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A collaborative review of the current concepts and challenges of anastomotic leaks in colorectal surgery

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Abstract

The reduction of the incidence, detection, and treatment of anastomotic leakage (AL) continues to challenge the colorectal surgical community. AL is not consistently defined and reported in clinical studies, its occurrence is variably reported and its impact on long-term morbidity and healthcare resources has received relatively little attention. Controversy continues about the best strategies to reduce the risk. Diagnostic tests lack sensitivity and specificity, resulting in delayed diagnosis and increased morbidity.

Intraoperative fluorescence angiography has recently been introduced as a means of real-time assessment of anastomotic perfusion with preliminary evidence suggesting that it may reduce the rate of AL. In addition, concepts are emerging about the role of the rectal mucosal microbiome in AL and the possible role of new prophylactic therapies.

In January 2016 a meeting of expert colorectal surgeons and pathologists was held in London, UK to identify the ongoing controversies surrounding AL in colorectal surgery. The outcome of the meeting is presented in the form of research challenges that need to be addressed.

Introduction

Anastomotic leakage (AL) is one of the most feared complications of colorectal surgery. Despite advances in anastomotic technique, postoperative monitoring and diagnostics, its incidence and consequences have not appreciably changed during the last fifty years. AL can have profound consequences for patients through mortality and short and long-term morbidity. It also has an effect on healthcare providers, through the immediate cost o management and the use of resources for remedial care. IALis considered by many surgeons to be the greatest single challenge in visceral surgery.

In January 2016, a meeting of expert colorectal surgeons and pathologists was held in London, UK to identify the challenges in preventing, diagnosing, and treating AL in light of recent innovations in this field. The meeting was sponsored by educational grants from Novadaq Technologies Inc. (Ontario, Canada) and Elemental Healthcare (Berkshire, UK). Participants were asked to give a short presentation on a specific topic related to AL, followed by an invited commentary from a second faculty member, as the basis for wider discussion. Each participant submitted a written narrative of their presentation. This manuscript, which each participant was invited to review and edit, reports the outcome of fthe meeting and the identified areas for further research.

Definition and Incidence

Previous research into AL has been hampered by the lack of a widely accepted definition, with twenty nine separate definitions reported from 1993 to 1999 and 59 from 200 to 2009 [1, 2]. An attempt to address this was made in 2010 by the International Study Group of Rectal Cancer (ISREC), who defined AL as ‘a communication between the intra- and extra-luminal compartments owing to a defect of the integrity of the intestinal wall at the anastomotic site’

[2]. In addition, a pelvic abscess adjacent to an anastomosis, even if no communication with the bowel lumen could be demonstrated, was considered to have originated from a leak. Recommendation was made for a simple grading system based on clinical management as follows: grade A, resulting in no change in management, grade B, requiring active therapeutic intervention and grade C, requiring re-laparotomy or laparoscopy. Subsequent validation in patients undergoing sphincter preserving surgery of the rectum demonstrated an overall leakage rate of 7.5% with a severity of 16% grade A, 23% grade B and 61% grade C [3]. Despite attempts at standardisation, AL continues to be variably reported, with an incidence ranging widely from 5% to 19%, depending on the site and type of anastomosis and the cohort under investigation [4]. To complicate the situation further, many studies fail to take into account subclinical or radiological leakage, despite the recognised association with poor bowel function and anastomotic stricture formation [5].

Research challenge:

- Integration of standard validated definition and reporting of AL into clinical trials.

Risk factors for anastomotic leakage

Much has been written about the risk factors for AL in an attempt to guide surgeons as to when anastomosis is appropriate. In an attempt to quantitate these following left-sided colorectal surgery a Colon Leakage Score (CLS) was developed and shown to have good predictive value [6]. The patient-related factors cited as increasing AL include male gender, smoking, obesity, alcohol abuse, pre-operative steroid and non-steroidal anti-inflammatory drugs, longer operation duration, pre-operative transfusion, contamination of the operative field and the urgency of the operation [4]. A recent meta-analysis of 23 studies and 110,272

patients found that AL was significantly associated with low rectal anastomosis (odds ratio (OR) 3.26, 95% CI 2.31, 4.62), male gender (OR 1.48, 95% CI 1.37, 1.60), and pre-operative radiotherapy (RT) (OR 1.65, 95% CI 1.06, 2.56), although the quality of evidence was regarded as moderate or low [7].

