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Anastomotic technique is not associated with leakage rate after right hemicolectomy

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ABSTRACT

INTRODUCTION: The present study aimed to evaluate the anastomotic leakage rate in relation to anastomotic technique in right hemicolectomy in a single high-volume centre.

METHODS: This was a retrospective single-centre study of prospectively collected data of patients undergoing right hemicolectomy or ileocecal resection in an acute or elective setting over a seven-year period in a large University Hospital. Anastomotic leakage, anastomotic technique (hand-sewn versus stapled anastomosis) and potential confounders were registered. The possible confounding risk factors were explored by univariate analysis. Any variables with a p value < 0.2 after univariate logistic regression analysis were included in a subsequent multivariate logistic regression analysis.

RESULTS: A total of 754 patients had a primary anastomosis performed. In 222 (29%) of the patients, anastomosis was hand-sewn and in 528 (70%) stapled. Overall, 26 patients (3.4%) developed an anastomotic leakage. The anastomotic leakage rate was similar following hand-sewn and stapled anastomoses (3.6% (8/221) versus 3.4% (18/527); p = 0.89). Univariate analyses failed to identify any significant risk factors for anastomotic leakage. A multivariate logistic regression analysis with all mentioned co-variates was performed. None of the included variables were significantly associated with anastomotic leakage.

CONCLUSIONS: In the present study, we found no significant difference between hand-sewn versus stapled anastomosis.

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Right hemicolectomy is a common procedure mainly performed in relation to malignancy and inflammatory bowel disease (IBD). After this procedure, one of the most serious surgical complications is anastomotic leakage, which severely increases morbidity, mortality and risk of cancer recurrence [1-3]. In one study, patients with anastomotic leakage after

colonic resection for cancer had a 7.2-fold higher risk of death than patients without complications, and the five-year overall survival was reduced from 67% to 51% in patients re-operated for anastomotic leakage [3]. In Denmark, the risk of anastomotic leakage after colonic resection for colon cancer with a primary anastomosis was approx. 4% in the years 2009 through 2016 (2009: 5.8%, 2016: 4.3%) [4]. The risk of anastomotic leakage after surgery due to IBD is reported to be 13%. This difference is thought to be due to malnutrition, steroid use and existing infection [5].

A range of risk factors have been associated with an increased risk of anastomotic leakage including male gender [6], diabetes, tobacco use, preoperative nutritional status and post-operative use of non-steroidal anti-inflammatory drugs [7, 8]. Furthermore, factors such as age, American Society of Anesthesiology (ASA) score [9], smoking habits [6], emergency versus planned surgery [10], circulatory instability, perioperative blood loss [6], blood transfusion [10] and anastomotic technique might influence the risk of anastomotic leakage. Some of the risk factors can be modified by the surgeon and are therefore interesting to explore.

In this study, we decided to focus primarily on anastomotic technique in right hemicolectomy. Despite many studies in this field, there is no consensus on whether stapled or hand-sewn anastomosis influences the anastomotic leakage rate [1, 11-13]. A systematic Cochrane review and meta-analysis from 2011 concluded that stapled anastomosis in right hemicolectomy was associated with fewer anastomotic leaks than hand-sewn anastomosis [11]. In contrast, over the past few years, several studies have shown an increased risk of anastomotic leakage with stapled anastomosis compared with hand-sewn anastomosis in right hemicolectomies [1, 12, 13]. In light of this controversy, the overall aim of this study was to examine the association between anastomotic technique and anastomotic leakage in a cohort of patients with right-sided hemicolectomy.

METHODS

This study was a retrospective single-centre study of prospectively collected data of patients undergoing right hemicolectomy or ileocecal resection in an acute or elective setting in the course of a seven-year period in a large university hospital. Data were extracted from a local in-house database on all emergency surgery patients as well as from the Danish Colorectal Cancer Group's (DCCG) nationwide database on colorectal cancer. All patients undergoing right hemicolectomy or ileocecal resection in our institution from January 2009 through December 2016 were included in the study. We included both elective and emergency cases as well as both benign and malignant indications. Demographic, pre-, per- and post-operative data were extracted from our in-house database and merged with data from the DCCG database. All patient charts were reviewed manually by two authors to confirm the reliability of the data extracted. In case of disagreement, the case was reviewed by a third author to

reach agreement. The primary end-point was an anastomotic leakage within 30 days of surgery. Anastomotic leakage was defined as a "clinical condition related to the anastomosis including fluid accumulation in close proximity to the anastomosis, which demands radiological, surgical or medical treatment" [14], and graded according to the Clavien-Dindo classification [15].

