



PREVENTION, DIAGNOSIS AND MANAGEMENT OF COLORECTAL ANASTOMOTIC LEAKAGE

March 2016

ISSUES IN PROFESSIONAL PRACTICE
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Association of Surgeons
of Great Britain and Ireland



The Association of Coloproctology
of Great Britain and Ireland

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PREVENTION, DIAGNOSIS AND MANAGEMENT OF COLORECTAL ANASTOMOTIC LEAKAGE

AUTHORS

F D McDermott, S Arora, J Smith, R J C Steele,
G L Carlson and D C Winter
(on behalf of the joint ASGBI/ACPGBI
Anastomotic Leakage Working Group)

PUBLICATION DATE

March 2016

PUBLISHED BY

Association of Surgeons of Great Britain and Ireland
35-43 Lincoln's Inn Fields, London, WC2A 3PE

SPONSORED BY AN EDUCATIONAL GRANT FROM

Baxter

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FOREWORD

Issues in Professional Practice (IIPP) is an occasional series of booklets published by the Association of Surgeons of Great Britain and Ireland to offer guidance on a wide range of areas which impact on the daily professional lives of surgeons. Some topics focus on clinical issues, some cover management and service delivery, whilst others feature broader aspects of surgical working life such as education, leadership and the law.

This latest IIPP booklet on the Prevention, Diagnosis and Management of Anastomotic Leakage, has been produced in partnership with the Association of Coloproctology of Great Britain and Ireland, and it is hoped that this joint collaboration will be of significant clinical benefit to members of both societies.

The Association intends that this publication, and others in the series (all of which are accessible at: www.asgbi.org.uk/publications), will provide concise advice and guidance on major current issues, and prove to be a helpful and accessible resource to support your professional practice. We welcome feedback on this and other booklets in the *Issues in Professional Practice* series, and proposals and contributions for future issues in the series.



Mr John Moorehead
President

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INTRODUCTION

An anastomotic leak, as all colorectal surgeons are aware, is a devastating complication that may not only result in severe morbidity, but can also unfortunately lead to the demise of the patient. We all fear it, and will do all we can to prevent it. However, no matter how skilled the surgeon may be, there are times when this complication will occur despite best efforts.

These guidelines, which have been developed by an exhaustive review of the literature and meticulous scientific process, provide extremely valuable advice as how to prevent, diagnose, treat and - very importantly - counsel patients about the possibility of this dreaded complication. The group have worked diligently to sift and interpret the information and are to be commended on producing a document that is clear, concise and balanced. If teams follow their advice there is no doubt in my mind that the incidence of anastomotic leakage will be reduced but also, when it occurs, lives will be saved.

I do hope that all practicing surgeons will heed the current thinking that is embodied in the document and apply it appropriately.



Professor Sir Norman Williams

MS, FRCS, FMed Sci, FRCP, FRCP (Edin), FRCA, FDS (Hon), FACS (Hon), FRCSI (Hon), FRCSEd (Hon)

Past President, The Royal College of Surgeons of England

Director, National Centre for Bowel Research and Surgical

Innovation, Barts & The London School of Medicine & Dentistry.

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Patient Perspective

Whilst this document is intended to review the clinical evidence on the prevention, diagnosis and management of anastomotic leakage, it is essential that the impact of anastomotic leakage on the patient and their family is also considered. Good communication remains an important aspect of care.

Careful history taking may elicit important risk factors for anastomotic leakage (e.g. a history of smoking or alcohol abuse), which may not otherwise be evident, and about which some patients may be reticent.

It is important to prepare patients and their families for surgery where an anastomosis is being considered, by giving a balanced assessment of the risk of anastomotic leakage. This will allow better-informed decision-making regarding whether the risk of an anastomosis (in particular a higher risk anastomosis) is acceptable, or whether a stoma may be preferable. This may enable patients to make a better-informed choice and to be better prepared to deal with the consequences of an anastomotic leak, should this occur.

Good quality, timely information before and after surgery is part of this process and should include input from an enterostomal therapist, which may help allay the patient's fears with regard to a stoma and its impact on future quality of life.

Patients who have suffered from anastomotic leakage should not only be offered prompt and appropriate medical attention, but a frank, open and honest discussion about the complication as soon as their condition permits. They should have access to psychological support, to help them deal with associated anger, grief and stress.

Jo Church

Patient Representative

Acknowledgements

The authors wish to thank the following members of the ASGBI/ACPGBI joint anastomotic leak working group, for generously giving their time and effort in assessing the clinical evidence and providing expert opinion:

Austin Acheson, Tan Arulampalam, Arnie Bhowmick, Cat Boereboom, Ken Campbell, Jo Church (Patient Liaison), Mark Coleman, Justin Davies, Michael Davies, Peter Dawson, Nicola Fearnhead, Nader Francis, Richard Guy, Nigel Hall, Athur Harikrishnan, Deena Harji, Charles Hendrickse, Stephen Holtham, Kourosh Khosraviani, Robin Kennedy, Anil Lala, Gerald Langman, Charles Maxwell-Armstrong, Brendan Moran, Neil Smart, Henry Tilney, Jared Torkington, Janindra Warusavitarne.

Thank you to Louise Hull for her assistance with the Delphi Methodology.

