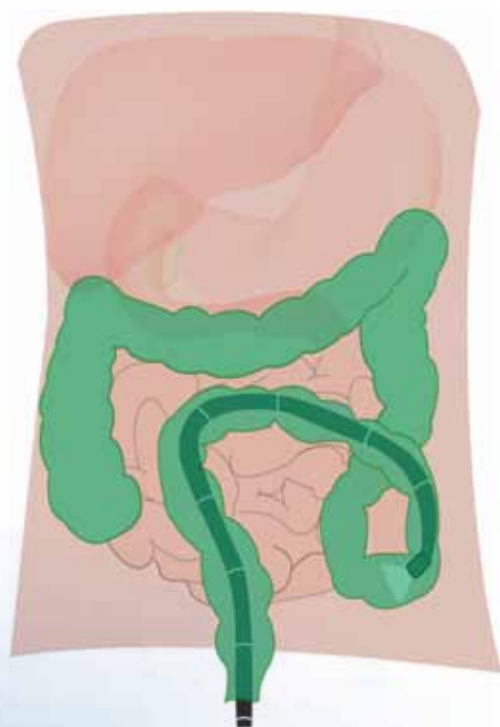
Sigmoid

In general, this is the most difficult segment during insertion. The sigmoid colon is more like an accordion than any other portion of colon and can be stretched to as much as 70-80cms, but will shorten to about 25-30cms with a straight scope located in the caecum (at 65-70cms of insertion). Thus precise anatomical location within the sigmoid by virtue of distance on insertion is very unreliable. It may be useful on withdrawal. If a polyp is not removed on insertion it is very important to precisely note its position with a straight scope so that it can be readily identified on withdrawal – its clock face position within the lumen may have completely changed. You may even consider to leave a suction mark on the adjacent mucosa or take a biopsy to aid localisation on withdrawal. The sigmoid mesentery is highly variable in length and mobility and thus in some individuals

the sigmoid colon can pass well into the upper abdomen before making a loop back down to the descending colon. In contrast after hysterectomy, the sigmoid tends to be rather angulated and may be fixed into the area previously occupied by the uterus. This can create difficulties during insertion.

Due to the shape of the pelvis with the curved sacrum, in general the colonoscope will naturally pass from posterior to anterior, and in more than 80% of cases will take a clockwise antero-posterior spiral into the descending colon. Some degree of upward looping with a convex arc forming towards the diaphragm always occurs as the colonoscope is advanced through the sigmoid. If one advances beyond the rectum into a long straight (often relatively featureless) segment, then this often reflects a lengthy or mobile sigmoid mesentery and a large loop may well be forming. In this situation the colonoscope will often pass relatively easily into the descending colon forming a relatively open N loop (Figure 3). Eventually such a loop will cause pain and the endoscopist will be aware of its formation due to non-progression up the descending colon, the excessive length of instrument inserted and the long straight insertion phase beyond the rectum. Such a loop is easily withdrawn by applying clockwise torque of between 90 and 180 degrees and withdrawing the instrument slowly. From this point it is often easy to advance up to the splenic flexure. Applying loop resolution techniques when half way through a loop will only cause the colonoscope to drop back below the loop without genuine progress being achieved.

Figure 3: An N sigmoid loop is forming. After the loop is passed this can be resolved by simultaneous clockwise torque and slow scope withdrawal.



Almost all colonoscopy procedures require some degree of sigmoid loop resolution. The scope must be straight at the splenic flexure so that the remainder of the procedure can proceed smoothly, but still a sigmoid loop may tend to re-form and thus whilst moving through the proximal colon it is important to repeatedly straighten and pull back to keep the sigmoid straight. On occasions non-specific left iliac fossa pressure may assist in maintaining a straight sigmoid.

Aim to completely avoid pushing blindly around corners, but rather rotate through these by torque steering. Enter the corner and rotate the IT slowly within the right hand up to 180 degrees whilst gently insufflating and pulling back very slightly. If a straight segment of lumen comes into view beyond this corner, try not to push directly into it but rather aspirate air and with small forward and backwards movements inch your way forward into the segment. This technique will concertina the colon onto the endoscope rather than stretching the colon over a forcefully inserted instrument. On occasions a “slide by” technique is acceptable for a few centimetres where one may see a “slide by” of the normal mucosal vascular pattern. If mucosal blanching occurs, this is indicative of excessive force by the colonoscope tip on the mucosa and perforation may well be imminent. The scope must be withdrawn.

In severe stenosing or tightly angulated diverticular disease, a change of instrument may be preferable. In general paediatric colonoscopes allow easier passage of the sigmoid and many use them as the preferred instrument. Sometimes even a gastroscope may be necessary. When compared to an adult colonoscope, the paediatric colonoscope or gastroscope have smaller tip diameters (12.3, 11.3 and 8.8mms respectively) and take a more compact arc with complete “up” movement to achieve 180° angulation (6.6 x 5.6cms for an adult colonoscope compared to 3.8 x 3.4cms for a gastroscope) (Figure 4). Hence narrow severely angulated corners can be traversed more easily. Even when using a gastroscope the caecum can often be easily reached as the relatively fixed sigmoid colon acts as a splint, tending not to loop and thus instruments with short insertion lengths will succeed.

Figure 4: Comparison of 180° turning arcs of adult and paediatric colonoscopes and a gastroscope. Narrow calibre instruments that are able to adopt a tighter arc are easier to manoeuvre through tightly angulated segments of colon such as severely stenosing diverticular disease.



Descending colon, splenic flexure and distal transverse

Often sigmoid loop resolution will paradoxically advance the colonoscope forward in the descending colon. Progress in the descending may also be direct. Right or left hypogastric pressure or left iliac fossa pressure may be necessary. Pressure should only be applied for 30 seconds initially to determine its effect. The colonoscope must be straight at the splenic flexure with only 45-50cms of instrument inserted. This flexure is usually relatively fixed by the phrenico-colic ligament (a peritoneal fold of variable length), but may be mobile. The transition to the transverse colon is usually relatively obvious when the patient is in the left lateral position as there is generally little fluid and the lumen has a triangular configuration. Passing beyond the splenic may be difficult. A convenient technique is to take a wider corner, aiming for the 12 o'clock position. As you insert the scope there will be 2-3cms of non-advancement, but then the "slack" will be taken up and the scope will then advance into the distal transverse. After 4-5cms one can pull back a little and straighten, aspirate air and then move onto the mid transverse. If available, applying the variable stiffener may help. This will stiffen the proximal shaft of the IT which at this point is within the sigmoid and thus prevent or minimise looping at this level. Occasionally change of position to supine will be necessary. Gentle forwards and backwards movements while aspirating will also assist.

On occasion much of the left colon is relatively mobile and a sense of the true anatomy may completely disappear. A clue to this situation is again the finding of a long straight segment of insertion at 20-50cms without obvious angulations. At the appropriate point where non-progression occurs it may be best to apply the less conventional counter clockwise torque on withdrawal to resolve what is actually a reverse alpha loop (Figure 6).

Proximal transverse, hepatic flexure and ascending colon

As the scope has often "buckled up" the splenic flexure, most often one can shorten into the proximal transverse by withdrawal and clockwise torque (beyond the mid transverse angulation). Try to enter the ascending colon with only 70-90cms of scope inserted. Often one can rotate clockwise into the ascending with gentle advancement and then by aspirating and gentle backwards and forwards movements proceed to the caecum. Remember that brisk or forceful movements when the scope is in the right colon will result in looping of the relatively unfixed left colon. If there is difficulty passing the hepatic flexure, rotate the patient first halfway back to supine (moving only the shoulders) and then if needed full supine (see below).

Caecum and ileo-caecal valve intubation

All landmarks should be confidently identified in the caecum. The scope should be able to comfortably touch the appendiceal orifice. This indicates that deep caecal intubation has been achieved. The ileo-caecal valve can be considered as being located on the medial or postero-medial wall and in consideration of this landmark generally the anterior and lateral walls of the caecum are easily seen. A frequent blind spot is the region immediately inferior to the ileo-caecal valve, and between here and the appendiceal orifice. Difficult to detect sessile lesions that may later lead to interval caecal cancers may lurk in this area. If difficulty is encountered it is crucial that a deliberate effort is made to view this area. This can be done by aspirating air and applying counter clockwise torque hugging the medial wall of the ascending colon and working gently backwards and forwards with 2cm movements to insert the tip of the colonoscope beyond the ileo-caecal valve.

A number of different techniques may be used to advance a straight colonoscope from the hepatic flexure down to the caecal pole. As a general principle, if difficulty is encountered in the ascending colon as a starting point it may often help to roll the patient's shoulders backwards towards the supine position (but not necessarily the hips), although full supine may be necessary but requires much more effort. This opens up the hepatic flexure and often will allow the scope to pass without difficulty unobstructed to the base of the caecum. Gentle forwards and backwards movements whilst aspirating air to concertina the colon onto the IT may also assist. Again applying counter clockwise torque whilst advancing along the medial wall of the ascending colon may also assist. In larger more voluminous right colons, for example in middle aged and elderly men with elevated BMI, on occasion it is helpful to advance the colonoscope in the 12 o'clock direction (this being the antero-lateral wall of the ascending colon/caecum). Sometimes pressure in the left iliac fossa and left upper quadrant is necessary. There may be 2-3cms of non-progression and then the scope will advance and you will reach the caecum and be able to shorten to an 80-90cm position at the anus indicating there has been a small amount of looping.

There are a number of techniques to achieve ileal intubation. If one draws an imaginary arrow on the curved "bow" opening of the appendiceal orifice then this arrow generally points directly to the orifice of the ileo-caecal valve. If the orifice of the valve cannot be seen en face (more than 50% of occasions) aspirating air for periods of 2 and 3 seconds at a time may encourage the flow of gas and luminal contents out of the valve and viewed from above this can also help to identify the precise location. My preferred technique for intubating the ileum is to identify the appendiceal orifice, rotate the IT gently counter clockwise a few degrees and slowly withdraw the instrument on the medial wall of the caecum until one comes across the inferior lip of the valve. It is then easy enough to pause for a moment, gently insufflate and drop into the orifice. Some prefer to de-flex the tip of the colonoscope and drag back into the valve. On occasion it is necessary to retroflex to identify an ileo-caecal valve, but such manoeuvres to identify the valve are only possible in those individuals who have a fairly deep (long) and capacious caecum.

Problem solving

The most common problems that result in failed caecal intubation and their potential solutions are listed in table 1. Knowledge (or a reasonable estimate) of the location of the scope tip and the IT's status is necessary to apply these strategies successfully. If this is not obvious it can be approximated by assessing the amount of scope inserted, the tension in the IT and knowledge of the colonic anatomy to that point. A resistance free insertion through featureless colon to 80cms with few angulations suggests the formation of a large sigmoid loop. This will need to be resolved before progress to the right colon. In contrast, a straight 50cms scope at the splenic with non progression on insertion suggests a mobile sigmoid or "high" splenic. Use of the stiffener or specific pressure will control the problem.

Table 1: Colonoscopy insertion problem/sequential response strategy.

Sequential Response

Problem	1	2	3
Stenotic or sharply angulated – fixed rectosigmoid junction or sigmoid colon	Right hypogastric pressure directed medially and downwards above the pubis (Fig 5)	Change position to supine \pm pressure as in 1	Right lateral position or change of scope
Long resistance free left colon forming an N, alpha or complex loop	Recognise, advance to the end of the loop and resolve with clockwise torque	Resolve with slow anti-clockwise torque often $>180^\circ$	Withdraw the scope to the rectum or until it is straight, apply specific pressure and re-insert slowly.
Trouble passing the splenic flexure, high and mobile splenic flexure	Apply variable stiffener and aim for 12 o'clock \pm left upper quadrant pressure just beneath the left costal margin pushing postero-inferiorly (Fig 6)	Supine position \pm pressure as in 1 or left iliac fossa pressure	Right lateral position \pm pressure as in 1 and/or 2
Non progression in mid/proximal transverse	Apply variable stiffener if available \pm left upper quadrant pressure	Right hypogastric or left iliac fossa pressure	Supine or right lateral position
Scope in the ascending colon but caecum in the distance	Use gentle forward and backward movements whilst aspirating air and applying anti-clockwise torque to pass the scope down the medial wall of the ascending colon, aiming for the ileo-caecal valve	Adopt a half way back position (shoulders rotated back towards the supine position but not the patient's hips) \pm left iliac fossa pressure and advance aiming for 12 o'clock	Supine or right lateral position

Figure 5: In a sharply angulated recto-sigmoid junction (usually around 20cms of insertion) right hypogastric pressure directed medially and downwards above the pubis will often resolve the difficulty.

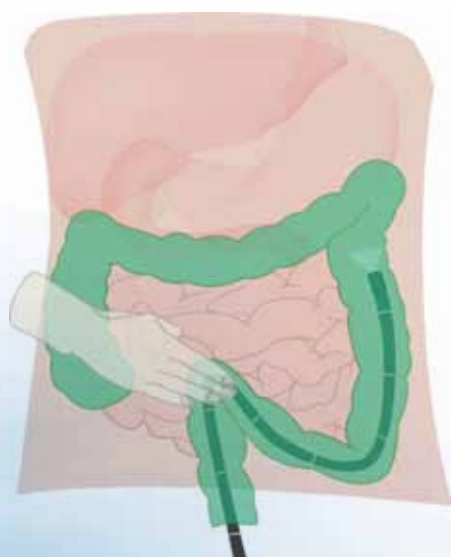
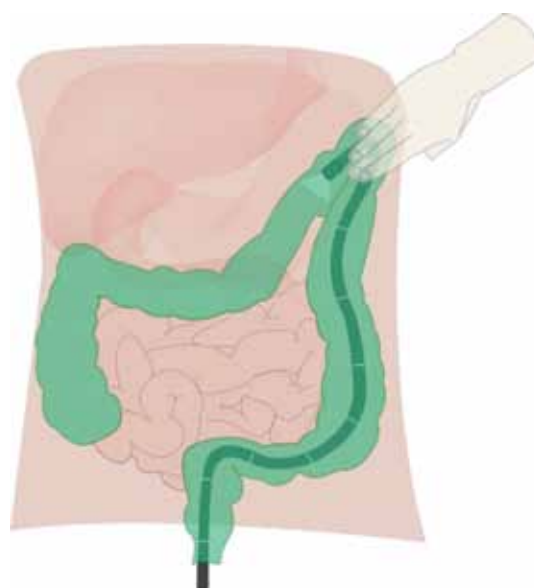


Figure 6: A sharply angulated or mobile splenic flexure that “loops” upward may be overcome by left upper quadrant pressure.



Assumptions: The patient is initially in the left lateral position, the scope is straight and the patient is sedated. On occasion a change in position may be a preferred strategy before pressure, especially when the patient can be re-positioned with relative ease. Attempt each response only once or twice. If it does not work after two attempts then you are unlikely to succeed with this strategy. The next logical step in the hierarchy should be chosen. Expert colonoscopists who quickly and painlessly intubate the caecum are generally not more dexterous than their less experienced colleagues, but make better decisions more quickly without repetition of manoeuvres that have failed previously. These are the preferred initial strategies, but this is not an exhaustive list. Other techniques may assist.

When to reconsider

As a general rule, if the caecum has not been reached within 20 minutes or progress during insertion comes to a halt for greater than 10 minutes then, particularly for trainee's, the situation should be reconsidered. Always remember that safety is the primary objective. Complete colonic examination (non-endoscopic alternatives exist) may not be necessary and as technical difficulty increases the balance of procedure related risk against clinical benefit may reach a tipping point where the benefit does not justify the risk. When difficulty is encountered trainees should involve their teacher/supervisor early as at this point he/she may be able to talk you through the resolution of the problem as an educational exercise. The trainees who ultimately complete their training with the most skill and technical insight are those that involve their teachers early. If assistance is delayed, then the consultant may need to take over or worse, the procedure may need to be aborted.

Withdrawal Technique

Colorectal cancer is the second leading cause of cancer death in Australia and many colonoscopies are now performed for screening and adenoma detection. Recent evidence confirms that even when performed under optimal conditions, colonoscopy is an imperfect test. Thus institution and adherence to quality measures that maximise mucosal visualisation and lesion detection are critical in optimising the efficacy of colonoscopy in cancer prevention and diagnosis. Although not a universal finding in all studies, an expanding body of evidence indicates that withdrawal times in excess of 6-7 minutes are associated with enhanced adenoma detection rates. Furthermore, evidence from large prospective studies indicate that within screening programs, endoscopists with an adenoma detection rate in excess of 20%, provide effective cancer prevention with a significantly lower or absent incidence of interval cancers when compared to endoscopists with a lesser adenoma detection rate. Thus adenoma detection rate is a valuable surrogate marker for the efficacy of colonoscopy in cancer prevention. Many experts and quality programs now report adenoma detection rates in excess of 50% for screening populations of average risk. In 2010, the consensus is that adenoma detection rates in screening populations should exceed 20% as a baseline with figures above 30% reflecting best practice.

It is intuitively obvious that bowel preparation is a critical factor in achieving an accurate colonoscopic assessment. The responsibility for the quality of the bowel preparation primarily rests with the endoscopist and his team. Patients who are likely to have poor bowel preparation (for example non-English speaking, inpatient bowel preparation, diabetics, patients with chronic constipation) should be identified pre-procedurally. (See preparation for colonoscopy).

All procedure reports should describe the quality of the bowel preparation. In some clinical situations considerations for repeating the procedure may be necessary. Photo documentation of poorly prepared areas helps to justify to patients and other 3rd parties alike the potential necessity for a repeat procedure, possibly with an enhanced bowel preparation.

Beyond time considerations, it is the authors view that in the future the withdrawal procedure will incorporate a protocol that mandates examination of known and potential "blind" spots. Some components of this "colonic mucosal visualisation" protocol will be completed on insertion. Ultimately such a protocol may be a standard feature of colonoscopy reports such as bowel preparation is. Areas where the mucosa may be incompletely visualised include the medial aspect of the caecum and the major flexures, particularly the infero-medial aspects. Two pass examination means that the endoscope is slowly withdrawn, slowly re-inserted and withdrawn again with the field of view centred on areas where visualisation was sub-optimal with the first pass. More than two passes may be required. A similar strategy can be applied to the sigmoid in selected cases. Skilful endoscopists achieve this easily and this underscores the importance of a good technique.

At the technical level, the key aspect is torque of the IT with the right hand and use of the up/down control with the left thumb. This should allow visualisation of the entire mucosal surface and deflection or flattening of mucosal folds to view the proximal side with an economy of movement. A slow staccato in and out movement may be used across sharp angulations or excessively telescoped portions of colon where mucosa may "fly past". Withdraw 3-5cms, then insert 2-3cms and slowly work your way past the corner. This technique can also be used in the transverse colon or other poorly visualised areas to provide an insertion component to the examination phase.

Although one does not wish to leave a patient uncomfortably distended, excessive suctioning of air during withdrawal may compromise mucosal visualisation. Successive folds that have collapsed onto each other may obscure lesions lurking in the space between them. Minimising unnecessary air insufflation on insertion will assist. Good insertion technique facilitates swift caecal intubation, reducing gas use. Periodic palpitation of the patients abdomen to assess distension is easily done and also assists. A useful technique is to deflate each segment when examination of that portion of the colon is complete. Thus having completed the assessment of the caecum, ascending and hepatic flexure, air is aspirated and the ascending colon completely deflated before moving back to the transverse. If at the end of the procedure a patient is clearly distended, a good endoscopist can easily intubate the colon beyond the sigmoid or splenic flexure to suction gas. Be aware that in very long procedures or patients with patulous ileocaecal valves, much of the gas trapping may be in the small bowel and removing colonic gas will not help greatly.

In contrast, adequately suctioning all pools of fluid and residue with irrigation as required, is very important. A significant lesion may be hidden beneath such collections. Unless the pool is large, use a two finger technique to avoid suctioning mucosa. Poorly distensible areas on withdrawal are often dependent or contain redundant colon. Even small changes in position significantly improve distension and visualisation.

A potential algorithm for colonoscopy withdrawal is summarised in Table 2. Certain areas of the colon are best seen on insertion, particularly the transverse colon when the patient is in the left lateral position. Optimal views on withdrawal may require placing the patient in the supine position. Similarly, the sigmoid is inflated in front of the endoscope on insertion, but is often concertina'd over the instrument on withdrawal.

Conclusion

With its increasing recognition as a pivotal component of colorectal cancer screening, diagnosis and therapy, high quality colonoscopy has become a critical part of endoscopic practice. All those training in colonoscopy should diligently apply themselves to becoming the best colonoscopists they can possibly be. Satisfying the training requirements of the relevant statutory bodies and qualifying for independent practice should not be seen as the end of one's training experience. Attaining this sort of formal approval also carries with it a substantial responsibility. Sadly, interval cancers and the attendant devastating impact on patients and families, remain a not infrequent occurrence in 2010. Quality assurance activities, either individual or as part of a group, are an important ongoing component of high quality endoscopic practice. Prospectively recording parameters such as adenoma detection and caecal intubation rate as well as bowel preparation adequacy provide important information on the quality of one's colonoscopy practice. This chapter is not an exhaustive summary of colonoscopy technique, but serves as a backbone upon which one can develop one's skills and also as a valuable resource for those involved in teaching colonoscopy.

Table 2: Suggested features of a standardised colonoscopy withdrawal protocol.

Withdrawal time of ≥ 6 minutes
Ileal intubation with careful inspection of the region immediately beneath the ileo-caecal valve, and between the valve and the appendiceal orifice
Consider retroflexion in the ascending colon and examination of the proximal aspect of folds up to the hepatic flexure. If not safely possible, careful inspection of the medial and anterior walls of the ascending colon.
Two pass examination of the hepatic flexure, i.e. reinsertion of the scope beyond the flexure and an additional withdrawal examination of this area once the first withdrawal examination has been completed
Two pass examination of the splenic flexure and distal transverse
Consider two pass examination of the sigmoid colon where it "flies past" quickly due to telescoping on the IT
Slow staccato withdrawal/insertion for areas that are difficult to visualise completely
Retroflexion in the rectum and inspection of the anorectal junction and distal rectum

Further Reading

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Polypectomy

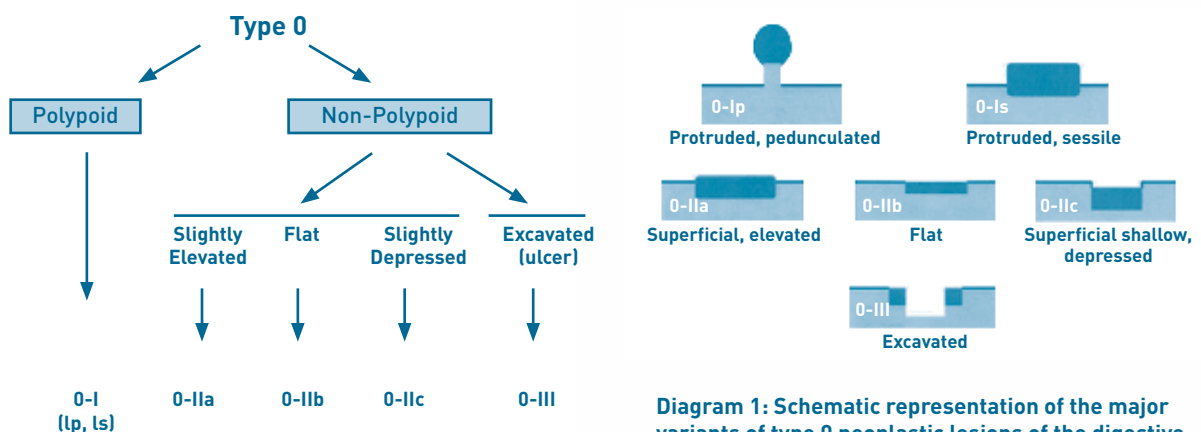
Michael Bourke

Polypectomy is a remarkably effective therapeutic intervention. It reduces the expected incidence of colorectal cancer amongst patients with colonic adenomas by the order of 75-90%. Approximately 70-80% of colorectal neoplasia arises from conventional adenomatous polyps and it is by this means that polypectomy exerts its influential effect. Colonic adenomas are common with a prevalence of greater than 30% amongst average risk 50 year olds. Most colonic polyps are relatively small at less than 1cm in diameter and this has facilitated the ease and success of their treatment by colonoscopy. Only 10-20% of polyps are over 10mms in size.

Lesion Assessment

Lesion assessment should routinely include a morphological description, size estimate and an assessment of the polyp's relationship to the surrounding mucosa if relevant. For example, polyps may have a saddle distribution over a fold or an invasive lesion may be relatively fixed with effacement of the surrounding mucosal folds. Colorectal polyps, particularly lesions >7mms, should be described morphologically according to the Paris system of endoscopic classification (see Figure 1). For significant polyps (>10mms) in the left colon, their distance from the anus with a straight scope (on withdrawal) should be precisely recorded. Below the splenic flexure this distance can be accurately reproduced.

Figure 1: (reproduced from the Paris classification of superficial neoplastic lesions).



General Principles of Polypectomy

Safe polypectomy implies the ability to resect and completely remove a polyp whilst achieving haemostasis and maintaining the integrity of the colonic wall. Two complementary forces operate during polypectomy, monopolar current delivered by the wire snare leads to cauterisation and haemostasis, whilst the tightening of the wire loop against the plastic sheath of the snare exerts a shearing force which ultimately will transect the polyp at the desired point. These two forces must operate simultaneously to result in a clean bloodless polypectomy without excessive thermal injury to the colonic wall. Either force alone will not safely sever a polyp or ensnared tissue $\geq 10\text{mm}$ s. Small polyps of $\leq 6\text{mm}$ s can be safely removed by cold snaring.

Closure of the snare around the pedicle of a polyp with the application of current seals vessels by the principle of coaptive coagulation. This is the means by which thermal probes are used to arrest peptic ulcer haemorrhage. As a result of firm pressure the walls of the bleeding vessel are coapted together with a small amount of heat being delivered to seal the union. Coagulating current alone is used by most experienced endoscopists on an approximate setting of 20-30 watts, although with older generators this is not standardised. Most endoscopists find a power setting they are comfortable with and use this for almost all their polypectomies, be it large sessile or small polyp. The delivery of energy is continuous once polypectomy is commenced and the snare is closed slowly over 2-3 seconds. Cutting current alone is not appropriate as this explodes cells and will result in immediate haemorrhage in a significant percentage. The use of blended current may be appropriate for situations where snare entrapment has occurred as a result of stalling during polypectomy or when removing polyps with very thick pedicles where stalling with the use of coagulating current alone is a significant risk (on the proviso that the endoscopist is prepared for immediate haemorrhage should it occur). More recently devices that continuously sense tissue resistance and adjust power output within a pre-determined range have become more widely utilised. Utilising a combination of short pulses of cutting current in combination with longer segments of coagulating current may provide a more controlled and safer polypectomy with less uncontrolled dispersion of thermal energy beyond the target area, particularly for large sessile lesions. Such microprocessor-controlled electrosurgical generators capable of alternating cycles of pulse cutting and coagulation current include: Erbe VIO 300 (Tübingen, Germany); Olympus ESG-100 (Olympus, Tokyo, Japan); or CONMED (Englewood, Colorado, USA). In theory these generators confer a significant safety and technical advantage for major endoscopic resection.