Factors and variables possibly associated with anastomotic leakage, including gender, age (median), smoking, alcohol consumption, BMI, acute/planned surgery, ASA score, tumour, node and metastasis (TNM) classification and type of anastomosis (stapled versus hand-sewn) were registered. Patient characteristics, anastomotic technique (stapled versus hand-sewn) and the other possible confounding risk factors mentioned above where analysed in a univariate analysis to assess any association between the variables and anastomotic leakage. Any variables with a p value < 0.2 after univariate logistic regression analysis were included in a subsequent multivariate logistic regression analysis. The statistical analyses were performed with the Statistical Package for Social Sciences. The study was approved by the Danish Data Protection Agency (I-Suite number: 06113 and ID-number: HGH-2018-003).

Trial registration: not relevant.

RESULTS

A total of 797 adult patients were included in the study. Of these, 754 (95%) patients had a primary anastomosis performed. The remaining excluded 43 patients (5%) received a stoma. A total of 292 (39%) were male and the median age of the whole population was 74 years (range: 16-97 years). There were 522 (69%) elective cases, 231 (31%) emergency cases and one patient with missing data (**Table 1**). All the elective cases were due to malignancy and 58% of the emergency cases were due to benign conditions such as IBD, bowel obstruction due to adhesions or appendicitis. Laparotomy was performed in 262 (35%) of the cases; laparoscopic surgery in 492 (65%) of the cases (Table 1). In the laparoscopic group, 81 patients (11%) received a robotic assisted resection. Laparoscopy was converted to laparotomy in 68/492 (14%) of the cases. There was no significant difference in the conversion rate in the robot-assisted laparoscopy group (6/81 (7.5%)) compared with the traditional laparoscopy group (60/411 (14.6%); p = 0.089).

In 222 (29%) of the cases, anastomosis was hand-sewn, and 528 (70%) had a stapled anastomosis. Four patients (1%) were excluded due to missing data. Overall, 26 patients (3.4%) developed an anastomotic leakage (Table 1). Among the 26 cases of anastomotic leak, two were Clavien Dindo minor (CD I-II) and 24 were major (CD III-IV). The 30-day mortality rate in patients with anastomotic leakage was 15.4%.

TABLE 1 / Demographic and tumour-specific variables.

		Missing

	Total (N = 754)	Missing data, %
Age, median (range), yrs	74 (16-97)	0
Gender, m/f, n (%)	292/462 (39/61)	0
BMI, median (IQR), kg/m^2	24.5 (22.0-26.8)	25
ASA group, n (%)		7
I	151 (22)	
II	360 (51)	
III	176 (25)	
IV	13 (2)	
Tobacco usage, n (%)		9
Never	335 (49)	
Former smoker	219 (32)	
Smoker	135 (20)	
Alcohol consumption, n (%)[a]		20
0 units	149 (25)	
1-14 units	377 (63)	
15-21 units	49 (8)	
〉21 units	27 (5)	
Year of surgery, n (%)		0
2009	63 (8)	
2010	80 (11)	
2011	89 (12)	
2012	93 (12)	
2013	92 (12)	
2014	119 (16)	
2015	124 (16)	
2016	94 (13)	
Open/laparoscopic procedure, n (%)	262/492 (35/65)	0
Perioperative transfusion?, y/n, n (%)	55/563 (9/91)	18
Timing of surgery, n (%)		0
Planned	522 (69)	

Planned	[illegible]	
Acute	231 (31)	
Type of resection, n (%)		0
Ileocoecal	46 (6)	
Right hemicolectomy	654 (87)	
Extended right hemicolectomy	52 (7)	
Type of anastomosis, n (%)		1
Stapled	528 (70)	
Hand-sewn	222 (30)	
Anastomotic leakage rate?		0
No	726 (97)	
Yes	26 (4)	
Only colorectal cancer patients		
T-stage, n (%):		0
0	5 (1)	
1	27 (4)	
2	65 (11)	
3	345 (56)	
4	176 (29)	
N-stage, n (%):		0.3
0	356 (58)	
1	134 (22)	
2	126 (21)	
Tumour fixation?, n (%):		0
No	511 (83)	
Yes, removable	103 (17)	
Yes, not removable	4 (1)	

ASA = American Society of Anesthesiologists; f = female;
IQR = interquartile range; m = male.
a) 1 unit = 12 g of alcohol.

