Mini-Review Article (Invited)

The risk factors and predictive factors for anastomotic leakage after resection for colorectal cancer: Reappraisal of the literature

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A brief title: The risk factors for anastomotic leakage after colorectal surgery

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Abstract

Anastomotic leakage is a serious complication that can occur after colorectal surgery. Several risk factors for anastomotic leakage have been reported based on the findings of prospective and retrospective studies, including patient characteristics, the use of neoadjuvant therapy, the tumor location, intraoperative events, etc. However, as these risk factors affect each other, the statistical results have differed in each study. In addition, differences in surgical methods, including laparoscopy versus laparotomy or stapling anastomosis versus handsewn anastomosis, may influence the incidence of anastomotic leakage. This mini-review summarizes the results of reported papers to clarify the current evidence of risk factors for anastomotic leakage.

Key words: Anastomotic leakage, Colorectal cancer, Risk factors

Introduction

Anastomotic leakage is a severe and potentially fatal complication that can occur after colorectal surgery. The rate of anastomotic leakage after colon and rectal resection is widely reported to be between 2% and 23 % [1-8]. Due to anatomical and technical reasons, the leakage rates differ between colonic and rectal surgery, having been reported to be 11-12% and 3-4%, respectively [9-15]. Furthermore, the leakage rates also differ from institution to institution, even when using the same surgical procedure.

Such differences do not indicate an inequality in surgical techniques, but rather depend on the patient conditions and many other factors. Although several risk factors for anastomotic leakage have been identified, including patient characteristics and the use of neoadjuvant chemoradiati on therapy and certain kinds of drugs such as steroids, the statistical results have been different in each report and the useful predictive factors for anastomotic leakage after colorectal surgery remain unclear. The aim of this mini-review is to summarize the results of recent reports evaluating the risk factors for anastomotic leakage.

General characteristics of risk factors for anastomotic leakage

Relevant studies were identified in a search of the MEDLINE (Pub-Med) databases with no restrictions. We also reviewed the reference lists of the retrieved articles. Many authors have prospectively or retrospectively investigated the risk factors for anastomotic leakage using their own data. Table 1 shows a list of relatively recent reports investigating these risk factors [10, 11, 16-27]. Five studies [10, 11, 18, 20, 25] collected data in multicenter trials, while the other studies [16, 17, 19, 21-24, 26, 27]

collected data from their own institution. Leakage appears to be a primary issue for rectal surgery in particular; therefore, six of the fourteen articles were restricted to the rectum only. This is one reason why the rates of leakage differ widely, as tumor localization in the left-sided colon or rectum is generally accepted to be a risk factor for anastomotic dehiscence [11, 17].

The correlations between the patient characteristics and anastomotic leakage are summarized in Table 2. Age was not found to be associated with an increased risk of anastomotic leakage in any study. A selection bias might account for this finding. For example, elderly patients tend to reject surgery, or are selected to undergo safer procedures without anastomosis. A male gender was found to be associated with an increased risk of leakage in some reports [11, 23, 25, 26]. Generally, the difficulty of performing surgery in the narrow male pelvis is associated with an increased risk of anastomotic leakage in patients with rectal cancer [23]. The American Society of Anesthesiologists (ASA) classification was shown to have statistical significance in two studies [11, 27]. Diabetes was not found to influence the anastomotic leakage in any of these series. Preoperative steroid use is widely accepted as a risk factor for developing anastomosis, and three studies showed statistical significance for this factor. On the other hand, some studies did not demonstrate an increased risk for anastomotic complications with steroid use [28]. The exact dosage and duration of steroid use may play an important role in the development of anastomotic leakage [19]. Although not shown in Table 2, Gorissen et al. [18] mentioned that nonsteroidal anti-inflammatory drugs may be associated with anastomotic leakage. Bowel resection in patients with chronic renal failure has been considered to be associated with an increase in anastomotic leakage [29]. However, only one recent study [27], shown in Table 2,

identified that renal failure was a risk factor, but the other studies did not examine whether it was a risk factor.

The correlations between surgical events and anastomotic leakage are also summarized in Table 2. The estimated amount of operative blood loss and the use of consecutive blood transfusions were both independently associated with an increased risk of anastomotic leakage [9, 30]. Blood loss may induce ischemia at the anastomoses and hence impair anastomotic healing. Blood transfusions may induce immunological suppression, thereby increasing the risk of infectious conditions around anastomoses. Three of the studies shown in Table 2 reported that blood transfusions were a risk factor [11, 25, 27]. Although other studies have reported that the use of intraoperative blood transfusions is unlikely to be a risk factor for anastomotic leakage, several studies have shown that substantial intraoperative blood loss, which is most likely a marker of the need for intraoperative blood transfusions, is associated with an increased risk of anastomotic leakage [27, 31, 32].

Emergency surgery, which intuitively should place patients at a higher risk of adverse postoperative events, was not found to be associated with anastomotic leakage in three studies (Table 2), whereas Choi et al. [33] reported that emergency surgery was a risk factor based on the univariate and multivariate analyses.

