

Original Article

Intraoperative Anastomotic Dye Test for Detecting Risks of Anastomotic Leakage in Patients Undergoing Colorectal Cancer Surgery

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Background. Anastomotic leakage remains a major complication of colorectal surgery. Prompt detection and immediate treatment of anastomotic leaks during surgery may reduce postoperative morbidity and mortality. The use of various intraoperative anastomotic tests has been proposed to reduce the incidence of this complication. Herein, we present our experience of conducting intraoperative dye tests in colorectal cancer surgery.

Methods. Data of 111 patients who underwent colorectal cancer surgery between 2019 and 2021 at a single medical center were retrospectively reviewed, of which 88 underwent elective surgery without the creation of a diverting stoma, and 23 patients, who received a diverting stoma either previously or during the same operation, were excluded from the study. Diluted dye was routinely introduced into the rectal lumen to test anastomotic integrity. If an intraoperative leak was identified, it was promptly repaired. No routine radiological survey or intraoperative colonoscopy was conducted to assess anastomotic integrity after colorectal anastomoses.

Results. Of the 88 patients, 12 (12.5%) presented anastomotic leaks, which were repaired using suture reinforcement. One of the 76 patients who had no intraoperative leaks developed clinical leaks during follow-up (leak rate: 1.3%). Of the 12 patients with intraoperative leaks, 2 developed clinical leaks during follow-up (16.6%). The overall rate of postoperative leakage was 3.4% (3/88).

Conclusions. Routine use of the intraoperative dye test to detect colorectal anastomoses following colorectal surgery may be advantageous.

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Key Words

Intraoperative anastomosis leakage test;
Postoperative leakage rate;
High risk of postoperative leakage;
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Anastomotic leakage (AL) is one of the most serious complications of colorectal surgery, and it may prolong hospital stay, increase treatment costs, reduce the quality of life of the patient; influence

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long-term outcomes of cancer surgery; and increase postoperative morbidity and mortality.¹⁻³ The incidence of AL in colorectal surgery varies from 1.8% to 19.2%, with the risk of low rectal anastomoses being the highest.⁴⁻⁶ The anastomosis technique is selected at the discretion of the surgeon and depends on the surgeon's experience and patient characteristics.⁷ Considering the problems associated with anastomotic leaks, various methods to detect intraoperative anastomotic leaks early, such as anastomotic integrity examination with normal saline, a staining solution, or air insufflation, have been proposed.⁸⁻¹¹ Although a positive anastomotic integrity test result may not always indicate the development of a postoperative leak, studies have recommended performing an intraoperative anastomotic leak test to reduce the leakage rate.^{7,12,13}

The rate of postoperative leakage is higher in anterior resection or low anterior resection performed for rectal lesions than in colonic resection;¹⁴ therefore, identifying a colorectal surgical technique that reduces the development of leakage is necessary. Because an intraoperative test can treat a potential leak perioperatively and thus reduce the risk of subsequent clinical leaks, we developed an intraoperative test to examine the anastomotic integrity and detect any anastomotic leaks in patients with colorectal cancer.¹⁴ In contrast to other tests that involve instilling saline or air insufflation into the rectum, we used diluted patent blue dye to examine anastomotic integrity and assessed the clinical value of the intraoperative dye test in this study.

Materials and Methods

Between August 2019 and July 2021, the data of 111 patients (49 men and 39 women; mean age, 63.3 years [range, 38-90 years]) with colorectal cancer who received stapled or hand-sewn anastomosis and who underwent the intraoperative dye test were reviewed. All operations and intraoperative anastomotic leak tests were performed by an experienced surgeon. Low anterior resection with total mesorectal excision was performed for the resection of tumors located in the mid- or lower-third of the rectum. No routine diverting stoma was planned preoperatively. Of the oper-

ated patients, 6 underwent diverting colostomy or ileostomy before the operation, and protective colostomy or intersphincteric resection was performed in 17 patients because their anastomosis site was located within 4 cm from the anal verge. Pelvic drainage through a rubber or Jackson-Pratt drain was routinely performed. The tumor location was the distal sigmoid colon in 30 patients, rectosigmoid colon in 19 patients, and rectum in 39 patients. According to the criteria of the American Joint Commission on Cancer Union for International Cancer Control, 2, 24, 13, and 44 patients were classified to have stage 0, stage I, stage II, stage III, and stage IV cancer, respectively. A total of 29, 11, and 48 patients underwent open surgery, laparoscopy surgery, and robotic surgery, respectively. The patient characteristics are presented in Table 1.

