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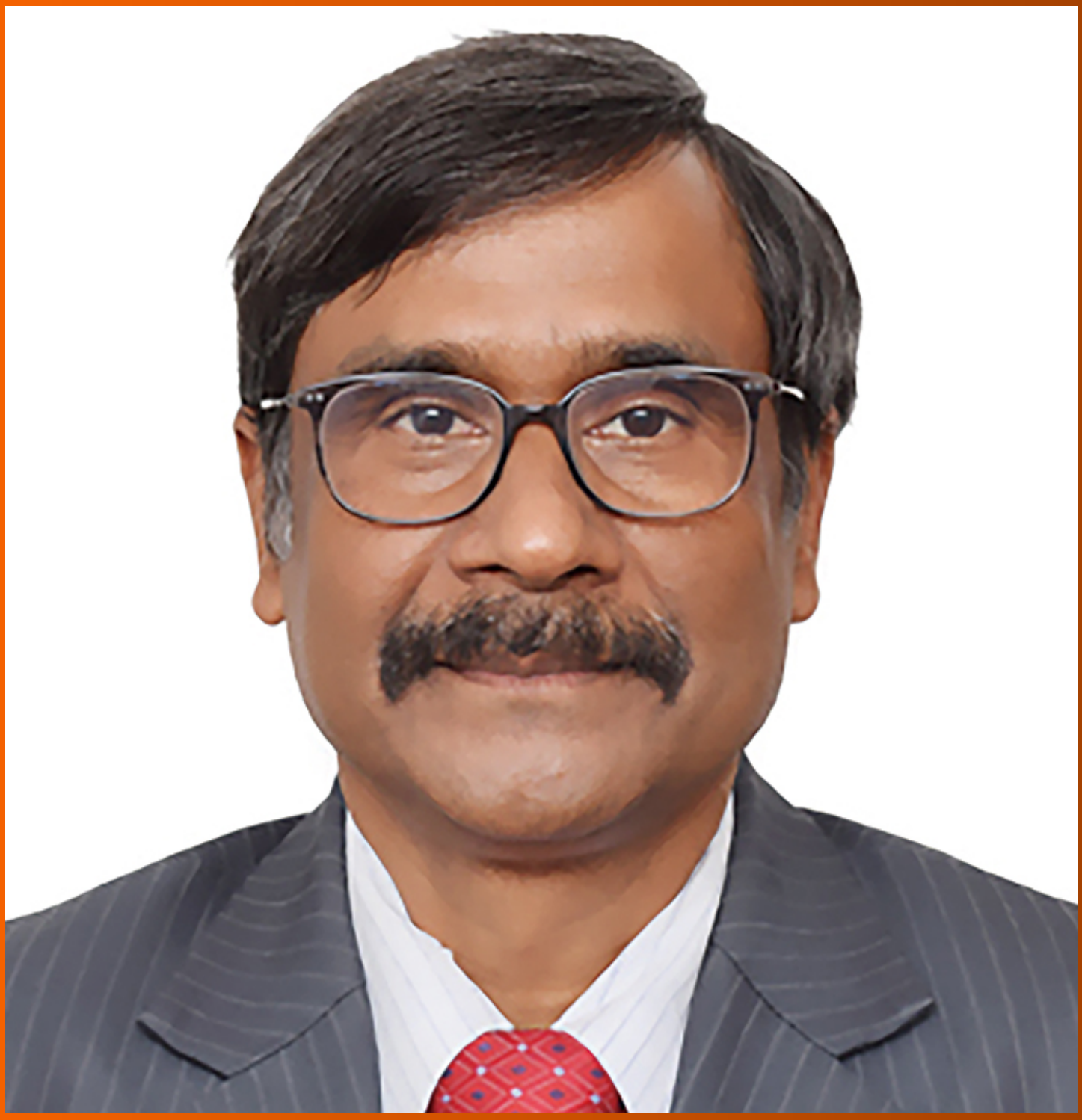

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REVIEW

Impact of anastomotic leakage on long-term prognosis after colorectal cancer surgery

Valeria Tonini, Manuel Zanni

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Valeria Tonini, Manuel Zanni, Department of Medical and Surgical Sciences, University of Bologna, Bologna 40138, Bologna, Italy

Corresponding author: Valeria Tonini, MD, PhD, Full Professor, Surgeon, Surgical Oncologist, Department of Medical and Surgical Sciences, University of Bologna, Via Massarenti 9, Bologna 40138, Bologna, Italy. valeria.tonini@unibo.it

Abstract

Colorectal cancer (CRC) is one of the most common malignancies in the world. Despite significant improvements in surgical technique, postoperative complications still occur in a fair percentage of patients undergoing colorectal surgery. The most feared complication is anastomotic leakage. It negatively affects short-term prognosis, with increased post-operative morbidity and mortality, higher hospitalization time and costs. Moreover, it may require further surgery with the creation of a permanent or temporary stoma. While there is no doubt about the negative impact of anastomotic dehiscence on the short-term prognosis of patients operated on for CRC, still under discussion is its impact on the long-term prognosis. Some authors have described an association between leakage and reduced overall survival, disease-free survival, and increased recurrence, while other Authors have found no real impact of dehiscence on long term prognosis. The purpose of this paper is to review all the literature about the impact of anastomotic dehiscence on long-term prognosis after CRC surgery. The main risk factors of leakage and early detection markers are also summarized.

Key Words: Anastomotic leakage; Colorectal surgery; Colon cancer; Rectal cancer; Long term prognosis; Long term survival

Core Tip: Colorectal cancer (CRC) is one of the most common malignancies in the world. Despite significant improvements in surgical technique, postoperative complications still occur in a fair percentage of patients undergoing colorectal surgery. The most feared complication is anastomotic leakage. It negatively affects short-term prognosis, with increased post-operative morbidity and mortality, higher hospitalization time and costs. Moreover, it may require further surgery with the creation of a permanent or temporary stoma. While there is no doubt about the negative impact of anastomotic dehiscence on the short-term prognosis of patients operated on for CRC, still under discussion is its impact on the long-term prognosis. Some authors have described an association between leakage and reduced overall survival, disease-free survival, and increased recurrence, while other authors have found no real impact of dehiscence on long term prognosis. The purpose of this paper is to review all the literature about the impact of anastomotic dehiscence on long-term prognosis after CRC surgery. The main risk factors of leakage and early detection markers are also summarized.

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INTRODUCTION

Definition, incidence and classification

Anastomotic leakage (AL) is a major cause of postoperative morbidity and mortality after colorectal cancer (CRC) surgery. AL is a defect of the intestinal wall integrity at the colorectal or colo-anal anastomosis site (including suture and staple lines of neorectal reservoirs) leading to a communication between the intra- and extraluminal compartments[1]. However, there are several definitions of AL in literature and most studies define it using clinical signs (pain, fever, tachycardia, peritonitis, purulent or fecal drainage), radiographic findings (fluid and/or gas-containing collections), and/or intraoperative features (peritoneal effusion and ruptured anastomosis)[1,2]. The use of different definitions in clinical studies can partly explain the considerable variations in AL reported rates. The incidence of AL reported in different studies is highly variable (2%-19%) and certainly influenced first of all by the surgeon's experience and the emergency or elective surgical setting. It is also influenced by the site of the anastomosis: It is lowest for ileocolic anastomoses (1%-3%) and highest for coloanal anastomoses (10%-20%)[3-5].

AL has been divided into "early" and "late" depending on whether AL is diagnosed within or after 30 d after surgery[6]. In general, early AL manifests with severe peritonitis and it is mainly related to a technical error in performing the anastomosis, usually due to mal vascularization of the intestinal stumps or tension at the anastomotic site[7]. In contrast, late AL is often associated with long-standing pelvic abscess[8] and is due to preexisting conditions in patients, such as local sepsis, poor nutrition, immunosuppression, morbid obesity, and radiation exposure[9].

AL is also classified according to severity into grade A, B and C. Grade A is represented by AL that does not require active therapeutic intervention, grade B by AL that requires active therapeutic intervention but manageable without re-laparotomy, and grade C by AL that requires re-laparotomy[1].

RISK FACTORS

Several risk factors for anastomotic dehiscence following colorectal surgery have been identified over the years. They can be classified for convenience into preoperative, intraoperative, and postoperative [10].

Preoperative risk factors commonly reported in the literature include male sex[7], obesity[11], tobacco habit, alcohol consumption, an American Society of Anaesthesiologistscore of 3 or higher[6], and prolonged corticosteroid intake[12]. Tumor location, size and stage must be considered among the risk factors. Akiyoshi *et al*[13] reported that tumor localization in the rectum, rather than the colon, was independently predictive of AL development on multivariate analysis.

The AL rate was 10 times higher (20.6% *vs* 2.3%) when the anastomotic region was located within 5 cm of the anal verge[14].

