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Health Sciences
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21st Annual Controversies and Problems in Surgery Symposium 2017

Making wise choices for difficult surgical problems

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Welcome Note: Message from the Head of Department of Surgery

Prof Taole Mokoena

I should once again welcome back those who have attended our Controversies and Problems in Surgery Symposium before, and a hearty welcome to novices and trust that they too will continue to support the Symposium.

This year we choose a theme that we trust will be thought provoking not only to the presenters but also to all the attendees. Medical practice is such that there is always an alternative to management of any particular clinical problem. It is thus sometimes difficult to make the correct choice. We hope the speakers will help us steer towards better and wise choices for different challenging clinical scenarios.

I should thank the presenters for accepting the challenge to present at this conference. We know that each and every one of you is busy but you thankfully devoted time to prepare for this.

We cannot thank the Trade enough for their support in these times of austerity. Keep digging deeper into your treasure troves to support continuing professional development in South Africa.

I thank the members of staff in the Department who toiled hard to put together the programme and its related logistics.

I wish you all an enjoyable and fruitful learning experience.

Yours Sincerely,

Prof Taole Mokoena

Message From **The Dean**

Prof BG Lindeque
Deputy Dean and Chair of School of Medicine, University of Pretoria

Dear Colleagues

On behalf of the Organisers, Dept. Surgery, University of Pretoria, and the School of Medicine, a hearty welcome to this year's edition of Controversies in Surgery.

Clinical practice is under constant pressure due to the number of patients we see, the intensity of disease that we encounter, and the width of the disease spectrum in our country. Add to this the limited half-life of knowledge and facts, the continuous inflow of new studies and data, the development of new perspectives, and new questions being asked about previously understood topics. Another perspective is added by the threat of litigation that hangs over our heads.

How do we maintain excellence? How do we ensure that our best is good enough? How do we remain conversant in our fields? The successful adult learner has internal drive, has interest in the subject matter, has stamina to go through programmes, has capacity to absorb and interpret new facts and perspectives.

Controversies are a tool to allow for this successful adult learning. It is a key CPD programme in this Faculty and is worthy of your support. Thank you for attending. Thanks to the organisers for producing. I trust we will all enjoy this meeting.

Kind regards,

Prof BG Lindeque

Massive Upper GIT Bleeding: Surgery or embolization after failed Endoscopic Management?

Prof Sandie Thomson CHM, FRCS (ED & ENG) FRCP(ED)

Professor Sandie Thomson Division of Gastroenterology Department of Medicine Faculty of Health Sciences, University of Cape Town

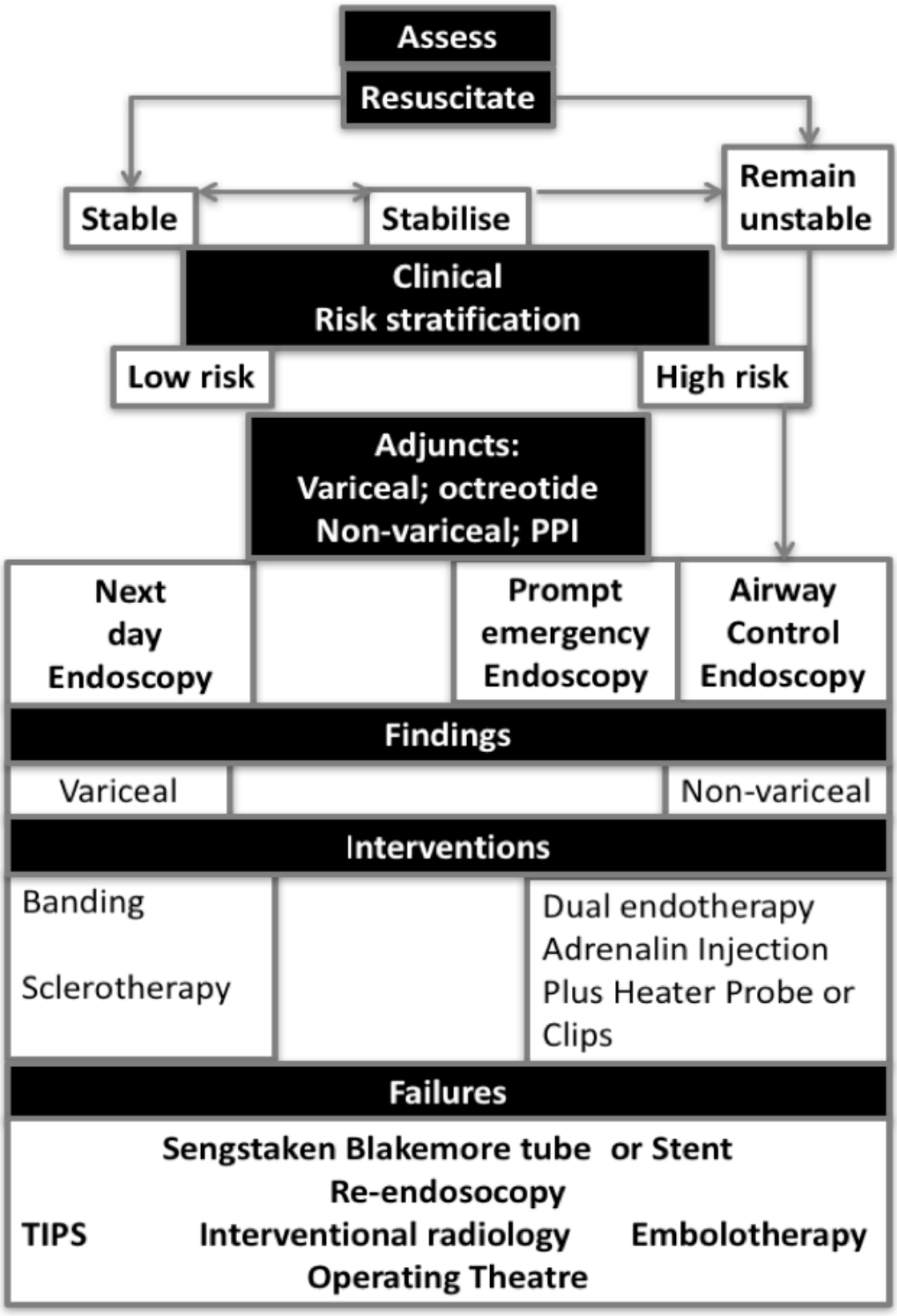
The causes

Upper gastrointestinal haemorrhage has a variety of causes (Table 1) and is the commonest complication of peptic ulceration and portal hypertension. Peptic ulceration in the duodenum or stomach and oesophageal and gastric varices are the conditions which most often present with life-threatening haemorrhage.

Tabel 1 Causes of Upper Gastrointestinal Bleeding related degree of bleeding severity

Degree	Site		
	Oesophageal	**Gastric**	**Duodenal**
Major Common	Varices	Gastric Varices	Benign Ulcer
	Mallory-Weiss Tear	Benign Giant Ulcers	
Major Uncommon		Dieulafoy's Lesion	Haemobilia
		GIST	Haemosuccus Pancreas
			Aotoenteric Fistula
Usually Minor/Chronic	Oesophagitis	Gastritis	
	Cancer	Gastric Antral Vasculat Ectasia	
		Gastric Cancer	

The key elements of an approach to this medico surgical emergency are outlined below


Assess
Resuscitate
Stable
Stabilise
Remain unstable
Clinical Risk stratification
Low risk
High risk
Adjuncts: Variceal; octreotide Non-variceal; PPI
Next day Endoscopy
Prompt emergency Endoscopy
Airway Control Endoscopy
Findings
Variceal
Non-variceal
Interventions
Banding
Sclerotherapy
Dual endotherapy Adrenalin Injection Plus Heater Probe or Clips
Failures
Sengstaken Blakemore tube or Stent
Re-endosocopy
TIPS
Interventional radiology
Embolotherapy
Operating Theatre

Resuscitation and assessment

Whatever the cause, the most important initial management is to assess the haemodynamic parameters and institute appropriate resuscitation measures early. In those who are haemodynamically unstable aggressive resuscitation has been shown to improve outcome. Ninety five per cent of patients will stabilise and it is important that they are fully assessed by history and physical examination. This allows management to be strategized based on whether the individual has variceal or non-variceal bleeding. The former is most likely if they have stigmata of chronic liver disease and portal hypertension and the latter assumed in the absence of these findings.

Risk stratification

A variety of clinical factors laboratory tests endoscopic findings can be incorporated into the risk stratification of patients who present with upper GI bleeding. These systems predict the likelihood of continuing to bleed or of rebleeding, and the risk of death. The most important clinical factors are age over 60, and shock on admission. Concurrent medical therapy in particular with NSAIDs and anticoagulants, which affects platelet function and clotting factors respectively increase rebleeding rates and require optimization

Monitoring and adjunctive measures

These stratification systems can also direct appropriate monitoring of high-risk patients prior to endoscopy, which is the next step. During resuscitation and stabilisation appropriate adjunctive measures are of proven benefit. In clinically high-risk patients with suspected non-variceal bleeding, intravenous PPI therapy elevates the pH to above 6, allowing stable clot formation and lessens lysis. In variceal haemorrhage benefit has been shown from the early use of vasopressors or somatostatin analogues, which lower portal venous pressure. Similarly antimicrobial therapy improves outcome by treating or preventing infection because variceal haemorrhage in patients with decompensated chronic liver disease is often precipitated or worsened by infection.

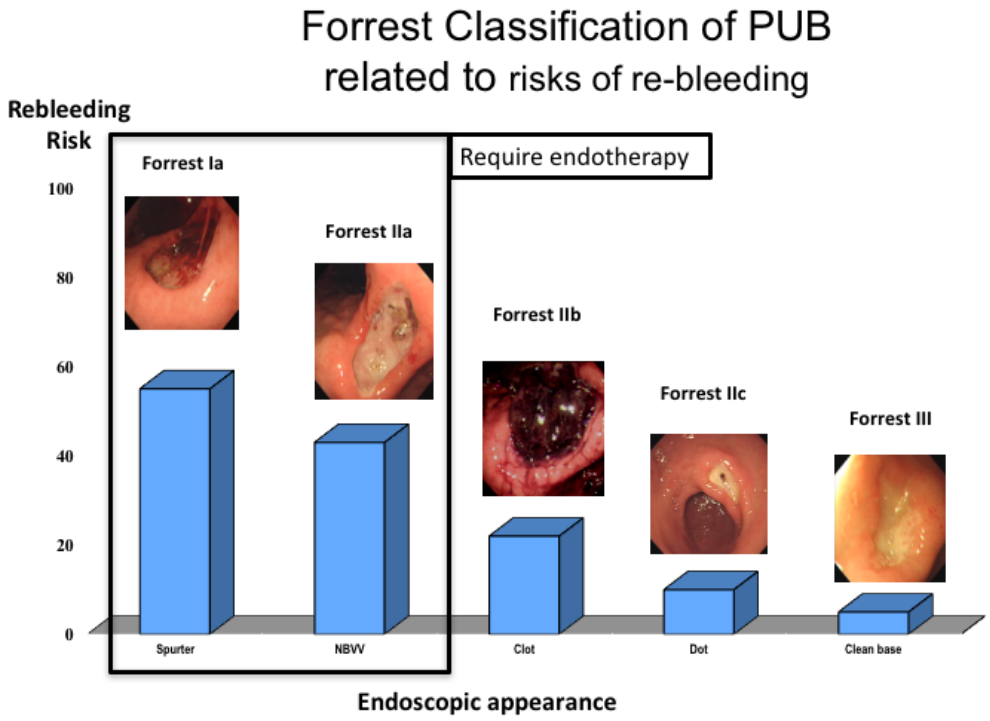
Endoscopy

The aim of endoscopy is to establish the cause of bleeding and, using endotherapy, control the bleeding or reduce the likelihood of further bleeding.

Endotherapy

Non-variceal haemorrhage

Ulcers can be classified into different categories according to the Forrest classification.



This defines the risk of rebleeding and is the determinant indicating which ulcers should have endotherapy to either control the bleeding or reduce the risk of it recurrent bleeding. Various endotherapies that have been used to control the bleeding.

More lasting control can be achieved by adding one of the following two techniques, clips or thermal co-aption with a heater or gold probe. For the majority of patients these methods should control even active bleeding 80 - 90% of the time.

Variceal

The method of choice for oesophageal varices is banding and for gastric varices cyanoacrylate. In patients with variceal bleeding, the bleeding often stops in those with good liver reserve. In those with massive bleeding and often decompensated liver disease the Sengstaken-Blakemore tube can be used when visualisation of the oesophagus is not possible due to active bleeding. Alternatively, a covered 30 mm oesophageal stent has been used as an alternative form of temporary tamponade. When these devices are removed endotherapy may well be successful. In the face of recurrent bleeding in this setting the interventional procedure of choice is a TIPS shunt which, when placed successfully, will reduce the portal pressure below 12 mmHg and control the bleeding.

Rebleeding Risk in Peptic Ulcer Patients

The vast majority of upper gastrointestinal bleeding episodes are not severe

Even those who present with hemodynamic instability usually stabilize with appropriate resuscitation. Experienced endoscopists can usually control the bleeding by endotherapy. Improvements in endoscopic hemostatic techniques and medication have meant that only 13% of patients develop rebleeding. As a result the requirement for emergency surgery has dropped from approximately 20% in the 1970s to less than 2% in the present day. Rebleeding is a significant predictor of risk for mortality and can often be salvaged by further therapeutic endoscopy. Patients who fail endoscopic hemostasis are often elderly with multiple comorbidities making them high risk for morbidity and mortality after emergency surgery. Mortality ranges from 10%−30% following operative management.

Major bleeding culprits

Overt and evident

The patients who have the most severe bleeding episodes are those who have esophageal varices under high pressure or those in whom the bleeding is from a major artery. Peptic ulcer sufferers at risk of severe bleeding are usually those

with giant ulcers which have eroded into one of the branches of the left gastric artery or the gastroduodenal artery. In these individuals the source of bleeding is readily identified at endoscopy.

It is in this category patient that consideration is being given for the use of interventional radiology rather than repeat endoscopy or surgery to control the recurrent haemorrhage. A collective review in 2014 which had one multicenter prospective and 8 retrospective cohort whose accrual times were approximately 6 years. The cohort sizes were between from 23 to 150 patients with a total of 711 patients 347 of whom had embolization and 364 who had surgery. Those who underwent TAE were significantly more likely to have IHD and be on anticoagulants. Compared with TAE, surgery was associated with a lower risk of re-bleeding but a similar mortality. In a recent Finnish national audit mortality and rebleeding rates did not differ between TAE and surgery. In their 1583 hospital admissions for bleeding gastric or duodenal ulcers TAE or surgery was necessary in 85 (5.4%) patients, 43 receiving surgery and 42 TAE. In 16 of the TAE's the procedure was prophylactic and two underwent TAE to localize and treat the bleeding. The remaining 24 received TAE for active or recurrent bleeding after endoscopy. The comparison included only patients with active or recurrent bleeding. Rebleeding rate was 25% after TAE and 16.3% after surgery. Mortality rate was 12.5% after TAE and 25.6% after surgery. Post-procedural complications were less frequent after TAE than surgery 37.5 vs. 67.4%. Out of 85 procedures, 14 (16.5%) took place between midnight and 8 a.m. with, all night time interventions being surgeries. With less postoperative complications they concluded that TAE should be the preferred hemostatic method when endoscopy fails. They identified that hypotension, hemoglobin of 10 g/dL, fresh blood in the stomach, ulcer size 4 2 cm, and active bleeding during endoscopy were factors which individually increased by 2-fold the risk of rebleeding. In a systematic review, Elmunzer et al also identified similar predictors of recurrent hemorrhage after endoscopic hemostatic therapy but also found comorbid illness, and posterior duodenum and lesser curve ulcers were significant additional risk factors.

Overt and Obscure

It is useful to categorize upper gastrointestinal bleeding as obscure when the source is not evident on upper endoscopy. These individuals with obscure

bleeding are further subdivided into those who have overt bleeding (haematemesis and or melaena) and those in whom the bleeding is occult most often presenting with anaemia. It is the former patient category that are particularly troublesome to manage. One must be guided by the history to identify the potential sources. A history of chronic pancreatitis should alert one to the possibility of bleeding from an inflammatory process which has eroded into an artery to form a false aneurysm which then ruptures into the pancreatic ductal system. These individuals are bleeding from either a pancreatico-duodenal arteries or from the splenic artery. Similarly a history of gastrointestinal bleeding following liver pathologies or interventions is important to elicit. Hepatic trauma, abscesses, PTC or liver biopsy should alert one to the potential for haemobilia. In this situation it is in the hepatic arteries or major parenchymal branches that false aneurysms are formed. These patients may also be jaundiced as clot in the bile duct can cause a biliary obstruction. The clue to the diagnosis here is the fact that there is usually no blood in the stomach. It is only if one inspects the second part of the duodenum with a side viewing scope that the diagnosis can be made by visualization of blood coming out of the ampulla of vater. In these two instances the treatment of choice is intervention radiology these lesions can be obliterated by platinum coils, gelfoam particles, cyanoacrylate, polyvinyl alcohol particles or combinations of these methods. It is important that collaterals are also embolized to prevent re bleeding. Specific catheters allow more precise delivery and stents enable control of bleeding when preservation of flow is essential.

Start and Stop

Many of the others with obscure overt bleeding have lesions which are particularly difficult to detect because they start stop and bleeding. The archetypal example of this is the Dieulafoy's lesion (calibre persistent artery) in which a very small artery which has eroded through the mucosa bleeds profusely and stops. It is important that these individuals stay until they can be endoscoped during their next bleeding episode when the lesion is likely to be detected and either clipped or banded. A gastrointestinal stromal tumour which has eroded through the mucosa can also present in this manner. These individuals may present with a minor herald bleed which is the typical presentation of an aortoenteric fistula of the third part of the duodenum. Though these are very occasionally due to a tuberculous or inflammatory aneurysm they invariably occur post aneurysmal surgery. Endoscopy in these

individuals is often negative as the bleeding is distal to the ampulla of vater. A high index of suspicion is needed in these cases so that an appropriate CT can be performed the diagnosis established and a surgical performed before a catastrophic bleeding episode occurs.

Portal hypertensive bleeding

These with high pressure varices particularly those due to decompensated cirrhosis are particularly problematic. These individuals can be risk stratified based on the endoscopic findings based on size and evidence of recent bleeding with red whale signs cherry red spots. Current evidence is that those with advanced cirrhosis are better served with TIPS as first line therapy than endotherapy.

Conclusion

Management of massive and recurrent upper gastrointestinal bleeding remains a challenge. Those with suggestive histories and a negative endoscopy should move to CTA to guide angioembolic/stent therapy, or surgery in the case or aortoenteric fistula. The lesions which stop and start are also problematic and for these repeat endoscopy at the time of bleeding is key establishing a diagnosis and planning intervention. The patients with varices have a variety of options but TIPS remains the interventional technique of choice unless the venous anatomy is unfavourable in which case an oesophageal transection is the only viable acute option. In those with a localizable source at endoscopy dual endotherapies have improved their efficacy in recent decades. Despite their low failure rate there are well quantified risk factors for failure of endotherapy. TAE has become increasingly popular with more evidence showing its safety and efficacy. TAE is associated with a higher failure rate than surgery. Microcatheters and glues have the potential to impact favorably on success rates of TAE. The use of TAE can avoid surgery in some patients and does not seem to adversely affect outcomes in patients who eventually require surgery. Whether in those patients with large ulcers with episodes of hypotension on admission whose bleeding is initially controlled by endotherapy merit a pre-emptive TAE or a wait and see approach is unclear.

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When is it justifiable to perform a Definitive Peptic Ulcer Surgery during emergency management to a Perforated or Bleeding Ulcer in the PPI and Helicobacter Pylori era, and which operation to do?

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Introduction

Peptic ulcer disease (PUD) is a significant cause of morbidity and mortality worldwide, although the global prevalence has decreased (1). This is partly explained by the recognition of the key role of Helicobacter pylori in the pathogenesis of PUD and the efficacy of H. pylori eradication (2). The decrease in prevalence of peptic ulcer disease has not, however, been mirrored by a decrease in complications. Bleeding from peptic ulcers remains the most frequent complication but perforation is associated with the highest mortality (3).

The management of peptic ulcer disease has evolved significantly comprising primarily medical treatment with proton pump inhibitors (PPIs) and the antibiotic eradication of H. pylori. The efficacy of medical management has mostly eliminated the need for acid reducing surgery (1). Surgery still has a role, with 33% of surgery for upper gastrointestinal pathology in a US review being for PUD. Of these surgeries, 81% were for bleeding or perforated ulcers with a 23% hospital mortality (4).

Epidemiology

PUD is responsible for seven times the number of deaths from appendicitis globally, with perforation responsible for 70% of those deaths (1). Complications are seen in approximately 11% of patients (5).

In low to middle income countries PUD is responsible for 230 000 deaths and seven million disability adjusted life years annually (6), this incidence is several times greater than in high-income countries (7). A review of literature from Sub-Saharan Africa showed 6594 patients undergoing surgery for PUD, and contrary to the US data the main indication was perforation(8). In low- and middle-income countries the presentation of PUD is similar to the patterns described in developed countries during the middle half of the 20th century; that is duodenal ulcers in male patients aged approximately 40 years old. In recent times the median age at diagnosis has increased by more than two decades and the sex distribution has evened out (7).

Duodenal ulcers remain more common than gastric although the greatest decrease in ulcer incidence was in duodenal ulcers (9). In the general population the incidence of bleeding is 0.27-1.06 per 1000 person-years while perforations are 0.03 – 0.30 per 1000 person-years (10).

The options

Surgery for PUD ranges from the simple oversew of a bleeding ulcer or primary closure of a perforated ulcer to acid-reducing procedures and gastric resections.

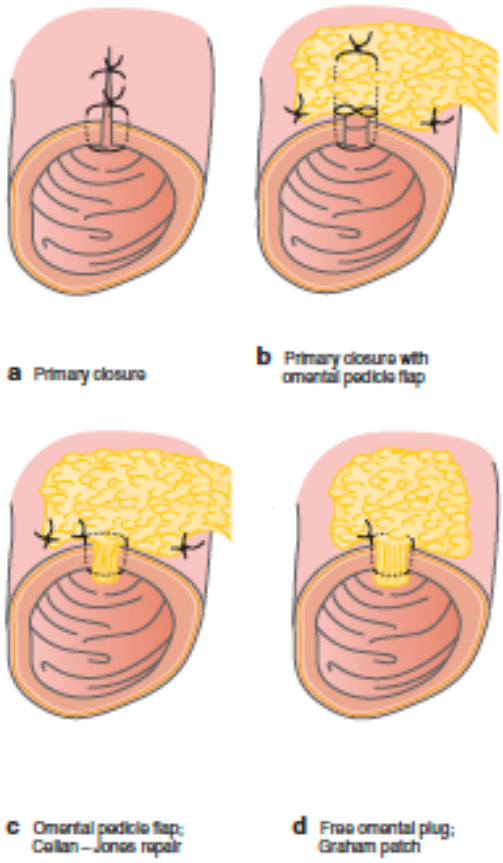
Bleeding PUD

Oversew – this consists of an anterior longitudinal duodenotomy or gastrostomy and a figure of eight suture at the superior and inferior borders of the ulcer. A second suture is placed for the transverse pancreatic branches that enter the gastroduodenal artery.

