

EFFECT OF NSAID IN ANASTOMOTIC LEAK AFTER RECTAL SURGERY:A STUDY

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Abstract

The AAR for colon cancer in women is 3.9/100,000. Men rank rectal cancer ninth and colon cancer eighth. Rectal cancer does not appear on the list, but colon cancer does. 2. Thiruvananthapuram, Bangalore, and Mumbai were the cities with the highest CRC AAR for men in 2013. (3.9). (3.7). The highest female CRC AAR (5.3) is found in Nagaland, followed by Aizwal (4.5) 2. In 224 colorectal cancers, the Cancer Genome Atlas Network discovered similar genetic alterations in colon and rectal tissues regardless of anatomic location and origin. Tumors of the colon and rectum were grouped by researchers. This study thoroughly examined the information connecting NSAID use to anastomotic leak. Animal experimental models and human clinical data were utilised to support this research. Clinical effects of NSAIDs on patients are measured using laboratory data. These inadequate instruments can measure the immeasurable. The second most frequent large intestine cancer is rectal carcinoma. CRC is a problem for world health. It is the second most common cancer in women (571000 cases, 9.5%) and the third most common cancer in men (663000 cases, 10.1% of all cancer cases). 1. 60% of incidents occur in developed countries. The fourth most common cause of death and the cause of 8% of all cancer deaths is CRC. Males in India had colon and rectal cancer AARs of 4.5 and 4.1 per 100,000, respectively.

Keyword: rectal cancer, diagnosis, health, Colorectal

Introduction

Colorectal cancer affects about 1.5 million people globally [1]. Colorectal cancer patients usually have surgery. After removing the diseased intestine, both ends of the colon are reconnected to restore continuity. Anastomotic leakage (AL), the most dreaded postoperative complication, produces significant morbidity following colorectal surgery. AL pathology is still poorly understood. Years of research have shown several AL risk factors, both modifiable and not [2e4]. NSAIDs for postoperative analgesia may lower risk [2e4]. The ERAS programs' multimodal approach to postoperative pain therapy relies heavily on nonsteroidal anti-inflammatory medications (NSAIDs) [5]. They generate analgesia by inhibiting COX-2 selectively or both COX-1 and COX-2 enzymes (non-selective). They create fewer prostaglandins, which improves hemostasis and inflammation [6]. NSAIDs relieve pain, restore gastrointestinal function, reduce adverse effects, and are cheap [7]. Opioids may induce respiratory depression, delayed bowel recovery, urine retention, and drug dependency, hence nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended for postoperative analgesia [8,9]. NSAIDs may impede anastomosis healing, however this is debated [10].

Five researchers reabstracted without quantifying interobserver variability. NSAIDs may increase AL risk following colorectal surgery, however studies disagree. Many cohort studies have suggested an elevated risk of AL, whereas others have not [11]. Systematic research have shown conflicting findings. Most study has methodological challenges due to the inclusion of varied gastrointestinal anastomoses (gastric, jejunal, ileum, colon, or rectum), each with a different risk profile. Colorectal resections leak more than small bowel resections [12]. The surgical pathology complicates the procedure. Large dosages of oral corticosteroids in IBD patients increase the risk of anastomotic leak following ileocecal resection. For example: Cancer, IBD, and other bowel diseases have immunological variations that may impact how individuals react to NSAIDs and their risk of AL. NSAIDs significantly inhibit COX-2 synthesis, which is elevated in colorectal cancers. Even though it is unclear how postoperative immunological changes affect AL risk and NSAID response, it is possible that they do. NSAID effects on AL in similar cohorts may reduce this bias and enhance data used to adjust therapy recommendations. Colorectal cancer accounts for 70% of colon resections [13].

Rectal cancer

The second most frequent malignancy is large intestine rectal cancer. Rectal cancer is one of the world's biggest public health issues due to its high incidence rate and increased number of young diagnosis. Modern screening methods increase the number of cases discovered each year. Rectal tumors are handled differently from colon or other gastrointestinal tract tumors. Due of the rectum's position and adjacent organs, 28% of large intestine malignancies are rectal, second only to proximal colon tumors (42%). Rectal cancer has traditionally been included in epidemiological studies of colorectal cancer. Colorectal cancer (CRC), the second most common disease in men and women globally, with a lifetime chance of 4.7-5%. (6). It is the third-leading cause of cancer deaths in men and women in the US, according to recent data.