Current snare nomenclature is misleading. The standard snare (truly a large snare) is 5.5-6cms in length and 2.5-3cms in width. It will not open to its full width to allow tissue capture until the snare has completely exited the sheath, this usually implies that there must be 5-6cms of lumen in front of the end of the sheath into which the snare can comfortably open. This is not always the case, particularly within stenotic diverticular disease (where the lumen is unable to completely accommodate the fully deployed snare). It can also be cumbersome to use, especially for the removal of small polyps or saddle type lesions which wrap over a fold. It was the first snare manufactured, but has been

superseded by the preferred snare for most polypectomies, i.e. the “mini-snare” (3 x 1-1.5cms – depending on the manufacturer). This smaller snare would be better termed the standard snare. It is a better “all purpose” snare and will easily remove more than 90% of polyps encountered by the average colonoscopist. It is far easier to manipulate and deploy than the larger snare. Smaller 10-15mm oval to circular snares are now also widely available. Endoscopists should familiarise themselves with the various snares available.

A mono-filament or thin wire cuts quicker and has an advantage in certain situations, either for cold guillotining of small polyps (not mandatory) or to avoid stalling and snare entrapment when transecting giant pedicles. However, most endoscopists use a braided wire (0.4 to 0.5mm diameter) and this manages most of the common situations very well. Many snares now come with a stopper or markers on the handle which allow one to estimate the degree of closure of the snare, i.e. how much tissue is entrapped. This can be rehearsed prior to inserting the snare down the working channel by closing the handle until the tip of the wire just abuts on the end of the plastic sheath. This is the desired position for most polypectomies. An ink mark on the snare handle could serve as an alternative should the stopper not be available. The author prefers to handle the snare myself whilst transecting the polyp. Although this is not common practice amongst endoscopists I feel the information gained is invaluable, particularly when removing large lesions.

The working channel of most colonoscopes exits between 5 and 6 o'clock, hence devices passed down this channel, including the polypectomy snare, will undergo an obligatory trajectory from 5 o'clock (on exiting the scope) towards 11 o'clock as the device is advanced. For large or difficult polyps the target lesion should generally be positioned between 5 and 6 o'clock. Smaller less challenging lesions can be comfortably ensnared along this 5 to 11 o'clock arc. Positioning of the target lesion is crucial to successful and safe polypectomy.

Small polyps, if in the appropriate field, can be removed quickly on the way through to the caecum. This has the advantage of eliminating the not uncommon difficulty of identifying a small lesion on withdrawal. It is however important to bear in mind that if a significant amount of time is spent trying to remove a diminutive polyp on insertion, then there is a risk of excessive air insufflation which could increase the difficulty of caecal intubation and lengthen the time for total colonoscopy. For this reason, amongst others, large lesions are probably best left and dealt with on withdrawal. Total colonoscopy is important as 50% of patients who have one adenoma in their colon will have at least one further adenoma elsewhere in the colon. Removing lesions on withdrawal has the additional advantage of a straight instrument. This means that movement of the wheels or torque of the shaft is transmitted directly to the tip of the instrument, rather than being absorbed by any loops that may have been created during insertion. If a target lesion is not within the preferred 5 to 11 o'clock arc, a straight scope can easily be rotated to deliver the lesion into the target zone.

Basic Polypectomy

More than 80% of polyps encountered at colonoscopy are $\leq 10\text{mm}$ in size. The vast majority of these are sessile and minimally elevated. A small (more correctly termed standard) snare, no more than 3 times larger than the lesion, is preferred.

The key steps are as follows:

1. Position the lesion 2-3cms beyond the distal tip of the scope and approximately at 6 o'clock by rotating the IT. Your assistant may need to hold the IT for you.
2. Advance the snare sheath above and slightly beyond the lesion
3. Ask your assistant to open the snare and gently withdraw it slightly and lower the open snare around the lesion.
4. In general there are 2 options for snare closure:
 - a. Standard approach (figure 2)
 - i. Gently advance the snare so that the polyp is at the base of the open snare/ tip of the sheath and slowly close.
 - ii. The snare sheath remains largely stationary in the fingers of the endoscopist and the wire snare captures the polyp under visual control. Minor adjustments of the sheath by the endoscopist may be necessary during the final stages of closure. This is the core technique for most polypectomy. It works well when the axis of the snare is parallel to the wall of the colon. It is safe, requires limited technical skill, and carries little risk of unintentional entrapment of tissue proximal to the polyp.

- b. Traction technique (figure 3)

This approach may be preferable when access to the lesion is difficult, especially if the projected axis of the snare is not parallel to the colonic wall ($>30^\circ$) and particularly where access to the lesion is often difficult.

- 1) Saddling a fold
- 2) Proximal to a fold that obscures the view, or
- 3) Narrow lumens where even a small snare cannot open completely

This technique avoids unintentional entrapment of tissue proximal to the polyp.

- i. Gently pull the open snare backwards until it abuts the target lesion and slightly distorts.
- ii. Working carefully with your assistant, maintain the anchor you have on the lesion and whilst your assistant closes the snare, you advance the sheath to closure.

Challenging Polypectomy

In general there are four types of polyps which can create therapeutic difficulties for even the most experienced and proficient endoscopist. These can be considered as follows:

1. **Small flat/sessile**
2. **Pedunculated polyps with very large pedicles**
3. **Large flat sessile lesions or laterally spreading tumours**

1. Small flat polyps (<10mm): Suction pseudopolyp technique

Technically challenging, minimally elevated or flat lesions between 2-10mms, can be found through the colon. There is always the temptation to use a hot biopsy forceps technique and the author strongly advocates that this urge be resisted. The hot biopsy forceps technique is associated with a small but unacceptable risk of transmural injury leading to either perforation or post-polypectomy serositis along with the significant risk of delayed post-polypectomy haemorrhage resulting from the ensuing occasionally deep unpredictable cautery ulcer. Numerous case reports attest to this problem. A better alternative is cold guillotining of these lesions. However, it can be difficult to discretely and precisely capture the target lesion within the snare. There is an easier way to do this, the suction pseudopolyp technique (SPT).

- a. Ensure that the bowel is not over distended. Distension of the bowel stretches these lesions out, placing them under tension and makes them difficult to ensnare.
- b. Ensure that the mini-snare is ready to be used, the diathermy plate is attached (if one desires to use this) and the foot pedal is in the correct position.
- c. Aspirate the lesion into the suction channel of the colonoscope. This requires precise targeting but is easily learnt. Once the polyp has entered the working channel (bearing in mind it is still attached to the mucosa and has not been resected) continuous suction is applied whilst pulling the colonoscope backwards for a distance of 3-5cms. The suction is then released, the colonic mucosa springs back to its original position but you will observe that instead of a flat lesion now there is a small pea-like polyp. This can be easily ensnared and cold guillotined (safe for polyps up to 6mms) or removed by standard polypectomy with diathermy.

This technique works particularly well in the colon because the mucosa is very loosely attached to the underlying muscularis propria, a feature which is not shared by the oesophagus or stomach.

2. Pedunculated polyps with very large pedicles – The concerns here are threefold

- a. The risk of post polypectomy haemorrhage; it may be worth considering a haemostatic intervention to the stalk either before or after polypectomy, particularly where the head of the lesion is in excess of 3cms.
- b. Stalling during transection, this occurs when despite the application of continuous current on appropriate settings the snare becomes embedded in the polyp stalk and will not make any further progress in transecting the stalk.
- c. Contra-lateral burn, this results from current leakage from the tip of the polyp into the contra-lateral wall where the head of the lesion abuts during polypectomy. This is an infrequent occurrence that can be avoided by moving the polyp back and forth during polypectomy. It will not be discussed further.

A. In current practice stalk pre-treatment is rarely performed, but if employed it entails the use of either a clip or an endo-loop. It may take more than one clip to secure the pedicle. Haemostasis is confirmed by a blue discolouration of the head of the lesion. The polyp stalk is then transected above the level of the clip. The endoloop is a detachable nylon snare with a noose which can be locked at the base of a large pedicle rendering the tissue above ischaemic and occluding the vessels within the stalk.

It is a useful tool, but suffers from the limitation of having limited expansile force, hence complete deployment of the loop in a stenotic segment may be difficult and a truly giant polyp may not be readily captured. Ironically they are easier to use in areas where they are less likely to be required such as the ascending colon where the lumen is more capacious but large lesions are not frequently pedunculated. A clip (or several) is a useful alternative but will not confer reliable pre-resection haemostasis for lesions with thick pedicles (>10-12mm) due to inability to completely capture the stalk.

B. Stalling during polypectomy: This may happen despite the appropriate diathermy settings with extremely thick stalks or where there is malignant invasion of the stalk. In lesions with thick pedicles the delivery of energy should generally be continuous once polypectomy is commenced, this decreases the chance of stalling. Smart generators that sense tissue resistance offer more greater flexibility in these situations and stalling is virtually impossible. Stalling occurs when the encircled tissue at the core of the snare has been completely desiccated, but the cell walls have not been disrupted. A thick core of desiccated tissue of woody consistency forms. Further application of coagulating current is unlikely to transect the stalk. In a pedunculated lesion it is usually very safe to simply change to a blended or pure/primarily cutting current (and by using the cut foot pedal) continue to transect the stalk with tension applied to the snare handle. Haemostatic devices should be on hand in case of bleeding. Pre-treatment of the polyp stalk with either a clip or endoloop provides additional confidence with this manoeuvre. The stalk shortens significantly during the application of diathermy and so the clip or loop acts as a reference point so that one does not become concerned about the application of current close to the true colonic wall. Prior to removing a polyp with a large stalk it is important to ensure that the snare retracts for at least 1.5-2cms into the plastic sheath of the snare. Mechanical force is also an important component of tissue transection.

3. Large sessile lesions or laterally spreading tumours

In general submucosal injection of saline or another solution during polypectomy should be considered:

- a. in the right colon when the base of the lesion exceeds 10mms
- b. in the left colon when the base of the lesion exceeds 15mms
- c. if a lesion is hidden behind a fold then pre-injection on the more proximal side beyond the lesion will often elevate it forwards towards the colonoscope and facilitate an easy resection.

Submucosal injection is uniquely successful in the colon, more so than any other mucosal surface throughout the gastrointestinal tract, due to the relatively loose attachment of the overlying mucosal layer to the deeper muscularis propria. The loose spongy areolar tissue of the submucosal layer allows the deposition of large amounts of fluid. The mucosa, muscularis propria or serosa will not accept any form of injected substance. An injection in the correct mucosal plain immediately results in a visible bleb. The use of a fluid cushion lifts the mucosa away from the underlying muscularis propria and creates a large vertical plane through which safe thermal transection can occur. The fluid also serves as a heat sink minimising transmission of thermal energy to the colonic serosa. The colonic wall is normally between 2 and 2.5mms in total thickness. With the use of a submucosal injection this can be increased substantially. This technique allows the safe piecemeal resection of extremely large sessile lesions. In the hands of experts it is possible to safely resect lesions in excess of 120cms maximum dimension extending over more than two haustral folds and occupying more than two thirds of the circumference of the colon. However, an endoscopist who does not perform this technique frequently should consider the options for removal of a polyp if it:

- occupies more than one third of the circumference of the colonic wall
- crosses over two haustral folds (as invariably the tissue caught in the valley between the folds will be difficult to remove)

During piecemeal endoscopic mucosal resection as the plane of excision is cutting through the loose areolar tissue of the submucosa which has been extensively infiltrated by fluid, the snare should transect this tissue easily. If there is stalling during polypectomy then this is due to either:

- a. malignant invasion (which is unlikely if the lesion has been properly assessed and has elevated well on injection)
- b. the snare is operating in a plane deeper than the submucosa, i.e. the muscularis propria. One should stop this part of the piecemeal polypectomy and reassess

It is also important to remember the “one chance rule”, i.e. the best opportunity of obtaining a discrete and clear resection without the need for subsequent excavating polypectomies and Argon plasma coagulation exists only with the first intervention. Once thermal energy has been applied to the polyp there is invariably submucosal fibrosis and this limits the ability of the submucosa to expand and makes further attempts at appropriate endoscopic mucosal resection at times extremely difficult. In this situation after multiple attempts have previously been undertaken at another institution a compromise position at the tertiary institution may be necessary where the adenomatous tissue is shaved closely away from the bowel wall and the defect is then widely treated with Argon plasma coagulation. This can be successful in eliminating all adenomatous tissue during longterm follow up, but does not represent optimal management for these types of lesions. In essence, lesions in excess of 30-35mms should only be attempted by experienced endoscopists who are confident they can safely and completely excise the lesion. If this is not the case the polyp should be referred on to an “expert”.

Injection Technique

The first few submucosal injections set the stage for a successful procedure and great care should be taken at this point. Poorly placed or excessive injections, particularly within relatively narrow lumens (e.g. stenosing sigmoid diverticular disease) may create major difficulties and potentially render the procedure impossible. A carefully placed submucosal injection should make the procedure easier by lifting the lesion out into the lumen and towards the colonoscope. This is particularly important for poorly accessible lesions located on the proximal sides of folds or within tight angulations. A transparent short cap can be used to deflect folds and facilitate access to the proximal aspect of lesions saddling folds. For extensive piecemeal ER the author prefers a sequential inject and resect technique and thus avoid elevating the entire lesion at the outset. The author performs one or two resections each 1-2 sequential injections. Elevating the entirety of a large lesion (>40mms) may create difficulty with access but also excessive tension within the cushion limiting purchase of the snare and decreasing the size of sequential piecemeal resections.

Where access is unrestricted and en-bloc excision is being considered (<20mms particularly distal colon and rectum) use the injection to elevate the lesion towards the colonoscope.

- Divide the lesion into thirds and make the initial injection at the junction of the middle and furthest thirds (from the scope tip).
- Position the needle tip tangentially to the mucosal surface and gently touch the surface.
- Ask your assistant to commence the injection whilst simultaneously “stabbing” the mucosa with the needle tip by a rapid 1-2cm movement with the right hand holding the injection catheter. This technique accesses the submucosal plane swiftly and accurately.
- The correct plane is confirmed by an immediate elevation of the mucosa. Ongoing injection without tissue elevation or intra-luminal fluid escape indicates transmural placement of the needle tip with extra-mural injection. Slowly withdraw the needle and the tissue should elevate.

- Pull back slightly on the injection catheter or colonoscope, whilst maintaining the position of the needle tip in the submucosal plane. This will reduce the deformity on the mucosal surface and maximise fluid deposition immediately beneath the lesion, limiting dispersion of the fluid cushion beyond the perimeter of the lesion. You may even gently rotate the mucosa (which is impaled on the needle tip) out into the lumen by torque on the endoscope shaft.
- After satisfactory tissue elevation (usually a 5-8ml submucosal injection), resect this area first.
- In cases of submucosal fibrosis where the needle tip is placed correctly, but the submucosal plane is obliterated by fibrosis, a “jet sign” may be seen; a jet of fluid exits the lesion at high pressure.
- Alternatively a canyoning effect may occur where the lesion remains anchored in its original position, but the tissue of the perimeter elevates. The injection should be terminated immediately. The peripheral elevation will make the lesion very difficult to access, ensnare and resect.
- For more extensive lesions, beyond or straddling haustral folds or angulations, plan to resect the least accessible area first and use the first injection to facilitate access to this area.

Resection Technique

After careful lesion assessment, an endoscopic resection plan is loosely formulated, taking into account the orientation, size and position of the lesion in relation to the endoscope and its location in the colon. Generally a more aggressive approach can be adopted in the rectum, whereas great care needs to be taken in the caecum. Plan to remove the lesion in as few pieces as safely possible. En-bloc and oligo piecemeal resections create fewer opportunities for error, more accurate histological assessment and theoretically a reduced risk of recurrence in comparison to when lesions are removed in numerous pieces (poly piecemeal excision). Figures 4-5 demonstrate some basic examples.

- Orientate the target so that it is in the 5-6 o'clock position.
- Resect the most inaccessible and difficult aspect first.
- Work sequentially from the point of first entry into the submucosal plane using the edge of the defect as the base for subsequent piecemeal resections.
- Excise a 2-3mm margin of normal tissue at the edge of the lesion, this eliminates the risk of small amounts of residual tissue at the edge of the defect. These can be difficult to treat.
- Align the snare at the edge of the advancing mucosal defect to minimise occurrence of tissue islands within the defect. These are difficult to remove subsequently.
- Open the snare completely above your target and push down firmly on the fluid cushion with the up/down control whilst aspirating air. Deflating the lumen reduces colonic wall tension and decreases the footprint of the neoplasm on that wall, maximising tissue capture.

- Close the snare tightly. If using a spiral or serrated snare of more than 10mm diameter, it is not possible to resect the tissue without the use of diathermy. Individual snares have different handling characteristics. Endoscopists who perform advanced endoscopic resection should become familiar with the performance characteristics of their preferred snares. The author uses the 20mm spiral snare as the general work horse of extended piecemeal and en-bloc EMR. Closing the snare maximally excludes muscularis propria from the captured tissue analogous to the use of rubber band ligation during multi-band mucosectomy in the oesophagus.
- Safe tissue capture is confirmed by three manoeuvres:
 - assessing mobility of the ensnared tissue relative to the adjacent colonic wall; the captured tissue should be able to move back and forth quickly and seemingly slide a short distance over the surface of the colon;
 - the degree of closure of the snare handle; for a spiral snare the snare handle should be such that the distance between the thumb and fingers is less than 1cm; and
 - the speed of transection; this phase should be short-lived. The snare is kept tightly closed whilst the foot pedal is depressed. With a microprocessor controlled generator, between 1-3 pulses transect the tissue. A more prolonged transection phase indicates either potential entrapment of the muscularis propria or deeper neoplastic invasion. In the right colon we generally tap the pedal, essentially cutting the tissue from the colonic wall in a fashion similar to ESD.

Conclusion

This chapter is not an exhaustive summary of polypectomy technique, but lays out the general principles and serves as a backbone upon which one can develop one's skills and also as a valuable resource for those involved in teaching colonoscopy and polypectomy. Some of the discussion in relation to the more advanced techniques will not be relevant to all, but it is helpful to have an understanding of the principles involved.

Further Reading

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Figure 2: Standard approach: the base of the open snare is positioned at the interface between the polyp and the surrounding normal mucosa. The snare is then closed slowly with gentle suction.



Figure 3a: Traction technique for polypectomy.



Figure 3b: Post polypectomy site.



Figure 4a: Paris 0-IIa 15mm Non Granular lesion.



Figure 4b: Following Indigo-Carmine Saline injection lifting lesion ready for resection.



Figure 4c: Enbloc resection, exposing submucosa.

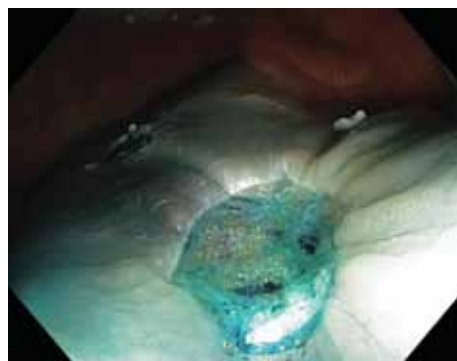


Figure 4d: End result showing no residual adenoma and clean margins, two lesions have been resected.

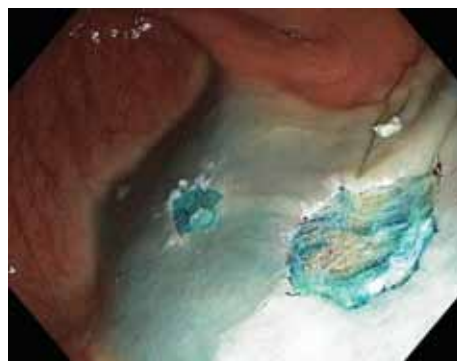


Figure 5a: Paris 0-IIa 15mm Sessile Serrated Adenoma (SSA).



Figure 5b: Following Indigo-Carmine Saline injection to lift lesion ready for resection.



Figure 5c: Enbloc resection, showing exposed submucosa.

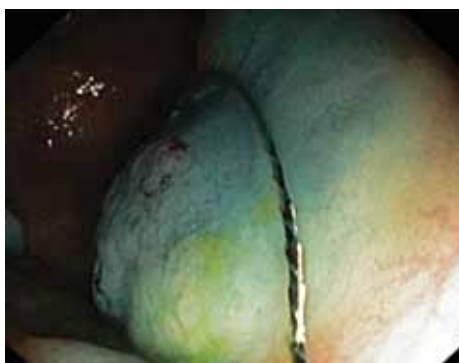


Figure 5d: End result showing no residual adenoma.



Figure 6a: Paris 0-IIa 30mm Granular lesion overlying fold in saddle disposition.



Figure 6b: Following Indigo-Carmine Saline injection to lift lesion ready for resection.



Figure 6c: Post 1st excision, exposing submucosa.



Figure 6d: End result, following 4 piece resection, showing no residual adenoma.



Colorectal Cancer Screening and Surveillance

Lennart Choo & Ian Norton

Introduction

Colorectal cancer (CRC) is the second leading cause of cancer related death in Australia. In 2006, there were more than 13,500 new diagnoses of colorectal cancer, and more than 3,800 deaths associated with the disease.

Survival is directly related to stage at diagnosis. Stage I (limited to mucosa and submucosa, T1) has a 5-year survival of nearly 100%. The 5-year survivals of stage 2 (penetration to the muscularis or serosa, T2-T3), 3 (lymph node involvement) and 4 (distant metastases) disease are 80%, 50%, and 5% respectively. Early discovery improves survival, but CRC is usually asymptomatic until late-stage disease.

It is well established that screening of asymptomatic persons who are at average risk can detect cancers at an earlier and therefore more curable stage, resulting in a reduction in mortality. Since its launch in May 2006, the National Bowel Cancer Screening Program (NBCSP) has had a measurable impact on colorectal cancer stage at diagnosis, where 40% of NBCSP detected cancers were stage I compared to only 14% of symptomatic cancers. Improvement in survival is anticipated. Furthermore, since CRC is preceded by a long premalignant phase (polyp) for which there is an effective intervention (polypectomy), this is an ideal disease for screening strategies.

Individual Risk of Colorectal Cancer

There are three risk categories to stratify patients to appropriate screening. These risk categories are high risk, increased risk, and average risk. Only 25% of new cases of CRC occur in those with easily identifiable risk factors. The remaining 75% occur in patients considered at average risk.

High Risk Group

Familial adenomatous polyposis

Though most patients with FAP have a family history of the disease, 20% of those affected are secondary to spontaneous mutations, and thus could be the first affected member in the family. It accounts for only 1% of all CRC, however, its penetrance is nearly always 100%, as is the risk of developing CRC. Though patients with classical FAP start to express their phenotype in the early teenage years, attenuated FAP is also being increasingly recognised. In this condition, fewer than 100 adenomas may be present, often only in the proximal colon, and they tend to develop at a later age, and progress to colorectal cancer slower.

Where an APC gene mutation has been identified in the family, individuals within the family may be evaluated by genetic testing for the APC mutation, or be enrolled into a colonic screening program from their second decade of life until such time when colectomy is deemed by both physician and patient as the best treatment. This screening involves annual flexible sigmoidoscopy until colonic adenomas are detected and thereafter annual colonoscopy.

It is important to note that these patients are also at increased risk of duodenal (and ampullary) cancer and adenomas, and gastric adenomas. Therefore, upper endoscopic surveillance is also recommended for FAP patients, including with a side-viewing scope to evaluate the ampulla, and this surveillance should continue post colectomy. Additionally, *Helicobacter pylori* infection should be sought in FAP patients and eradicated due to the increased risk of chronic active gastritis and subsequent gastric adenomas.

Hereditary non-polyposis colorectal cancer

Hereditary non-polyposis colorectal cancer (HNPCC) comprises of 3-5% of all colorectal cancers, and tends to cause more right-sided cancers than in the sporadic population. HNPCC is associated with multiple other cancers including endometrial, ovarian, pelvi-ureteric, gastric, small bowel, pancreatic, and hepatobiliary. Although disease penetrance is less than FAP, nearly 70% of HNPCC individuals will eventually develop a malignancy.

Patients may be clinically screened for the possibility of HNPCC by using the revised Bethesda criteria (Table 1). Individuals who fulfil the criteria should have any tumour stained immunohistochemically for the mismatch repair gene products (proteins hMLH1, hMSH2, hMSH6, hPMS2), and those in whom a negative stain suggests a deficient protein should be offered genetic testing. Those patients with positive genetic testing should undergo colonoscopy every 2 years beginning at age 20-25 years or 5 years younger than the youngest case or colorectal cancer in the family, until age 40 years, then annually thereafter. Separate screening guidelines exist for the multiple other cancers affecting HNPCC patients.

Table 1. Revised Bethesda criteria for clinical evaluation of risk for HNPCC.

Individuals with any of the following:
1. CRC before age 50
2. Synchronous or metachronous CRC or other HNPCC-related tumours,* regardless of age
3. CRC with MSI-high morphology before age 60
4. CRC with one or more first-degree relatives with CRC or other HNPCC-related tumours, one cancer diagnosed before age 50, or an adenoma before age 40
5. CRC with two or more relatives with CRC or other HNPCC-related tumours, regardless of age
*Colorectal, endometrial, ovarian, pelvi-ureteric, gastric, small bowel, pancreatic, and hepatobiliary CRC-colorectal cancer HNPCC- hereditary nonpolyposis colorectal cancer MSI- microsatellite instability

Increased Risk Groups

Individuals may be at increased risk of CRC based on family history, personal history of previous adenomatous polyps or CRC, and a history of inflammatory bowel disease. These patients have a 2-6 fold increased risk of CRC, and should ideally be screened by colonoscopy.

Family History

Patients with one first-degree relative with CRC before the age of 55 years, or two first-degree relatives at any age, should be screened beginning at the age of 50 years, or 10 years before the earliest CRC in the family. These patients should be screened every 5 years with a colonoscopy assuming a normal preceding colonoscopy.

Individuals with one first-degree relative with CRC at the age of 55 years or older or two second-degree relatives with CRC at any age should be screened as the average risk individual, as their lifetime risk is increased only 1.5 fold compared to the general population.

Personal History

Individuals with a history of a CRC who have undergone a surgical resection for curative intent should ideally have had a full colonoscopy prior to resection, as 5% will harbour a synchronous cancer and 15% a synchronous adenomatous polyp. If complete colonoscopy was not performed prior to resection, it may be performed intra-operatively, or 2-6 months after resection. Thereafter, patients should undergo colonoscopy within 3 to 5 years. If adenomatous polyps are identified, these patients are surveyed for future disease based on the polyp size, histopathology, and number.

Patients with adenomatous polyps which were incompletely excised, or were excised by piecemeal nature have a high rate of recurrence, and as such, should be re-evaluated with another colonoscopy in 2-6 months. Patients with polyps which cannot be completely excised, or have multiple recurrences should be considered for surgical resection.

Individuals with more than 10 adenomas on a single examination should have a repeat colonoscopy in 3 years, and consideration of a possible hereditary syndrome.

Patients with 3 to 10 adenomas, or 1 adenoma ≥ 1 cm, or any adenoma with villous features or high-grade dysplasia should have a repeat colonoscopy in 3 years. If the follow-up colonoscopy is normal or shows only 1 or 2 small tubular adenomas with low-grade dysplasia, then the interval for the subsequent examination should be 4-6 years.

Patients with 1 or 2 small tubular adenomas with low grade dysplasia should have repeat colonoscopy in 4-6 years time.

Individuals with hyperplastic polyps should be subsequently screened as average risk individuals except in the case of a hyperplastic polyposis syndrome.

Inflammatory Bowel Disease

Patients with idiopathic inflammatory bowel disease (IBD); either ulcerative colitis or Crohn's colitis; are at an increased risk of developing CRC after 8-10 years of chronic colitis. This risk is estimated at 0.25% per year of disease, and is 4 times higher in the presence of primary sclerosing cholangitis. Colonoscopy should be performed 1-2 yearly beginning 8 years after the onset of pan-colitis or 12 to 15 years after the onset of left-sided colitis; and if primary sclerosing cholangitis is present, to begin surveillance from the time of diagnosis is recommended.