Perforated PUD

Simple closure without an omental patch – this is the simplest technique.

Omental patch – there are various options for placing an omental patch. They are a simple suture with a pediculised omental patch, interrupted sutures reninforced with an omental overlay or a free omental patch (Graham technique) (11).



(1)

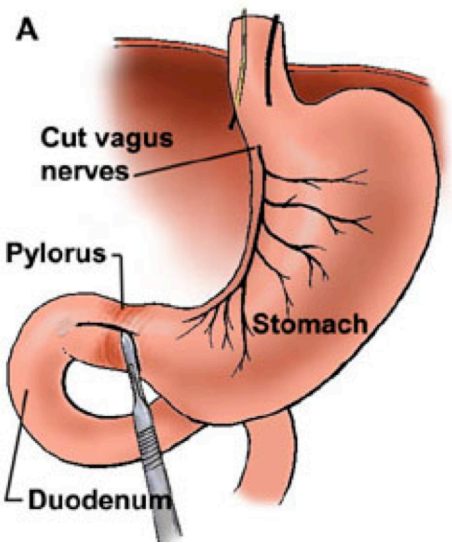
A perforated ulcer of greater than 2 centimetres in the duodenum presents a challenge. There is no standard management and the options include a controlled tube duodenostomy, jejunal pedicle graft or serosal patch, pedicle omental plug, partial gastrectomy and gastric disconnection (9).

Acid reducing surgery

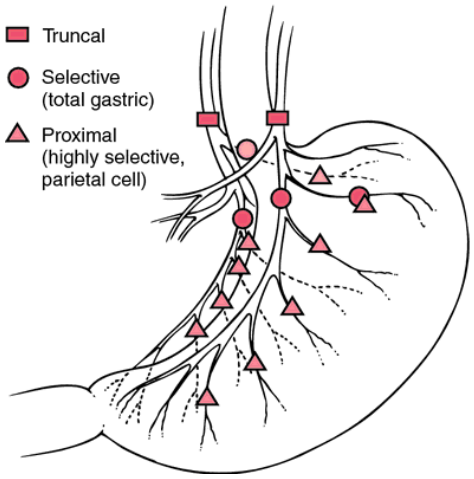
Truncal vagotomy and pyloroplasty - this procedure is the easiest to perform but has a 10% - 15% ulcer recurrence rate (9). The major complications are dumping, diarrhea, bile reflux and post vagotomy syndrome (12).

Truncal vagotomy and antrectomy – this procedure is associated with very low recurrence rates but a higher operative mortality rate (9).

Highly selective vagotomy - this procedure is also known as a parietal cell vagotomy and a proximal gastric vagotomy. It is a more challenging procedure with high ulcer recurrence rates in inexperienced hands (9).



The aim of the procedure is to denervate the proximal stomach where the bulk of parietal cells are located and leave the muscular antrum with its normal nerve supply (12). To achieve this six centimetres of the oesophagus and six centimetres along the fundus must be denervated, leaving only the distal branch of the nerve of Laterjet (13). The ulcer recurrence rate has not been shown to be higher in emergency rather than elective surgery but a level of expertise is required (12).



Laparoscopy

Laparoscopy for repair of a perforated ulcer was first described in 1990 (1). The repair is a simple closure with or without an omental patch.

The trends

A review of surgery for PUD in Sub-Saharan Africa showed that the main procedure performed was a vagotomy and drainage (60%), followed by primary repair (31%), resection and reconstruction (6%) or drainage (3%). These results, however, include surgery for gastric outlet obstruction and chronic disease in 58% of patients (8). These results may reflect limited access to PPIs and the eradication of H. pylori. The estimated infection rate of H. pylori in Sub-Saharan Africa is 91% (14), the 1 year recurrence rate of PUD is 5% with eradication and 35% without (1). The drop in incidence of PUD in high-income countries is attributed to the wide spread use of PPIs (15).

In Europe the incidence of surgery for bleeding ulcers ranges from 2.8 to 10 per 100 000 inhabitants, and this incidence has remained fairly stable (16).

The evidence

Bleeding PUD

A French study compared oversewing and vagotomy vs. gastrectomy for bleeding PUD and showed increased recurrence with the lesser surgery (17% vs. 3%) but a higher rate of duodenal leak with gastrectomy. The overall mortality was similar and higher than other studies (22% vs. 23%) (5). A multicenter study from the early 1990s showed no statistical differences between conservative and more extensive surgery for rebleeding and mortality (17). It is worth noting that these are older studies and predate the prevalent use of PPIs, and that the mortality in both studies is high. These studies also predate some of the endoscopic therapies that are now considered standard (18). A meta-analysis performed around the same time concluded that the type of surgery did not affect mortality but bleeding was more common in conservative surgery (19).

The current understanding of the pathogenesis of PUD and subsequent technical improvements and early effective medical management have made the need for surgical reduction of acid secretion less clear and largely made vagotomy a redundant procedure(9) (16). This is reflected in the decrease in definitive acid-suppressing procedures performed, especially in the emergency situation (18).

Perforated ulcers

Surgery is almost always indicated in a perforated ulcer, and is associated with a high mortality rate of 6% - 30% (9). The site of the ulcer often dictates the surgical procedure. There does not appear to any difference in suture line leak rate or morbidity and mortality according to the type of omental patch used (11).

The technical challenges of ulcers on the lesser curvature and antrum have led to distal gastrectomy being more commonly performed – this has been shown to have a similar mortality to a patch or simple closure (20).

There are three landmark trials on the outcome of simple vs. definitive surgery for perforated PUD, all are from the 1980s. Boey et al. compared simple closure (35 patients) to vagotomy and drainage (32 patients) and proximal gastric vagotomy (34 patients). There was no difference in mortality or post-operative course but ulcer recurrence was 63.3%, 11.8% and 3.8% at 39 months. They conclude that a definitive acid-reducing procedure is indicated in good risk patients (21).

Tanphiphat et al. randomized 33 patients to simple closure and 32 patients to a vagotomy and drainage with only one patient undergoing a proximal gastric vagotomy. They also showed no difference in mortality and complications. The group with simple closure had an 83% recurrence rate vs. 8% in the vagotomy and drainage group. Their caveat was that definitive surgery was not indicated in high risk patients or if the surgeon was inexperienced (22).

The study by Hay et al. looked at the mortality of the various procedures for the management of a perforated ulcer and concluded that there was no difference in complication or mortality rates (23). These studies were, however, all performed before modern understanding of the role of H. pylori and the accessibility of PPIs.

The eradication of H. pylori vs. PPI alone results in a significantly lower ulcer relapse rate in perforated ulcers closed with simple closure (4.85 vs. 38.1%), which argues against the need for definitive acid reducing surgery (24). In present times with the evidence for the medical management of H. pylori and acid suppression few surgeons would perform definitive PUD surgery in an emergency setting (5).

Laparoscopy

The advantages of laparoscopic surgery for PUD are decreased analgesic use, shorter hospital stay, fewer wound infections and lower mortality (25). These results are, however, based on small studies and prior to rigorous guidelines for systematic reviews; more studies are required (1). The highest level and most recent evidence is from a Cochrane meta-analysis showing a 92% success rate for laparoscopic surgery and no major significant differences in complication rates (26).

Patients with shock on admission, delayed presentation more than 24 hours, older than 70 years and ASA grade III-IV are poor candidates for laparoscopic surgery (27).

Gastric ulcers

The concern with complicated gastric ulcers is the risk of malignancy as 4-5 % of benign appearing ulcers are malignant (28). The surgical approach can be a simple wedge excision for an ulcer on the greater curvature to a distal gastrectomy for a distal ulcer (9). The tyoe of surgical procedure does not appear to be a risk factor for poor prognosis for gastric cancer and two-stage approach should be considered (11).

The latest evidence

One of the most recent reviews of emergency surgery for complicated PUD come in 2014 from the American College of Surgeons National Surgical Quality Improvement Program which holds more than one million patient records from more than 250 facilities. 3611 patients had emergency surgery between 2005 and 2010. Perforation was the indication for surgery in 2374 patients and bleeding in 775.

64.3% of patients with bleeding ulcers had a local procedure, 15.6% had a vagotomy with drainage, and 20.9% had a vagotomy and gastric resection. There was no significant difference in postoperative morbidity or early

rebleeding rate, although the mortality was significantly less for those patients who had a vagotomy and drainage than a local procedure. This was more pronounced in high-risk patients (12.3% vs. 26.7%).

A local procedure was the choice in 89.0% of patients with a perforation, 1.9% had a vagotomy and drainage and 9.1% had a vagotomy and resection. Patients who had a resection had a significantly higher morbidity than the other two procedures, this included surgical site infection, prolonged ventilation, septic shock and major bleeding. There was no difference in mortality. There was no benefit in outcomes of adding a vagotomy and drainage over simple closure.

For both complications resection was associated with significantly longer length of hospital stay (18).

Conclusion

There is limited evidence for one surgical procedure over another in the management of bleeding and perforated PUD. A simple closure appears to the best procedure for perforated PUD without risk factors. In ulcers with significant bleeding the addition of a vagotomy and drainage conveys some benefit. There is little evidence for resection in either situation. Laparoscopy is a safe alternative to open surgery for perforated ulcers. In an era where surgeon exposure to definitive acid-suppressing surgery in an elective setting is decreasing, the role of these procedures in emergency surgery should be carefully considered.

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Prevention of Anastomotic Breakdown after Colorectal Surgery

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Anastomotic failure is an inevitable consequence of performing an anastomosis. There are only 2 causes of anastomotic failure, inadequate surgical technique or incorrect surgical judgement. The surgeon is directly responsible for all anastomotic failures.

The consequences of anastomotic failure may vary from a patient who has a mildly prolonged postoperative recovery to overwhelming sepsis with multiple reoperations and a high mortality. In addition, anastomotic leakage in rectal cancer surgery is associated with worse long term bowel function and increased local recurrence rates with reduced survival (Mirnezami, Mirnezami et al. 2011)

What is an anastomotic leak? There are at least 29 different definitions in the literature. A reasonable definition comes from the International Study Group of Rectal Cancer (Rahbari, Weitz et al. 2010). They defined an anastomotic leak as a defect in the intestinal wall at the anastomotic site leading to a communication between the intra and extra-luminal compartments. They graded leaks as:

Grade A: Leaks that do not change patient management

Grade B: Leaks that require intervention but not re-laparotomy

Grade C: Require repeat laparotomy

Incidence: Reported leak rates for colorectal surgery vary widely from 1%(Paun, Cassie et al. 2010) to 50%(Goligher, Graham et al. 1970) depending on how they are detected and the site of the anastomosis. The closer the anastomosis is to the anus in rectal surgery, the higher the leak rate. A clinical leak rate of around 10% for coloanal anastomosis is generally accepted, but for more proximal anastomoses, leak rates should not be any higher than 1 to 2%.

Defunctioning proximal to an anastomosis with a colostomy or ileostomy does not appear to alter leak rates, but it does decrease the morbidity of a leak

(Huser, Michalski et al. 2008, Montedori, Cirocchi et al. 2010). It however adds to morbidity and mortality by adding a second operation for closure.

Factors affecting leak rates

1. Technical factors:
    a. Leak rates vary between surgeons.
    b. Meticulous technique
    c. No tension
    d. Good blood supply
    e. No contamination
    f. Single layer better than double layer
    g. Lower leak rate for stapled anastomosis
    h. Appropriate suture material
    i. High IMA ligation

2. Management factors:
    a. Peri-operative hypotension
    b. NSAIDs
    c. Over use of perioperative fluids
    d. Inotropes
    e. Long operation time
    f. Blood loss
    g. Transfusions

3. Patient factors
    a. Emergency surgery
    b. Significant pre-operative weight loss
    c. Low albumin
    d. Obesity
    e. Diabetes
    f. Liver disease
    g. Renal failure
    h. Myocardial infarction
    i. Cardiac failure
    j. Peripheral vascular disease
    k. Cerebrovascular disease

l. Dementia
m. Chronic pulmonary disease
n. Any tumour
o. Immunosuppression
    i. Steroids
    ii. Other causes
p. Crohn's disease
q. Peritonitis

The important questions a surgeon needs to ask when performing an anastomosis are:

1. How important for the patient is this anastomosis?
2. What is the likely chance of a leak in this patient?
3. Does the patient have the reserve to survive a leak should it occur?

On re-operating or a patient who has had a leak, a surgeon has to establish the cause of the leak. If it is due to a technical error and there is little contamination, it may be reasonable to re do the anastomosis. In most other situations, the surgeon has to change the approach and take the anastomosis down.

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Management of obstructed advanced rectosigmoid tumours.

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Introduction

Symptoms of acute intestinal obstruction may be the initial presentation in up to 20% of all patients with colorectal cancer necessitating emergency surgery, which in this setting may be associated with significant morbidity, mortality and a high percentage of stoma creation (temporary or permanent). While treatment of right-sided malignant colonic obstruction is often resection and primary anastomosis in suitable patients, controversy persists on the emergency management of obstructed left sided colorectal cancer. Earlier obstruction is noted in recto-sigmoid tumors due to the smaller size of the lumen.

Management options

Various options have been used in the management of left colon malignant obstruction, these include:

- Loop colostomy and subsequent resection (2 or 3 staged procedure)
- Loop ileostomy and subsequent resection (2 or 3 staged procedure)
- Primary resection with end colostomy (Hartmann's procedure)
- Primary resection and anastomosis (with colonic irrigation or manual decompression)
- Use of endoscopic colonic self-expanding metallic stents (SEMS) as palliation or as a bridge to surgery.

Patient's age, ASA grade, Operative urgency and Duke's stage, were identified in the ACPGBI study of large bowel malignant obstruction to be the 4 main predictors of outcome.

Pros and cons

Loop colostomy and Hartmann's procedure have similar mortality and hospitalization. Advantages of loop colostomy include that it is easy technically

thus can be competently done by surgical trainees/Registrars, it provides colonic decompression,

It involves minimal surgical trauma, there is reduced risk of contamination from unprepared bowel and it allows staging and multidisciplinary MDT evaluation prior to definitive treatment.

In a German study by Kube et al, 743 patients underwent emergency surgery for rectosigmoid malignant obstruction in which resection was done. The treatment options included; Resection and primary anastomosis 57.9%, Resection, primary anastomosis and covering stoma 11.7%, Resection and Hartmann's procedure 30.4%. No statistical significant difference was noted with regards to morbidity and intra-hospital mortality. The rate of anastomotic leak was also not improved by the presence of a covering stoma.

Hartmann's procedure (with high ligation of the lympho-vascular pedicle) should be reserved for patients who are elderly, high risk (high ASA) or have advanced lesions and in cases where the surgery is being conducted by a surgeon with limited experience and expertise e.g. trainees.

Placement of pre-operative self-expanding metallic stents SEMS as a bridge to surgery allow for bowel decompression and subsequent surgery (laparoscopic or open) in a semi-elective setting with the possibility of primary anastomosis. The semi-elective surgery compared to emergency surgery resulted in decreased rates of colostomy and post –operative complications e.g. surgical site infections SSI coupled with increased rate of primary anastomosis. SEMS as a bridge to surgery for left sided colon cancer do not adversely affect oncological outcomes or patient survival.

Recommendations

The guidelines in management of obstructing cancer of the left colon include:

- Resection and Hartmann's procedure is preferred to diverting colostomy with out resection as colostomy alone is associated with a cumulative longer overall hospital stay and the need for multiple operations but not decreased peri-operative morbidity (during all the other staged procedures).
- There is no survival benefit offered by Hartmann's procedure compared to resection and primary anastomosis, thus Hartmann's procedure should be reserved for patients with high surgical risk.

- Manual decompression or intra-operative colonic irrigation done during segmental resection and primary anastomosis are associated with similar morbidity and mortality. The surgeon's experience and preference is recommended, though manual decompression is a shorter simpler procedure.
- For palliation, SEMS are associated with shorter hospital stay thus preferred to colostomy in patients with anticipated poor prognosis or short survival time. For surgically fit patients with anticipated longer survival and who may be eligible for bevacizumab-based treatment, SEMS should be used with caution, rather offer the patient a colostomy.
- In referral centers or hospitals with the relevant expertise, SEMS should be used as a bridge to surgery.

Conclusion

The literature and RCT data on management of obstructing rectosigmoid cancer is relatively poor. Patients should be stratified according to surgical risk (age and ASA grade), surgeon's skill, Operative urgency and Duke's stage. Based on these factors, treatment should be individualized.

Where clinical and technical expertise is available, SEMS as a bridge to surgery is recommended. If unavailable, primary resection and anastomosis following manual decompression is recommended for good surgical risk patients while a Hartmann's procedure is recommended for those who are high surgical risk. Total colectomy and ileorectal anastomosis should be considered in patients with synchronous colorectal cancer, young patients less than 40yrs who may possibly have lynch syndrome and in cases with impending or actual caecal and right colon perforation.

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Laparoscopic surgery for Rectal Cancer; What are the challenges?

Challenges in Rectal Cancer Surgery.
Oncology vs Functionality

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The ideal characteristics of rectal cancer management focus on achieving both optimal oncologic outcomes while maintaining the highest possible quality of life. In the distal rectum (approx. 1Ocm from the anal verge) preventing a permanent colostomy is a challenge. The key to extending sphincter preservation without compromising oncological outcomes comprise a combination of: high dose pre-operative chemo radiation, prolonged interval to surgery, use of post-radiation characteristics to design the operation (controversial) and optimizing the surgical approach.

Since I did my first laparoscopic Colectomy for cancer in 2001, followed by laparoscopic rectal resection in 2005 (after the publication of the CLASICC and COLOR II trials) the rectal cancer treatment landscape has changed dramatically. Initially it was TME type dissection as described by Heald et al, that changed the way we do proctectomies, followed by the different approaches (open, laparoscopic, robotic, Trans-anal)

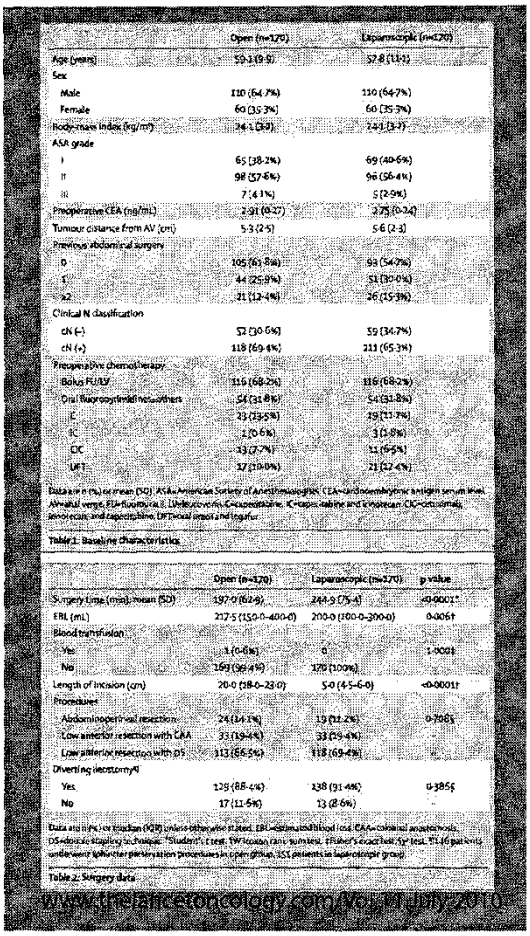
For colonic laparoscopic surgery, good quality studies show at least the same oncologic outcome but better short-term outcome. The same cannot be said for mid and low rectal cancer and there is a definite need for these patients to be managed in high volume centers.

The optimal surgical approach is still a matter of contention, all the major randomized controlled trials (CORBAN, CLASICC, COLOR II, ACO-SOG Z6051 (USA) ALaCaRT

(AUS) has not showed laparoscopy or open surgery to be superior. The Robotic study ROLARR is underway and the results are not available yet.

In the COREAN study, T3 tumors,wererandomized for open orlaparoscopic surgery,

170 patients in each arm. There was a low conversion rate, blood loss was marginally better, operative time longer (laparoscopic group). No difference in oncological markers (CRM, macroscopic margin, harvested lymph nodes or morbidity) There were short term benefits to laparoscopy in micturition, fatigue, mobility, and defecation problems



	Open (n=170)	Laparoscopic (n=170)
Age (years)	59·1 (9·5)	57·8 (11·1)
Sex		
Male	110 (64·7%)	110 (64·7%)
Female	60 (35·3%)	60 (35·3%)
Body-mass index (kg/m²)	26·1 (3·9)	24·1 (3·7)
ASA grade		
I	65 (38·2%)	69 (40·6%)
II	98 (57·6%)	96 (56·4%)
III	7 (4·1%)	5 (2·9%)
Preoperative CEA (ng/mL)	2·91 (0·27)	2·75 (0·24)
Tumour distance from AV (cm)	5·3 (2·5)	5·6 (2·5)
Previous abdominal surgery		
0	105 (61·8%)	93 (54·7%)
1	44 (25·9%)	51 (30·0%)
≥2	21 (12·4%)	26 (15·3%)
Clinical N classification		
cN (–)	52 (30·6%)	59 (34·7%)
cN (+)	118 (69·4%)	111 (65·3%)
Preoperative chemotherapy		
Bolus FU/LV	116 (68·2%)	116 (68·2%)
Oral fluoropyrimidine/others	54 (31·8%)	54 (31·8%)
C	33 (19·5%)	29 (17·1%)
X	2 (0·6%)	3 (1·8%)
CC	13 (7·7%)	11 (6·5%)
UFT	37 (10·0%)	21 (12·4%)

Data are n (%) or mean (SD). ASA=American Society of Anesthesiologists. CEA=carcinoembryonic antigen serum level. Annual vergl. FU=fluorouracil. L=leucovorin. C=capecitabine. X=capecitabine and irinotecan. CC=oxaliplatin and capecitabine. UFT=oral uracil and tegafur.

Table 1: Baseline characteristics

	Open (n=170)	Laparoscopic (n=170)	p value
Surgery time (min), mean (SD)	197·0 (62·9)	244·9 (75·4)	<0·0001†
EBL (mL)	217·5 (150·0–400·0)	200·0 (100·0–300·0)	0·006†
Blood transfusion			
Yes	1 (0·6%)	0	1·000‡
No	169 (99·4%)	170 (100%)	
Length of incision (cm)	20·0 (18·0–23·0)	5·0 (4·5–6·0)	<0·0001†
Procedure‡			
Abdominoperineal resection	24 (14·1%)	19 (11·2%)	0·798§
Low anterior resection with CAA	33 (19·4%)	33 (19·4%)	
Low anterior resection with DS	113 (66·5%)	118 (69·4%)	
Diverting ileostomy¶			
Yes	129 (88·4%)	138 (91·4%)	0·385§
No	17 (11·6%)	13 (8·6%)	

Data are n (%) or median (IQR) unless otherwise stated. EBL=estimated blood loss. CAA=colonic anastomosis. DS=endoscopic stapling technique. †Student's t test. ‡Wilcoxon rank sum test. §Fisher's exact test (or less). ¶1 (6 patients) underwent sphincter preservation procedures in open group, 151 patients in laparoscopic group.