Abbreviations

AL: Anastomotic leak

ASA: American Society of Anaesthesiologists Physical Status Classification

BMI: Body mass index

CI: Confidence intervals

CRP: C-reactive protein

DFS: Disease free survival

IR: Interventional radiology

NSAID: Non-steroidal anti-inflammatory drug

OS: Overall Survival

OR: Odd Ratio

RCT: Randomised Control Trial

SDD: Selective decontamination of the digestive tract.

TNF: Tumour necrosis factor

WHR: Waist: hip ratio

Introduction

Anastomotic leaks (AL) are potentially catastrophic complications of colorectal surgery. The spectrum of clinical severity associated with AL is broad, however, ranging from a small-contained leak without sepsis in a patient with a defunctioning stoma, to a patient with four-quadrant peritonitis and septic shock. ALs increase the need for reoperation, the risk of local recurrence¹, and reduce both overall (OS) and disease free survival (DFS)²⁻⁴. Despite the gravity of the complication and potential sequelae, data regarding risk factors and optimal perioperative management of ALs are relatively poor and few attempts have been made to bring together the data which are available, in order to provide clinical guidance. This document aims to present the current best evidence, and utilised Delphi methodology to provide expert colorectal opinion.

Development Of Methodology & Delphi Meeting

A systematic review of the literature searching for colorectal anastomotic leaks was performed⁵. Due to low quality evidence across multiple domains of risk factors, assessment and management of ALs, a Delphi methodology was proposed. Following the review and Delphi process it was agreed that formal grading/strength of recommendation would be inappropriate, due to the lack of high quality evidence. A formal cut-off for consensus was not used: rather the evidence was discussed and the percentage consensus after 3 rounds of discussion is presented in brackets.

A steering group of colorectal consultants and trainees was formed and met at the Tripartite meeting in Birmingham in July 2014. Current evidence was presented, and on the basis of this, it was agreed that a Delphi format would be beneficial to help develop guidelines. A questionnaire was developed using Survey Monkey⁶ and distributed to ACPGBI members covering all ACPGBI regional chapters. The initial round was completed on-line by participants prior to a meeting with a further 2 rounds. (See Table 7, Appendix).

Definitions and epidemiology of AL

Definition

The preferred definition for anastomotic leaks was: 'A leak of luminal contents from a surgical join between two hollow viscera'⁷.

Epidemiology

The prevalence of AL varies from 1% to 19%, depending upon anatomical site, pre, intra and postoperative factors⁵. These are discussed below.

Avoidance of Anastomotic Leakage

Preoperative considerations

Identification of significant preoperative risk factors may guide the proposed treatment and allow modification of risk. Preoperative alteration of lifestyle and/or treatment may not always be possible, particularly in the emergency setting. However, consideration of risk factors is relevant in the decision-making process with regard to whether an anastomosis is a safe option, and whether a defunctioning (or permanent) stoma should be considered. At the very least, if a patient opts for a "high risk" anastomosis, despite the identification of significant risk factors for AL, this should be on the basis of clearly documented discussion regarding the alternative, safer options. Preoperative risk factors for AL may be modifiable or non-modifiable.

Modifiable risk factors

Alcohol

Ethanol consumption in excess of recommended levels (>105g alcohol per week) is associated with an increased risk of AL⁸. In the UK 1 unit of alcohol is the equivalent of 8 grams of pure alcohol.

Smoking

Tobacco smoking, both current and historical, is associated with an increased risk of AL. Several studies have demonstrated current smoking to be an independent risk factor⁹⁻¹³. Additionally, a previous smoking history (>40 pack years) is an independent risk factor for AL¹⁴.

Obesity

Several studies have shown obesity to independently increase the risk of AL¹⁵⁻¹⁸. While obesity has often been poorly defined in these studies and the degree of obesity and associated increase in risk may consequently be open to interpretation, it is nevertheless clearly associated with a measurable increase in the risk of AL. Measures of central obesity, such as waist circumference and waist-hip ratios may be more sensitive than BMI in predicting AL¹⁹.

Medication

Table 1 details medication reportedly associated with an increased risk of AL. Some of the evidence is, however, weak or contradictory. There is experimental evidence of increased risk of AL for several immunosuppressant drugs used in patients who have undergone organ transplantation. This is consistent with reports of a higher AL rate in immunosuppressed patients after renal transplantation²⁰.

Medication	Type	Evidence & Recommendations
Corticosteroids	Steroid	Prolonged use may increase AL ^{21, 22}
Infliximab	Anti-TNF α monoclonal anti-body	Slows wound healing but no impact on AL rate ^{23, 24}
Mycophenolate mofetil ²⁵ Cyclosporine A ²⁶ Tacrolimus ²⁷ Everolimus ²⁸	Immunosuppressant	Mycophenolate AL risk based on clinical observational study. For other drugs experimental evidence suggests increased AL risk
Azathioprine	Purine analogue immunosuppressant	Contradictory evidence ^{29, 30}
Bevacizumab	VEGF inhibitor	Should be stopped and not restarted for at least 28 days either side of surgery (manufacturer advice) ³¹

Table 1. Medication associated with increased risk of AL.