Low anterior resection (LAR) involves surgery in an anatomically confined space and when tumor size and/or stage increases, intrapelvic manipulation becomes limited and rectal dissection more challenging. In a series of 154 patients with rectal carcinoma, tumor size ≥ 5 cm in diameter was associated with a 4-fold increased risk of leakage[15]. Zhu *et al*[16] found that tumors greater than 3 cm

in diameter, as well as TNM stage, were independently associated with leakage.

Intraoperative risk factors include: The surgeon experience (and hospital size)[7], the number of linear stapler firings[7], left colic artery ligation[17], emergency surgery (patients with peritonitis and/or bowel obstruction are at higher risk of postoperative adverse events)[18], operative time[19] and blood loss during surgery. Intra-operatively, it is also important to ensure good vascularization of the anastomosed bowel segments. Indocyanine green (ICG) fluorescence angiography may help in this evaluation. In a recent meta-analysis, an incidence of anastomotic dehiscence was observed in 3.8% of cases in the ICG group and 7.8% in the control group in which ICG was not used[20].

Postoperative risk factors are anemia, hypoalbuminemia, and late initiation of enteral nutrition[21].

EARLY DETECTION AND MARKERS

Early detection of AL is crucial to treat patients limiting negative effects. Baeza-Murcia *et al*[22] analyzed the accuracy of C-reactive protein (CRP) and procalcitonin (PCT) for early detection of AL and have found that CRP is more accurate than PCT on both postoperative day (POD) 3 and 5. According to this study CRP measured on POD 5 is the most useful test for early diagnosis of AL and that values above 9.1 mg/dL are indicative of anastomotic dehiscence.

In a recent meta-analysis by Yeung *et al*[23] a CRP cutoff level of 14.8 mg/dL at POD 3 had a sensitivity and specificity of 95%, while CRP cut-off levels of 12.3 mg/dL at day 4, 11.5 mg/dL at day 5, 10.5 mg/dL at day 6, and 9.6 mg/dL at day 7 had a sensitivity and specificity of 100% for anastomotic dehiscence.

According to Garcia-Granero *et al*[24] and El Zaher *et al*[25], PCT is also a very good predictor of anastomotic dehiscence, particularly from POD 5 or higher. The predictive power of PCT may also be enhanced in combination with CRP or white blood cell, or both (area under the curve 0.92, 0.92, 0.93, respectively)[25]. A recent meta-analysis by Xu *et al*[26] shows that PCT at POD 3 has potential clinical value in the early diagnosis of AL and has better diagnostic accuracy in patients undergoing laparoscopic surgery. Cut-off values are recommended in the range of 0.7-1.3 ng/mL to ensure accurate diagnosis and safe discharge. However, PCT is a valid predictor only for patients with major clinical losses confirmed by radiology and presenting with severe clinical signs and symptoms that require a change in therapeutic management and in most cases a reintervention. Cousin *et al*[27] conducted a meta-analysis and concluded that PCT does not add value to CRP in the diagnosis of AL.

It can be said that CRP and PCT at POD 5 have a high negative predictive value, which would allow early and safe discharge.

Tavernier *et al*[28] considered 5 criteria for safe early discharge after laparoscopic colorectal surgery: A CRP level of less than 15 mg/dL, absence of fever during the entire hospital stay (temperature < 38 °C), return of bowel function (flatus with or without stool), adequate pain control with oral analgesics (pain less than 5 out of 10 on a 10-point visual analog scale) and tolerance of a solid diet. The negative predictive value in ruling out an anastomotic leak was 98.4% for all 5 criteria combined. The false-negative rate was 13.3%.

RELATIONSHIP BETWEEN AL AND SHORT-TERM PROGNOSIS

AL affects the outcome of surgery, worsening the short-term outcomes and increasing the time and cost of hospitalization[29,30]. The mortality related was reported to be between 0.8% and 27%[31]. Mortality was higher after leak from a colonic anastomosis than after leak from a rectal anastomosis (43.8% *vs* 7.1%)[31]. Bertelsen *et al*[32] found in a multicenter study a 4-fold increase in 30-d mortality in patients with AL[32]. According to a Cochrane review, AL is associated with a perioperative mortality rate of 2% to 24% and high morbidity, with the risk of a definitive ostomy exceeding 25%[33]. Warps *et al*[34] found an overall AL rate of 4.8%, ranging from 4.0% (right hemicolectomy) to 15.4% (subtotal colectomy). AL was predominantly managed with reintervention, ranging from 81.2% of cases after transversectomy to 92.4% after sigmoid resection. After reintervention, the highest mortality rates were observed for transversectomy (15.4%) and right hemicolectomy (14.4%) and the lowest for sigmoid resection (5.6%) and subtotal colectomy (5.9%). The intensive care unit admission rate was 62.6% overall (range 56.7%-69.2%) and the stoma rate ranged from 65.5% (right hemicolectomy) to 93.0% (sigmoid resection).

RELATIONSHIP BETWEEN AL AND LONG -TERM PROGNOSIS

While the short-term consequences of AL are well known, its impact on long-term prognosis in CRC patients is still debated.

In the literature, the first authors to concern themselves with outcomes related to anastomotic dehiscence after resective surgery for CRC were Phillips *et al*[35] and Sauven *et al*[36]. In both cases, the parameter evaluated was local recurrence (LR). In the first study, AL did not appear among the significant risk factors for recurrence, while in the second, anastomotic dehiscence was associated with an increased rate of LR. In the same years, Amato *et al*[37] evaluated the association between CRC and AL by focusing exclusively on patients with rectal tumors operated with an anterior resection. In this study, AL did not influence the recurrence rate.

In 1991, Akyol *et al*[38] performed a study on patients operated for left colon or rectal cancer and demonstrated an important influence of AL on recurrence and cancer-specific survival (CSS) at 24 mo. The independence of the impact of dehiscence on outcomes from tumor stage was highlighted. This was the first study that analyzed local and distant recurrence separately and used multivariate Cox regression.

Two years later, a study published by Fujita *et al*[39] showed the impact of AL on LR and disease-free survival (DFS). DFS is significantly lower in the AL group for patients with Duke stage A and B cancers but not for C and D. The importance of this work also lies in the separate evaluation of subjects with colon and rectal cancer.

Petersen *et al*[40] studied the influence of leakage on LR, CSS, overall survival (OS) and postoperative mortality. AL influence only LR and CSS, confirming the previous findings of Akyol *et al*[38]. Branagan *et al*[41] reached similar conclusions in 2005. Further studies[42-44] showed a correlation between AL and higher 30-d mortality, lower OS and CSS.

Law *et al*[45] in 2007 found a significant association between AL and 5-year CSS, 30-d mortality and recurrence (local and systemic).

According to the study by Eberhardt *et al*[46], AL does not change the risk of recurrence and mortality for colon cancer, whereas it does for rectal cancer. The article also offers an assessment of OS, CSS, LR and overall recurrence for each stage, as well as an analysis of these outcomes at both 1 and 5 years after surgery.

According to Marra *et al*[47], AL significantly reduces OS without affecting the risk of recurrence, while other studies[48-58] have found an impact of leakage on OS, recurrence, and DFS. However, Katoh *et al*[50] evaluated only patients with stage II CRC and Breugom *et al*[54] only patients with stage I-III colon cancer. To be precise, Park *et al*[56] in 2016 found an effect of AL on OS and DFS only for patients with rectal cancer. Nachiappan *et al*[52] found a reduction in OS in patients with AL who required reoperation compared with subjects without AL. Ramphal *et al*[58] demonstrated that LR develops with the same frequency in symptomatic and asymptomatic dehiscence.

Krarup *et al*[59-60] identified in patients with AL an increase in distant recurrence (DR) and in mortality. However, there was no significant association with LR. Nordholm-Carstensen *et al*[61] and Ng *et al*[62] evaluated the impact of AL in patients with stage IV CRC. The 3-year survival rate is affected by dehiscence for both colon (18.7% *vs* 44.6%) and rectum (53.7% *vs* 73.3%).

The first meta-analysis on this topic was performed by Mirnezami *et al*[63] on 22 studies. It reported an association between AL and LR, DR and cancer-specific mortality.

The subsequent meta-analysis by Ha *et al*[64] evaluated 34 studies and divided the results into two categories. In the first group rectal anastomosis data were analyzed, and AL was associated with increased LR and reduced OS, CSS, and DFS. There were no significant effect on distant recurrence. In the second group colic anastomoses were analyzed and AL was associated with reduced OS and DFS and there was no correlation with local or distant recurrence.

The studies by Sammour *et al*[65] and Goto *et al*[66] also analyzed CSS. They showed a significant reduction in 5-year OS for patients with AL, without finding differences in LR, CSS and postoperative mortality (in rectal carcinoma, leakage affects only the latter). The second one documented instead a reduction in OS (80. 8% *vs* 90.3%) and CSS (89.6% *vs* 95.1%), an increase in LR and no correlation with distant recurrence.