Table 2: Surgery data

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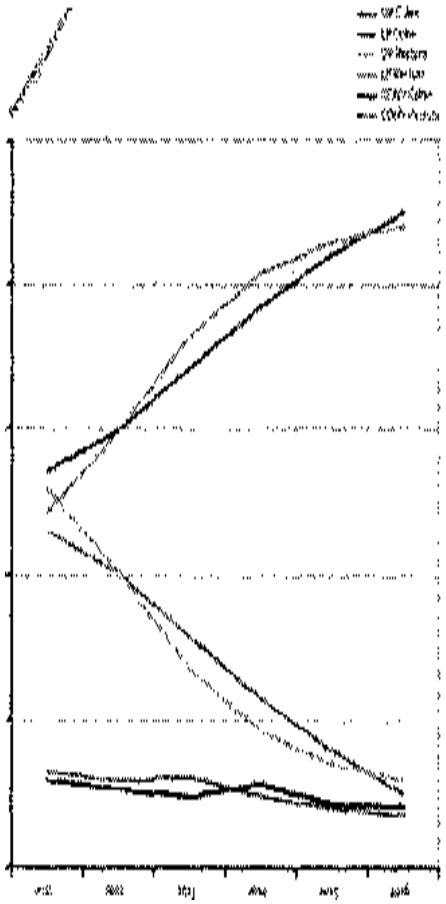


What do surgeons actually do?

What access is used to resect rectal cancers around the world? I do not know of data in South Africa but: In the Netherlands, more than 90% of rectal resections is now performed laparoscopically.

In the USA, a minimally invasive surgical (MIS) approach is utilized in less than half of all colon resections in this national database, which accounts for over 70% of all diagnosed cancers in g—,Darmkanker the US. Significant variability exists among age, race, insurance status, socioeconomic status, region, and facility type. (Surg Endosc. 2017 Aug 24 .Barriers to laparoscopic colon resection for cancer: a national analysis, Hawkins et al

In Austria, the proportion of colorectal resections that are carried out laparoscopically is low (26.1%). Technical challenges and a learning curve with a significant number of cases may be reasons for the slow adoption of laparoscopic colonic surgery. (Current State of Laparoscopic Colonic Surgery in Austria: A National Survey, Klugsberger et al)

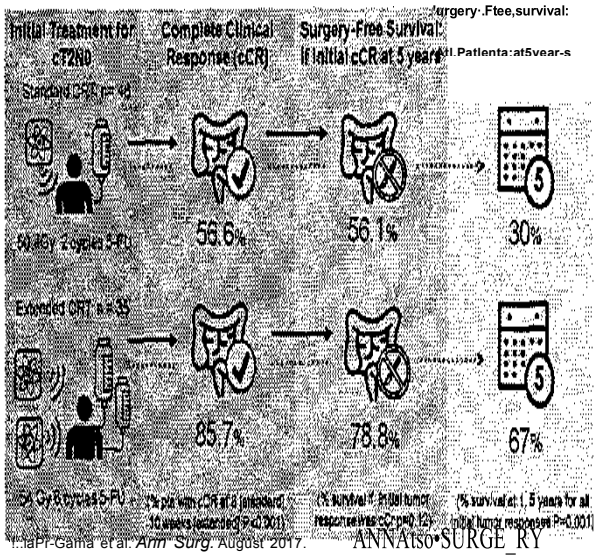
Even though we might think colo-rectal cancer surgery is performed laparoscopically in the world, it does not seem to be the cas

Three important new developments have been introduced to rectal cancer surgery in the past decade: I. Watchful waiting after neo-adjuvant chemo radiotherapy, 2. TAMIS and

3. TaTME.

1. Watchful Waiting.

Correct staging is of critical importance in this subgroup of patients, MRI and possibly ERUS for early lesions are mandatory. Approximately 10 to 30% of patients with extended neo-adjuvant chemo radiation protocols have complete pathological response (pCR). Only this subgroup of patients can be included in watchful waiting protocols. Macroscopic evidence of complete response is controversial but a white scar without any ulceration is considered complete, this at 8- 10 weeks after therapy with



Organ Preservation in cT2NO Rectal Cancer:

Radiation Dose-escalation & Consolidation Chemo

regular endoscopic and MRI (accuracy 92%). Follow-up 3 monthly for 2 years and then 6 monthly up to 5 years. This is intensive and expensive

Patients treated with TME with a ypTO status (after chemo radiation) have a local recurrence rate of less than 1% and a 5 year survival of 95%. Watchful waiting need to be compared to this excellent long-term outcome.
Patients need to be fully informed of choices, and definitely all options must be considered. Potentially up to 20% of patients with rectal cancer can benefit from this approach. There is always salvage surgery to fall back on. If indeed follow-up is properly performed, local recurrence is higher but overall survival is the similar to surgery.

2. TAMIS (Trans-anal minimally invasive surgery)

Several different platforms are available for local excision of certain early tumors. TEO, TEM and excision with an endoscope is used with good success. The advent of TAMIS with the use of endoscopic instruments via a trans anal platform and an air seal system have significant advantages. Higher lesions can

be removed, the instruments are readily available and it is relatively inexpensive. If the patients are chosen well and staged as early rectal cancer confined to the submucosa, excellent results can be achieved.

TAMIS is a relatively new procedure and complications have been described: entry into the peritoneum, recto-vaginal fistula, bleeding, sepsis and urinary retention.
Follow-up is important and should be done at 3/6/9/12 months and six monthly for another two years.
In future, more of these procedures will be done even though it has not been validated. Currently it is used mostly for benign disease but one can imagine local resection in this manner post chemo radiation.

In a recently published study (Quality of Local Excision for Rectal Neoplasms Using Trans-Anal Endoscopic Microsurgery Versus Trans-Anal Minimally Invasive Surgery:
A Multi-Institutional Matched Analysis by Lawrence Lee et al} published in Diseases of the Colon and Rectum September 2017, no difference could be found between TAMIS and TEM. The matched cohort included benign and malignant lesions in 428 patients. 181 TAMIS and 247 TEM. Poor quality excisions were similar as were peritoneal violation and post-operative complications. Cumulative 5-year survival were also similar at 80%and 78%. Salvage surgery for local recurrence was needed in 7% of patients in both groups. TAMIS is easier and cheaper and does not need extra equipment.

3. Trans anal TME (TaTME)

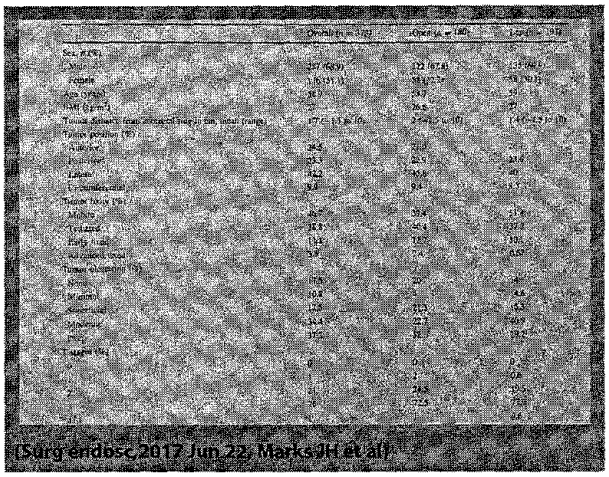
As part of the laparoscopic revolution rectal cancer surgery was enthusiastically adopted by many. Unfortunately, the technical limitations of operating in a narrow pelvis, combined with limited staplers and a very steep learning curve often led to longer operating times, high conversion rates and anastomotic leaks due to multiple firings of the stapler. There are some concerns with oncologic safety and possibly long-term recurrences especially for the low rectal tumors. Despite multiple studies marked advantage in favor of laparoscopy has proven elusive.

The robot was supposed to alleviate these problems in a narrow pelvis, but until now has not been proven to be superior to standard laparoscopy. It is also prohibitively expensive and this prevented widespread adoption thus far. The results of the robotic vs laparoscopic approach for the resection of rectal cancer study is awaited (ROLARR). For now, robotics should be confined to educational programs.
Against this background TaTME or a bottom-up approach was introduced.

TaTME occurs when at least the distal third of the rectum is resected trans-anal according to TME principles. It is said to take all the major developments in colo- rectal cancer care of the last three decades into one procedure (TME, laparoscopy and NOTES). Advantages include easier management of

obese patients and the narrow pelvis.

Introduced in 2010 several publications have shown the feasibility and short- term outcomes that are comparable to other forms of access. Caution however is needed as the initial results from the international registry (23 countries, registered units and 720 procedures) shows conversion in 9.1 %, intact TME specimens in 85%, mortality and morbidity of 0,5% and 32.6%.



(Surg endosc 2017 Jun 22; Marks JH et al)

In the only long-term study (more than 5 years follow-up) TaTME is not only feasible but has low recurrence rates and good quality mesorectal excision. 96% of the TME specimens were complete, 94% had a negative circumferential resection margin and 98.6% had a negative distal resection margin. Morbidity and mortality (13.4% and 0.3%) was acceptable. This large trial of TaTME included 373 patients, form a prospectively maintained database. Trans-abdominal access was open in 180 patients and laparoscopic in 193. Mean follow-up was 5.5 years, 91% of the cancers were in the distal rectum. 68,9 % were men and 53.2% of tumors were fixed at presentation. Almost all patients (97.7 %) received neo- adjuvant chemo-radiotherapy (5405Gy and 5FU based). (John Marks et al)

Summary

Much has changed in the management of rectal cancer in the past 20 years. Multimodality management of rectal cancer has become the norm.

This patient-specific approach, along with efforts aimed at early diagnosis, should further improve surgical

outcomes while preserving quality of life. MRI and different methods of surgery has made a big difference in both oncological and functional outcomes. There is now an opportunity to individualize treatment for different patient groups. This can only happen with standardized pre-treatment work-up and adjuvant therapy and provides unprecedented local tumor control and patient survival. This intense multimodality treatment is associated with significant morbidity and long-term sequelae that permanently impair quality of life. High volume centers are obviously better equipped to handle these new surgical approaches and multidisciplinary treatments. Finding predictors of tumor response and ways to identify response early in the treatment course should help improve the treatment of patients.

References available on request

Extralevator Abdominal Perineal Excision (ELAPE) for low Rectal Cancer.

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Indications

Abdominoperineal resection (APR) is used to resect rectal cancer where the anus cannot be saved due to either tumour invasion, close resection margins or substantial risk for poor functional outcome. It involves resecting the rectum with it's mesentery en bloc with the anus and creation of a permanent colostomy.

History

Patients undergoing APR were found to have increased recurrence rates when compared to low anterior resection (LAR) patients[(1)]. It was postulated that the reason for this was the way in which the mesorectum was dissected off the pelvic diaphragm.

When the plane of dissection comes up against the pelvic diaphragm, it starts to taper in towards the rectum. This causes "waisting" of the specimen and directs the line of operation into the tumour itself. Since the last 2-3cm of rectum has no fascia-covered mesorectum (the so called "no-man's land"), this may result in early spread of the tumour to surrounding structures as well as incision of the tumour with very low dissection.

In 2006, it was proposed that this could be avoided by the introduction of the extralevator abdominoperineal excision (ELAPE)[(1)]. This operation required en bloc excision of the levator ani muscles with the mesorectum to avoid this "waisting". This practise was then widely adopted but with little good data to support its use.

Controversy #1: Is ELAPE oncologically superior to APR?

A recent study done in South Africa[2] has shown no difference in intraoperative tumour perforation rates (TPR), involved circumferential resection margin rates (CRM) or wound complications when comparing ELAPE to APR. The patients in this trial were followed up for 2 years.

Internationally, results have been conflicting. Oncological outcomes have been subjected to the most scrutiny with some studies favouring ELAPE[3-7] while others have shown no difference[8-9]. A recent meta-analysis has shown no difference in CRM but improved TPR in ELAPE[10].

While some studies have shown superiority of ELAPE to APR, none have demonstrated inferiority in terms of oncological resection.

Controversy #2: Is quality of life worse in EALPE than APR?

ELAPE leaves the patient with a large defect in the pelvic diaphragm. This has the potential for increased risk of pelvic herniation of abdominal contents. It is thought that APR carries a lower risk of this complication[11]. While it is exceedingly rare for perineal herniae to strangulate, there is a small and unpublished rate of this scenario. Some studies suggest that prophylactic biologic mesh inserted into the pelvis may prevent this type of hernia[12] while others do not[11]. Flap reconstruction seems to be as effective at preventing pelvic herniation[13].

Quality of life has been reported as equivalent in studies that have judged short and long term follow up of patients who have undergone ELAPE or APR[4,6-7,13]. Erectile dysfunction seems to rank higher than pelvic hernia in most quality of life scores and is equivalent in both groups[4].

Controversy #3: Is perineal wound healing worse in ELAPE?

80-90% of patients who undergo APR or ELAPE receive neoadjuvant chemoradiotherapy. This impacts on healing of the perineal wound. There are several ways to manage this wound: primary closure, omentoplasty or flap

closure. Whether an APR or ELAPE are performed does not seem to make any difference in the rate of wound complications[1,3-5].

Conclusions

ELAPE remains a controversial solution to a difficult and common problem. While it has been widely adopted despite limited data, there have been recent studies examining it's use. These seem to indicate that ELAPE is safe and effective in most cases where excision of the anus is necessary. Most data seem to show that it has superior rates of tumour perforation but little difference in circumferential resection margin involvement. Long term data is limited but shows that it is not inferior to APR.

Complications of ELAPE do not seem to make it an unattractive method to deal with this problem. Rates of pelvic herniation seem to be higher in ELAPE but this does not impact on either quality of life or complication risk.

As with most aspects of medicine, it is dangerous to prescribe one operation for all patients. The future may involve tailoring your resection to the needs of the patient.

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Complete Mesocolic Excision vs Traditional Colectomy: Is there Oncologic difference.

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Introduction

In the last 30 years, probably the greatest advance in the management of colorectal cancer provided by surgeons has been the development of the total mesorectal excision of the rectum. Over time Heald's contribution in this field clearly demonstrated that such a technique improved the overall survival and certainly the local recurrence of rectal malignancies when used in management of rectal cancer. The translation of his idea from opinion through to irrefutable evidence is a description of collaborative European based research at its best (8).

More recently the concept of a careful anatomical dissection of the meso-intestinal package has been extrapolated to the management of colonic malignancy. Using the technique of complete mesocolic excision greater precision can be exercised in the surgery of colon cancer and may enable a decreased chance of local recurrence and possible improvement in overall survival. The work of the Japanese has led the way in the clear documentation of surgical procedures (10). In this instance their guidelines for the surgical management of colonic resection has been a point of reference for the development of complete mesocolic excision in Europe. Their obsessive documentation of technique has helped initiate the concept of complete mesocolic excision in the west. This procedure has therefore taken off in the last 10 years and has been debatably advantageous in improving overall survival in patients with colonic malignancy.

Surgical Technique

There are 3 main principles in performing a complete mesocoloic excision. These include:

1. Careful resection of the colon and its mesentery in an embryological dissection of the oncologically affected package. In so doing the surgeon will mobilize the tumour off the retroperitoneal structures along Toldt's fascia. This avascular plane is used as a means to lift the involved colon and its mesentery away from surrounding structures and at the same time preserve the integrity of those tissues both apparently and potentially affected by the malignancy.
2. There after the surgeon will remove enough of the mobilized colon and mesocolon to include D1 (peri-colonic lymph nodes) , D2 (intermediate nodes) and D3 (central nodes at the root of the main vessels origin) (*fig 1)*. This necessitates the dissection of the specimen down to the root of the closest feeding vessel going to the tumour. Debate continues around whether the surgeon needs to extend dissection beyond these limits; in particular to D4 nodes around the aorta, vena cava and portal vessels. Besides this interest remains in vascular variations: particularly in the region of the right/transverse colon and the rectosigmoid junction; leading enthusiasts to suggest the removal of infraduodenal and epiploic nodes in the former instance and ileac nodes in the latter (3).
3. An adequate length of bowel on either side of the malignancy will be removed with the resection. The Japanese have suggested this should be 5cm beyond the feeding vessel in the direction of lymphatic spread and at least 10cm in the opposite direction. This is thought to ensure adequate removal of pericolic lymphadenopathy (D1 nodes). These guidelines have been based on outcomes of retrospective patient samples.

This surgical technique has initially been described in open surgery and, understandably, has been extrapolated into surgeries performed laparoscopically (7). There has been some debate as to whether laparoscopic technique worsens the overall outcome of this surgical technique, although it is now accepted that it probably does not and may even contain some advantage of decreased pain and complication related to the event these studies at least showing oncological equivalence. Changing objectives and techniques have resulted in a need to define complete mesocolic resection as a single entity (1,4)

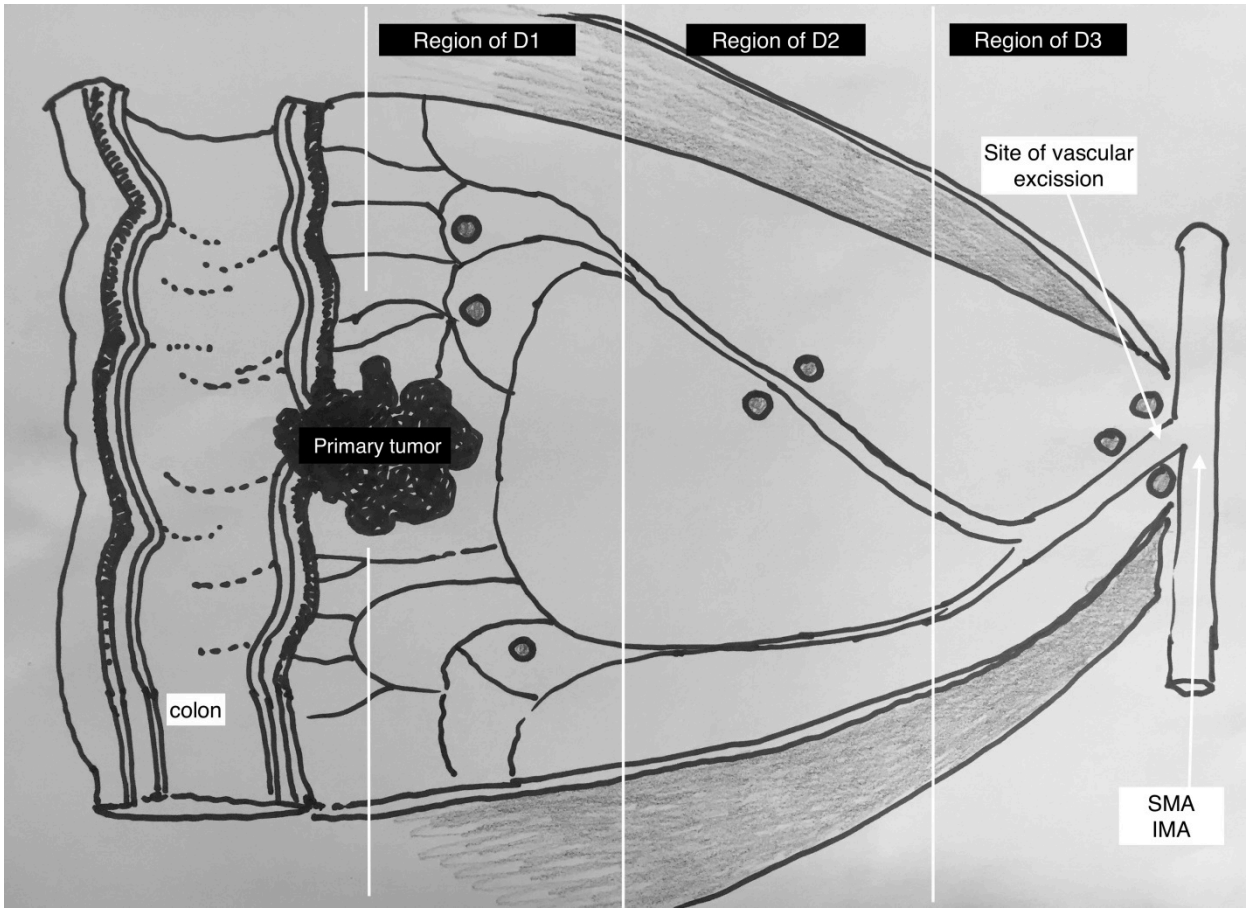

Figure 1: depicting levels of lyphnodes in colorectal cancer

Evidence for the oncological worth of CME

All considered, there is no hard evidence as yet that this surgical method and allied techniques have any convincing impact on oncological outcome even though they are increasingly being performed in multiple Centers (9,5). In evaluating the impact of CME on overall survival, one would want to see whether surgical procedure has significantly improved death rates as well as disease free survival and local recurrence. This would indirectly then, account for changes in the disease associated life years' assessment for colorectal cancer. Does this evidence exist? Answering this question is the objective of this presentation.

To date, what is most evident is the opinion of the enthusiasts.(4) This has been fuelled in part by the Japanese methodology already discussed.Change in western surgical management has required not only a more asciduous application of techneque but also greater care in documentation of events. This has filtered down into teaching platforms in these countries where the rational

and advatages of complete mesocolic dessection has been punted. Advocates and teachers have in particular moved towards a more extended longitudinal excision and a resection of a carefully dissected package to the level of the main arterial feeder, so achieving at least a D3 resection. D4 resection has not been considered to be of advantage as its oncologicl benefit is dubious and its' associated morbidity significant.

But what then of the evidence for an impact on the disease process? Certainly, the nature of the histological specimen has been evaluated by a multi-centered European team . They have demonstrated that the complete mesocolic excission produces specimens of a significantly better quality than their counterparts. This is particularly so with regard the longitudinal margin as well as the number of lymph nodes harvested for the assessement of stage (11). This however, is not direct evidence for superiority. As is often the case, in the past the best European based population studies have come out of the Scandinavian countries and, certainly, there have been attempts to assess complete mesocoloic excision. These papers suggest that since the introduction in 2003/2004 of complete mesocoloic excision as a structured methodology, the overall survival rate for colonic malignancy has improved (6,2). Understandably, this improvement is not unifactorial. There have been many new developments and innovations introduced in the management and understanding of colonic malignancy that may responsible for the improvements seen. It is therefore difficult to justify that this technique, alone, has initiated the improvement in survival of patients with colonic malignancy in this period (9). The question posed to us" Has CME improved the outcomes of the management in patients with colonic malignancy?" is still subject to scrutiny and debate.

But even more questionable is the relevance of this surgical nuance in our setting when considering management of patients with colorectal cancer in South Africa. In an environment where the delay to diagnosis and the barriers to care are the biggest determinants of outcome, the subtleties of impact of this surgical approach are of diminished overall significance.

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Evolving Management of the Axilla in invasive Breast Cancer

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Synopsis

Breast cancer management and prognosis are governed by both the stage of disease at presentation and, more latterly, tumour molecular biology. One of the strongest indicator for prognosis is the axillary stage at presentation, and response to any neo-adjuvant therapy. Axillary lymph node dissection has been the standard of care historically for two purposes: to determine stage of disease and therefore prognosis, and to eradicate or reduce local tumour burden. Advances in the last 20 years have challenged both this procedure, and the necessity of its outcomes, and this talk will examine both these changes in practice.

