

# After-hours colorectal surgery: a risk factor for anastomotic leakage

Niels Komen · Jan-Willem Dijk · Zarina Lalmahomed · Karel Klop · Wim Hop · Gert-Jan Kleinrensink · Hans Jeekel · W. Ruud Schouten · Johan F. Lange

Accepted: 26 February 2009 / Published online: 21 March 2009  
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## Abstract

**Purpose** This study aims to increase knowledge of colorectal anastomotic leakage by performing an incidence study and risk factor analysis with new potential risk factors in a Dutch tertiary referral center.

**Methods** All patients whom received a primary colorectal anastomosis between 1997 and 2007 were selected by means of operation codes. Patient records were studied for population description and risk factor analysis.

**Results** In total 739 patients were included. Anastomotic leakage (AL) occurred in 64 (8.7%) patients of whom nine (14.1%) died. Median interval between operation and

diagnosis was 8 days. The risk for AL was higher as the anastomoses were constructed more distally ( $p=0.019$ ). Univariate analysis showed duration of surgery ( $p=0.038$ ), BMI ( $p=0.001$ ), time of surgery ( $p=0.029$ ), prophylactic drainage ( $p=0.006$ ) and time under anesthesia ( $p=0.012$ ) to be associated to AL. Multivariate analysis showed BMI greater than 30 kg/m<sup>2</sup> ( $p=0.006$ ; OR 2.6 CI 1.3–5.2) and “after hours” construction of an anastomosis ( $p=0.030$ ; OR 2.2 CI 1.1–4.5) to be independent risk factors.

**Conclusion** BMI greater than 30 kg/m<sup>2</sup> and “after hours” construction of an anastomosis were independent risk factors for colorectal anastomotic leakage.

**Keywords** After-hours · Colorectal surgery · Anastomotic leakage · Body mass index

This work was presented at the Dutch Surgical Days, May 22nd 2008, Veldhoven, the Netherlands.

N. Komen (✉)  
Department of Surgery, ZNA Middelheim,  
Lindendreef 1,  
2020 Antwerp, Belgium  
e-mail: nielskomen@hotmail.com

N. Komen · J.-W. Dijk · Z. Lalmahomed · K. Klop · H. Jeekel · W. Ruud Schouten · J. F. Lange  
Department of Surgery, University Medical Center Rotterdam,  
Erasmus MC, Dr. Molewaterplein 50,  
3015 GE Rotterdam, The Netherlands

G.-J. Kleinrensink  
Department of Neurosciences and Anatomy,  
University Medical Center Rotterdam,  
Erasmus MC, Dr. Molewaterplein 50,  
3015 GE Rotterdam, The Netherlands

W. Hop  
Department of Epidemiology and Biostatistics,  
University Medical Center Rotterdam,  
Erasmus MC, Dr. Molewaterplein 50,  
3015 GE Rotterdam, The Netherlands

## Introduction

Anastomotic leakage (AL) is the major complication after colorectal surgery. It is poorly understood as illustrated by the vast body of confirming and contradicting publications on virtually every known potential risk factor. The great variation of reported incidences of AL, between 3% and 19% [1, 2], illustrates this as well.

The poor understanding of AL may be due to its multifactorial aspect. In addition, studies on potential risk factors are performed in different populations throughout the world and, therefore, show many different independent risk factors for anastomotic leakage, varying from diverticular disease [3] and rectal resection [4] to weight loss [5], urgent operation [6], smoking [7] and BMI [8]. The factor “surgeon” is important as well since it is shown that leakage risk is lower when patients are operated upon by a high-volume surgeon [9].

The group of potential risk factors for AL that is studied in literature is generally quite similar and contains, in addition to the aforementioned factors, mechanical bowel preparation (MBP) [10], prophylactic drainage (PD) [11], ASA-score [4], prolonged operating time [4], use of corticosteroids [12], anastomotic configuration [13], hand-sutured vs. stapled anastomosis [14], neoadjuvant radiotherapy [15], laparoscopic vs. open surgery [16], and gender [8].