Nutrition and Hypoalbuminaemia

Malnutrition (defined as an unintentional loss of weight of >10% in the preceding 6 months), and a serum albumin concentration of <35g/L increases the risk of AL³²⁻³⁶. Hypoalbuminaemia is more likely to be associated with a systemic inflammatory response secondary to necrotic or perforated tumours, or sepsis (see below), than related to nutritional depletion *per se*. Nutritional assessment should be undertaken in all patients being prepared for surgery, and an attempt made to correct malnutrition. The underlying cause of hypoalbuminaemia should also be corrected where possible (for example by treating infection). It should be noted that it is not the hypoalbuminaemia itself which confers the additional risk, but the metabolic conditions which lead to it (systemic inflammation and increased capillary permeability). Thus, preoperative administration of albumin to temporarily increase serum albumin concentration will not abnegate the associated increase in risk of AL. In the event that it is not possible to correct significant malnutrition (>10% unintentional weight loss) and/or hypoalbuminaemia (<32g/L) preoperatively (for example, in a patient with a large necrotic tumour, and/or because of impending intestinal obstruction or perforation), the operative strategy should be modified so as to avoid undertaking an anastomosis at that time if it is possible to do so.

Mechanical Bowel Preparation (MBP)

Mechanical bowel preparation (MBP) has traditionally been used to reduce stool burden in the colon, with the additional benefits of improving visualisation for intraoperative endoscopy and facilitating the insertion of stapling devices. Withholding MBP does not appear to have resulted in increased AL rate in several randomised trials and a systematic review³⁷⁻⁴¹. The GRECCAR III RCT demonstrated an overall reduction in septic complications in rectal surgery alone in patients receiving MBP, although there was no difference in AL⁴². Bowel preparation is unpleasant for patients and is not essential for colorectal surgery.

Radiotherapy

Neoadjuvant radiotherapy, usually in combination with chemotherapy, has been demonstrated to reduce local recurrence and to downstage rectal tumours⁴³. Retrospective series have previously suggested that chemoradiotherapy might increase AL^{44, 45}. However, this has not been supported by several RCTs, including the MRC CR07 and Dutch TME trials⁴⁶⁻⁴⁸. A previous history of pelvic radiotherapy does, however, increase AL rate and is discussed in Table 2.

Preoperative antibiotics and selective decontamination of the digestive tract

Preoperative broad-spectrum intravenous antibiotics are routinely used in elective and emergency colorectal surgery, with the goal of reducing postoperative infective complications and this practice is recommended by ACPGBI⁴⁹. In the USA, some surgeons routinely use non-absorbable oral antibiotics such as Tobramycin and Amphotericin B - also known as selective decontamination of the digestive tract (SDD). A systematic review has indicated that SDD reduces anastomotic leak rates from 7.4% to 3.3%⁵⁰. This finding has also been replicated in a recent study of over 8,000 colorectal resections, demonstrating both lower surgical site infection and anastomotic leak rates in the treatment group⁵¹. Despite this, SDD is not currently in widespread practice in the United Kingdom and Ireland.

Non-modifiable risk factors

Gender and age

Male gender and increasing age (especially age over 60) may increase the risk of AL. While the effect of gender on rectal anastomotic leakage might be attributable to greater technical difficulty of undertaking surgery in the narrower male pelvis, this does not explain the higher rate of AL seen in colonic surgery. The effect of chronological age is not observed consistently and is most probably accounted for by co-morbidity (Table 2).

Risk Factor	Evidence
Gender	Male gender increases AL rate in colonic ¹⁰ and rectal ^{45, 52} anastomoses.
Age	Some studies have demonstrated that increasing age or age >60 is associated with an increased risk of AL ^{53, 54} . Other studies in elderly populations have failed to report this ⁵⁵ . It is probably more important to consider the biological age of the patient and other risk factors, rather than chronological age <i>per se</i> .
History of radiotherapy	Patients previously treated with radiotherapy, e.g. for cervical or prostate cancer have AL rates documented to be as high as 36% ⁵⁶ . This must be considered when planning an anastomosis.
Diabetes Mellitus	The evidence is contradictory. Two studies have suggested an increased AL rate in ileocolic anastomoses ¹⁵ or low anterior resection ⁵⁷ , whereas another paper has demonstrated no change in AL rate but higher mortality in those who do sustain a leak ⁵⁸ .
Co-morbidity	<p>Increase in AL rate:</p> <ul style="list-style-type: none"> • Pulmonary disease^{21, 22, 59} • Vascular disease⁴⁴ • Renal disease/renal replacement therapy/ immunosuppressed renal transplant patients^{20, 60, 61} (Haemodialysing patients pre and post-surgical intervention reduces surgical complications but not anastomotic leaks, anastomosis should be avoided in emergency cases). • ASA of greater than 2⁶², 3¹⁵ and 4⁶³ have been demonstrated to increase risk of AL.

Table 2. Summary of non-modifiable risk factors for anastomotic leak.

History of Radiotherapy

While immediate preoperative radiotherapy might represent a modifiable risk factor, a history of previous pelvic radiotherapy clearly does not. Previous radical pelvic radiotherapy is associated with a very high risk of AL in the radiotherapy field. Consideration should be given to avoiding anastomoses in bowel previously subjected to radiation (however many years earlier), particularly in the presence of other risk factors.

Diabetes

Although there is conflicting evidence for an increased risk of AL in patients with diabetes (see Table 2), there is evidence for increased perioperative mortality⁶⁴ and increased length of stay⁶⁵. In addition, there is evidence of increased perioperative morbidity due to pre-existing complications, including cerebrovascular, cardiovascular disease and nephropathy⁶⁶⁻⁶⁸. There are NHS guidelines, published in conjunction with ASGBI and other organisations, for the optimum perioperative management of diabetes⁶⁹.