A subsequent meta-analysis conducted in 2020 by Bashir Mohamed *et al*[67] demonstrated a lack of significant effect of AL on recurrences, however it reduced OS, DFS and CSS.

Recent articles on this topic were written by Stormark *et al*[68] and Kryzauskas *et al*[69]. The former concluded that leakage only after surgery for stage III CRC is able to reduce survival, whereas the latter demonstrated that AL impaired disease-free and OS in patients undergoing sigmoid and rectal surgery.

Regarding rectal cancer alone, the first data of the new millennium showed an increase in LR and a decrease in CSS[70,71]. Subsequent studies can be divided into 3 categories. In the first group, there are studies that supported the absence of an impact of AL on cancer outcomes such as OS, CSS, DFS, LR and DR[72-79]. The second group covers studies defining AL as an independent prognostic factor for reduced OS, CSS, DFS and increased recurrence[80-83]. In the third group, we can place studies[84-88] midway between the first two categories, as the study of Noh *et al*[88], demonstrating that AL is associated with increased LR and reduced DFS, whereas its relationship with OS and distant recurrence is not significant. These findings were confirmed in a recent study by Peltrini *et al*[89].

To the above groups, we must also add studies evaluating also perioperative mortality. Ptok *et al*[90] and Hain *et al*[91] found an impact of dehiscence on 30-d mortality, DFS, and LR, whereas Eriksen *et al* [92] and Bertelsen *et al*[32] found an increase in 30-d mortality, but without a significant increase in LR. Bertelsen *et al*[32] also noted the lack of reduction in OS and impact on distant recurrence[32].

Lim *et al*[93] in 2015 classified ALs into 3 categories based on the consequences: (1) Generalized peritonitis; (2) Localized peritonitis with or without abscess; and (3) Fistula. Oncologic outcomes were evaluated separately for each type and reduced OS and LRFS (LR-free survival) were identified. According to Boström *et al*[94], leaks only impact OS if they require intervention.

In 2022, Dulskas *et al*[95] evaluated AL in patients undergoing right colectomy for CRC and concluded that AL is a factor that negatively affects long term prognosis. In contrast, a Dutch retrospective study found that disease recurrence is not associated with AL after CRC resection[96].

Koedam *et al*[97], analyzing data from the COLOR and COLOR II studies, show that ALs after rectal cancer surgery are associated with an increased rate of LR and a decreased DFS at 5-year follow-up. DR and OS are not significantly affected. Regarding colon cancer surgery, no significant effect of AL on long-term oncologic outcomes was observed, presumably because of a relatively low leakage rate. Strengths of this study include the randomized, multicenter design of the two included studies[98,99] and uniform study protocol for perioperative care and follow-up to limit practice variability.

All studies on this topic are summarized in Table 1.

CONCLUSION

AL appears to be an independent risk factor influencing long-term oncologic outcomes after rectal cancer surgery. On the other hand, regarding colon cancer, the results are still extremely heterogeneous and unclear. Further studies on patients undergoing resection for CRC are needed to confirm the oncological impact of AL.

Based on these data, we would recommend more frequent follow-up for patients with AL after CRC cancer surgery.

Table 1 Summary table of all studies reporting on anastomotic leakage and outcomes after colorectal cancer surgery

Ref.	Study	Period	Cancer	Patients	LR	DR	OS	CSS	DFS	30 d mortality	Follow-up (mo)	Stage	Leak's definition	AL rate (%)	LR rate (%)	Multivariate analysis
Phillips *et al* [35], 1984	PCS	1976-1980	C + R	1627	Yes	No	No	No	No	No	≥ 60	I, II, III	NR	8	14	No
Sauven *et al* [36], 1989	RCS	1978-1981	C + R	53	Yes	No	No	No	No	No	36	I, II, III, IV	Clin, Rad	19	13	No
Amato *et al* [37], 1991	PCS	1981-1995	R	78	Yes	No	No	No	No	No	≥ 24	I, II, III	Clin, Rad	17	12	No
Akyol *et al* [38], 1991	RCS	1985-1989	C + R	167	Yes	Yes	No	Yes	No	No	25	I, II, III, IV	Clin, Rad	19	18	Yes
Fujita *et al* [39], 1993	PCS	1970-1991	C/R	980	Yes	Yes	No	No	Yes	No	NR	I, II, III, IV	Clin, Rad	3	3	Yes
Pakkastie *et al*[100], 1995	PCS	1981-1990	R	116	Yes	No	Yes	No	Yes	No	48	I, II, III	Clin, Rad	16	28	No
Petersen *et al* [40], 1998	RCS	1985-1995	C + R	331	Yes	No	Yes	Yes	No	Yes	32	I, II, III, IV	Clin	8	9	Yes
Merkel *et al* [70], 2001	RCS	1978-1996	R	814	Yes	No	No	Yes	No	No	90	I, II, III	Clin	11	14	Yes
Bell *et al* [101], 2003	PCS	1971-1991	R	401	Yes	No	No	No	No	No	≥ 60	I, II, III	Clin, Rad	13	12	Yes
Law *et al* [102], 2004	PCS	1993-2002	R	622	Yes	No	No	Yes	No	No	39, 6	I, II, III	Clin, Rad, Endo	6	10	Yes
Walker *et al* [43], 2004	PCS	1971-1999	C + R	1722	No	No	Yes	No	No	No	≥ 60	I, II, III	Clin, Rad	5	NR	Yes
Branagan *et al*[41], 2005	PCS	1991-1995	C/R	1834	Yes	No	Yes	No	No	No	≥ 60	I, II, III	Clin, Rad	4	10	Yes
Eriksen *et al* [92], 2005	PCS	1993-1999	R	1958	Yes	No	Yes	No	No	Yes	45	I, II, III	Clin, Rad	12	11	Yes
McArdle *et al* [42], 2005	PCS	1991-1994	C + R	2235	No	No	Yes	Yes	No	Yes	≥ 60	I, II, III	Clin, Rad	4	NR	Yes

Choi *et al* [44], 2006	PCS	1996-2004	C + R	1417	No	No	Yes	No	No	No	NR	I, II, III, IV	Clin, Rad	2	NR	Yes
Ptok *et al*[90], 2007	RCS	2000-2001	R	2044	Yes	No	No	No	Yes	Yes	40	I, II, III	Clin, Rad, Endo	15	6	Yes
Law *et al*[45], 2007	PCS	1996-2004	C + R	1580	Yes	Yes	No	Yes	No	Yes	46	I, II, III, IV	Clin, Rad	4	6	Yes
Jung *et al* [71], 2008	RCS	1997-2003	R	1391	No	No	Yes	Yes	No	No	40	I, II, III	Clin, Rad	3	10	No
Lee *et al*[79], 2008	PCS	1996-2004	R	1278	Yes	No	Yes	No	Yes	No	45	I, II, III, IV	Clin, Rad, Endo	4	NR	Yes
den Dulk *et al* [87], 2009	RCS	1987-2002	R	2726	Yes	Yes	Yes	Yes	Yes	No	71	I, II, III	Clin, Rad, Endo	10	9	Yes
Eberhardt *et al*[46], 2009	PCS	1979-2007	C/R	468	Yes	Yes	Yes	Yes	No	No	94	I, II, III	Clin, Rad	33	6	Yes
Marra *et al* [47], 2009	RCS	1991-2004	C	440	Yes	Yes	Yes	No	No	Yes	63	I, II, III	Clin, Rad	3	6	No
Bertelsen *et al* [32], 2010	PCS	2001-2004	R	1494	Yes	Yes	Yes	No	No	Yes	45	I, II, III	Clin, Rad, Endo	11	7	Yes
Kube *et al* [48], 2010	PCS	2000-2004	C	28271	No	No	Yes	No	Yes	Yes	23	NR	Clin, Rad	3	NR	No
Boccola *et al* [49], 2011	PCS	1984-2004	C + R	1576	No	No	Yes	Yes	Yes	No	67	I, II, III, IV	Clin, Rad	7	NR	Yes
Jörgren *et al* [72], 2011	PCS	1995-1997	R	250	Yes	Yes	Yes	Yes	No	Yes	≥ 60	I, II, III	Clin, Rad, Endo	9	8	Yes
Katoh *et al* [50], 2011	RCS	1990-2000	C/R	207	No	No	No	No	Yes	No	116	II	Clin, Rad	6	NR	Yes
Lin *et al*[80], 2011	PCS	1993-2003	R	999	Yes	Yes	Yes	Yes	Yes	Yes	≥ 60	I, II, III	Clin, Rad	5	5	Yes
Smith *et al* [73], 2012	RCS	1991-2010	R	1127	Yes	No	Yes	Yes	No	Yes	74	I, II, III	Clin, Rad	4	5	Yes
Smith *et al* [103], 2013	RCS	1992-2010	R	184	Yes	No	Yes	Yes	No	No	30	IV	Clin, Rad	7	13	Yes
Krarup *et al* [59], 2014	RCS	2001-2008	C	8589	Yes	Yes	Yes	No	No	No	≥ 60	I, II, III	Clin, Rad	6	10	Yes
Bakker *et al* [104], 2014	RCS	2009-2011	C	15667	No	No	No	No	No	Yes	NR	I, II, III, IV	Clin, Rad	8	NR	Yes
Jäger *et al* [81], 2015	RCS	2003-2010	R	108	No	No	Yes	Yes	Yes	No	70	I, II, III	Clin, Rad	18	NR	Yes
Ke *et al*[78], 2015	RCS	2007-2011	R	653	Yes	Yes	No	No	Yes	No	47	I, II, III, IV	Clin, Rad	6	4	Yes
Ebinger *et al* [74], 2015	RCS	1991-2010	R	584	Yes	Yes	Yes	Yes	No	No	62	I, II, III	Clin, Rad, Endo	11	17	Yes
Jannasch *et al* [84], 2015	PCS	2000-2010	R	17867	Yes	No	Yes	No	Yes	No	30	I, II, III	Clin, Rad	12	9	Yes
Nachiappan *et al*[52], 2015	PCS	2004-2013	C + R	1048	Yes	Yes	Yes	No	Yes	No	40	I, II, III, IV	Clin, Rad	9	2	Yes
Kang *et al* [82], 2015	RCS	2006-2009	R	1083	Yes	No	Yes	No	Yes	Yes	54	I, II, III	Clin, Rad	6	2	Yes
Kulu *et al* [85], 2015	RCS	2002-2011	R	570	Yes	No	Yes	No	No	No	56	I, II, III	Clin, Rad, Endo	9	4	Yes
Krarup *et al* [60], 2015	RCS	2001-2008	C	8597	No	No	No	No	No	Yes	≥ 60	I, II, III	Clin, Rad	6	NR	Yes
Lim *et al*[93], 2015	RCS	2007-2011	R	2510	No	No	Yes	No	No	No	33	I, II, III, IV	Clin	6	NR	Yes
Kim *et al*[53], 2015	RCS	2008-2013	C + R	809	Yes	Yes	Yes	No	No	Yes	NR	I, II, III	Clin, Rad	4	4	Yes