Despite the vast body of evidence on these potential risk factors AL remains poorly understood. Therefore, risk factor analysis should not be limited to these factors.

Since ischemia is considered to be one of the causes of AL, studying vascular disease, i.e., atherosclerosis, could be a new approach as suggested by Foster et al. [17]. Analysis of known risk factors for atherosclerosis like hypertension [18], dyslipidemia [19], smoking [20], diabetes mellitus [21] could be an interesting addition to the group of potential risk factors.

More and more publications show the danger of after-hours medical activity. Gray et al. showed after-hours surgery to be related to higher complications rate [22]. Fechner et al. showed that night time kidney transplantation enhances the risk for complications and graft failure [23]. In addition, several studies have shown that proficiency and situational awareness of physicians is less at night [24–27]. On the matter of colorectal surgery, the time of day at which the patient is operated has never been related to AL.

In short, risk factors for AL vary between different populations and, since it is a multifactorial problem, there are probably several unknown risk factors.

This means that more studies on this matter, from different hospitals throughout the world should be performed, published and compared in order to improve understanding of this complication.

This study aims to describe the population of patients with primary colorectal anastomosis treated in a Dutch tertiary referral center and to determine the incidence and risk factors of AL in this population.

## Materials and methods

All patients who have undergone surgery on the colon or rectum in the period 1997–2007 were selected in the electronic archive by means of operation code of the relevant operations. In this population, patients whom received a primary anastomosis, involving colon and or rectum, were selected. The electronic- and paper patient records were used to score patient-, surgery-, and disease-related factors for risk factor analysis and description of the patient population.

The patient-related factors analyzed in this study were body mass index (BMI), age, gender, diabetes mellitus (DM), smoking, cardiac- and pulmonary comorbidity,

history of vascular disease, ASA-score, use of steroids, statins, and anti-hypertensive medication (Table 1).

The surgery-related factors analyzed in this study were prophylactic drainage (PD), time of surgery, type of operation, anastomotic configuration, blood transfusion, surgeon vs. assistant, mechanical bowel preparation (MBP), laparoscopic vs. open operation, duration of surgery, stapled vs. hand-sutured anastomosis, urgent vs. elective operation (Tables 1 and 2). Operations were considered urgent when it was indicated in anaesthesiologists' records and the patient's file. Examples of included surgical emergencies were mechanical obstruction due to colorectal cancer and perforated diverticulitis.

The disease-related factors analyzed in this study were the type of neoadjuvant therapy, radio- or chemotherapy or a combination, surgical indication (Table 1).

In addition, several outcome parameters like wound infection, pneumonia, urinary tract infection, abdominal wound dehiscence, hospital stay and stay on the intensive care unit were analyzed as well

The primary outcome measure was clinically manifest anastomotic leakage, confirmed by imaging or relaparotomy. In case of imaging, leakage was considered to be present when free air or contrast was visible around the anastomosis. In case of relaparotomy, leakage was considered to be present when a dehiscent anastomosis was visualized.

Results are summarized as means and standard deviations or medians and ranges for the continuous variables; the categorical variables are summarized in frequencies. Median and mean values were compared between groups with and without AL by means of the Mann–Whitney test or Chi-square test in univariate analyses. Multivariate analysis was performed with factors that were significant in univariate analysis and consisted of multiple logistic regression with backwards elimination. In the final model, multiple logistic regression with backwards elimination with all factors, significant or non-significant in univariate analysis, was performed.

Operation duration was transformed logarithmically in this analysis to reduce the influence of outlying observations. A *p* value of 0.05 (two-sided) was considered the limit of significance. Analyses were performed with “SPSS 15.0” statistical software.