In considering the clinically node-negative axilla, an axillary dissection was deemed to be overtreatment with only 22% positive lymph nodes therefore exposing 78% of early breast cancer patients to excessive surgery and the 15-20% risk of lymphoedema long-term. Therefore, a sentinel lymph node biopsy (SLNB) technique localisation and biopsy was conceived. The sentinel node is the first draining lymph node that receives lymph from an anatomic region. If a macromolecular tracer is introduced to that area, it will be taken up (by the antigen presenting cells) and delivered through drainage to the regional lymph nodes, starting at the sentinel. The accuracy of this procedure in the breast, which was first documented in 1993, and has been proven in large multicentre trials to be good with a sensitivity of 90-95% and a false negative rate less than 5-10%. In addition to the clinical advantage of a reduction in negative axillary dissections and patient morbidity, with less quantity of node dissection greater attention could be paid to the node specimen pathologically. Immunohistochemistry and serial sectioning led to the identification of micro metastatic disease and isolated tumour cells. The impact of these cells on prognosis and implication on treatment is still undetermined despite multiple

studies (mostly retrospective analysis of previously “node-negative” specimens). Many authors now recommend a ‘don’t look, don’t find’ policy. Despite these controversies, in clinically N0 breast cancer, the SLNB has become the standard of care to determine metastatic disease.

In node-positive disease, the axillary lymph node dissection (ALND) continued to be the standard of care, and still in our practice outside of a clinically trial or multi-disciplinary context, it remains the recommended practice. However, the landscape of breast cancer management continues to evolve, and both advances in neo/adjuvant therapies and increasing survivor advocacy for limited surgery influence current studies and future practice. With the increasing success of new chemotherapeutic agents and novel biologicals given to node-positive patients prior to surgery, the continued benefit of a full axillary dissection, where nodes were clinically down-staged to negative, was uncertain and provided equipoise for ongoing trials. In clinically node-negative (prior to neoadjuvant therapy) it is well established that a SLNB is suitable. In the GANEA prospective study an identification rate of 90% and false negative rate of 9.4% (all patients had a confirmatory full dissection) in clinically node-negative axillae.

Where the node has remained positive clinically after chemotherapy, there also remains little debate that a full dissection is beneficial in reducing local tumour burden, followed by radiation. The remaining dilemma is how to treat an axilla that was clinically node-positive prior to chemotherapy but has been rendered node negative by response to treatment. The increasing incidence of negative axillary dissections in this group led to two prospective trials: SENTINA and ACOSOG-Z1071. ACOSOG-Z1071 found a false negative rate of 12.6% reduced to 10.8% if dual agents were used. In further analysis of procedures where two or more (true) sentinel nodes were excised, the false negative rate is 8.7% and deemed acceptable. Where positive nodes were marked prior to chemotherapy and excised during nodal biopsy the false negative rate further decreased to 6.8% (if the node was not found the false negative rate was up to 39%).

In contrast, SENTINA found an identification rate of only 80.1% and a false negative rate of 14.2% reduced by finding three or more nodes or using dual tracer to under 10%. The conclusions of these studies and meta-analysis of smaller similar groups is summed up by the conclusion of the most recent meta-analyses in the European Journal of Surgical Oncology, which states “In conclusion, based on current evidence it seems not justified to omit further

axillary treatment in every clinically node positive breast cancer patients with a negative sentinel lymph node biopsy after neoadjuvant systemic therapy". Therefore, the SLNB can be safe after neo-adjuvant chemotherapy but in limited controlled circumstances. It is important to note that the effect of a false negative axilla and erroneous omission of a full ALND is on increased local recurrence. However, because multi-modality therapy is conceived on the initial presentation with both chemotherapy (given prior to surgery) and radiation indicated for node-positive patients, it would not affect systemic treatment decision-making.

In patients with axillary node-positive disease, but with low tumour burden (small tumours, favourable biology, less than three nodes involved) two trials investigated the need for further dissection. The ACOSOG- Z0011 trial in the USA recruited nearly 900 patients after positive SLNB and randomised them to further ALND or observation alone. Two important caveats to the trial were that all patients received whole-breast irradiation as all patients underwent breast-conserving surgery, and that the trial was unblinded therefore radiation oncologists knew which patients had not received a full ALND (and may have increased their radiation fields to compensate. In addition, the trial was heavily underpowered. It did find however, that there was no difference in recurrence between those with and those without a full ALND (0.9% vs. 0.5%, $p>0.05$). Note also that those numbers for recurrence are extremely low, and on a personal note, are far lower that we reproduce in the South Africa government system. This cautions us to interpret USA data in a South African context. The principle remains that, where a patient is having whole-breast irradiation with low volume good biology disease, it remains possible, in fact favourable, to omit a full dissection.

The second important study was the AMAROS trial which compared axillary dissection in these low-risk node-positive tumours to radiation alone. The results found no additional benefit in recurrence (86.9% vs. 82.7%, $p=0.18$) and more complications in the surgery group, around shoulder movement particularly if radiation and surgery were both administered.

The final evolution is how to carry out the sentinel procedure in 2017. Despite the improved patient reported outcomes and proven accuracy of SLNB, it is estimated that only 60% of eligible patients undergo this procedure in developed countries and less than 5% in other countries. One of the main barriers to

increased access to radioisotope labels. Therefore, new novel technologies are being developed to overcome this obstacle using hybrid tracers. The most promising novel technique is SPIO which has again shown non-inferiority in a meta-analysis of six multicentre trials, however the cost of the probe and single-use Sienna+ tracer is far more than current radioisotope costs at face value, and no in-depth costs studies have been carried out as yet. It is currently being introduced to South Africa in government and private.

The future landscape for the management of the axilla may not focus on which technique is best, and at what time, but whether clinically node-negative axillae require any surgery at all. Routine axillary ultrasound is invaluable in determining the presence and extent of axillary disease, particularly when impalpable. In the UK, the NICE guidelines recommend routine evaluation, and in South Africa, whilst the accompaniment of an ultrasound to mammography is routine, although axillary assessment is more variable. Non-surgical evaluation with ultrasound, and confirmed by FNA or core needle biopsy can prevent unnecessary SLNB in patients who may be better managed with NAC prior to definitive axillary surgery. The SOUND trial has also been designed to determine whether patients with a clinically and radiologically node negative axilla can be safely observed with no further management. It is currently recruiting in Europe at present.

In summary, the role of the sentinel lymph node is expanding and maturing. Whilst previous controversies regarding full ALND or SLNB biopsy have been resolved, new areas of debate are evolving. Prospective trial results and expert consensus guidelines help guide the breast surgeon as to current recommendations and standard of care, whilst future studies may continue to challenge our understanding of the management of the axilla in breast cancer.

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Management choices for CBD Stone induced Jaundice, with or without Cholangitis in Laparoscopic surgery era.

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Common bile duct (CBD) stones are present in 8-20% of patients with cholecystolithiasis[1]. In patients with no evidence of obstruction, a third of these stones will pass spontaneously[2]. Few would argue about an interventional approach in symptomatic patients. These patients are at risk of potentially fatal complications including cholangitis and pancreatitis.

Courvoisier and Thomton performed the first open common bile duct explorations in 1889. This tradition continued during the 1900's and was the preferred approach for cholecysto-choledocholithiasis. In 1974 endoscopic retrograde cholangiopancreatography (ERCP) was introduced but did not affect the management of CBD stones in the open era. The advent of laparoscopy resulted in a minimally invasive approach to removing the gallbladder at the expense of difficulty in accessing the bile duct. This led to what is now the preferred approach[3] in the management of these patients: ERCP with sphincterotomy for removal of CBD stones followed by laparoscopic cholecystectomy (LC).

However, as skills in minimally invasive surgery have improved, laparoscopic bile duct exploration (LCBDE) has now become a useful tool in the management of CBD stones. This has resulted in the development of a variety of therapeutic approaches. These include:

Single stage procedures

- Open CBD exploration and cholecystectomy
- LCBDE (Transcystic or transcholedochal approaches) + LC
- Intra-operative ERCP + LC

Two stage procedures

- Pre-operative ERCP + LC
- LC + post operative ERCP

Open CBD exploration

Open CBD exploration (OCBDE) and cholecystectomy was the “gold standard” for the management of patients with combined cholecysto-choledocholithiasis prior to the advent of laparoscopy. It obviated the need for pre-operative endoscopic therapy and its associated morbidity. However, it has been associated with significant morbidity and occasional mortality.

There is only one randomized trial that compares OCBDE to LCBDE. Grubnik[4] found that in a group of 256 similar patients, open surgery was associated with a non-significant increase in morbidity. The lack of statistical significance is likely only due to a small sample size. There were no significant differences in operative duration or stone clearance rates. However, LCBDE was associated with a significantly lower intra-operative blood loss and length of stay.

In one of the largest reports on bile duct exploration, 2635 CBDE’s (52% OCBDE, 48% LCBDE) were analyzed from the NSQIP database[5]. OCBDE was associated with significantly increased morbidity, mortality, return to theatre and re-admission. Multivariate logistic regression to control for potential confounders continued to suggest an increase regardless of indication for OCBDE. However it is important to note that stone clearance rates were 2.8 times higher in the OCBDE group.

Single stage Therapy

Potential advantages of a single procedure include a single anaesthetic, the ability to address both the gallbladder and bile duct at the same time and obviate the need for any bile duct intervention (CBDE or ERCP) when an intra-operative cholangiogram (IOC) is negative. Patient compliance is improved with a single stage procedure by preventing dropout associated with two stages.

However, LCBDE and particularly the transcholedochal approach is a technically demanding procedure with a significant learning curve (See below). Furthermore

the adoption of a single stage strategy is still questionable in patients with acute cholangitis.

Two stage Therapy

Two-stage therapy has several drawbacks. ERCP may not be possible in patients with altered anatomy (Roux en Y gastric bypass, previous biliary diversion, Billroth II gastrectomy). Despite various stratification methods to predict intra-ductal stones, up to 68% of patients may have an unnecessary ERCP exposing patients to significant morbidity (bleeding, perforation, pancreatitis) and occasional mortality[6]. Delays between ERCP and LC risk recurrence of symptoms.

A theoretical risk of endoscopic sphincterotomy is bacterobilia and recurrent stone formation[7,8]. LC after ERCP is also more difficult possibly due to bacterobilia leading to chronic inflammation and scarring[9].

With regard to post-operative ERCP, the fundamental drawback would be when one is unable to clear the duct and thus the patient would then require a second operative procedure for ductal clearance.

Single stage versus two staged approaches – An analysis of the literature

Two Cochrane reviews[10,11] have attempted to analyze randomized data comparing different methods to address cholecysto-choledocholithiasis in patients fit for surgery.

OCBDE versus ERCP + LC

Studies comparing *OCBDE to ERCP* + LC found no significant difference in morbidity or mortality. However open surgery was significantly superior in achieving clearance of the bile duct. It is important to remember that these trials were conducted in the early era of endoscopic therapy with limited experience and may not be applicable currently. It is relevant though if a patient is undergoing a planned open procedure for whatever reason and if stones are detected on IOC that OCBDE would be applicable.

LCBDE versus post-op ERCP

Two trials with 166 were included. No differences were noted in morbidity or mortality. The LCBDE group had a significantly lower number of retained stones and a shorter hospital stay.

LCBDE versus pre-operative ERCP + LC

An updated meta-analysis of *LCBDE versus ERCP + LC* was recently published[12]. Eight RCT's including 1130 patients were identified. All trials included a proportion of patients with jaundice. No significant differences were found in mortality and morbidity. Bile leaks were more common in the LCBDE arm with pancreatitis more common in the ERCP arm.

However, LCBDE was significantly better with regard to total operating times, stone clearance and length of hospital stay. Stone clearance was largely influenced by a single study[14] which when excluded caused there to be no difference between the two arms.

The RCT by Noble and a prospective study by Zheng both demonstrated safety of LCBDE in high risk and elderly patients.

One has to interpret this meta-analysis with caution as it is limited by the studies included. The studies are likely underpowered with only two studies with more than 50 patients in each arm. Furthermore they also likely to be subject to publication bias.

Hybrid procedure

Intra-operative ERCP (IOERCP) was first attempted in the early 90's. Advantages for this are similar to those of other single stage techniques. Furthermore, the passage of a guide wire down the cystic duct into the duodenum, the so-called laparo-endoscopic rendezvous (LERV), avoids manipulation of the pancreatic duct. This may decrease the incidence of acute pancreatitis, which represents the majority of the complications associated with 2 stage techniques[12].

A recent meta-analysis of five RCT's with 629 patients compared *IOERCP to ERCP + LC*[15]. Stone clearance rates were similar between the two groups. However significant differences were found in favour of the IOERCP group with regard to acute pancreatitis, overall morbidity and length of hospital stay. In a trial from Cuba[16], 134 patients were randomized to one of three approaches (ERCP + LC, LCBDE and IOERCP). IOERCP was found to be superior to both ERCP + LC and LCBDE with fewer retained stones, post-operative complications and a decreased length of stay.

Despite these results, IOERCP has several drawbacks. Insufflation during ERCP may lead to bowel distension prohibiting adequate visualization during the laparoscopic procedure. Clamping the proximal bowel and using CO2 insufflation may mitigate this complication. The supine position also requires an extra rotation by the endoscopist to achieve adequate positioning for cannulation[15]. Perhaps the most important prohibitive factor is the logistical problems and co-ordination required with two different teams in the theatre.

Cost

As stated above, single stage strategies have equivalent clinical outcomes to two staged procedures. However single stage strategies were associated with a significantly shorter length of stay. Only two randomized studies assessed cost with both finding LCBDE to be more cost effective than ERCP + LC[21,38]. In the US study[21] this was due to higher professional fees associated with the two staged procedure and not hospitalization costs. Topal[39] reported on 53 consecutive patients, finding a single stage procedure to be significantly more cost effective.

Acute cholangitis

Endoscopic therapy for the management of acute severe cholangitis is clearly superior to open surgery with a significant difference in mortality[19]. No RCT's have looked specifically at the use LCBDE in the management of cholangitis although a small number of patients were included in some of the trials in the above mentioned meta-analysis[8,13,14,20,21] Specific outcomes for this group of patients was not provided. Several studies have looked at outcomes for patients

managed laparoscopically for acute non-severe cholangitis. Atstupens[22] found similar outcomes for patients with and without cholangitis who were treated emergently. Zhu[23] demonstrated that both early (< 72 hours) or delayed LCBDE for cholangitis had similar outcomes. However patients in the early group had a shorter length of stay and total cost. Chan[24] also found no significant differences in mortality, morbidity, conversion rates or length of stay in patients managed with emergency LCBDE. It is important to note that all these studies excluded patients with severe cholangitis. Furthermore amongst the non-severe cholangitis population, these were managed in high volume centers by experienced surgeon and thus may not be generalizable.

Learning curve

Many surgeons and trainees in established teaching programmes may have not be exposed to LCBDE during their training[27]. Laparoscopic training using simulators have been validated as a training tool for various operations. They have been shown to improve operative skill, theatre performance and have shown a reduction in complications[28]. Studies have looked at training simulators together with didactic teaching for LCBDE[29–31]. It was found that these low cost models allow for improvement in performance and confidence for both surgical trainees and practicing surgeons. A group from Veneuzuela[32] described the building of a cost effective training model using urinary catheters which may work well in the South African context.

An interesting observation in studies that have looked at training found that less experienced surgeons are able to perform LCBDE safely with similar stone clearance rates as experienced colleagues provided that they are proficient in performing LC and IOC[33,34]. They did however have significantly longer operating times.

In the study by Tutton[33], it was suggested that the learning curve was reached at 50 cases. Quaresima[35] suggests that the learning curve was complete at a more modest 30 cases (20 transcholedochal and 10 transcystic LCBDE). Keeling[36] also suggested that the learning curve for transcystic LCBDE would be reached at 10 cases. Hong[37] suggested that the learning curve for transcholedochal LCBDE was 25 cases. Zhu[26] used Cumulative sum (CUSUM) methodology to assess learning curves for transcystic LCBDE. Overall, operative times and length of stay

decreased significantly as surgeon volume increased. They found that mastery for a unit of multiple surgeons occurred after 250 cases.

Transcystic LCBDE versus Transcholedochal LCBDE

LCBDE may be carried out in two ways. In the transcystic method a choledochoscope is advanced via the cystic duct into the bile duct with subsequent removal of stones via the cystic duct. The transcholedochal approach mimics the open approach using an anterior choledochotomy.

In a meta-analysis of 18 trials, Feng[17] found no difference between transcystic and transcholedochal LCBDE in terms of stone clearance, conversion to other procedures, operative time or morbidity. However, the transcystic approach allowed for a shorter hospital stay and expense. Furthermore transcholedochal approaches resulted in a significantly increased rate of biliary morbidity. It must be noted that a transcystic approach will only be successful in about 85% of patients.

Many groups have described criteria for a transcystic approach over a transcholedochal approach. These include number, size and location of stones, cystic duct insertion and diameter and diameter of the common bile duct. However these “standards” are different for different units as they are impacted by anatomy and the use of adjunctive surgery (e.g. micro-incision) or technology (various forms of lithotripsy).

A personal view of the data

The available data appears to show clinical equivalency between LCBDE and traditional ERCP + LC. However, LCBDE is associated with a shorter length of stay and is more cost effective. LCBDE has been dogged by the perception of high technical skill requirement. Several studies have shown equivalent clinical outcomes for competent laparoscopic surgeons attempting LCBDE when compared to their more experienced counterparts especially when proctored. Transcystic LCBDE is not difficult and is marginally different from doing an IOC, hence the low numbers needed to attain proficiency. The use of simulators may also shorten the learning curve required for a transcholedochal approach. In

most cases it is probably appropriate to start with a transcystic approach and convert to a transcholedochal approach as needed. With continued refinement in technique and increased teaching, LCBDE has the potential to become the gold standard in the management of choledocholithiasis. ERCP will continue to have a role, particularly in patients presenting with acute severe cholangitis. IOERCP has demonstrated good results but will unlikely become mainstream practice due the logistics issues. An alternative approach to achieve some of the benefits would be scheduling ERCP and LC a day or two apart. Currently, the best approach will be one that balances the expertise and resources available with the safety and comfort of the patient in front of you.

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Feasibility and efficacy of Laparascopic vs open Liver Resections

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The first laparoscopic liver resection (LLR) was reported in 1993 (Gagner 1993), however the uptake has only recently increased markedly. (Vigano 2009) The vast majority of hepatic resections are stand-alone procedures, without any need for reconstruction, which should make them good candidates for a laparoscopic approach. The probable reasons for the slow uptake may be summarized by (i) technical difficulties especially with controlling haemorrhage and elementary maneuvers of open hepatic surgery (manual palpation, organ mobilization, and parenchymal transection) (ii) pneumoperitoneum may increase the risk of gas embolism especially when having haemorrhage from the hepatic veins or inferior vena cava, (iii) possibility of oncological inadequacy and tumor spread. (Cherqui 2000)

Feasibility

In general the indications for laparoscopic hepatectomy do not differ from those for open surgery, however feasibility is limited by the technical ability to perform the laparoscopic surgeries. (Kaneko 2005) Most high volume liver resection units report a 5-30% laparoscopic surgery resection rate (Topal 2008; Dagher 2007), and a select few report a rate of 50-80% laparoscopic liver resection. (Buell 2008; Cho 2008)

Tumor location

Lesions located in the antero-lateral segments of the liver (segments 2–6, the so-called “laparoscopic segments”) and scheduled for wedges, segmentectomies,

and left lateral sectionectomies are the best indications for the laparoscopic approach. (Vibert 2006)

Laparoscopic right hepatectomy can be planned for lesions located anywhere in the right lobe, with the exception of those close to the liver hilus or the hepato-caval junction because of the risk of major vascular or biliary injury. The role of laparoscopy for lesions requiring resections of segments 7, 8 and 1 is not yet codified. These segments have been traditionally considered as non-laparoscopic segments because of difficult visualization of the surgical field. (Sasaki 2009)

Tumor size

Except for exophytic lesions which are easy to resect by laparoscopy, and is not recommended for lesions exceeding 5 cm in diameter. (Chen 2008)

Morbidity

Gas embolism

The risk of gas embolism due to lesions of the hepatic veins during parenchymal transection has been suggested, however, the occurrence of gas embolism in clinical practice is extremely low. (Farges 2002) In a review of approximately 200 LLR surgeries only two cases of gas embolism were reported. (Biertho 2002) Carbon dioxide pneumoperitoneum minimizes the risk of gas embolism as compared to air, and low pneumoperitoneum pressure further reduces its incidence, which is now standard practice for LLR. (Palmer 1993)

Bleeding

The main technical challenge of LLR remains controlling significant intraoperative hemorrhage during parenchymal transection. Some cases of severe hemorrhagic complications have been reported in the literature, usually related to hepatic veins injuries (Vibert 2006), and are usually managed (either laparoscopically or) by conversion to laparotomy. Only ten (<0.5%) postoperative

deaths have been reported in more than 2000 published LLR's. (Vigano 2009) The causes of death included three liver failures in cirrhotic patients, one brain death after major intraoperative hemorrhage, one sepsis, and one acute respiratory distress, the rest were not listed.

Oncological results

The proper use of oncological surgical principles has reduced the problem of peritoneal seeding and port site recurrence to the level that there are no more differences relative to open surgery. (Vibert 2006) Some studies have compared oncological results of laparoscopic and open surgery, including those of any kind of malignant lesion, and reported a similar margin width, recurrence risk, and overall survival rates (Lee 2007; Gigot 2002). The addition of intraoperative laparoscopic ultrasonography has been specifically associated with an increased rate of negative margins (Gigot 2002). It is important that oncological principles are strictly followed during LLR: 'no touch', no direct manipulation of the tumor, immediate conversion in the case of locally advanced cancer, and protection for extraction.

Conclusion

Good candidates for LLR are patients with peripheral lesions requiring limited hepatectomy or left lateral sectionectomy. In these cases, intra- and postoperative outcomes are better, including reduced blood loss, morbidity rates, need for analgesic, and hospital stay, than those of their open resection counterparts. The benefits of the laparoscopic approach have also been demonstrated in cirrhotic patients. However, the rules of oncological surgery must be followed for minimally invasive operations, just as in open surgery.

Must read

Recommendations for Laparoscopic Liver Resection: A Report From the Second International Consensus Conference Held in Morioka. Wakabayashi G et al.. Annals of Surgery 2015, 261(4); 619-29.

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The indications for surgery and surgical options in Chronic Pancreatitis.

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Introduction

Chronic pancreatitis (CP) is a pathologic fibro-inflammatory syndrome of the pancreas in patients with genetic, environmental and/or other risk factors who develop persistent pathologic responses to parenchymal injury or stress. Although alcohol is the predominant aetiological factor it is increasingly recognized that CP is a multifactorial disease in which the interplay between genetic and environmental factors plays an important role. In the alcohol-induced group psychosocial and economic factors are often coupled with substance abuse, including tobacco, which add to the complexity of their management. Pathological features of CP are pancreatic atrophy, fibrosis, duct distortion, strictures, calcifications, fluid collections, ascites and obstruction of adjacent structures. In longstanding disease, pancreatic exocrine and endocrine dysfunction are inevitable and there is an increased risk of malignancy. Some or all of these features may be present in individual cases but are more likely to be present in those with longstanding or advanced disease.
Pain is the predominant symptom. Pain patterns vary from minimal to intermittent during flares, to persistent and intractable requiring opioids for control resulting in impaired lifestyle and quality of life. The exact pathogenesis of pain remains poorly understood. Ductal obstruction and hypertension, parenchymal tissue fluid hypertension, inflammatory cytokines producing visceral and central nerve stimulation and sensitization, and tissue hypoxia causing oxygen-derived free radicals damage are the major aetio-pathogenic postulates. A recent review coalesces the role these various factors play.