Average Risk Group

Individuals without a personal or family history of CRC or polyps and no IBD have an increasing risk of CRC with increasing age (Table 2). Population screening is recommended from the age of 50 years in completely asymptomatic individuals. The available options for CRC screening with their advantages and disadvantages are summarised in table 3.

Table 2. Absolute risk of colorectal cancer in people without risk factors.

Risk of colorectal cancer within a time period				
Age (years)	5 years	10 years	15 years	20 years
30	1 in 7000	1 in 2000	1 in 700	1 in 350
40	1 in 1200	1 in 400	1 in 200	1 in 90
50	1 in 300	1 in 100	1 in 50	1 in 30
60	1 in 100	1 in 50	1 in 30	1 in 20
70	1 in 65	1 in 30	1 in 20	1 in 15
80	1 in 50	1 in 25	–	–

Guaiac based Faecal Occult Blood Testing (gFOBT)

gFOBTs detect blood in the stool based on a reaction with the pseudoperoxidase activity of heme. The test is not specific for human haemoglobin and can cross react with peroxidases in fruits, vegetables, and non-human blood, thus requiring a strict 3 day elimination diet of all meats and some raw vegetables before testing. Nonsteroidal anti-inflammatory drugs (NSAIDs) and vitamin C should also be avoided prior to testing to minimise false positive and negative results respectively. These tests also require collection of a sample of stool over 3 consecutive days, and does not distinguish upper from lower gastrointestinal bleeding. Despite these limitations, in a systemic review of four randomised, controlled trials involving more than 320,000 individuals, a 16% reduction in the relative risk of CRC death was noted overall, and a 25% reduction was seen when adjusted for screening attendance. The Hemoccult SENSa kit has been shown to be the most sensitive and efficacious. Its sensitivity for cancer and advanced adenomas is 86.7% and 87.5% respectively, with a specificity of 87.5% for both.

Faecal Immunohistochemical Testing (FIT)

FIT specifically detects non-degraded human globin and is thus identifies bleeding in the colon and rectum only (blood from the upper gastrointestinal tract is degraded to heme products prior to its transit to the colon). It does not require dietary and medicinal exclusion pre-testing, and only requires one sample. This has translated to increased participation rates in population screening studies. Sensitivity for cancer has been reported at 94% and specificity 87.5%. Two large randomised controlled trials have recently shown the superiority of FIT over gFOBT, detecting advanced neoplasms and cancer at a rate of 2-2.5 times more when used as a screening tool.

Flexible Sigmoidoscopy

Flexible Sigmoidoscopy is an endoscopic procedure that examines the distal part of the colon lumen; nevertheless, this is where most cancers are found. It is typically performed without sedation (thus no prior fasting is required) and with a more limited bowel preparation than colonoscopy (usually just an enema prior to investigation). Since sedation is not required, it can be performed in office-based settings, and patients do not require the whole day off work, nor are they restricted in requiring an escort home. Any adenoma identified on flexible sigmoidoscopy requires a subsequent colonoscopy for further evaluation. **Sigmoidoscopy is associated with a 60% to 80% reduction in CRC mortality.** Emerging evidence has also shown that as a once off screening tool, despite lower participation rates, flexible sigmoidoscopy detects 3 or 6 times more advanced neoplasia or CRC than FIT or FOBT respectively.

Colonoscopy

Colonoscopy is the common end-point for all screening studies, and is considered the gold standard for the diagnosis of both colon and rectal polyps and malignancy. Although effective at both diagnosis and treatment, colonoscopy requires a large amount of patient participation. A liquid diet is generally recommended the day before with the ingestion of a large volume of lavage or laxative solutions. During the procedure, patients typically receive sedation to decrease the discomfort, and this disallows the patient to work the same day, and requires them to be escorted home by a family member. Many large population studies have demonstrated the decreased incidence of CRC post clearance colonoscopy, though there have been no randomised controlled trials of colonoscopy screening to assess benefit over risks. The reduction in incidence has been estimated at 70% to 90%. Despite it being the best investigation for diagnosis and treatment, however, colonoscopy is not infallible. Controlled studies have demonstrated a miss rate of about 6-12% for 10mm polyps, and this is where optimal bowel preparation and adequate training of proceduralist is paramount. Additionally, complications are more frequent and severe than the previously mentioned investigations, with a significant bleeding rate of 1 in 500, bowel perforation of 1 in 1,000, and death rate of 1 in 10,000 colonoscopies.

Table 3. Summary of screening tests for colorectal cancer.

Test	Advantages	Disadvantages
FIT	Non invasive No time off work Inexpensive	Non bleeding polyps and cancers will not be detected Requires continued yearly testing
gFOBT	Non invasive No time off work Inexpensive	Requires multiple samples Requires dietary restrictions Lower sensitivity and specificity than FIT
Flexible sigmoidoscopy	Minimal bowel preparation No fasting required	No sedation, thus uncomfortable
Colonoscopy	Complete bowel examination Diagnostic and therapeutic	Complete bowel prep required Conscious sedation used; day off work and chaperone required Risks include perforation and bleeding Expensive
FIT- faecal immunohistochemical testing gFOBT- guaiac based faecal occult blood test (HAEMOCULT SENSa) CRC- colorectal cancer		

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Colonoscopic Stenting

Michael K.L. Suen & Christopher J. Young

Introduction

Large bowel obstruction (LBO) is a common initial presentation among colorectal cancer patients. Its prevalence varies between 8 and 29% in the literature. Traditional management involves urgent surgery, and quite often decompressing procedures such as colostomy or Hartmann's procedure. In such an emergency setting, urgent surgery is often associated with worse clinical outcomes. Patients with LBO will have fluid and electrolyte depletion and possibly renal failure. Faecal loading and distension of the colon can make the operation technically more difficult, with impending colonic ischaemia and perforation if the obstruction is not relieved, while nutritional deficiency will affect wound healing. Morbidity and mortality for emergency surgery is widely quoted at 45–50% and 15–20% respectively. The traditional surgical management involves one to three operations with a significant proportion of patients ending up with a permanent stoma.

Colonic stenting has the potential to immediately relieve large bowel obstruction, and to avoid emergency operations in these sick patients which may in turn improve their clinical outcomes.

General Principles

A self-expandable metallic stent (SEMS) is a tubular metal mesh stent that expands radially upon deployment. Similar stents were first used in the management of malignant biliary obstruction with great success. Its use in the management of large bowel pathology was first described by Dohmoto in 1991 for an obstructing rectal cancer. They are usually inserted under fluoroscopic or endoscopic guidance, or a combination of both to relieve the obstruction, which can provide permanent relief in the palliative setting and temporary relief in the curative setting.

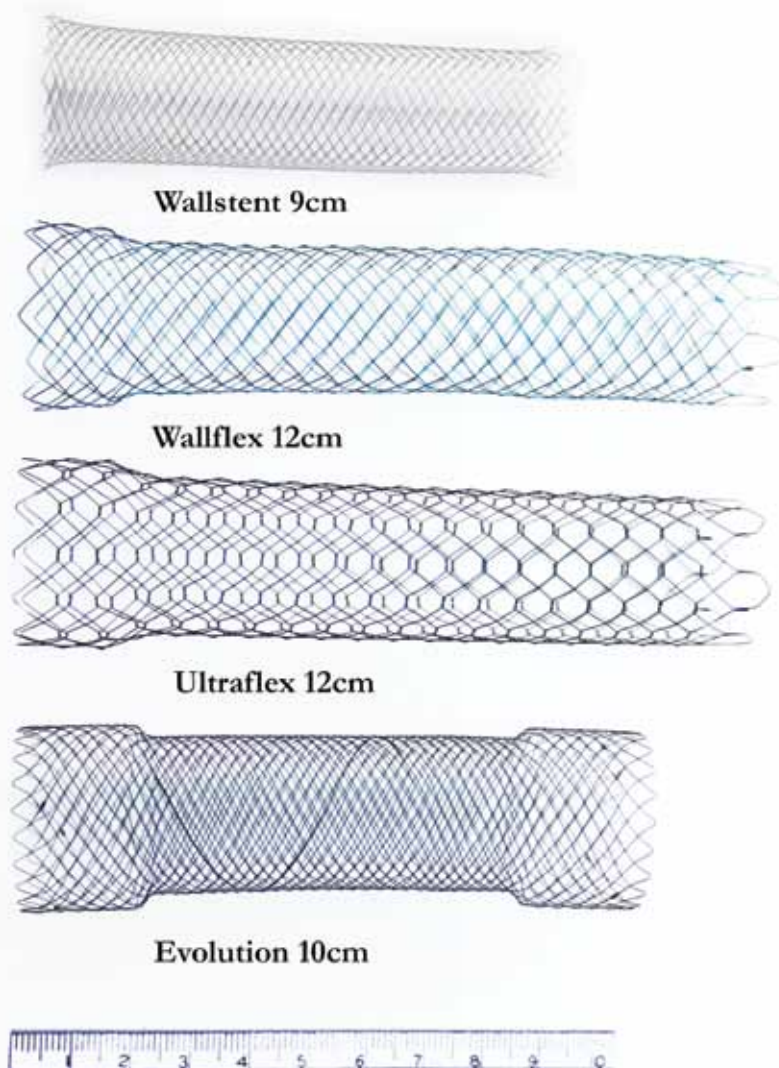
In the palliative setting, patients can benefit from the avoidance of having an open procedure and the high likelihood of stoma formation in this setting. Their quality of life should improve as a result.

In the curative setting, patients can first recover from the physiological stress caused by the bowel obstruction. A more thorough pre-operative workup can be completed, a bowel preparation can be given and their definitive surgery can be performed in a semi-elective setting.

Techniques

There are a few different types of stents available. The ones that the authors have used include the Wallstent, Wallflex and Ultraflex (all three from Boston Scientific, Natick, MA) stents, and Evolution (Cook Medical, Winston-Salem, NC) stents (Fig.1). The authors no longer use the Wallstent.

Fig 1. Four different types of self expanding metallic stents used by the authors. Top three stents supplied by Boston Scientific, Natick, MA, and lower stent supplied by Cook Medical, Winston-Salem, NC.



The key difference is that the Wallflex, Wallstent and Evolution stents can be placed through the biopsy channel of a colonoscope, which is 3mm or 10FG in diameter, while the Ultraflex stent cannot be placed through the colonoscope. This allows the Wallflex, Wallstent and Evolution stents to be placed anywhere in the colon or rectum that the colonoscope can reach.

The Wallflex and Evolution stents are made of Nitinol (Nickel-Titanium alloy) and has rounded metal ends and a proximal flare that may make it less likely to dislodge if placed through a stricture. The Wallstent stent is made of a cobalt-chromium alloy and the ends are potentially sharp barbs that can penetrate probing fingers or soft bowel.

The Ultraflex stent is made of nitinol and comes on a larger delivery system and cannot be placed through the colonoscope, and so is limited more to the rectum and sigmoid colon.

The difference between the Wallflex and Ultraflex stents is created by the weave of the nitinol wires that create the differences in the parameters of these nitinol stents. The Ultraflex stent does not lengthen when radial pressure is applied externally unlike the Wallflex, Wallstent and Evolution systems, so that while it cannot be placed down a narrow delivery system to go down a biopsy channel, it has a greater radial force to withstand the forces placed on it by lower bowel strictures and propulsive forces.

The author prefers to perform the procedure in the operating theatre under combined endoscopic and fluoroscopic guidance. All patients are placed on a trans-x operating table in a supine position, with the legs placed in a "frog-leg" position for ease of access of equipment. The patient is usually brought down towards the foot of the table so that the abdomen can be viewed with the fluoroscopic machine.

The fluoroscopic screen is placed to the top left of the table and the video monitor of the colonoscope and the endoscopist to the right of the table. The C-arm of fluoroscopic image intensification machine comes in from the left hand side of the patient, along with the radiographer.

Nursing staff are usually on the right hand side of the patient as well, and one assistant at the foot of the table to help hold the scope, guidewire or stent in a particular position if required.

Under the colonoscopic view, a guidewire is inserted. Air or a 50/50 solution of Ultravist with saline can be used as a contrast medium to confirm the length of the stricture. A triple lumen ERCP cannula is used if contrast needs to be injected. Access to angulated strictures may be facilitated by the use of a bowed sphincterotome. The 5cm guidewire tip is the best judge of distance, considering the disproportions that arise from fluoroscopy and the screen, to adequately measure stricture length and allow appropriate stent selection.

The endoscopist needs to commit to deploy the stent using either the colonoscopic view or the fluoroscopic view. As the Wallflex or the Evolution stent is deployed the stent pushes away from the end of the colonoscope and the colonoscope is pushed away from the stricture. This therefore pushes the video image further away. Simultaneous viewing of the video image while deploying the stent requires the colonoscope to be reinserted 2 to 5cm and the stent apparatus pulled back into the colonoscope by the same amount. The Wallflex, Wallstent and Evolution stents are approximately twice their final length while in the delivery device. This all needs to be taken into account while deploying the stent (Fig.2). The Ultraflex stent is already at its full length in the delivery device, and so the proximal and distal markers either end of the stent reveals exactly where the stent will end up once deployed (Fig.3).

The guidewire should not be removed from the stricture or the deployed stent until the endoscopist is satisfied with the position of the stent.

Fig 2. Wallflex stent used in palliative treatment of ASA grade 4 elderly male with obstructing sigmoid colon carcinoma. (Top left) AXR on presentation, (Top middle) CT scan coronal view of tumour, (Top right) tumour viewed through colonoscope, (Bottom left) Guide-wire placed, (Bottom middle) Image intensification of partly deployed stent and (Bottom right) AXR of fully deployed stent.

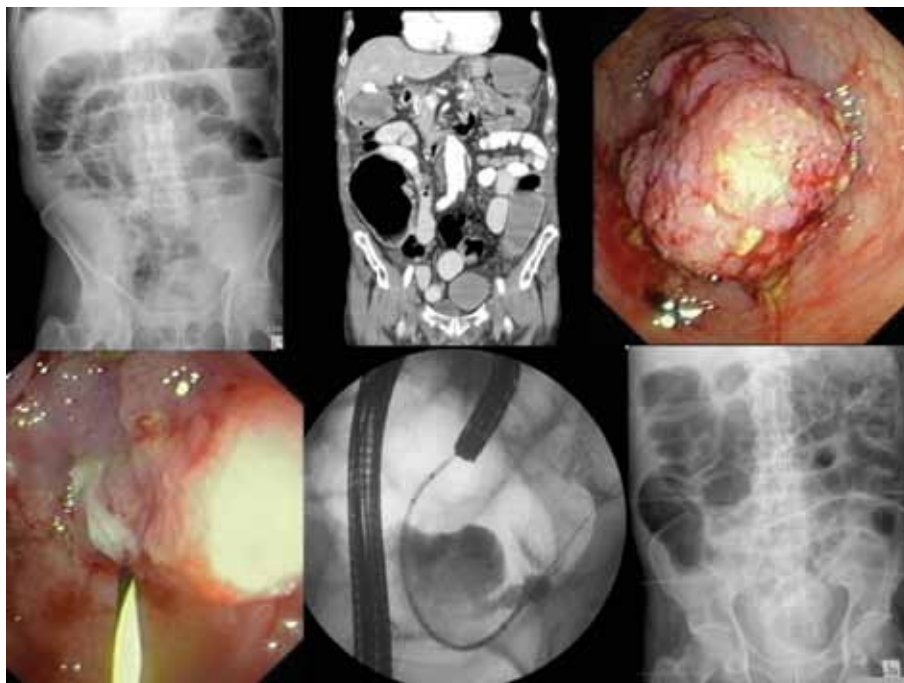
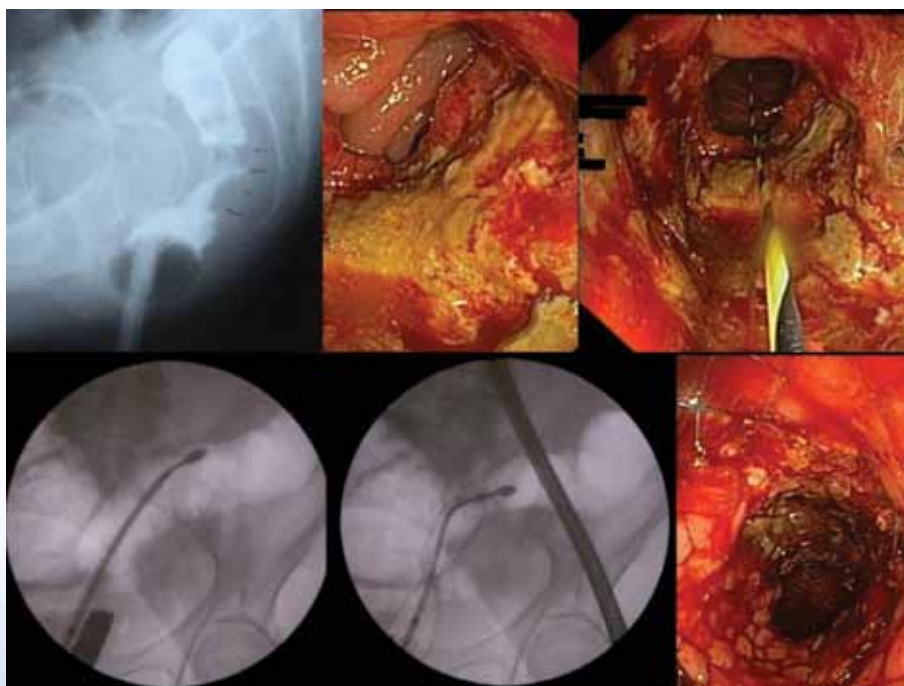


Fig 3. Ultraflex stent used in palliative treatment of ASA grade 4 elderly female with obstructing mid-rectal carcinoma. (Top left) Gastrograffin enema image of stricture, (Top middle) Colonoscopic view of tumour, (Top right) Guide wire through stricture, (Bottom left) Image intensification of stent apparatus prior to deployment and (Bottom middle) fully deployed stent and (Bottom right) Colonoscopic view through deployed stent.



Relevant Literature and Outcomes

Sebastian et al reported the largest pooled analysis of SEMS in 2004, combining results for 1,198 patients from 54 studies, 66% with palliative and 34% with temporary intent. They report an overall technical success rate, defined as a successful stent placement at the first attempt with correct deployment confirmed radiologically of 93%, with a technical success rate in the palliative group of 93%, and in the “bridge to surgery” group of 92%, with a higher success rate seen in primary CRC cases of 94% than in extrinsic compression cases with 78%. Reasons for technical failure include inability to place a guidewire, and long and tortuous strictures making adequate stenting difficult.

The overall clinical success rate, defined as clinical and radiological evidence of colonic decompression within 48 hours of stent insertion without the need for re-intervention, was 89%. These rates of technical and clinical success were very similar to the rates reported in systematic reviews by Khot et al in 2002 and by Tilney et al in 2007.

The use of colonic stents in obstructed patients was also associated with significant reductions in mortality rate and medical complications. In the systematic review specifically on comparing stent and open surgery for malignant large bowel obstruction, Tilney et al reported a mortality rate of 5.7% in the stent group versus 12.1% in the group treated by emergency surgery. Less medical complications were found in the stent group, with a reported odds ratio of 0.18.¹²

Stoma formation at any point during management in the stent group was reported as 8.2%. Although a direct comparison was not made in the literature, this is much lower than those reported by Seah et al with a 68% permanent stoma rate after patients having Hartmann’s procedure.

When colonic stents were used as a ‘bridge to surgery’, single-stage surgery with primary anastomosis was achieved in 72% of patients. Most common reasons for failure of single-stage surgery included locally advanced tumour, inadequate bowel preparation, stent perforation and migration. Long-term survival data is still lacking in the literature, although a few studies including Saida et al showed no significant difference in overall survival between emergency surgery and the stent procedure at 3 years (50% vs 48%, respectively) and 5 years (44% vs 40%).

Cost effectiveness of up to 50% reduction in the palliative group and 12% in the bridge to surgery group was reported in the literature. Most cost reduction was attributable to shorter hospital stays, fewer days in the intensive care unit, and fewer surgical procedures.

Potential Complications and Adverse Events

Reported complications associated with SEMS insertion include death, perforation, migration, obstruction, bleeding, pain, incontinence and faecal impaction. The study by Sebastian reports a 4% perforation rate, 12% migration rate, a 7% obstruction rate, and a 0.6% stent related mortality rate.

The most important factor associated with stent-related perforation is balloon dilatation. Migration rates can be reduced by stents with proximal flare, such as the Wallflex, Ultraflex and Evolution stents, which may enhance stent retention. Most stent obstruction is associated with tumour ingrowth, which can be treated by laser therapy or repeat stenting, without the need for open surgery. Most stent related bleeding resolves spontaneously. Pain and incontinence are problems specifically related to lower rectal stents, Baron in 2004 states that in general stent insertion greater than 2cm proximal to the anal canal does not interfere with anal function.

An important consideration with stent insertion used as a 'bridge to surgery' is the potential for the dilatation, or even worse a perforation, resulting from self-expanding metal stents to cause dissemination of otherwise localised curable tumours. Although no difference in long-term survival was reported in a few studies, a lack of matching in the studies analysed for this outcome could have caused this finding to be affected by selection bias.

Conclusion

Colonic stents are safe and effective and associated with lower morbidity and mortality rates compared to open surgery in the management of large bowel obstruction. It also has the potential to reduce stoma formation rates and lower the overall management cost in this group of patients. They are a useful adjunct to colorectal surgery. The majority of the literature reported is on their usage for palliative indications. Its use as 'bridge to surgery' still needs to be further assessed.

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Acute Colonic Bleeding

Simon Zanati

Introduction

Acute lower gastrointestinal bleeding, defined as bleeding from distal to the Ligament of Trietz, accounts for approximately 20-25% of major GI bleeding. This chapter will focus primarily on those patients with large volume acute lower GI bleeding who require hospitalisation and emergency care.

The aetiology of lower GI bleeding can be generally classified as anatomical, vascular, inflammatory/autoimmune, neoplastic, and iatrogenic with the incidence varying in different age groups (Table 1). The majority of lower gastrointestinal bleeding will spontaneously resolve, requiring non-specific resuscitation and circulatory support acutely, followed by early colonoscopy to establish the diagnosis. Mortality from lower gastrointestinal bleeding is approximately 4%, with advanced age, comorbid illness and ischaemic aetiology increasing the risk of death.

Table 1: Major causes of large volume lower GI bleeding.

Major Causes of Colonic Bleeding
Diverticular disease
Vascular malformations (angiodysplasia)
Ischaemic colitis
Haemorrhoids
Inflammatory bowel disease (Ulcerative colitis, Crohn's Disease)
Neoplasia (polyps or carcinoma)
Radiation enteropathy

All patients presenting with rectal bleeding require a full history, respiratory, cardiac and abdominal examination including digital rectal examination and anal inspection. Up to 40% of rectal carcinomas are palpable. Generally left colonic bleeding produces bright red blood while right colonic bleeding is coloured maroon and can be mixed with stool. Upper GI bleeding typically presents with melaena. However, approximately 15% of patients presenting with severe acute haematochezia will have an upper GI cause diagnosed at upper endoscopy. Small bowel causes of severe haematochezia account for up to 9% of cases. **The location for gastrointestinal bleeding cannot be solely determined on stool blood colour.**

General Principles

Initial management of patients with lower GI bleeding is the same as for patients with acute upper GI haemorrhage. Early assessment of the severity of bleeding and haemodynamic stabilisation occurs concurrently. Subsequent consideration of the site, likely pathology and specific therapy of bleeding follows and should be guided by the locally available expertise in gastroenterology, radiology and surgery.

Overt rectal bleeding requires investigation in all cases. For severe acute bleeding (>2 units transfusion requirement), persistent active bleeding, or where a patient has evidence for an acute abdomen or serious comorbidities, hospitalisation, resuscitation and early involvement of gastroenterological and surgical units is necessary. Consideration needs to be given towards intensive care admission in haemodynamically unstable patients.

Resuscitation involves insertion of two large bore (>18 Gauge) peripheral intravenous catheters. Blood investigations including an urgent full blood count, cross-match, coagulation profile, and electrolytes/ BUN should be collected. Thrombocytopaenia with platelet count of <50,000 should be given platelet transfusion. Coagulopathy (INR>1.5) should be corrected with FFP. If a patient is on warfarin reversal with vitamin K intravenously and prothrombinex is indicated. Anaemia may require packed red cell transfusion. Target haemoglobin varies depending on a patient's background cardiorespiratory status and the likelihood that there is active bleeding. Significant comorbid illness or active bleeding warrants transfusion up to 10g/dl whereas the absence of these features make a target haemoglobin of at least 7g/dl desirable. If there is concern regarding the possibility of colonic perforation or acute bowel obstruction, a plain abdominal film and erect chest xray should be obtained.

Where the history suggests anorectal pathology, proctoscopy or sigmoidoscopy may provide the diagnosis and offer therapeutic options. Investigation of large volume haematochezia should commence with upper endoscopy to exclude an upper GI source with the intention of proceeding to colonoscopy if the examination is negative

Technique

Colonoscopy

Emergency colonoscopy allows for accurate localisation of the bleeding site, collection of any required pathological specimens and the application of haemostatic therapy which is required in 10-15% of cases. Such interventions have been demonstrated to control colonic bleeding and reduce the risk of rebleeding from diverticular disease when compared with conservative therapy. Early colonoscopy (within 12 hours) reduces morbidity and length of hospital stay. Colonoscopic localisation and diagnosis direct further management and, where surgery is required, directed segmental resection is associated with superior clinical outcomes.

Complete colonoscopy should be performed to the level of the caecum and is achievable for acute lower GI bleeding in greater than 95% of cases. Blood is a powerful cathartic and some experts advocate proceeding to colonoscopy without any bowel preparation. In our experience, rapid colon cleansing achieves superior results and can be achieved with

1-2 litres of polyethylene glycol-based purge taken orally or via nasogastric tube over 60 mins. Administration of a pro-motility agent such as erythromycin or metoclopramide may reduce the risk of vomiting. A period of 2 hours is recommended between ingestion of a clear fluid and administration of anaesthetic agents.

The therapeutic modalities to control bleeding in the lower GI tract are the same as those in the upper GI tract. These include local injection of 1:10,000 adrenaline, thermal coagulation using heater or gold probes, haemostatic mechanical clipping and argon plasma coagulation (APC).

Unlike the thick muscular wall of the stomach, the right colon is relatively thin. Prolonged thermal effect at higher power carries the increased risk of necrosis and bowel perforation. This risk can be significantly decreased by submucosal injection of saline to act as a buffer as well as a reduction in power settings. Visible vessels can be treated by bipolar coagulation at 10 to 15W of power, applying moderate appositional pressure directly on the vessel, and one-second pulses until good coagulation and flattening of the vessel is achieved.

APC allows for a non-contact method of thermoablation which achieves superficial thermal injury with reduced risk for colonic perforation. For this reason it has become very popular in the management of vascular lesions such as angiodysplasia and radiation proctopathy where it can be used to quickly and safely ablate diffuse pathology and has been shown to decrease transfusion requirements.

Overall, therapeutic manoeuvres in lower gastrointestinal bleeding have a technical success rate of 90-100% and a clinical success rate of 70-100% with rare complications. The rates of successful treatment are increased in the setting of post-polypectomy haemorrhage where bleeding origin is already known.

Imaging

Various imaging modalities may be utilised when massive haemorrhage precludes colonoscopy or when a bleeding source cannot be identified at colonoscopy.