The impact of RT on AL rates is a contentious issue particularly as the common practice of creating a defunctioning stoma in RT patients can introduce bias into studies [8]. The UK Medical Research Council (MRC) CR07 randomised controlled trial (RCT) reported no difference in AL rates between patients having pre-operative RT or selective post-operative RT in a multicentre, multinational randomised analysis of 1,350 rectal cancer patients [9]. In an interim analysis of the Stockholm III trial in rectal cancer comparing short course RT, short course RT with delay and long-course RT, the effect of radiotherapy on AL appeared to be related to the timing of surgery, with a significant increase if it was performed between 11 and 17 days following the start of RT [10].

In addition to patient-related factors and non-specialist colorectal surgeons, [11] low institutional cancer case load are associated with higher AL rates [12]. A meta-analysis including 13,040 rectal cancer patients demonstrated a significantly lower risk of AL in favour of high volume hospitals (OR 0.72, 95% CI 0.48, 1.09). There was no significant difference among colon cancer patients [12].

Research challenges:

- Further validation of the Colon Leakage Score as a universal tool for predicting AL.
- Improved understanding of the detrimental effects of radiotherapy on anastomotic healing

Anastomotic construction

The role of specialisation in reducing leakage rates highlights the importance of surgical technique in anastomotic construction. One meta-analysis of reconstruction techniques after low anterior resection compared straight coloanal anastomosis, side-to-end coloanal anastomosis, transverse coloplasty and colonic J pouch and did not demonstrate superiority of any technique in terms of leakage [13].

Several Cochrane reviews and meta-analyses have failed to demonstrate a benefit for either hand sewn or stapled anastomosis [14-17]. Stapled anastomosis is increasingly being used because of technical ease, reproducibility and speed. In the era of increasing laparoscopic surgery, stapled low rectal anastomosis presents a particular problem due to the confines of the bony pelvis. Numerous studies suggest that the number of stapler firings used to transect the distal rectum in double-stapled anastomosis increases the rate of AL [18-23], whilst others have failed to show this [24, 25]. There does not appear to be any benefit of single over double-stapled low rectal anastomosis [26].

Transanal total mesorectal excision (TaTME) has been suggested to result in lower rates of ALdue to the avoidance of cross stapling [27, 28]. More data from large international cohort studies and randomised trials are awaited to confirm this. Other techniques for anastomosis have been tried, including anastomotic compression. First described by Denans almost two centuries ago [29], the AKA-2 device, developed in the 1980s, comprised two plastic rings applied with a transanal applicator. Compression of the inverted bowel edges produces simultaneous necrosis and healing. After four to six days the rings separate from the anastomosis [30]. The AKA-2 was superseded by the biofragmentable anastomotic ring (BAR) made of absorbable polyglycolic acid and barium sulphate [31]. When the device is closed a

small gap remains between the rings to limit tissue necrosis. The ring fragments are passed with the stool tow to three weeks postoperatively. The limitations of the device include retained foreign material within the tissue, luminal narrowing, necrosis at the anastomotic site and problems with introducing the deployment device [32]. Most recently the nickel-titanium (Nitinol; NiTi) ColonRing device has been introduced [32] with compression rings that possess shape memory and elasticity to provide more uniform compression of the tissue. Despite a large multicentre, multinational study involving 1,180 patients [33] and a prospective multicentre study reporting leakage rates of just over 3% [34] the device has not gained widespread application.