Like other health care registries, the SCRCR is valuable for research, quality control, and benchmarking. Colorectal cancer rates vary globally, but men and women have the similar tendency. CRCs are now more common in wealthy countries. Western Africa has the lowest estimated rates, 4.5 and 3.9 per 100,000 for men and women. Australia and New Zealand will have the highest rates, with 44.9 and 32.3 per 100,000 for men and women, respectively (6). Recent US data shows that 40,000 of the 136,830 new colorectal cancer cases each year are rectal. In 2014, 26,270 men and 24,040 women will die from colorectal cancer, while 71,830 men and 65,000 women will be diagnosed. During the last decade, screening and standard treatment have increased access and reduced the incidence rate by 3% annually. Rectal cancer incidence has grown by 1.9% yearly among those under 50, despite a significant drop in those over 65 (-4.3% and -1.5%, respectively). Rectal cancer is diagnosed substantially younger than proximal and distal colon tumors (63 years in men and 65 years in women). Rectal tumors are rarer as individuals become older. Male-to-female rectal cancer incidence rates by age group: 1.10 for adults 0–49, 1.19 for 50–64, 1.37 for 65–79, and 1.39 for 80+.

While stage-specific survival is essentially comparable, rectal cancer has a slightly better 5-year survival rate than colon cancer (64.3%). Men and women survive similarly. Men and women die 30–40% differently, however this gap decreases with age. Race and ethnicity may affect mortality. According to US data, black individuals die more than twice as often as Asian and Pacific Islanders. CRCs are more frequent in wealthy countries, but their fatality rate is greater in developing nations. These nations' lower survival rates may explain this. Central and Eastern Europe has the highest estimated death rates for men (20.3 per 100,000) and women (11.7 per 100,000). Western Africa has the lowest mortality (3.5 and 3.1, respectively).

Research Methods

Literature lists several anastomotic leak risk factors. The searches "colorectal surgery," "anastomotic leak," and "risk factors" yield over 500 PubMed articles. Most research are low-quality, many have inconsistent findings, and few variables have been firmly linked to anastomotic leak. Nonetheless, perioperatively minimizing potential modifiable risk factors may reduce their cumulative impact.

Several patient variables have been linked to anastomotic leak, but few have been shown to enhance leak rates. Numerous large retrospective investigations have shown modifiable and nonmodifiable patient variables that may enhance anastomotic leak risk. [14,15] Examples: Diabetes, perioperative hyperglycemia, and high hemoglobin A1c ASA score 3 Smoking Serum albumin Young age.

Variations in the postoperative time frame at which leaks first become noticeable are one factor that contributes to the variability. According to the conventional school of thought, leaks almost often become apparent within seven days of surgery. Nevertheless, a comprehensive prospective analysis that included 1,223 patients and was conducted over the course of ten years by two different surgeons indicated a leak rate of 2.7% and that leaks were identified at a mean of 12.7 days after surgery.

Anastomotic Leak Risks

Further patient variables are discussed below. Extraperitoneal anastomotic leaks were associated with men. Due of technical difficulties operating in the small male pelvis. Male gender does not raise intraperitoneal anastomosis leak risk. [16] Obesity also causes anastomotic leak. Obesity was linked to anastomotic leak after low colorectal anastomoses in one retrospective analysis.[17] Larger, recent, retrospective investigations that include all anastomoses have not proven this connection. Obese people may have the same issues as thin, masculine pelvic leakers. Anastomotic leak is linked to perioperative corticosteroids. Steroid usage and anastomotic leak varied in retrospective research. Nevertheless, the greatest comprehensive analysis (12 trials) found that preoperative corticosteroids increased anastomotic leak (6.8% vs. 3.3%). NSAIDs are often used in multimodality, nonnarcotic pain treatment after colorectal surgery, and their connection with postoperative problems has been examined. 2016 comprehensive review and meta-analysis examined 6 randomized controlled trials (473 patients) and 11 observational studies (including more than 20,184 patients). In observational studies, NSAID usage increased anastomotic leak risk (OR: 1.46, 95% CI: 1.14–1.86, I 1/454%). NSAID usage was not linked with leakage in