Elective vs. Emergency Surgery

Emergency surgery is, predictably, associated with higher AL rates compared with elective practice. However, an emergency operation *per se* is not an absolute contraindication to an anastomosis, with several studies demonstrating, for example, that an anastomosis with a defunctioning stoma is a safe option for perforated diverticulitis⁷⁰⁻⁷². However, the risk factors outlined in this document, and, in particular, haemodynamic instability, shock, inotrope requirements and hypoalbuminaemia must be taken into account when considering an anastomosis and the need for a defunctioning stoma. Whenever possible, the risks and benefits of, and alternatives to a primary anastomosis should be discussed with the patient before surgery, so that an appropriately informed decision can be made. However, there will be some emergency circumstances when this may not be possible.

Tumour factors

Distal anastomoses, particularly those of infraperitoneal rectum have the highest anastomotic leak rates. Distance from the anorectal junction is an independent predictive risk factor for AL^{9, 45, 73}. Other factors that increase AL rate are tumour size >3cm⁷⁴ or >4cm⁷⁵, advanced tumour stage⁴⁵ and, in particular, the presence of distant metastases¹¹. It is likely that many of these factors are interrelated. For example, late presentation with advanced disease is likely to be associated not only with lower socioeconomic status, but also poor nutritional status, smoking and medical comorbidity.

Intraoperative considerations

Operative Technique

Poor operative technique, for example, failing to avoid tension on, or poor vascularity at an anastomosis will impact negatively on anastomotic healing and is likely to result in AL. Operative duration of greater than 4 hours, intraoperative contamination, blood loss over 100ml and blood transfusion are risk factors for AL⁷⁶⁻⁷⁹, as is hypoxia⁸⁰. The use of vasopressors is associated with a threefold increase in AL⁸¹.

Goal directed fluid therapy

The National Institute for Health and Care Excellence (NICE) recommends the use of goal directed therapy e.g. the use of oesophageal doppler⁸². Goal directed therapy has been shown to

reduce postoperative complications for major surgery but it has not been shown to reduce anastomotic leak rates *per se*^{83, 84}.

Interventions

Suturing, as opposed to stapling an anastomosis may be associated with a higher risk of AL, although the difference may be only detected radiologically, and is not manifest clinically⁸⁵. Specifically, meta-analysis favours stapled anastomosis in ileocolic resections⁸⁶, but no superiority has been demonstrated between anastomotic techniques for anterior resection of the rectum⁸⁷. Other technical interventions that may reduce the risk of AL include utilising air leak tests⁸⁸, low versus high ties on vascular pedicles⁸⁹, and open compared to laparoscopic surgery⁹⁰, although the last finding has not been substantiated on meta-analysis⁹¹.

Irrespective of the quality of scientific evidence, it is appropriate to note that a recent legal judgement in England regarding the routine use of air leak testing in rectal anastomoses (Shortall-v-Mid Essex Hospital Services NHS Trust 2014) concluded that failure to use this technique was held to be negligent. While the technique may not be supported by sufficient weight of clinical evidence (and clearly cannot provide reassurance regarding leakage caused by excessive tension or ischaemia), it seems sensible to recommend that all rectal anastomoses (and probably all left sided colonic anastomoses) for which a defunctioning proximal stoma is not being undertaken should routinely be tested for immediate “technical” defects by air insufflation (or a similar technique).

The use of a defunctioning stoma and/or an omentoplasty to isolate the anastomosis may reduce the adverse consequences of AL, but does not appear to reduce the likelihood of AL *per se*^{92, 93}.

Drains have historically been used following colorectal anastomoses with the perceived benefit of identifying and potentially reducing postoperative complications. The use of drains for both colonic and infraperitoneal rectal anastomoses is debated. However, there have been several large systematic reviews including a Cochrane review on the use of drains for colorectal anastomoses, that do not demonstrate a significant reduction in AL rate⁹⁴⁻⁹⁶. The Cochrane review assessed 1,140 patients from 6 RCTs and showed no reduction in clinical or radiological anastomotic leaks (or any other complications for colorectal anastomoses). Specific to rectal infraperitoneal anastomoses, a meta-analysis combining 3 RCTs and 5 retrospective studies demonstrated a reduction in anastomotic leak (OR 0.51; 95% CI 0.36 – 0.73)⁹⁷. This effect was not seen, however, when the 3 RCTs were analysed in isolation⁹⁶. In summary, drainage is not routinely required for colonic anastomoses, but to properly assess their use in infraperitoneal rectal anastomoses would require an appropriately powered RCT. Their use in this setting, specifically with respect to avoidance of AL is therefore currently a matter of personal choice.

Preoperative considerations	Intraoperative considerations
Non-modifiable risk factors <ul style="list-style-type: none"> • Male gender • Distal rectal anastomosis • Tumour size >3cm • Advanced tumour stage • Metastatic disease • History of radiotherapy • ASA >2 • Diabetes • Pulmonary disease • Vascular disease • Emergency surgery • Ex-smoker (>40 pack years) 	Increase risk <ul style="list-style-type: none"> • Intraoperative contamination • Duration >4 hours • Inotropes • Blood loss • Blood transfusion
Potentially modifiable risk factors <ul style="list-style-type: none"> • Smoking • Obesity • (High BMI/ Waist: hip ratio/ Visceral fat) • Alcohol excess (>21units/ 105g alcohol/ week) • Corticosteroids • Bevacizumab • Malnutrition/ hypoalbuminaemia 	Reduce risk <ul style="list-style-type: none"> • Preoperative antibiotics (intravenous and selective decontamination digestive tract)

Table 3. Summary of preoperative and intraoperative risk factors.

