Abstract. Background: Anastomotic leak rates following colorectal anastomosis range from 4 to 26%, and the development of a leak is known to be correlated with worse prognosis after a curative resection for colorectal cancer. In addition, anastomotic leakage has been associated with increased mortality and risk of permanent stoma. While techniques to improve the leakage rates in colorectal surgery have been described, these have largely been through isolated case series. We sought to undertake an evidence-based approach to reviewing the use of such techniques. Methods: A systematic review of the literature was performed, evaluating the current evidence for techniques to improve leakage following colorectal anastomosis. Results: There is Level I evidence to support the use of intra-operative leak testing, defunctioning ileostomy and drain tube insertion in the correct settings, including those associated with poor patient, disease and/or operative factors. There is no clear evidence to support the use of handsewn techniques, stapling techniques or laparoscopy over other techniques. Conclusion: Reductions in morbidity and mortality from colorectal anastomotic leaks can be gained by performing intra-operative leak testing, defunctioning ileostomy and drain tube insertion in the correct settings. The technique for performing the anastomosis remains at the discretion of the surgeon and largely depends on experience, patient characteristics and the operative setting, rather than there being any clear evidence for one technique over another. New techniques and devices that overcome drawbacks in current practice are consistently being developed and tested, making further risk reduction in colorectal anastomosis of great future promise.
Review of Techniques in Colorectal Anastomosis

Handsewn. A Cochrane review of nine randomised control trials in 2001 established handsewn colorectal anastomosis as a safe and cost-effective technique (4). The advantages of handsewn anastomoses are also corroborated by a substantial bulk of Level IV evidence, with Law et al. reporting a leak rate as low as 1.4% in a retrospective review of single layer absorbable monofilament sutures in 492 patients (6). This finding confirmed earlier large prospective studies that report incidence of fistula in supra-peritoneal anastomoses to be as low as 0.6% (7). Despite the efficacy of handsewn colorectal anastomosis, creating them is noted to be relatively time consuming.

As such, much effort has been spent in the quest to find a rapid approach to anastomosis that can potentiate a low leak rate. Substances such as intraperitoneal gentamycin, alloderm, propolis, bioactive polypeptides, pentoxifylline and polyester stents (8-13) have each been tested recently in animals with variable results. Despite the fact anastomotic compression devices such as the biofragmentable anastomotic ring (BAR) have received much attention, including prospective randomized controlled trials (14, 15) and are reported to be safe and efficacious in both emergency and elective surgery (16), they have not yet achieved widespread acceptance. The most widely practised and tested methods are stapling techniques. The level of technical difficulty is more marked the more distal the anastomosis lies, and in such a setting the use of a stapler may make the colorectal anastomosis easier to perform. There are a variety of proposed benefits from a stapled technique: better blood supply, reduced tissue manipulation, less edema, uniformity of sutures, and rapidity. These factors are believed to facilitate sound healing of the anastomosis without increasing the incidence of postoperative complications such as anastomotic leak, prolonged ileus or stricture (4).

Level I evidence has demonstrated that when handsewn methods are compared to mechanical suturing, no significant statistical differences are found, except that stricture is more frequent with stapling, especially in infraperitoneal anastomoses, and the time taken to perform the anastomosis is longer with handsewn techniques. The majority of studies consider stenosis to be irrelevant from a clinical point of view by virtue of the fact that no patients in any series were required to return to theatre for correction (4). This finding confirmed results of a similar Level I meta-analysis by MacRae and McLeod that covered all types of mechanical anastomoses (17). The authors found no relevant clinical differences between stapling and handsewn techniques, although intraoperative technical problems and postoperative strictures were more common with stapled anastomoses. Similarly, Level I evidence for colon-penetrating injury and emergency colorectal operations found that the method of anastomosis did not affect the incidence of abdominal complications (18, 19). The current evidence is insufficient to demonstrate the superiority of the stapling method over

<table>
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<tr>
<td>Lastosa et al. 2001 (4)</td>
<td>IA</td>
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<td>Brisinda et al. 2009 (3)</td>
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<td>Ricciardi et al. 2009 (59)</td>
<td>IIB</td>
<td>Clinical trial of leak testing. Anastomotic leaks were identified in 7.7% of anastomoses with positive air leak test results compared with 3.8% of anastomoses with negative air leak test results.</td>
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<td>Rondelli et al. 2009 (2)</td>
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<td>Review of 12 comparative studies (5 RCTs and 7 observational studies). Defunctioning stoma can reduce the risk of prolapse (OR= 0.21) and sepsis (OR=0.54), but was associated with an excess risk of occlusion and dehydration.</td>
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<td>Jesus et al. 2004 (81)</td>
<td>IA</td>
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RCT, Randomized controlled trial.
handsewing for a reduction in anastomotic leakage rates. Based on this evidence, the decision can remain at the discretion of the surgeon based on personal experience, circumstantial facts and available resources (20).