## Results

### Patient population

A total of 739 patients received a primary colorectal anastomosis over the selected period. This number included 90 ileocecal resections, 27 transverse colon resections, 250 right hemicolectomies, 30 subtotal colectomies, 64 left hemicolectomies, 155 sigmoid resections, 18 rectosigmoid

**Table 1** Description of operated population and univariate analysis

Factor		Anastomotic leakage	No anastomotic leakage	<i>p</i> value
Population description and univariate analysis				
BMI (kg/m <sup>2</sup> ) <sup>a</sup>	<25	33 (9%)	343 (91%)	0.001
	25-30	13 (6%)	217 (94%)	
	>30	15 (20%)	62 (81%)	
Age (years) <sup>b</sup>		61 (22 – 84)	60 (18 – 99)	0.953
Gender (M/F)		32(9%)/ 32 (9%)	346 (91%)/ 329 (91%)	0.951
Smoker <sup>c</sup>		Yes: 16 (9%) No: 44 (8%)	Yes: 163 (91%) No: 485 (92%)	0.918
Use of steroids <sup>c</sup>		Yes: 13 (12%) No: 51 (8%)	Yes: 96 (88%) No: 569 (92%)	0.277
Use of Anti-hypertensive medication <sup>c</sup>		Yes: 7 (5%) No: 55 (9%)	Yes: 137 (95%) No: 532 (91%)	0.116
Use of statines <sup>c</sup>		Yes: 6 (9%) No: 56 (8%)	Yes: 63 (91%) No: 608 (92%)	1.000
ASA-score <sup>c</sup>		I: 13 (20%) II: 27 (42%) III: 20 (31%) IV: 1 (2%) V: 0 (0%)	I: 162 (24%) II: 303 (45%) III: 125 (19%) IV: 20 (3%) V: 1 (0,1%)	0.203
History of vascular disease <sup>c</sup>		Yes: 11 (9%) No: 51 (8%)	Yes: 106 (91%) No: 564 (92%)	0.831
Cardiac comorbidity <sup>c</sup>		Yes: 13 (9%) No: 49 (8%)	Yes: 134 (91%) No: 539 (92%)	0.974
Pulmonary comorbidity <sup>c</sup>		Yes: 8 (9%) No: 49 (8%)	Yes: 85 (91%) No: 563 (92%)	1.000
Diabetes mellitus <sup>c</sup>		Yes: 6 (9%) No: 57 (9%)	Yes: 60 (91%) No: 606 (91%)	1.000
Blood transfusion <sup>c</sup>		Yes: 14 (13%) No: 48 (8%)	Yes: 91 (87%) No: 550 (92%)	0.114
Mechanical bowel preparation <sup>d</sup>		Yes: 37 (8%) No: 16 (10%)	Yes: 436 (92%) No: 142 (90%)	0.460
Neoadjuvant radiotherapy		Yes: 1 (8%) No: 63 (9%)	Yes: 11 (92%) No: 664 (91%)	1.000
Anastomotic configuration <sup>c</sup>		E-E 7 (12%) E-S 2 (2%) S-E 21 (11%) S-S 33 (9%)	E-E 52 (88%) E-S 90 (98%) S-E 170 (89%) S-S 345 (91)	0.075
Surgical indication		Cancer: 37 (9%) IBD: 6 (5%) Diverticular disease: 3 (5%) Other: 18 (12%)	Diverticular disease: 53 (95%) IBD: 109 (95%) Cancer: 374 (91%) Other: 139 (89%)	0.249
Approach		Laparotomy: 59 (9%) Laparoscopy: 5 (5%)	Laparotomy: 588 (91%) Laparoscopy: 87 (95%)	0.328
Surgeon vs. assistant		Surgeon 13 (10%) Assistant 51 (8%)	Surgeon 114 (90%) Assistant 561 (92%)	0.603
Stapled vs. hand-sutured <sup>c</sup>		Stapled 5 (8%) Sutured 57 (9%)	Stapled 57 (92%) Sutured 617 (91%)	1.000
Urgent vs. Elective		Urgent: 19 (12%) Elective: 45 (8%)	Urgent: 137 (88%) Elective: 538 (92%)	0.110
Prophylactic drainage	Yes	21 (15%)	121 (85%)	0.006
	No	43 (7%)	554 (93%)	
Time of surgery <sup>e</sup>	During-hours	49 (8%)	584 (92%)	0.029
	After-hours	15 (14%)	91 (86%)	
Duration of operation (minutes) <sup>b</sup>		163 (70 – 365)	144 (49 – 497)	0.038
Time under anesthesia (minutes) <sup>b</sup>		226 (110 – 426)	195 (75 – 630)	0.012