Radionuclide Imaging

Radionuclide scanning is more sensitive than angiography, able to detect bleeding rates of 0.1 to 0.5ml/minute. However it only has the ability to localise bleeding to an area of the abdomen as opposed to a definitive anatomic site. Localisation is further hampered by blood moving in either peristaltic or anti-peristaltic directions in the colon lumen. Overall, accuracy has been reported between the ranges of 24-91%. Two types of radio-labelling substrate can be used with different benefits. Technetium sulphur colloid has a short half-life so the patient needs to be actively bleeding at the time of injection. However, it is extremely sensitive being able to detect bleeding rates as low as 0.1ml/minute. ^{99m}Tc pertechnetate- labelled red cells, although less sensitive, can allow for repeated scanning up to 24 hours after infusion so may be more useful in detecting intermittent bleeding.

Radionuclide imaging is acknowledged to be less specific than a positive finding at colonoscopy or angiography. Its primary use may be to determine if there is sufficient active bleeding likely to result in a positive angiographic study.

Multidetector Computed Tomography (MDCT)

Computed tomography has been evaluated in cohort studies suggesting an evolving role for localising acute lower GI bleeding as well as predicting the treatment potential of arteriography and embolisation. Sensitivity and specificity of 90 and 99 percent respectively have been reported in severe/massive bleeding. It has the benefit of anatomical correlation to determine bleeding site. Like angiography, a positive scan requires active bleeding. Image quality may be limited by artefact resulting from contrast extravasation. Depending on local expertise, MDCT may be preferable to radionuclide imaging as the first line diagnostic imaging modality to localise bleeding for subsequent directed angiographic or surgical therapy.

Angiography

Angiography requires a rate of bleeding of 1-1.5 ml/minute for accurate bleeding localisation. The overall yield of angiography for the detection of a bleeding source ranges from 40-78%. A positive result confers a high likelihood for the need for surgery.

50-80% of diverticular bleeds and 100% of angiodysplastic bleeds are fed by the superior mesenteric artery. Therefore, this is the first vessel interrogated during angiography, followed by the inferior mesenteric and coeliac systems, giving an overall success rate in localisation of 14-72%.

The major advantages of angiography are that it does not require bowel preparation and that it may permit therapy at the one procedure. Historically, intra-arterial infusion of vasopressin was successful in achieving control in up to 91% of patients with lower GI haemorrhage. However, vasopressin has been largely abandoned due to rebleed rates as high as 50% and significant drug toxicity.

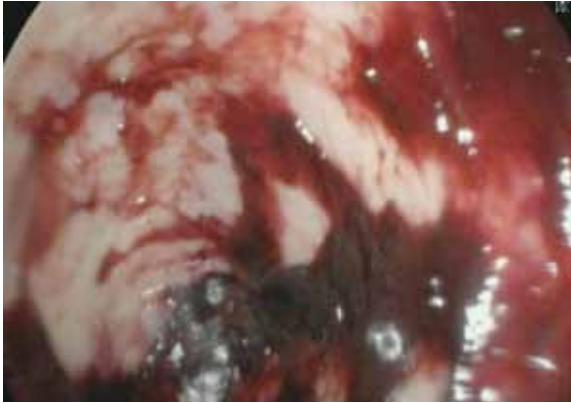
Transcatheter embolisation is a more definitive means of controlling haemorrhage and is clinically effective in 80-91% of cases. This is at the risk of bowel infarction that complicates 10-20% of procedures and, in a recent review, 7% of "superselective" procedures. Other complications include arterial thrombosis, embolisation of vessels distal to the intended target and renal failure. The low sensitivity of the test and significant complication rates when compared with colonoscopy, make angiography a second line investigation in lower gastrointestinal bleeding.

Surgery

Most patients will not require surgery. Occasionally, severe life-threatening lower GI bleeding does not spontaneously abate or respond to the aforementioned interventions and surgical management is unavoidable. In the acute setting, such surgery is associated with significant morbidity and mortality, particularly in the elderly patient with multiple comorbidities. Wherever possible, all efforts to localise the lesion should be undertaken so as to direct the appropriate surgical intervention. Directed segmental resection is preferable to a blind subtotal colectomy (which will not manage a small bowel source for bleeding), being associated with lower rates for rebleeding, preserved bowel function and less overall morbidity and mortality.

Colonic Bleeding Images

Unprepped bleeding colon.



Bleeding colonic angiodysplasia.



Blood clot at mouth of diverticulum.



Post polypectomy bleeding site Treated with adrenaline and haemoclips.



Bleeding colonic angiodysplasia treated with adrenaline and gold probe diathermy.



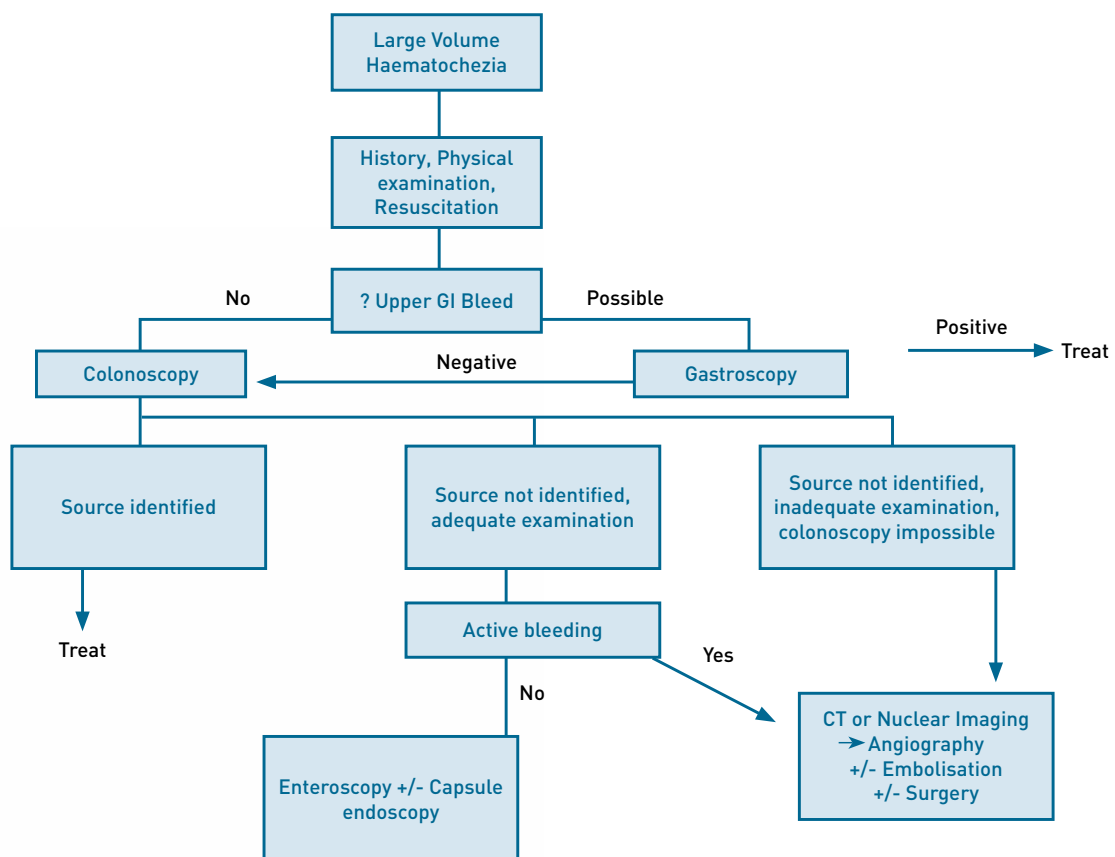
Radiation proctopathy



Summary

An aging population and increasing reliance upon anti-platelet agents is likely to make management of lower GI bleeding an important skill for the gastroenterologist. Advances in interventional techniques have expanded the role for early colonoscopy which is central to management but dependent on locally-available expertise. Where a bleeding source is not detected or unabated brisk bleeding precludes colonoscopy, nuclear or CT imaging may guide angiographic intervention or definitive surgery. A management algorithm is proposed (see Fig).

Adapted from Farrell and Freidman 2005.



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SECTION 4

ERCP

- Biliary Obstruction Due To Malignancy (*Tony Speer*)
- Benign Biliary Strictures and Biliary Leaks (*Philip Craig*)
- Chronic Pancreatitis (*Cameron Bell*)
- Endoscopic Management of Peripancreatic Collections (*Vu Kwan*)

Biliary Obstruction Due To Malignancy

Tony Speer

The most common malignancy causing biliary obstruction is carcinoma of the pancreas. Other malignancies include cholangiocarcinoma, carcinoma of the gallbladder and tumours metastases to lymph nodes or the liver. Biliary obstruction due to malignancy is conveniently divided into low and hilar obstruction, the investigation and treatment of these two groups differs.

Identifying Obstruction: Stones and Strictures

The initial liver function tests roughly triage patients into those with chronic liver disease, hepatitis and those with "cholestasis". Cholestatic liver function tests typically have moderate elevations of ALP & GGT and minor elevations of transaminases (2-5X). Cholestatic liver function tests may be due to biliary obstruction or hepatocellular disease. A careful history often identifies a likely cause of hepatocellular disease.

Abdominal ultrasound is the initial investigation to triage patients to obstruction or hepatocellular disease.

If the bile duct is obstructed ultrasound will usually show a dilated duct and usually identify the level of obstruction. Good quality ultrasound may also identify the lesion itself, particularly carcinoma of the pancreas, gallbladder carcinoma, metastases or less frequently cholangiocarcinoma. In low bile duct obstruction due to malignancy the gallbladder is usually dilated. Ultrasound readily identifies stones in the gallbladder but their presence does not necessarily signify bile duct obstruction due to stones. Ultrasound has good specificity (90-95%) for identifying stones in the duct but a lower sensitivity: 30 to 70%. That is, ultrasound misses stones in the common bile duct in approximately 50% of cases.

A common scenario is jaundice with ultrasound demonstrating a dilated bile duct but no causative lesion. The clinical presentation usually separates patients into two broad groups, stones or malignancy.

Low Bile Duct Obstruction

If the ultrasound shows the bile duct dilated down to the pancreas and a dilated gallbladder the most likely cause is carcinoma of the pancreas. Important differential diagnoses are carcinoma of the ampulla, autoimmune pancreatitis, other pancreatic tumors and occasionally an impacted gallstone. A pancreatic protocol abdominal CT scan will help differentiate between these diagnoses and stage carcinoma.

After intravenous contrast injection fine cuts are taken through the pancreas during arterial and portal venous phases. A pancreatic carcinoma is best seen on the arterial phase. Involvement of arterial and venous structures can also be identified. It should be noted that a routine CT abdo/pelvis does not usually include arterial phase imaging and the slices through the pancreas are much broader, showing less detail. A standard CT Abdo/pelvis may miss small pancreatic tumours.

If the pancreatic protocol CT does not identify a mass lesion or is equivocal, then endoscopic ultrasound (EUS) may identify a small lesion. EUS shows detailed images of the pancreas and a fine needle aspiration biopsy can be performed on suspicious mass lesions and enlarged lymph nodes under ultrasound control. An impacted gallstone or carcinoma of the ampulla are readily identified at EUS.

Carcinoma of the ampulla is a less common cause of low bile duct obstruction but is an important differential diagnosis. The tumour is less aggressive than carcinoma of the pancreas and a surgical resection provides a cure in the majority of patients. The tumour is slower growing and imaging often demonstrates marked dilation of the common bile duct and pancreatic duct. It is difficult to identify a mass lesion within the lumen of the duodenum with any confidence on CT or ultrasound. The level of jaundice is often lower than with carcinoma of the pancreas and cholangitis and pancreatitis are common symptoms. Diagnosis can be confirmed by direct biopsy at either EUS or ERCP.

Autoimmune Pancreatitis

Autoimmune pancreatitis is a relatively recently described condition. A sub group of these patients present with obstructive jaundice and imaging suggesting a mass in the head of the pancreas. Despite the name the condition rarely presents with acute pancreatitis. Patients are usually mildly jaundiced and there may be other features of systemic IgG4 disease such as retroperitoneal fibrosis, salivary gland involvement or renal disease. The pancreatic duct is not dilated and may have irregular stricturing. The pancreas is diffusely enlarged rather than atrophied as seen in carcinoma of the pancreas and MRCP may show intrahepatic strictures if autoimmune cholangitis is present as well as autoimmune pancreatitis. IgG4 levels are elevated in between 30-70% but also can be elevated in 10% of carcinoma of the pancreas. A pancreatic biopsy will show a lymphoplasmacytic infiltration in most patients. A diagnosis of autoimmune pancreatitis is best made after a careful review of imaging, serum IgG levels and perhaps a true cut biopsy of the pancreas. If there is any doubt about the diagnosis the lesion should be treated as a carcinoma and resected if possible.

Staging

A confident diagnosis of carcinoma of the pancreas can usually be made on history plus imaging. Typically an elderly patient presents with painless progressive jaundice with associated weight loss and ultrasound shows a dilated bile duct and gallbladder, CT confirms a mass in the head of the pancreas and a dilated pancreatic duct. If the patient is considered fit for surgery, then the tumour should be staged. A TNM staging system has been developed for carcinoma of the pancreas, however, this is difficult to apply and

is seldom used. A clinical staging system based on common radiological investigations is shown in table 1. Resectable lesions are those with no extra pancreatic disease and no involvement of the coeliac axis, superior mesenteric artery, and common hepatic artery and no involvement of the superior mesenteric vein or portal vein. Locally advanced tumour is defined as those with tumour extension to involve the coeliac axis or superior mesenteric artery or venous occlusion of either the superior mesenteric vein or portal vein. Metastatic disease is the presence of extra pancreatic disease, usually liver metastases.

Treatment

At the time of diagnosis 40% of patients have locally advanced disease, 40% have metastatic disease and 20% present with a possibly resectable lesion.

Resection

Resectable lesions should be managed with a Whipple's operation (proximal pancreaticoduodenectomy with antrectomy) or a pylorus preserving pancreaticoduodenectomy. Surgery should be performed by an experienced hepatobiliary surgeon in a high volume centre to achieve optimum resection rates and to minimise morbidity and mortality. Resection has a 30 day mortality of approximately 3% and a five year survival of 10 to 20%. Imaging often underestimates the amount of disease and patients should be advised that laparotomy is the final staging procedure. Unresectable local disease or distant metastases are found in up to 50% of patients submitted for a Whipple's resection, surgical bypass, hepaticojejunostomy with or without a gastroenterostomy provides palliation in these patients.

Patients considered for Whipple's resections have been managed with pre-operative biliary stents in the past. A recent randomised trial of pre-operative endoscopic drainage found an increased rate of overall complications in the pre-operative drainage group. The patients selected for this study had mild to moderate jaundice with a bilirubin level less than 200, pre-operative drainage is not beneficial in this group. Pre-operative drainage could be considered in selected patients with deep jaundice, renal impairment or cholangitis.

Palliation

The majority of patients present with unresectable disease and are managed with palliation.

Biliary obstruction causes jaundice, pruritis, malabsorption, poor appetite and prolonged obstruction may lead to renal impairment. These symptoms resolve with biliary decompression. Endoscopic biliary stenting is the treatment of choice. This can be achieved in 90 to 95% of patients with relief of jaundice in 90%, a 30 day mortality of 5-7% and a median survival of 5.5 months. Expanding metal stents are more expensive than plastic stents but have a lower early complication rate, better drainage and a lower late blockage rate and are cost effective when these advantages are taken into account. Late stent blockages occur in 25-30% of those with metal stents causing recurrent jaundice and/or cholangitis and are easily managed with repeat ERCP and dilation of the stricture and insertion of another stent.

Chemotherapy for advanced pancreatic cancer

Gemcitabine is a nucleoside analog with activity across a broad range of solid tumours. Gemcitabine reduces symptoms in carcinoma of the pancreas and provides a modest survival benefit with a low toxicity.

Chemoradiotherapy for locally advanced pancreatic cancer

The optimal therapy for patients with locally advanced unresectable pancreatic cancer remains controversial. Chemoradiotherapy could be considered for those with a good performance status.

Other palliative measures

Duodenal obstruction is often best palliated with expanding metal stents or a laparoscopic bypass in patients with a good performance status.

Persistent severe pain is a common problem and treatment should start with regular analgesia and other management that could be added include chemo or radiotherapy, and coeliac plexus block.

Malabsorption secondary to pancreatic duct obstruction responds well to enzyme replacement.

Histology

Not all tumors in the pancreas are adenocarcinomas. Histological proof of malignancy should be obtained in all unresectable lesions. EUS guided fine needle aspiration biopsy has a sensitivity of between 80-95% and a specificity of 95-100%. Ultrasound or CT guided percutaneous biopsy can also be performed either of the primary or a metastasis. If a lesion is resectable and the imaging is typical of a carcinoma of the pancreas then it is not necessary to obtain histological confirmation pre-operatively. A negative biopsy does not necessarily exclude a carcinoma.

Tumour Markers

Tumour makers are of limited diagnostic value. Ca 19 9 is often elevated in carcinoma of the pancreas but is also elevated in biliary obstruction, cholangitis or liver failure. Ca 19 9 is often performed as a base line in order to guide treatment follow up. If a neuroendocrine tumor is suspected chromogranin A should be requested.

Hilar Strictures

Hilar strictures are defined as those involving the proximal 2cm of the common hepatic duct and or the left or right hepatic ducts and their branches. Cholangiocarcinoma (50%) carcinoma of the gallbladder (20%) and metastases to lymph nodes or liver (20%) are the most common malignancies that obstruct the hilum. Important differential diagnosis are benign strictures including sclerosing cholangitis, Mirrizi's syndrome and benign idiopathic stricture.

Most patients present with jaundice, pruritis, pale stools and dark urine. Right upper quadrant pain occurs in carcinoma of the gallbladder but not cholangiocarcinoma. Fatigue, malaise and weight loss are common in advanced disease.

Ultrasound is the first imaging procedure. Carcinoma of the gallbladder and cholangiocarcinoma can be detected as mass lesions. Small tumours may be missed, ductal dilation with an abrupt change in duct diameter may indicate the presence of the tumour.

MRI with gadolinium contrast gives excellent visualisation of the hepatic parenchyma as well as the biliary tree and vascular structures. MRCP has replaced ERCP and PTC as the best imaging modality to demonstrate biliary anatomy and should be performed on all suspected hilar strictures.

Abdominal CT may provide additional information on mass lesions, vascular involvement and lobar atrophy.

Staging depends on the extent of the stricture, vascular involvement and lobar atrophy/hypertrophy and is best performed in consultation with an experienced hepatobiliary surgeon and hepatobiliary radiologist. Criteria for unresectability are shown in table 2.

Tumour Markers

There are no tumour markers specific for cholangiocarcinoma. Ca 19 9 is elevated in up to 85% of patients with cholangiocarcinoma, however, Ca19 9 is also elevated in benign biliary obstruction and hepatic injury.

Histology

Biliary brushings performed at ERCP have a specificity of 95-100% but a low sensitivity of only 50%. Histology is not necessary prior to resection but biliary brushings should be performed on unresectable lesions when a stent is being inserted. Ultrasound or CT guided biopsy can be performed on mass lesions in unresectable disease.

Surgical resection has a 9-18% five year survival with a 5-12% thirty day mortality. Routine use of pre-operative biliary drainage is not recommended. Three randomised trials have been performed, two showed no difference in outcomes and one showed the pre-operatively drained patients did worse.

Patients with unresectable lesions should be assessed to see whether they would benefit from biliary drainage with an endoscopic stent. The risks of attempted stenting may outweigh benefits in those with multiple intrahepatic strictures, multiple liver metastases causing impaired hepatocellular function as judged by ascites, hypo albumin anaemia or prolonged INR and those who are only mildly jaundiced. Discussions with the patient and their family should include realistic expectations of the benefits of stenting and an appreciation of the risks. If the patient decides to proceed then the imaging is reviewed to identify the best segment to drain. Atrophied segments and those replaced by metastatic disease should be avoided. A randomised trial has confirmed that a single stent placed in the best segment provides effective palliation and has a lower risk of cholangitis than attempting to place two stents. A single stent can be placed successfully in 75-90% of patients with a thirty day mortality of 10-20% and an overall mean survival of about 6 months.

Table 1: Staging Carcinoma of the Pancreas.

Stage	Clinical/Radial Criteria	Long Term Survival	Median Survival
1 - II	Resectable – no encasement Of coeliac axis or patient SMV/portal vein xylol pancreatic disease	10-20%	13-20m
III	Locally advanced tumour Includes coeliac or /portal vein involvement No extra pancreatic disease	0	10m
IV	Distant metastases usually liver	0	3-6m

Table 2: Cholangiocarcinoma – criteria unresectability.

Bilateral extensions into or beyond second order ducts
Significant lobar atrophy with insufficient remaining liver
Involvement of main or both right and left portal veins or hepatic arteries
Biliary stricture involves more than three hepatic segments
Metastatic spread beyond the liver or bile ducts

Further Reading

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Excellent review of diagnosis and staging of hilar strictures. 92 references.
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A single stent had less complications (less cholangitis) and achieved successful drainage more often. A single stent inserted into the best segment is optimal management.

Illustration 1: Most patients with carcinoma of the pancreas are elderly and frail. The gallbladder is often palpable but not so often palpated, and occasionally visible.

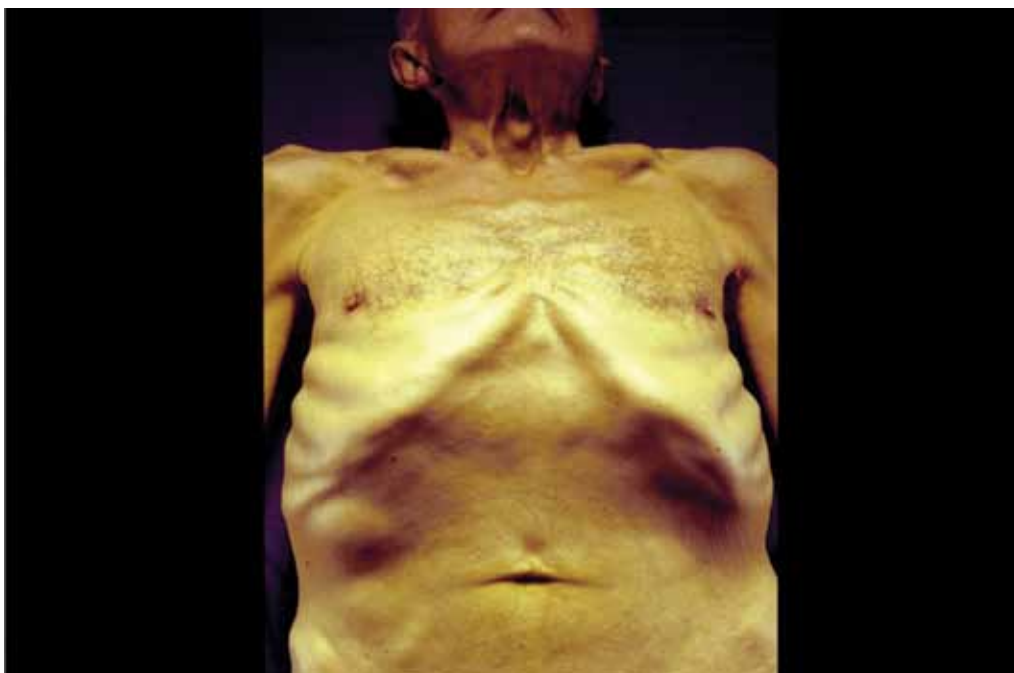
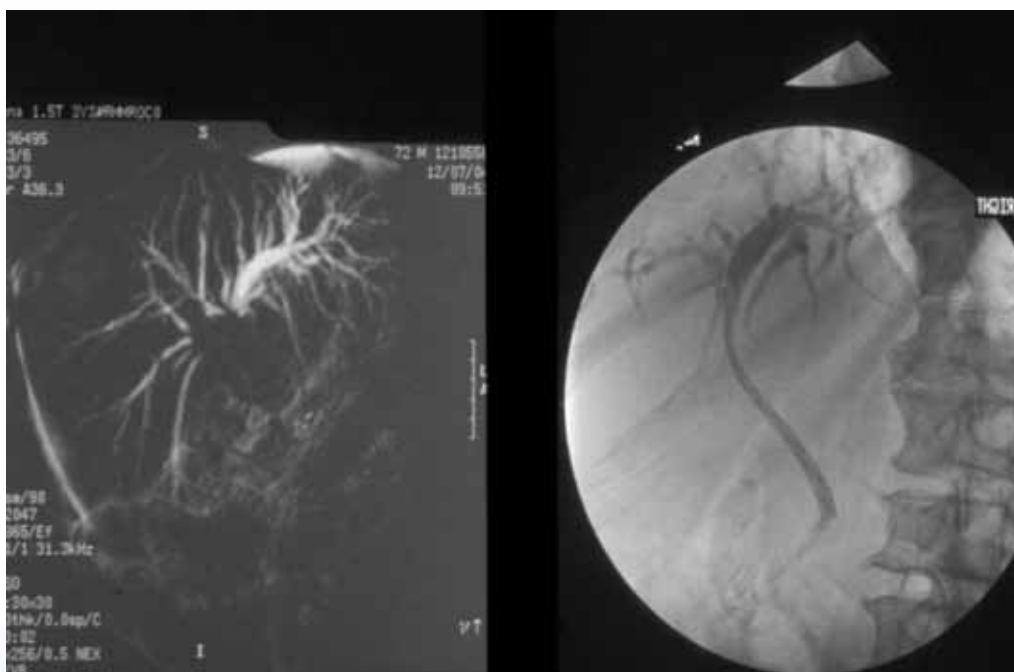


Illustration 2: MRCP shows the hilar stricture with a stricture in the left hepatic duct and multiple right hepatic duct strictures. The left duct is best for stenting.



Benign Biliary Strictures and Biliary Leaks

Philip Craig

The aetiology of benign biliary strictures and leaks is diverse (Table 1). Most commonly subjects present with symptomatic cholestasis or cholangitis and it is important at presentation to exclude an underlying malignancy. Many strictures are suitable for endoscopic therapy which is usually indicated to prevent the development of cirrhosis. The focus of this chapter is the management of biliary strictures and leaks.

Table 1: Causes of benign biliary strictures.

Post operative
Post endoscopic sphincterotomy
Chronic Pancreatitis
Primary sclerosing cholangitis
Secondary sclerosing cholangitis Oriental cholangitis HIV-associated Hepatic arterial chemotherapy (Floxuridine)
IgG4-associated cholangitis
Portal biliopathy
Radiation induced
Ischaemia (including vasculitis)

Post operative biliary leaks and strictures

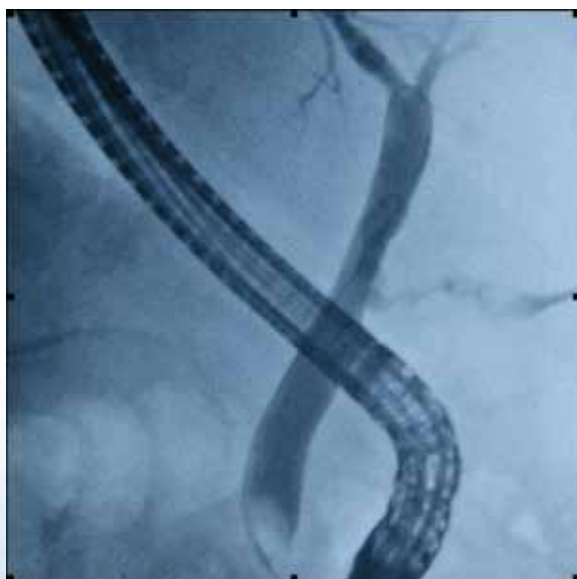
Although bile leaks and strictures may occur after any operation on the biliary tract, they most commonly follow laparoscopic cholecystectomy (LC). The risk of bile duct injury following LC is 0.5% which appears to be 2-5x higher than for open cholecystectomy. Strictures may also develop at the site of biliary anastomoses following hepatic resections or liver transplantation. The types of biliary injury are assessed as being either major or minor and have been classified by Bergman into 4 types: A) Biliary leaks involving either the cystic duct or peripheral hepatic radicles (*minor*); B) Bile leaks with or without biliary strictures (Major); C) Bile duct strictures without leaks (*major*) or; D) Complete transection with or without excision of part of the biliary tree (*major*).