Non-surgical management of CP

The mainstays of medical management include lifestyle modification emphasizing abstinence from alcohol, cessation of smoking and dietary modification utilizing a low fat, balanced protein carbohydrate diet. Exocrine and endocrine failure need to be monitored for and effectively managed. A step up approach for pain relief utilizing standard non-opioid analgesics and anti-inflammatories progressing to opioid containing medications the traditional approach however some evidence is accruing in favor of earlier surgery prior to opiate dependency as an alternative strategy. Neurolysis by thoracoscopy or image guided techniques are also employed in selected cases for pain control.

Cross sectional imaging prior to surgery

Careful evaluation of the patient's general state of health, severity of symptoms and detailed imaging of the pancreas and biliary system are required to individualize treatment. CT and MRI/MRCP are the key investigations used to select the appropriate treatment while ERCP is now reserved for endoscopic interventions. Endo-ultrasound (EUS) has become an important adjunct to endoscopic drainage procedures and to exclude an underlying malignancy.

Complications

Complications occur in about a third of patients with chronic pancreatitis (CP) during the course of the disease and may lead to considerably morbidity if not managed appropriately. Modern imaging has become invaluable in the assessment of the nature and extent of these complications while radiological and endoscopic interventional procedures have broadened the treatment armamentarium. These complications occur not only in the gland but also in adjacent structures due to extension of the inflammatory process, particularly to the common bile duct and the duodenum.

Bile Duct Obstruction

Bile duct obstruction (BDO) is commonly seen during the advanced stages of CP when there is an associated inflammatory mass and calcification in the head of the pancreas. The obstruction can be caused by oedema during an acute on chronic attack, compression of a contiguous intra-pancreatic fluid collection or by fibrosis. The presentation and natural history may thus vary according to the predominant underlying pathology. The clinical spectrum ranges from an incidental finding on imaging with a disproportionately raised alkaline phosphatase level to overt obstructive jaundice with associated severe pain. The natural history is unpredictable but it should be noted that jaundice may resolve in half of patients after resolution of an acute on chronic attack. There are conflicting reports on the risk of developing secondary biliary cirrhosis but, when all publications are considered, the incidence is low amongst those patients with low grade BDO.
Cholecystectomy and hepaticojejunostomy is the treatment of choice in patients with persistent jaundice and minimal pain. However fully covered removable self expanding metal stents have also been shown to be efficacious in well selected patients.

Pancreatic fluid collections (PFCs)

Pancreatic fluid collections (PFCs) and pancreatic ascites, may be the result of duct obstruction and/or disruption secondary to focal necrosis. In addition, rupture of the collection usually presents as ascites or rarely as an isolated pleural or pericardial effusion secondary to a retroperitoneal leak. PFCs may cause duodenal or biliary obstruction or become secondarily infected. Another serious complication is haemosuccus pancreaticus that occurs when inflammatory erosion into neighbouring arteries results in a false aneurysm. whose rupture into the pancreatic duct presents as an upper gastrointestinal bleed.
Most patients with symptomatic PFCs will require drainage but under certain circumstances conservative treatment can be tried first if, for example, there is concern about the “maturity” of the PFC or when major surgery is being considered to address associated pancreatic pathology.
There is very little level I evidence to support any particular method of drainage but there is now accumulated evidence that when feasible, endoscopic drainage (ED) either transduodenal or transgastric should be the first line of treatment

preferably with EUS guidance. ED is less invasive than surgical drainage, is safe in skilled hands and has a high success rate. Intuitively, surgery with a lateral pancreatic-jejunostomy would seem to be the first choice if there is associated pancreatic duct obstruction with pancreatic dilatation. There is very little data to support this approach other than that surgical drainage of the pancreatic duct in this setting is all that is required. On the other hand, It could be argued that considering the safety record and high success rate of endoscopic drainage of CP PFCs, patients have nothing to lose by having endoscopic drainage first and then reserve surgery for failures.

Haemorrhage

Haemorrhage associated with CP may be due to analgesic-induced peptic ulcer disease, false aneurysms related to PFCs or gastric varices secondary to segmental portal hypertension. Surprisingly the risk of bleeding from gastric varices is low and there is no need for prophylactic intervention. Most cases with bleeding from false aneurysms can be successfully managed by selective angiographic embolization. Surgery should be the last resort and is aimed at vascular control rather than performing a major resection unless the aneurysm is situated towards the body or tail of the pancreas.

Duodenal obstruction

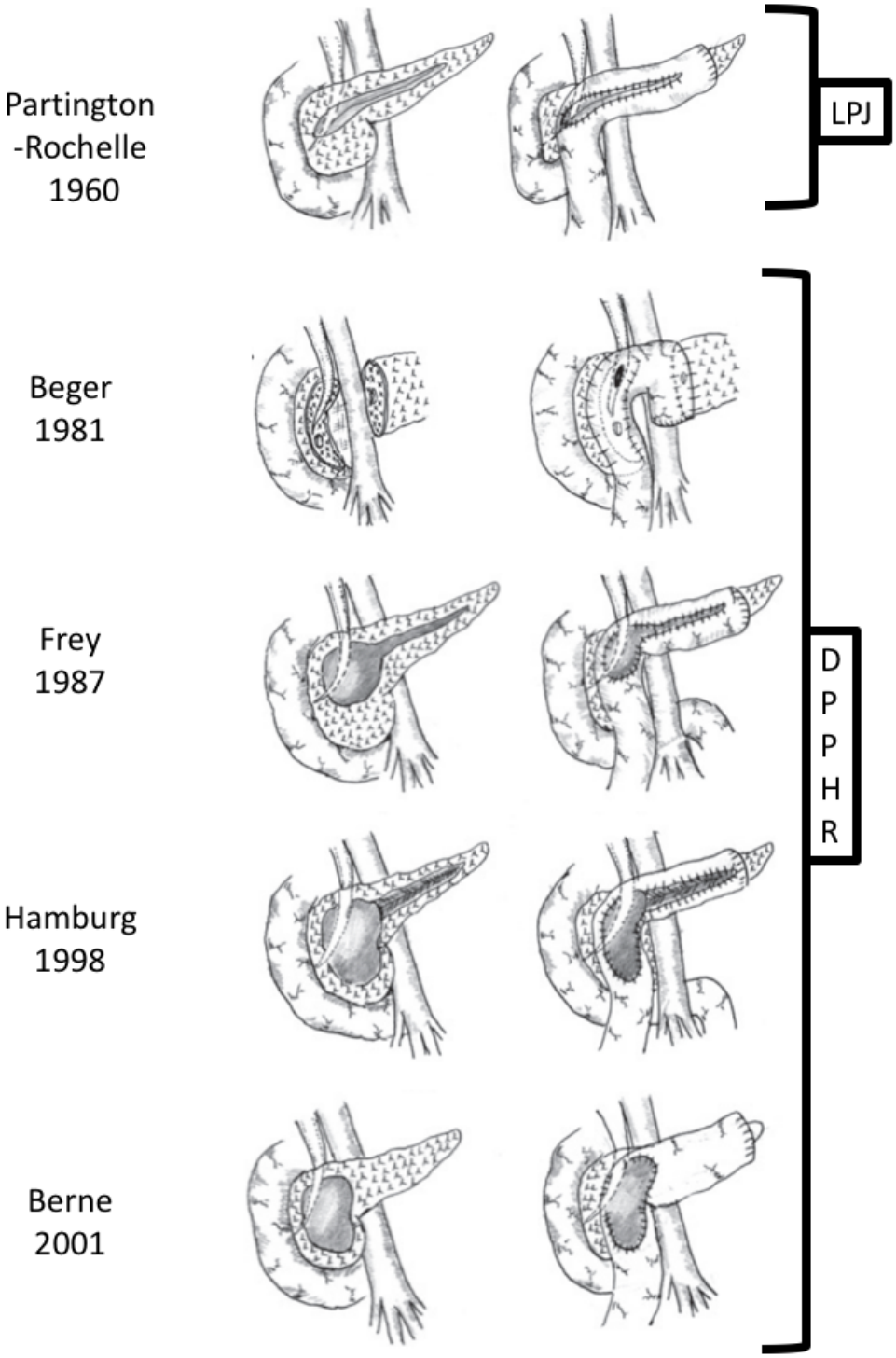
Overt duodenal obstruction is less frequently seen in CP but many patients with advanced disease will have subclinical evidence of delayed gastric emptying. A PPPD should be considered when duodenal obstruction is associated with a BDO and an inflammatory mass in the head of the pancreas. Minimal-access options are now integrated into management algorithms. These include utilizing ERCP and EUS for endotherapy of Pancreatic Fluid Collections (PFC), ductal strictures, and pancreatic calculi removal (with or without ESWL).

Surgical management for pain

Pain is the leading symptom of CP. After failure of initial limited conservative treatment operative treatment for CP is indicated. The current focus is on the

timing of minimally invasive interventions or surgery in relation to when conservative treatment has failed. A systematic review
suggests that earlier intervention may improve the outcome. This is based on the fact that the pain pathways become centrally autonomous rather than locally mediated with time and that local interventions are less likely to be effective when this has occurred. This concept is currently being explored in the Dutch Pancreatitis Research group in the ESCAPE trial which started recruiting in 2013 and finished recruiting in July of this year.

Surgical Intervention of CP is performed to address pain and/or complications. Surgical procedures can be classified as drainage procedures, resective procedures or a combination of both. In the absence of an inflammatory pancreatic head mass lateral pancreato-jejunostomy (LPJ) (Partington Rochelle operation) remains a commonly performed procedure in the presence of a dilated main pancreatic duct (Figure 1). The simplest of the resections is a distal pancreatectomy when the disease is confined to the body and tail of the pancreas. Approximately 30% of patients presenting with CP will have an inflammatory mass in the head of the pancreas that can be addressed by resective procedures such as pancreato-duodenectomy (PD) or pylorus-preserving pancreato-duodenectomy (PPPD). Duodenal preserving pancreatic head resections (DPPHR) with or without drainage of the pancreatic duct are now increasingly performed. These were originally described by Frey and Beger (9, 10) though more recently a number of modifications, often referred to as hybrid procedures, have been devise. These DPPHR variations are shown schematically in Figure 1. PPPD can lead to complete pain relief in about 75%–82% of patients in the short and long term with a mortality rate of less than 3% and excellent long-term survival. Ongoing exocrine and endocrine deterioration appears to be unrelated to the type of resection or whether resection is combined with a drainage procedur. While no apparent difference in mortality rates has been found among standard PD, PPPD and DPPHR, the duodenal-preserving procedures are associated with significantly lower morbidity rates than pancreatico-duodenectomy (9% to 22% versus 20 to 70%) (8). The current trend therefore is to favour drainage or combination procedures. A few centres with the experience and technical expertise have the option to perform a total pancreatectomy and carry out autologous islet cells isolation and transplantation. A technique applicable to small duct disease, hereditary pancreatitis with its high risk malignant transformation or as a salvage technique for failed prior surgery.



LPJ = lateral pancreato-jejunostomy

DPPHR = duodenal preserving pancreatic head resections

Conclusion

Strategies to get CP sufferers to stop smoking is paramount as it is a major driver of disease progression. Many of the complications of CP can be managed with a variety of minimally invasive approaches without having to resort to major complex surgery. When pain is the overarching symptom alone or in combination with other complications, a morphological and comorbidity assessment allow the surgical approach to be tailored to the patient. The concept of that surgery should be considered before opiate dependency is gaining gaining credence. It should be remembered that all surgical therapy remains an interlude in a disease which requires a holistic multidisciplinary approach and requires life long follow up.

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Pros and cons of surgery vs Therapeutic Arterial Embolization in Splenic Trauma

Current Concepts In Splenic Injuries Update

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Splenic injuries are still the most common solid organ injury in blunt trauma, followed by liver trauma. Haemodynamically unstable patients who do not respond to fluid management require urgent surgical intervention i.e. splenectomy. There is still no role in re-implanting the splenic tissue under these circumstances. The splenic tissue regenerated after splenic re-implantation, does not offer any immunity benefit.

Splenic preservation is the standard for haemodynamically stable patients. Even in the elderly patients, the spleen can be preserved following current non-operative management (NOM) standards. Contrast CT scan remains the essential investigation of choice to evaluate solid organs and exclude hollow viscus injury. Presence of fluid without solid organ involvement should prompt surgical or laparoscopic exploration. The haemodynamic status, and not the grade of splenic injury is the key factor in successful outcomes of NOM. The amount of fluid in the abdomen is not an independent determinate of outcome.

Haemodynamic status is determined by not just looking at the blood pressure and the pulse status of the patient (see table 2), but also the other markers of perfusion. These markers include lactate, BE, cardiac output monitoring (invasive and minimally invasive). The more normal these values are, the greater the success of NOM. There is a need for ongoing monitoring under these circumstances to optimize outcome. Monitoring in NOM is best done in an ICU or High dependency unit. There is no science to determine how long a patient should be observed for in a high care environment; the most common practice is at least a day per grade of injury before transferring to an ordinary ward.

Well-resourced units have been able to push the envelope of haemodynamic status to include more borderline patients. However, this practice should not compromise overall patient outcome in the name of new and available technology. A non-responder will still need to have their bleeding stopped immediately in a controlled environment i.e. theatre. The transient responder should be evaluated within the availability of resources in an institution. These resources may vary depending on the time of the day or the day of a week.

Other than splenectomy, surgery should play a minor role in the management of splenic injuries. The low grade splenic injuries that are diagnosed should preferably be managed without surgery. If in theatre for other indications, the spleen should be handled with care to minimize further trauma during mobilization. Local haemostatic agents can play a role in controlling minor to moderate bleeders during surgery. The traditional splenorrhaphy techniques, and even the use of mashes to wrap the spleen, should rarely be practiced in modern medicine.

Advances in interventional radiology has offered further adjunct to management of these injuries. This advantage has been further enhanced by availability of Hybrid suites (RAPTOR) that allow for combination of radiological and surgical approaches in a controlled environment while resuscitation continues in a multiple injured patient. This still requires logistics of getting trained personnel in theatre without compromising care. Most centres do not enjoy this luxury, and therefore need to keep management protocols simpler.

Radiology is indicated in the presence of a vascular blush, which is indicative of ongoing bleeding. Care must be taken to make sure that there is no delay to embolization, while appropriate fluid resuscitation with blood products is maintained. What is debatable, is whether the embolization should be central or highly selective. The available expertise will influence the choice between these approaches.

Highly selective embolization, preferably with coils, will minimize tissue damage and splenic necrosis. This requires sophisticated skill and may take much longer with less experienced individuals. Radiological confirmation of control of bleeding will be accompanied by appropriate improvement in haemodynamic status. Less tissue necrosis implies better splenic preservation, and continued immunity functional state. A Japanese study showed good immunity in embolized patients with a follow up to 2,9years.

The central embolization of the splenic artery is a less complex procedure. This results in overall decrease in the pressure flow within the injured spleen, thus allowing for slowdown of bleeding. This approach has been shown to be successful and can also be achieved with minimal radiological apparatus, like a normal C-arm. The blood supply is also re-established from the collateral, via the short gastric. Unfortunately, there is a chance of causing significant tissue necrosis, with resultant septic complication. Abscess formation and complete disintegration of the spleen have been reported. Studies have shown that the immunological function can still be preserved with this approach.

Catheter related vascular complications should always be anticipated. Local vascular wall damage at the site of insertion of the catheter can be complicated by simple haematomas, to significant wall damage with resultant ischaemic complication to the limb. This is complicated by the occasional coagulopathy that is associated with the bleeding trauma patient. We prefer to compress locally before applying locally compressive dressings that can be removed later in the ward. Very rarely do we need to leave the catheter in situ, to have it removed once coagulation has been corrected.

Controversy persists regarding the role of pre-emptive angiogram in the absence of a blush on contrast CT scan. This practice is aimed at doing formal angiogram in all major splenic injuries of grade III and above, with an intention of embolizing if there is evidence of bleeding. There is no Level I or II evidence that this strategy improves outcomes compared to standard embolization based on finding first a blush on CT scan. However, some of the Level III evidence shows a superior splenic salvage rate of greater than 90% even in grade IV and Grade V injuries.

There is further debate about the role of repeat CT scan in these injuries. Concerns for later complications increase with the grade of injury. This is further complicated by the concern for delayed splenic rupture in NOM. Some of the splenic ruptures have been reported as late as two months after the trauma, although majority will happen within a week. Ability to detect pseudo-aneurysms on Ct scan before they rupture is beneficial. However, increased irradiation with repeat CT scan should be balanced with the advantages of the yield from such an investigation. In resource limited conditions, the automatic repeat CT scan is not economical. The CT scan is then only requested for symptomatic cases (e.g. drop in Hb level) and also for those involved in professional sports.

Irrespective of NOM, early mobilization in the absence of other contraindications is standard of care. The use of thrombo-prophylaxis with appropriate pharmacology is safe in 24-48 hrs in the presence of normal coagulation and normal platelet function. The use of aspirin in only relevant in those patients who have a platelet function of greater than 1000 count post-splenectomy. Overwhelming post-splenectomy infection (OPSI) is reported in 0,05-2% of the cases, and may happen as late as 65yrs of age. The mortality rate of 50% has been reported in OPSI cases. If splenectomy is performed, then the patient receives immunization with Pneumococcal vaccine, Meningococcal vaccine as well as Haemophilus influenza vaccine (see table 3). The timing for these vaccines is best performed at two weeks after the surgery when they are able to mount a good immune response. Lack of follow-up in most of the discharged trauma patient dictates immunization at discharge, should the patient be discharged before the two-week period.

The resuscitative endovascular balloon occlusion of the aorta (REBOA) has the potential benefit of decreasing bleeding from the associated splenic injury. The impact of this technique in improving haemodynamic status is well established. The role in improving salvage rates of splenic injuries is not yet clarified. The role of laparoscopy in splenic management still needs to be determined. Surgical principles should not be altered by availability of less invasive techniques.

Conclusion

Management of splenic injuries should be based on the haemodynamic status of the patient. Availability of resources can allow for more splenic preservation. Angio-embolization techniques, whether central or highly selective, can improve the splenic preservation rate for high grade injuries. The role of laparoscopy and REBOA is yet to be defined.

Table 1: AAST SPLENIC INJURY GRADE	
Grade I	Laceration <1cm or subscapular haematoma<1cm
Grade II	Laceration 1-3cm or subscapular haematoma1-3cm

Grade III	Laceration <3-10cm or subscapular haematoma<3-10cm
Grade IV	Laceration <10cm or subscapular haematoma<10cm
Grade V	Devascularized spleen

Table 2 Western Association approach to Hemodynamic Instability Score	
Grade 0:	No significant hypotension (systolic blood pressure SBP 90 mm Hg) or serious tachycardia (heart rate HR 130)
Grade 1:	Hypotension or tachycardia by report but none recorded in emergency department
Grade 2:	Hypotension or tachycardia responsive to initial volume loading with no ongoing fluid or PRBC requirement
Grade 3:	Hypotension or tachycardia responsive to initial volume loading with modest ongoing fluid (250 mL/h) or PRBC requirement
Grade 4:	Hypotension or tachycardia only responsive to 2 L of volume loading and the need for vigorous ongoing fluid infusion (250 mL/h) and PRBC transfusion
Grade 5:	Hypotension unresponsive to fluid and PRBC transfusion

Table 3: POST SPLENECTOMY VACCINATIONS	**Dose**	**Route**	**Revaccination**
Polyvalent pneumococcal	0.5 mL	SC	Every 6 years
Quadra valent meningococcal/diphtheria conjugate (16-55yr old)	0.5 mL	IM upper deltoid	Every 3-5 years
Quadra valent meningococcal polysaccharide (55yr old)	0.5 mL	SC	Every 3-5 years
Haemophilus b conjugate	0.5 mL	IM	None

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Role of Inferior Vena Cava (IVC) Filter in Trauma

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Inferior vena cava filters (IVCF) in trauma

Pulmonary embolisms (PE) occur in up to 1.5 – 9 % of patients who survive their initial trauma. Chemical strategies in combination with mechanical compression devices have been well described in decreasing the risk of venous thromboembolism (VTE)

The trauma patient presents additional challenges with regards to prophylaxis. Often these patients are coagulopathic and have intracranial bleeds. In addition they have extremity fractures which prevent the application of mechanical compression devices.

Vena caval filters have been proposed as an alternative not only for prophylaxis but for therapy as well. Vena cava filters can be placed into the superior vena cava (SVC) or more commonly into the inferior vena cava (IVC) for either preventing or treating pulmonary embolism. Two types of filters are available namely permanent or retrievable.

Although vena caval filters seem a logical alternative for both prophylaxis and therapy the studies have been controversial.

Decousus et al in the PREPIC study enrolled 400 patients with acute proximal DVT. The addition of IVC filter placement to routine anticoagulation for patients with proximal DVT leads to a 4% absolute reduction in PE risk. The benefit of IVC filter placement was offset by doubling the rate of recurrent DVT at 2 years.

The follow – up PREPIC 2 study enrolled 399 patients with a confirmed acute PE. Patients either received a retrievable fliter or not. There was no difference in the primary outcome of recurrent symptomatic PE at 3 months (3% vs. 1.5%; P=0.50), nor were there significant differences at 6 months. The authors

conclude that among patients with acute PE at high risk of recurrence, temporary placement of a retrievable IVC filter should not be routinely performed; IVC filters should generally be reserved for patients with contraindications to anticoagulation.

In view of these large studies the role of IVCF in both prophylaxis and therapy in VTE remain controversial. Presently there is more consensus on the indications for IVCF use in therapy with different organisations having similar guidelines

ESC Guidelines on the Diagnosis and Management of Acute Pulmonary Embolism, 2014

- Routine use of IVC filters is not recommended (Grade 3A)
- IVC filters should be considered in patients with acute PE and absolute contraindications to anticoagulation (Grade 2C)
- IVC filters should be considered in cases of recurrence of PE, despite therapeutic levels of anticoagulation (Grade 2C)

ACCP Antithrombotic Therapy for VTE Disease, 2012

- In patients with acute PE who are treated with anticoagulants, we recommend against the use of an IVC filter (Grade 1B).
- In patients with acute PE and contraindication to anticoagulation, we recommend the use of an IVC filter (Grade 1B).

The use of IVCF as prophylaxis for VTE had initially gained favor in the early 2000s. However the data has not been convincing. Complications associated with the use of the device have been an ongoing concern. Filter migration, thrombosis, fracture, and perforation have been documented. The most concerning problems with filters are the low retrieval rate with retrieval rates as low as 30%. Most common reasons are the risk of haemorrhage, injury to IVC, filter in growth and poor follow-up of the patients – seen most commonly in trauma patients.