No significant difference in the leakage rate was observed between hand-sewn and stapled anastomoses (3.6% (8/221) versus 3.4% (18/527); p = 0.89) (**Table 2**). As shown, the hand-sewn and stapled groups differed in certain aspects. There were fewer smokers in the hand-sewn group (45% versus 54 %, p = 0.03) and most of the stapled anastomoses were performed after laparoscopic resection (27% versus 82 %; p < 0.01). The latter distribution was caused by an over-representation of hand-sewn anastomoses in the acute setting where most resections were open. Also, for the patients with colorectal cancer, the hand-sewn approach was more frequently used in patients with more advanced disease (N-stage 0 in 63% versus 41%; p < 0.001 and T-stage 4 in 23% versus 47%; p < 0.001).

TABLE 2 / Demographic and tumour-specific variables according to type of anastomosis.

	Stapled (N = 528)	Hand-sewn (N = 222)	p-value
Age, median (range), yrs	75 (16-97)	73 (22-95)	0.13
Gender, m/f, n (%)	212/316 (40/60)	79/143 (36/64)	0.24
BMI, median (IQR), kg/m^2	24.6 (22.0-27.0)	24.1 (22.0-26.1)	0.15
ASA group, n (%)			0.07
I	101 (20)	50 (26)	
II	271 (54)	88 (45)	
III	124 (25)	50 (26)	
IV	6 (1)	6 (3)	
Tobacco usage, n (%)			0.03
Never	228 (46)	107 (55)	
Former smoker	170 (35)	47 (24)	
Smoker	94 (19)	40 (21)	
Alcohol consumption, n (%)[a]			0.97
0 units	120 (25)	29 (24)	
1-14 units	295 (62)	79 (64)	
15-21 units	38 (8)	10 (8)	
〉21 units	22 (5)	5 (4)	
Year of surgery, n (%)			0.01
2009	35 (7)	28 (13)	
2010	51 (10)	29 (13)	
2011	54 (10)	35 (16)	
2012	65 (12)	26 (12)	
2013	67 (13)	25 (11)	
2014	91 (17)	28 (13)	
2015	93 (18)	29 (13)	
2016	72 (14)	22 (10)	
Open/laparoscopic procedure, n (%)	97/431 (18/82)	163/59 (73/27)	〈 0.01
Perioperative transfusion?, y/n, n (%)	40/447 (8/92)	15/112 (12/88)	0.21
Timing of surgery, n (%)			〈 0.001
Planned	464 (88)	56 (25)	
Emergency	63 (12)	166 (75)	
Type of resection, n (%)			〈 0.01

Ileocoecal	15 (3)	31 (14)	
Right hemicolectomy	471 (89)	179 (81)	
Extended right hemicolectomy	40 (8)	12 (5)	
Anastomotic leakage rate?, n (%)			0.89
No	509 (97)	213 (96)	
Yes	18 (3.4)	8 (3.6)	
Only colorectal cancer patients			
T-stage, n (%):			⟨ 0.001
0	4 (1)	1 (1)	
1	24 (5)	3 (2)	
2	58 (12)	7 (6)	
3	287 (59)	56 (44)	
4	114 (23)	60 (47)	
Unknown	41 (8)	95 (43)	
N-stage, n (%):			⟨ 0.001
0	303 (63)	52 (41)	
1	102 (21)	31 (24)	
2	80 (17)	44 (35)	
Tumour fixation?, n (%):			0.01
No	411 (84)	98 (77)	
Yes, removable	75 (15)	27 (21)	
Yes, not removable	1 (0)	3 (2)	
Unknown	41 (8)	94 (42)	

ASA = American Society of Anesthesiologists; f = female; IQR = interquartile range; m = male.
a) 1 unit = 12 g of alcohol.

Univariate analyses (including the following covariates: gender, tobacco use, alcohol intake, blood transfusion, ASA group, acute vs elective surgery, laparoscopic versus open surgery, TNM stages and anastomotic technique) failed to identify any significant risk factors for anastomotic leakage (**Table 3**). Also, as none of the registered variables had a p-value < 0.2, no multivariate analysis could be performed as planned. Instead, to minimise the risk of missed interactions between factors, multivariate logistic regression analyses with combinations of all mentioned co-variates were performed.