Table 1. Patient characteristics (N = 88)

Patient-related factors	Mean (SD)	N (%)
Age (years)	63.3 (11)	
Male		49 (56%)
female		39 (44%)
TMN classification		
0		2 (2.3%)
I		24 (27.4%)
II		13 (14.7%)
III		44 (50%)
IV		5 (5.6%)
Location of tumor		
Distal sigmoid colon		30 (34.1%)
Rectosigmoid junction		19 (21.6%)
Rectum		39 (44.3%)
Preoperative radiation		43 (38.7%)
Preoperative hemoglobin (g/dl)	12.2 (1.6)	
Preoperative albumin level	3.6 (0.4)	
Preoperative HbA1c	5.63 (1)	
Underlying disease		
Hypertension		40 (45.9%)
Cardiovascular disease		3 (3.6%)
Diabetes		20 (23.4%)
Chronic renal disease		7 (8.1%)
Cerebrovascular accident		2 (2.7%)
Social behavior		
Smoking		8 (9.1%)
Alcohol		3 (3.4%)
Betal nut		2 (2.3%)
Procedure-related factors		
Open surgery		29 (33%)
Laparoscopy surgery		11 (12.5%)
Robotic surgery		48 (54.5%)
Diverting stoma after leakage		3 (3.4%)

Anastomotic dye test

Patent blue dye, commonly used in lymphangiography to stain lymph ducts, is diluted with sterile water or saline (1:500). A 22-French Foley catheter is inserted into the anus, and the balloon is inflated to prevent the staining solution from spilling outside. The diluted preparation is then introduced into the rectal lumen while the bowel lumen proximal to the anastomotic site is occluded using a bowel clamp or the surgeon's fingers. Approximately 120-180 mL of staining solution is usually sufficient to distend the collapsed rectum.¹⁴ Leaks are observed as overt, blue-stained spillage, which most at staple crossing point. The detected leaks are then reinforced using interrupted sutures, and a retest for anastomotic leakage is performed as described previously.

Postoperative evaluation

No routine radiological survey or intraoperative colonoscopy was conducted for the assessment of anastomotic integrity after bowel anastomosis. If clinical signs or symptoms such as fever, leukocytosis, abdominal pain, elevated C-reactive protein (CRP), intra-abdominal infection, or intestinal content from the drain tube were observed, contrast-enhanced abdominal computed tomography was used to confirm anastomotic leakage.

Results

Among the 110 patients who underwent colorectal surgery, any intraoperative leak detected was repaired intraoperatively with suture reinforcement. After repair, the anastomotic dye test was performed again to ensure that no leakage remained; 12 patients presented with dye leaks from anastomosis, and 2 patients developed a clinically relevant anastomotic leak. Of the 76 patients who exhibited no leakage during the test, one developed leakage postoperatively (Table 2). Of the 88 patients who underwent elective surgery without the creation of a diverting stoma, 3 had postoperative leakage, with the overall leakage rate of

3.4% (Fig. 1). Two of these three patients with postoperative leakage had received robotic surgery (4.2%), and one had received conventional surgery (3.4%). The incidence of post-operative leakage was 16.6% in positive leakage group, and in negative leakage group was observed in 1.3% of the patient ($p = 0.06$, chi-square with Yates correction). After oral intake of diet, drainage revealed stool-like contents, but no abdominal pain was reported. However, fever, leukocytosis, and elevated CRP were noted. Three post-operative anastomosis leakage details as following: first patient, 56 year old female who had rectal cancer underwent robotic associated low anterior resection. Second, 87 year old male who had rectal cancer underwent robotic associated low anterior resection. Third, 75 year old male who had recto-sigmoid junction underwent open low anterior resection. Exploratory laparotomy or diagnostic laparoscopy was performed, followed by diverting colostomy.