Table 2 summarizes the final conclusions regarding the risk factors associated with anastomotic leakage in each article.

Preoperative preparation

Fecal contamination of the anastomosis is believed to be a major contributing factor to septic conditions and anastomotic dehiscence, and several types of mechanical

bowel preparation are routinely used before colorectal surgery in order to reduce bacterial bowel translocation. In the US, the most commonly used regimens of mechanical bowel preparation include polyethylene glycol solutions and sodium phosphate. Despite the widespread use of mechanical bowel preparation, the necessity of bowel cleansing before colectomy has been questioned. European surgeons, in particular, have advocated abandoning this practice. Several small studies have suggested that mechanical bowel preparation does not decrease the risk of postoperative wound infection or anastomotic dehiscence.

Slim et al. [34] reviewed seven studies and concluded that mechanical bowel preparation using polyethylene glycol before colorectal surgery increases the rate of anastomotic leakage compared to that observed with no preparation. However, as this review included only a small number of subjects, larger prospective trials are needed to determine whether mechanical bowel preparation before colectomy is necessary. Slim et al. updated their data and reevaluated the role of mechanical bowel preparation in colorectal surgery [35]. In this meta-analysis, which included almost 5,000 patients, there were no statistically significant differences between the mechanical bowel preparation group and the no preparation group with respect to anastomotic leakage, intra-abdominal abscess formation and wound infection. Van't Sant et al. [36] also demonstrated that there was not a higher risk of anastomotic leakage or septic complications among the patients who underwent low colorectal surgery, with or without mechanical bowel preparation. Therefore, the occurrence of anastomotic leakage following mechanical bowel preparation remains controversial.

Large bowel obstruction due to colorectal cancer

The surgical strategy for left-sided large bowel obstruction depends on the state of the patients and the policy of the surgeon. In most cases, an emergency operation is required, and after removal of the affected section of the bowel with lymph node dissection, there are various possible procedural options for reconstruction, including primary anastomosis, with the use of a protective stoma if necessary, and Hartmann's procedure. However, there have been few studies showing validated results with regard to which procedure is the best for each patient [37-39]. One of the prospective multicenter observational studies from Germany [40] described a recommended surgical procedure for obstructive left-sided colon cancer. They suggested that in cases with advanced obstruction and in high-risk cases, Hartmann's procedures should be used, however, a protective stoma did not appear to confer any advantage.

Although Hartmann's procedure seems to be safe from the point of view that there is no risk of anastomotic dehiscence, it requires a second operation to reverse the colostomy, and therefore, adversely affects the patients' quality of life. The preoperative placement of a self-expanding metallic stent can decompress the oral side colon, and allow for primary resection and anastomosis [41, 42]. The use of a stent may lead to the development of some complications such as perforation, however, as a bridge to surgery, it has higher successful primary anastomosis and lower overall stoma rates [41].

Neoadjuvant chemoradiation therapy for rectal cancer surgery

There has been concern that neoadjuvant chemoradiation affects the leakage rate. In particular, preoperative radiotherapy seems to be implicated in the development of anastomotic leakage following rectal surgery [22]. However, several prospective studies failed to show that a short course of preoperative radiation increases

anastomotic leakage [43, 44]. Nevertheless, the absence of concomitant chemotherapy and the liberal use of a protective stoma may have influenced these data. In a recent study which analyzed the risk factors for anastomotic leakage following laparoscopic rectal cancer excision [25], the univariate analysis of the whole data showed that anastomotic leakage was not associated with neoadjuvant chemoradiation. However, the results for the patients without a protective stoma showed that it was a powerful risk factor for leakage. Chang et al. [45] also examined the association by using a propensity score matching analysis and concluded that preoperative chemoradiation therapy did not affect the risk of anastomotic leakage after rectal cancer resection.

A diverting stoma should be strongly considered for patients who have received preoperative chemoradiation therapy, especially in males, those with cancer in a low location or the patients who have used steroids.

Laparoscopic versus open surgery

A previous multicenter study suggested that the use of laparoscopic rectal cancer resection should be discouraged due to the high anastomotic leakage rate [46]. However, laparoscopic colorectal surgery has recently become so popular that many surgeons have the case volume needed to complete the learning curve. Such experience may improve the surgical results. Two randomized clinical trials [47, 48] compared the laparoscopic approach with open surgery for colonic cancer and reported equal rates of anastomotic leakage. Furthermore, according to recent studies, the short-term outcomes, including morbidities such as anastomotic leakage, do not differ between laparoscopic and open surgery [49, 50].