randomized controlled trials (risk ratio: 1.96, 95% CI: 0.74–5.16, I² 1/4%). NSAID users had a 5.2% leak rate, compared to 2.5% for non-NSAID users. Ketorolac is a popular NSAID used intra- and postoperatively to speed healing. Ketorolac usage was linked with a greater risk of anastomotic complications-related readmissions in a recent research (55% colorectal patients). Nevertheless, a previous analysis of 731 patients with primary anastomoses, 48.6% of whom took ketorolac perioperatively, found no change in leak rate (3.2 vs. 3.4%, OR: 1.06, 95% CI: 0.43–2.62; *p* = 0.886). [18] Considering their frequent usage in accelerated recovery routes in colorectal surgery, further well-powered randomized trials are needed to evaluate whether NSAIDs increase anastomotic leak rate. Several technical and patient conditions may contribute to anastomotic leak. Surgeons should first conduct a tension-free anastomosis without vascular compromise. They should pick a laparoscopic, open, handsewn, or stapled method they can safely do. The index surgery should be repeated if the anastomosis is suspect. Use a diverting ostomy if the anastomosis or patient has many leak risk indicators. It may not reduce anastomotic leak rate, but it will reduce patient clinical effect.

Technological Risks

Leak risk is closely linked to anastomosis location—intraperitoneal or extraperitoneal. Over 1,600 individuals underwent 1,639 anastomoses in one of the biggest prospective investigations on this topic. Anastomotic leak was 6.6% after extraperitoneal anastomosis and 1.5% after intraperitoneal. Ultralow or coloanal anastomoses leaked 8%. Intraoperatively, leaky anastomoses may be identified by their appearance. Intraoperatively, Sujatha-Bhaskar et al. categorized 106 stapled colorectal anastomoses as grade 1: circumferentially normal looking mucosa, grade 2: ischemia or congestion of 30% of the colon or rectal mucosa or both sides of the staple line. 4/106 grade 3 anastomoses were reworked. The remaining group included 92 rated 1 anastomoses and 10 graded 2. The cohort had a 12.2% anastomotic leak rate, 9.4% for grade 1 and 40% for grade 2. Grade 2 anastomosis was associated with anastomotic leak in multivariate logistic regression (OR: 4.09, 95% CI: 1.21–13.63, *p* ¼ 0.023). Intraoperative correction of grades 2 and 3 anastomoses was recommended. 8 Leak rates were examined in 382 colorectal resection patients. One stapler load divided the rectum in 58.4% of cases, two in 33.5%, and three or more in 8.1%. Several stapler firings were more common in men, rectal cancer, laparoscopy, and surgeries lasting over 200 minutes. 4.7% leaked. Three or more stapler loads to separate the rectum were the sole risk factor for anastomotic leak. Murray et al examined leak rate in 23,568 elective colorectal resections in the ACS-NSQIP database. The laparoscopic group leaked 2.8% and the open group 4.5%. After correcting for patient, illness, and procedure characteristics using propensity-score matching (OR: 0.73, 95% CI: 0.58–0.91) and multivariate analysis (OR: 0.69, 95% CI: 0.58–0.82), this substantial difference maintained. Despite surgeons being early in their laparoscopic learning curve, two randomized studies found no difference in leak rates between laparoscopic and open surgery. [19] Anastomotic leak is linked to anastomotic ischemia. For a tension-free anastomosis, the proximal bowel must be completely mobilized (splenic flexure takedown) and the inferior mesenteric artery and vein high-ligated. Before anastomosis, the mesentery or mesocolon might be severely divided to ensure bowel blood flow. Following mesenteric division, palpating a pulse or using a Doppler may confirm arterial blood supply. Fluorescence angiography may verify blood supply before and after an anastomosis.