Discussion

Due to the high risks of leaks in untested anastomoses in clinical settings, the intraoperative leak test is widely conducted.^{7,12} In our study, we performed the intraoperative dye test immediately after anastomosis and identified 12 intraoperative leaks; of them, two patients developed a postoperative anastomotic leak (16.6%), which is considerably higher than the overall incidence (3.4%) in our study. By detecting the leak site with patent blue dye, we could repair preventable anastomotic leaks in 10 of 12 patients (83.3%). Our results were similar to those of a previous study by Smith et al.,⁹ in which among 229 patients who underwent the intraoperative dye test, none of the 10 patients found to have intraoperative leaks that were

Table 2. Comparison of results of postoperative and intraoperative leaks

Intraoperative leak	Postoperative leak		
	No leak	Leak	Total No. (leak %)
No leak	75	1	76 (1.3%)
Leak	10	2	12 (16.6%)
Total No.	86	3	88 (3.4%)

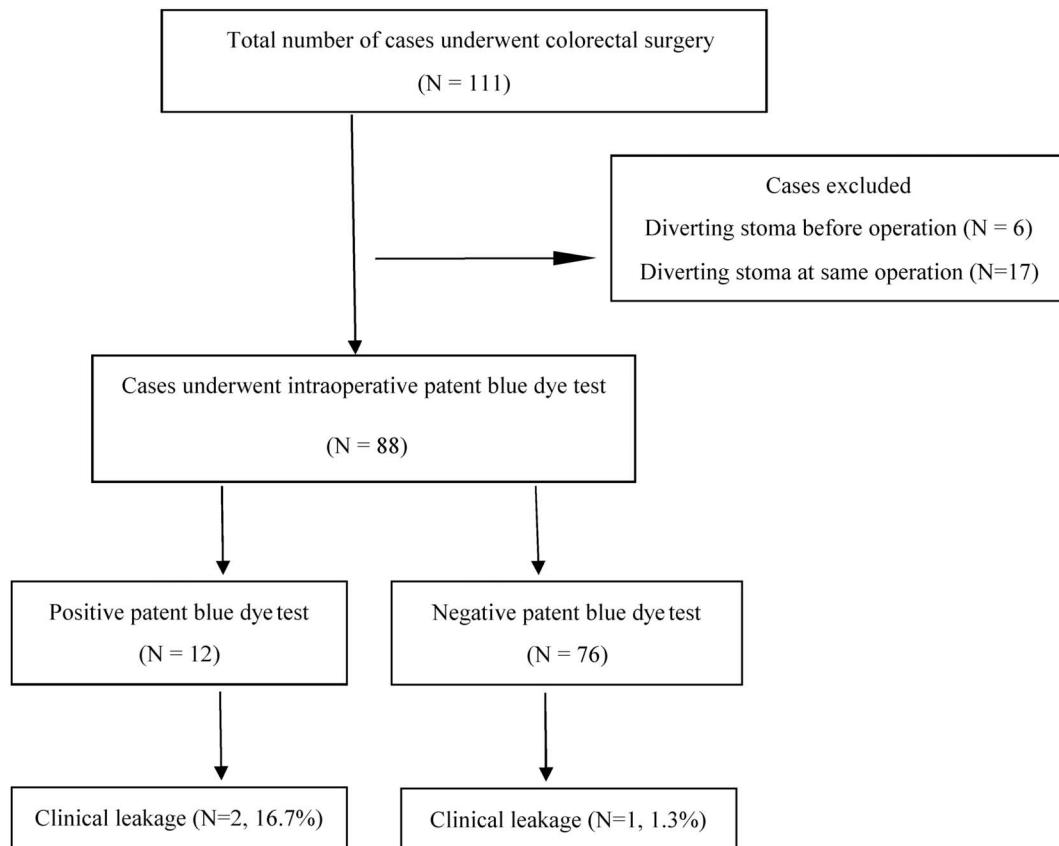


Fig. 1. Patient enrollment and incidence of anastomosis.

immediately repaired developed postoperative leaks. By contrast, in a cohort of 998 patients who underwent left-sided colorectal anastomosis, Ricciardi et al. reported that the highest risk of clinical leaks was found in those who had positive air leak tests and merely received suture repair.¹²