The timing and presentation of postoperative biliary injuries is varied, depending on the nature of the injury. Patients may present acutely with either jaundice, cholangitis, an external fistula or intraperitoneal collection. The majority (70-80%) of strictures however have a delayed presentation, often 6 to 12 months after surgery with symptoms of cholestasis or LFT elevation. At cholangiography, biliary strictures are usually short with sharp edges, located near the cystic duct stump. Strictures resulting from ischaemic injury are usually longer and extend to the hilum.

In the early postoperative period, ERCP has both a diagnostic and therapeutic role in both defining and treating biliary injuries. If ERCP is unsuccessful or does not fully define the biliary tree then MRCP provides useful information to classify types of injury. When the presentation of biliary strictures is delayed, then abdominal ultrasound, MRCP or CT cholangiography prior to ERCP, help plan management. Percutaneous transhepatic cholangiography, an alternative therapeutic approach to ERCP, is limited by lower success rates and higher complication rates; it is reserved for failed endoscopic procedures. Causes of biliary injury in the setting of cholecystectomy include: 1) Anatomical variations in the origin of the cystic duct and right sided biliary segments; 2) Previous surgery and; 3) Active cholecystitis or cholangitis.

Apart from Type D Bergman injuries where it is impossible to gain access to the proximal biliary tree with a guide wire, all other biliary injuries are worth attempted endoscopic therapy. To treat early postoperative biliary leaks, appropriate ERCP techniques include slow contrast injection to define the level of the injury and to detect associated calculi (Figure 1). The aim of therapy is to abolish the transpapillary pressure gradient thereby promoting the flow of bile into the duodenum. Leaks from the cystic duct stump are the most common and are often associated with a retained bile duct calculus. Severing of the ducts of Luschka, which are peripheral ducts connecting the intrahepatic system within the gallbladder bed, also produce minor leaks. Careful inspection during early CBD injection will differentiate between cystic duct leak versus gall bladder fossa duct injury. Both situations can be managed by a combination of endoscopic sphincterotomy (ES) and/or short-term biliary stenting with resultant leak closure within a week. Both ES and stenting have specific advantages and disadvantages. Type B biliary injuries produce leaks from either the CBD or one of the intrahepatic ducts. These injuries usually require large bore plastic stents with or without ES to cover the hole and help prevent late stricture formation. These stents should be left for at least 2 months with expected resolution in 70-80%.

Figure 1: Post cholecystectomy cystic duct leak managed with endoscopic sphincterotomy.



Late biliary strictures are usually managed by a combination of balloon dilatation and the placement of multiple stents since dilatation alone is associated with high recurrence rates. These strictures are often tight and need to be traversed with narrow hydrophilic guide wires. An ES is required to allow placement of multiple stents and repeat procedures. The biliary stents are exchanged every 3 months to avoid cholangitis and usually left in place for 1 year until stricture resolution on cholangiography. For difficult cases, an initial combined percutaneous-endoscopic approach may be required for initial stent placement. Bergman et al reported that using two 10 French (FG) plastic stents for 12 months, enabled 80% of postoperative stenoses to resolve endoscopically. However, Costamagna's group advocated even more aggressive management with balloon dilatation and the placement of as many 10Fr stents as possible (mean 3.2) over a mean 12 month period, until complete stricture resolution. This regime confirmed by Kuzela et al produced long-term stricture resolution in 90-100% over a 16-48 month follow up. Early complications in 9% were all managed conservatively. Overall surgical and endoscopic approaches appear at least equivalent in treating benign biliary strictures although there have been no comparative trials. However, since initial endoscopic therapy does not preclude later surgical intervention it is therefore usually the initial treatment of choice. Although multiple endoscopic procedures are usually required, the morbidity and mortality from surgery are higher.

Post transplant anastamotic biliary strictures are managed with similar endoscopic approaches combining biliary dilatation with the placement of multiple plastic stents. Post sphincterotomy distal biliary strictures may occur in up to 2% of patients. Again, stricture dilatation using multiple plastic stents produces stricture resolution in 90%. Uncovered self-expanding metal stents (SEMs) are not indicated for most benign biliary strictures as they cannot be removed and may develop a late granulation reaction which can preclude surgery. In contrast, promising preliminary data in BBS using short-term (3 month) stenting with large bore, *covered* SEMS before stent removal suggest, an alternative to plastic stenting however, long term follow up data is unavailable.

Chronic Pancreatitis

Symptomatic biliary stenoses develop in 10-30% of chronic pancreatitis patients. Acute biliary obstruction from either pancreatic inflammation or pseudocysts usually resolve with short-term biliary stenting. The long-term results of endoscopic therapy for fibrotic stricture in chronic pancreatitis are however, disappointing. Thus, Cahen's overall success rate for aggressively stenting 58 patients with distal strictures for 12 months was just 38%. Similarly, results with SEMs have been mixed and can only be recommended for poor operative candidates.

Primary sclerosing cholangitis (PSC)

PSC is a chronic inflammatory disease characterised by stricturing and dilatation of the intra- and/or extrahepatic biliary tree. It is associated with IBD in two thirds. PSC leads to chronic cholestasis however, subjects may present at anytime with asymptomatic elevation of SAP, pruritus, jaundice or upper abdominal pain. The disease may progress to cirrhosis and 10-30% will develop cholangiocarcinoma. Traditionally,

ERCP has been used to radiologically diagnose PSC however in expert hands, MRCP or CT cholangiography are almost as sensitive. Thus, MRCP in comparison to ERCP has a diagnostic accuracy of 83-90%. MRCP however, has difficulties diagnosing early PSC, in assessing extrahepatic disease, in differentiating strictures due to cholangiocarcinoma and, it does not allow therapeutic interventions in cholestatic patients. CT cholangiography appears more sensitive than MRCP at diagnosing PSC (sensitivity 94% versus 63%) and it is superior in diagnosing extrahepatic involvement (69% versus 25%). Secondary causes of sclerosing cholangitis need exclusion. In addition other conditions such as multicentric cholangiocarcinoma or IgG4 associated cholangitis may mimic the cholangiographic appearances of PSC.

The role of ERCP in PSC is: 1) To aid diagnosis in difficult case; 2) To help differentiate between benign and malignant strictures and; 3) To treat symptomatic dominant biliary strictures, which develop in 15-20% of patients. At presentation, 25% of dominant strictures are dysplastic or malignant. In a cohort of Swedish patients with PSC followed for 5.7 years after diagnosis, the frequency of cholangiocarcinoma was 13%. Confirmation of cholangiocarcinoma in PSC is often difficult but should be suspected with the development of progressive cholestasis or a sudden rise in tumour markers such individuals should undergo cross sectional imaging and cholangiography with brushings and biopsies of any suspicious strictures. A CEA over 5.2 ng/mL had a sensitivity of 68% and specificity of 82% for cholangiocarcinoma while a CA19-9 level over 180 U/mL has a sensitivity of 67% and specificity of 98%. The sensitivity of brush cytology for diagnosing cholangiocarcinoma is around 50%. PSC patients with cytological high grade dysplasia and possibly low grade dysplasia should be strongly considered for liver transplantation. Other modalities used to diagnose cholangiocarcinoma in PSC include intraduct ultrasound which appears superior to ERCP for the detection of malignancy (sensitivity 88% versus 63% and specificity 91% versus 53%). Similarly, cholangioscopy appears superior to ERCP for the detection of malignancy (sensitivity 92% versus 66% and specificity 93% versus 51%). In contrast, the role of PET scanning is less clear cut.

The prognosis of PSC patients may be assessed using a scoring system combining the initial cholangiographic features with age at first ERCP. Patients undergoing ERCP should be covered for several days with broad spectrum antibiotics to prevent cholangitis while care should be taken to avoid overfilling obstructed intrahepatic biliary segments unsuitable for drainage. Some patients have either co-existent biliary pigment stones or a papillary stenosis which respond to ES. The optimal endoscopic management of dominant biliary strictures is however controversial. The literature consists of case series and a variety of techniques have been used. The term, 'dominant biliary stricture' usually refers to a stenosis <1.5mm diameter involving the extrahepatic duct or <1mm of the right or left hepatic ducts. Biliary dilatation upstream of a stricture may not be present in PSC. In patients without significant cholestasis it is controversial whether dominant strictures should be endoscopically treated. However, in jaundiced subjects with symptoms of biliary obstruction however, or those likely to have cholangiocarcinoma, endoscopic tissue sampling and therapy of dominant strictures should be undertaken. Most experts recommend initial ES and then narrow hydrophilic guide wires are used to traverse the stricture before dilatation. Some series suggest that dilatation alone is superior to prolonged endoscopic stenting with lower rates of cholangitis. Moreover, since the bile ducts in PSC subjects are usually narrow, these are usually not amenable to the placement of multiple stents. However, more recent series employing short-term plastic

stenting suggest improved benefits extending several years. Hence Ponsioen et al described 32 patients with dominant strictures receiving a plastic stents for a mean of just 11 days; 60% of subjects were intervention free at 3 years follow up. The addition of ursodeoxycholic acid to endoscopic therapy for dominant biliary strictures may also improve survival as assessed by the Mayo Clinic model. Overall complications for therapeutic procedures in PSC are no more common than for other groups having ERCP although episodes of post-procedure cholangitis appear more common. Liver transplantation should be considered in cirrhotic patients with dominant biliary strictures. Unfortunately, most PSC patients who develop symptomatic cholangiocarcinomas are unsuitable for either liver transplantation or curative resection. In this situation, most subjects are best managed with long term biliary stenting, most commonly using a SEMs.

Acquired immunodeficiency syndrome (AIDS) cholangiopathy

AIDS cholangiopathy produces RUQ pain (90%) and cholestasis. The cholangiography often develops late in AIDS, with CD4 counts below 200/mm³. Biliary opportunistic infections such as *Cryptosporidium Parvum* (two thirds) or CMV are often implicated. Abdominal US may detect biliary dilatation or acalculous cholecystitis. The diagnostic appearances of AIDS cholangiography at ERCP include, papillary stenosis with extrahepatic biliary dilatation and stricturing of the intra- and extrahepatic biliary tree. Other features include abnormal pancreatograms in 50% and an increased incidence of cholangiocarcinoma. Organisms are found in over 90% of cases from relevant duodenal, papillary and biliary samples. Therapies include appropriate antimicrobial agents, antiretroviral therapy and ursodeoxycholic acid. ES often palliates pain without improving the LFTs.

IgG4 cholangitis

IgG4 cholangitis was recently described and is characterised by segmental biliary strictures usually in the setting of autoimmune pancreatitis (Figure 2). The usual presentation is obstructive jaundice with over 80% of affected subjects being males aged over 60 years. Thus, the common differential diagnosis is biliary malignancy. There is histological evidence of bile duct fibrosis with a lymphoplasmacytic infiltrate with positive IgG4 staining. These histological findings may be noted in biliary, liver or ampullary biopsies. Additional features include multi-organ involvement and elevated serum IgG4 levels (Table). Jaundiced subjects respond to biliary stenting while the strictures usually disappear with corticosteroids. Long-term immunosuppression is eventually required however, in 20% of subjects with IgG4 cholangitis.

Conclusion

The management of benign biliary strictures is generally dependent upon the underlying stricture aetiology. Endoscopic approaches are usually indicated for diagnosis, and therapy consists of a combination of stricture dilatation and/or biliary stenting.

Figure 2: Post cholecystectomy cystic duct leak managed with endoscopic sphincterotomy.



Table 2: Diagnostic features of IgG4 cholangitis.

Location of segmental biliary strictures:	
Distal bile duct	70%
Proximal bile duct	34%
Intrahepatic	36%
Histology:	
Lymphoplasmacytic infiltrate	
Obliterative phlebitis and bile duct fibrosis	
IgG4 positive plasma cells	
Other organ IgG4 organ involvement:	
Autoimmune pancreatitis	92%
Tubulointerstitial nephritis	26%
Sjogren's	6%
Lymphadenopathy	6%
Elevated serum IgG4 levels	80%
Response to steroids	

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Chronic Pancreatitis

Cameron Bell

Background

In chronic pancreatitis (CP), progressive inflammation of the gland leads to irreversible structural damage, resulting in the possible development of exocrine and/or endocrine impairment. Alcohol, autoimmune pancreatitis and hereditary disorders (including cystic fibrosis gene mutations, SPINK-1 and cationic trypsinogen mutations) are common causes. Some patients have so-called idiopathic CP. CP can arise as a consequence of recurrent bouts of acute pancreatitis (clinical or subclinical). The main clinical features of CP are abdominal pain and pancreatic insufficiency, manifesting as diabetes, malabsorption or steatorrhea. ERCP and EUS have both diagnostic and therapeutic roles to play in patients with CP.

Diagnostic Endoscopic Procedures in Chronic Pancreatitis

(I) ERCP

In patients without evidence of pancreatic insufficiency and in whom CT does not demonstrate typical changes (microcalcification, duct dilatation and irregularity), the diagnosis of CP can be elusive. The commonest situation is a patient with upper abdominal pain but neither diabetes nor steatorrhea. Historically, ERCP was often used diagnostically in this situation to outline the ductal anatomy. Beading (irregular dilatations and strictures of the main duct) and clubbing or ectasia of side-branches are characteristic features of the pancreatogram in CP. Ductal changes demonstrated at ERCP have been used as the basis for distinguishing groups of patients suspected of having CP. For instance, categories (I) "equivocal changes", (II) "mild to moderate changes" and (III) "considerable changes" were described in the Cambridge classification system. Correlations were reported between severity of ductal changes and pancreatic dysfunction. However, not all patients with CP have demonstrable abnormalities at ERCP, meaning that a normal ERCP does not exclude the diagnosis, particularly in patients with symptoms of short duration.

MRCP is being used more and more to visualise the pancreatic ductal system, limiting any clearcut role of ERCP to patients in whom some therapeutic potential exists. Currently, limited sensitivity and specificity of MRCP restrict its place in the diagnosis of CP but this may change in the future, particularly in patients whose ducts are inaccessible endoscopically. Given the limitations of pancreatic function testing, including availability, other modalities to interrogate the structure of the pancreas have been sought, in an effort to confidently diagnose CP.

(III) EUS

EUS has allowed evaluation of ductal and parenchymal features of the pancreas, some of which, in particular the parenchymal characteristics, have not been appreciated by other imaging modalities. Some features (such as hyperechoic duct margins, ectatic side branches, subtle lobularity and small cystic changes of the parenchyma) have been suggested to correlate with the presence of CP. Diagnostic criteria for CP, based on the number of EUS features identified in a given patient, have emerged. For instance, an international consensus panel developed the Rosemont criteria for EUS features of CP. Both major criteria (hyperechoic foci with shadowing, main pancreatic duct calculi, lobularity with honeycombing) and minor criteria (cysts, ducts dilated to more than 3.5mm, irregular pancreatic duct contour, side branches dilated to more than 1mm, hyperechoic duct walls, strands, hyperechoic foci without shadowing and lobularity, with noncontiguous lobules) have been described. The proposed classification scheme based on these criteria has still to be validated.

One difficulty in evaluating the diagnostic accuracy of EUS in CP is the absence of a clear gold standard, against which EUS criteria can be evaluated. Other potential shortcomings are that the EUS features are in part qualitative and that they might not all carry equal diagnostic weight when “scoring” an individual patient’s pancreas. Furthermore, some EUS features of the pancreas change with age, meaning some may be more or less significant when assessing patients of different ages.

However, in general, the greater the number of EUS criteria found in a given patient, the higher the likelihood they have CP. For instance, CP is unlikely if zero or only one EUS criterion is evident, while the presence of 5 or more criteria makes CP likely. The clinical significance of an intermediate number of criteria is uncertain. The sensitivity, specificity, positive and negative predictive values of EUS in the setting of CP diagnosis are difficult to quantify, again because of the lack of an absolute gold standard, and they depend on the set of criteria being used as well as the “threshold” number of criteria used.

EUS may be over-sensitive in diagnosing CP. In studies comparing ERCP and EUS in groups of patients, while agreement between the two tests is found in most patients, in most cases of discordance, EUS was “positive” while ERCP was “normal”. It is unclear whether EUS is better than ERCP at diagnosing mild or early cases of CP or whether it is oversensitive compared with ERCP.

Therapeutic Endoscopic Procedures in Chronic Pancreatitis

(I) ERCP

ERCP has potential therapeutic application to CP patients in several settings, including relief of ductal obstruction to treat pain, relief of obstructive jaundice by biliary stenting and treatment of pancreatic fistulae.

(a) Relief of Pancreatic Ductal Obstruction

Several reports have suggested that endoscopic decompression of an obstructed pancreatic duct can relieve pain in some CP patients. The basis for this approach is the hypothesis that ductal hypertension, due to strictures of the main pancreatic duct or stones within it, may lead to pain. The endoscopic therapy in this setting is similar in principle to that used for stones and strictures in the bile duct, namely stricture dilatation, stone removal and stent placement. However, the link between main ductal stones and pain is not straightforward; many patients with stones are pain-free and pain may be due to side-branch obstruction or parenchymal ischaemia or inflammation, factors obviously not amenable to endoscopic manoeuvres.

Relief of pain has been the main outcome goal in endoscopic studies; slowing of the deterioration in pancreatic function has not been demonstrated. Indeed, only one surgical study has suggested that surgical decompression of the pancreatic duct might delay progressive deterioration of pancreatic function in CP. Others have noted loss of endocrine and exocrine function despite a lateral pancreaticojejunostomy.

The utility of endoscopic therapy in CP is controversial. In a large multicentre study of over 1000 patients followed up for 2-12 years, endoscopic ductal decompression was reported to provide relief of pain in 2/3 of patients, when used as the sole form of therapy, whether the patients had strictures (47%), stones (18%) or both (32%). One-quarter of patients came to surgery during the course of the study. Ductal decompression failed to improve pancreatic function. However, the results of these observational studies are somewhat dubious given the tendency for chronic pancreatitis pain to "burn out" with time.

A recent though much smaller trial published in 2007, comparing endoscopic and surgical drainage of the pancreatic duct in patients with CP, concluded that the surgical approach was more effective. Amongst 39 randomised patients followed for 2 years, those in the surgical arm had lower pain scores and better physical health summary scores. The proportion of patients with complete or partial pain relief at 2 years was higher in the surgical group (75% versus 32%) while rates of complications, length of hospital stay and changes in pancreatic function were no different between the two groups. Patients in the endoscopic group required more procedures than those in the surgical group. Although this study directly compared the surgical and endoscopic approaches, it was relatively small in size and it should be remembered that (i) in reports of surgery in CP, pain relief lasting more than two years is only seen in about 60% of patients and (ii) even total pancreatectomy does not achieve pain relief in all patients.

Endoscopic decompression of ductal obstruction does seem to be beneficial, from the point of view of analgesia and reduction in the number of episodes of acute pancreatitis, in patients with hereditary pancreatitis, at least during 2-3 years of follow-up.

Another study sounded a note of caution, suggesting that patients undergoing PD stenting who subsequently required surgical drainage had significantly more peri-operative complications than those without prior stenting. Were this true, then endoscopic therapy in patients with CP would have to be much more carefully considered and not simply undertaken on the basis that it would at least do no harm.

Extracorporeal shock wave lithotripsy may have an adjunctive role in patients with stones in the pancreatic duct, allowing easier endoscopic removal. It has been reported to result in significant improvement in clinical outcomes in most patients with CP.

The role that pancreatic endotherapy should have in the management of pain in patients with CP is not straightforward. Since the techniques involved can be technically difficult, pancreatic endotherapy in this setting should probably be performed only in a small number of expert centres.

(B) Relief of Biliary Obstruction

Biliary obstruction occurs in up to 5-10% of patients with CP. Abdominal pain, jaundice and cholestatic elevation of liver enzymes can result. Secondary biliary fibrosis, which is reversible if the biliary obstruction is relieved, can supervene. The obstruction is usually due to strictures of the distal common bile duct resulting from involvement of its intrapancreatic portion in the inflammatory/ fibrotic process affecting the head of the gland. Pseudocysts may be responsible in a minority of patients.

ERCP has potential roles in these patients, to obtain a cholangiogram, to brush distal biliary strictures for cytology and to decompress the biliary tree by stent insertion. A major difficulty in treating biliary strictures due to CP has been the need to perform multiple ERCPs to repeatedly replace plastic stents. In a study of 58 CP patients with biliary strictures, long-term success with plastic stents was found to be poor. Patients with calcifications in the pancreatic head had a much higher risk of plastic stent failure than those without.

Recently, the possibility of using fully covered, removable SEMSs, to “dilate” and splint the strictured distal CBD more effectively for longer, has emerged. Certainty of removability without bile duct injury must be established before the technique is accepted. Stent migration is another potential concern. A recent study is encouraging, at least with regard to safety. Only 1 out of 19 patients with CP experienced stent migration and no acute bile duct injury was described in these or 25 additional patients with benign biliary strictures due to other causes. Only 58% of CP strictures resolved, however, and the authors reported the stents to be challenging to deploy. They also reported duct mucosal bleeding during removal related to anchoring fins.

(C) Therapy of Fistulae and Pseudocysts

Pseudocysts develop in about 10 percent of patients with CP, as a result of pancreatic ductal disruption. Most communicate with the pancreatic ductal system. While the majority of pseudocysts are asymptomatic, they can become problematic and require therapy, because of pain, or the development of complications, such as duodenal or biliary obstruction, infection, pseudoaneurysm, pancreatic ascites or pleural effusion.

Conservative management in this situation (e.g. TPN, octreotide and percutaneous aspiration) often fails. If the pancreatic ductal system is disrupted, relief of ductal hypertension, by stricture dilatation or by transpapillary stenting of the pancreatic duct (to remove the trans-sphincteric pressure gradient) may be beneficial, at least in the short term.

(III) EUS

(a) Therapy of Pseudocysts

EUS has come to play a central therapeutic role in many patients whose pseudocysts require treatment. Using EUS, pseudocysts can be characterised and local vessels identified. It also allows localisation of the pseudocyst, to facilitate therapy, when it does not produce a visible bulge into the upper gastrointestinal tract lumen. Pseudocyst puncture and fistula formation can be achieved and pigtail stents placed to maintain the created pseudocyst-gastrostomy or -duodenostomy. Published series report high success rates of drainage, cyst resolution and overall clinical outcome and low rates of complications.

(B) Coeliac Nerve Block

Another potential role for EUS in patients with CP with intractable pain is in the performance of coeliac plexus block. EUS can be used to localise the plexus and guide infiltration with either corticosteroids or alcohol. Success has been limited, analgesic benefits are often restricted to the short to medium term and serious complications have been reported. These shortcomings should be borne in mind in deciding whether such therapy is worthwhile for an individual CP patient.

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Endoscopic Management of Peripancreatic Collections

Vu Kwan

Introduction

Whilst numerous innovative techniques for the endoscopic management of peripancreatic collections have emerged in recent years, the principles of management remain unchanged: a clear clinical indication for treatment should exist, a distinction between pseudocyst and pancreatic necrosis should be made and drainage procedures should only be performed in experienced centres with multidisciplinary support.

General principles

Four important questions should be posed in the assessment of a peripancreatic collection:

- 1) Is there a clinical indication for drainage of the collection?
- 2) What is the nature of the collection?
- 3) Is it suitable for endoscopic drainage?
- 4) Is there communication with the main pancreatic duct?

1. Clinical indication

It is imperative to keep in mind that 50% of acute peripancreatic collections will resolve spontaneously. Therefore, a clear clinical indication should exist for draining persistent collections. Important clinical indications for drainage include: gastric outlet obstruction, infection and abdominal pain. Additionally, asymptomatic collections that have not resolved after 13 weeks warrant consideration for drainage as early surgical literature suggests that spontaneous resolution after this period is rare and the complication rate rises sharply.

2. Nature of the collection

The distinction between pseudocyst and walled-off pancreatic necrosis is of utmost importance. A pseudocyst is a collection of pancreatic juice encased in reactive granulation tissue - simple drainage utilising stents usually suffice. Pancreatic necrosis is nonviable pancreatic parenchyma that becomes walled-off. It may be sterile or infected. *Sterile* pancreatic necrosis may be managed conservatively in the first instance: in fact, this is an ideal approach as liquefaction may occur, converting it from a solid debris collection to a fluid collection that can be drained. However, *infected* pancreatic necrosis is a distinctly different situation that carries with it significant morbidity and mortality and generally requires both drainage *and* debridement.

3. Suitability for endoscopic drainage

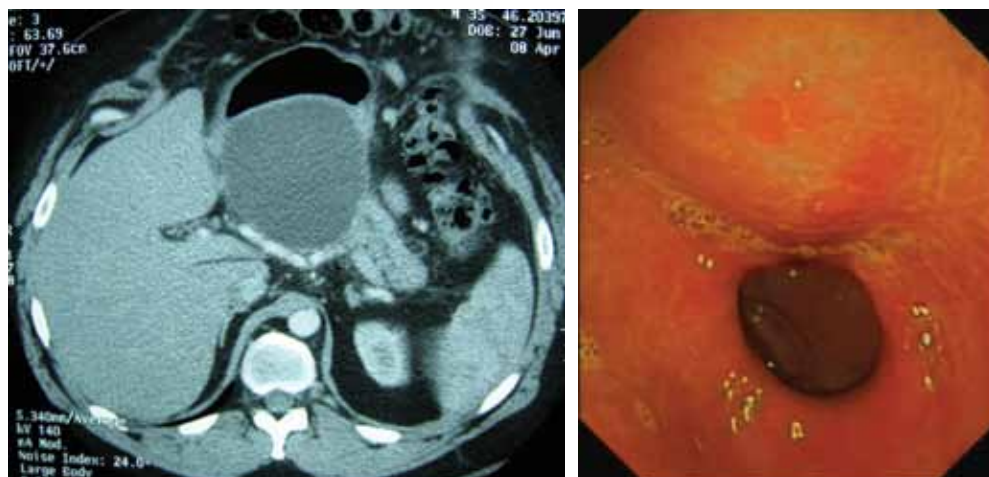
Maturity

It is important that the collection is mature with a defined circumscribing wall: a poorly defined collection is not an enclosed system of fixed pressure and will not decompress into the gut lumen when a tract is created.

Location

Proximity to the gut wall is of great importance, but the requirement for the collection to be causing a 'bulge' of compression into the gut lumen (Figures 1a & 1b) is no longer imperative with the advent of EUS. EUS allows clear visualisation of structures lying adjacent to the gut wall and has Doppler ultrasound to detect the presence of blood vessels lying in between the gut wall and the collection.

Figures 1a & 1b: A perigastric collection creating a bulge of external compression upon the antrum of the stomach.



Collection composition

As discussed above, the nature of the collection's internal contents needs to be considered: if the collection is composed purely of fluid then a simple endoscopic drainage procedure will suffice. However, the presence of solid necrotic tissue debris requires debridement. The differentiation of solid versus liquid material is readily made on EUS or MRI but may be difficult on CT. Previously, open necrosectomy has been advocated but this is associated with significant morbidity and mortality. Endoscopic necrosectomy has emerged as an effective minimally invasive modality and is discussed below. Thickness of the collection's wall should also be considered. Previously, a wall thickness of greater than 10mm was thought to be excessive; however, the advent of large diameter puncture devices with diathermic rings (cystoenterostomes) may allow passage through thicker cyst walls by using electrosurgical current.