Research challenges:

- Identification of new materials and methods for performing anastomosis with minimal collateral tissue trauma.
- Development of devices that accommodate the confines of the pelvis and facilitate low rectal anastomosis

Anastomotic reinforcement

Several innovations have been tried to reinforce an anastomosis and so reduce the occurrence of leakage. These include the use of tissue adhesives, bio-absorbable materials and intraluminal stents. None has shown clinical efficacy or entered into routine practice. Notably, two randomised comparisons of Seamguard® (W.L. Gore & Associates Inc., Flagstaff, Arizona, USA) against standard circular stapling for rectal anastomosis failed to show any difference in the AL rate [35, 36]. The most recent technology, LifeSeal™ (LifeBond, Caesarea Industrial Park, Israel), uses enzyme-based catalytic breakdown of a gelatin-based

product to seal an anastomosis; the results of early phase clinical trials are awaited. Recent studies in rat models of AL have demonstrated that cyanoacrylate-based adhesives show the greatest mechanical strength and lowest rate of ileus, bowel wall destruction and immunohistopathological tissue reaction compared with other adhesive materials [37, 38].

In a related strategy, omental wrap [39] and mesenteric flap formation [40] have been used to seal anastomoses and provide a cellular scaffold for healing. In a meta-analysis of three studies including 943 patients, the use of an omental wrap resulted in a significant three-fold reduction in the rate of clinical AL but no difference in the reoperation rate or mortality [39].

Research challenge:

- Improved methods to seal an anastomosis and support tissue healing

Defunctioning stoma

A defunctioning stoma is used to protect a rectal anastomoses by diverting the faecal stream. Whether it prevents AL or merely reduces the consequence of leakage is debated. There is no agreement whether a defunctioning stoma should be constructed for all rectal anastomoses or just for those that are low. A defunctioning ileostomy can cause morbidity, most notably dehydration and sodium depletion owing to excessive output. Reversal of the stoma is associated with a complication in some 40% of patients [41]. Many patients will be left with a stoma for several months due to the low clinical priority for reversal [42] and 20% of patients are left with a permanent stoma owing to postoperative complications of anterior resection [43].

Several studies have suggested that a defunctioning stoma decreases the incidence of clinical leakage of a colorectal anastomosis [44, 45], others on the other hand have reported no difference in leakage but a reduced incidence of reoperation has been recorded[46]. A recent propensity-matched scoring analysis of 936 patients who underwent low anterior resection confirms that defunctioning ileostomy does not influence the rate of clinical AL but does mitigate against the consequences, reducing the need for urgent reoperation [47].

The technique of pre-stage ileostomy, also known as 'ghost' ileostomy, has been described whereby a terminal ileal loop is exteriorized through the abdominal wall but is left unopened [48]. Should a complication of the anastomosis develop it can be rapidly transformed into a definitive ileostomy under local anaesthesia. If this is not needed, the morbidity of an ileostomy is avoided. Although the ghost ileostomy appears to be feasible in cohort studies [49, 50], its role is yet to be determined by randomised controlled evidence.

Research challenge:

- Improved selection criteria for patients undergoing a defunctioning stoma
- Further determine the role of 'ghost' ileostomy in association with a high risk anastomosis

Intraoperative prediction of anastomotic leakage

The air leak test is a well established technique to check intraoperatively the anastomotic integrity immediately after completion of the anastomosis.. It is easy, cheap and quick to perform with very little risk. The evidence suggests that the air test is effective in predicting satisfactory healing when it demonstrates an intact anastomosis [51, 52]. Thus a randomised

study by Beard et al. [51] reported more clinical and radiological leaks in patients who did not undergo an air test than those who did (clinical 14% vs. 4%, radiological 29% vs. 11%). In a retrospective cohort study, Ricciardi et al. [52] analysed 998 consecutive left sided anastomoses performed without diversion. The clinical leak rate of 8% in patients with a positive air test was significantly higher than the 4% in patients with a negative result, with the leak rate in patients with untested anastomoses being similar (8%) to those with a positive test. In the event of a positive air test, suture repair alone may be associated with a high AL rate and the evidence suggests that in this situation the anastomosis should be revised and/or defunctioned [52-54].