Postoperative considerations

NSAIDs

There is growing evidence that NSAIDs should be used with caution in the postoperative period. A meta-analysis has demonstrated that non-selective NSAIDs were associated with an increased risk of AL. However many of the studies included were flawed and had selection bias⁹⁸. More recently a retrospective cohort study of over 13,000 bariatric and colorectal operations has demonstrated a 24% increase in the likelihood of AL with NSAID use. This effect appears to have

been attributable to emergency colorectal operations 12.3% vs. 8.3% in the NSAID and non-NSAID group respectively (OR 1.7 [95% CI 1.11 – 2.68], $p = 0.01$)⁹⁹.

Diagnosis of Anastomotic Leakage

Prompt diagnosis of AL is essential for effective management. Delayed diagnosis of AL is associated with worse outcomes¹⁰⁰. Clinicians must therefore be alert to early and subtle signs of AL, including non-specific signs, notably cardiac arrhythmias including atrial fibrillation^{101,102}. Postoperative ileus is unusual after uncomplicated laparoscopic colorectal surgery and should lead to urgent assessment for anastomotic leakage. Rectal bleeding or passage of bloody mucus per rectum should cause suspicion of anastomotic leakage after a rectal anastomosis. It cannot be emphasised strongly enough that failure to make anticipated postoperative progress in any patient with a colorectal anastomosis should, above all, raise the suspicion of anastomotic leakage.

In patients in whom there is a departure from the expected pattern of postoperative recovery, frequently repeated assessment by a senior, experienced clinician, and careful analysis of trends in observations remain the most valuable and reliable means of establishing early diagnosis of AL. It can be difficult for any surgeon to remain entirely objective when considering the likelihood of leakage from an anastomosis they have created themselves. Asking a similarly experienced colleague to provide a second opinion in these circumstances is therefore extremely valuable and is strongly recommended¹⁰³.

Raised concentrations of serum C-reactive protein and procalcitonin may be useful (but non-specific) markers for AL, particularly if CRP is very high ($>150\text{mg/L}$) on postoperative days 3-5^{104, 105} and especially if the serum albumin continues to fall or fails to return to normal postoperatively. The negative predictive value of a normal CRP in this context may be particularly useful. In contrast, white cell count appears to be less reliable as a marker of AL⁴⁴.

Diagnostic imaging is not essential when a patient is unwell and a leak is clinically evident, and imaging under these circumstances may give rise to unnecessary delay in management. The sensitivity of common imaging modalities, such as CT scanning and water-soluble contrast enema is dependent on the timing of investigations, the quality of the technique used and the skill and experience of the radiologist. The diagnostic accuracy of CT for suspected leakage from the distal colon may be improved with the addition of rectal and intravenous contrast¹⁰⁶. Cross sectional imaging should not be undertaken in the presence of haemodynamic instability, unless invasive monitoring is available and the patient is accompanied throughout by critical care personnel who can provide immediate cardiorespiratory support. Intravenous contrast should be used with caution (or avoided) in the presence of dehydration, hypotension or acute kidney injury.

Scoring systems

A variety of scoring systems have been developed to assist in prediction, diagnosis, or grading the severity of AL. None has proved sufficiently valuable to gain widespread acceptance or incorporation into routine practice. The colon leakage score (CLS) attempts to predict AL for left sided colonic resection using 11 patient and operative factors¹⁰⁷. The modified DULK score is an aid to the diagnosis of AL but has a low positive predictive value¹⁰⁸. The International Study group of Rectal Cancer devised a grading system for severity of leak, but this is relatively simplistic, suggesting only “no intervention, active non-operative intervention or re-laparotomy”¹⁰⁹.

Treatment of Anastomotic Leakage

Initial Management

There is an international drive to improve the management of sepsis, which remains the major cause of morbidity and mortality associated with AL. Systemic inflammatory response syndrome (SIRS) consists of 6 criteria: temperature $>38.3^{\circ}\text{C}$ or $<36^{\circ}\text{C}$, respiratory rate $>20/\text{min}$, heart rate $>90/\text{min}$, white cell count $<4 \times 10^9/\text{l}$ or $>12 \times 10^9/\text{l}$, altered mental state and a blood glucose level of $>7.7\text{mmol/l}$ in the absence of diabetes. Sepsis is currently defined as the presence of at least 2 of the SIRS criteria as a result of infection. Severe sepsis is defined as sepsis with evidence of super-added organ dysfunction (hypotension, oliguria, high serum lactate). Septic shock is defined as failure of these parameters to respond to adequate fluid resuscitation. Patients with severe sepsis are at particular risk of developing septic shock and it is imperative that septic shock is avoided in order to avoid associated high mortality rate. A delay of source control in excess of 12 hours after the development of hypotension, compared with less than 3 hours has been previously shown to increase mortality from 25% to 60%¹¹⁰.

Timely and appropriate intervention is therefore imperative if a patient develops sepsis as a consequence of AL. Initial management should include the “sepsis six” care bundle¹¹¹. “Sepsis six” is a set of 6 criteria, which, when implemented, have been shown to result in a 46.6% reduction in the relative risk of mortality from sepsis¹¹². These interventions are administering high flow oxygen, taking blood cultures, measuring lactate and full blood count, urine output, administration of broad-spectrum antibiotics and intravenous fluid challenge.

