Staple Line/Anastomotic Reinforcement and Other Adjuncts: Do They Make a Difference?

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Abstract

Since the development of the stapled intestinal anastomosis, efforts have been aimed at reducing complications and standardizing methods. The main complications associated with stapled anastomoses include bleeding, device failure, and anastomotic failure (leaks and strictures). These complications are associated with increased cost of care, increase in cancer recurrence, decreased overall survival, poor quality of life, and in some cases the need for further procedures including a diverting ostomy. Reducing these complications therefore has important implications. To this end, techniques to reduce the incidence of anastomotic complications have been the focus of many investigators. In this review, we summarize the current staple line reinforcement technology as well as other adjunctive measures, and specifically discuss the role of biologic materials in this realm.

Keywords
- ► anastomotic complications
- ► staple line reinforcement
- ► stapled anastomosis

CME Objectives: At the completion of this article the reader should be able to summarize the complications of stapled anastomoses and the various staple line reinforcement agents.

The first gastrointestinal anastomosis was performed over 200 years ago.[1] Since then, there has been a push to improve anastomotic techniques with the goals of reducing complications, standardizing methods, and reducing operative time. These goals led to the development of the surgical stapler and the subsequent technological improvements by Ravitch and Steichen.[2] Before the use of circular staplers, many patients were treated with sphincter extirpation. Staple technology has allowed for these patients to be treated with low colorectal anastomoses. However, anastomotic complications, especially leaks, remain the Achilles heel of these procedures. These complications have the potential to be devastating, and the rate of anastomotic leak in colorectal surgery has remained significant, hence the pursuit of adjuncts and reinforcements for stapled anastomoses.

Complications Associated with Stapled Anastomoses

Complications related to stapled anastomoses include bleeding, device failure, and anastomotic failure, which include stricture or leak (►**Table 1**). Some of these complications can be directly related to the device itself, with at least 112 deaths resulting from 20,000 malfunctions in a recent review.[3] Most of the complications are related to problems with anastomotic blood supply, tension, or inappropriate device choice. Other factors include poor nutrition, radiation, and immunosuppression.[4] Anastomotic strictures can be bothersome for patients and the rate of stricture is fourfold higher for stapled anastomoses than for those that are hand sewn in colorectal anastomoses.[5] Ultimately, anastomotic leak remains the most feared complication in colon and rectal surgery.

The implications of anastomotic leak have been widely researched, and in an analysis by Phillips et al, there was an 18.6% rate of local recurrence of malignancy in patients without an anastomotic leak, and a 19.5% rate of recurrence in patients with a leak.[6] This was not statistically significant, but further series has shown a local recurrence of 17.2% in patients with a leak compared with 8.6% for patients without an anastomotic leak.[7] The impact on overall survival as a consequence of anastomotic leak has also been quantified. In a series of 1,722 patients who underwent curative resection for colorectal cancer, 5.1% had an anastomotic leak. For this subgroup, the 5-year overall survival rate was 44.3%, compared with a survival rate of 64% for those patients without a leak.[8] Multiple similar studies have been completed, and a

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Table 1 Complications of stapled anastomoses

Complication	Sequelae
Stricture	Patient discomfort, need for additional procedures
Bleeding	Hemodynamic implications, difficult intraoperative visualization
Anastomotic leak	Increase in local recurrence, decreased overall survival, sepsis, need for diverting ostomy, increased hospital cost, increased use of hospital resources, decreased quality of life

meta-analysis of these series confirmed that both local recurrence and overall survival are negatively impacted by anastomotic leakage.[9] Surgical complications in general are costly, and a large series evaluating this showed an increase in mean cost of major colorectal surgery from $26,420 to $66,929 for those patients with a complication.[10] The economic implications of anastomotic leak have been specifically studied. Ashraf et al showed a €6,319 cost for low anterior resection without complications, compared with €17,220 for those patients who suffered an anastomotic leak after anterior resection.[11] While the increased costs after anastomotic leak have a significant economic impact, the effect on hospital resource allocation is equally important. A recent study showed that anastomotic leak negatively impacts total critical care days, days of parenteral nutrition, ventilator days, and total hospital stay.[12] Specific studies on quality of life (QOL) after colorectal surgeries have indicated that complications after colorectal surgery negatively impact QOL in terms of mobility, self-care, and pain/discomfort.[13] When anastomotic leak was specifically explored, patients with anastomotic leak had significant decreases in QOL in terms of emotional function, social function, and overall QOL.[14]