The EAST guidelines 2002 provide similar guidelines as the ESC and ACCP to for the use of IVC filters as a therapy.

Its role in the prophylaxis of VTE in trauma patients like in the other patient populations remains weakly supported. EAST guidelines recommend its use in the prophylaxis of high risk trauma patients who have injury patterns rendering them immobilized for a prolonged period of time, namely:

a. Severe closed head injury (GCS score < 8).

b. Incomplete spinal cord injury with paraplegia or quadriplegia.

c. Complex pelvic fractures with associated long bone fractures.

d. Multiple long bone fractures

Kidane et al in a systematic review on the use of prophylactic IVCF's in trauma patients concluded the literature is still plagued by a lack of high quality data.

Therefore the true efficacy of prophylactic IVC filters for prevention of PE in

trauma patients remains unclear. Further studies are required to determine the true role of prophylactic IVC filters in trauma patients.

Sarosiek et al in 2017 retrospectively reviewed 451 patients with IVC filters inserted over a 9 year period. They matched 1343 controls. They concluded there was no significant difference in survival in trauma patients with vs without placement of an IVC filter, whether in the presence or absence of venous thrombosis. The use of IVC filters in this population should be reexamined because filter removal rates are low and there is increased risk of morbidity in patients with filters that remain in place.

It is becoming clearer that the indications for use of IVCF's in therapy is limited to a few indications as supported by both ESC and the ACCP guidelines.

On the other hand the data to support the prophylactic use of IVCF in all patient populations, including trauma patients, is progressively diminishing. Appropriate and judicious patient selection is advocated for the insertion of the IVCF. Chemical anticoagulation in combination with mechanical compression devices remains the mainstay for both prophylaxis and therapy in VTE.

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Management of complex Pancreatic-Duodenal injuries

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Introduction

Pancreatic and duodenal injuries occur in 3-5% of abdominal injuries. Although high grade pancreas and duodenal injuries are uncommon, they often present as diagnostic and surgical management challenges and are prone to developing devastating complications requiring prolonged hospital stay. In a review of 15 papers describing more than 1400 patients, the mortality for penetrating duodenal injuries was 9% and 18% for blunt injuries. In a review of 76 case series describing nearly 5000 patients, the mortality rate attributed to pancreatic injuries was 20 percent for penetrating injury and 19 percent for blunt injury. (Asensio JA, Feliciano DV, et al 1993) (Asensio, Demetriades et al 1999)

Increasing grades of injury are associated with an increase of morbidity and mortality, especially related to infectious complications. Most injuries to the pancreas and duodenum are of low grade and can be managed nonoperatively or using relatively simple surgical techniques, though more complex injuries may require pancreatic and/or duodenal resection and reconstruction

Complex pancreatico-duodenal injuries are for practical purposes those that can be classified as Grade 4 and 5 on the duodenal and/or pancreas AAST Organ Injury Scale, and may include various permutations of combined injuries to the pancreas head, pancreatic ducts, duodenum, ampulla, distal bile duct, and often other adjacent structures as well. The exact anatomical diagnosis and extent of the injury is often unclear at the time of emergency surgery. This is, in fact, one of the significant dilemmas associated with injuries to the region of the head of the pancreas. Both blunt and penetrating pancreatico-duodenal injuries are frequently associated with injuries to liver, colon, diaphragm and small bowel. Up to 37% of penetrating injuries to this region may be associated with some of the most challenging vascular injuries, such as injuries to the portal vein,

proximal mesenteric vessels, IVC or peri-hiatal aorta. (Vasquez, Coimbra, Hoyt et al, 2001)

Diagnosis

Information regarding the mechanism of injury plays an important role in suspecting retroperitoneal injuries, as they may initially not present with significant peritonism or immediate indications for surgery. A history of high speed deceleration injuries, seat belt pattern bruising and bicycle handlebar related injuries should always prompt further investigation, as should injury patterns that include epigastric bruising, lumbar vertebral body fracture, persistent or progressive pain, abdominal pain radiating to the back, unexplained tachycardia and ileus. No clinical findings are specific for or unique to pancreatico-duodenal injuries, nor are biochemical parameters such as serum amylase or lipase levels.

In unstable patients, FAST may confirm non-specific intra-peritoneal free fluid, but is unlikely to demonstrate injury to retroperitoneal structures. Abdominal X-ray, in the case of concomitant duodenal injury, classically may show a ground glass appearance or retroperitoneal air outlining the duodenum or kidney.

Hemodynamically unstable patients should proceed to urgent surgery, with rapid control of bleeding and contamination. The presence of a central retroperitoneal hematoma, however small, mandates exploration, to inspect the whole of the duodenum as well as the head and tail of the pancreas.

In hemodynamically stable patients, high quality contrasted CT scanning may confirm the diagnosis, although sensitivity may vary from 59% to 92%. (Rekhi et al 2010). (Velmahos et al 20019)

CT findings suggestive of duodenal injury include duodenal wall thickening, extra-luminal air, peri-duodenal fluid, fluid in the right anterior para-renal space, diminished enhancement of the injured duodenal wall segment, extraluminal contrast and collections of blood, seen as heterogenous fluid accumulation near the injured area. Pancreatic laceration, hematoma or fluid extravasation, edema or poor pancreatic attenuation are indicative of pancreatic injury.

The critical question is whether the pancreatic ducts and/or bile ducts are intact, as this will determine further management. Despite high resolution scanning,

between 5 to 10 percent of pancreatic ductal injuries are missed with abdominal CT. In a multicentre study of 206 patients, the sensitivities of 16-channel and 64-channel multidetector abdominal CT were 54.0 and 52.4% respectively, with specificities of 94.8 for 16-channel and 90.3% for 64-channel CT scanners. (Phelan HA et al 2009)

In hemodynamically stable patients, where CT or surgery cannot confirm the integrity of the pancreatic duct, and pancreatic injury is suspected, ERCP or MRCP can be performed. ERCP offers the benefit of diagnosis and treatment, such as stenting of pancreatic and bile duct injuries, or utilising other endoscopic techniques such sphincterotomy to facilitate drainage. (Lin BC et al 2006) MRCP has the advantage of being non-invasive. Disadvantages of MRCP is that the injured patient is inaccessible for the duration of the procedure and it does not offer treatment options.

Injury Grading

The American Association for the Surgery of Trauma (AAST) injury grading system provides a universal practical way to describe the severity of the injury, but does not always relate to treatment recommendations.

Duodenal injury scale

Grade I: Hematoma involving a single portion of duodenum or partial thickness laceration without perforation

Grade II: Hematoma involving more than one portion or disruption <50 percent circumference or major laceration without duct injury or tissue loss

Grade III: Laceration with disruption of 50 to 75 percent circumference of 2nd portion or disruption of 50 to 100 percent circumference of 1st, 3rd, 4th portion

Grade IV: Laceration with disruption >75 percent circumference of 2nd portion or involving ampulla or distal common bile duct

Grade V: Massive laceration with disruption of the duodeno-pancreatic complex or devascularization of the duodenum

Pancreas injury scale

Grade I: Minor contusion without duct injury or superficial laceration without duct injury

Grade II: Major contusion without duct injury or tissue loss, or major laceration without duct injury or tissue loss

Grade III: Distal transection or parenchymal/duct injury

Grade IV: Proximal transection or parenchymal injury involving ampulla

Grade V: Massive disruption of the pancreatic head

Non-operative management

Only indicated for Gr 1 and 2 pancreas / duodenal injuries and duodenal hematomas. Patients with duodenal hematomas require nutritional support and nasogastric drainage for up to 10 days. If they remain obstructed beyond 10-14 days, surgical drainage is required.

Operative management

Urgent surgery is required for hemodynamically unstable patients, signs of peritonism, as well as grades 3 to 5 duodenal injuries, grades 3 to 5 pancreatic injuries and the vast majority of penetrating injuries.

Access and assessment

Midline laparotomy, mobilisation of the hepatic flexure of the colon is followed by Kocherisation of the duodenum, with or without a full right medial visceral rotation, to inspect the anterior and posterior aspects of the pancreatic head and neck, as well as D1, 2 and 3. In addition, the gastro-colic omentum should be divided to inspect the posterior aspect of D1, the medial aspect of D2 and the surface of the body and tail of the pancreas. If distal pancreatic injury is suspected, mobilisation of the ligaments of the spleen to a point where it can be elevated into the laparotomy wound, together with mobilizing and lifting the inferior edge of the pancreas, will allow the tail to be inspected and resected if

required. To expose the 4th part of the duodenum, mobilize the ligament of Treitz.

All retroperitoneal haematomas, however small, in the peri-duodenal and peri-pancreatic areas need to be carefully inspected. Pancreatic lacerations bleed and will present with a significant hematoma in the area. Pancreatic clear fluid leaks are difficult to see although saponification (white streaks on fatty tissue) of adjacent tissues may be present. Signs of duodenal injury include bile staining of the retroperitoneal tissues or duodenal wall and air in the retroperitoneum. A duodenal hematoma should be carefully assessed, taking care not to inadvertently convert a closed injury into an open injury, as these hematomas usually resolve with conservative management.

Secretin, (1 unit/kg intravenously) can be given to stimulate pancreatic secretion. Intraoperative ultrasound can also be used to detect pancreatic parenchymal or pancreatic duct injury If a pancreatic duct injury is suspected but cannot be confirmed, cholangiopancreatography (or cholecystopancreatography) may be performed. (Subramanian A, et al 2007) (Wind P, et al 1999) (Hikida S et al, 2004)

Intra-operative assessment of the pancreatic and bile ducts may be simple: look for a more than 50% transection of the pancreas, or a penetrating wound through the centre of the pancreas head. For unconfirmed injuries, further investigations, either intra- or post operatively, may be required.

Intraoperative cholangiopancreatography during trauma exploration is performed through an existing duodenal wound, or via anterior duodenotomy. A small catheter is inserted into the common bile duct or pancreatic duct injecting 2 to 5 mL of soluble contrast into the duct while imaging using fluoroscopy or shooting a plain film.

Intraoperative endoscopic retrograde cholangiopancreatography (ERCP) can also provide the necessary imaging but would require the abdomen to be closed and the patient to be re-positioned in lateral decubitus position on a radiolucent table.

An alternative approach is to apply temporary abdominal closure and then obtain a postoperative study (ERCP or MRCP) to evaluate the ductal anatomy. Positive findings are then surgically managed as soon as practically possible.

Damage control options

Patients who require damage control for reasons of coagulopathy, shock and physiological decompensation, should have duodenal injuries repaired, excised, ligated or stapled, sometimes without restoring continuity. Pancreas and bile duct injuries are drained. All other injuries are managed with the principles of haemorrhage control, control of contamination and temporary closure. In selected cases, with distal pancreatic ductal injury or obvious transection, especially with concomitant splenic injury, damage control may include distal pancreatectomy with splenectomy. Bleeding from the pancreas distal to the neck of the pancreas can usually be controlled with packing. High grade injuries to the head of the pancreas, which may also involve the duodenum, are often associated with bleeding that cannot be controlled by packing, consequently resection without reconstruction may be needed. To resect the proximal duodenum and pancreas, the pylorus, pancreatic neck, and proximal jejunum are stapled across and transected, the common bile duct is ligated, and the biliary tract is drained with a tube cholecystostomy. Closed suction drains are placed to control duodenal and pancreatic secretions. Following resuscitation, stabilization and imaging, definitive resection and reconstruction (Whipple) can be done.

Extensive pancreatic head injuries may be difficult to assess, as the integrity of the pancreatic duct, bile duct and ampulla may be unsure. The preferred option is drainage, temporary closure, physiological stabilisation and planned assessment with ERCP, followed by definitive surgery.

Emergency surgery in the hemodynamically stable patient

If damage control is not indicated, distal pancreatic duct injuries (to the left of the superior mesenteric vessels) are treated with distal pancreatectomy and drainage. Spleen preserving pancreatectomy is only indicated if there are no other significant injuries and the patient is hemodynamically and physiologically normal.

Massively disruptive or devascularizing injuries of the duodenal pancreatic complex, ampulla and intra pancreatic ducts that are not amenable to repair, in physiologically stable patients, require pancreaticoduodenectomy. This can be

performed at the time of the first procedure, or a few hours later for practical reasons.

In injuries such as a gunshot wound or blunt disruption of the head of the pancreas, where the integrity of the ducts are questionable, other significant injuries should be sought. In such cases, it may be wise to deal with other injuries first and leave a drain to the pancreas head and apply a temporary closure. ERCP should be done as soon as the patient is stable enough, alternatively, re-operation with expert assistance in more favourable conditions, may allow better assessment and decision making.

Intra-operative contrast studies such as cholangiography via the gall bladder, the common duct or cannulation of the ampulla via the open duodenum or duodenotomy may be considered at the time of emergency surgery. Creating a duodenotomy for the sake of a contrast study carries a risk of pancreatitis, duodenal leaks and fistulas, therefore the risks and potential benefits should be carefully weighed up.

Repair of duodenal injury

Most duodenal lacerations can be managed by simple debridement and tension-free primary closure in one or two layers, or resection and re-anastomosis Extensive duodenal disruptions should be carefully inspected to define the anatomy, assess the blood supply of the duodenum and integrity of the ampulla. Most duodenal lacerations can be carefully debrided and transversely approximated, provided there is good blood supply. If the injury is judged to be too extensive for primary repair (eg, >3 cm) after debridement, the injured segment should be resected and the duodenal ends brought together with a primary end-to-end duodeno-duodenostomy. Once repaired, high risk duodenal lacerations can be bolstered with omentum, or a jenunal loop as serosal patch, with nasogastric drainage, drainage of the retroperitoneum near the duodenal repair, and a feeding jejunostomy or naso-jejunal feeding tube inserted at the time of surgery.

Duodenal devascularisation or complete disruption will require formal resection and diversion, depending on the position of the injury related to the ampulla. Consider the possibility of anatomical variations of the ampulla:10% of the

population may have 2 ampullas, 5% have the bile duct and pancreatic duct opening separately on the ampulla, 85% have a common channel.

Complex duodenal injuries are rare, but carry a high risk of postoperative complications including suture line leak and enteric fistula formation. Increased mortality is often related to associated injuries and sepsis.

Ampullary and peri-ampullary injuries

Limited injuries to the ampulla may be amenable to treatment options such as stenting or sphincteroplasty. Avulsion of the ampulla can be managed with choledochoduodenostomy.

Extensive periampullary injuries, such as intraduodenal bile duct injury, intrapancreatic bile duct injury, or Grade V injury often require classical or staged pancreaticoduodenectomy. (Harris JP, et al 1986) (Cooke HS, et al 1990) (Cox MR et al 1994)

Procedures to protect the duodenal repair

Pyloric exclusion, duodenal decompression and duodenal diverticularization have been utilised in the hope of decreasing the likelihood of leak following repair. This remains controversial, as none of these techniques have demonstrated a clear benefit. Under most circumstances, these adjunctive techniques are not needed. Given a lack of data, pyloric exclusion may be useful in rare situations as it is a relatively simple and less extensive procedure to perform inan already seriously injured patient.

Pyloric exclusion entails the temporary closure of pylorus with sutures or staples via an antral gastrotomy to exclude gastric secretions from the duodenal repair. It may have a role in high grade duodenal or combined injuries and requires an additional loop gastrojejunostomy. The pylorus will usually reopen spontaneously within three to six weeks, even when non-absorbable sutures or staples are used. In a retrospective review of 29 patients with penetrating duodenal injuries, no significant differences in clinical outcomes were seen in patients who underwent pyloric exclusion compared with those who underwent primary repair alone. Although pyloric exclusion is a relatively simple procedure,

it carries the risk of marginal ulceration at the gastrojejunostomy site. (Seamon MJ et al 2007)

Duodenal diverticulization refers to suture closure of the duodenal injury, antrectomy with end-to-side gastrojejunostomy, and tube duodenostomy. It is a complex, time-consuming procedure that is generally unnecessary, except where there is destructive injuries of D1, with preservation of the ampulla in D2. The tube duodenostomy may be omitted or replaced with a retrograde jejunostomy decompression tube.

Duodenal decompression refers to the antegrade (duodenostomy) or a retrograde (jejunostomy) drainage of the duodenum after repair. The rationale for duodenal decompression is to decrease the pressure and volume of secretions in the duodenum, thereby protecting the duodenal repair. There are no randomized trials evaluating duodenal decompression following duodenal injury and the outcomes of retrospective reviews are mixed. There is a risk of duodenal fistula and other complications and therefore routine duodenal decompression is not recommended.

Treatment of pancreatic injuries

Most pancreatic injuries are Grade I or Grade II and if isolated, can be managed nonoperatively. When injury to the pancreas is identified during abdominal exploration, the location and duct integrity should be evaluated. Treatment principles include wide closed suction drainage for grades 2 and upwards (2 drains), avoiding pancreatico-enteric anastomoses, distal pancreatic resection for ductal injuries to the left of the SMV, and conservative management of proximal duct injuries unless other indications for resection of the pancreas-duodenal complex are present.

Pancreatic transection or parenchymal injury to the left of the superior mesenteric vein is managed with distal pancreatectomy without splenectomy in hemodynamically stable patients with isolated pancreatic injury. To salvage the spleen, the splenic artery branches and venous tributaries draining the posterior surface of the pancreas are isolated and ligated, working from distal to proximal, followed by division of the pancreas. Management of pancreatic duct injury to the right of the superior mesenteric vessels depends upon the presence and extent of pancreatic tissue devitalization and concomitant duodenal injury.

Options include debridement and wide suction drainage, extended distal pancreatectomy with division of the pancreas to the right of the superior mesenteric vessels, and pancreaticoduodenectomy. Due to the high incidence of endocrine insufficiency and diabetes with removal of >90 percent of the pancreas, some authors have advocated Roux-en-Y distal pancreaticojejunostomy (with oversewing of the proximal segment) for proximal duct transections (ie, central pancreatectomy). Central pancreatectomy has an advantage over distal or subtotal pancreatectomy in preserving the tail of the pancreas and its endocrine and exocrine function, as well as the spleen. However, the risks of anastomotic leak and other complications are significant. In a review of 134 patients with blunt pancreatic duct injury, 34 patients with proximal injuries (not Grade V) were treated with closed suction drainage alone. Complication rates were no different compared with more aggressive approaches. Favorable results have also been reported for proximal duct injury due to gunshot wounds using debridement, suture repair, and closed suction drainage. These considerations and the complexity of the procedure make central pancreatectomy unsuitable for many patients, particularly multiply-injured patients. (Patton JH et al 1997) (Degiannis E, et al 1996)

Anterior Roux-en-Y pancreaticojejunostomy has been advocated for internal drainage of main pancreatic duct injuries with extensive injury to the pancreatic head (provided there is sufficient preserved parenchyma). However, this procedure has been associated with a high incidence of pancreatic leak and abscess formation. (Campbell et al, 1980)

Combined pancreaticoduodenal injuries

In certain combined pancreas and duodenal injuries, the duodenal injury and pancreatic injury can be approached separately using relatively simple procedures. When combined pancreatoduodenal injuries are more extensive, the risk of postoperative pancreatic and/or duodenal fistula is high. Adjunctive procedures should be considered to decrease the amount of secretions in the duodenum such as pyloric exclusion as well as extensive closed suction drainage to control possible leaks and avoid fluid collections and secondary infections.

Severe, combined pancreatoduodenal injury, such as destruction of the ampulla of Vater or intrapancreatic common bile duct or extensive devitalization of the

duodenum or head of the pancreas, pancreatico-duodenal resection is required. Associated injuries may indicate a damage control approach, which entails simple drainage followed by a planned urgent Whipple procedure, or a staged procedure. (Koniaris LG et al 2000) (Asensio JA et al 2003)

The head of the pancreas and proximal duodenum are easily resectable. At the initial exploration, the pylorus, proximal jejunum, and pancreatic stump are stapled and transected. The common bile duct is ligated or a drain placed within it. The patient is stabilized in ICU and after 24 to 48 hours, brought back to the operating room for reconstruction.

An alternative to pancreatic resection or pancreatic-enteric anastomosis is drainage and management of the resultant fistula with medication, nutritional support (preferably enteral) and endoscopic interventions such as sphincterotomy and stenting of the pancreatic duct or bile ducts.

Early enteral nutrition

Not all pancreatico-duodenal injuries require jejunostomy feeding, but the surgical management of complex injuries creates the opportunity to place a feeding jejunostomy for early enteral nutritional support. In rare cases one may consider placement of the “triple ostomy”: decompressing gastrostomy, retrograde jejunostomy for duodenal decompression and antegrade jejunostomy for enteral feeding. (Dissanaike et al, 2008)

Complications

In a review of more than 1400 cases, complications were reported in 64%, including intraabdominal abscess, posttraumatic pancreatitis, and duodenal fistula. The risk of complications increases with the grade of injury, associated injuries, excessive delays, and shock. (Asensio, Feliciano, Britt 1993)

The most life-threatening complication of duodenal injury is duodenal fistula, in about 7% of cases. Management includes controlled drainage of the fistula output, drainage of intraabdominal collections, broad spectrum antibiotics, fluid and nutritional support. Re-exploration should be considered in persistent high-output duodenal fistula as pyloric exclusion may be useful, if diversion was not already done.

Complication rates for pancreatic injuries range from 24 to 50% and include pancreatic fistula, pancreatic pseudocyst and intraabdominal abscess, which typically do not require reoperation.

Pancreatic fistula is the most common complication of a pancreatic injury (5 to 37% of pancreatic injury cases). Diagnostic options include CT, ERCP or MRCP. Management options include TPN for high output fistulas and enteral nutrition for low output fistulas (<20Ml daily). Octreotide does not increase the rate of healing, but it does decrease the amount of fistula output, which may be useful in patients with high output fistulas with hypovolemia and electrolyte abnormalities. Persistent fistulas may require re-exploration and distal pancreatic resections.

Pancreatic pseudocyst is very common after blunt injury– occurs in up to 30%. Early management consists of percutaneous drainage of fluid collections and treatment of infectious complications. Late management options are ERCP with pancreatic duct stenting, internal drainage, external drainage, and resection

Intraabdominal abscess occurs in 7 to 18 percent of patients with pancreatic injuries and are usually treatable with percutaneous drainage.

Conclusions

Injury to the duodenum and pancreas is uncommon, but severe degrees of injury are associated with high morbidity and mortality

CT may miss up to 10 % of pancreatic duct lesions. ERCP and MRCP are sensitive, but not always practical for acutely injured patients.

Grade 1 and 2 injuries may be treated conservatively, and simple surgical options are applicable to most injuries. Penetrating injuries require surgical intervention.

Several adjunctive techniques to decrease potential leaks following duodenal repair have been described, but no studies have proven any benefit.

Surgical management of pancreatic ductal injuries depends on location: distal duct injuries require distal pancreatectomy and proximal duct injuries require closed-suction drainage and possible endoscopic interventions.

High-grade injuries to the pancreatic head or combined severe injuries of the duodenum and pancreas are managed with resection (pancreaticoduodenectomy) and interval (or immediate) reconstruction, depending on the physiology and other risks for a prolonged surgical procedure.