Subsequent and Definitive Management

1. *General principles*

Subsequent management requires a thorough assessment of the patient's clinical stability. A stable patient may initially be adequately managed conservatively, with fluids, antibiotics and oxygen, together with close clinical observation. Conversely, an urgent attempt to achieve source control should be undertaken in any patient with an AL and severe sepsis or septic shock, within the time frame indicated below.

A patient with an AL should be nursed in an environment appropriate to their level of systemic illness and the consequent need for monitoring. Recommended time limits for intervention in the treatment of abdominal sepsis associated with AL have been identified previously, and are determined by the severity of sepsis¹¹³. In the absence of organ dysfunction, surgical or radiological intervention to achieve source control should be undertaken as soon as possible (where this is required), but always within 18 hours of diagnosis. If sepsis is complicated by evidence of organ dysfunction, source control should be achieved as soon as possible, but always within 6 hours of diagnosis. Septic shock should result in source control immediately, and always within 3 hours, if preventable death is to be avoided.

2. *Source control*

Control of the source of infection associated with AL may occasionally be unnecessary. Such patients will usually be stable and well, without evidence of sepsis, but may have some localised abdominal tenderness, raised inflammatory markers and gastrointestinal dysfunction (for example, ileus and/or diarrhoea). Imaging in these cases usually shows no evidence of anastomotic discontinuity and little more than a small perianastomotic collection. Complete resolution can be expected in most cases with conservative treatment, including intravenous antibiotics, intestinal rest (oral fluids only or parenteral nutrition) and close monitoring in the ward environment for signs of sepsis.

A small, contained AL in a haemodynamically stable patient without radiological evidence of anastomotic discontinuity may be managed successfully by radiologically guided drainage, and/or washout and defunctioning, rather than taking down the anastomosis and creating a stoma, provided there is continued close observation and evidence of improvement. Radiological drainage should not be undertaken when there is radiological evidence of complete anastomotic discontinuity, as it is unlikely to control sepsis adequately and anastomotic healing cannot occur. Multiple separate foci of intraabdominal infection associated with AL are not usually suitable for radiological drainage and if present on cross sectional imaging, generally

represent an indication for surgical source control. Laparotomy is usually required.

In low rectal ALs transanal drainage may be effective. Endoscopic placement of vacuum devices into the presacral cavity (e.g. an Endo-SPONGE®) may also be of benefit under these circumstances but adequate evaluation of the efficacy and cost effectiveness of this technique is required¹¹⁴.

Development of, or deterioration in, the severity of sepsis in a patient treated conservatively or by radiological drainage for AL should be considered “failed” treatment and a low threshold maintained for taking a patient urgently to theatre and taking down the anastomosis. Attempts to “repair” an AL should never be undertaken in the presence of severe sepsis or septic shock, in patients with AL requiring inotropes and in those with significant hypoalbuminaemia (<32g/L). A repair should not be attempted if there is an established abscess cavity at the anastomosis. Satisfactory healing under these circumstances is unlikely to occur and it is far safer to exteriorise the affected segments. Similarly, enterotomies made during laparotomies under these circumstances are unlikely to heal adequately and injured bowel should be resected and/or exteriorised if further abdominal sepsis and intestinal failure is to be prevented¹⁰³. Operating upon a patient with an AL can not only be technically challenging, but also emotionally difficult for the surgeon who constructed the “failed” anastomosis. It may be associated with significant feelings of guilt and can impair objective decision-making. Involving the assistance of a second consultant colleague in re-operative procedures is not an admission of failure or inadequacy but is good practice under these circumstances and is strongly encouraged¹⁰³.

Association of Surgeons of Great Britain and Ireland

ISSUES IN PROFESSIONAL PRACTICE

PREVENTION, DIAGNOSIS AND MANAGEMENT OF COLORECTAL ANASTOMOTIC LEAKAGE

Management of Specific Patterns of Anastomotic Leakage

1. Intraperitoneal Anastomotic Leakage

Table 4 details grades of increasing severity for intraperitoneal AL. Table 5 presents suggested management of these leaks based on the Delphi process.

Grade	Clinical status	Clinical signs of peritonitis	Haemodynamic changes	Setting	Inotropes
1	Infection or sepsis without need for interventional procedure	No	None	Level 0 (Ward)	No
2	Infection or sepsis with ileus responsive to abscess drainage	No	None (or tachycardia rapidly responsive to treatment)	Level 0 (Ward)	No
3	Sepsis with ileus, requirement for nasogastric drainage & urinary catheterisation	Single quadrant	Persistent tachycardia but normotensive	Level 1/2 (Ward with critical care input/HDU)	No
4	Severe sepsis	More than single quadrant, but not generalised	Tachycardia & hypotension (responsive to fluid therapy)	Level 2 (HDU)	No
5	Septic shock	Generalised	Tachycardia, hypotension, and shock	Level 3 (ITU)	Yes

Table 4. Grades of clinical severity for AL.