Double stapling technique. Performing an end-to-end low rectal anastomosis with the linear single stapling technique (SST) was first reported by Ravitch and Steichen in 1979 (21), and the double-stapling technique (DST) involving horizontal closure of the lower rectal segment with a linear stapler and performing an anastomosis using a circular stapler across the linear row of staples was reported by Knight and Griffen in 1980 (22). The circular stapling device has now been generally acknowledged as an important advance in reconstruction after low anterior resection for rectal cancer. Level IV evidence has begun to emerge regarding the reliability of the triple-staple technique in colorectal anastomosis (23, 24).

Stapled techniques of colorectal anastomosis in anterior resection have gained widespread acceptance, many patients who might previously have been candidates for Miles’ operation with a permanent colostomy can now receive sphincter-saving operations with the DST. DST offers the advantages of eliminating the distal purse string suture and reducing the operation time in an ultralow anastomosis (25). Conventional DST is mainly performed for tumors greater than six centimeters from the anal verge (26), however, in a recent prospective case series Sato et al describe a variation of DST for extra-low anterior resection involving vertical transection of the rectum followed by an anastomosis with a circular stapler which results in a vertically oriented elliptical anastomotic orifice. This configuration may have accounted for the lower bowel frequency that resulted when compared with previous reports (27). New devices and techniques are emerging that allow trans-anal delivery of the specimen and total intraperitoneal anastomosis (48, 49). Laparoscopic (total mesorectal excision) TME has also been demonstrated to show that the most common reasons for conversion were excessive tumor fixation and extensive adhesions (37, 43, 46). Intra-operative Leak Testing

Anastomotic leak testing has been proposed to reduce the development of anastomotic leak by identifying anastomoses that are not air or water tight. An array of techniques have been tested in the past including Doppler flowmetry (51), scanning laser flowmetry (52, 53) fluorescence videography (54), near-infrared spectroscopy (55) and intramucosal pH measurements (56, 57). None of these methods have demonstrated sufficient efficacy to become widely accepted,

Laparoscopy. Laparoscopic colon surgery was first described by Redwine and Sharpe in 1991 (33), and multiple Level I studies show the advantages include less intraoperative trauma, reduction in postoperative adhesions, decreased postoperative pain, decreased length of ileus, better cosmesis, early discharge from the hospital and early return to work (34-37). Operating room costs are significantly higher, but the difference in overall hospital charges has not been found to be statistically significant (36). Similarly, Level IIIb evidence has been demonstrated to show that in robotic colon surgery, it takes significantly longer to prepare the operating room and patient, taking 24±12 minutes longer than in laparoscopic resection 18±7 minutes (38). Anastomotic leak rates in laparoscopic colorectal surgery are reported to range from 2.5-12% (39-42).

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While open preparation of the proximal bowel for circular stapler anastomosis, through a Pfannenstiel or left-lower quadrant incision, has gained popularity (47) new techniques that allow trans-anal delivery of the specimen and total intracorporeal anastomosis are being reported (48, 49). Laparoscopic (total mesorectal excision) TME has also been employed for the treatment of rectal cancer without lateral lymph node metastasis or invasion to the adjacent organ, as laparoscopy has the advantage of providing a good view, even in a narrow pelvis and allowing more precise autonomic nerve preservation (50).
due largely to high inter-observer variability and the long duration of the measurements (58). The evidence surrounding anastomotic air leak testing is also poor despite its relatively high rate of adoption (59). Level IV studies demonstrate that when intraoperative insufflation of the anastomosis reveals it is intact, clinical leaks are frequently averted (60-62). A review of 998 left sided colorectal anastomoses by Ricciardi et al. established that untested anastomoses had twice the rate of postoperative clinical leaks compared with those that were tested (59). This review confirmed findings from a bulk of Level IV evidence that had accrued through several smaller retrospective studies (63-67).