Anastomotic Healing

Similar to healing elsewhere in the body, anastomotic healing can be divided into distinct phases. These include the inflammatory phase, followed by the proliferative phase, and, finally, the remodeling phase. Initially, collagen is broken down by matrix metalloproteinases, but after about 7 days, collagen synthesis predominates.[15] Many factors influence the healing of gastrointestinal anastomoses, and these include lack of tension, adequate blood supply, and control of systemic illness.[4] With regard to systemic illness, both burst pressure and collagen content of colonic anastomoses are negatively affected in the presence of abdominal sepsis.[16] To prevent anastomotic breakdown in the critical first week, adjuncts to anastomoses have been investigated. Burst pressure has been used to evaluate anastomotic strength, and staple line buttressing in animal models has been shown to significantly increase anastomotic burst pressure. Downey et al reported a series in which small intestinal submucosa (SIS) was used to buttress porcine intestinal anastomoses. Burst pressure increased from 53 to 83 mm Hg after reinforcement.[17] Bovine pericardium can similarly be used to buttress anastomoses. In a rabbit model using bovine pericardial (BP) buttress, burst pressure was 125 mm Hg for buttressed staple lines compared with 58.4 mm Hg for anastomoses without pericardial bolster.[18]

Anastomotic bleeding is a common complication of stapled anastomoses, and it can lead to hemodynamic instability and anemia, sometimes requiring transfusion or additional procedures. To this end, there are efforts aimed at reducing staple line hemorrhage by using buttressing techniques. In a 20-patient series where an absorbable polymer membrane was used to buttress gastrointestinal staple lines, perioperative blood loss decreased from 210 to 120 mL after staple line reinforcement.[19] While this finding may not seem to be clinically significant, it may be an indication that reinforcement may reduce perioperative bleeding along the staple line. A prospective randomized trial evaluating the use of glycolide copolymer reinforcement of staple lines in gastric bypass anastomoses showed an improved rate of staple line bleeding, with a decrease in mean blood loss from 129 to 84 mL, and a decrease in time to hemostasis (from 10.1 to 1.2 minutes) in those patients who underwent staple line reinforcement.[20] Similar results have been shown using bioabsorbable reinforcement during stapled transection of mesenteric vessels in colorectal surgery. In one series, 25 patients had reinforcement with no reported episodes of staple line bleeding.[21] Clinically, relevant reductions in bleeding have not been shown by staple line reinforcement for colorectal anastomoses.[22]

Staple Line Reinforcement

Given the complications associated with stapled anastomoses, efforts are ongoing to develop reinforcement agents that can be helpful in the prevention or attenuation of anastomotic leaks and bleeding staple lines. Staple line reinforcement has been used to reduce air leaks in pulmonary surgery[23] and this technology is now being applied to surgery of the colon and rectum. The aim of this technology has been to develop products that are effective and logical with regard to gastrointestinal physiology and healing. Many products are available for operative staple line reinforcement. These products fall into three main categories: permanent, semiabsorbable, and bioabsorbable[24] (►**Table 2**).

Permanent staple line reinforcement has been described, notably with lung resections. The mainstay of permanent staple line reinforcement is utilization of expanded polytetrafluoroethylene (ePTFE) sleeves. The sleeves are attached to the arms of the surgical stapler, and the stapler is used in the routine fashion to compress tissue. After compression, but before firing, the excess ePTFE is removed along the edges of the stapler. Use of ePTFE reinforcement does not require any adhesive, and removal of excess is facilitated by the perforated edges of the sleeve. ePTFE sleeves are effective in reducing staple line air leak in lung surgery. In a head-to-head comparison of ePTFE sleeves versus BP patch reinforcement, the local inflammatory response to the pericardial patch was

Table 2 Staple line reinforcement and adjunctive options

Bioabsorbable reinforcement	Semiabsorbable reinforcement	Permanent reinforcement	Other adjunctive measures
Fibrin glue	Bovine pericardial patches	ePTFE sleeves	Omentoplasty
Polyglycolic acid	Small intestinal submucosa patches		Laser and dye-enhanced fibrinogen
	Semiabsorbable acellular dermal matrices		Intraluminal stents including C-seal

much more significant than that for the ePTFE sleeve. Additionally, there was no evidence of air leak with the use of the ePTFE reinforcement in animal models.[25] In a study using fresh cadaveric human lungs to predict the relationship between airway pressure and staple line leak, ePTFE and BP reinforcement were compared with stapled anastomoses without reinforcement. Both methods of buttressing were superior to the nonbuttressed group in preventing air leak at specified airway pressures, with ePTFE reinforcement being the sturdiest of the three methods.[23] Use of ePTFE for staple line reinforcement in lung surgery is well described, but erosion of the nonabsorbable material into the surrounding tissues has been described, resulting in bronchial obstruction.[26]