Case Scenario	Management	Source Control	Setting
1	<i>No sepsis (Grade 1)</i>		
	Conservative (89%)	None	Level 0/ 1 (96%)
2	<i>Sepsis/ contained leak/ abscess (Grade 2)</i>		
	Drainage needed (80%)	Radiological drainage if possible. If unavailable, laparoscopy/ laparotomy, washout, drain and repair AL with proximal defunctioning stoma, or resect anastomosis and create stoma (85%)	Level 0 -2 (100%)
3	<i>Sepsis, ileus/Single quadrant peritonitis (Grade 3)</i>		Level 2
	Resuscitate and operation (85%)	Laparoscopy/ Laparotomy washout, drain and proximal defunctioning stoma or resect anastomosis and create stoma (92%)	(96%)
4	<i>Severe sepsis/more than single quadrant peritonitis (Grade 4)</i>		
	Resuscitate and operation (100%)	Laparoscopy/ Laparotomy washout, resect anastomosis and create stoma (85%)	Level 2/3 (100%)
5	<i>Septic shock/generalised peritonitis (Grade 5)</i>		
	Resuscitate and operation (100%)	Laparoscopy/ Laparotomy washout, resect anastomosis and create stoma (100%)	Level 3 (96%)

Table 5. Suggested management of intraperitoneal AL based on Delphi meeting (percentage consensus in brackets). In these scenarios it is assumed in all cases that patients are being appropriately resuscitated with oxygen, intravenous fluids and antibiotics.

2. Extra-peritoneal Anastomotic Leakage

The highest leak rates occur with extra-peritoneal (low pelvic) anastomoses^{9, 45, 115, 116}. However, because peritoneal contamination is less likely to occur, and the majority of patients will have a covering loop stoma, the clinical signs may be more subtle. Management (Table 6) will depend upon the patient's clinical

stability as indicated above (Table 6). Take down of the anastomosis is recommended for all patients who develop severe sepsis or septic shock after an extraperitoneal AL.

Case Scenario	Management	Source Control	Setting
1	<i>No sepsis (Grade 1)</i>		
	Conservative (89%)	Drainage (IR/transperineal/transanal) ± proximal defunctioning stoma (76%)	Level 0/ 1 (96%)
2a	<i>Sepsis with contained leak/ abscess <3cm (Grade 2)</i>		
	Drainage needed (70%)	<ul style="list-style-type: none"> • Transperineal/transanal drainage ± proximal defunctioning stoma (56%) • Laparoscopy/laparotomy and drain ± proximal defunctioning stoma (33%) 	Level 0 -2 (100%) Level 1 (56%)
2b	<i>Sepsis with contained leak/ abscess >3cm (Grade 2)</i>		
	Drainage needed (93%)	<ul style="list-style-type: none"> • Radiological drainage (37%) • Surgical drainage (56%) <ul style="list-style-type: none"> ◦ Laparoscopy/Laparotomy washout, drain and proximal defunctioning stoma (44%) ◦ Transperineal drainage ± proximal defunctioning stoma (26%) ◦ Laparotomy and take down anastomosis (22%) 	Level 2 (67%)
3	<i>Sepsis, ileus/Single quadrant peritonitis (Grade 3)</i>		
	Resuscitate and operation (82%)	<ul style="list-style-type: none"> • Drain and proximal defunctioning stoma (30%) • Take down anastomosis (48%) 	Level 2 (74%)
4	<i>Severe sepsis, more than one quadrant peritonitis (Grade 4)</i>		
	Resuscitate and operation (100%)	Laparoscopy/ Laparotomy washout, and take down anastomosis (93%)	Level 2/3 (100%)
5	<i>Septic shock, generalised peritonitis (Grade 5)</i>		
	Resuscitate and operation (100%)	Laparoscopy/ Laparotomy washout, and take down anastomosis (100%)	Level 3 (100%)

Table 6. Suggested management of extraperitoneal AL based on Delphi meeting (percentage consensus in brackets). In these scenarios it is assumed in all cases that patients are being appropriately resuscitated with intravenous fluids and antibiotics.

Appendix

Summary of findings from Delphi process for colorectal anastomotic leakage

- Initial meeting at Tripartite meeting in Birmingham (July 2014)
- Delphi meeting held on 14th October 2014, RCS England
- Invited Consultants and colorectal trainees from ACPGBI
- Round 1 completed prior to meeting with on-line questionnaire
- Further 2 rounds completed at meeting
- Results presented here are after 3 rounds of questionnaires.

Key (SD strongly disagree, D –disagree, N – neither agree or disagree, A – agree, SA – strongly agree)

Demographics and Format of Delphi Process

	Round 1	Round 2	Round 3
No of participants	36	31	31
Format	On-line	Meeting	Meeting

Table 7. Format and numbers completing rounds of Delphi process.



Figure 1. Age groups of surgeons within anastomotic leak working group

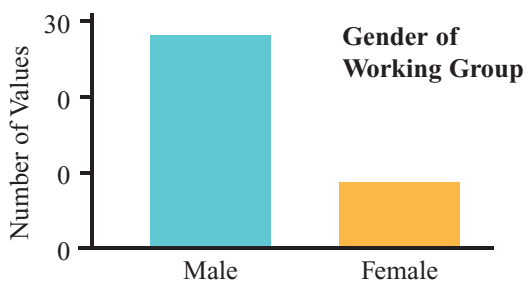


Figure 2. Gender of anastomotic leak working group

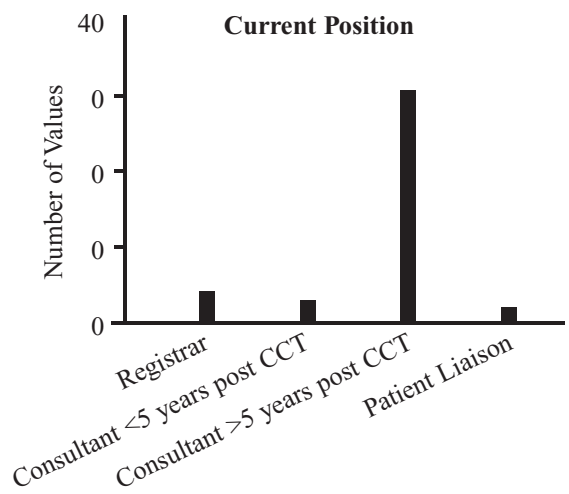


Figure 3. Seniority of anastomotic leak working group

Regions

All regions of the UK and Ireland were represented, based on ACPGBI chapters:



Figure 4. Regional representation of anastomotic leak working group

Delphi Process:

Definition of anastomotic leaks:

A leak of luminal contents from a surgical join between two hollow viscera ⁷ .	63%
A breach in a surgical join between two hollow viscera with or without active leak of luminal contents.	37%

Table 8. Percentage agreement of definitions for anastomotic leak.