With respect to laparoscopic colorectal surgery, anastomotic leakage is more

likely to occur in patients undergoing surgery for low rectal cancer. One reason for this is that laparoscopic surgery for rectal cancer is associated with technical difficulties. In cases of laparoscopic surgery for rectal cancer, intracorporeal stapling devices are used to transect the rectum, which is technically difficult due to the width and limited articulation of the devices. Technical failure in this step appears to be one of the explanations for the increased rates of anastomotic leakage following laparoscopic procedures. Additionally, an increased risk of anastomotic leakage in stapled anastomoses using multiple firing has also been reported [51]. However, these technical problems can be overcome by experience and the development of new devices. In fact, the just recent results of a randomized phase Ⅲ trial [52] demonstrated that the comparable short-term outcomes, including the morbidity, of laparoscopic and open rectal surgery. The authors reported that anastomotic leakage was noted in 13% of patients who had undergone laparoscopic surgery and 10% of patients who had undergone open surgery, with no statistically significant differences between the groups [52].

From these data it appears that the laparoscopic approach in general may not increase the risk of anastomotic leakage, although additional monitoring is required to draw definitive conclusions.

Diverting stoma

The creation of a stoma should effectively divert the fecal stream from a healing anastomosis and it may mitigate the influence of anastomotic failure. However, the relationship between a diversion stoma and anastomotic leakage is controversial. Only two randomized studies have examined the effects of the use of temporary

diverting stomas on the leakage rates after low anterior resection, neither of which showed negative results [53, 54]. However, these studies included only small numbers of patients, and the high rate of leakage may have influenced these results. Eberl et al. [17] reported that proximal diversion is associated with lower leakage rates and lower reoperation rates. However, other authors have reported that the presence of a stoma is associated with postoperative mortality in cases of anastomotic leakage [19, 23].

On the other hand, stomas made temporally sometimes become permanent. The procedure for stoma reversal usually requires a second hospital stay and sometimes results in morbidity. Koperna et al. [55] reported that, in their study, the hospital stays were significantly prolonged in the stoma group. For this reason, diverting stomas are not routinely used in patients undergoing rectal surgery. Law et al. [23] reported that the absence of a stoma is associated with a significantly increased rate of leakage in male, but not female patients, and in male patients, the leakage rates among those with and without proximal diversion were 5% and 27%, respectively. The authors concluded that diverting stomas should be routinely used in males.

It is well known that anastomotic leakage tends to occur following low rectal anastomosis. Karanjia et al. [56] showed that, according to their data, all cases of major anastomotic leakage occurred at an anastomotic height of less than 6 cm. Therefore, they recommended that proximal diverting stomas should be created in patients with an anastomosis below 6 cm. Park et al. [25] reported that tumors located less than 7 cm from the anal verge had an increased risk of anastomotic leakage.

Therefore, the construction of a diverting stoma should be considered in patients with suspected risk factors for anastomotic leakage such as male patients and patients with an anastomotic height of less than 6 cm. However, this procedure should

be selected according to the discretion of the surgeon based on his/her experience and the characteristics of the individual patients and tumors.

Stapled and handsewn methods of anastomosies

Stapling devices have been in use since the late 1970's. Linear cutter staplers are commonly used to divide tissue between two lines of staples at the same time, while circular staplers are used to create anastomoses, especially in sigmorectal lesions. However, linear cutter staplers are also used to create anastomoses, such as functional end-to-end anastomoses. This anastomotic technique is commonly used for colocolic and ileocolic anastomoses today. Puelo et al. [57] retrospectively analyzed the type of anastomosis technique used for ileocolic anastomosis. Their results showed that the rate of anastomotic leakage is higher in patients with handsewn anastomoses than in those with stapled anastomoses. Moreover, the authors analyzed the type of stapled anastomoses in detail and concluded that the end-to-side configuration is associated with a lower incidence of leakage than the side-to-side configuration. The intervention review edited by the Cochrane Colorectal Cancer Group [58] reported that stapled anastomoses are associated with significantly fewer cases of anastomotic leakage than handsewn anastomoses with respect to ileocolic anastomoses. In a subgroup analysis of cancer patients, the use of a stapled anastomosis led to a significantly lower rate of anastomotic leakage [58].

The development of circular staplers has enabled the easy and safe creation of anastomoses during low anterior resection for rectal cancer; however, anastomotic leakage continues to be encountered occasionally. Peeters et al. [10] attempted to identify the risk factors for symptomatic anastomotic leakage in patients undergoing

total mesorectal excision for rectal cancer. In that article, the authors compared the use of a stapled anastomosis with the hand-sewn method with respect to the risk of anastomotic leakage. However, they could not find any statistically significant differences. Law's study [23] showed the same results for these anastomotic techniques.