The literature on leak rates and handsewn vs stapled anastomoses varies by location. For benign and cancer diagnosis, handsewn ileocolic anastomoses leaked more than stapled ones, according to a Cochrane evaluation of seven studies. Stapled and handsewn colorectal anastomoses leaked similarly clinically and radiologically. [20] Lastly, diverting ostomies have been tested to reduce anastomotic leak risk. Diverting ostomy lessens the clinical consequences of a leak (reoperation, death, etc.), although few studies have proven a decreased leak incidence. In a 2014 prospective analysis of 2,364 patients receiving 2,994 anastomoses, diverting stomas did not reduce leak rate but did reduce clinical severity and the need for reoperation. This supported a prospective research. 37 In a meta-analysis of four randomized studies, patients with protective stomas had a reduced leak rate (9.6 vs. 22.8%) and a lower need for reoperation (OR: 0.27, 95% CI: 0.17–0.59).

Anastomotic Leak Surgery

Location, patient stability, degree of leaking (contained vs. free perforation), and surgical findings determine how to manage anastomotic leaks. Modern intraperitoneal anastomotic leak therapy strategy. If an anastomotic leak is detected, patient stabilization is primary. Hemodynamically unstable patients should be resuscitated with IV fluids and broad-spectrum IV antibiotics. Invasive monitoring and ICU transport may be needed. If the patient stabilizes after resuscitation, imaging like a CT scan with Intravenous, oral, and rectal contrast may help therapy. If the patient remains unstable or has diffuse peritonitis, continue resuscitation with emergent surgical investigation.

Most anastomotic leak patients have fever, leukocytosis, increased abdominal discomfort, and tachycardia without hemodynamic instability. Imaging should be explored before intervention in this population to confirm leak. Due to its widespread availability in hospitals and ability to consistently detect pathologies such free air, perianastomotic air

or fluid, and collections/abscesses, CT scan with contrast is the most used imaging modality. If imaging shows a confined leak with moderate surrounding inflammation/phlegmon or a collection less than 3 cm, bowel rest and broad-spectrum antibiotics may be started with serial abdominal and clinical checks to monitor for free perforation. Percutaneous drainage and antibiotics may treat organized abscesses larger than 3 cm. Surgery is needed if conservative treatment fails. Boyce et al. managed 44 anastomotic leaks in 555 laparoscopic low anterior resection patients with anastomosis within 10 cm of the anus. Just four patients with leaks needed reoperation. Sixteen had diverting stomas. Twenty-four of the 28 leak patients without diverting stomas required reoperation. Seventy-four percent of laparoscopic surgical re-explorations included ileostomy or colostomy. patients (2.5%, 18% with anastomotic leakage) needed permanent stomas.

Surgical investigation should focus on safely and effectively detecting and treating the leak, laparoscopically or openly. If there is a big phlegmon and the bowel is matted, mobilizing and exploring the anastomosis may cause further damage. Washout, drainage, and proximal diversion are recommended in these circumstances. Safely accessing the anastomosis allows bowel viability and integrity examination. Primary repair of the anastomosis with proximal diversion may be considered if a clearly marked defect is smaller than 1 cm and the surrounding bowel is healthy without severe inflammation. If the remaining bowel is healthy and non-edematous, remove and re-create the anastomosis. Even with a healthy new anastomosis, proximal diversion should be considered, especially with distal leakage.

New anastomoses are not recommended for sick or edematous bowels. Hartmann's pouch or distal bowel amucous fistula should establish an end stoma. If a colorectal anastomosis leaks, the rectum cannot be raised as a mucous fistula. A rectal tube and pelvic drains should be left if a colorectal anastomosis is removed. Low colorectal, coloanal, and ileoanal anastomoses without a diverting stoma are very impossible to heal. Proximal diversion, washout, and perianastomotic drainage commonly manage sepsis. As mentioned, leak severity determines therapy in patients who were proximally diverted at the index procedure. Percutaneous or transanal drainage may treat perianastomotic abscesses. If transanal drainage is suitable, the abscess may be drained through the anastomosis with a drain (usually a Penrose drain) left in place in the operating room under general anesthesia or sedation. CT scans should be done to check for a collection in individuals with subclinical leaks, such as those seen on contrast enema. If feasible, drain a collection. Expectant care with repeat imaging after 3–6 weeks is possible for a confined leak without a collection. Anastomotic leak therapy should control sepsis. Throughout therapy, remember this aim.