Espín *et al* [77], 2015	RCS	2006-2008	R	1181	Yes	No	Yes	Yes	No	Yes	60	I, II, III	Clin	9	5	Yes
Breugom *et al* [54], 2016	RCS	2006-2008	C	761	No	No	Yes	No	Yes	No	60	I, II, III	NR	5	NR	Yes
Park *et al* [56], 2016	RCS	2000-2011	C/R	10477	Yes	Yes	Yes	No	Yes	Yes	45	I, II, III, IV	Clin, Rad	3	2	Yes
Sammour *et al*[65], 2018	PCS	1988-2015	C/R	4892	Yes	No	Yes	Yes	No	Yes	60	I, II, III, IV	Clin, Rad	4	C = 5/R = 2	Yes
Noh *et al*[88], 2016	RCS	2006-2012	R	1258	Yes	Yes	Yes	No	Yes	No	50	I, II, III, IV	Clin, Rad	8	5	Yes
Nordholm *et al*[61], 2017	RCS	2009-2013	C/R	774	No	No	Yes	No	No	Yes	36	IV	Clin, Rad	9	NR	Yes
Goto *et al* [66], 2017	RCS	2007-2008	C	3364	Yes	Yes	Yes	Yes	No	Yes	96	I, II, III, IV	Clin, Rad	3	1	Yes
Hain *et al* [91], 2017	RCS	2005-2014	R	428	Yes	No	No	No	No	Yes	40	I, II, III, IV	Clin, Rad	28	8	Yes
Hüttner *et al* [51], 2018	RCS	2001-2014	C	628	No	No	Yes	No	Yes	No	60	I, II, III	Rad	4	NR	Yes
Voron *et al* [57], 2019	RCS	1990-2015	C	1025	No	No	Yes	No	Yes	No	60	I, II, III, IV	Clin, Rad	4	NR	Yes
Boström *et al* [94], 2018	RCS	2007-2016	R	6948	No	No	Yes	No	No	No	60	I, II, III, IV	NR	10	NR	Yes
Ng *et al*[62], 2018	RCS	2002-2015	C + R	843	No	No	Yes	No	No	Yes	150	I, II, III, IV	Clin, Rad	6	NR	Yes
Ramphal *et al* [58], 2018	RCS	2005-2015	C + R	1984	Yes	Yes	Yes	No	Yes	Yes	48	I, II, III, IV	Clin, Rad	8	2	Yes
Furnée *et al* [86], 2019	RCS	2011	R	746	Yes	Yes	Yes	No	Yes	Yes	42	I, II, III	Rad	14	4	Yes
Allaix *et al* [83], 2020	RCS	1998-2013	R	532	Yes	Yes	Yes	No	Yes	No	80	I, II, III	Clin, Rad	8	6	Yes
Zimmermann *et al*[55], 2019	RCS	2001-2014	C + R	1122	Yes	Yes	Yes	No	Yes	No	63	I, II, III, IV	NR	8	1	Yes
Jang *et al*[76], 2019	RCS	2000-2013	R	698	Yes	Yes	Yes	Yes	Yes	No	48	I, II, III	Clin, Rad	7	17	Yes
Crippa *et al* [75], 2020	RCS	2000-2013	R	787	Yes	No	Yes	Yes	Yes	No	64	I, II, III, IV	Clin, Rad	5	2	Yes
Kryzauskas *et al*[69], 2020	PCS	2014-2018	C/R	900	No	No	Yes	No	Yes	Yes	NR	I, II, III, IV	Clin, Rad, Endo	C = 5/R = 11	NR	Yes
Dulskas *et al* [95], 2022	RCS	2014-2018	C	488	No	No	Yes	No	No	No	48	I, II, III, IV	Clin, Rad, Endo	5	NR	Yes
Arron *et al* [96], 2022	RCS	2008-2018	C/R	88154	No	No	No	Yes	Yes	No	NR	I, II, III, IV	Clin, Rad	C = 5/R = 8	NR	Yes
Koedam *et al* [97], 2022	RCS	1997-2010	C/R	1832	Yes	Yes	Yes	No	Yes	No	60	I, II, III (No T4)	Clin, Rad	C = 3/R = 11	C = 15/R = 13	Yes
Peltrini *et al* [89], 2022	RCS	2011-2017	R	367	Yes	Yes	Yes	No	Yes	No	60	I, II, III, IV	Clin, Rad, Endo	17	23	Yes

AL: Anastomotic leakage; LR: Local recurrence; DR: Distant recurrence; OS: Overall survival; CSS: Cancer-specific survival; DFS: Disease-free survival; PCS: Prospective cohort study; RCS: Retrospective cohort study; C: Colon cancer; R: rectal cancer; C + R: Colon and rectal cancer analyzed together; C/R: Colon and rectal cancer analyzed separately; NR: Not reported; Clin: Clinical; Rad: Radiological; Endo: Endoscopic.

FOOTNOTES

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Country/Territory of origin: Italy

ORCID number: Valeria Tonini 0000-0003-3130-2928; Manuel Zanni 0000-0001-7732-7739.

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REFERENCES

1 **Rahbari NN**, Weitz J, Hohenberger W, Heald RJ, Moran B, Ulrich A, Holm T, Wong WD, Tiret E, Moriya Y, Laurberg S, den Dulk M, van de Velde C, Büchler MW. Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. *Surgery* 2010; **147**: 339-351 [PMID: 20004450 DOI: 10.1016/j.surg.2009.10.012]

2 **Bruce J**, Krukowski ZH, Al-Khairy G, Russell EM, Park KG. Systematic review of the definition and measurement of anastomotic leak after gastrointestinal surgery. *Br J Surg* 2001; **88**: 1157-1168 [PMID: 11531861 DOI: 10.1046/j.0007-1323.2001.01829.x]

3 **Phitayakorn R**, Delaney CP, Reynolds HL, Champagne BJ, Heriot AG, Neary P, Senagore AJ; International Anastomotic Leak Study Group. Standardized algorithms for management of anastomotic leaks and related abdominal and pelvic abscesses after colorectal surgery. *World J Surg* 2008; **32**: 1147-1156 [PMID: 18283511 DOI: 10.1007/s00268-008-9468-1]

4 **Hyman N**, Manchester TL, Osler T, Burns B, Cataldo PA. Anastomotic leaks after intestinal anastomosis: it's later than you think. *Ann Surg* 2007; **245**: 254-258 [PMID: 17245179 DOI: 10.1097/01.sla.0000225083.27182.85]

5 **Crafa F**, Smolarek S, Missori G, Shalaby M, Quaresima S, Noviello A, Cassini D, Ascenzi P, Franceschilli L, Delrio P, Baldazzi G, Giampiero U, Megevand J, Maria Romano G, Sileri P. Transanal Inspection and Management of Low Colorectal Anastomosis Performed With a New Technique: the TICRANT Study. *Surg Innov* 2017; **24**: 483-491 [PMID: 28514887 DOI: 10.1177/1553350617709182]