Akiyoshi et al. [16] identified the risk factors for leakage following surgery for rectal cancer with respect to the use of circular staplers, namely, intracorporeal rectal transection and double-stapling anastomoses. In their results, there were no significant differences in the rate of anastomotic leakage when comparing either the number of cartridges used to transect the rectum or the length of the cartridges. Park et al. [25] reported the finding that multiple firings of a linear stapler was significantly associated with anastomotic leakage. Some surgeons have attempted to modify the double-stapling technique (DST) in order to reduce the risk of anastomotic leakage. Kang et al. [59] converged the staple line on the middle portion using running sutures and removed the staple line after circular stapler firing. They concluded that this modified method achieves better outcomes with respect to reducing anastomotic leakage than DST. Another comparative study of single-stapled and double-stapled anastomoses reported that there were no statistically significant differences between these anastomotic methods [60]. Some surgeons recommend performing a colonic J-pouch anastomosis, rather than a straight coloanal anastomosis, in order to minimize the symptoms of increased stool frequency, urgency and incontinence. A number of studies that compared those two techniques showed the functional superiority of the pouch [61-63]. Several studies found no significant differences in the incidence of anastomotic leakage between the J-pouch and straight coloanal anastomosis [62, 64, 65]. Furthermore, Hallbook et al. [61] reported a significantly lower incidence of anastomotic leakages after a colonic

J-pouch anastomosis than after a straight coloanal anastomosis.

Therefore, many reports have shown that a stapled anastomosis is superior to the handsewn method in terms of the risk of anastomotic leakage. However, anastomotic region recurrence caused by free cancer cells is a concern when using stapling devices [66]. Yajima et al. [67] reported two instances of staple line recurrence in the same case, in which curative resection was required twice. In addition, the stapled anastomosis is generally associated with important economical expenditures. In cases that require a hand-sewn method, such as intersphincter resection (ISR), the best procedure should be selected for the individual anastomosis. In particular, it has been reported that the rate of anastomotic leakage is 6.4% among cases of ISR with handsewn anastomoses [68].

The ligation level of the inferior mesenteric artery

During the complete lymph node dissection in cases of left-sided colon cancer or rectal cancer, the inferior mesenteric artery is often ligated at the origin from the aorta (high ligation). However, as the proximal portion of the anastomosis relies on the marginal blood flow coming from the middle colic artery, there is particular concern regarding whether high ligation may increase the risk of the anastomotic leakage. For this reason, the inferior mesenteric artery is ligated while preserving the left colic artery (low ligation). Tsujinaka et al. [69] reported that 2 % of the patients with high ligation developed proximal bowel necrosis, while the patients with low ligation did not suffer from this complication. Trencheva et al. [26] noted that, in their study, the patients with high ligation had a 3.8-fold higher risk of developing leakage than those with low ligation. On the other hand, Corder et al. [70] reported that there was no

statistically significant difference in the anastomotic leakage rates between the patients with high ligation and low ligation. Furthermore, Hida et al. [71] reviewed the pertinent literature, and concluded that a high ligation did not represent a source of increased anastomotic leak in rectal surgery.

In cases of high ligation, the poor blood supply may be further exacerbated by the vessel condition of the patients, such as the presence of atherosclerosis or the anatomical variations of the major mesenteric blood vessels and collaterals. A high ligation may be necessary for several reasons, including the need to create a tension-free low rectal anastomosis or to perform an *en bloc* lymphadenectomy for advanced cancer. However, the indications should be considered carefully in patients with risk factors for poor blood flow during the postoperative period.

Conclusions

Based on recent studies, multiple risk factors for anastomotic leakage have been identified. Such factors should be taken into consideration before and during colorectal surgery in order to comprehensively assess the risk for anastomotic leakage. Surgeons should therefore be aware of high-risk patients so that they can select appropriate measures, such as the use of diverting stomas, during surgery.

Table 1. Recent studies evaluating the risk factors for anastomotic leakage after colorectal surgery

Reference	Year	Country	Location	Study type	No. Pts	Rate Leakage(%)
Law [23]	2000	China	rectum	prospective	196	10.2
Alves [27]	2002	France	colon, rectum	retrospective	707	6
Peeters [10]	2005	Netherlands	rectum	retrospective	924	11.6
Konishi [19]	2006	Japan	colon, rectum	prospective	391	2.8
Law [24]	2007	China	colon, rectum	prospective	1580	3.8
Eberl [17]	2008	Austria	rectum	retrospective	472	10.4
Akiyoshi [16]	2011	Japan	rectum	prospective	396	3.6
Leichtle [20]	2012	USA	colon	prospective	4340	3.1
Gorissen [18]	2012	Netherlands	colon, rectum	retrospective	795	9.9
Krarup [11]	2012	Denmark	colon	prospective	9333	6.4
Smith [21]	2012	USA	rectum	retrospective	1127	3.5
Trencheva [26]	2012	USA	colon, rectum	prospective	616	5.7
Park [25]	2013	Korea	rectum	retrospective	1609	6.3
Kobayashi [22]	2013	Japan	colon, rectum	prospective	918	6.3

Pts, patients

Table 2. The statistical results: Perioperative risk factors for anastomotic leakage and final conclusions