According to our experience, an air bubble easily disappears in a water-drained pelvic cavity; therefore, air is less effective than dye in indicating the exact leak site, consequently resulting in less precise leakage repair. Nevertheless, placing gauze stained with dye on the posterior wall of the anastomosis allows the easy identification of the leakage side. In addition, Kryzauskas et al. evaluated the mechanical integrity of anastomosis and reported that methylene blue tests through the Foley catheter are cheaper and easier to perform than intraoperative endoscopy. Moreover, they reported a positivity of 14.3% in the methylene blue leak test in patients who received a negative result in the air leak test.^{16,17}

According to our preliminary experience, the patent blue dye has excellent applicability to colorectal anastomoses. Compared with other test methods involving povidone-iodine solution, saline, or air, the patent blue dye test enables the overt localization of the leak site. The diluted povidone-iodine solution might be mistaken for serosanguineous fluid. Sodium chloride solution is too transparent to be detected. Furthermore, air bubbles in a water-filled pelvic cavity can easily escape from a leak site, necessitating repeated tests.¹⁶ The use of patent blue dye can overcome these drawbacks because this dye is easily identified in the adipose tissue as well as the anastomotic bowel wall due to the contrast of the blue color against yellow.

Accordingly, based on our experience, the test need not be repeated if no stained tissue is visualized after the bowel segment is well distended. A limitation of our study is that because of the retrospective design, our data may not be sufficient to generate infer-

ences regarding differences between different intraoperative tests for leakage. However, the present study has the following strengths. First, we excluded emergency cases, and all operations were performed by a single surgeon. Therefore, confounders such as the operative setting, preoperative septicemia or peritonitis, surgical techniques, placement of pelvic drain tubes, and personal experience or expertise that might influence the development of postoperative leaks were well controlled. Second, we only focused on patients with colorectal cancer.

The overall postoperative leakage rate of 3.4% was comparable with that reported in a similar study, which used a methylene blue test in a mixed population composed of patients with benign and malignant cancer managed with various operations.⁹ Nevertheless, we demonstrated that the postoperative leakage was considerably higher in patients who received a positive leakage test than in those who received a negative leakage test. In addition, in a review of 3023 cases by Schiff et al., a higher postoperative AL rate was observed in those with a positive leakage test result.¹⁹ Therefore, a positive intraoperative leak test result may be associated with a higher risk of postoperative leakage.

Conclusions

The patent blue test can be used to efficiently detect anastomosis leakage. Although this procedure does not significantly reduce the risk of anastomosis leakage, it can be used to identify patients at a high risk of leaks. Moreover, this method is suitable for use in both conventional and mini-invasive surgical procedures. Thus, routine use of the intraoperative dye test may be beneficial for the confirmation of anastomotic integrity intraoperatively in patients undergoing colorectal surgery.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

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The authors declare no role of the funding source in the study results.

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原 著

大腸直腸癌手術之病患行術中吻合處染色測試 可檢測術後高滲漏風險

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目的 大腸直腸癌術後吻合處滲漏都會帶來嚴重的併發症甚至提高死亡率，藉由術中滲漏測試，判斷高滲漏風險因子，藉由了解高風險病人而提早發現滲漏及提早治療減少併發症及降低死亡率，目前已經提出使用各種術中吻合試驗來減少這種並發症的發生率。在此，介紹我們在大腸直腸癌手術中進行術中染料測試的經驗。

方法 藉回溯性觀察，於 2019 年到 2021 間蒐集 111 名在本院行大腸直腸癌手術的病患，除去術前或同次手術行腸造口之病患，共 23 人無須術中行染色檢測，一共分析 88 名患者。稀釋的染劑由肛門灌入直腸來測試吻合的完整性。如果發現術中滲漏，及時修復。沒有進行常規放射檢查或術中大腸鏡檢查來評估結直腸吻合術後的吻合的完整性。

結果 在 88 位病患中有 12 位有發現術中染色滲漏之情況 (12.5%) 且在術中再行加強縫合，在術中滲漏為陰性的病患共有 76 位，在這 76 位當中有一位病患有術後吻合處滲漏發生 (1.3%)，在術中測試陽性病患有 12 位裡面有兩位病患發生術後吻合處滲漏 (16.6%)，在術後總體滲漏率是 3.4%。

結論 在大腸直腸癌手術中常規使用吻合處染色測試是一種有利的術後滲漏檢測。

關鍵詞 術中吻合處滲漏測試、術後滲漏率、高風險術後滲漏、藍染測試。