6 **Yang SY**, Han YD, Cho MS, Hur H, Min BS, Lee KY, Kim NK. Late anastomotic leakage after anal sphincter saving surgery for rectal cancer: is it different from early anastomotic leakage? *Int J Colorectal Dis* 2020; **35**: 1321-1330 [PMID: 32372379 DOI: 10.1007/s00384-020-03608-9]

7 **Park JS**, Choi GS, Kim SH, Kim HR, Kim NK, Lee KY, Kang SB, Kim JY, Kim BC, Bae BN, Son GM, Lee SI, Kang H. Multicenter analysis of risk factors for anastomotic leakage after laparoscopic rectal cancer excision: the Korean laparoscopic colorectal surgery study group. *Ann Surg* 2013; **257**: 665-671 [PMID: 23333881 DOI: 10.1097/SLA.0b013e31827b8ed9]

8 **Lim SB**, Yu CS, Kim CW, Yoon YS, Park IJ, Kim JC. Late anastomotic leakage after low anterior resection in rectal cancer patients: clinical characteristics and predisposing factors. *Colorectal Dis* 2016; **18**: O135-O140 [PMID: 26888300 DOI: 10.1111/codi.13300]

9 **Sparreboom CL**, van Groningen JT, Lingsma HF, Wouters MWJM, Menon AG, Kleinrensink GJ, Jeekel J, Lange JF; Dutch ColoRectal Audit group. Different Risk Factors for Early and Late Colorectal Anastomotic Leakage in a Nationwide Audit. *Dis Colon Rectum* 2018; **61**: 1258-1266 [PMID: 30239395 DOI: 10.1097/DCR.0000000000001202]

10 **Sciuto A**, Merola G, De Palma GD, Sodo M, Pirozzi F, Bracale UM, Bracale U. Predictive factors for anastomotic leakage after laparoscopic colorectal surgery. *World J Gastroenterol* 2018; **24**: 2247-2260 [PMID: 29881234 DOI: 10.3748/wjg.v24.i21.2247]

11 **Nugent TS**, Kelly ME, Donlon NE, Fahy MR, Larkin JO, McCormick PH, Mehigan BJ. Obesity and anastomotic leak rates in colorectal cancer: a meta-analysis. *Int J Colorectal Dis* 2021; **36**: 1819-1829 [PMID: 33796958 DOI: 10.1007/s00384-021-03909-7]

12 **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**: O154-O160 [PMID: 24215329 DOI: 10.1111/codi.12490]

13 **Akiyoshi T**, Watanabe T, Ueno M. Risk factors for and long-term outcomes of anastomotic leakage after colorectal cancer surgery. *World J Surg* 2011; **35**: 1689-90; author reply 1691 [PMID: 21290123 DOI: 10.1007/s00268-011-0973-2]

14 **Choi DH**, Hwang JK, Ko YT, Jang HJ, Shin HK, Lee YC, Lim CH, Jeong SK, Yang HK. Risk factors for anastomotic leakage after laparoscopic rectal resection. *J Korean Soc Coloproctol* 2010; **26**: 265-273 [PMID: 21152228 DOI: 10.3393/jksc.2010.26.4.265]

15 **Kawada K**, Hasegawa S, Hida K, Hirai K, Okoshi K, Nomura A, Kawamura J, Nagayama S, Sakai Y. Risk factors for anastomotic leakage after laparoscopic low anterior resection with DST anastomosis. *Surg Endosc* 2014; **28**: 2988-2995 [PMID: 24853855 DOI: 10.1007/s00464-014-3564-0]

16 **Zhu QL**, Feng B, Lu AG, Wang ML, Hu WG, Li JW, Mao ZH, Zheng MH. Laparoscopic low anterior resection for rectal

carcinoma: complications and management in 132 consecutive patients. *World J Gastroenterol* 2010; **16**: 4605-4610 [PMID: 20857534 DOI: 10.3748/wjg.v16.i36.4605]

17 **Hinoi T**, Okajima M, Shimomura M, Egi H, Ohdan H, Konishi F, Sugihara K, Watanabe M. Effect of left colonic artery preservation on anastomotic leakage in laparoscopic anterior resection for middle and low rectal cancer. *World J Surg* 2013; **37**: 2935-2943 [PMID: 24005279 DOI: 10.1007/s00268-013-2194-3]

18 **Sánchez-Guillén L**, Frasson M, García-Granero Á, Pellino G, Flor-Lorente B, Álvarez-Sarrado E, García-Granero E. Risk factors for leak, complications and mortality after ileocolic anastomosis: comparison of two anastomotic techniques. *Ann R Coll Surg Engl* 2019; **101**: 571-578 [PMID: 31672036 DOI: 10.1308/rcsann.2019.0098]

19 **Silva-Velazco J**, Stocchi L, Costedio M, Gorgun E, Kessler H, Remzi FH. Is there anything we can modify among factors associated with morbidity following elective laparoscopic sigmoidectomy for diverticulitis? *Surg Endosc* 2016; **30**: 3541-3551 [PMID: 26541732 DOI: 10.1007/s00464-015-4651-6]

20 **Liu D**, Liang L, Liu L, Zhu Z. Does intraoperative indocyanine green fluorescence angiography decrease the incidence of anastomotic leakage in colorectal surgery? A systematic review and meta-analysis. *Int J Colorectal Dis* 2021; **36**: 57-66 [PMID: 32944782 DOI: 10.1007/s00384-020-03741-5]

21 **Sripathi S**, Khan MI, Patel N, Meda RT, Nuguru SP, Rachakonda S. Factors Contributing to Anastomotic Leakage Following Colorectal Surgery: Why, When, and Who Leaks? *Cureus* 2022; **14**: e29964 [PMID: 36381751 DOI: 10.7759/cureus.29964]

22 **Baeza-Murcia M**, Valero-Navarro G, Pellicer-Franco E, Soria-Aledo V, Mengual-Ballester M, Garcia-Marin JA, Betoret-Benavente L, Aguayo-Albasini JL. Early diagnosis of anastomotic leakage in colorectal surgery: prospective observational study of the utility of inflammatory markers and determination of pathological levels. *Updates Surg* 2021; **73**: 2103-2111 [PMID: 34018141 DOI: 10.1007/s13304-021-01082-8]

23 **Yeung DE**, Peterknecht E, Hajibandeh S, Torrance AW. C-reactive protein can predict anastomotic leak in colorectal surgery: a systematic review and meta-analysis. *Int J Colorectal Dis* 2021; **36**: 1147-1162 [PMID: 33555423 DOI: 10.1007/s00384-021-03854-5]

24 **Garcia-Granero A**, Frasson M, Flor-Lorente B, Blanco F, Puga R, Carratalá A, Garcia-Granero E. Procalcitonin and C-reactive protein as early predictors of anastomotic leak in colorectal surgery: a prospective observational study. *Dis Colon Rectum* 2013; **56**: 475-483 [PMID: 23478615 DOI: 10.1097/DCR.0b013e31826ce825]

25 **El Zaher HA**, Ghareeb WM, Fouad AM, Madbouly K, Fathy H, Vedin T, Edelhamre M, Emile SH, Faisal M. Correction to: Role of the triad of procalcitonin, C-reactive protein, and white blood cell count in the prediction of anastomotic leak following colorectal resections. *World J Surg Oncol* 2022; **20**: 64 [PMID: 35232431 DOI: 10.1186/s12957-022-02540-2]

26 **Xu Z**, Zong R, Zhang Y, Chen J, Liu W. Diagnostic accuracy of procalcitonin on POD3 for the early diagnosis of anastomotic leakage after colorectal surgery: A meta-analysis and systematic review. *Int J Surg* 2022; **100**: 106592 [PMID: 35257965 DOI: 10.1016/j.ijsu.2022.106592]

27 **Cousin F**, Ortega-Deballon P, Bourredjem A, Doussot A, Giaccaglia V, Fournel I. Diagnostic Accuracy of Procalcitonin and C-reactive Protein for the Early Diagnosis of Intra-abdominal Infection After Elective Colorectal Surgery: A Meta-analysis. *Ann Surg* 2016; **264**: 252-256 [PMID: 27049766 DOI: 10.1097/SLA.0000000000001545]

28 **Tavernier C**, Flaris AN, Passot G, Glehen O, Kepenekian V, Cotte E. Assessing Criteria for a Safe Early Discharge After Laparoscopic Colorectal Surgery. *JAMA Surg* 2022; **157**: 52-58 [PMID: 34730770 DOI: 10.1001/jamasurg.2021.5551]

29 **Paun BC**, Cassie S, MacLean AR, Dixon E, Buie WD. Postoperative complications following surgery for rectal cancer. *Ann Surg* 2010; **251**: 807-818 [PMID: 20395841 DOI: 10.1097/SLA.0b013e3181dae4ed]