Reference	Age	Gender	BMI	ASA	DM	NAT	Steroid use	TL	LS	EBL	OT	BPT	ES	Conclusions
Law [23] †	N	Y	-	-	-	-	-	N	-	-	-	-	-	gender, DV
(n=196)		0.049												
Alves [27] †	-	-	-	Y	-	Y	Y	Y(transverse)	-	-	Y	Y	-	renal failure, septic condition
(n=707)				0.04		0.02	0.01	0.02			0.001	0.006		
Peeters [10] †	N	N	-	-	-	N	-	N	-	N	N	-	-	DV, pelvic drain
(n=107)														
Konishi [19] †	N(>60)	N	N(26>)	N	N	N	Y	N	N	-	Y(>240)	N	-	steroid, OT, fecal contamination
(n=391)							0.023				0.006			
Law [24] †	N	N	-	N	-	-	-	Y	N	-	-	-	N	poor survival, high recurrence rate
(n=1580)								<0.001						
Eberl [17] †	N(>70)	N	N(25>)	N	-	N	-	N	-	-	N(>150)	N	-	tumor size, location, DV
(n=472)														
Akiyoshi [16] †	N(>70)	N	N	N	N	N	-	Y	-	N(>50)	N(>280)	-	-	location, pelvic drain
(n=363)							-	0.041						
Leichtle [20]†	N	N	N	N	N	N	Y	-	N	Y(>300)	N(>120)	N	N	fecal contamination, EBL
(n=4340)							0.02			0.001				
Gorissen [18] †	N	-	-	-	N	N	N	-	-	-	-	-	-	NSAIDs, stapled anastomoses
(n=795)														
Krarup [11] †	N	Y	-	Y	-	-	-	N	N	Y	-	Y	N	age, gender, location, LS, EBL, BPT
(n=9333)		0.001		<0.001						<0.001		<0.001		
Smith [21] †	N	N	-	-	-	N	-	N	-	-	-	-	-	DV
(n=1127)														

Trencheva [26] † (n=616)	N	Y 0.0085	-	N	-	Y 0.0049	-	Y(<10cm) <0.0001	N	-	-	-	-	Charlson Comorbidity Index, DV
Park [25] † (n=1609)	N	Y <0.001	N	N	-	N	-	N	-	-	Y 0.015	Y <0.001	-	gender, chemoradiation, tumor stage
Kobayashi [22] † (n=918)	N	N	N	N	-	Y(radiation) 0.029	N	-	N	Y 0.0022	Y 0.0024	-	-	radiation, OT, EBL

Significant differences: Yes(Y) or No(N), the number is the p value, BMI: body mass index, ASA: American Society of Anesthesiologists, DM: diabetes mellitus, NAT: neoadjuvant therapy, TL: tumor location, LS: laparoscopic surgery, EBL: estimated blood loss, OT: operating time, BPT: blood product transfusion, ES: emergency surgery, NSAIDs: nonsteroidal anti-inflammatory drugs, DV: diverting stoma

†: a univariate analysis to determine the association with anastomotic leakage

References

1. Byrn J C, Schlager A, Divino C M, Weber K J, Baril D T and Aufses A H, Jr., The management of 38 anastomotic leaks after 1,684 intestinal resections. Dis Colon Rectum, 2006. 49(9): 1346-53.
2. Hedrick T L, Sawyer R G, Foley E F and Friel C M, Anastomotic leak and the loop ileostomy: friend or foe? Dis Colon Rectum, 2006. 49(8): 1167-76.
3. Hyman N, Manchester T L, Osler T, Burns B and Cataldo P A, Anastomotic leaks after intestinal anastomosis: it's later than you think. Ann Surg, 2007. 245(2): 254-8.
4. Kanellos I, Vasiliadis K, Angelopoulos S, Tsachalis T, Pramateftakis M G, Mantzoros I, et al., Anastomotic leakage following anterior resection for rectal cancer. Tech Coloproctol, 2004. 8 Suppl 1: s79-81.
5. Lim M, Akhtar S, Sasapu K, Harris K, Burke D, Sagar P, et al., Clinical and subclinical leaks after low colorectal anastomosis: a clinical and radiologic study. Dis Colon Rectum, 2006. 49(10): 1611-9.
6. Matthiessen P, Hallbook O, Andersson M, Rutegard J and Sjodahl R, Risk factors for anastomotic leakage after anterior resection of the rectum. Colorectal Dis, 2004. 6(6): 462-9.
7. Phitayakorn R, Delaney C P, Reynolds H L, Champagne B J, Heriot A G, Neary P, et al., Standardized algorithms for management of anastomotic leaks and related abdominal and pelvic abscesses after colorectal surgery. World J Surg, 2008. 32(6): 1147-56.
8. Blumetti J, Chaudhry V, Prasad L and Abcarian H, Delayed transanal repair of persistent coloanal anastomotic leak in diverted patients after resection for rectal cancer. Colorectal Dis, 2012. 14(10): 1238-41.
9. Bertelsen C A, Andreasen A H, Jorgensen T and Harling H, Anastomotic leakage after anterior resection for rectal cancer: risk factors. Colorectal Dis, 2010. 12(1): 37-43.
10. Peeters K C, Tollenaar R A, Marijnen C A, Klein Kranenbarg E, Steup W H, Wiggers T, et al., Risk factors for anastomotic failure after total mesorectal excision of rectal cancer. Br J Surg, 2005. 92(2): 211-6.
11. Krarup P M, Jorgensen L N, Andreasen A H and Harling H, A nationwide study on anastomotic leakage after colonic cancer surgery. Colorectal Dis, 2012. 14(10): 661-7.
12. Buchs N C, Gervaz P, Secic M, Bucher P, Mugnier-Konrad B and Morel P, Incidence, consequences, and risk factors for anastomotic dehiscence after colorectal surgery: a prospective monocentric study. Int J Colorectal Dis, 2008. 23(3): 265-70.
13. Golub R, Golub R W, Cantu R, Jr. and Stein H D, A multivariate analysis of factors