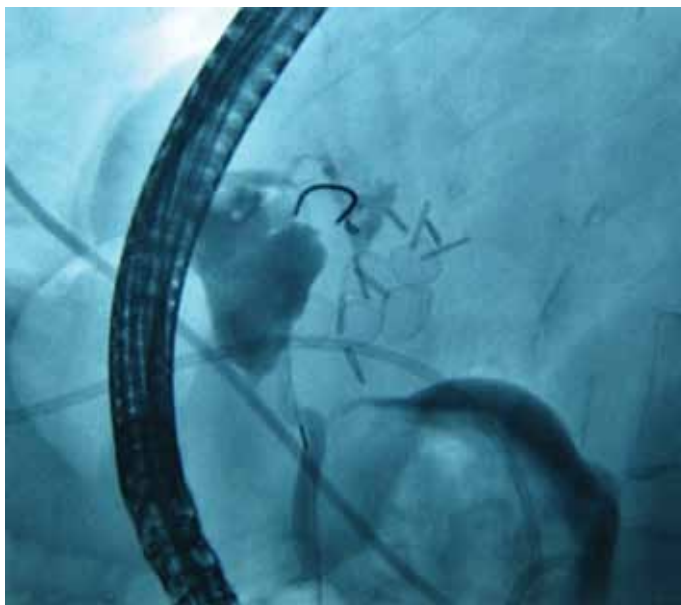
Portal hypertension, pseudoaneurysm

The presence of portal hypertension is a relative contraindication to performing endoscopic drainage without EUS guidance as small varices may lie in the trajectory of the needle. Pseudoaneurysm of the splenic or other artery, which occurs in up to 10%, is a definite contraindication to drainage without prior embolisation.

4. Communication with the main pancreatic duct

Collections that arise as a result of pancreatic duct (PD) disruption are composed of amylase-rich pancreatic secretions. PD disruption can occur due to severe pancreatitis, pancreatic trauma, following pancreatic surgery or due to pancreatic injury at laparotomy (Figure 2). Collections communicating with the main PD have a constant source of fluid because the pancreas continuously produces secretions. Drainage of the collection therefore needs to be accompanied by some form of pancreatic endotherapy: this decreases resistance to flow via the transpapillary route and 'encourages' secretions to flow in this direction rather than into the collection. Leaving the pseudocyst stents in indefinitely has also been suggested to reduce the chance of collection recurrence when there is pancreatic duct communication. Demonstrating communication between the collection and the main pancreatic duct can be done via pancreatogram at ERCP.

Figure 2: Pancreatic duct disruption due to inadvertent injury to the pancreas (repair to injury of the inferior mesenteric vein during an anterior resection for colorectal carcinoma). Injection of contrast into the pancreatic duct results in filling of a large cavity. Incidental finding of calcified gallstones.



Technique

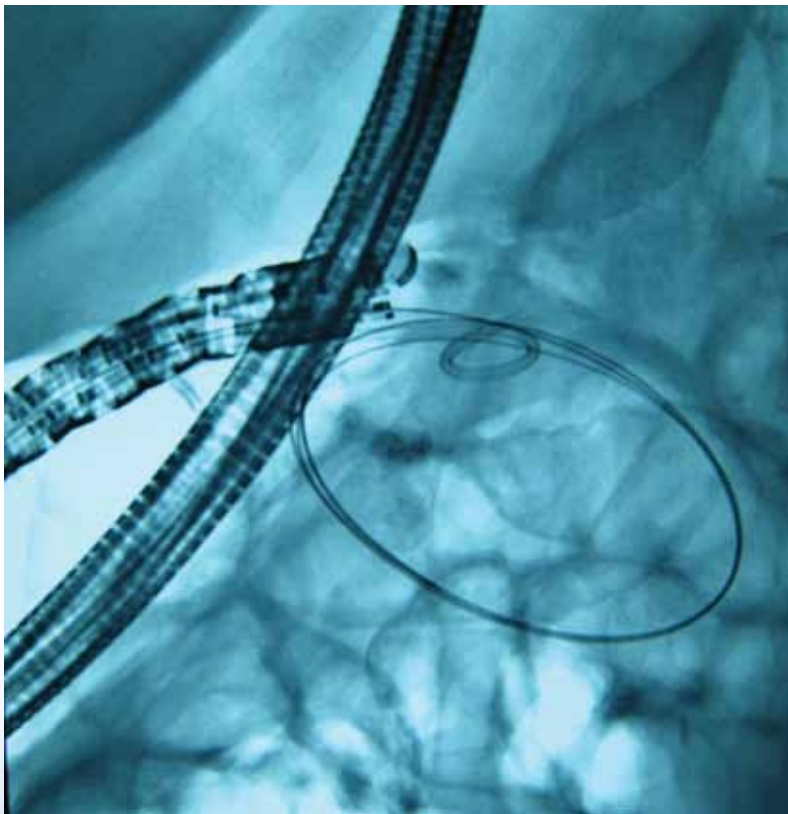
Equipment

Endoscopes

Previously, the therapeutic duodenoscope has been the major workhorse for pseudocyst drainage, but this relatively blind technique requires the presence of visible 'bulge' into the gut lumen (Figures 1a & 1b). The advent of EUS has significantly altered the practice of transluminal drainage, with the following advantages:

- clear visualisation of the collection and its relationship to the gut wall
- assessment of internal composition: presence of solid debris that requires debridement, presence of features that suggest an alternative diagnosis (e.g. septation of a cystic tumour)
- detection of intervening vessels/varices using Doppler ultrasound
- real-time visualisation of the needle as it is passed into the collection

Figure 3: Insertion of 1st stent: the first stent is deployed over the first guidewire, leaving in situ the 2nd guidewire over which the second stent can be placed immediately thereafter.



Post-procedural care

Uncomplicated pseudocyst drainages in well patients can be performed as a day-stay procedure if it is performed early in the morning and the patient is observed post-procedure for the remainder of the day. However, sick or septic patients must be observed as inpatients. If the collection is infected, ongoing intravenous antibiotics appropriate to the organisms cultured from the fluid should be administered. The patient remains nil by mouth for 24 hours post-procedure.

Follow-up imaging should be performed in 1-2 months time to determine whether or not the collection has resolved. If the collections do not recur after approximately 3 months, the stents are generally removed. A small randomised controlled trial suggested that collection recurrence could be reduced by leaving stents in indefinitely particularly in patients with communication with the PD. If the collection has not resolved in 4-6 weeks, repeat dilatation and stent replacement, perhaps with larger calibre stents, can be performed.

Necrosectomy

This can be performed as part of the initial drainage procedure, or as a two-stage procedure allowing time for the tract to be well-established and for decompression of any infected fluid component.

A forward-viewing gastroscope is used. The existing tract is dilated to 15-20mm using a balloon dilator. The gastroscope is then entered into the cavity. A variety of equipment can then be used to remove the necrotic tissue:

- Basket devices (Roth Net®, biliary stone extraction devices) (Figure 4)
- Polypectomy snare
- Tripod foreign body grasping forceps

It is important that only the necrotic pancreatic tissue is removed (black in colour) and not the healthy granulation tissue (pink in colour) (Figure 5). If there is adherent tissue that cannot be removed, a repeat procedure after further nasocystic catheter irrigation is advisable. The aim is to have no residual necrotic tissue, leaving behind only a cavity lined by healthy granulation tissue.

Figure 4: A Roth Net® basket being opened within the collection of necrotic material.

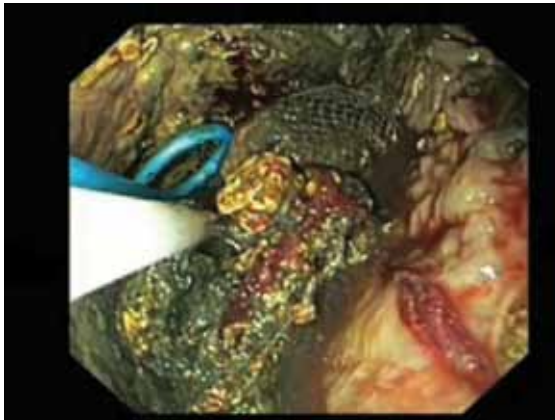


Figure 5: The interior of a collection of infected pancreatic necrosis: note the pink granulation tissue lining the cavity- this need not be debrided. The black solid debris in the body of the cavity is the necrotic pancreatic tissue: this is the target of debridement.



Literature

No randomised-controlled trials exist regarding the best way to manage peripancreatic collections. However, endoscopic drainage has become an accepted alternative to surgery when conducted in experienced centres.

The outcomes of endoscopic drainage of pseudocysts have been documented by several expert centres. The initial landmark report in 1989 described its use in patients with pseudocysts in the setting of chronic pancreatitis. Whilst it has previously been considered that higher success rates are achieved in chronic pancreatitis (>90%) as compared to acute pancreatitis (70-80%), a more recent series examining larger numbers of patients does not suggest this is the case, with equivalent success rates for both groups (~90% overall). However, a lower long-term success rates in achieved patients with pancreatic necrosis, also shown in data from other centres. However, with the development of endoscopic debridement techniques, success rates of over 90% have been demonstrated.

Complications of transmural drainage include:

- Acute and delayed bleeding
- Perforation
- Systemic infection
- Stent migration

The frequency of these complications is variable amongst the published literature, ranging from 11 to 37%. No controlled data exist to compare EUS-guided and conventional drainage techniques. The literature available is not designed to detect such a difference as both series selected patients who had failed non-EUS guided drainage or had features such as non-bulging collections and portal hypertension to undergo EUS guided drainage; nonetheless, both series showed that the two groups had comparable complication rates.

Conclusion

The endoscopic management of peripancreatic collections offers patients a safe and effective alternative to major surgery. Refinements in technical aspects and equipment over recent years have rendered the practice easier to execute, with excellent long-term results. Nonetheless, it remains a technique that should only be performed in expert centres with adequate multidisciplinary support.

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SECTION 5

BASIC PRINCIPLES OF ENDOSONOGRAPHY AND EQUIPMENT

- Introduction to Endoscopic Ultrasound (*Ian Norton*)
- EUS for Oesophageal and Mediastinal Indications
(*Alina Stoita & David Williams*)
- Endoscopic Ultrasound (EUS) and its use in Submucosal Lesions
in Upper Gastrointestinal (GI) Tract (*Robert Y. Chen*)
- EUS for Biliary Disease and Choledocholithiasis
(*Jillian Rosenstengel & Patrick R Walsh*)

Introduction to Endoscopic Ultrasound

Ian Norton

Endoscopic Ultrasound (EUS) has rapidly evolved over the past 15 years. In the rapidly shifting field of medical imaging some areas of EUS have become more limited (e.g. staging of oesophageal and pancreatic malignancy) while others have grown (e.g. suspected choledocholithiasis and non-small cell carcinoma of the lung). This review will outline the common diagnostic and therapeutic scenarios for which EUS is currently utilised.

Equipment

Endoscopic ultrasound utilises a flexible endoscope to pass an ultrasound probe to a point in the gastrointestinal tract adjacent to an area of interest. The procedures are performed on an out-patient basis, usually with titrated conscious sedation. Frequencies used range from 5.5MHz to 30MHz. Higher frequencies produce high resolution images with limited depth of view, whereas lower frequencies provide imaging of lower resolution, but greater penetration (up to ~5cm). Acoustic coupling with the mucosal surface is achieved by a water-filled balloon attached to the instrument tip and/or infusion water into the lumen. Three types of instruments are currently in routine practice:

1. **Radial Scanning Endoscopes.** This is the diagnostic “workhorse” of EUS. It comprises a modified endoscope with a circular ultrasound array around the instrument near the tip. This provides a circular ultrasound image (with the instrument at the centre of the circle) perpendicular to the long axis of the endoscope. Previously, these instruments involved a mechanical rotating transducer, but most instruments in use now have a solid-state transducer. These instruments do not have FNA capability. The solid state instruments have Doppler capability.
2. **Linear Scanning Endoscopes.** These have a solid state, curved linear array transducer in the endoscope tip providing an image parallel to the axis of the endoscope. The ultrasound beam is aligned with the endoscope’s biopsy channel, such that a needle (or other accessory) is in the ultrasound beam as it passes through tissue. This permits sampling of tissues deep the lumen (such as lymph nodes) under real-time ultrasound control. Similarly, periluminal cystic lesions can also be aspirated for diagnostic and therapeutic purposes. The solid-state nature of these transducers also permits Doppler interrogation of the area of interest.
3. **Catheter Probes.** These are small caliber catheters (~7 French) that are passed through a routine endoscope. They have a mechanical rotating transducer at the tip. In particular, high frequency probes (12 to 30MHz), are used to obtain fine detail of mucosal lesions. Wire-guided versions of these probes have been used to perform intraductal ultrasound within the pancreatobiliary system. In general, catheter probes are not widely used since they require a separate drive motor and their main application (high frequency definition of mucosal lesions) has largely been superseded by endoscopic mucosal resection techniques.

Luminal Applications

1. **Mucosal Lesions:** Standard endoscopic ultrasound scanning resolves the gastrointestinal wall into five layers, representing the mucosa, submucosa, muscularis propria and serosa, together with the layer interfaces. Higher frequency probes provide more definition, with the muscularis mucosa visible as well as separation of muscularis propria into circular and longitudinal layers. Therefore, EUS becomes a very sensitive modality for determining the layer in which a lesion arises as well as the depth of penetration of a mucosal-based lesion (T-staging).

- i. *T-staging of Luminal Malignancy:* In general, T-staging of mucosal-based tumours is dependent upon the relationship of the lesion to the muscularis propria. T₁ lesions are superficial to the muscle layer, T₂ lesions invade the muscle and T₃ lesions extend beyond the muscle. EUS has been shown to be more accurate than computerised tomography in the detection and T-staging of oesophageal, gastric and rectal malignancies. The T-stage accuracy of EUS for early gastric cancer is 80-89% and 76-96% for rectal lesions. However, EUS is poor at differentiating mucosal based disease from submucosal involvement (both T1). This distinction is important since oesophageal lesions with submucosal invasion have a high risk of lymphatic involvement (up to 30%). Therefore, since EMR techniques have advanced (definitively sub-staging T1 tumours pathologically) EUS is not commonly used for assessment of early oesophageal neoplasia.

Nonetheless, since T-staging has direct prognostic significance, accurate T-staging of malignancy by EUS may assist in the pre-operative stratification of patients enrolled in oncologic trials. Furthermore, preoperative diagnosis of locally advanced (T₄) lesions may prevent explorative surgery of incurable lesions.

- ii. *Mucosal Thickening:* Thickened gastric folds are easily characterised by EUS. Loss of normal acoustic layering may suggest malignant infiltration. Unfortunately, Zollinger Ellison syndrome, Menetriere's disease, diffuse gastric malignancy, and MALT lymphoma may all cause gastric wall thickening with preservation of wall layers, making EUS differentiation of these conditions difficult. However, EUS can be useful in targeting appropriate areas for large particle endoscopic biopsy (or EMR) as well as confirming whether the process is in the mucosal or submucosa and thus amenable to endoscopic biopsy. In situations where endoscopic mucosal biopsies are negative needle biopsy under EUS guidance may be performed, yielding a diagnostic accuracy in this situation of about 65%.

2. **Submucosal lesions with normal overlying mucosa:** These are a frequent indication for EUS which can differentiate lipoma (hyperdense) from leiomyoma (hypodense). EUS imaging cannot differentiate leiomyoma from GIST tumours, but FNA may be used for immunostaining to differentiate these lesions. EUS criteria for determining high-risk GISTS (size >3cm, irregular border, heterogeneous structure and cystic spaces) have been published.

Less common submucosal lesions that are also well characterised by EUS include carcinoid tumours, duplication cysts and pancreatic rests. EUS is also occasionally used to assess gastroesophageal varices or other vascular lesions.

3. **Assessment of Peri-Luminal Tissues:** EUS may be helpful in assessing sphincter integrity in patients with faecal incontinence. Preliminary data also suggest that EUS may be as sensitive as MRI or examination under anaesthesia for characterisation of peri-rectal fistulae in patients with Crohn's Disease. EUS has also been used in the differentiation of primary from secondary (malignant) achalasia of the oesophagus.

Assessment of Peri-Intestinal Lymph Nodes and Masses

Endoscopic ultrasound with or without EUS guided fine needle aspiration (FNA) biopsy provides the most sensitive and specific means of nodal staging of periluminal malignancy. N-stage accuracy rates of 70-85% for rectal tumors and 79-93% for oesophageal tumors have been reported. Of particular note, a recent study demonstrated that EUS-FNA increased diagnostic accuracy for N-staging of oesophageal malignancy from 70% to 93% compared to radial EUS alone. EUS-guided FNA proving malignant involvement of selected node groups is particularly important in cases where the nodal staging precludes resection with curative intent (e.g. coeliac or cervical lymphadenopathy in oesophageal cancer and contralateral mediastinal adenopathy in non-small cell carcinoma of the lung).

Multiple studies have documented the safety and efficacy of transoesophageal EUS guided biopsy of mediastinal masses. EUS-FNA has been demonstrated to be at least as accurate as transbronchial biopsy in the diagnosis of mediastinal masses. Furthermore, cost analysis of EUS-FNA of mediastinal masses has demonstrated significant savings compared to mediastinoscopy. Therefore, EUS is a safe and relatively inexpensive method of sampling mediastinal masses and lymph nodes, particularly those relatively inaccessible to other modalities (e.g. subcarinal and posterior mediastinum).

Extraluminal Applications

1. **Diagnosis and Staging of Pancreatic Malignancy:** EUS is the most sensitive test for detection and characterisation of pancreatic masses, especially those less than 3cm in diameter. The accuracy of detection of vascular involvement has been reported to be as high as 80-85%. However, locoregional staging by multislice CT has replaced EUS in most units. Linear scanning EUS permits biopsy of suspicious pancreatic lesions.
2. **Pancreatic Neuroendocrine Tumors:** EUS is a sensitive test for the detection of neuroendocrine tumors. One comparative study reported EUS to be superior to CT or transabdominal ultrasound, and equivalent to somatostatin receptor scintigraphy (SRS) for gastrinomas, and superior to SRS for insulinomas. Biopsy of suspicious lesions via EUS is also straightforward, though usually not necessary.
3. **Pancreatic Cystic Lesions:** EUS is the most accurate imaging technique in the characterisation of pancreatic cysts. This is important since some lesions are benign (post-inflammatory and serous cystadenomas), while others have malignant potential (mucinous tumours). Cyst CEA level has been shown to be the most accurate test for differentiating benign from malignant lesions.

4. **Choledocholithiasis:** EUS is at least as sensitive as endoscopic retrograde cholangiography or magnetic resonance cholangiography in the diagnosis of common bile duct stones. EUS does not carry the risk of pancreatitis associated with endoscopic retrograde cholangiopancreatography. This is a very important area of development of EUS. As such, ERCP should rarely be performed as a diagnostic test.
5. **Chronic Pancreatitis:** Sonographic changes in the pancreatic parenchyma and duct system in chronic pancreatitis have been reported and characterised. Although several studies have advocated its use as a means of early diagnosis of chronic pancreatitis, these studies have lacked a “gold standard” for early disease and have ignored age-related changes that may occur in the pancreas. More data is needed before advocating EUS as a standard diagnostic test for chronic pancreatitis. It should also be noted that the differentiation of focal chronic or acute pancreatitis from malignancy can be difficult even with EUS.

Therapeutic Interventions via EUS

The ability to place a needle under real-time guidance using the linear-scanning instrument has opened up the possibility of therapeutic intervention using EUS, specifically, the drainage of fluid collections and injection of therapeutic substances into specific areas.

1. **Drainage of Peripancreatic Fluid Collections:** Endoscopic drainage of symptomatic pancreatic pseudocysts has become widely established. EUS may be of use to confirm the diagnosis of pseudocyst as well as determining the most advantageous site of cyst/gut apposition. EUS also has the advantage of delineating adjacent vascular structures to be avoided during cyst puncture and aspiration. Several recent studies have reported successful drainage and stenting of cyst gastrostomy entirely under EUS real time guidance using linear EUS scanning.
2. **Coeliac Ganglion Neurolysis:** The coeliac ganglion drapes across the coeliac artery, an area easily visualised during EUS and within several millimeters of the posterior gastric wall. Coeliac plexus neurolysis under direct EUS guidance has been advocated for patients with unresectable pancreatic cancer. EUS may stage the lesion, obtain biopsy confirmation and perform neurolysis all in one procedure.

Complications of Endoscopic Ultrasound

Complications with EUS relate to either the endoscopic portion of the procedure or those associated with fine needle aspiration biopsy. Dilatation of oesophageal malignancies to a diameter sufficient to pass the EUS instrument (12mm) is associated with risk of perforation. Large pancreatic neoplasms may invade and fix the second part of the duodenum, leading to increased risk of perforation at this site.

Three large published series (totaling over 1100 patients) have addressed complications of EUS-FNA. Comprising over 900 EUS-FNA biopsies of solid tissue structures, there were no complications relating to the biopsy. In a large multicenter trial involving 554

consecutive mass or lymph node biopsies, only five complications were observed, all of which were nonfatal. Two patients had endoscope-induced perforation, two had febrile episodes following aspiration of cystic lesions, and one had haemorrhage from the wall of a pseudocyst. Pneumoperitoneum has been reported when endoscopy closely followed EUS-FNA, suggesting that intestinal insufflation should be minimised soon after EUS-FNA. A risk (<2%) of pancreatitis (usually mild) has been observed following biopsy of pancreatic lesions.

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EUS for Oesophageal and Mediastinal Indications

Alina Stoita & David Williams

I. General principles

Endoscopic ultrasound (EUS) combines endoscopic visualisation with high frequency ultrasound. This allows precise differentiation of the individual layers of the oesophageal wall and direct imaging of the surrounding tissues. As such, EUS is an ideal imaging modality for cancer staging (TNM classification), allows extraluminal tissue diagnoses (EUS guided fine needle aspiration) and therapeutic procedures can be performed with EUS guidance (coeliac plexus neurolysis, mediastinal abscess drainage).

There are several types of echoendoscopes available:

1. **Radial scanner** (5-20 MHz) provides a 360 degree view oriented perpendicularly to the shaft of the echoendoscope. A balloon fits over the tip of the scope to allow for water filling and acoustic coupling.
2. **Curvilinear array scanner** (5-10MHz) provides sector images in the same plane as the long axis of the endoscope and has colour Doppler capabilities. This instrument allows real time EUS guided fine needle aspiration and therapeutic procedures.
3. **High frequency catheter mini-probes** (20-30MHz) can be inserted through the therapeutic channel of a normal endoscope and can be used for assessment of small mucosal lesions and tight malignant oesophageal strictures.

EUS is performed under conscious sedation and is an outpatient procedure. The instructions for preparation are the same as for standard endoscopy. Anticoagulant and antiplatelet drugs (not aspirin) are usually stopped 5-7 days before EUS guided biopsy and in high risk patients bridging therapy with low molecular weight heparin is instituted. Antibiotic prophylaxis is required before aspirating any cystic lesion or draining an extramural collection.

II. Technique

The oesophagus can be evaluated either with a radial or a linear scope but if tissue acquisition is not needed a radial echoendoscope is preferable. The mediastinum is usually evaluated with a linear scope as in most cases a biopsy is required to diagnose mediastinal lesions and to stage non-small cell lung cancer (NSCLC). EUS guided fine needle aspiration (FNA) biopsy is usually performed with 22FG or 25FG needles, albeit larger gauge needles (19FG, Quik-core) can be used where core specimens are considered preferable (e.g. diagnosis of lymphoma). On-site cytopathologic interpretation of the sample improves the diagnostic accuracy of EUS guided FNA and minimises the number of passes.

An oesophageal cancer and mediastinal study starts with inserting the endoscope in the stomach and imaging the liver, left adrenal and coeliac axis for metastases (M stage). The scope is then slowly withdrawn into the oesophagus looking for mediastinal lymph nodes (N stage). Once the oesophageal tumor is reached the frequency is adjusted to obtain detailed images of the wall layers (T stage). Positive and relevant negative findings are carefully documented in the report.

III. Complications

EUS is a safe procedure with rare complications. The reported risk of perforation is 0.4%, mostly related to insertion of the oblique viewing echoendoscope with a long rigid tip by an inexperienced operator. The risk of infection after aspirating mediastinal cysts has been reported to be as high as 9% and as a result cyst aspiration is avoided or is performed under antibiotic cover.

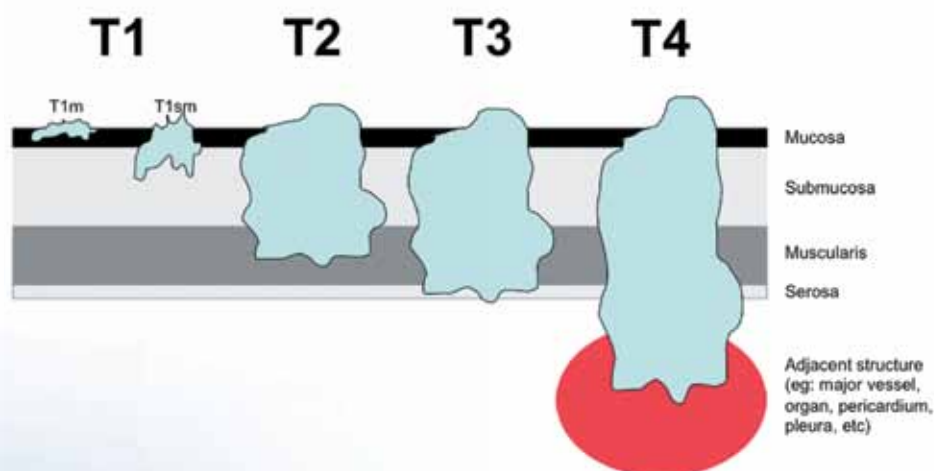
IV. Indications

1. Oesophagus

A. EUS in oesophageal cancer staging

Oesophageal cancer represents a significant health problem in Australia with 25% increase in incidence from 1993 to 2003. Oesophageal cancer is a devastating disease with overall 5 year survival of only ~20%. Accurate tumour staging is essential since it helps define treatment options and patient outcomes.

Fig 1: Staging of oesophageal cancer.



Therapeutic impact studies show the benefit of EUS staging by:

- avoiding unnecessary surgery in patients with advanced disease (e.g. previously unidentified metastases, T4 disease).
- selecting patients with nodal involvement for neoadjuvant therapy (meta-analyses have shown that for stage II A, IIB and III disease, neoadjuvant chemoradiotherapy followed by surgery rather than surgery alone improves 2 and 3 year survival) .
- identifying patients with early cancers for definitive endoscopic mucosal resection (e.g. T1mN0 disease).

EUS in oesophageal cancer has a T stage accuracy of 85% and N stage accuracy of 80%. When EUS FNA of lymph nodes (LN) is performed the N stage accuracy increases to 87%. Standard endosonographic criteria for a malignancy include nodes that are round, well defined, hypoechoic and larger than 5-10mm. When all four criteria are present the chance of malignancy is 80%, albeit this occurs in <25% of cases. Recently suggested modified criteria (the four standard ones plus presence of coeliac LN, >5 LN and EUS T3/T4 tumour) can better differentiate malignant LN. The presence of >6 or <1 modified criteria has 100% accuracy of predicting if a LN is malignant or benign, respectively.

Elastography is an emerging EUS technology relying on variations in tissue stiffness to identify malignant LN. However, the reported sensitivity and specificity of this technique is only 80-87% and EUS FNA remains the gold standard in confirming malignant adenopathy.

Numerous studies have shown that EUS is consistently superior to computer tomography (CT) in detecting tumour stage and locoregional adenopathy. In addition EUS has been reported to be superior to positron emission tomography (PET) in detecting nodal metastases.