*BMI* Body mass index (kg/m<sup>2</sup>), *SD* standard deviation, *ASA* American Society of Anesthesiologists

<sup>a</sup> BMI missing 47 (6,4%)

<sup>b</sup> Expressed in median and range

<sup>c</sup> Data do not add up to 739 due to occasional missing of data

<sup>d</sup> MBP unknown in 108 (14,5%) patients

<sup>e</sup> During-hours is defined as the hours in which a new elective procedure was allowed to start (i.e. between 7.45 h and 15.30 h). After-hours is defined as the period in which patients were operated upon by the operating team that is on call (i.e. between 15.30 h and 7.45 h).

<sup>f</sup> The group with nine non-traditional resections (“other” in Table 2) was excluded for risk factor analysis

resections and 96 low anterior resections after the total mesenterial excision principle (TME). Nine patients underwent non-traditional resections, consisting of eight anastomosis without resection when intraoperatively, the tumor appeared to have progressed to far and one resection of

transverse and descending colon. These nine patients were excluded for further risk factor analysis. A total of 92 (13%) operations were performed laparoscopically, of which 38 (41%) were converted. The population is described in Table 1.

**Table 2** The incidence of anastomotic leakage stratified for the performed operations

“Other” contained eight anastomoses without resection when, intraoperatively, the tumor appeared to have progressed to far and one resection of transverse and descending colon

Analysis of the anastomotic leakage rate per operation showed a significant trend ( $p=0.019$ ), regarding the expected increase in leakage rate going from top to bottom in the table (the group “other” was not included in this calculation).

Performed operations			
Procedure	No anastomotic leakage	Anastomotic leakage	Total
(Neo)-ileocecal resection	86 (96%)	4 (4%)	90
Resection transverse colon	23 (85%)	4 (15%)	27
(Extended) Hemicolectomy right	235 (94%)	15 (6%)	250
Subtotal colectomy	26 (87%)	4 (13%)	30
Hemicolectomy left	56 (88%)	8 (12%)	64
Resection sigmoid	142 (92%)	13 (8%)	155
Rectosigmoid resection	15 (83%)	3 (17%)	18
LAR/TME	83 (87%)	13 (13%)	96
Other	9 (100%)	0 (0%)	9
Total	675 (91.3%)	64 (8.7%)	739

Overall, the median duration of anesthesia was 217 min (range 75–630 min) and the median duration of operation was 162 min (range 49–497 min). A total of 633 (86%) patients were operated upon during-hours, which was defined as the hours in which a new elective procedure was allowed to start (i.e., between 7.45 h and 15.30 h). This means that generally, the elective program ended around 17.30 h–18.00 h. A total of 106 patients (14%) were operated upon after-hours, which was defined as the period in which patients were operated upon by the operating team that is on call (i.e., between 15.30 h and 7.45 h).

A total of 156 (21%) patients were operated upon in an emergency setting, 583 (79%) patients were operated upon in elective setting. The median hospital stay after the operation was 13 days (range 1–180 days) and the median stay on ICU was 0 days (range 0–72 days). The overall in hospital mortality rate was 4.7%.

#### Incidence of anastomotic leakage

Anastomotic leakage was diagnosed in 64 (8.7%) patients, of which nine patients (14%) died due to consequences of anastomotic leakage (AL).

As depicted in Table 2, the highest incidence of AL occurred after resection of the rectosigmoid (17%), followed by resection of the transverse colon (15%) and low anterior resection (13%). The median interval between operation and diagnosis of anastomotic leakage was 8 days (range 2–61 days).