Intraoperative endoscopy allows assessment of anastomotic integrity, bleeding from the staple line and the detection of any additional pathology. [52] [55]. Although intra-operative endoscopy has been shown to be a safe and reliable technique, studies comparing its routine with selective use have been underpowered [55, 56]. Without a large randomised control trial any benefit of routine intraoperative endoscopy in preventing AL cannot be determined.

Research challenge:

- A randomised evaluation of intraoperative endoscopy to assess anastomotic integrity.

Anastomotic healing

Understanding the pathophysiology of anastomotic healing is crucial to the development of new treatment and preventative strategies. Owing to the complex biological processes involved, it is difficult to mimic anastomotic healing *in vitro* and a recent systematic review showed that animal research on AL is of poor quality [57]. Although many components of the

healing process, such as the initial inflammatory response, organisation, collagen deposition and wound remodelling, are common to all tissues and have been studied extensively in skin, certain aspects of anastomotic healing differ considerably [58]. Caution is therefore advised in translating cutaneous models of wound healing to healing in the gastro-intestinal (GI) tract.

Collagen in the GI tract is produced both by fibroblasts and smooth muscle cells compared with fibroblasts alone in the skin. Despite increased shear stress and bacterial load, wound healing is far more rapid in the GI tract [58]. The capacity of collagen synthesis in anastomotic tissue [59] is significantly impaired in sepsis and an anastomosis should be avoided in such circumstances. Furthermore, collagenase, which is less important in cutaneous healing, plays a critical role. Collagenase is upregulated in the colonic mucosa following anastomosis, contributing to lysis of collagen and decreased anastomotic strength [60]. It has been suggested that some patients are at increased risk of AL due to pre-existing changes in the extracellular matrix, such as a lower collagen type I/III ratio and higher expression of several collagenase subtypes in both mucosa and submucosa [61].

Research challenge:

- Improved understanding of the molecular and biochemical pathways controlling the early balance of collagen synthesis and breakdown in anastomotic healing

Optimising anastomotic vascularity

Optimal blood supply to the anastomosis is critical for healing. At operation, perfusion is assessed clinically by inspecting the colour of the bowel and bleeding from its cut ends and the marginal vessels. Several attempts have been made to apply more sophisticated means of

assessing anastomotic perfusion. Such methods include analysis of tissue oxygenation using light spectroscopy [62] and modified pulse oximetry [63, 64]. A fall in tissue oxygen tension appears to be associated with subsequent AL. Interestingly, in patients who do not suffer AL there is a reactive rise in the tissue oxygen tension in the proximal part of the anastomosis, suggesting a protective compensatory mechanism at the tissue level [62].

In patients undergoing chemoradiotherapy for rectal cancer, computed tomographic (CT) perfusion scanning was used to assess parameters of microvascular perfusion, including blood flow and blood volume [65]. Both parameters were increased in the cancers compared with normal rectal wall and showed a significant reduction in response to chemoradiotherapy. Similar techniques may be applicable to assessing the risk of AL particularly after radiotherapy.

The development of fluorescence perfusion angiography has enabled the surgeon to 'visualise' tissue perfusion in real time. This allows the surgeon to assess bowel perfusion and to select an appropriate segment of bowel for anastomosis and then to check perfusion endoscopically on completion of the anastomosis [66]. Typically, a fluorophore is injected intravenously and visualized with a near-infrared (NIR) camera. NIR imaging has the advantage over other wavelengths of electromagnetic radiation in providing deep tissue penetration without causing thermal damage [67]. The most commonly used fluorophore is indocyanine green (ICG), which absorbs light at 790-810nm and re-emits fluorescence at 835nm [67]. ICG is safe for human use and has US Food and Drug Administration (FDA) approval for a variety of imaging applications, including assessment of hepatic function, measurement of cardiac output, and ophthalmic angiography [68]. When administered intravenously it binds rapidly to plasma proteins and is limited to the intravascular

compartment. It has a plasma elimination half-life of three to five minutes and is metabolized in the liver with a half-life of 15 to 20 minutes, making it suitable for multiple evaluations [69, 70].