Evidence for routine intra-operative colonoscopy (IOC) is currently being established as it allows direct visualization for anastomotic bleeding, inadvertent bowel wall injury near the anastomosis, adequacy of distal margins, vascularity of the anastomosis, and unsuspected distal lesions or stricture at the preoperative assessment. A recent Level IV study of IOC with stapling anastomosis has shown that following the introduction of IOC, there were no cases of postoperative anastomotic hemorrhage, and only one case of anastomotic leakage (1.4%) (68). Another Level IV study examining colonoscopy during laparoscopic colorectal anastomosis found that routine IOC was able to frequently detect abnormalities at and around the anastomosis. Although the selective IOC group showed a tendency toward more anastomotic complications than the routine IOC group (5.1% vs. 0.9 %), no significant difference could be demonstrated in any of the measured outcomes between the two groups (69). Other novel techniques such as intraoperative visible light spectroscopy (VLS) that uses a shallow-penetrating visible light to measure hemoglobin oxygen saturation in small tissue volumes, are easy to perform, have repeatable results and await further study (58).

Defunctioning Stomas

While it is evident that numerous factors have been associated with the occurrence of anastomotic leakage, a protective stoma should be considered under several specific conditions. The literature highlights specific operative factors as indications for a defunctioning stoma, including poor initial condition of the patient, low-lying tumour, narrow male pelvis, complications during construction of the anastomosis, devascularization of the rectal stump and/or the wide space created by TME (70-73). However, the majority of large series that have investigated such risk factors report the experience of highly specialized surgeons over a long period of time, focus on a specific technique, or are retrospective in nature. Inclusive studies are sparsely reported, however a single large prospective series of 1,018 consecutive patients undergoing all types of colorectal anastomosis identified predictive factors associated with anastomotic leakage to include American Society of Anesthesiologists (ASA) score, rectal location and prolonged operative time, recommending a defunctioning stoma in these cases (74).

There is not enough data currently available to determine if omentoplasty to reduce anastomotic leakage is worthwhile (75), however there is Level IB evidence to support the creation of a proximally diverting stoma in order to protect a low pelvic or technically inadequate anastomosis. Although it does not alter the risk for dehiscence, it does reduce the septic effects of the leak (71, 76-79). A Cochrane review in 2007 reported that current evidence could not determine a difference in outcomes between loop colostomy and loop ileostomy (80). A wide spectrum of complications can arise from stoma formation such as: wound infection, prolapse, retraction, stenosis, necrosis, parastomal hernia or fistula, skin irritation, ileus or obstruction, increased length of hospital stay and poor patient adaptation. The relevance of these complications is significant, as some complications usually demand a reintervention, while others are time-limited complications often managed with non-invasive treatments. Level IA evidence presented in a recent meta-analysis by Rondelli et al. concluded that, regarding the above mentioned parameters, it is believed that loop ileostomy has a minor impact on the quality of life, since prolapse and sepsis which are associated with loop colostomy are much worse complications than dehydration (2).

Drain Tubes

The purpose of drainage is to prevent accumulation of fluids in the pelvic or peritoneal cavity and to permit early detection of anastomotic dehiscence by faecal or purulent discharge from the drain (81). There is robust Level I evidence that routine pelvic drainage is not justified in colorectal surgery, as it does not preclude anastomotic leak nor minimize the severity of related complications (82, 83). This finding was supported by a large prospective study where anterior resection with pelvic drainage was identified as an independent risk factor for leak (84). A Cochrane review in 2004 analysed 1140 patients enrolled in six RCTs, of which 573 were allocated for drainage and 567 no drainage, they concluded that for the outcome measures mortality, clinical dehiscence, radiological dehiscence, wound infection and reintervention there was insufficient evidence showing that routine drainage prevents complications (81). However, these findings were refuted in the Dutch TME trial (Level IB evidence) which showed that the lack of a pelvic drain was an independent risk factor for anastomotic dehiscence and in fact reduced the need for surgical reintervention in patients with an anastomotic leak (71). On reviewing the published work, most authors agree on the selective use of a pelvic drain in patients where there has been technical difficulties during surgery, uncontrollable bleeding or peritonitis due to perforation, especially in the emergency setting (85).
Conclusion

Reductions in morbidity and mortality from colorectal anastomotic leaks have been clearly shown to be gained by performing intra-operative leak testing, defunctioning ileostomy and drain tube insertion in the correct settings. These high risk settings include those associated with poor patient, disease and/or operative factors. The decision to perform the anastomosis with traditional handsewn techniques, stapling techniques or laparoscopically remains at the discretion of the surgeon and largely depends on experience, patient characteristics and the operative setting, rather than there being any clear evidence for one technique over another. New techniques and devices that overcome drawbacks in current practice are consistently being developed and tested, making further risk reduction in colorectal anastomosis of great future promise.

Conflicts of Interest

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