Non-modifiable risk factors:

- All >70%: Male gender, distal anastomosis, advanced tumour stage, metastatic disease, historical radiotherapy, ASA>2, diabetes, vascular disease, emergency surgery, ex-smoker (>40 pack years).
- Others: Tumours >3cm (15%), pulmonary disease (63%).

Modifiable risk factors:

- All >70%: Smoking, obesity, alcohol excess, corticosteroids, biological agents, biologics in combination with steroids, malnutrition/hypoalbuminaemia, pre-op short and long course DXT.
- Others: Bevacizumab (62.9%), Age >60 (42%).

Peri/intraoperative risk factors:

- All >70%: contaminated surgery, single and multiple inotropes, blood loss.
- Others: Duration >2 hours (23%), blood transfusion (48%).

Reduce risk of anastomotic leaks:

- Preoperative intravenous antibiotics: 26% agree or strongly agree.
- Selective decontamination of digestive tract: 74.1% (A/SA).
- Goal directed fluid therapy: 78% (A/SA).

Preoperative	Intraoperative
Non-modifiable risk factors <ul style="list-style-type: none"> • Male • Distal anastomosis, particularly rectal • Tumour size >3cm • Advanced tumour stage • Metastatic disease • Historical radiotherapy • ASA >2 • Diabetes • Pulmonary disease • Vascular disease • Emergency surgery • Ex-smoker (>40 pack years) 	Increase risk <ul style="list-style-type: none"> • Intraoperative contamination • Duration >4 hours • Inotropes • Blood loss • Blood transfusion
Potentially modifiable risk factors <ul style="list-style-type: none"> • Smoking • Obesity • (High BMI/ Waist: hip ratio/ Visceral fat) • Alcohol excess (>21units/ 105g alcohol/week) • Corticosteroids • Bevacizumab • Malnutrition/ hypoalbuminaemia 	Reduce risk <ul style="list-style-type: none"> • Preoperative antibiotics (intravenous and selective decontamination digestive tract) • Cardiac monitoring/goal directed fluid management

Table 9. Pre and postoperative non-modifiable and modifiable risk factors.

Risk factors required to consider defunctioning

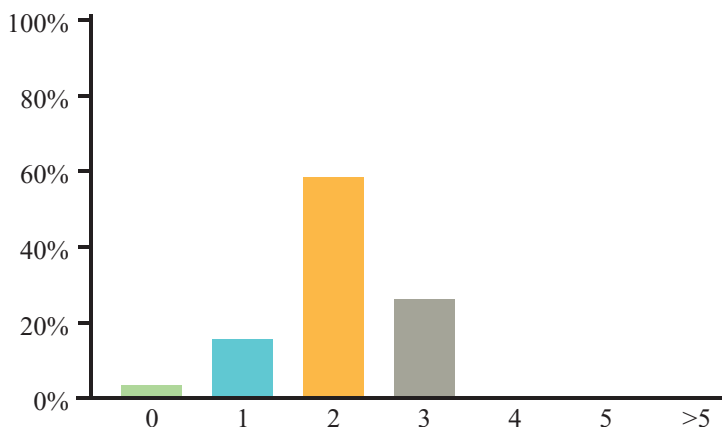


Figure 5. How many risk factors from Table 9 would a patient require to consider defunctioning an anastomosis?

Air Leak Testing

	A/ SA
Anterior resections	100%
Other colonic anastomoses	36%
Small bowel anastomoses	4%
All patients without a defunctioning stoma	29%

Table 10. Percentage agreement with statement: should air leak testing be performed on the following anastomoses?

Intraoperative endoscopy

22% agreed or strongly agreed that endoscopy should be performed following anterior resections.

Useful indicators for anastomotic leaks

Over 70% agreed or strongly agreed that: Tachycardia, Pyrexia, CRP, WCC, pain out of proportion, arrhythmia, ileus, and failure to progress are useful indicators for anastomotic leak. Others indicators included Pro-calcitonin (19%) and urinary retention (27%).

Investigation of anastomotic leak

- Contrast enhanced CT (Oral or rectal contrast): 100% A/SA
- Right hemicolectomy: contrast CT (100%)
- High anterior resection: contrast CT (96%)
- Low anterior resection: contrast CT (92%)

Factors to determine whether to resect an anastomosis

- >70%: Generalised pus, faecal peritonitis, severe sepsis
- Others: localised pus 16%, elderly age of patient 63%
- Other comments: size of defect, ischemia of anastomosis

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Association of Surgeons of Great Britain and Ireland

35-43 Lincoln's Inn Fields, London, WC2A 3PE

Tel: 020 7973 0300 Fax: 020 7430 9235

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