Intra-operative NIR-ICG for assessment of anastomotic perfusion has been shown to be feasible and safe in several non-randomised studies using laparoscopic (PINPOINT™ (Novadaq, Mississauga, Ontario, Canada) [69, 71], NIR/ICG system (Karl Storz [72], Tuttlingen, Germany)) and robotic (Firefly™ (Intuitive Surgical Inc., Sunnyvale, California, USA)) systems [73]. In white light mode these systems act as a conventional laparoscope and in NIR mode the ICG is visualized as a white fluorescence on a black background. The PINPOINT™ system provides a dual display mode, where green ICG fluorescence is superimposed on the white light image to provide an augmented view of tissue perfusion. All commercially available NIR imaging systems lack the capability to quantify tissue perfusion, which remains subjective with no clear cut-off to guide the surgeon on the adequacy or inadequacy of anastomotic perfusion [67].

The largest non-randomised multicentre trial to use NIR fluorescence angiography with the PINPOINT system to assess anastomotic viability during laparoscopic left colectomy is the Perfusion Assessment in Laparoscopic Left Anterior Resection (PILLAR II) trial [71]. This feasibility study in 147 patients conducted in the United States achieved successful imaging in 98.6% of cases and resulted in a change of surgical plan in 7.9% of the patients. There was a low clinical leak rate of 1.4% at 30-days with no complications attributable to the use of ICG or the device. A European phase II study of the role of NIR fluorescence angiography in assessing anastomotic perfusion is ongoing (clinical trials identifier NCT02459405) [74].

A RCT evaluating ICG-NIR in rectal surgery, the PILLAR III trial, is due for completion in 2017 (clinical trials identifier NCT02205307) [75]. Patients planned for open or minimally invasive low anterior resection for rectal or rectosigmoid cancer with an anastomosis at 10cm or less from the anal verge, are eligible. They are stratified according to neo-adjuvant therapy and randomised to receive intra-operative fluorescent angiography with the PINPOINT® or SPY® Elite system or white light laparoscopy. The primary endpoint is the anastomotic leakage rate.

Research challenges:

- Validation of NIR-ICG efficacy in reducing AL
- Methods to quantify NIR-ICG perfusion
- Multi-spectral laparoscopic systems for detection of different fluorophores
- Novel pharmacological methods to enhance anastomotic perfusion

Anastomotic leakage as an infective complication

There has been much interest in a return to the concept of anastomotic leakage as an infective complication. Using a rat model, Shogan et al have shown that anastomotic injury results in a change in anastomotic tissue-associated microbiota with a notable 500-fold and 200-fold increase in the relative abundance of Enterococcus and Escherichia/Shigella species [76]. Importantly, this difference was only apparent in tissue from the anastomosis and not in luminal faecal samples. AL was associated with increased bacterial virulence-associated pathways, including production of matrix-degrading enzymes and cytotoxic necrotizing factors. Work by the same group, again in a rat model, showed that Enterococcus faecalis contributed to AL by upregulation of collagenase activity and activation of tissue matrix metalloproteinase-9 (MMP-9) and that AL was prevented by administration of an antibiotic

enema or MMP-9 inhibitor [77]. Furthermore, in a small cohort of 11 patients undergoing colonic surgery, E. faecalis and other bacteria with collagen-degrading and MMP-9-activating ability could be isolated from the anastomotic site and were unaffected by the use of standard intravenous prophylactic antibiotics.

The concept of upregulation of bacterial virulence pathways with increased collagenase production leading to AL is supported by work from the 1980s conducted by Young and Wheeler [78, 79]. Using a collagenase inhibitor (Aprotinin) they were able to demonstrate an increase in anastomotic burst pressure and breaking strength in a rat model [78] and a significant reduction of radiological and clinical AL in a RCT involving 100 patients [79].