Result

It is nearly never feasible to repair an anastomotic leak in low colorectal, coloanal, or ileoanal anastomoses that do not already have a diverting stoma in situ. Sepsis may typically be managed with the use of proximal diversion, washout, and perianastomotic drainage. Management of patients who have already had proximally diverted surgery at the index procedure relies on the degree of the leak, as was already mentioned. Percutaneous or transanal drainage techniques can be used to treat a perianastomotic abscess. If transanal drainage is necessary, it can be done in the operating room while the patient is under general anaesthesia or sedation, and the abscess can be drained through the anastomosis with a drain (usually a Penrose drain) left in place, if necessary. In individuals with a subclinical leak, such as those

Conclusion

Anastomotic leak is an undesirable but common complication that may arise after colorectal surgery. There are a large number of risk factors that have been documented for anastomotic leak, but only a handful have been conclusively proved in high-quality research on a constant basis. While assessing a patient's individual risk for leak, the surgeon will need to use their clinical judgment since it is very probable that these risk variables interact with one another. Before to beginning with a surgery, measures should be done to optimize the patient wherever there are modifiable elements involved. In the end, an evaluation of each individual patient's risk for leak must be performed at the time of the surgery. Decisions about anastomosis and the use of proximal diversion should be made in accordance with the results of this evaluation. The treatment for an anastomotic leak should begin with determining the patient's level of stability. Then, the patient should undergo resuscitation, diagnostic imaging, or surgical investigation. In order to treat sepsis and stabilize the patient, the results of the operation will govern the surgical strategy that will be used.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA A Cancer J Clin* 2018;68(6):394e424.