contributing to leakage of intestinal anastomoses. J Am Coll Surg, 1997. 184(4): 364-72.

14. Kube R, Mroczkowski P, Granowski D, Benedix F, Sahm M, Schmidt U, et al., Anastomotic leakage after colon cancer surgery: a predictor of significant morbidity and hospital mortality, and diminished tumour-free survival. Eur J Surg Oncol, 2010. 36(2): 120-4.

15. Marra F, Steffen T, Kalak N, Warschkow R, Tarantino I, Lange J, et al., Anastomotic leakage as a risk factor for the long-term outcome after curative resection of colon cancer. Eur J Surg Oncol, 2009. 35(10): 1060-4.

16. Akiyoshi T, Ueno M, Fukunaga Y, Nagayama S, Fujimoto Y, Konishi T, et al., Incidence of and risk factors for anastomotic leakage after laparoscopic anterior resection with intracorporeal rectal transection and double-stapling technique anastomosis for rectal cancer. Am J Surg, 2011. 202(3): 259-64.

17. Eberl T, Jagoditsch M, Klingler A and Tschmelitsch J, Risk factors for anastomotic leakage after resection for rectal cancer. Am J Surg, 2008. 196(4): 592-8.

18. Gorissen K J, Benning D, Berghmans T, Snoeijs M G, Sosef M N, Hulsewe K W, et al., Risk of anastomotic leakage with non-steroidal anti-inflammatory drugs in colorectal surgery. Br J Surg, 2012. 99(5): 721-7.

19. Konishi T, Watanabe T, Kishimoto J and Nagawa H, Risk factors for anastomotic leakage after surgery for colorectal cancer: results of prospective surveillance. J Am Coll Surg, 2006. 202(3): 439-44.

20. Leichtle S W, Mouawad N J, Welch K B, Lampman R M and Cleary R K, Risk factors for anastomotic leakage after colectomy. Dis Colon Rectum, 2012. 55(5): 569-75.

21. Smith J D, Paty P B, Guillem J G, Temple L K, Weiser M R and Nash G M, Anastomotic leak is not associated with oncologic outcome in patients undergoing low anterior resection for rectal cancer. Ann Surg, 2012. 256(6): 1034-8.

22. Kobayashi M, Mohri Y, Ohi M, Inoue Y, Araki T, Okita Y, et al., Risk factors for anastomotic leakage and favorable antimicrobial treatment as empirical therapy for intra-abdominal infection in patients undergoing colorectal surgery. Surg Today, 2013.

23. Law W I, Chu K W, Ho J W and Chan C W, Risk factors for anastomotic leakage after low anterior resection with total mesorectal excision. Am J Surg, 2000. 179(2): 92-6.

24. Law W L, Choi H K, Lee Y M, Ho J W and Seto C L, Anastomotic leakage is associated with poor long-term outcome in patients after curative colorectal resection for malignancy. J Gastrointest Surg, 2007. 11(1): 8-15.

25. Park J S, Choi G S, Kim S H, Kim H R, Kim N K, Lee K Y, et al., Multicenter

analysis of risk factors for anastomotic leakage after laparoscopic rectal cancer excision: the Korean laparoscopic colorectal surgery study group. Ann Surg, 2013. 257(4): 665-71.

26. Trencheva K, Morrissey K P, Wells M, Mancuso C A, Lee S W, Sonoda T, et al., Identifying important predictors for anastomotic leak after colon and rectal resection: prospective study on 616 patients. Ann Surg, 2013. 257(1): 108-13.

27. Alves A, Panis Y, Trancart D, Regimbeau J M, Pocard M and Valleur P, Factors associated with clinically significant anastomotic leakage after large bowel resection: multivariate analysis of 707 patients. World J Surg, 2002. 26(4): 499-502.

28. Schrock T R, Deveney C W and Dunphy J E, Factor contributing to leakage of colonic anastomoses. Ann Surg, 1973. 177(5): 513-8.

29. Piecuch J, Wiewiora M, Jopek J, Szrot M, Mazur I, Zurawinski W, et al., Mortality and anastomotic leakage after anterior resection for rectal cancer. Hepatogastroenterology, 2012. 59(115): 721-3.