Another interesting observation, with relevance to rectal cancer surgery, is the change in composition and virulence of the rectal flora following radiotherapy [80]. The adverse influence of radiotherapy on AL is usually attributed to tissue inflammation and microvascular injury, but it is possible that radiotherapy-induced changes in the rectal flora result in a pro-AL microenvironment. This is supported by the work of Olivas et al (2012) who showed in a model of low anterior resection that pre-operative radiation and intestinal inoculation of Pseudomonas aeruginosa (a collagenase producing bacterium) resulted in high rates of AL, whereas radiation alone or P. aeruginosa alone did not cause leakage [81].

Research challenges

- To establish cause and effect for the role of the microbiome in AL
- Exploit protease inhibition as a mechanism to reduce AL
- Further investigation of the change in microbiome induced by radiation, its role in AL, and strategies for mitigation.

The role of mechanical bowel preparation

The role of mechanical bowel preparation (MBP) prior to surgery is an area of contention, with opinions varying either side of the Atlantic. The disadvantages of MBP are the unwanted complications, including hypovolaemia, metabolic disturbance and poor patient compliance [82-85]. The advantages include the ability to perform intraoperative endoscopy and to avoid a faecally loaded colon. Evidence against the use of routine MBP in colonic surgery includes a meta-analysis performed in 2009 and a subsequent Cochrane review [86, 87].

The evidence for MBP in rectal surgery is less clear-cut. Randomised evidence in rectal cancer is confined to one trial, GRECCAR III, which randomised patients to MBP (oral laxative and enema) or no MBP [84]. Although no difference in the rates of AL and major morbidity were demonstrated, patients with no MBP had a higher 30-day morbidity and more infectious complications. Other studies have confirmed the lack of association between MBP and AL in rectal surgery [88, 89] and suggested that a rectal enema alone may be as effective [90]. This is the focus of an ongoing Italian RCT in which patients are randomised to either full MBP or rectal enema alone (clinical trials identifier NCT00940030) [74].

Research challenge:

- Optimal method of bowel cleansing prior to rectal surgery
- Clarification on the role of MBP when an upstream stoma is to be fashioned

Pre-operative antibiotics and selective gut decontamination

The pre-operative administration of non-absorbable oral antibiotic preparations (OAP) has been demonstrated to reduce the risk of AL following elective GI surgery (OR 0.42, 95% CI 0.24 to 0.73) [91]. The co-administration of MBP with OAP may reduce the faecal load allowing increased delivery of OAP to the colonic mucosa [92, 93]. Several recent large retrospective studies using the National Surgical Quality Improvement Program (NSQIP) database suggest that OAP in combination with MBP is effective in reducing AL [93-95]. There are, however, methodological limitations with these studies, including differences in the study populations, lack of data on systemic antibiotic usage and lack of detail regarding type and dose of MBP and OAP. Further evidence is needed and might be forthcoming from the SELECT study (clinical trials identifier NCT01740947), which is investigating whether oral non-absorbable antibiotics reduce clinical AL, and is due to complete in 2018 [96].

Research challenge:

- The optimal administration and antibiotic combination for reducing AL and surgical site infections

Early diagnosis

Early diagnosis of anastomotic leakage allows timely remedial intervention and reduces morbidity and mortality [97]. The difficulty is that AL presents in a variety of ways, ranging from rapid fulminant sepsis to a more insidious onset with failure to progress in the postoperative period. The main radiological modalities used to diagnose AL are water-soluble contrast enema (WSCE) and CT, but data on their accuracy are limited by the timing of the study and the expertise of the radiologist [98]. WSCE is safe despite fears concerning

anastomotic disruption [99], but its sensitivity and specificity can be poor with reported figures of 52% and 87% respectively in left-sided anastomoses [100]. In comparison, the sensitivity and specificity of CT scanning has been reported to be 57% and 100% after total mesorectal excision for rectal cancer [101]. It is possible that a combination of the techniques, using CT with rectal contrast, improves diagnostic accuracy [102].