TABLE 3 / Univariate logistic regression analyses, odds ratios indicating the risk of anastomotic leak.

	p-value	OR (95% CI)
Hand-sewn (vs stapled)	0.89	1.06 (0.46-2.48)
Year of surgery	0.37	
2009	-	Reference
2010	0.14	4.95 (0.58-42.2)

2011	0.80	0.70 (0.04-11.4)
2012	0.54	2.03 (0.21-20.0)
2013	0.81	1.36 (0.12-15.3)
2014	0.70	1.58 (0.16-15.5)
2015	0.23	3.65 (0.44-30.3)
2016	0.55	2.01 (0.20-19.8)
Tumour fixated?	0.93	
No	-	Reference
Yes	0.70	0.79 (0.23-2.70)
Yes, tumour not removed	1.00	
ASA group	0.70	
I	-	Reference
II	0.24	2.14 (0.61-7.49)
III	0.31	2.03 (0.52-7.99)
IV	-[a]	-[a]
Male gender (vs female)	0.97	1.02 (0.46-2.27)
Emergency surgery (vs planned surgery)	0.34	0.67 (0.27-1.70)
Intraoperative transfusion	0.51	0.50 (0.07-3.81)
Laparoscopic resection (vs open)	0.21	1.81 (0.72-4.55)
Alcohol consumption[b]	0.35	
0 units	-	Reference
1-14 units	0.796	0.87 (0.30-2.54)
15-21 units	0.174	2.56 (0.66-9.94)
〉21 units	0.927	1.11 (0.12-9.87)
Smoking	0.47	
Never	-	Reference
Former smoker	0.71	0.83 (0.30-2.26)
Smoker	0.34	1.60 (0.61-4.22)
BMI	0.89	1.00 (0.95-1.05)
Age	1.00	1.00 (0.97-1.03)
T-stage	1.00	
0	-[a]	-[a]
1	-[a]	-[a]

2	1.00	Reference
3	0.80	1.22 (0.27-5.5)
4	0.98	1.01 (0.20-5.2)

ASA = American Society of Anesthesiologists; CI = confidence interval; OR = odds ratio.
a) Too few cases to calculate.
b) 1 unit = 12 g of alcohol.

DISCUSSION

The overall anastomotic leakage rate after right hemicolectomy in our single-centre study was 3.4%, which is acceptable compared with national and international standards. On a nationwide basis in Denmark, the anastomotic leakage rate after right hemicolectomy performed on malignant indication was 4.9% in 2009 and 2.7% in 2016 [4]. In previous studies of right hemicolectomies, the risk of anastomotic leakage ranges 1.5%-8.1% [13, 16, 17].

A recently presented snapshot study performed by the European Society of Colo Proctology concerning anastomotic leakage rate [13] reported more hand-sewn anastomoses in the acute cases, but unlike our study, there the authors recorded a significantly increased risk of an anastomotic leakage in the group with stapled anastomosis. The explanation for a higher leakage-rate in stapled anastomoses has been suggested to be crushing of the tissue, coarser tissue manipulation and haematomas in the intestinal wall, all of which will lead to poor blood supply at the anastomotic site and subsequent anastomotic leakage [18, 19]. Conversely, the Cochrane systematic review and meta-analysis on stapled versus hand-sewn anastomosis from 2011 reported a higher risk of anastomotic leak after hand-sewn ileocolic anastomoses [11]. The reason for this finding may be reduced time spent performing the anastomosis, less manipulation of tissue and less foecal spillage when performing a stapled anastomosis [20]. As mentioned, in the present study, we found no significant difference between hand-sewn and stapled ileocolic anastomosis.

In our univariate and multivariate logistic regression analyses, we were not able to identify risk factors for anastomotic leakage. This may indicate that the level of detail in our data could have been higher and that leakages occurred unpredictably and possibly due to technical failures and/or special cases or circumstances that cannot be detected in the analysis of an entire cohort. In contrast, diabetes, tobacco and stapled anastomosis seemed to be a risk factor for anastomotic leakage in a similar study from 2016 [17].

Our study has several limitations. This was a retrospective review of prospectively recorded data, no randomisation between the two types of anastomosis was performed which

introduces a risk of selection bias. This is underlined by the uneven distribution of hand-sewn anastomoses in the acute cases compared with the planned cases. There was, however, no difference in leakage rate after elective and acute resection. This may, however, be a result of selection bias as a larger proportion of the acute cases than of the planned cases received a stoma - probably due to selection where the surgeon does not choose to perform an anastomosis in the more acute and ill patients. Furthermore, more specific details concerning the anastomotic techniques (type of stapler, number of firings, one- or two-layered hand-sewn anastomosis, etc.) were not registered and therefore not used in our study. Thus, we cannot know if these details concerning anastomotic technique have affected the results. Some of the cofounders have a high percentage of missing values, which is related to the DCCG database and was taken into account by excluding the missing values from the multivariate analysis.