30. Makela J T, Kiviniemi H and Laitinen S, Risk factors for anastomotic leakage after left-sided colorectal resection with rectal anastomosis. Dis Colon Rectum, 2003. 46(5): 653-60.

31. Boccola M A, Buettner P G, Rozen W M, Siu S K, Stevenson A R, Stitz R, et al., Risk factors and outcomes for anastomotic leakage in colorectal surgery: a single-institution analysis of 1576 patients. World J Surg, 2011. 35(1): 186-95.

32. Telem D A, Chin E H, Nguyen S Q and Divino C M, Risk factors for anastomotic leak following colorectal surgery: a case-control study. Arch Surg, 2010. 145(4): 371-6; discussion 6.

33. Choi H K, Law W L and Ho J W, Leakage after resection and intraperitoneal anastomosis for colorectal malignancy: analysis of risk factors. Dis Colon Rectum, 2006. 49(11): 1719-25.

34. Slim K, Vicaut E, Panis Y and Chipponi J, Meta-analysis of randomized clinical trials of colorectal surgery with or without mechanical bowel preparation. Br J Surg, 2004. 91(9): 1125-30.

35. Slim K, Vicaut E, Launay-Savary M V, Contant C and Chipponi J, Updated systematic review and meta-analysis of randomized clinical trials on the role of mechanical bowel preparation before colorectal surgery. Ann Surg, 2009. 249(2): 203-9.

36. Van't Sant H P, Weidema W F, Hop W C, Oostvogel H J and Contant C M, The influence of mechanical bowel preparation in elective lower colorectal surgery. Ann Surg, 2010. 251(1): 59-63.

37. Cross K L, Rees J R, Soulsby R H and Dixon A R, Primary anastomosis without colonic lavage for the obstructed left colon. Ann R Coll Surg Engl, 2008. 90(4): 302-4.
38. David G G, Al-Sarira A A, Willmott S, Cade D, Corless D J and Slavin J P, Use of Hartmann's procedure in England. Colorectal Dis, 2009. 11(3): 308-12.
39. ReMine S G and Dozois R R, Hartmann's procedure. Its use with complicated carcinomas of sigmoid colon and rectum. Arch Surg, 1981. 116(5): 630-3.
40. Kube R, Granowski D, Stubs P, Mroczkowski P, Ptok H, Schmidt U, et al., Surgical practices for malignant left colonic obstruction in Germany. Eur J Surg Oncol, 2010. 36(1): 65-71.
41. Grundmann R T, Primary colon resection or Hartmann's procedure in malignant left-sided large bowel obstruction? The use of stents as a bridge to surgery. World J Gastrointest Surg, 2013. 5(1): 1-4.
42. Tan C J, Dasari B V and Gardiner K, Systematic review and meta-analysis of randomized clinical trials of self-expanding metallic stents as a bridge to surgery versus emergency surgery for malignant left-sided large bowel obstruction. Br J Surg, 2012. 99(4): 469-76.
43. Kapiteijn E, Kranenbarg E K, Steup W H, Taat C W, Rutten H J, Wiggers T, et al., Total mesorectal excision (TME) with or without preoperative radiotherapy in the treatment of primary rectal cancer. Prospective randomised trial with standard operative and histopathological techniques. Dutch ColoRectal Cancer Group. Eur J Surg, 1999. 165(5): 410-20.
44. Marijnen C A, Kapiteijn E, van de Velde C J, Martijn H, Steup W H, Wiggers T, et al., Acute side effects and complications after short-term preoperative radiotherapy combined with total mesorectal excision in primary rectal cancer: report of a multicenter randomized trial. J Clin Oncol, 2002. 20(3): 817-25.
45. Chang J S, Keum K C, Kim N K, Baik S H, Min B S, Huh H, et al., Preoperative Chemoradiotherapy Effects on Anastomotic Leakage After Rectal Cancer Resection: A Propensity Score Matching Analysis. Ann Surg, 2013.
46. Scheidbach H, Schneider C, Konradt J, Barlehner E, Kohler L, Wittekind C, et al., Laparoscopic abdominoperineal resection and anterior resection with curative intent for carcinoma of the rectum. Surg Endosc, 2002. 16(1): 7-13.
47. Guillou P J, Quirke P, Thorpe H, Walker J, Jayne D G, Smith A M, et al., Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet, 2005. 365(9472): 1718-26.
48. Veldkamp R, Kuhry E, Hop W C, Jeekel J, Kazemier G, Bonjer H J, et al.,

Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. Lancet Oncol, 2005. 6(7): 477-84.

49. Jayne D G, Guillou P J, Thorpe H, Quirke P, Copeland J, Smith A M, et al., Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC Trial Group. J Clin Oncol, 2007. 25(21): 3061-8.

50. Laurent C, Leblanc F, Wutrich P, Scheffler M and Rullier E, Laparoscopic versus open surgery for rectal cancer: long-term oncologic results. Ann Surg, 2009. 250(1): 54-61.