The use of biosensors to sample the anastomotic environment via an intraluminal or microdialysis catheter may allow early detection of anastomotic disruption [55]. This technique allows rapid analysis at multiple time points. Studies have reported a lower pH [103] and concentration of ischaemia-related metabolites [104] and increased levels of lysozyme [105], bacterial cell wall lipopolysaccharide [106] and cytokines [107] in patients who develop AL. These findings suggest that bacterial translocation has occurred within the first three to five days of the anastomosis being constructed, even if the frank leakage of intraluminal contents has not occurred by that time.

Changes in electrical resistance have also been associated with anastomotic disruption [108]. The use of serum C-reactive protein (CRP) as a marker of AL is probably limited by its poor specificity, but it has been suggested that a CRP above 150mmol/l on postoperative days 3 to 5 may be predictive and a trigger for further investigation [4].

Research challenges:

- The optimal radiological techniques to detect AL
- Identification of the preferred biomarkers for detecting early AL
- Development of real-time, bed-side methods for detecting early AL

Management strategies for anastomotic leakage

Many factors have to be considered when deciding the best treatment for a patient with AL. These include age, comorbidity, level of the anastomosis, the interval from the primary operation and the degree of anastomotic dehiscence [109]. The treatment options include one or more of antibiotic therapy, transanal drainage, percutaneous drainage, laparoscopy/laparotomy with anastomotic repair and defunctioning stoma, and take-down of the anastomosis with end stoma. A survey of 350 members of the Dutch Society of Gastrointestinal Surgery suggested heterogeneity in the strategies employed to manage leakage with a preference to try and preserve a left sided anastomosis in fitter and younger patients [110].

In an analysis of the American College of Surgeons (ACS) NSQIP 2012 database, 56% of patients with AL required re-operation, 25% received a non-surgical intervention and 19% were treated medically [111]. The need for re-operation was found to be greater in patients with anastomotic leakage from a colo-colonic anastomosis than with an ileo-colonic or colo-rectal anastomosis, and was reduced in patients with a stoma. In patients with a high-risk profile, a repair or construction of new anastomosis should probably not be performed without a protective stoma [112]. McDermott et al proposed an AL severity score to aid clinical decision-making regarding the escalation of care, use of inotropes and intervention [4]. This score ranges from a patient deviating from his or her expected course with biochemical abnormalities (grade 1), where the recommendation is close observation to a patient in septic shock (grade 5) where intensive care and emergency laparotomy are required.

AL following rectal surgery, particularly in the presence of a diverting stoma, may present as a pre-sacral abscess that can leave a chronic sinus after it has drained. Treatment options include a watch and wait policy, take down of the anastomosis and creation of an end colostomy or laying open of the sinus into the neorectum. Newer techniques include endoluminal endosponge vacuum-assisted systems, which provide continuous drainage and encourage by suction the bowel wall of the neorectum to obliterate the cavity [113]. This should, however, be undertaken early whilst the tissues are still flexible and can respond to the negative pressure. Vacuum—assisted treatment is effective with and without a diverting stoma [113, 114]. The use of sutures or endoscopic clips to close the residual defect following endosponge therapy may reduce the time to healing [115].

Research challenges

- Validation of endoluminal therapies for anastomotic leakage

Summary and future perspectives

ALis a substantial problem for clinicians, patients and healthcare providers. Little progress has been made over the last ten years in our understanding or management of the condition. A concerted effort is required by surgical researchers, working in collaboration with industry, basic scientists and healthcare partners. Several new techniques have emerged that hold promise in reducing AL although their exact role is yet to be established by prospective randomised evidence. The emerging concept of AL as an infective complication warrants further investigation and if it is shown to be valid it may hold the key to future prophylactic therapies.

The aim of this manuscript has been to present the current thinking amongst leading colorectal surgeons and pathologists on the most pressing areas for further research. It is hoped that this manuscript will stimulate the research that is needed to make an impact on a clinical problem that has defied the efforts of previous generations.

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