2. Kang CY, Halabi WJ, Chaudhry OO, Nguyen V, Pigazzi A, Carmichael JC, et al. Risk factors for anastomotic leakage after anterior resection for rectal cancer. *JAMA Surg* 2013;148(1):65e71.
3. Bakker IS, Grossmann I, Henneman D, Havenga K, Wiggers T. Risk factors for anastomotic leakage and leak-related mortality after colonic cancer surgery in a nationwide audit. *Br J Surg* 2014;101(4):424e32. discussion 32.
4. Frasson M, Flor-Lorente B, Rodriguez JL, Granero-Castro P, Hervas D, Alvarez Rico MA, et al. Risk factors for anastomotic leak after colon resection for cancer: multivariate analysis and nomogram from a multicentric, prospective, national study with 3193 patients. *Ann Surg* 2015;262(2):321e30.
5. Gustafsson UO, Scott MJ, Hubner M, Nygren J, Demartines N, Francis N, et al. Guidelines for perioperative care in elective colorectal surgery: enhanced recovery after surgery (ERAS((R))) society recommendations: 2018. *World J Surg* 2019;43(3):659e95.
6. Zhao-Fleming H, Hand A, Zhang K, Polak R, Northcut A, Jacob D, et al. Effect of non-steroidal anti-inflammatory drugs on post-surgical complications against the backdrop of the opioid crisis. *Burns Trauma* 2018;6:25.
7. Yu YD, Hwang JH, Seo YE, Song BD, Jung YS, Lee DH, et al. Effects of nonsteroidal anti-inflammatory drugs as patient controlled analgesia on early bowel function recovery after radical cystectomy. *Sci Rep* 2018;8(1):4658.
8. Kurz A, Sessler DI. Opioid-induced bowel dysfunction: pathophysiology and potential new therapies. *Drugs* 2003;63(7):649e71.
9. Martinez V, Beloeil H, Marret E, Fletcher D, Ravaud P, Trinquart L. Non-opioid analgesics in adults after major surgery: systematic review with network meta-analysis of randomized trials. *Br J Anaesth* 2017;118(1):22e31.
10. Koughnett JAMV, Wexner SD. NSAIDs and risk of anastomotic leaks after colorectal surgery. *Nat Rev GastroenterolHepatol* 2014;11(9):523e4.
11. Gorissen KJ, Benning D, Berghmans T, Snoeijs MG, Sosef MN, Hulsewe KW, et al. Risk of anastomotic leakage with non-steroidal anti-inflammatory drugs in colorectal surgery. *Br J Surg* 2012;99(5):721e7.
12. Klein M, Andersen LPH, Harvald T, Rosenberg J, Gogenur I. Increased risk of € anastomotic leakage with diclofenac treatment after laparoscopic colorectal surgery. *Dig Surg* 2009;26(1):27e30.
13. EuroSurg Collaborative. Safety and efficacy of non-steroidal anti-inflammatory drugs to reduce ileus after colorectal surgery. *Br J Surg* 2020;107(2): e161e9.
14. Parthasarathy M, Greensmith M, Bowers D, Groot-Wassink T. Risk factors for anastomotic leakage after colorectal resection: a retrospective analysis of 17 518 patients. *Colorectal Dis* 2017;19(03): 288–298
15. van Rooijen SJ, Huisman D, Stuijvenberg M, et al. Intraoperative modifiable risk factors of colorectal anastomotic leakage: why surgeons and anesthesiologists should act together. *Int J Surg* 2016;36(Pt A):183–200
16. Law WI, Chu KW, Ho JW, Chan CW. Risk factors for anastomotic leakage after low anterior resection with total mesorectal excision. *Am J Surg* 2000;179(02):92–96 23 Choi HK, Law WL, Ho JW. Leakage after resection and intraperitoneal anastomosis for colorectal malignancy: analysis of risk factors. *Dis Colon Rectum* 2006;49(11):1719–1725
17. Rullier E, Laurent C, Garrelon JL, Michel P, Saric J, Parneix M. Risk factors for anastomotic leakage after resection of rectal cancer. *Br J Surg* 1998;85(03):355–358
18. Eriksen TF, Lassen CB, Gögenur I. Treatment with corticosteroids and the risk of anastomotic leakage following lower gastrointestinal surgery: a literature survey. *Colorectal Dis* 2014;16(05): O154–O160
19. Smith SA, Roberts DJ, Lipson ME, Buie WD, MacLean AR. Postoperative nonsteroidal anti-inflammatory drug use and intestinal anastomotic dehiscence: a systematic review and meta-analysis. *Dis Colon Rectum* 2016;59(11):1087–1097.
20. Kotagal M, Hakkarainen TW, Simianu VV, Beck SJ, Alfonso-Cristancho R, Flum DR. Ketorolac use and postoperative complications in gastrointestinal surgery. *Ann Surg* 2016;263(01):71–75
21. Saleh F, Jackson TD, Ambrosini L, et al. Perioperative nonselective non-steroidal anti-inflammatory drugs are not associated with anastomotic leakage after colorectal surgery. *J Gastrointest Surg* 2014;18(08):1398–1404
22. Siewert B, Tye G, Kruskal J, et al. Impact of CT-guided drainage in the treatment of diverticular abscesses: size matters. *AJR Am J Roentgenol* 2006;186(03):680–686

23. Boyce SA, Harris C, Stevenson A, Lumley J, Clark D. Management of low colorectal anastomotic leakage in the laparoscopic era: more than a decade of experience. *Dis Colon Rectum* 2017;60(08): 807–814.
24. Jafari MD, Wexner SD, Martz JE, et al. Perfusion assessment in laparoscopic left-sided/anterior resection (PILLAR II): a multiinstitutional study. *J Am Coll Surg* 2015;220(01):82–92.e1.
25. Choy PY, Bissett IP, Docherty JG, Parry BR, Merrie A, Fitzgerald A. Stapled versus handsewn methods for ileocolic anastomoses. *Cochrane Database Syst Rev* 2011;7(09):CD004320.
26. Neutzling CB, Lustosa SA, Proenca IM, da Silva EM, Matos D. Stapled versus handsewn methods for colorectal anastomosis surgery. *Cochrane Database Syst Rev* 2012;15(02):CD003144.