30 **Ashraf SQ**, Burns EM, Jani A, Altman S, Young JD, Cunningham C, Faiz O, Mortensen NJ. The economic impact of anastomotic leakage after anterior resections in English NHS hospitals: are we adequately remunerating them? *Colorectal Dis* 2013; **15**: e190-e198 [PMID: 23331871 DOI: 10.1111/codi.12125]

31 **Thornton M**, Joshi H, Vimalachandran C, Heath R, Carter P, Gur U, Rooney P. Management and outcome of colorectal anastomotic leaks. *Int J Colorectal Dis* 2011; **26**: 313-320 [PMID: 21107847 DOI: 10.1007/s00384-010-1094-3]

32 **Bertelsen CA**, Andreasen AH, Jørgensen T, Harling H; Danish Colorectal Cancer Group. Anastomotic leakage after anterior resection for rectal cancer: risk factors. *Colorectal Dis* 2010; **12**: 37-43 [PMID: 19175624 DOI: 10.1111/j.1463-1318.2008.01711.x]

33 **Wallace B**, Schuepbach F, Gaukel S, Marwan AI, Staerkle RF, Vuille-Dit-Bille RN. Evidence according to Cochrane Systematic Reviews on Alterable Risk Factors for Anastomotic Leakage in Colorectal Surgery. *Gastroenterol Res Pract* 2020; **2020**: 9057963 [PMID: 32411206 DOI: 10.1155/2020/9057963]

34 **Warps AK**, Dekker JWT, Tanis PJ, Tollenaar RAEM. An evaluation of short-term outcomes after reoperations for anastomotic leakage in colon cancer patients. *Int J Colorectal Dis* 2022; **37**: 113-122 [PMID: 34559290 DOI: 10.1007/s00384-021-03996-6]

35 **Phillips RK**, Hittinger R, Blesovsky L, Fry JS, Fielding LP. Local recurrence following 'curative' surgery for large bowel cancer: I. The overall picture. *Br J Surg* 1984; **71**: 12-16 [PMID: 6689962 DOI: 10.1002/bjs.1800710104]

36 **Sauven P**, Playforth MJ, Evans M, Pollock AV. Early infective complications and late recurrent cancer in stapled colonic anastomoses. *Dis Colon Rectum* 1989; **32**: 33-35 [PMID: 2642789 DOI: 10.1007/BF02554722]

37 **Amato A**, Pescatori M, Butti A. Local recurrence following abdominoperineal excision and anterior resection for rectal carcinoma. *Dis Colon Rectum* 1991; **34**: 317-322 [PMID: 2007349 DOI: 10.1007/BF02050591]

38 **Akyol AM**, McGregor JR, Galloway DJ, Murray GD, George WD. Anastomotic leaks in colorectal cancer surgery: a risk factor for recurrence? *Int J Colorectal Dis* 1991; **6**: 179-183 [PMID: 1770281 DOI: 10.1007/BF00341385]

39 **Fujita S**, Teramoto T, Watanabe M, Kodaira S, Kitajima M. Anastomotic leakage after colorectal cancer surgery: a risk factor for recurrence and poor prognosis. *Jpn J Clin Oncol* 1993; **23**: 299-302 [PMID: 8230754]

40 **Petersen S**, Freitag M, Hellmich G, Ludwig K. Anastomotic leakage: impact on local recurrence and survival in surgery of colorectal cancer. *Int J Colorectal Dis* 1998; **13**: 160-163 [PMID: 9810519 DOI: 10.1007/s003840050158]

41 **Branagan G**, Finnis D; Wessex Colorectal Cancer Audit Working Group. Prognosis after anastomotic leakage in colorectal surgery. *Dis Colon Rectum* 2005; **48**: 1021-1026 [PMID: 15789125 DOI: 10.1007/s10350-004-0869-4]

42 **McArdle CS**, McMillan DC, Hole DJ. Impact of anastomotic leakage on long-term survival of patients undergoing

curative resection for colorectal cancer. *Br J Surg* 2005; **92**: 1150-1154 [PMID: 16035134 DOI: 10.1002/bjs.5054]
43 **Walker KG**, Bell SW, Rickard MJ, Mehanna D, Dent OF, Chapuis PH, Bokey EL. Anastomotic leakage is predictive of diminished survival after potentially curative resection for colorectal cancer. *Ann Surg* 2004; **240**: 255-259 [PMID: 15273549 DOI: 10.1097/01.sla.0000133186.81222.08]
44 **Choi HK**, Law WL, Ho JW. Leakage after resection and intraperitoneal anastomosis for colorectal malignancy: analysis of risk factors. *Dis Colon Rectum* 2006; **49**: 1719-1725 [PMID: 17051321 DOI: 10.1007/s10350-006-0703-2]
45 **Law WL**, Choi HK, Lee YM, Ho JW, Seto CL. Anastomotic leakage is associated with poor long-term outcome in patients after curative colorectal resection for malignancy. *J Gastrointest Surg* 2007; **11**: 8-15 [PMID: 17390180 DOI: 10.1007/s11605-006-0049-z]
46 **Eberhardt JM**, Kiran RP, Lavery IC. The impact of anastomotic leak and intra-abdominal abscess on cancer-related outcomes after resection for colorectal cancer: a case control study. *Dis Colon Rectum* 2009; **52**: 380-386 [PMID: 19333035 DOI: 10.1007/DCR.0b013e31819ad488]
47 **Marra F**, Steffen T, Kalak N, Warschkow R, Tarantino I, Lange J, Zünd M. Anastomotic leakage as a risk factor for the long-term outcome after curative resection of colon cancer. *Eur J Surg Oncol* 2009; **35**: 1060-1064 [PMID: 19303243 DOI: 10.1016/j.ejso.2009.02.011]
48 **Kube R**, Mroczkowski P, Granowski D, Benedix F, Sahm M, Schmidt U, Gastinger I, Lippert H; Study group Qualitätssicherung Kolon/Rektum-Karzinome (Primärtumor) (Quality assurance in primary colorectal carcinoma). 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**: 120-124 [PMID: 19775850 DOI: 10.1016/j.ejso.2009.08.011]
49 **Boccola MA**, Buettner PG, Rozen WM, Siu SK, Stevenson AR, Stitz R, Ho YH. Risk factors and outcomes for anastomotic leakage in colorectal surgery: a single-institution analysis of 1576 patients. *World J Surg* 2011; **35**: 186-195 [PMID: 20972678 DOI: 10.1007/s00268-010-0831-7]
50 **Katoh H**, Yamashita K, Wang G, Sato T, Nakamura T, Watanabe M. Anastomotic leakage contributes to the risk for systemic recurrence in stage II colorectal cancer. *J Gastrointest Surg* 2011; **15**: 120-129 [PMID: 21086058 DOI: 10.1007/s11605-010-1379-4]
51 **Hüttner FJ**, Warschkow R, Schmied BM, Diener MK, Tarantino I, Ulrich A. Prognostic impact of anastomotic leakage after elective colon resection for cancer - A propensity score matched analysis of 628 patients. *Eur J Surg Oncol* 2018; **44**: 456-462 [PMID: 29396327 DOI: 10.1016/j.ejso.2018.01.079]
52 **Nachiappan S**, Askari A, Malietzis G, Giacometti M, White I, Jenkins JT, Kennedy RH, Faiz O. The impact of anastomotic leak and its treatment on cancer recurrence and survival following elective colorectal cancer resection. *World J Surg* 2015; **39**: 1052-1058 [PMID: 25446478 DOI: 10.1007/s00268-014-2887-2]
53 **Kim IY**, Kim BR, Kim YW. The impact of anastomotic leakage on oncologic outcomes and the receipt and timing of adjuvant chemotherapy after colorectal cancer surgery. *Int J Surg* 2015; **22**: 3-9 [PMID: 26283295 DOI: 10.1016/j.ijsu.2015.08.017]
54 **Breugom AJ**, van Dongen DT, Bastiaannet E, Dekker FW, van der Geest LG, Liefers GJ, Marinelli AW, Mesker WE, Portielje JE, Steup WH, Tseng LN, van de Velde CJ, Dekker JW. Association Between the Most Frequent Complications After Surgery for Stage I-III Colon Cancer and Short-Term Survival, Long-Term Survival, and Recurrences. *Ann Surg Oncol* 2016; **23**: 2858-2865 [PMID: 27075325 DOI: 10.1245/s10434-016-5226-z]
55 **Zimmermann MS**, Wellner U, Laubert T, Ellebrecht DB, Bruch HP, Keck T, Schlöricke E, Benecke CR. Influence of Anastomotic Leak After Elective Colorectal Cancer Resection on Survival and Local Recurrence: A Propensity Score Analysis. *Dis Colon Rectum* 2019; **62**: 286-293 [PMID: 30540662 DOI: 10.1097/DCR.0000000000001287]
56 **Park JS**, Huh JW, Park YA, Cho YB, Yun SH, Kim HC, Lee WY. Risk Factors of Anastomotic Leakage and Long-Term Survival After Colorectal Surgery. *Medicine (Baltimore)* 2016; **95**: e2890 [PMID: 26937928 DOI: 10.1097/MD.0000000000002890]
57 **Voron T**, Bruzzi M, Ragot E, Zinzindohoue F, Chevallier JM, Douard R, Berger A. Anastomotic Location Predicts Anastomotic Leakage After Elective Colonic Resection for Cancer. *J Gastrointest Surg* 2019; **23**: 339-347 [PMID: 30076589 DOI: 10.1007/s11605-018-3891-x]
58 **Ramphal W**, Boeding JRE, Gobardhan PD, Rutten HJT, de Winter LJMB, Crolla RMPH, Schreinemakers JMJ. Oncologic outcome and recurrence rate following anastomotic leakage after curative resection for colorectal cancer. *Surg Oncol* 2018; **27**: 730-736 [PMID: 30449500 DOI: 10.1016/j.suronc.2018.10.003]
59 **Krarup PM**, Nordholm-Carstensen A, Jorgensen LN, Harling H. Anastomotic leak increases distant recurrence and long-term mortality after curative resection for colonic cancer: a nationwide cohort study. *Ann Surg* 2014; **259**: 930-938 [PMID: 24045445 DOI: 10.1097/SLA.0b013e3182a6f2fc]
60 **Krarup PM**, Nordholm-Carstensen A, Jorgensen LN, Harling H. Association of Comorbidity with Anastomotic Leak, 30-day Mortality, and Length of Stay in Elective Surgery for Colonic Cancer: A Nationwide Cohort Study. *Dis Colon Rectum* 2015; **58**: 668-676 [PMID: 26200681 DOI: 10.1097/DCR.0000000000000392]
61 **Nordholm-Carstensen A**, Rolff HC, Krarup PM. Differential Impact of Anastomotic Leak in Patients With Stage IV Colonic or Rectal Cancer: A Nationwide Cohort Study. *Dis Colon Rectum* 2017; **60**: 497-507 [PMID: 28383449 DOI: 10.1097/DCR.0000000000000761]
62 **Ng SC**, Stupart D, Bartolo D, Watters D. Anastomotic leaks in stage IV colorectal cancer. *ANZ J Surg* 2018; **88**: E649-E653 [PMID: 29895100 DOI: 10.1111/ans.14494]
63 **Mirnezami A**, Mirnezami R, Chandrakumaran K, Sasapu K, Sagar P, Finan P. Increased local recurrence and reduced survival from colorectal cancer following anastomotic leak: systematic review and meta-analysis. *Ann Surg* 2011; **253**: 890-899 [PMID: 21394013 DOI: 10.1097/SLA.0b013e3182128929]
64 **Ha GW**, Kim JH, Lee MR. Oncologic Impact of Anastomotic Leakage Following Colorectal Cancer Surgery: A Systematic Review and Meta-Analysis. *Ann Surg Oncol* 2017; **24**: 3289-3299 [PMID: 28608118 DOI: 10.1245/s10434-017-5881-8]
65 **Sammour T**, Hayes IP, Jones IT, Steel MC, Faragher I, Gibbs P. Impact of anastomotic leak on recurrence and survival after colorectal cancer surgery: a BioGrid Australia analysis. *ANZ J Surg* 2018; **88**: E6-E10 [PMID: 27255690 DOI:

10.1111/ans.13648]
66 **Goto S**, Hasegawa S, Hida K, Uozumi R, Kanemitsu Y, Watanabe T, Sugihara K, Sakai Y; Study Group for Nomogram of the Japanese Society for Cancer of the Colon and Rectum. Multicenter analysis of impact of anastomotic leakage on long-term oncologic outcomes after curative resection of colon cancer. *Surgery* 2017; **162**: 317-324 [PMID: 28433249 DOI: 10.1016/j.surg.2017.03.005]
67 **Bashir Mohamed K**, Hansen CH, Krarup PM, Fransgård T, Madsen MT, Gögenur I. The impact of anastomotic leakage on recurrence and long-term survival in patients with colonic cancer: A systematic review and meta-analysis. *Eur J Surg Oncol* 2020; **46**: 439-447 [PMID: 31727475 DOI: 10.1016/j.ejso.2019.10.038]
68 **Stormark K**, Krarup PM, Sjövall A, Søreide K, Kvaløy JT, Nordholm-Carstensen A, Nedrebø BS, Kørner H. Anastomotic leak after surgery for colon cancer and effect on long-term survival. *Colorectal Dis* 2020; **22**: 1108-1118 [PMID: 32012414 DOI: 10.1111/codi.14999]
69 **Kryzauskas M**, Bausys A, Degutyte AE, Abeciunas V, Poskus E, Bausys R, Dulskas A, Strupas K, Poskus T. Risk factors for anastomotic leakage and its impact on long-term survival in left-sided colorectal cancer surgery. *World J Surg Oncol* 2020; **18**: 205 [PMID: 32795348 DOI: 10.1186/s12957-020-01968-8]
70 **Merkel S**, Wang WY, Schmidt O, Dworak O, Wittekind C, Hohenberger W, Hermanek P. Locoregional recurrence in patients with anastomotic leakage after anterior resection for rectal carcinoma. *Colorectal Dis* 2001; **3**: 154-160 [PMID: 12790981 DOI: 10.1046/j.1463-1318.2001.00232.x]
71 **Jung SH**, Yu CS, Choi PW, Kim DD, Park IJ, Kim HC, Kim JC. Risk factors and oncologic impact of anastomotic leakage after rectal cancer surgery. *Dis Colon Rectum* 2008; **51**: 902-908 [PMID: 18408971 DOI: 10.1007/s10350-008-9272-x]
72 **Jörgren F**, Johansson R, Damber L, Lindmark G. Anastomotic leakage after surgery for rectal cancer: a risk factor for local recurrence, distant metastasis and reduced cancer-specific survival? *Colorectal Dis* 2011; **13**: 272-283 [PMID: 19912285 DOI: 10.1111/j.1463-1318.2009.02136.x]
73 **Smith JD**, Paty PB, Guillem JG, Temple LK, Weiser MR, Nash GM. Anastomotic leak is not associated with oncologic outcome in patients undergoing low anterior resection for rectal cancer. *Ann Surg* 2012; **256**: 1034-1038 [PMID: 22584695 DOI: 10.1097/SLA.0b013e318257d2c1]
74 **Ebinger SM**, Warschkow R, Tarantino I, Schmied BM, Marti L. Anastomotic leakage after curative rectal cancer resection has no impact on long-term survival: a propensity score analysis. *Int J Colorectal Dis* 2015; **30**: 1667-1675 [PMID: 26245949 DOI: 10.1007/s00384-015-2331-6]
75 **Crippa J**, Duchalais E, Machairas N, Merchea A, Kelley SR, Larson DW. Long-term Oncological Outcomes Following Anastomotic Leak in Rectal Cancer Surgery. *Dis Colon Rectum* 2020; **63**: 769-777 [PMID: 32109914 DOI: 10.1097/DCR.0000000000001634]
76 **Jang JH**, Kim HC, Huh JW, Park YA, Cho YB, Yun SH, Lee WY, Yu JI, Park HC, Park YS, Park JO. Anastomotic Leak Does Not Impact Oncologic Outcomes After Preoperative Chemoradiotherapy and Resection for Rectal Cancer. *Ann Surg* 2019; **269**: 678-685 [PMID: 29112004 DOI: 10.1097/SLA.0000000000002582]
77 **Espín E**, Ciga MA, Pera M, Ortiz H; Spanish Rectal Cancer Project. Oncological outcome following anastomotic leak in rectal surgery. *Br J Surg* 2015; **102**: 416-422 [PMID: 25619499 DOI: 10.1002/bjs.9748]
78 **Ke H**, Chi P, Lin H, Lu X, Huang Y, Xu Z, Huang S, Chen Z, Sun Y, Ye D, Wang X. [Influence of anastomotic leakage on long-term survival after resection for rectal cancer]. *Zhonghua Wei Chang Wai Ke Za Zhi* 2015; **18**: 920-924 [PMID: 26404691]
79 **Lee WS**, Yun SH, Roh YN, Yun HR, Lee WY, Cho YB, Chun HK. Risk factors and clinical outcome for anastomotic leakage after total mesorectal excision for rectal cancer. *World J Surg* 2008; **32**: 1124-1129 [PMID: 18259805 DOI: 10.1007/s00268-007-9451-2]
80 **Lin JK**, Yueh TC, Chang SC, Lin CC, Lan YT, Wang HS, Yang SH, Jiang JK, Chen WS, Lin TC. The influence of fecal diversion and anastomotic leakage on survival after resection of rectal cancer. *J Gastrointest Surg* 2011; **15**: 2251-2261 [PMID: 22002413 DOI: 10.1007/s11605-011-1721-5]
81 **Jäger T**, Nawara C, Neureiter D, Holzinger J, Öfner-Velano D, Dinnewitzer A. [Impact of anastomotic leakage on long-term survival in mid-to-low rectal cancer]. *Chirurg* 2015; **86**: 1072-1082 [PMID: 26428227 DOI: 10.1007/s00104-015-0090-0]
82 **Kang J**, Choi GS, Oh JH, Kim NK, Park JS, Kim MJ, Lee KY, Baik SH. Multicenter Analysis of Long-Term Oncologic Impact of Anastomotic Leakage After Laparoscopic Total Mesorectal Excision: The Korean Laparoscopic Colorectal Surgery Study Group. *Medicine (Baltimore)* 2015; **94**: e1202 [PMID: 26200636 DOI: 10.1097/MD.0000000000001202]
83 **Allaix ME**, Rebecchi F, Famiglietti F, Arolfo S, Arezzo A, Morino M. Long-term oncologic outcomes following anastomotic leak after anterior resection for rectal cancer: does the leak severity matter? *Surg Endosc* 2020; **34**: 4166-4176 [PMID: 31617094 DOI: 10.1007/s00464-019-07189-9]
84 **Jannasch O**, Klinge T, Otto R, Chiapponi C, Udelnow A, Lippert H, Bruns CJ, Mroczkowski P. Risk factors, short and long term outcome of anastomotic leaks in rectal cancer. *Oncotarget* 2015; **6**: 36884-36893 [PMID: 26392333 DOI: 10.18632/oncotarget.5170]
85 **Kulu Y**, Tarantio I, Warschkow R, Kny S, Schneider M, Schmied BM, Büchler MW, Ulrich A. Anastomotic leakage is associated with impaired overall and disease-free survival after curative rectal cancer resection: a propensity score analysis. *Ann Surg Oncol* 2015; **22**: 2059-2067 [PMID: 25348782 DOI: 10.1245/s10434-014-4187-3]
86 **Furnée EJB**, Aukema TS, Oosterling SJ, Borstlap WAA, Bemelman WA, Tanis PJ; Dutch Snapshot Research Group. Influence of Conversion and Anastomotic Leakage on Survival in Rectal Cancer Surgery; Retrospective Cross-sectional Study. *J Gastrointest Surg* 2019; **23**: 2007-2018 [PMID: 30187334 DOI: 10.1007/s11605-018-3931-6]
87 **den Dulk M**, Marijnen CA, Collette L, Putter H, Påhlman L, Folkesson J, Bosset JF, Rödel C, Bujko K, van de Velde CJ. Multicentre analysis of oncological and survival outcomes following anastomotic leakage after rectal cancer surgery. *Br J Surg* 2009; **96**: 1066-1075 [PMID: 19672927 DOI: 10.1002/bjs.6694]
88 **Noh GT**, Ann YS, Cheong C, Han J, Cho MS, Hur H, Min BS, Lee KY, Kim NK. Impact of anastomotic leakage on long-term oncologic outcome and its related factors in rectal cancer. *Medicine (Baltimore)* 2016; **95**: e4367 [PMID: 27472726