51. Kayano H, Okuda J, Tanaka K, Kondo K and Tanigawa N, Evaluation of the learning curve in laparoscopic low anterior resection for rectal cancer. Surg Endosc, 2011. 25(9): 2972-9.

52. van der Pas M H, Haglind E, Cuesta M A, Furst A, Lacy A M, Hop W C, et al., Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. Lancet Oncol, 2013. 14(3): 210-8.

53. Graffner H, Fredlund P, Olsson S A, Oscarson J and Petersson B G, Protective colostomy in low anterior resection of the rectum using the EEA stapling instrument. A randomized study. Dis Colon Rectum, 1983. 26(2): 87-90.

54. Pakkastie T E, Ovaska J T, Pekkala E S, Luukkonen P E and Jarvinen H J, A randomised study of colostomies in low colorectal anastomoses. Eur J Surg, 1997. 163(12): 929-33.

55. Koperna T, Cost-effectiveness of defunctioning stomas in low anterior resections for rectal cancer: a call for benchmarking. Arch Surg, 2003. 138(12): 1334-8; discussion 9.

56. Karanjia N D, Corder A P, Bearn P and Heald R J, Leakage from stapled low anastomosis after total mesorectal excision for carcinoma of the rectum. Br J Surg, 1994. 81(8): 1224-6.

57. Puleo S, Sofia M, Trovato M A, Pesce A, Portale T R, Russello D, et al., Ileocolonic anastomosis: preferred techniques in 999 patients. A multicentric study. Surg Today, 2012.

58. Choy P Y, Bissett I P, Docherty J G, Parry B R, Merrie A and Fitzgerald A, Stapled versus handsewn methods for ileocolic anastomoses. Cochrane Database Syst Rev, 2011(9): CD004320.

59. Kang J, Lee H B, Cha J H, Hur H, Min B S, Baik S H, et al., Feasibility and impact on surgical outcomes of modified double-stapling technique for patients undergoing laparoscopic anterior resection. J Gastrointest Surg, 2013. 17(4): 771-5.

60. Kim H J, Choi G S, Park J S and Park S Y, Comparison of intracorporeal

single-stapled and double-stapled anastomosis in laparoscopic low anterior resection for rectal cancer: a case-control study. Int J Colorectal Dis, 2013. 28(1): 149-56.

61. Hallbook O, Pahlman L, Krog M, Wexner S D and Sjodahl R, Randomized comparison of straight and colonic J pouch anastomosis after low anterior resection. Ann Surg, 1996. 224(1): 58-65.

62. Mehrvarz S, Towliat S M, Mohebbi H A, Derakhshani S and Abavisani M, Comparison of Colonic J-pouch and Straight Coloanal anastomosis after Low Anterior Resection. Iran Red Crescent Med J, 2013. 15(1): 32-5.

63. Steffen T, Tarantino I, Hetzer F H, Warschkow R, Lange J and Zund M, Safety and morbidity after ultra-low coloanal anastomoses: J-pouch vs end-to-end reconstruction. Int J Colorectal Dis, 2008. 23(3): 277-81.

64. Joo J S, Latulippe J F, Alabaz O, Weiss E G, Nogueras J J and Wexner S D, Long-term functional evaluation of straight coloanal anastomosis and colonic J-pouch: is the functional superiority of colonic J-pouch sustained? Dis Colon Rectum, 1998. 41(6): 740-6.

65. Seow-Choen F and Goh H S, Prospective randomized trial comparing J colonic pouch-anal anastomosis and straight coloanal reconstruction. Br J Surg, 1995. 82(5): 608-10.

66. Gertsch P, Baer H U, Kraft R, Maddern G J and Altermatt H J, Malignant cells are collected on circular staplers. Dis Colon Rectum, 1992. 35(3): 238-41.

67. Yajima K, Matsuo H, Kobayashi T, Ajioka Y and Hatakeyama K, Curative resection performed twice for circular-staple-line recurrence after colorectal carcinoma surgery: report of a case. Surg Today, 2007. 37(1): 61-5.

68. Fujii S, Yamamoto S, Ito M, Yamaguchi S, Sakamoto K, Kinugasa Y, et al., Short-term outcomes of laparoscopic intersphincteric resection from a phase II trial to evaluate laparoscopic surgery for stage 0/I rectal cancer: Japan Society of Laparoscopic Colorectal Surgery Lap RC. Surg Endosc, 2012. 26(11): 3067-76.

69. Tsujinaka S, Kawamura Y J, Tan K Y, Mizokami K, Sasaki J, Maeda T, et al., Proximal bowel necrosis after high ligation of the inferior mesenteric artery in colorectal surgery. Scand J Surg, 2012. 101(1): 21-5.

70. Corder A P, Karanjia N D, Williams J D and Heald R J, Flush aortic tie versus selective preservation of the ascending left colic artery in low anterior resection for rectal carcinoma. Br J Surg, 1992. 79(7): 680-2.

71. Hida J and Okuno K, High ligation of the inferior mesenteric artery in rectal cancer surgery. Surg Today, 2013. 43(1): 8-19.