

Are We Getting Better at Preventing Anastomotic Leak?

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Bowel resection is one of the commonly performed procedures in modern day surgery. Common indications include gastrointestinal cancers, diverticular disease, inflammatory bowel disease and intestinal obstruction, etc. Restoring gastrointestinal continuity is an essential step after resection. Unfortunately to surgeons and patients, there is a relatively low, yet inescapable risk of anastomotic leakage (AL) despite improvement in the standard of surgery over the years. AL is certainly a demoralizing complication. It significantly increases morbidity and mortality [1]. There is a surge of health costs [2]. Studies also demonstrated a negative impact on local recurrence, distant metastasis and survival after AL [3,4].

AL rate generally ranges from 1 to 24% for colorectal resections [5]. Widely accepted technical factors that increase the chance of AL include poor blood supply and excessive tension to an anastomosis [6]. Other factors that predispose to AL include male gender, obesity, malnutrition, chronic steroid use, intraoperative blood transfusion, preoperative radiation, low rectal anastomosis and surgeons' level of experience [1,7-10]. However, it is not unusual for surgeons to encounter a patient who suffered from AL and yet had no apparent risk factors for it. Gross technical mistakes with obviously under-perfused anastomosis or unacceptably high tension were indeed uncommon. As a matter of fact, it has been shown that intra-operative evaluation by surgeons was a poor predictor of subsequent AL [11]. The fact is our understanding for AL is still very limited. So, in the last 10 to 20 years, have we figured out ways to reduce the incidence of AL?

The debate over hand-sewn and stapled anastomosis was quite settled, as many would have thought. Studies conducted over the years failed to prove superiority in either method and the choice is largely up to surgeon's personal preference [12,13]. Just when we were so complacent about the findings of the studies mostly conducted in the nineties, more recent studies showed otherwise. Choy et al. published a meta-analysis, which included a total of seven randomized control trials with a total of 1125 patients: 441 stapled and 684 hand-sewn ileocolic anastomosis. Stapled anastomosis were found to have a lower incidence of AL, 2.5% versus 6.1%, with an odds ratio of 0.48, 95% CI 0.24, 0.95 [14]. Similar conclusion was reached by another meta-analysis, with a 2.4% leakage rate for stapled anastomosis compared to 6.1% for hand-sewn anastomosis [15]. There was also evidence favoring stapled anastomosis with regard to a lower incidence of bowel obstruction and shorter operating time [16]. We expect

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a continuous improvement in stapling technology and staplers should be more reliable. More research should therefore be conducted on the newer generation stapling devices.

Kiran et al. published a retrospective cohort study on 8442 patients undergoing colorectal resections [17]. The study aimed to investigate the impact of mechanical bowel preparation and oral antibiotics on surgical site infections. The study demonstrated the use of mechanical bowel preparation and oral antibiotics were associated with a lower incidence of AL, with an odds ratio of 0.45, 95% confidence interval of 0.32, 0.64. Similar conclusion was reached by another study by Althumairi et al. [18]. Not only do these findings support the use of bowel preparation and antibiotics, they prompted a question as to why mechanically and chemically cleansing the bowel helps reduce AL.

The answer may lie within the microbes living inside our body. There is an increasing interest in the role of microbiome in AL. Shogan et al. demonstrated high collagen-degrading activity from microbes in leaking anastomosis in rats [19]. Leaked anastomosis was noted to have colonized by *Enterococcus faecalis*, a commensal in gut, with high collagen-degrading activity and ability to activate host intestinal matrix metalloproteinase 9 (MMP9). A study by van Praagh et al. found there was a lower microbial diversity and higher gut concentration of *Lachnospiraceae* in those with AL [20]. These studies provided a possible explanation of the effect on AL by gut decontamination.

Fluorescence imaging has been recently applied to assess microperfusion of bowel before and after fashioning of anastomosis. It involves intravenous injection of indocyanine green (ICG). ICG binds to plasma proteins and stays in the intravascular compartment. It absorbs near infra-red light at 800 nm and emits fluorescence. The presence of fluorescence therefore indicates perfusion. With that surgeons can transect at well-perfused bowel for fashioning an anastomosis. In one multicenter study, by using fluorescence imaging, there was a change in surgical decision in 8% of the cases [21]. The overall leakage rate was 1.3%. In another similar study, the anastomotic leakage rate was only 0.9% out of a total of 107 patients [22].

Biodegradable devices have been designed to mechanically shield the intraluminal contents from anastomoses. C-seal, is

one of such devices with the appearance of a thin-walled sheath. It is deployed after firing a circular stapler and is expelled in 10 to 15 days time. It theoretically protects a distal colorectal anastomosis similar to a diversion stoma. Only feasibility study is available and ongoing trial is currently underway to investigate its effects [23,24]. Other novel methods including sealant, e.g., cyanoacrylate, and doxycycline-coated sutures, which inhibit MMP, are over the horizon in the hope to decrease AL [25,26]. However, these are still largely experimental.

A dramatic reduction in AL is still far-fetched at present. Novel techniques like fluorescent imaging have emerged to optimize anastomosis. There are still a lot that we do not understand about AL. Hopefully, better understanding of the role of microbiome in AL provides us the missing piece of the puzzle.

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