DOI: 10.1097/MD.0000000000004367]

89 **Peltrini R**, Carannante F, Costa G, Bianco G, Garbarino GM, Canali G, Mercantini P, Bracale U, Corcione F, Caricato M, Capolupo GT. Oncological outcomes of rectal cancer patients with anastomotic leakage: A multicenter case-control study. *Front Surg* 2022; **9**: 993650 [PMID: 36171821 DOI: 10.3389/fsurg.2022.993650]

90 **Ptok H**, Marusch F, Meyer F, Schubert D, Gastinger I, Lippert H; Study Group Colon/Rectum Carcinoma (Primary Tumour). Impact of anastomotic leakage on oncological outcome after rectal cancer resection. *Br J Surg* 2007; **94**: 1548-1554 [PMID: 17668888 DOI: 10.1002/bjs.5707]

91 **Hain E**, Maggiori L, Manceau G, Mongin C, Prost À la Denise J, Panis Y. Oncological impact of anastomotic leakage after laparoscopic mesorectal excision. *Br J Surg* 2017; **104**: 288-295 [PMID: 27762432 DOI: 10.1002/bjs.10332]

92 **Eriksen MT**, Wibe A, Norstein J, Haffner J, Wiig JN; Norwegian Rectal Cancer Group. Anastomotic leakage following routine mesorectal excision for rectal cancer in a national cohort of patients. *Colorectal Dis* 2005; **7**: 51-57 [PMID: 15606585 DOI: 10.1111/j.1463-1318.2004.00700.x]

93 **Lim SB**, Yu CS, Kim CW, Yoon YS, Park IJ, Kim JC. The types of anastomotic leakage that develop following anterior resection for rectal cancer demonstrate distinct characteristics and oncologic outcomes. *Int J Colorectal Dis* 2015; **30**: 1533-1540 [PMID: 26260482 DOI: 10.1007/s00384-015-2359-7]

94 **Boström P**, Haapamäki MM, Rutegård J, Matthiessen P, Rutegård M. Population-based cohort study of the impact on postoperative mortality of anastomotic leakage after anterior resection for rectal cancer. *BJS Open* 2019; **3**: 106-111 [PMID: 30734021 DOI: 10.1002/bjs5.50106]

95 **Dulskas A**, Kuliavas J, Sirvys A, Bausys A, Kryzauskas M, Bickaite K, Abeciunas V, Kaminskas T, Poskus T, Strupas K. Anastomotic Leak Impact on Long-Term Survival after Right Colectomy for Cancer: A Propensity-Score-Matched Analysis. *J Clin Med* 2022; **11** [PMID: 35955993 DOI: 10.3390/jcm11154375]

96 **Arron MNN**, Greijdanus NG, Bastiaans S, Vissers PAJ, Verhoeven RHA, Ten Broek RPG, Verheul HMW, Tanis PJ, van Goor H, de Wilt JHW. Long-Term Oncological Outcomes After Colorectal Anastomotic Leakage: A Retrospective Dutch Population-based Study. *Ann Surg* 2022; **276**: 882-889 [PMID: 35930021 DOI: 10.1097/SLA.0000000000005647]

97 **Koedam TWA**, Bootsma BT, Deijen CL, van de Brug T, Kazemier G, Cuesta MA, Fürst A, Lacy AM, Haglind E, Tuynman JB, Daams F, Bonjer HJ; COLOR COLOR II study group. Oncological Outcomes After Anastomotic Leakage After Surgery for Colon or Rectal Cancer: Increased Risk of Local Recurrence. *Ann Surg* 2022; **275**: e420-e427 [PMID: 32224742 DOI: 10.1097/SLA.0000000000003889]

98 **Veldkamp R**, Kuhry E, Hop WC, Jeekel J, Kazemier G, Bonjer HJ, Haglind E, Påhlman L, Cuesta MA, Msika S, Morino M, Lacy AM; COlon cancer Laparoscopic or Open Resection Study Group (COLOR). Laparoscopic surgery *vs* open surgery for colon cancer: short-term outcomes of a randomised trial. *Lancet Oncol* 2005; **6**: 477-484 [PMID: 15992696 DOI: 10.1016/S1470-2045(05)70221-7]

99 **van der Pas MH**, Haglind E, Cuesta MA, Fürst A, Lacy AM, Hop WC, Bonjer HJ; COlorectal cancer Laparoscopic or Open Resection II (COLOR II) Study Group. Laparoscopic *vs* open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. *Lancet Oncol* 2013; **14**: 210-218 [PMID: 23395398 DOI: 10.1016/S1470-2045(13)70016-0]

100 **Pakkastie TE**, Luukkonen PE, Järvinen HJ. Anterior resection controls cancer of the rectum as well as abdominoperineal excision. *Eur J Surg* 1995; **161**: 833-839 [PMID: 8749216]

101 **Bell SW**, Walker KG, Rickard MJ, Sinclair G, Dent OF, Chapuis PH, Bokey EL. Anastomotic leakage after curative anterior resection results in a higher prevalence of local recurrence. *Br J Surg* 2003; **90**: 1261-1266 [PMID: 14515297 DOI: 10.1002/bjs.4219]

102 **Law WL**, Chu KW. Anterior resection for rectal cancer with mesorectal excision: a prospective evaluation of 622 patients. *Ann Surg* 2004; **240**: 260-268 [PMID: 15273550 DOI: 10.1097/01.sla.0000133185.23514.32]

103 **Smith JD**, Butte JM, Weiser MR, D'Angelica MI, Paty PB, Temple LK, Guillem JG, Jarnagin WR, Nash GM. Anastomotic leak following low anterior resection in stage IV rectal cancer is associated with poor survival. *Ann Surg Oncol* 2013; **20**: 2641-2646 [PMID: 23385965 DOI: 10.1245/s10434-012-2854-9]

104 **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**: 424-32; discussion 432 [PMID: 24536013 DOI: 10.1002/bjs.9395]

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