CONCLUSIONS

In conclusion, we found no difference in risk of anastomotic leakage after hand-sewn versus stapled ileocolic anastomosis and therefore see no reason to refrain from the stapled anastomosis in our institution. The choice between hand-sewn and stapled anastomosis should therefore depend on the clinical circumstances and the surgeon's preference and experience.

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LITERATURE

1. Krarup P-M, Jorgensen LN, Andreasen AH et al. A nationwide study on anastomotic leakage after colonic cancer surgery. Colorectal Dis 2012;14:e661-e667.
2. Mirnezami A, Mirnezami R, Chandrakumaran K et al. Increased local recurrence and reduced survival from colorectal cancer following anastomotic leak. Ann Surg 2011;253:890-9.
3. Kube R, Mroczkowski P, Granowski D 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;36:120-4.
4. Group TDCC. https://dccg.dk/aarsrapporter-2/ (8 Jan 2020).
5. Yamamoto T, Allan RN, Keighley MR. Risk factors for intra-abdominal sepsis after surgery in Crohn's disease. Dis Colon Rectum 2000;43:1141-5.
6. Bertelsen CA, Andreasen AH, Jørgensen T et al. Anastomotic leakage after anterior resection for rectal

cancer: risk factors. Color Dis 2010;12:37-43.

7. Trencheva K, Morrissey KP, Wells M et al. Identifying important predictors for anastomotic leak after colon and rectal resection. Ann Surg 2013;257:108-13.
8. Frasson M, Granero-Castro P, Ramos Rodŕiguez JL et al. Risk factors for anastomotic leak and postoperative morbidity and mortality after elective right colectomy for cancer: results from a prospective, multicentric study of 1102 patients. Int J Colorectal Dis 2016;31:105-14.
9. Buchs NC, Gervaz P, Secic M et al. Incidence, consequences, and risk factors for anastomotic dehiscence after colorectal surgery: a prospective monocentric study. Int J Colorectal Dis 2008;23:265-70.
10. Golub R, Golub RW, Cantu R et al. A multivariate analysis of factors contributing to leakage of intestinal anastomoses. J Am Coll Surg 1997;184:364-72.
11. Choy PYG, Bissett IP, Docherty JG et al. Stapled versus handsewn methods for ileocolic anastomoses. In: Bissett IP, ed. Cochrane Database Syst Rev. Chichester, UK: John Wiley & Sons, Ltd, 2011.
12. Gustafsson P, Jestin P, Gunnarsson U et al. Higher frequency of anastomotic leakage with stapled compared to hand-sewn ileocolic anastomosis in a large population-based study. World J Surg 2015;39:1834-9.
13. 2015 European Society of Coloproctology Collaborating Group. Relationship between method of anastomosis and anastomotic failure after right hemicolectomy and ileo-caecal resection: an international snapshot audit. Color Dis 2017;19:e296-e311.
14. DCCG. https://dccg.dk/wp-content/uploads/2017/10/kirurgiskema_2015_vejledning.pdf (8 Jan 2020).
15. Clavien PA, Barkun J, de Oliveira ML et al. The Clavien-Dindo Classification of Surgical Complications. Ann Surg 2009;250:187-96.
16. Bakker IS, Grossmann I, Henneman D et al. Risk factors for anastomotic leakage and leak-related mortality after colonic cancer surgery in a nationwide audit. Br J Surg 2014;101:424-32;
17. Jessen M, Nerstrøm M, Wilbek TE et al. Risk factors for clinical anastomotic leakage after right hemicolectomy. Int J Colorectal Dis 2016;31:1619-24.
18. Kashiwagi H. The lower limit of tissue blood flow for safe colonic anastomosis: an experimental study using laser Doppler velocimetry. Surg Today 1993;23:430-8.
19. Vignali A, Gianotti L, Braga M et al. Altered microperfusion at the rectal stump is predictive for rectal anastomotic leak. Dis Colon Rectum 2000;43:76-82.
20. Suturing or stapling in gastrointestinal surgery: a prospective randomized study. West of Scotland and Highland Anastomosis Study Group. Br J Surg 1991;78:337-41.