Malignant oesophageal strictures can sometimes be problematic as they can prevent insertion of the large bore echoendoscope (outer diameter ~13mm) and hence prevent a complete staging study. However, if it is felt that EUS findings would significantly alter patient management (e.g. celiac nodal metastases, T4 disease), dilatation to allow passage of the echoendoscope can be performed before EUS, albeit risk of perforation needs to be weighed up.

Restaging of oesophageal cancer with EUS imaging alone after neoadjuvant therapy is less accurate as compared to primary TN staging as it is difficult to differentiate tumour from necrosis or inflammation. However, EUS FNA can be used to exclude patients from undergoing surgery as those with persistent extensive disease or new metastases.

EUS is the best locoregional staging modality for oesophageal cancer and should be incorporated into the staging plan of patients considered suitable candidates for treatment. The Cancer Institute NSW supports this central role in oesophageal cancer by acknowledging that most quality-adjusted-life-years for patients are achieved when EUS FNA in staging strategies.

B. EUS in Barrett's oesophagus

The tasks of staging Barrett's related early cancers or high grade dysplasia are to detect occult cancers, identify submucosal invasion (T1sm) and define nodal disease (N1). It is particularly important to identify submucosal invasion as tumours limited to the mucosa have <5% chance of metastasising to lymph nodes whereas tumours invading to submucosa have up to 27% chance of nodal disease. Multiple studies suggest that EUS cannot readily detect dysplasia nor occult cancers and cannot reliably enough distinguish T1m from T1sm invasion, particularly in flat lesions. As such, EUS is perhaps best served as a staging adjunct to careful high quality endoscopy and endoscopic mucosal resection of defined lesions, whereby histologically proven T1sm disease or beyond can be assessed for nodal disease. At present there is no defined role for EUS in the assessment of non-dysplastic Barrett's mucosa or low grade dysplasia.

C. Submucosal lesions

EUS is important in the assessment of submucosal lesions in the oesophagus, with more common lesions including mesenchymal tumours, granular cell tumours and mediastinal cysts. EUS can readily differentiate mural lesions and extraluminal compression from mediastinal mass lesions. With respect to mural lesions, it can provide information concerning layer of origin, size, borders, homogeneity and vascularity, whereby differential diagnoses can be defined. Whilst not often required, EUS FNA can confirm diagnosis, albeit cytologically samples obtained are often only small. In addition EUS can indicate whether endoscopic resection is appropriate. The commonest oesophageal lesion is leiomyoma and this appears as a well defined hypoechoic homogeneous lesion that arises from layer 4. GISTs are not common in the oesophagus.

EUS can help differentiate pseudoachalasia from achalasia. Patients with achalasia have a thickened muscularis propria in the distal esophagus but otherwise normal wall architecture. In pseudoachalasia, tumor infiltration into the esophageal wall is evidenced by an irregular hypoechogenic infiltration with loss of the normal wall architecture and possible adjacent mass lesion.

2. Mediastinum

A. EUS in diagnosing and staging of non-small cell lung cancer (NSCLC)

Lung cancer is the fourth most common cancer in Australia and has the highest cancer related mortality, with 5 year survival rates of <20% for mediastinal (N2, N3) nodal disease. Since prognosis of lung cancer is directly related to disease TNM stage, accurate staging is essential for choosing the most beneficial therapies. Unfortunately up to 25% patients undergoing thoracotomy after staging CT and bronchoscopy alone are found to have mediastinal disease that would normally preclude them from resection or allow consideration of neoadjuvant treatment.

The role of EUS FNA in NSCLC:

- diagnosis of lung cancer with tumour near the oesophagus
- diagnosis of suspected lung cancer with enlarged mediastinal LN
- assessment of tumour invasion (T4) in centrally located tumours
- mediastinal nodal staging of lung cancer (N2/3 disease)
- mediastinal restaging after induction chemotherapy
- assessing PET positive lymph nodes

According to the AJCC lung cancer classification, patients with stage I and II disease are offered surgery alone and those with stage III A (N1 and minimal N2 disease) can be considered as candidates for neoadjuvant therapy. Patients with stage III B disease (T4 or N3) are in general not considered suitable candidates for resection.

Staging modalities for NSCLC include CT, PET, EUS FNA, endobronchial ultrasound (EBUS) and mediastinoscopy. For mediastinal staging EUS FNA is more sensitive (88% versus 57%) and specific (91% versus 82%) than CT and percutaneous biopsy carries risk of pneumothorax. EUS FNA and PET have similar sensitivities but EUS is more specific (100% versus 72%) and can detect malignant LN <1cm in longest axis. Any lymph nodes >1cm on X-sectional imaging or any positive nodes on PET should be sampled in order to exclude malignancy. EUS and mediastinoscopy have similar accuracy (90%) but they are complementary as they provide access to different mediastinal nodal stations. EUS provides access to posterior stations 5, 7, 8 and 9 and mediastinoscopy provides access to stations 2, 4 and ventral part of station 7. However, since mediastinoscopy is an invasive procedure requiring general anaesthesia with 2% complication rates, it should be considered only when EUS FNA has not provided definitive diagnosis. Studies confirm that EUS FNA can thereby reduce unnecessary thoracotomies and mediastinoscopies in a substantial number of patients.

EBUS is an emerging endoscopic modality that can evaluate subcarinal and anterior mediastinal lymph nodes (stations 7, 2, 3, 4). The combination of EUS and EBUS FNA carries the promise of complete endoscopic mediastinal nodal staging with reported 93% sensitivity and 100% specificity.

ASGE guidelines recommend EUS FNA as the procedure of choice for sampling subcarinal, aortopulmonary window and periesophageal lymph nodes (stations 5,7,8) in lung cancer patients with enlarged lymph nodes on X-sectional imaging. EUS FNA should also be considered in preoperative staging of patients with negative mediastinal adenopathy on imaging as significant number of mediastinal nodal metastasis can be detected by EUS.

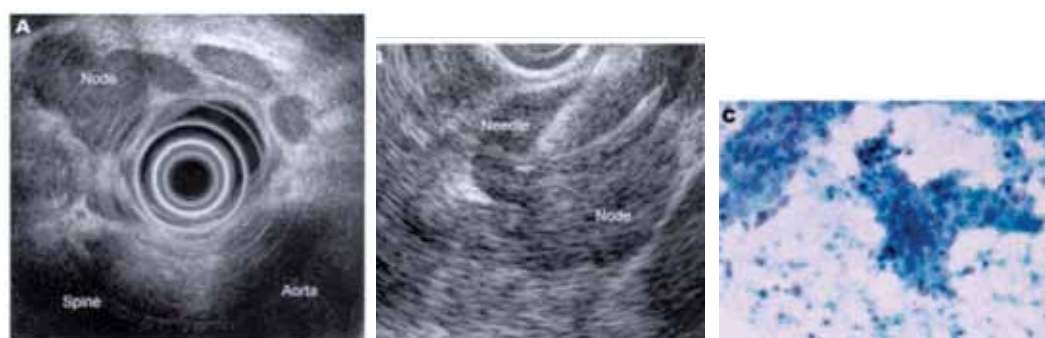
B. Unexplained mediastinal lymphadenopathy and mediastinal mass lesions

As with mediastinal staging of known lung cancer, EUS FNA is an important modality for assessment of unexplained mediastinal adenopathy and mass lesions.

Differential diagnosis of mediastinal adenopathy includes:

- *Reactive lymph nodes* with benign EUS features: draping, triangular, hyperechoic centre
- *Granulomatous LN* (sarcoid, tuberculosis, histoplasmosis, coccidioidomycosis). The appearance is of benign LN sometimes with internal calcifications. Cytology is usually sufficient identify granulomata and further samples can be sent for special stains, culture and TB PCR.
- *Malignant LN*: The overall accuracy of EUS FNA in diagnosing malignant mediastinal LN is 93% (Fig. 2).
- *Lymphoma*: Usually presents as diffuse mediastinal lymphadenopathy. Biopsies can be sent for flow cytometry and immunohistochemistry. EUS guided trucut biopsies (Quikcore) can provide additional architectural details to confirm diagnosis of lymphoma.

Fig 2: Malignant mediastinal lymphadenopathy (our photo).



Mediastinal mass lesions are often incidental findings on CT with differential diagnoses including:

- *Mediastinal cysts* appear as oval, anechoic structures with acoustic enhancement. FNA is in general avoided as most are benign and there is a reasonably high risk of infection.

- *Mediastinitis and abscess:* An abscess is suggested by an inhomogenous, well demarcated hypoechoic area in a patient with fever and appropriate history, usually after surgical intervention. There are case reports of successful EUS guided drainage of a mediastinal abscess, utilising much the same technique as for drainage of pancreatic and pelvic fluid collections.
- *Primary neoplasms of the posterior mediastinum* are rare. The majority are neurogenic and arise from peripheral nerves (schwannoma, neurofibroma), sympathetic ganglia (ganglioneuroma, ganglioneuroblastoma, neuroblastoma) parasympathetic ganglia (paraganglioma) or sarcoma.
- *Metastases* from lung, breast, oesophageal, colon, renal and testicular cancers

Conclusion

EUS +- FNA is an established, highly effective and safe method for diagnosing and staging lesions of the oesophagus and mediastinum that significantly impacts on patient management.

Tables

Table 1: American Joint Commission on Cancer staging for esophageal cancer.

Definition of TNM			
Primary tumor (T)			
TX	Primary tumor cannot be assessed		
T0	No evidence of primary tumor		
Tis	Carcinoma in situ		
T1	Tumor invades lamina propria or submucosa		
T1a	Tumor invades mucosa or lamina propria		
T1b	Tumor invades submucosa		
T2	Tumor invades muscularis propria		
T3	Tumor invades adventitia		
T4	Tumor invades adjacent structures		
Regional lymph nodes (N)			
NX	Regional lymph nodes cannot be assessed		
N0	No regional lymph node metastasis		
N1	Regional lymph node metastasis		
Distant metastasis (M)			
MX	Distant metastasis cannot be assessed		
M0	No distant metastasis		
M1	Distant metastasis		
Tumors of the lower thoracic esophagus:			
M1a	Metastasis in celiac lymph nodes		
M1b	Other distant metastasis		
Tumors of the midthoracic esophagus:			
M1a	Not applicable		
M1b	Nonregional lymph nodes and/or other distant metastasis		
Tumors of the upper thoracic esophagus:			
M1a	Metastasis in cervical nodes		
M1b	Other distant metastasis		
Stage grouping for oesophageal cancer			
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2	N0	M0
	T3	N0	M0
Stage IIB	T1	N1	M0
	T2	N1	M0
Stage III	T3	N1	M0
	T4	Any N	M0
Stage IV	Any T	Any N	M1
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b

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Endoscopic Ultrasound (EUS) and its use in Submucosal Lesions in Upper Gastrointestinal (GI) Tract

Robert Y. Chen

Introduction

It is not uncommon to see a submucosal (SM) lesion on routine endoscopy. This is characterised by protrusion of a lesion into the lumen of the esophagus or stomach, i.e. “lump” or “nodule” with a normal appearing overlying mucosa. Endoscopic appearance and biopsy are generally non-diagnostic. Often CT scan can only visualise large lesion and certainly cannot locate small lesions and cannot give detailed information regarding nature of a SM lesion.

EUS is a combination of endoscopy and ultrasonography. It uses an echoendoscope which has an ultrasound transducer mounted at the tip of the endoscope. As a result, submucosal lesion can be scanned in close range (by endoscopically placing the tip of the echoendoscope close to the lesion) with high frequency. As a result, detail images of the layers of the wall and lesion can be obtained.

Differential Diagnoses of SM lesions

The differential diagnosis of submucosal lesion can be divided into lesions arising from outside the wall (extramural) or arising from within the wall (intramural). The sensitivity and specificity of EUS in differentiating intramural lesion and extramural compression are 92% and 100% respectively.

The extramural lesions can be: indentation by normal structures such as surrounding organ, (e.g. gall bladder, liver) vessels or indentation by tumour/mass/aneurysm.

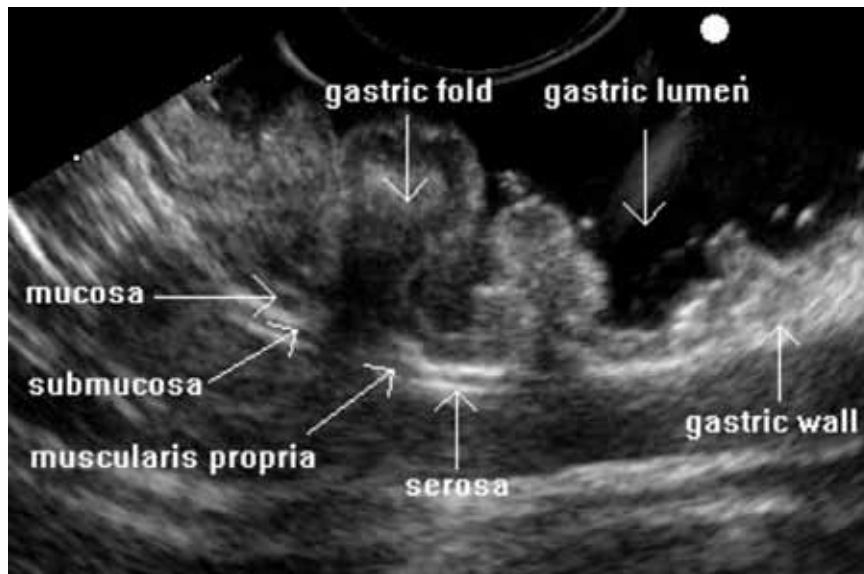
The intramural lesions have multiple differential diagnoses and include: gastrointestinal stromal tumour (GISTs), leiomyoma, leiomyosarcoma, lipoma, cyst, pancreatic rest, carcinoid, granular cell tumor and blood vessel (varices). Other rare lesions can also be found: metastasis, fibroma, haematoma.

General principles of performing EUS for SM lesions

The specific technique used whilst doing EUS for SM tumours is that fluid (either water or saline) instillation into the gastrointestinal lumen (for gastric and duodenum, not oesophagus) should be used to “submerge” the lesion and intraluminal air should be aspirated. This allows the lesion to be visualised clearly by optimising acoustic coupling with no interference by intraluminal air. In addition, a miniprobe can be used for small SM lesions.

Figure 1: Normal Gastric wall

- 1st layer: Hyperechoic, superficial mucosa
- 2nd layer: Hyperechoic, deep mucosa
- 3rd layer: Hyperechoic, submucosa
- 4th layer: Hyperechoic, muscularis propria
- 5th layer: Hyperechoic, serosa



EUS features of SM lesions

Extramural lesions

On EUS, the extramural lesions can be seen to be arising from the outside the wall of the stomach or oesophagus and compressing into the lumen. The normal wall layers are preserved between the GI lumen and the extramural lesion.

The most common organs/vessels that inadvertently give rise to an impression of SM lesions are: splenic artery (at posterior wall of upper stomach), liver (anterior wall), spleen (fundus) and gall bladder (antrum). The important features to note is that SM lesions arising from compression from external organ/vessels tend to be present only at significant inflation of the stomach with air and disappear on deflation of the stomach.

Pathological extramural lesions could arise from liver tumour, splenic aneurysm, pancreatic pseudocysts or tumour, intra-abdominal lymphadenopathy.

Intramural lesions

Gastrointestinal stromal tumour (GIST)

Even though GIST account for less than 1% of all primary gut tumours, it is the most common SM lesions found. GISTs are mesenchymal tumour believed to be originated from malignant transformation of the interstitial pacemaker cells (interstitial cells of Cajal). Microscopically, it can be either of spindle cell tumour appearance (70%) or epithelioid in appearance (20%) or both. The most characteristic feature is the presence of positive immunohistochemistry marker, cell surface antigen CD117 (KIT) a growth factor transmembrane receptor, is a product of proto-oncogene c-kit (chromosome 4).

The estimated incidence of GISTs is 10-20 cases per million. GIST can occur throughout the gastrointestinal tract, approximately 60% of the GISTs occurring in the stomach, 35% in the small intestine and 5% in esophagus and rectum.

On EUS, it is usually hypoechoic, arises from the muscularis propria layer (i.e. the fourth echo-layer), homogeneous and has a smooth/well defined margin (Figure 2). It can, however, involve or arise from other layers (such as muscularis mucosa).

Most of the GISTs are homogeneous in echo-texture features suggestive of a high-risk lexion include inhomogeneity of the echo-texture, or presence of pockets of anechoic areas, and indistinct/irregular margin.

Figure 2: GIST



Leiomyoma and leiomyosarcoma

Endoscopically, there is no clear cut discriminating feature between GIST and leiomyoma. Histologically, GIST tends to have both spindle and epithelioid cell types whereas leiomyoma tend to have spindle cell types only. On immunohistochemistry stain, GISTs are positive to CD117, whereas leiomyoma SM lesions are positive to smooth muscle actin and desmin.

Lipoma

Lipomas are benign tumors of mature lipocytes. They have no malignant potential. On EUS, it arises from the submucosal layer i.e. the third echo-layer, and is hyperechoic, with smooth margin (Figure 3).

Figure 3: Lipoma



Cyst

Duplications cyst are benign embryonic remnant that are usually found incidentally, most often for investigation of other pathology. On EUS, they are anechoic and can be arising from the submucosal layer or extramural. They usually have a smooth and regular margin. They tend to be pliable and its shape could be changed with indentation using the echoendoscope (Figure 4).

Pancreatic rest

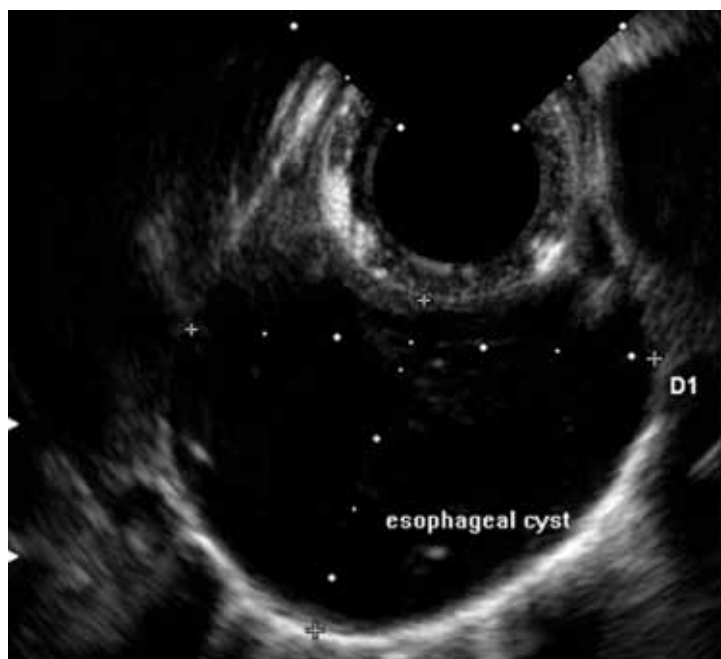
Pancreatic rest is ectopic pancreatic tissue arising as embryonic remnant. They compose of exocrine cells with cystic dilatation. It is usually located on the inferior aspect of the antrum or occasionally in the duodenum. Endoscopically, it usually has a central “umbilicus”.

On EUS, it arises from the submucosal layer (third echo-layer) in the majority of cases. It is of mixed echogenicity with isoechoic areas mixed with anechoic areas corresponding to small ducts.

Carcinoid

Carcinoid lesions are intramucosal tumours with malignant potential. These lesions tend to be small and found incidentally. On EUS, it is usually hypoechoic or isoechoic and arises from the deep mucosal (second echo-layer) and may involve submucosal layer (third echo-layer).

Figure 4: Esophageal cyst



Granular cell tumor

It is an uncommon oesophageal tumor and in general runs a benign course. It tends to be located at oesophagus and rarely in stomach. On EUS, it is usually hypoechoic, arising mainly from the deep mucosa (second echo-layer) and sometimes the submucosal layer (third echo-layer).

Varices

Varices usually appears as bluish, tortuous SM lesions on endoscopic appearance. Clinical information also in general helps with the diagnosis. On EUS, varices appear as anechoic areas, that are positive on Doppler ultrasound, arising from the deep mucosa (second echo-layer) or submucosa (third echo-layer). During scanning it can be appreciated that these form a tubular structure rather than spherical.

Role of EUS-guided fine needle aspiration (EUS-FNA)

Even though EUS-FNA is very accurate in obtaining tissue diagnosis of pancreatic or mediastinal lesions, the yield of EUS-FNA of solid intramural gastric or oesophageal lesion is not high and varies significantly from as low as 19% to up to 100%. The overall average yield is around 60%.

This is due to a combination of factors: the lesion are often small, more mobile (especially in stomach) during FNA, and there are scanty cells within the lesion. In addition, the aggressiveness of the GIST lesions is difficult to predict with cytology obtained on EUS-FNA alone. Factors that may be playing a role in determining aggressiveness of GIST include tumour size, mitotic activity, tumor necrosis, histological and immunochemistry characteristics. Thus, even if FNA showed evidence of cells supporting the diagnosis of GIST, it is hard to determine the malignant nature/aggressiveness of the lesion.

Although trucut biopsies can be done via EUS, the yield is not ideal either and is reported to be about 63%.

Thus, EUS-FNA or trucut biopsy is not done routinely and whether tissue sampling is performed depends on the preference of the echoendoscopist and is based on individual clinical scenario.

Approach to managing submucosal lesion

GIST

Management of GIST is controversial. Although there are many factors affecting the aggressiveness/malignant tendency of the GISTs, the most easily applicable factors are size and mitotic activity.

If a GIST is more than 5cm, surgery should be considered, as lesion is at least of intermittent risk of having metastasis or malignant tendency [29]. If lesion is between 2-5cm, some endoscopist will elect to monitor the lesion whilst others will consider surgery, depending on the individual clinical situation. GIST less than 2cm may not grow rapidly in size or change in size significantly. Thus, a significant amount of endoscopists will elect to observe the lesion without surgery. However, one should bear in mind that GIST can be associated with malignant change/metastasis even if it is small in size if the mitotic activity is high.

Leiomyoma

As it is hard to distinguish leiomyoma from GIST endoscopically or on EUS. Management will be similar to description above regarding GIST. If leiomyosarcoma is suspected on EUS, surgery obviously needs to be considered.

Lipoma

If lipoma is found and is confidently diagnosed on EUS, no further follow up is needed as it is benign.

Cysts

Cysts are in general benign and do not need regular follow up by EUS.

Pancreatic rest

In general, pancreatic rests are mostly benign. It is not routinely recommended to follow up pancreatic rest regularly with surveillance.

Carcinoid

Carcinoid lesion can be either sporadic or associated with atrophic gastritis or MEN syndrome. Management will depend on the type of carcinoid lesion. In general, lesion should be removed, either endoscopically or via surgery.

Treatment

Generally, submucosal lesions are followed up endoscopically or removed by surgery. There is a small amount of literature on endoscopic submucosal dissection of submucosal lesions [32], however, this technique is very time consuming and technically challenging. It may be considered if surgery is not able to be carried out and should be performed in centres with expertise well trained in endoscopic submucosal dissection. Other methods such as band ligation has been described, but should not be performed on lesions arising from the muscularis propria layer. Large GIST or GIST with metastasis can be treated with imatinib.

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EUS for Biliary Disease and Choledocholithiasis

Jillian Rosenstengel & Patrick R Walsh

Introduction

EUS is an ideal modality for assessment of biliary disease and choledocholithiasis due to its high sensitivity, specificity and low morbidity. Traditional approaches have included cross sectional imaging and ERCP. ERCP is not a good diagnostic tool as it has a high complication rate (2-5% risk of pancreatitis). Cross sectional imaging also has limitations. Stones are not well seen on CT, variable on MRI. Transabdominal ultrasound is sensitive and specific for stones in the gallbladder but not for the CBD, due to air artefact from the duodenum and ultrasound attenuation in obese patients. With respect to biliary disease, EUS is complimentary to cross sectional imaging. It is usually used to confirm an abnormality seen on other imaging modalities.

General principles

Ultrasound imaging of tissue is achieved by transmitting short pulses of ultrasound energy into tissue and receiving reflected signals. Fluid filled structures (gallbladder) have few reflections or refractions and are therefore dark or "anechoic". Solid structures (stones) lead to reflection and scattering and therefore appear bright or "hyperechoic" with posterior shadowing. Tissues containing fat are also brighter (more echogenic) than lean tissues.

Stones are seen as echogenic structure with or without posterior acoustic shadowing. They may be mobile. There may be associated signs; dilated CBD, thickened CBD walls, cholelithiasis, and pericholecystic fluid. "Sludge" is hyperechoic but does not have shadowing.

Strictures are seen as narrowing of the CBD. The narrowing may be extrinsic (mass or chronic pancreatitis) or intrinsic (tumour or benign). Often the duct is dilated above the stricture.

Test performance

Procedure

The procedure is usually done as a day only procedure under deep sedation (propofol and/or midazolam and fentanyl).

Stones

MRCP is a non-invasive imaging technique regarded as superior to CT for the diagnosis of CBD stones. MRCP has limited spatial resolution (misses small stones) and can miss stones in the peri ampullary region. Performance comparison is complicated by the absence of a true gold standard for comparison (both ERCP and intraoperative cholangiogram can miss small stones).

The specificity of EUS in ruling out the presence of CBD stones is in the 92-98% range. In addition it can detect sludge /microlithiasis which is often missed with other imaging techniques. Sensitivity is also high (>90%) and superior to MRCP. EUS is therefore the most accurate test for CBD stones, especially small stones.

In the work up of patients with suspected stones, cross sectional imaging is first line. Those with stones seen go straight to ERCP. Those with history and biochemical data suggestive but negative imaging are suitable for EUS prior to ERCP. EUS therefore avoids unnecessary ERCP's.

Strictures

Strictures can be divided into benign and malignant causes. They can further be separated into ductular lesions and compression from nearby processes. EUS can readily visualise the CBD and can help in the differentiation of a stricture into benign or malignant causes (especially with EUS FNA). IDUS and cholangioscopy provide detailed assessment of biliary strictures but are not widely available. (see part 2).

Complications

Complications from EUS are extremely rare. The standard risk for a diagnostic EUS is similar to that of conventional endoscopy. The risks include risks associated with sedation (aspiration, anaphylactic reactions, etc), scope related and FNA related. Scope related causes include minor trauma, bleeding and perforation. Perforation occurs at the high cervical region or in the duodenal bulb. FNA related complications include infection, bleeding and pancreatitis. Infection risk is highest if a non draining fluid structure is punctured. Antibiotic prophylaxis may be given in these cases.

Part 2: For those interested in further training

Technique

Assessment of the CBD for stones and other pathology has traditionally been performed using the radial instrument. This provides a “long” view of the CBD from the CHD and cystic duct take off to the ampulla. In more recent times as EUS becomes a more therapeutic procedure the CBD is often examined using a linear instrument. The linear instrument gives a piecemeal view of the CBD. In experienced hands accuracy is similar regardless of what scope is used.

Both techniques involve the placement of the probe in such a way as to obtain key anatomical land marks or “stations”. They are similar for both radial and linear instruments.

Radial

The scope is placed into the duodenal bulb. The balloon is inflated and wedged at the apex of the D1/D2 junction with maximal downwards deflection of the large wheel on the scope. The portal vein is then identified and placed on the left side of the screen. The liver and gall bladder should be on the superior half of the image. The scope is then slowly advanced with a gentle clockwise torque to provide an image of the CBD. Once this is obtained the CBD is traced both towards the ampulla and towards the liver until a long view is obtained. As the CBD is traced to the ampulla the MPD will come into view. This completes the stack view (portal vein, CBD and PD). The CBD is traced to the duodenal fall off (where the CBD enters the duodenum).