Despite the theoretical advantages of using a permanent reinforcement material, the persistence of the foreign substance has deterred its use in gastrointestinal surgery. Semiabsorbable staple line reinforcement agents can offer some of the advantages of permanent buttress while mitigating some of the risks of foreign body reaction. One example of a semiabsorbable option is SIS. SIS has been shown to be a suitable patch for gastric perforation in animal models. In an evaluation using rats, 12 rats had surgically created gastric defects that were repaired only with porcine SIS. Over the 3-week postoperative period, none of the rats developed peritonitis, and on necropsy all of the gastric defects were completely closed.[27] Kini and Gagner published a series of 14 patients who had porcine intestinal submucosal reinforcement of gastrojejunostomies. In their study, the anastomosis was created with a circular stapler, and SIS was used to wrap the anastomosis after rehydration in sterile saline. This feasibility study showed similar complication rates in the study and control groups, demonstrating the safety of SIS use for anastomotic reinforcement.[28] SIS has also been studied in colonic anastomoses. In an animal study using pigs, a colocolonic anastomosis was created using a circular stapler. The anastomosis was then either reinforced with a 360-degree SIS patch or left unbuttressed. Necropsy was performed on postoperative day 30. Neither group had major complications, but the SIS buttressed group showed an increased rate of anastomotic mucosal coverage and a greater quantity of granulation tissue.[29] A similar study was completed in rat models. SIS buttressed anastomoses were compared with unbuttressed anastomoses with regard to burst pressure, leak rate, stricture rate, and histological appearance. Burst pressure on postoperative day 4 was significantly higher (148 vs. 108 mm Hg) in the buttressed group, and histological appearance showed an increase in neovascularization, and collagen content in the anastomoses reinforced with SIS. There was no appreciable difference in the rate of leak or stricture.[30] Alloderm (Lifecell, Bridgewater, NJ, USA), a semiabsorbable acellular dermal matrix derived from cadaveric human skin, has also been used in animal studies as a bolster to colorectal anastomoses. Here, a circular stapler was used to create a colorectal anastomosis and an Alloderm bolster was fixed to the stapler pin after passage through the rectal stump. There were two experimental groups: one group had meshed Alloderm bolsters and the other had unmeshed, and a control group in which no bolster was used. In this series, postoperative day 14 burst pressure was 263 mm Hg in the unmeshed Alloderm bolstered group, 272 mm Hg for the meshed Alloderm bolstered group compared with 198 mm Hg in the unbolstered group.[31] BP collagen matrices have also been studied for use as staple line reinforcement. A multicenter trial evaluated the efficacy of BP buttress of pulmonary staple lines in 60 patients. The results of this study showed a numerical but not statistically significant decrease in duration of air leak from 3 to 2 days ($p = 0.27$), and a mean time to chest tube removal from 6.3 to 5.9 days ($p = 0.62$) after use of BP buttressing.[32] This technology has been applied to gastrointestinal staple line reinforcement. In a prospective randomized clinical trial evaluating bleeding from gastric staple lines, the mean number of clips for bleeding staple lines decreased from 23 to 5 ($p < 0.001$) and the total operating time decreased from 220 to 120 minutes ($p < 0.01$) in the staple line buttressed group.[33] BP collagen matrices have been specifically described in colonic anastomoses; burst pressure after buttressing increased from 204 to 362 mm Hg. The use of BP is a bit more cumbersome than the other potential options. In this study, anastomoses were created with a circular stapler. BP collagen matrix was fastened to the stapler cartridge before firing. These strips must be prepared with a gel adhesive, adding an additional step to the buttressing process.[34] Additionally, there are cases of migration of both the pericardial strips[35] as well as the staples themselves[36,37] when reinforced with bovine pericardium.