Mortality rates are between 15 to 20 percent and is multifactorial. Complications are common and include abscess, fistula, pancreatitis and pseudocyst. High rates of late infectious complications are common.

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Traumatic Aortic Rupture: What is the best repair

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Traumatic Aortic injury is the second most common causes of death due to blunt force There is high pre-hospital mortality with aortic trauma rupture.[1,2] Less than 25% survive pre hospital setting and those that do up to 50% do not survive 24 hours. 29% have major abdominal injuries and 31% have major head injury this creates a major challenge in the management of blunt thoracic aortic injury.

Classification:

Blunt thoracic Aortic injury is classified into 4 categories depending on aortic wall disruption:

Grade I : Intimal tear

Grade 11 : Intramural haematomas

Grade III : Aortic pseudo-aneurysm

Grade IV : Free rupture of aorta

Management

Grade I injury cam be managed medically with blood pressure control, with Beta Blockade [3] and follow up imaging at 7days then at 30 days to confirm healing at 6 months and 1 year until healing occurs.

Grade 11, 111 and IV will need intervention.

Prior to 2005 most traumatic aortic injuries underwent open surgical repair. Since 2005 when Endovascular stent grafts became available, their use has

increased significantly, so much so that in 2011 the Society for Vascular Surgery suggested that Endovascular repair be performed preferably over open surgical repair .[4]

What was the evidence to this recommendation? Murad et al [5] were commissioned by the Society for Vascular Surgery to evaluate and compare different modalities (non-operative, open and Thoracic Endovascular aortic Repair (TEVAR) for the treatment of patients with traumatic aortic injuries.

This was a systematic review of 7768 patients from 139 previously published studies. TEVAR was associated with a lower mortality rate of 9% and open repair of 19% (RR 0.61; 95%, CI :0.46 -0.80. Spinal cord ischaemia (RR 0.34) and End Stage renal disease as well as systemic graft infections were lower with TEVAR. TEVAR was associated with increased secondary intervention for Endo graft related complications.

Further studies [6,7,8,9] have confirmed that TEVAR for blunt thoracic injuries is associated with lower mortalities, lower spinal cord ischaemia and earlier hospital discharge.

The other controversial issue with TEVAR was the coverage of Left subclavian artery and selective revascularization is recommended. Routine follow-up with CT Angiography at yearly intervals also recommended.

The recommendations today would be to offer TEVAR to Grade 11, 111 and 1V injuries of the thoracic aorta if anatomy allows. In stable patient's selective treatment of the other associated injuries is prioritized.

Unfortunately due to lower complications of TEVAR, it is unlikely that a randomized study comparing TEVAR to Open Surgery will ever take place.

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Management choices of delayed presentation of Acute Arterial Occlusion where Limb Viability is Doubtful

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Acute limb ischemia (ALI) is defined as a sudden decrease in limb perfusion (less than 2 weeks) causing a potential threat to limb viability, with a risk of major limb loss. It is one of the most serious problems surgeons encounter and is a source of significant medical legal risk[1]. Paramount to the treatment of this disease entity are prompt recognition and diagnosis, followed by rapid restoration of blood flow to the ischemic extremity to minimize risk of limb loss and subsequent reperfusion-related local and remote organ injury. This disease most often occurs in aged patients, who often have significant comorbidities, and can lead to their demise even after successful revascularization of a limb

The pathophysiology of ALI is due to an abrupt and complete blockage of the main arterial supply to the extremity. Causes of ALI are diverse, including traumatic occlusion or disruption of the peripheral arteries, aneurysm by embolism or thrombosis, cardiogenic embolism, native artery thrombosis, and reconstruction thrombosis. The distal tissue bed in the limb becomes ischemic with energy metabolism shifting from an aerobic to an anaerobic process. Progressive ischemia leads to cell dysfunction and death. Nervous tissue cells, skin, and subcutaneous tissue are the most susceptible, followed by muscle cells. Traditionally, it is accepted that a patient without underlying vascular disease and an acute arterial blockage has approximately 6 hours for revascularization before irreversible functional damage occurs; however, the time frame depends upon the degree of collateral perfusion in any given patient. Generally, ALI does not occur in young people outside of trauma, but it may occur in those in their 30s and 40s due to unusual circumstances, such as paradoxical emboli, hypercoagulable disorders, HIV vasculopathy, bacterial endocarditis with embolism, or in those with severe early onset cardiac disease[2].

Evaluation of ALI by Rutherford

Category	Prognosis	Findings		Doppler signals	
		Sensory loss	Muscle weakness	Arterial	Venous
I. Viable	Not immediately threatened	None	None	Audible	Audible
II. Threatened					
a. Marginal	Salvageable if promptly treated	Minimal (toes) or none	None	(Often) inaudible	Audible
b. Immediate	Salvageable with immediate revascularization	More than toes, associated with rest pain	Mild, moderate	(Usually) inaudible	Audible
III. Irreversible	Major tissue loss or permanent nerve damage inevitable	Profound, anesthetic	Profound, paralysis (rigor)	Inaudible	Inaudible

Category IIB is an immediately threatened limb that requires rapid revascularization, and is associated with sensory loss and associated mild muscle weakness with inaudible arterial signals. Category III is considered irreversible limb ischemia, with major tissue loss or permanent nerve damage, a profoundly anaesthetic and paralyzed limb, with rigor and inaudible signals. Patients whose disease falls into this category usually require amputation.

Factors Associated with Mortality and Limb Loss from ALI

Two primary factors underlie the morbidity and mortality that results from ALI; namely, the patients' underlying comorbid illness and delay in recognition and revascularization of the limb(s)[4, 6]. It is uncommon that the procedure itself to revascularize the affected limb, whether endoluminal or surgical, causes death. Men and women are equally affected by ALI.

Ischemia reperfusion injury (IRI) is a well-recognized clinical entity with a wide range of impact across nearly all organ systems that significantly affect the practice of surgeons, anaesthesiologists, and intensivists alike. Reperfusion of ischemic tissues carries with it a significant physiologic debt that contributes to systemic complications, such as cardiac depression, acute lung injury, renal failure, and poorer limb related functional outcomes. The primary interest in IRI in the context of ALI and limb salvage surrounds potential serum marker identifiers of severity, and then therapies to reduce this physiologic debt, making IRI a modifiable factor. Thus, this could improve morbidity and mortality associated with lower-limb revascularization.

Biochemical markers of ischemia reperfusion injury have been of interest to vascular surgeons and researchers for many years. Acute limb ischemia is the quintessential clinical scenario where these markers would seem relevant.

The use of biomarkers to preoperatively or perioperatively predict which patients will not tolerate limb-salvage efforts or who will have poor functional outcomes after salvage is of immense interest. Creatinine phosphokinase, myoglobin, lactate, lactate dehydrogenase, potassium, bicarbonate, and neutrophil/leukocyte ratios are a few of the studied biomarkers available. Currently, the most well-studied aspect of ischemia reperfusion injury is rhabdomyolysis leading to acute kidney injury. The last 10 years have seen significant progression and improvement in the treatment of rhabdomyolysis, from minor supportive care to use of continuous renal replacement therapy. Identification of specific biomarkers with predictive outcome characteristics in the setting of ischemia reperfusion injury will help guide therapeutic development and potentially mitigate pathophysiologic changes in acute limb ischemia, including rhabdomyolysis. These may further lead to improvements in short- and long-term surgical outcomes and limb salvage, as well as a better understanding of the timing and selection of intervention.

Currently, there is no specific biomarker that portends the attendant morbidity of IRI in the context of lower-extremity ischemia. The traits of such a specific biomarker include a rapidly available test obtained expeditiously at the onset of care, which continues to be available throughout all arenas of care and is inexpensive and ubiquitously available

Choosing the appropriate therapy is important to decrease amputation and mortality. Level I evidence suggests equivalence of endovascular or surgical therapies, as measured by mortality and amputation; however, the ethology of ALI needs to be factored into this equation. Two landmark articles were published in the 1990s that suggested thrombolytic therapy had equivalent outcomes to surgical therapy in patients with ALI. These were the Surgery or Thrombolysis in Lower Extremity Ischemia (STILE) and Thrombolysis or Peripheral Artery Surgery (TOPAS) trials, which randomized patients to catheter-directed thrombolytic therapy or best surgical therapy[3, 5]

A large national database suggested younger age (younger than 63 years) and use of heparin reduced mortality, whereas need for amputation was associated with an increased risk of death. In those patients with an embolic eatiology (generally stage IIb ischemia), amputation is significantly less likely with embolectomy, but not thrombolytic therapy. In this same study, patients who failed thrombolytic therapy had a significantly greater risk of amputation and

death, unlike the observations from the randomized STILE trial. The bottom line is to choose carefully the appropriate therapy for patients with ALI, integrating all aspects of good clinical judgment

Laboratory markers have also been used to predict major amputation in those with ALI. Consistent with previously stated clinical risk factors, prior vascular surgery, skin mottling, sensory and motor loss, muscle tenderness, and absent ankle Doppler signals all predicted amputation. Creatinine phosphokinase (CPK) elevation and neutrophilia upon presentation conferred an increased risk of amputation, associated with 50% risk as compared with 5% risk without CPK elevation. It is not clear if CPK elevation after revascularization carries the same prognosis, but it is unlikely because washout of the ischemic tissue bed normally occurs. Thus, initial plasma CPK levels may assist prognostic evaluation in patients with ALI[7].

Surgical Therapy

Most patients with lower extremity embolic occlusion can be approached through a standard common femoral artery exposure, which permits access for balloon catheter thrombo-embolectomy from the aortic bifurcation to the ankle. Occasionally, below-knee trifurcation arterial exposure with tibial-peroneal arterial thrombo-embolectomy may be required. Similarly for the upper extremity, brachial artery exposure is straightforward, usually on the distal medial upper arm or just below the antecubital crease

Endovascular therapy

Arteriography and thrombolysis should be considered in patients in whom the ethology of ALI is unclear or the history and physical exam strongly suggests a diagnosis of arterial or graft thrombosis in situ. Endovascular therapy is also appropriate in most instances of non-embolic ALI (stage IIA), such as popliteal artery thrombosis, as mean thrombus lysis times may be 12 to 24 hours. Pharmaco-mechanical therapy has improved the lysis time as it mechanically breaks the clot while at the same time infusing thrombolytic drug.

Lower extremity four-compartment fasciotomies are routinely performed to prevent a post reperfusion compartment syndrome, in the setting of class IIb and III ischemia with surgical thrombo-embolectomy. Fasciotomy may be required after successful thrombolysis as well. Thus, frequent extremity exams are essential during on-going lytic therapy.

Conclusions

It is likely that much of ALI treatment will be a mix of open and endovascular techniques that can be performed by in the operating room/endovascular suite. While technology continues to advance, making interventions easier and safer, the biggest gain in improving outcomes with ALI will be by more consistent recognition and rapid, standardized therapy for all patients with disease. The primary educational message that surgeons need to put forth to non-surgeon colleagues and trainees is that recognition of ALI is essential. Lastly, it is important to remember to save life over limb, and emergent amputation is sometimes required to save a patient's life.

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Indications for Thrombo-Prophylaxis and when to stop Anticoagulation before elective Surgery

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This paper is based on guidelines as per the references, be aware that the Vascular Society of Southern Africa Guidelines should come out early in 2018.

Introduction

Hospital acquired VTE has been considered the most common cause of preventable death. VTE is an important cause of morbidity and mortality in surgical patients. Due to the multitude of both patient specific risk factors and procedural risk factors it can be difficult to determine what populations are considered high risk for VTE. Studies have reported hospital acquired VTE prevalence rates anywhere between 0.8% - 11% depending on the patient population evaluated. There have been many risk factors identified in both the medical and surgical patient populations that can increase the risk of developing VTE.

DVT prevalence in various patient populations:

Patient information	***DVT prevalence %***
Internal medicine	10 - 20
General surgery	15 - 40
Major gynaecological surgery	15 - 40
Major urological surgery	15 - 40
Neurosurgery	15 - 40
Stroke	15 - 40
Hip and knee replacement surgery	40 - 60
Hip fractures	40 - 60

Polytrauma	40 - 80
Spinal cord injury	60 - 80
Critical care	10 - 80

Reducing the risk of VTE

- Do not allow patients to become dehydrated unless clinically indicated.
- Encourage patients to mobilise as soon as possible.
- Do not regard aspirin or other antiplatelet agents as adequate prophylaxis for VTE.
- Consider offering temporary inferior vena caval filters to patients who are at very high risk of VTE (such as patients with a previous VTE event or an active malignancy) and for whom mechanical and pharmacological VTE prophylaxis are contraindicated.
- Advise patients to consider stopping oestrogen-containing oral contraceptives or hormone replacement therapy 4 weeks before elective surgery. If stopped, provide advice on alternative contraceptive methods.
- Assess the risks and benefits of stopping pre-existing established antiplatelet therapy 1 week before surgery. Consider involving the multidisciplinary team in the assessment.
- Consider regional anaesthesia for individual patients, in addition to other methods of VTE prophylaxis, as it carries a lower risk of VTE than general anaesthesia. Take into account patients' preferences, their suitability for regional anaesthesia and any other planned method of VTE prophylaxis.
- If regional anaesthesia is used, plan the timing of pharmacological VTE prophylaxis to minimize the risk of epidural haematoma. If antiplatelet or anticoagulant agents are being used, or their use is planned, refer to the summary of product characteristics for guidance about the safety and timing of these agents in relation to the use of regional anaesthesia.
- Do not routinely offer pharmacological or mechanical VTE prophylaxis to patients undergoing a surgical procedure with local anaesthesia by local infiltration with no limitation of mobility.

Types:

- Pharmacological

- Aspirin
- LMWH
  - ✓ Enoxaparin 40mg SC dly starting 12 to 24 hrs after surgery
  - ✓ Dalteparin 2500 U SC dly starting 2h before surgery
- LDUFH
  - ✓ Proven to reduce incidence of VTE by 50 to 70% in moderate risk general surgery and medical patient's
  - ✓ Incidence of major haemorrhagic events was 1.8% vs 0.8% in controls – not statistically significant
  - ✓ 5000U SC q12h OR q8h beginning 2hrs before surgery until patient is fully ambulatory/discharged
- Fondaparinux
  - ✓ 2.5mg SC dly starting 6hrs after surgery
- Warfarin
  - ✓ 5mg dly adjusted to INR of 2.0 – 3.0 starting day before/on day of surgery
  - ✓ Continued for 35 days

▪ Non-pharmacological
- Studies have shown them to be effective in reducing rate of DVT, but not PE or death
- Less effective than pharmacologic prophylactic modalities
- Main advantage is lack of potential for bleeding
- Lack of compliance with these devices has been observed

- Types
  - ✓ Early ambulation
  - ✓ Intermittent pneumatic compression stockings (IPC)
    - Inflatable bladders that are wrapped around lower leg
    - Reduce stasis in gastrocnemius-soleus pump
    - Creates 35mmHg external compression at ankle and 20mmHg external pressure at thigh
    - Creates pumping action by inflating and deflating at regular intervals
    - Placed on patient on morning of surgery and are worn throughout surgical procedure and

continuously in postoperative period until patient is ambulatory or anticoagulant is started.
    - Most common complaints – local discomfort caused by increased warmth, sweating, disturbance of sleep
- ✓ GCS
    - 18mmHg external pressure at ankles, 8mmHg external pressure in thigh
    - Resulting 10mmHg pressure gradient acts as driving force for venous outflow from legs
- ✓ Mechanical foot compression
    - Compressing sole of foot which activates physiologic pump mechanism and improves venous return in lower extremity
    - Not as effective as external pneumatic compression sleeves
- ✓ IVC filters

Risk Assesment

All hospitalized patients should be evaluated for both bleeding and VTE risk within 24 hours of admission, upon transferring level of care, and periodically during the hospital stay

- 2012 ACCP guidelines recommend using risk assessment scoring system to grade patient's into 3 categories
    - LOW
    - MODERATE
    - HIGH

Risk factors should be divided into:

1. Patient-related risk factors
2. Procedure-related risk factors

The Caprini Risk Assessment Model should be used to assess VTE risk in general and abdominal-pelvic surgery patients.

Caprini Risk Assessment

1 Point	2 Points	3 Points	5 Points
Age 41-60	Age 61-74	Age ≥ 75	Acute spinal cord injury (< 1 mo)
Acute MI (<1 mo)	Central venous access	Established thrombophilia	Elective lower extremity arthroplasty
BMI > 25	Immobile > 72 hrs	HIT	Hip, pelvis, or leg fracture (< 1 mo)
CHF exacerbation (<1 mo)	Leg plaster cast or brace	Hx of VTE	Stroke (< 1 mo)
Hx of inflammatory bowel disease	Malignancy	Family hx VTE *(1 degree relative)*	
Procedure with local anesthesia	Surgery-arthroscopic		
Swollen legs or Sepsis (< 1 mo)	Varicose veins	Surgery > 45 mins	
Serious lung dx *ex. Pneumonia* (<1 mo)			
1 point **(For Women Only)**			
Oral contracePatientives or HRT			
Pregnancy or postpartum (< 1 month)			
Hx of unexplained stillborn infant, spontaneous abortion (≥3), premature birth with toxemia or growth restricted infant			

Caprini Risk Assessment Score

Points	Risk	Recommendation
0	Very Low VTE Risk	Early and frequent ambulation
1-2	Low VTE Risk	Mechanical Prophylaxis
3-4	Moderate VTE Risk and Low Bleed Risk	Pharmacologic Prophylaxis
> 5	High VTE Risk and Low Bleed Risk	Mechanical AND Pharmacologic Prophylaxis
> 2	High **Bleed** Risk	Mechanical Prophylaxis

VTE Prophylaxis Regimens for High VTE Risk General Surgical Patients

Surgical Patients	Enoxaparin 40 mg SQ every 24 hours OR Heparin 5000 units SQ every 8 to 12 hours
Renal impairment (CrCl < 30 mL/min)* *Not on renal replacement therapy	Enoxaparin 30 mg SQ every 24 hours OR Heparin 5000 units SQ every 8 to 12
Bariatric Surgery	Enoxaparin 40 mg SQ every 12 hours
Major Trauma	Enoxaparin 30 mg SQ every 12 hours
Abdominal/Pelvic Surgery for Cancer	Enoxaparin 40 mg SQ every 24

The Modified Padua Risk Assessment Model should be used to assess VTE risk in medical patients.

What to do once the risk is calculated?

a) Low risk (2-3)

- IPC peri-operatively
- Early mobilisation

b) Moderate risk (3-4)

- UFH/LMWH
  - Start 12-24 hrs post-op
- Foot pump/IPC

c) High risk (5-8)

- UFH/LMWH + IPC during hospitalisation
  - Start anticoagulation 12h pre-op
  - Continue anticoagulation for 7 – 10 days post-op

d) Very high risk (>8)

- UFH/LMWH + IPC during hospitalisation
  - Start anticoagulation 12h pre-op
  - Continue anticoagulation for 30 days post-op
    - In an open-label study conducted in Patient's undergoing major abdominal surgery, LMWH was administered once dly for 1 or 4 weeks
    - At 28 ± 2 days DVT was detected in 16% of patient's who had 7 days of prophylaxis versus 6% in those receiving LMWH for 4 weeks

Risk of Bleeding

The risk of developing VTE should always be weighed up against the risk of bleeding. While all hospitalized patients should be evaluated for both bleeding and VTE risk within 24 hours of admission. There is no universally validated model to assess bleeding risk; However certain risk factors increase once chances:

Medical patients	*Surgical patients*
Active gastroduodenal ulcer Bleeding in the 3 months prior to admission Platelet count < 50 x109/L	Active bleeding or previous major bleeding Renal failure (CrCl < 30 mL/min) Hepatic failure (INR > 1.5 without anticoagulants) Thrombocytopenia Acute stroke Uncontrolled systemic hypertension Concomitant use of anticoagulants, antiplatelets or thrombolytics

Peri-Operative Management of Antithrombotic Therapy

1) WARFARIN THERAPY

- Stop Warfarin 5/7 pre-op
- Restart Warfarin 12-24 hrs post-op, if there is adequate haemostasis
- Mechanical valves/AF
    - High risk for VTE
        - ✓ Bridging anticoagulation
    - Low risk for VTE
        - ✓ No bridging anticoagulation
    - Intermediate risk
        - ✓ Management on case by case basis

- Minor dental procedures
    - Continue with Warfarin with coadministration of prohaemostatic agent OR
    - Stop Warfarin 2-3 days pre-op

- Dermatological procedures

- Continue with Warfarin and optimize local haemostasis rather than interrupting treatment

2) UFH/LMWH

- Bridging anticoagulation
  - UFH
    - ✓ Stop 4-6 hrs pre-op
  - LMWH
    - ✓ 24 hrs pre-op (therapeutic dose)
    - ✓ Resume 12-24 hrs post-op
    - ✓ High risk of post-op bleeding
      - Resume 48-72 hrs post-op

3) ASPIRIN THERAPY

- High risk cardiovascular condition
  - Continue with aspirin around time of surgery, rather than stopping 7 – 10 days pre-op
- Low risk cardiovascular condition
  - Stop aspirin 7 – 10 days pre-op
- Requiring CABG
  - Continue aspirin
- Coronary artery stents (on dual antiPLT Tx)
  - Defer surgery for at least 6/52 – bare metal stent
  - Defer surgery for at least 6/12 – drug-eluting stent

Planning for discharge

As part of the discharge plan, provide written information:

- Signs and symptoms of deep vein thrombosis and pulmonary
- Recommended duration of use of VTE prophylaxis at
- Importance of using VTE prophylaxis correctly

Special Populations

Acute kidney injury (AKI) or chronic kidney disease (CKD)

- UFH is the preferred agent for patients who are on renal replacement therapy
- Enoxaparin 30 mg every 24 hours may be considered
- Consider monitoring anti-Xa level after 7-10 doses to evaluate for accumulation
- Goal anti-Xa 0.2-0.4 units/mL

Extreme Obesity

- Optimal thromboprophylaxis has not been established
- Preferred method for VTE prophylaxis is with LMWH
- Enoxaparin 40 mg every 12 hours
- Routine anti-Xa monitoring is not recommended
- Consider monitoring anti-Xa level after 7-10 doses to evaluate for accumulation (goal 0.2 – 0.4 units/mL)
- Prophylactic UFH has not been adequately studied in morbidly obese patients
- May consider heparin 7,500 units every 8 hours

History of Heparin Induced Thrombocytopenia
Unfractionated and low molecular weight heparins is not recommended.

Extended duration VTE prophylaxis: VTE prophylaxis prescribed on discharge.

Bariatric surgery

- Patients with high VTE risk, low bleed risk and BMI > 55 kg/m2
- Enoxaparin 40 mg SQ every 12 hours for 10 days

Abdominal or pelvic surgery for cancer

- Patients with a cancer diagnosis who received a traditional laparotomy or vulvectomy and is either > 60 years or < 60 years old with a history of VTE
- Enoxaparin 40 mg SQ every 24 hours for 28 days

- If patient refuses 28 days of prophylactic therapy then enoxaparin or UFH may be considered for 14 days

Orthopaedic surgery for VTE prophylaxis

- Total hip arthroplasty: 10-14 days
- Total knee arthroplasty: 10-14 days
- Hip fracture surgery: 10-14 days
- For major orthopaedic surgery may consider extended prophylaxis to 35 days
- If patient refuses extended duration parenteral prophylaxis then oral prophylaxis may be considered.