The scope is then placed to the D2 and the scope is straightened (as in ERCP). The ampulla is visualised endoscopically. The balloon is inflated and maneuvered so it “kisses” the ampulla. Air is aspirated. The scope is then slowly withdrawn. The ampulla will come into view as a relatively hypoechoic area containing 2 ovoid type anechoic structures close to one another. The one closest to the probe is the CBD, the deeper structure is the pancreatic duct. The ducts can then be traced from the ampulla.

Linear

The same stations are used. Often counter clockwise rotation and withdrawal of the scope is needed to visualise the CBD from the duodenal bulb. The CBD is seen as a circular/ovoid anechoic structure laying close the transducer. Long views are difficult to obtain, the duct is often viewed in a piecemeal fashion. Withdrawal of the scope gives views towards the hilum, advancing the scope gives views of the duct towards the ampulla. Doppler can help distinguish duct from adjacent vascular structures. Sometimes it is easier to obtain perpendicular views of the ampulla with the linear instrument.

Biliary Disease

Biliary abnormalities detected at EUS include stones, sludge, structures, thickened walls and related disorders in the ampulla and gallbladder.

Stones and sludge have been covered in the first section.

Bile duct strictures and masses

Differentiating benign from malignant biliary strictures remains extremely difficult. EUS improves the diagnosis in the setting of a known, or, suspected bile duct strictures with negative ERCP brushings and biopsies with cross-sectional imaging which did not demonstrate a cause for the stricture. In this setting the sensitivity and specificity for malignancy for the finding of a pancreatic head mass and/or and irregular bile duct wall was 88% and 100% respectively, a bile duct wall thickness $\geq 3\text{mm}$ had a sensitivity of 79% for malignancy and a specificity of 79% and the sensitivity of EUS-FNA for malignancy was 47% with a specificity of 100%. The sensitivity of EUS-FNA improved from 36% to 57% when a pancreatic mass was seen at EUS (as opposed to a thickened bile duct wall alone). In suspected hilar cholangiocarcinoma where ERCP brushings are negative, the accuracy, sensitivity and specificity of EUS-FNA is reportedly 91%, 89% and 100% respectively. EUS-FNA resulted in avoidance of major surgery in 20% of cases. In a similar series of proximal biliary strictures subjected to EUS-FNA, the sensitivity, specificity and accuracy of EUS-FNA were 77%, 100% and 79% respectively. EUS-FNA has a low negative predictive value, therefore a negative FNA result does not permit reliable exclusion of malignancy.

The question of what endoscopic technique to use to diagnose biliary strictures is not always straightforward. In the setting of biliary obstruction requiring decompression, ERCP is the obvious first step with subsequent EUS if a tissue diagnosis is not made. A reasonable approach is to start with ERCP when a biliary tumour is suspected and EUS when a pancreatic tumour is suspected.

Although not readily available, intraductal ultrasound features of malignancy include a hypoechoic appearance of the stricture with irregular margins, whereas benign strictures are more commonly hyperechoic or isoechoic with smooth borders. Endoscopically placed stents make the interpretation of findings at both EUS and intraductal ultrasound more difficult.

Ampulla

EUS is a very sensitive modality for detecting periampullary tumours. The sensitivity of EUS for detecting ampullary tumours ranges from 95% to 100%, compared to transabdominal US (5%-24%), CT (19%-68%) or MRI (81.3%). The sensitivity of ERCP for detection of ampullary tumours is equivalent to EUS. The utility of EUS for determining endoscopic respectability of ampullary lesions has not been thoroughly evaluated but currently it lacks accuracy as a single test. EUS used in combination with duodenoscopy and intraductal ultrasound may improve accuracy of staging of early lesions.

Gallbladder

The gallbladder is best seen from the antrum at EUS. It is essential to obtain a history of cholecystectomy from a patient prior to EUS to avoid confusing the gallbladder with cystic lesions of the liver or biliary tree. The sensitivity and specificity of EUS for the diagnosis of gallstones when previous imaging has been negative is 96% and 86% respectively.

4-7% of the healthy population have gallbladder polyps and these are classified either as neoplastic (adenomas and adenocarcinomas) or non-neoplastic (cholesterol polyps, inflammatory polyps, adenomyomatosis). EUS can depict the two-layer structure of the gallbladder wall with high resolution and is superior compared with transabdominal ultrasound for definition of small polypoid lesions and staging of gallbladder carcinoma has been reported in several studies. A proposed endosonographic scoring systems to differentiate benign from malignant polyps has been published. More recently Cho and colleagues describe the finding of hypoechoic foci as a sensitive and specific predictor of malignancy in gallbladder polyps (90% and 89% respectively).

Malignant gallbladder lesions tend to be sessile and broad based rather than pedunculated. Imaging appearances at EUS include hypoechoic heterogeneous masses, thickening of the wall, polypoid masses, loss of border between the liver and gallbladder and focal calcification of the gallbladder wall. The accuracy of EUS for the T staging of gallbladder carcinoma in one study was 100% for pTis, 75.6% for pT1, 85.3% for pT2 and 92.7% for pT3-4. EUS-FNA of gallbladder has been reported in small series without complication but caution should be exercised due to the risk of bile leak with peritonitis and tumour seeding.

Summary

EUS is a highly accurate imaging modality for the biliary tree. It is the most sensitive method for detection of small stones in the CBD. EUS is also useful in further defining biliary strictures identified on cross section imaging. It provides additional information to ERCP and is less invasive. EUS FNA allows cytological confirmation of the nature of the stricture or surrounding nodes. EUS is also useful in the assessment of gallbladder and ampullary tumors.

Further Reading

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SECTION 6

IMAGING OF THE SMALL INTESTINE

- Approach to Obscure Bleeding of the Gastrointestinal Tract *(Gregor Brown)*
- Endoscopic Imaging of the Small Intestine *(Mark Appleyard)*

Approach to Obscure Bleeding of the Gastrointestinal Tract

Gregor Brown

Introduction

“Obscure Gastrointestinal Bleeding” (OGIB) is defined as clinically significant GI bleeding for which no cause is found at gastroscopy and colonoscopy. The implication is that the bleeding is from the small bowel, although a range of pathologies may be ‘missed’ at routine endoscopy. OGIB may be overt (melaena or haematochezia) or non-overt (iron deficiency anaemia (IDA) without the obvious passage of blood per rectum), which to some extent will dictate the causes of the bleeding, and the urgency with which it should be investigated.

Over the past 5 years, the investigation and management of OGIB has undergone a paradigm shift due to spectacular advances in endoscope technology, namely capsule endoscopy and balloon enteroscopy (double or single), as well as the increasing availability of accurate CT angiography. Previously patients with OGIB faced a choice between repeated blood transfusions and iron infusions, or (often speculative) laparotomy with or without on-table enteroscopy. The management of OGIB in the current era is not only less morbid but also more successful, although it must be said that the outcome data remain incomplete.

Causes of OGIB

The causes of OGIB may be divided into those within reach of standard endoscopy, and those beyond (i.e. in the small bowel). Routine gastroscopy and colonoscopy have known miss rates, which will depend on the pathology, endoscopist factors (experience, skill, care, equipment, time taken, etc), and patient factors (ease of intubation, quality of prep, tolerability of the procedure, etc). More commonly missed pathologies include portal hypertensive gastropathy, vascular malformations, either isolated (particularly in the fundus or caecum) or multiple (such as GAVE – gastric antral vascular ectasia), ulcers of the stomach (Dieulafoy lesions, or hiatus hernia-associated Cameron’s ulcers) or duodenum (posterior cap or 2nd part), and colorectal cancer. Occasionally routine endoscopy may need to be repeated before embarking on a search for true small bowel causes of OGIB.

The causes of “true” OGIB are listed in Table 1. The list is not exhaustive. By far the most common lesions are vascular malformations, usually found in the proximal jejunum, and inflammatory lesions due either to NSAIDs or small bowel Crohn’s. Small bowel malignancy remains rare.

Table 1: Small Bowel Causes of OGIB.

Angiodysplasia
Non-steroidal enteropathy
Crohn's
Polyps (adenoma, hyperplastic, hamartoma)
Benign tumours (lipoma, leiomyoma)
Malignancy (adenocarcinoma, lymphoma, GIST, carcinoid, metastases - especially melanoma)
Jejunal diverticulae
Radiation enteritis
Enteric varices
Dieulafoy's lesion
Parasites
Meckel's diverticulum
Aorto-enteric fistula
Blue rubber bleb naevus syndrome
Osler-Weber-Rendu syndrome (hereditary haemorrhagic telangiectasiae)

Investigating OGIB

As noted above, capsule endoscopy (CE) and balloon enteroscopy (BE) have changed the approach to investigation of OGIB, as has the introduction of highly sensitive and routinely available CT angiography (CTA). How these tools are used depends on the clinical scenario, local expertise and availability. Broadly, the heavier the bleeding, the more accurate and relevant CTA becomes, however the mainstay of investigation of OGIB remains endoscopy.

All patients with anaemia should have at least a gastroscopy, which should be done urgently if there is heavy bleeding. Even bright rectal bleeding (if heavy) can derive from an upper GI source, and gastroscopy can not only be diagnostic but therapeutic.

Overt OGIB

In overt heavy GI bleeding, the next diagnostic step after a normal gastroscopy will depend on the factors alluded to previously. If the patient is cardiovascularly unstable, then CTA may be the next most appropriate step. If a bleeding point can be identified, it can be followed by formal angiography and embolisation. Colonoscopy in this situation is difficult, time-consuming and potentially risky, and should only be undertaken by those with suitable experience, expertise in colonic haemostasis, and equipment (i.e. a water pump and a colonoscope with a flushing channel). From a therapeutic perspective, the time to do such colonoscopy is when the patient is actively bleeding, although this necessarily limits the diagnostic capability. Importantly, the most common cause of haematochezia is diverticular haemorrhage, and the majority of these will settle spontaneously, so it is very reasonable to simply observe the stable patient with haematochezia and a normal

gastroscopy. "Urgent" CE may have a role for the actively bleeding patient with a normal gastroscopy, particularly when colonoscopy and ileoscopy shows transported blood from the ileum. However, the delay implicit in CE means CTA is usually more appropriate, being not only quicker but also more likely to accurately localise the lesion for therapeutic angiography (or surgery), if the study is positive.

Non-Overt OGIB

CE comes into its own for non-overt OGIB (i.e. iron deficiency anaemia), when good-quality gastroscopy and colonoscopy (often done in combination on the same occasion) are unhelpful and there is less urgency. In this setting, the yield of CE for causative small bowel lesions is over 50%. CE is also simple, safe and well tolerated. As with any form of endoscopy, expertise is required to accurately review and report CE studies. In its current form CE is purely diagnostic, having no therapeutic capability. It also struggles to accurately localise small bowel lesions, unless at either extremity of the small intestine. In experienced hands, however, it can provide uniquely useful information to guide BE, which offers the full gamut of endoscopic interventional therapeutics deep in the small bowel.

There is debate around the world as to the interplay between CE and BE, and how they should be used. In Australia we are lucky that CE is fully funded for this indication, provided certain clinical criteria are met, so we are able to use it as a screening tool for the more risky and time-consuming (from a proceduralist perspective, if not the patient's) BE. Thus, by using CE we are able to select those patients with lesions that are likely to be reachable with BE, which thereby can offer its therapeutic potential more fully and consistently. As such, the two modalities are very much complementary, not adversarial.

Notes on Specific Modalities used in OGIB

Gastroscopy

Careful and timely gastroscopy is essential in the work-up of OGIB. It should be done urgently (<24 hours) for overt bleeding, and within 30 days for IDA. It is the best diagnostic modality for upper GI bleeding, and can often be therapeutic also. Blood in the upper GI tract mandates a careful search for a source – if one cannot be found the examination should be repeated once the blood has cleared. Important lesions to consider are varices, ulcers (particularly hiatus hernia-associated Cameron's ulcers, subtle duodenal ulcers) and vascular malformations. Duodenal biopsies should routinely be taken for Coeliac disease in IDA.

Colonoscopy

Colonoscopy is often combined with gastroscopy in the investigation of IDA, because of the risk of dual pathology, as well as patient convenience. The yield diminishes in younger women, where it can be restricted to those with significant anaemia or relevant symptoms at the clinician's discretion.

In persistent or severe overt bleeding with anaemia urgent colonoscopy carries significant risk as well as being difficult and time-consuming. Bowel preparation is useful if time allows, and appropriate equipment (water pump and suitable colonoscope with a flushing channel) and experience are essential. A strong argument can be made for observing stable patients with haematochezia, as the majority will be diverticular in origin and will settle spontaneously. In unstable or persistently bleeding patients CTA may be more suitable as a means of localising bleeding to direct therapy (colonoscopy, angiography, or surgery) depending on the clinical circumstances and local availability and expertise.

Capsule Endoscopy

CE is fully funded by Medicare in Australia for recurrent or persistent bleeding and anaemia as long as a gastroscopy and colonoscopy (within 6 months) have not revealed a cause and the patient is over 10 years old. The yield in this situation is over 50%.

With the 'standard preparation' for CE (clear fluids after lunch the day before, fast from midnight), approximately 20% of studies are incomplete (i.e. the capsule has not entered the colon by the end of the study – usually 8 hours). Drugs that enhance gastric emptying (e.g. metoclopramide) or bowel preparation may improve the completion rate, but the data are mixed.

The major complication of CE is non-excretion of the capsule, although this occurs in <1% of studies. Usually it is due to small bowel strictures (Crohn's Disease, NSAIDs or malignancy), but overt small bowel obstruction is extremely rare. If reachable endoscopically the capsule can be removed, but surgery may be required – importantly the cause of the capsule retention (i.e. the stricture) can usually be dealt with at the same time.

Balloon Enteroscopy

There are two balloon enteroscopy systems (double (DBE) and single (SBE)) from different manufacturers. Both have a flexible overtube with a balloon on the tip; the DBE has an additional balloon on the tip of the scope itself. The balloons are independently inflated and deflated by a pump under the control of the operator, gently fixing the instrument to the otherwise mobile small bowel wall to allow deep small bowel intubation. Performing BE is complex and time consuming (often an hour or more), and generally requires two operators. The risk of aspiration is significant, and many choose to routinely intubate patients having antegrade BE. Post-procedure discomfort is common, but is reduced by the use of CO₂ for insufflation – this also improves insertion depth.

In Australia, BE is usually performed to further investigate or treat a small bowel abnormality identified by CE (or another imaging modality). The 'direction' of BE is determined by the CE findings – if the lesion(s) are in the proximal 60% of the small bowel by transit time, antegrade BE is used; if in the distal 40%, retrograde BE is used. If the lesion is not reached a tattoo is placed at the limit of insertion, and the alternative direction can be used (usually as a separate procedure), but total enteroscopy is rarely achieved in the Australian setting.

As BE usually follows CE to define suspected lesions, the rate of therapeutic intervention is higher than 'routine' endoscopy, with a concomitant increase in the risk of the procedure, particularly bleeding and perforation. Pancreatitis is a rare risk of BE, possibly due to traction on the ampulla during repeated insertion/withdrawal cycles. While virtually the full gamut of endotherapy is available with BE, the length of the scope (210cm), current narrowness of the working channel (2.8mm) and routine formation of loops when deep in the small bowel mean that some interventions may be difficult or impossible (e.g. balloon dilatation). Hopefully technical developments both in the enteroscopes and relevant therapeutic consumables will improve these negative aspects of BE, but currently it is a procedure that should only be performed in referral centres with the necessary interest, expertise and case volume.

CT Angiography

As multislice CT scanners become routine, CTA has become increasingly available, and can usually be performed quickly and without preparation or sedation. It is not limited by 'access' to the GI tract that can be problematic for endoscopy. The major risk is of contrast-related renal impairment, and the major limitation is the need for active bleeding at the time of the scan to accurately define a bleeding source. Once defined, however, therapeutic angiography is an immediate option where available and clinically appropriate. The major risk of embolisation is infarction of the target organ, but this is diminishing with increasingly selective embolisation.

Conclusion

The approach to OGIB has changed dramatically in recent years to be less morbid and more successful. Gastroscopy remains the index investigation, with subsequent investigations determined by the clinical scenario, in particular whether the bleeding is overt or occult, and whether the patient is stable or not. When the presentation is of IDA, colonoscopy is the next investigation, and if not informative is followed by CE as a screening test for BE or surgery. When the bleeding is overt, watchful waiting may be appropriate, with elective colonoscopy to clarify the cause of bleeding once it has settled. If the bleeding persists or the patient is unstable, CTA can be useful to localise the bleeding for therapeutic angiography. Urgent colonoscopy in the right hands can be both diagnostic and therapeutic, but comes with an increased risk of harm. CE is of limited utility in this setting due to the inherent delays and difficulty identifying and localising causative lesions in the presence of large amounts of blood.

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Endoscopic Imaging of the Small Intestine

Mark Appleyard

Introduction

Endoscopic imaging of the small bowel has until recently been limited to duodenal examination during upper GI endoscopy, terminal ileal examination during colonoscopy and push enteroscopy of the proximal small bowel. These modalities had both diagnostic and therapeutic roles. Even though the entire small bowel could be examined with tools such as the sonde enteroscope, they were limited to diagnostic roles in highly specialised research centres.

In the last decade, there has been a revolution in the endoscopic arena of the small bowel. This was first seen with the development of capsule endoscopy (CE) quickly followed by balloon assisted enteroscopy (BAE). Since then, there has been extensive research work clarifying the role of these tools in the management and therapeutics of the small bowel. These new tools play a vastly superior diagnostic role in patients with obscure gastrointestinal bleeding (OGIB) with BAE providing an effective therapeutic endoscopy alternative to more traditional therapeutic modalities such as embolisation during angiography and surgery. The role of intra-operative enteroscopy (IOE) is becoming more limited with the improved diagnostic and therapeutic capabilities of these newer techniques. This is reserved for rare cases and will not be discussed further in this chapter.

The management algorithms now available for small bowel disease include both these endoscopic developments with many new indications and innovations on the horizon.

General Principles

There are two key issues that will help decide which endoscopic tool is best. The indication and the need for a diagnosis or therapy are crucial elements. CE is essentially a diagnostic test with BAE being both diagnostic and therapeutic. The more traditional and available push endoscope plays a similar role for proximal small bowel lesions.

Indication

The vast majority of small bowel endoscopy is performed for OGIB bleeding. In Australia, OGIB was the only Medicare rebatable indication for CE until PJS was recently added to the MBS. In 2007 the American Gastroenterological Association (AGA) position paper on management of OGIB places CE as the first diagnostic test and the most pivotal step in the investigation of this problem. The traditional techniques of small bowel x-ray, CT and angiography play a very limited role and should not precede CE. Depending on the result of CE the next appropriate step can then be determined. The majority of patients will not need endoscopic intervention and hence more invasive diagnostic and therapeutic modalities can be limited.

Another common indication is small bowel Crohn's Disease. CE can play an important role in the diagnosis of this disease however the risks of a retained capsule rises significantly if a patient is known to have Crohn's Disease so disease assessment is not usually an indication. Hence, the endoscopic role of CE is limited. BAE however plays a very important role in this disease. It can not only play an important diagnostic role with the additional of endoscopic biopsies and mucosal histological assessment but the therapeutic role for structuring disease cannot be underestimated.

Small bowel polyposis is a growing indication whereas most studies show non-specific pain to have a very low yield for both procedures.

Diagnosis or therapy?

Bidirectional BAE has a similar diagnostic rate to a single CE with inferior total enteroscopy rates hence CE is the first step for diagnosis. The ideal endoscopic tool to deliver targeted endoscopic therapy varies according to the location and type of lesion(s) found. The most available and longstanding tool is push enteroscopy. This endoscopic tool is used primarily for antegrade enteroscopy with a depth of insertion limited to the proximal small bowel. In the case of OGIB, up to 44% of identified lesions can be managed with PE.

The most recent endoscopic innovation for the small bowel is a group of enteroscopic techniques now known as BAE. The first described is the double balloon enteroscope (Fujinon) and was described in 2001 by Yamamoto. This technique allowed for deeper small bowel intubation from both the antegrade and retrograde approaches. Studies have shown that the ideal approach can be determined by the timing of the lesion as seen by CE, a figure determined by achieving total enteroscopy. Olympus developed the SBE with preliminary studies showing promise with similar results to DBE. Newer endoscopic tools included in the BAE category include the Spirus system and the Pentax system both not yet in use in Australia.

Technique

Capsule Endoscopy (CE)

CE does not require traditional endoscopic techniques and can be performed in the clinician's rooms easily and without sedation. The placement of recording equipment and swallowing the capsule is simple and easy. The key technical issues are more related to the preparation for this technique with cleansing and prokinetic use. The general consensus is that bowel preparation improves the quality of the capsule imaging, however, it does not improve yield or total enteroscopy rates. There is ongoing controversy about prokinetic use with many authors supporting the regular use of prokinetics to maximise total enteroscopy rates with others rejecting this notion.

Reading the capsule images requires time and experience, there is no agreed minimum number of procedures reviewed to enable determination of competency.

Push Enteroscopy (PE)

This relatively simple and readily available technique is a very good option for proximal small bowel lesions. It is performed in the typical endoscopy left lateral position mainly under conscious sedation. There are no good guidelines to determine which proximal lesions are best targeted by PE but lesions more than 25% down the small bowel are unlikely to be reached by PE.

Balloon Assisted Enteroscopy (BAE)

BAE essentially includes new enteroscopes and techniques utilising balloons with overtubes. The first described is double balloon enteroscopy (Fujinon), with the recent addition of single balloon enteroscopy (Olympus). Alternatives such as Spirus are not currently available in Australia. DBE and SBE require more a more traditional endoscopic setup and skill set even though they have technical nuances. In most circumstances these procedures will be used to target known pathology and this most often is diagnosed by CE or CT scanning.

As a general principle, a lesion in the proximal two-thirds of the small bowel should be approached orally (antegrade procedure) whereas the distal third should be approached anally (retrograde procedure). Antegrade procedures require fasting for at least 8 hours unless a small bowel stricture is suspected so a fluid diet for 24 hrs prior is recommended so food debris is not encountered. Retrograde procedures require a comprehensive bowel preparation as any residual stool can often create friction between the enteroscope and overtube thus making the procedure difficult.

Most procedures can be performed under sedation however anaesthetic support and even endotracheal intubation should be considered for patients who are at risk from co-morbidities, difficult to sedate patients and procedures expected to be prolonged and therapeutic. Antegrade procedures are more likely to need anaesthetic support compared to retrograde procedures. Patient positioning is similar to routine endoscopy however the supine position can make retrograde BAE easier.

Relevant literature and outcomes

OGIB is the main indication for small bowel endoscopy and the vast majority of the literature is based upon these patients. The initial studies for CE in OGIB showed clear diagnostic superiority of CE over traditional tools such as small bowel series, CT and push enteroscopy. The overall diagnostic yield of CE in OGIB was approximately 60% and this figure has remained consistent amongst most series except in cases of acute ongoing OGIB where the diagnosis can approach 100%.

Depending on the CE finding, a decision can be then made if a therapeutic endoscopy procedure is required. The vast majority of patients will not require enteroscopy, however, in those who do need it accurate targeting by CE can limit the endoscopic interventions required to treat the lesion. The average number of BAE procedures required for those who need endoscopic intervention is about 1.3 procedures per person. The CE findings can also help determine the most appropriate endoscopic tool with proximal lesions

being suitable for PE whilst deeper or very distal lesions best suited for BAE. One key step in targeting lesions endoscopically after CE is to have achieved total small bowel views with the capsule endoscope study. Using the total small bowel transit time and placing the time a lesion is seen it can be easy to calculate the position of the lesions. This is very useful when making a decision for route of entry for BAE.

Patients with Crohn's disease often have small bowel involvement and determining diagnosis, disease extent and severity is very important for managing their disease. In comparison to OGIB these patients have a higher rate of retained CE with about 2% retention if patients are suspected of having CD and up to 10% retention if they are known to have CD. Hence CE can be problematic in these patients and alternatives are often required. One good option is the patency capsule to "test run" the small bowel prior to the real capsule and this has proven very effective. Unfortunately SBS remains unreliable if used for stricture exclusion. PE and BAE do offer the benefit of histology and therapy for small bowel strictures however good workup of patients is required in all cases prior to using any of these small bowel modalities.

Polyposis syndromes are emerging as a group of patients who can really benefit from these small bowel enteroscopy techniques. Currently in Australia, PJS is approved for surveillance CE. It is clear that CE is the single most accurate test for polyp detection, size estimation and positioning. PE or BAE can then be used to remove lesions hence avoiding the need for small bowel surgery in many cases. IOE can be used in those patients where prior surgery has made BAE difficult and for lesions that cannot be reached.

Emerging indications for both CE and BAE include exciting areas such as capsule colonoscopy and BAE ERCP in altered anatomy with new modifications and accessories improving success rates at a very rapid rate.

There are two categories of patient that pose great difficulty in OGIB. Firstly, patients with negative CE who have ongoing bleeding and also, patients who have ongoing bleeding despite multiple endoscopic evaluations and endoscopic interventions. One important fact is that despite our best efforts some 25% will have ongoing bleeding as seen in one cohort who underwent IOE to manage their OGIB. In addition, several studies show that up to 25% of patients will have a "missed lesion" found on subsequent enteroscopy that was not detected on routine endoscopy and colonoscopy. The difficulty is when to repeat procedures and how many times despite ongoing bleeding and deciding when to stop can be a very difficult to do.

Potential complications and adverse events

Complications of CE are rare with retained capsule being the best recognised. Depending on the indication the risks of retained capsule can be as high as 10% in cases on known Crohn's Disease. Many argue that surgery for retained capsules is not a complication because surgery would have been the definitive intervention in these cases anyway.

Enteroscopy literature is now extensive with good data regarding complications. In the case of BAE it is expected that any complication for a diagnostic BAE should be less than 1% however therapeutic procedures can have complication rates up to 4% and include perforation, bleeding, pancreatitis and anaesthetic complications.

Conclusions

Endoscopic imaging of the small bowel has developed rapidly over the last decade with new diagnostic and therapeutic options. New algorithms have been developed to guide patient's management and these vary according to indication. Future developments in this field will probably be in refining the use of these tools, however, exciting new modifications and accessories will expand their indications for both small bowel and non-small bowel use.

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Figures 1a, 1b, 1c:

1a: Capsule study shows a stricture prior to non-passage of the capsule.



1b: DBE identifies the stricture and shows similar endoscopic features.



1c: After successful endoscopic balloon dilatation the capsule is retrieved with a standard endoscopic snare.



Figure 2: Multiple classic angioectasia in the proximal small bowel have been successfully ablated using APC during standard push enteroscopy.

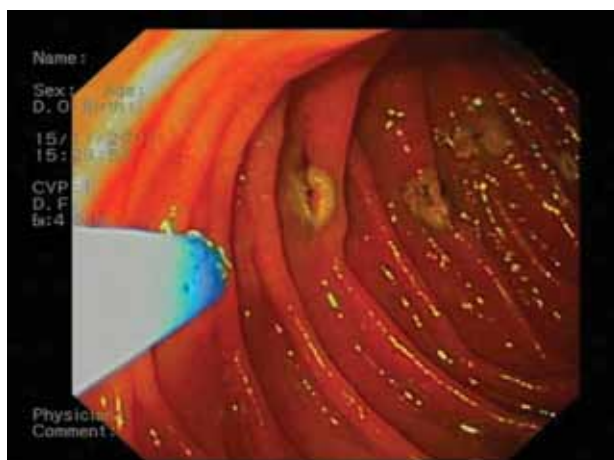


Figure 3: Successful polypectomy during antegrade DBE after capsule endoscopy identified the lesion in the proximal small bowel performed for OGIB.