Bioabsorbable anastomotic reinforcement materials are also being investigated to provide the benefit of anastomotic buttress, but further mitigate the risk of using foreign material portends. Fibrin sealant has been used in animal studies to cover iatrogenic anastomotic leaks. In an investigation by Nguyen et al, the fibrin product sealed anastomotic leaks in 10/10 swine.[38] The use of fibrin sealants has been applied clinically and multiple studies have supported its use in obesity surgery.[39,40] The product gaining the most momentum is polyglycolic acid felt which has been well described for use in lung volume reduction surgery. Originally, the felt pads were fixed to the stapler cartridges with the use of fibrin glue.[41] Development of a polyglycolic acid/trimethylene carbonate sleeve (Gore-Tex Bioabsorbable Seamguard, W.L Gore and Associates, Flagstaff, AZ) has made application of a bioabsorbable buttress simpler. Its use in colorectal surgery is being heavily investigated. In a study of 30 patients undergoing colorectal anastomoses buttressed with Seamguard, there were no clinical leaks, strictures, or bleeding episodes.[42] Another analysis of Seamguard reinforcement showed an anastomotic leak rate of 3.4% in 117 patients who underwent anastomotic buttressing, compared with a historical 6 to 12% leak rate reported for low colorectal resections.[22] Senagore et al recently published a randomized trial comparing outcomes in patients undergoing a colorectal anastomosis with or without bioabsorbable staple line reinforcement.[43] This was a 17-center study that enrolled 258 patients. A circular stapler was used for all anastomoses, and patients were randomly assigned to Seamguard reinforcement sleeves or nonbuttressed staple lines. There was no difference in anastomotic leak rate between the two groups. The only significant finding was that the reinforced group had a lower rate of small bowel obstruction and anastomotic stricture. However, this study was stopped at the first planned interim analysis due to insufficient power to detect a difference in anastomotic leak rates.[43]

Other Adjunctive Measures

Given the questionable efficacy of direct staple line reinforcement with commercial products, other adjuncts have been studied to prevent complications of the stapled anastomoses. The use of omentum as a buttressing agent has long been described. With regard to esophagogastric anastomoses, Sepesi et al published data from a large series of intrathoracic anastomoses with omental reinforcement. Their retrospective review of data collected prospectively showed an anastomotic leak rate of 4.7% in the buttressed population, compared with 9.8% in the nonbuttressed population.[44] Omentoplasty was specifically studied in the colorectal population, with favorable results. In a study of 112 patients, 3.8% of patients who had omentoplasty had clinically evident anastomotic leaks, compared with 11.8% of patients who underwent anastomosis without omental buttress.[45] Laser and dye-enhanced fibrinogen has also been investigated for use in colonic surgery. Moazami et al published a study of rabbits in which indocyanine green dye–enhanced fibrinogen was applied to colonic anastomoses followed by laser exposure. The idea was that fibrin glue would reinforce the sutured anastomoses, while the laser welding technique would create more water tight chemical bonds by increasing fibroblast response at the anastomotic staple lines. While this did lead to an increase in burst pressure, the technique has failed to catch on in the performance of colonic anastomoses.[46]

In addition to external protection, there are a few devices that can be used as an internal buttress to protect gastrointestinal anastomoses. Internal stents have been studied in animal models. In one study, endoscopic stents were placed across porcine colorectal anastomoses created with a circular stapler. Leaks were then intentionally created in the anastomoses and the animals were observed. At necropsy, none of the pigs in the stented cohort developed anastomotic leaks. In the pigs treated without an endoluminal stent, five of eight pigs developed either an intra-abdominal abscess or a fistula.[47] A similar animal study was performed using a soluble intraluminal stent. In this study, the internal stents dissolved quickly, but led to a better histological appearance on microscopic review. There was less tissue gap, less inflammation, and a higher breaking strength in the stented population, supporting the idea of internal stenting to prevent anastomotic leak.[48] A multicenter randomized control trial is ongoing to study the efficacy of the C-seal device (Polyganics BV, Groningen, the Netherlands) in preventing anastomotic leak. This device is an intraluminal soluble sheath that prevents content extravasation in the event of an anastomotic dehiscence. In the pilot study of 15 patients testing the product, there were no clinical anastomotic leaks. Further data are needed to support the use of C-seal, but preliminary results are promising.[49]

Conclusion

Complications associated with stapled anastomoses result in increased cost of care, poor QOL, increased need for colostomies/enterostomies, increased cancer recurrence, and decreased overall survival. Efforts are ongoing to improve surgical technique to lower these risks, and among these efforts are staple line buttressing and other anastomotic adjunctive measures. A front runner has not emerged, but the implications of anastomotic complications necessitate further research in this area. Biomaterials may represent a promising technology in this arena.

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