Patients With Major Trauma: Traumatic Brain Injury, Acute Spinal Injury, and Traumatic Spine Injury

For major trauma patients, it is suggested you use LDUH, LMWH, or mechanical prophylaxis, preferably with IPC, over no prophylaxis; if no contraindication exists.

Conclusion

All decisions must include a risk benefit evaluation. No 'one solution fits all' is acceptable. Methods, timing etc. for every patient must be clearly understood.

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Best Medical Therapy vs Carotid Endarterectomy vs Carotid Stenting

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Millions of people are affected by stroke every year with a large number dying from it(1, 2). For those that survive more than half will require assistance in their day to day activities. Stroke puts a huge financial burden on state and family(3). It has a major physical, psychological and social adverse effects.

Extra cranial cerebrovascular disease affects mainly older patients with typical risk factors for atherosclerosis(4, 5). Atherosclerotic occlusive carotid artery disease could be managed with best medical therapy (BMT) or surgical intervention. Surgical intervention could either be carotid endarterectomy (CEA) or carotid artery stenting (CAS). The decision on the form of therapy is based on the presence or absents of symptoms and the degree of stenosis. During the European Carotid Surgery Trial (ECST) and the North American Symptomatic Carotid Endarterectomy Trial (NASCET) intra-arterial angiography was used to measure the degree of stenosis but had a stroke rate of 1.2%(6). The degree of stenosis is today based mainly on duplex ultrasound(4, 5, 7, 8). Table 1 summarizes some of the duplex ultrasound criteria used for the degree of stenosis(9).

Table 1: Diagnostic velocity criteria for NASCET-based carotid stenosis measurement.

% stenosis NASCET	PSV ICA cm/s	PSVICA/ PSVCCA ratio	St Mary's ratio PSVICA/EDVCCA
<50%	<125	>2	<8
50 – 60%	>125	2 - 4	8 - 10
60 – 69%			11 - 13
70 – 79%	>230	>4	14 - 21

80 - 90%			22 - 29
>90% but not near occlusion	>400	>5	>30
Near Occlusion	High, low string flow	Variable	variable
Occlusion	No flow	Not applicable	Not applicable

NASCET: North American Symptomatic Carotid Endarterectomy Trial

1. Best Medical Therapy vs Carotid Artery Endarterectomy

Best Medical Therapy (BMT) entails statins, antiplatelet, angiotensin converting enzyme inhibitors and risk fact modification. CEA could be done under general or local anaesthesia mainly dependent on surgeon preference(4, 10).

The discussion will look at those with asymptomatic disease separately from symptomatic disease.

1a. BMT vs CEA in asymptomatic patients

Several randomized trials were conducted assessing BMT alone versus CEA plus BMT in asymptomatic patients.

The major trails are the Veteran's Affairs Co-operative Study (VACS), Asymptomatic Carotid Atherosclerosis Study (ACAS) and Asymptomatic Carotid Surgery Trial-1 (ACST-1)(6, 11, 12). These trails were conducted in the 1980s and 1990s. there was no standardized BMT then and few patients in both trails were on BMT as we know it today. Table 2 summarizes the outcome of these major trails(13).

Table 2: Perioperative and late outcomes following CEA and BMT in VACS, ACAS, and ACST.

RCT	30-day death/stroke	Ipsilateral stroke plus perioperative death/stroke	Any stroke plus perioperative death/stroke

	After CEA	CEA + BMT	BMT alone	CEA + BMT	BMT alone
VASC	4.6%	7.0% at 4 yrs	9.4% at 4 yrs	10.4% at 4 yrs	12.0% at 4 yrs
ACAS	2.3%	5.1% at 5 yrs	11% at 5yrs	12% at 5yrs	17.8% at 5yrs
ACST-1	2.8%	Not vailable	Not available	6.4% at 5yrs	11.8% at 5yrs

Guidelines from these studies were that CEA should be performed with a morbidity/mortality rate of <3% on a patient with an expected life expectancy of >5 years(6, 12, 13).

Subgroup analysis in the ACST-1 trail looked at those >75 years old(12). It was found that half of these patients had died within 5 years and had a higher post CEA stroke risk of 5.5%. The conclusion was that there is no benefit for CEA in asymptomatic patients older than 75 tears.

The ACAS and ACST-1 also assessed if gender influenced the risk of stroke(6, 12). It was found that males had twice the risk for stroke if on BMT alone. At 5 years women did not demonstrate any benefit from CEA. It was adviced not to offer CEA to women with asymptomatic disease.

VACS, ACAS and ACST-1 are the only randomized controlled trials to compare to compare CEA plus BMT and BMT alone. These were conducted in the era when BMT did not include statins and most of the candidates were smokers. Today some question if data from these studies is still relevant with BMT as we know it today(14-16). Several studies have shown a decline over the years in the risk of stroke since the ACAS and ACST-1 trials with the use of BMT. The rate of ipsilateral stroke declined from 2.3/100 person year to 1/100 person year with p value of 0.009 (15). This is a 39% reduction in ipsilateral stroke rate.

This called for the need for randomized controlled trials but ongoing trials are failing to recruit patients at a faster pace. Until such time that we get results from these studies several factors that are thought to increase the risk for stroke have been suggested; silent infarction on CT/MRI, stenosis progression, large plaque area, large juxta-luminal black area, plaque echolucency, intra-plaque haemorrhage, impaired cerebral vascular reserve and spontaneous

embolization on transcranial Doppler monitoring(13). It is suggested these patients could benefit from CEA.

1b. BMT vs CEA in symptomatic patients

Three major trails compared BMT and CEA in symptomatic patients, these were the Symptomatic Veterans Affairs Co-operative Study (SVACS) Trial, North American Symptomatic Carotid Endarterectomy Trial (NASCET) and European Carotid Surgery Trial (ECST)(17-19). Symptomatic patients were considered those who have had symptoms within the six months period. The SVACS was stopped prematurely when the NASCET and ECST results were published in 1991. The finding of these trails are summarized in table 3(13, 17-20).

Table 3: Individual patient meta-analysis of the 5-year risk of any stroke (including the perioperative risk) from pooled ESCT, NASCET, and SVACS Trial data.

Stenosis severity	5-year risk of any stroke (inc. perioperative)		ARR	RRR	NNT to revent one stroke	No. of strokes prevented per 1000 CEA
NASCET	CEA + BMT	BMT alone	@ 5 yrs	@ 5 yrs	No benefit	@ 5 yrs
0 – 30%	18.4%	15.7%	-2.7%	No benefit	No benefit	None
30 – 49%	22.8%	25.5%	+2.7&	No benefit	No benefit	27
50 – 69%	20.0%	27.8%	+7.8%	28%	13	78
70 – 99%	17.1%	32.7%	+15.7%	48%	6	156
Near occlusion	22.4%	22.3%	-0.1%	No benefit	No benefit	None

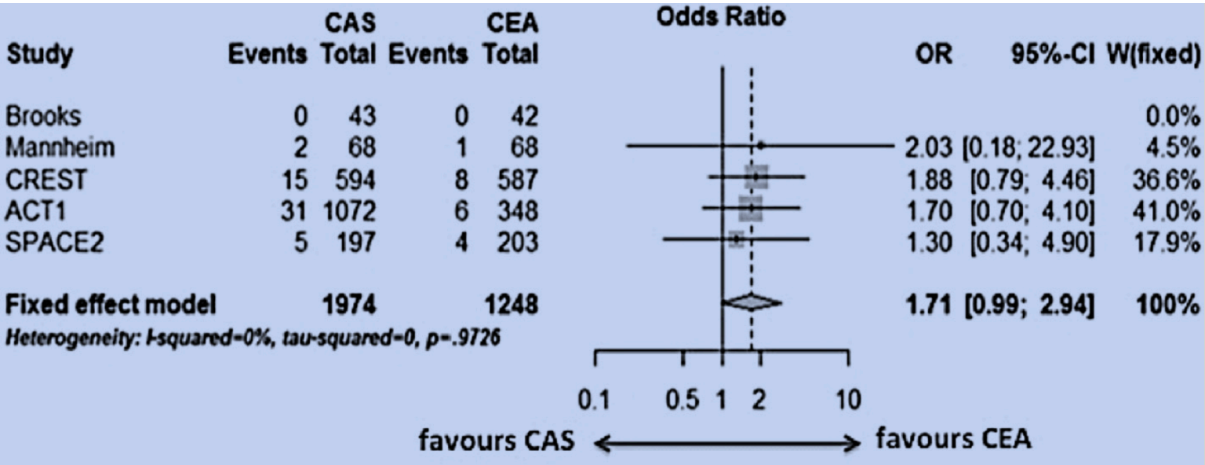
ARR = Absolute Risk Reduction in stroke; RRR = Relative Risk Reduction in stroke; NNT = number needed to treat to prevent one stroke

2. Carotid endorterectomy vs Carotid artery stenting

2a. CEA vs CAS in asymptomatic patients

Several randomized controlled trials looked at CEA vs CAS in asymptomatic patients. A meta-analyses of the data from these studies showed a 30 day death/stroke rate of 1.6% for CEA versus a 2.7% for CAS with the p value of 0.0553(13). Figure 1 shows the different studies and their results(21-24). Results from these studies favour CEA over CAS. Results from our own non-randomized study, but of carefully selected patients for CAS as in clinical practice showed similar outcome as that of CEA(25). It included both asymptomatic and symptomatic patients but majority were symptomatic. This study just confirms with careful patient selection CAS could have similar outcome as CEA.

Figure 1: Forest Plot comparing 30-day death/stroke in four randomised trials comparing carotid endarterectomy and carotid artery stenting in asymptomatic patients.



2b. CEA vs CAS in symptomatic patients

There are several randomized controlled trials comparing CEA to CAS in symptomatic patients. Most studies combined both symptomatic and asymptomatic patients and had small numbers. There are four major trials on which the management guidelines are based on, Endarterectomy versus Stenting in patients with Symptomatic Severe carotid Stenosis (EVA-3S), the Stent Protected Angioplasty versus Carotid Endarterectomy (SPACE) trial, the International Carotid Stenting Study (ICSS), and Carotid Revascularization versus Stenting Trial (CREST)(13, 26-29). Table 4 summarizes the meta-analyses from

these trials(30). The results showed significantly less stroke rate after CEA than CAS and there was increases death/stroke rate with increasing age. Recommendation from this meta-analysis was for CEA to be the first choice for these patients.

30-day outcomes	Symptomatic patients	
	hazard ratio (95% CI)	
Any stroke	1.81 (1.40-2.34)	favouring CEA
Death/stroke	1.72 (1.29-2.31)	favouring CEA
Death/stroke (males)	1.86 (1.19-2.91)	favouring CEA
Death/stroke (females)	1.53 (1.02-2.29)	favouring CEA
Death/stroke/MI	1.44 (1.15-1.80)	favouring CEA
Cranial nerve palsy	0.08 (0.04-0.14)	favouring CAS

Table 4: Summary of statistically significant findings in the perioperative period from meta-analyses of RCTs comparing CEA with CAS.

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New therapies for Sepsis

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Globally the incidence of sepsis is on the increase, yet the mortality remains substantive. As such the focus has shifted towards an improved understanding of the pathophysiology of the disease, its recognition and the implementation of specific therapeutic strategies in an individualized manner. The lecture will in particular address:

1. Pathophysiology of sepsis
2. Redox balance: Vitamin C, melatonin
3. Metabolic resuscitation: thiamine, melatonin
4. Microbiome manipulation: feeding, fecal transplant
5. Immunomodulation: via extracorporeal techniques
6. B Blockade

References available on request

Is Prophylactic Neck Dissection in Papillary CA of the Thyroid justifiable

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The treatment of Papillary thyroid cancer remains controversial. Treatment differs from total thyroidectomy and lymph node dissection to removing only the tumor and careful follow up.

In most of the western world the treatment of a papillary ca of the thyroid with no lymph nodes detected on imaging would be total thyroidectomy followed by ablation with radioactive Iodine and follow up

The follow up is with the help of serum thyroglobulin levels

Repeat iodine scanning, Ultrasound and FNA can then be used to determine the extent of recurrence and further treatment with Radioactive Iodine can then be repeated.

For this reason prophylactic neck dissection for the N0 neck is not usually done. The occurrence of occult metastases in papillary cancers found at prophylactic neck dissections range from 18 -92 %.

Papillary carcinoma is the most common malignancy arising from thyroid follicular cells. In the western world papillary carcinoma comprises 85% in whites and 72% in Blacks. In Japan the incidence is 92%. It generally has an indolent character. Frequent multicentricity and also lymph node metastases are a prominent biologic characteristic. Therefore the extent of thyroidectomy and also lymph node dissection is controversial.

In Japan limited thyroidectomy such as subtotal thyroidectomy or lobectomy and Isthmusectomy is frequently the standard surgical procedure. The use of Radioactive Iodine therapy is limited due to legal restrictions and to cost constraints. In Japan extensive prophylactic lymph node dissection of the central and lateral compartment has been widely adopted. This is due to the fact that the most common recurrence is to the lymph nodes and extensive dissections

can decrease the recurrence rates of these carcinomas. In spite of this these patients still develop lymph node recurrences due to incomplete lymphadenectomies. To date there have not been any studies comparing the outcome in patients who have recurrent disease after neck dissections versus patients who did not have prophylactic neck dissection and then developed recurrent disease.

Regional lymph nodes are located in 3 compartments; central, lateral and mediastinal. Mediastinal dissections are seldom done - usually only when there is radiological evidence of metastases. The central compartment is the most adjacent to the thyroid and this compartment can usually be dissected without extension of the wound. In a study of 5805 patients who underwent central neck dissections, the positive predictive value and specificity of preoperative ultrasonography was high at 92% and 98% respectively but negative predictive value and sensitivity were low at 37% and 12% respectively - this means that in 63% of patients where the ultrasound did not demonstrate lymph nodes they were positive on pathological evaluation.

The lateral compartment is more distal from the thyroid than the central compartment and therefore extension of the wound is necessary. It is considered that papillary thyroid cancer initially metastasizes to the central compartment and then to the lateral compartment but this has not been proven to be correct.

It has also been documented that patients who have clinical lymph node metastases are likely to have recurrences in spite of undergoing therapeutic lymph node dissection and thus very meticulous dissections must be done.

It is now recommended that the treatment of papillary carcinomas should be determined on a case by case basis. Primary lesions and nodal disease can be evaluated pre operatively with high resolution ultrasound High risk cases should undergo total thyroidectomy and neck dissection, It is recommended that prophylactic neck dissection be performed in patients with tumors larger than 3 cm or where extra-thyroid extension is demonstrated.

The complications of neck dissection in thyroid surgery can be devastating. The main complications are Hypoparathyroidism, Recurrent laryngeal nerve damage, Thoracic duct injury, accessory nerve damage with loss of shoulder movement and loss of sensation in the neck.

Radioactive Iodine has been shown to improve survival and reduce tumor recurrence in iodine-avid advanced stage well differentiated thyroid cancer.

What is my recommendation after all the reading I have done on the subject.

1 Papillary thyroid carcinoma is usually an indolent disease with a relatively low mortality but probably a high morbidity if not treated correctly

2. There is debate on the extent of thyroid resection – from lobectomy to total thyroidectomy

3. Radical central neck dissection is indicated in the node positive neck.

4. Due to the relatively high incidence of occult nodal metastases found at prophylactic neck dissection the nodal disease is important and has to be addressed

5. Radical neck dissection is only beneficial if it is performed meticulously and even then there still is a high recurrence rate.

6. Radical neck dissection combined with total thyroidectomy increases the incidence of complications exponentially.

7. Radioactive iodine is a very effective alternative for the treatment of occult nodal metastases in the neck.

8. If Radioactive Iodine fails the recurrent disease in the neck can usually be dealt with by neck dissection in a "virgin" neck

9. Radioactive iodine is cost effective.

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When should a dominant Thyroid Nodule be subjected to surgery? Review of current guidelines

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The definition of a “thyroid nodule” is defined as a discrete lesion within the thyroid gland that is radiologically distinct from the surrounding normal thyroid parenchyma. Thyroid nodules occur in 4-8% of the general population. Thyroid nodules may be a single dominant nodule (solitary thyroid nodule) or a dominant nodule in a multinodular goiter.

Indications for surgery

Indications for surgery include: very large goiters, compression symptoms (e.g. tracheal or oesophageal compression), patient’s request (mainly for cosmesis), non-resolving hyperthyroidism (failed medical treatment; failed radio-active iodine ablation (RAI) or where RAI is contra-indicated) and suspicion or confirmed malignancy.

Factors that increase the suspicion of malignancy includes:

- Age less than 20 or greater than 70 years
- Family history of thyroid cancer
- Rapid growth
- Nodules larger than 4 cm in size
- Firm and irregular consistency on palpation
- Fixation of the nodule to adjacent tissues
- Vocal fold paralysis
- History of neck irradiation
- Ipsilateral cervical lymphadenopathy

All the guidelines [American Thyroid Association (ATA), American Association of Clinical Endocrinologists (AACE), American College of Endocrinology (ACE), Associazione Medici Endocrinologi Medical guidelines (AME), British Thyroid

Association (BTA) and European thyroid cancer consensus] do agree that the ultrasound (U/S) findings in conjunction with fine needle aspiration (FNA) cytology results are the two main determinants for the work-up of malignancy.

The thyroid committees are not always in agreement with other supporting investigations such as serum calcitonin levels, radioisotope scanning, thyroid U/S elastography, 99mTc-sestamethoxyisobutylisonitryl (sestaMIBI) scan, 18F-fluorodeoxyglucose positron emission tomography-computed tomography (FDG-PET scan) and molecular testing.

Ultrasound (U/S) of the thyroid

The ultrasound assessment can provide detailed information that may indicate benign or malignant nodules. The U/S signs characteristic of papillary thyroid cancer or medullary cancer include hypoechogenicity, solid composition, irregular margins, taller than wider shape, fine micro-calcifications and central blood flow on a Doppler U/S. Cervical lymph nodes assessment under U/S has the highest sensitivity in diagnosing malignancy.

Comparison of the risk of malignancy in the different Ultrasound Classification Systems for Thyroid Nodules

ATA	BTA	AACE/ACE-AME	TIRADS
Benign. <1%	U1. Not defined	1. 1%	TR1. Not defined
Very low suspicion. <3%	U2. Not defined		TR2. Not defined
Low suspicion. 5-10%	U3. Not defined		TR3. Not defined
Intermediate suspicion. 10-20%	U4. Not defined	2. 5-15%	TR4. Not defined
High suspicion. >70-90%	U5. Not defined	3. 50-90%	TR5. Not defined

American Thyroid Association (ATA), American Association of Clinical Endocrinologists (AACE), American College of Endocrinology (ACE), Associazione Medici Endocrinologi Medical guidelines (AME), British Thyroid Association (BTA), Thyroid Imaging Reporting and Data System (TIRADS).

Each of the Society recommendations uses the U/S features as well as the size of the nodule to determine if FNA should be performed.

The American Thyroid Association (2015) size indication for FNA

Classification	Size indication for FNA
Benign.	No FNA
Very low suspicion. ≥2cm	≥2cm
Low suspicion. ≥1.5cm	≥1.5cm
Intermediate suspicion. ≥1cm	≥1cm
High suspicion. ≥1cm	≥1cm

Thyroid nodule biopsy

FNA is considered to be the most accurate to diagnose the type of pathology in the thyroid nodule with a sensitivity of 89% to 98% and a specificity of 92%. The Bethesda system for reporting thyroid cytopathology was formulated in 2007 and is well known. The Bethesda system consists of 6 grades, Bethesda 6 considered as malignant.

Bethesda system with malignancy rates and management plan.

Bethesda categories	Malignancy rate	Management

I.	Nondiagnostic or Unsatisfactory	1-4%	Repeat FNA with U/S guidance.
II.	Benign	0-3%	Clinical follow-up.
III.	Atypia of Undetermined Significance or	5-15%	Repeat FNA.
	Follicular Lesion of Undetermined Significance		
IV.	Follicular Neoplasm or Suspicious for a Follicular Neoplasm	15-30%	Surgical lobectomy.
V.	Suspicious for Malignancy	60-75%	Near-total thyroidectomy or surgical lobectomy.
VI.	Malignant	97-99%	Near-total thyroidectomy.

Should all cytopathological reports with a diagnosis of follicular cells in a dominant thyroid nodule be subjected to surgery? No, the cytopathologist can diagnose benign follicular cells which would then classify as Bethesda II (Benign). For the FNA to be diagnosed as benign, there has be a minimum of 6 groups of benign follicular cells, each group composed of a minimum of 10 cells with or without colloid; or any FNA specimen that contains abundant colloid, even if less than 6 groups of follicular cells are present on 1 or more smears. The benign FNA has the follicular cells arranged as macrofollicles and macrofollicle fragments.

The indeterminate group

The indeterminate group, Bethesda III (atypia of undetermined significance or follicular lesion of undetermined significance)/IV (follicular neoplasm or suspicious for a follicular neoplasm). Cytological features do not allow for

follicular carcinoma to be distinguished from follicular adenoma. Certain features may suggest carcinoma such as abundant follicular cells arranged in sheets, microfollicular or trabecular pattern, with minimal background colloid; following which the FNA is categorised as follicular neoplasm (Bethesda IV). Follicular carcinoma can only be diagnosed on histological samples where vascular or capsular invasion can be seen.

The different thyroid societies have different recommendations for the indeterminate group including: considering FNA results together with the U/S findings and clinical findings, repeating FNA under U/S guidance, close observation, or surgery. Further investigations; such as sestaMIBI scan, FDG-PET, and molecular testing; may assist the clinician in the decision to subject the patient for surgery.

Conclusion

The step-wise approach for the work-up of a patient thyroid nodule tends to vary according to which recommendations is followed. U/S and cytopathology are the two most appropriate investigations to diagnose malignancy in a dominant thyroid nodule. The concern is the indeterminate group where a definitive diagnosis cannot be made. There are further investigations that may assist in deciding on the risk that a dominant thyroid nodule may be malignant, but the clinician needs to be aware of the limitations of these investigations. The combination of history, clinical findings, recommendation guidelines, and appropriate investigations will influence the final decision whether to operate on a patient with a thyroid nodule or not.

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Anatomical and psychological challenges in the management of the intersex child or adolescent: which gender to assign?

Making wise choices in difficult surgical problems

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It is often a challenge to decide which gender to assign during the management of the intersex child or adolescent. Some, but not all children with intersex develop gender dysphoria. The World Professional Association for Transgender Health's (WPATH) latest Standards of Care indicates that "(I)n children and adolescents, a rapid and dramatic developmental process (physical, psychological, and sexual) is involved and there is greater fluidity and variability in outcomes, particularly in prepubertal children." Gender dysphoria during childhood does not inevitably continue into adulthood. Gender dysphoria may be associated with comorbid psychiatric pathology including suicidality associated with mental disorder. Most adults who present with gender dysphoria do not have a comorbid psychiatric diagnosis according to world literature and my own research. However, initial gender assignment in the intersex child or adolescent still seems to be the best predictor of adult gender identity.

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