#### Risk factor analysis

Analysis of the anastomotic leakage rate per operation showed a significant trend, indicating that higher leakage rates occurred as the anastomosis was constructed further downstream ( $p=0.019$ ; Table 2). Other potential risk factors for anastomotic leakage that reached significance in the

univariate analysis were BMI ( $p=0.001$ ), PD ( $p=0.006$ ), time of surgery ( $p=0.029$ ), duration of operation and anesthesia ( $p=0.038$ ,  $p=0.012$ ; Table 1).

Multivariate analysis showed body mass index (BMI) and time of surgery, classified in “during-” and “after hours”, to be independent risk factors (Table 3). Prophylactic drainage was significantly associated with anastomotic leakage as well (Table 3).

Adjusted for these factors, no relation was found between leakage rate and the level of anastomosis.

#### Patient outcome

Mortality rate amongst the patients with anastomotic leakage (14.1%) was significantly higher than amongst the

**Table 3** Significant results of multivariate analysis

Multivariate analysis				
Factor		OR	95% CI	<i>p</i> value
BMI (kg/m <sup>2</sup> )	<25	1	–	–
	25–30	0.6	0.3–1.14	0.115
	>30	2.6	1.3–5.2	0.006
Time of surgery	During-hours <sup>a</sup>	1	–	–
	After-hours	2.2	1.1–4.5	0.030
Prophylactic drainage	No	1	–	–
	Yes	2.8	1.5–5.1	0.001

The group “other” was excluded for the risk factor analysis; therefore, the total number of patients included is 730. Reference categories are indicated by OR=1

OR Odds Ratio, CI Confidence interval

<sup>a</sup> Time of surgery is defined as the hours in which a new elective procedure was allowed to start (i.e. between 7.45 h and 15.30 h). After-hours is defined as the period in which patients were operated upon by the operating team that is on call (i.e., between 15.30 h and 7.45 h).

patients without AL (3.9%;  $p=0.001$ ). The incidence of urinary tract infections, pneumonia, ileus, and wound infections did not differ significantly. Abdominal wound dehiscence (AWD), however, occurred more often in the group of patients with AL (8% vs. 5%,  $p=0.046$ ).

The mean hospital stay after operation and the stay at the ICU of patients with AL were 47 days and 7 days, respectively, whereas patients without AL stayed in the hospital 14 days and 1 days at the ICU, respectively ( $p=0.000$ ).

## Discussion

Leakage of a colorectal anastomosis still is a vast problem despite decades of research on this matter. This study was performed in order to improve understanding of this complication and to study new potential risk factors.

### Incidence of anastomotic leakage

In this study, an overall incidence of 8.7% was found over a period of 10 years. In literature leakage rates between 3% and 6% are reported for colonic anastomosis [28, 29], while leakage rates between 16% and 19% for low colorectal anastomosis are reported [2, 30]. Therefore this finding can be considered “average” considering anastomoses in the colon as well as in the rectum were included. The trend that was found in our study, i.e., higher leakage rates with lower anastomosis, is well-known too [31].

The leakage rate after resection of the transverse colon (four of 27) is remarkably high, which is not confirmed in literature [6]. Possibly the involvement of the watershed area at the splenic flexure and Griffiths’ critical point (insufficient marginal artery at splenic flexure) contribute to this high leakage rate [32]. However, since this group is relatively small and the 95% confidence intervals for the leakage rate is wide (4–34%), this finding should be considered only as an indication for further research.

### Risk factor analysis

The multivariate risk factor analysis showed BMI, time of operation and prophylactic drainage to be major factors, independently associated with anastomotic leakage.

A BMI higher than 30, which is considered obese according to the Centers of Disease Control and Prevention (CDC) [33], increased the risk for developing leakage almost three-fold. As to the explanation of this correlation, it remains unclear whether obesity indicates a defect of tissue structure and healing, whether the increased intra-abdominal pressure plays a role or whether construction of an anastomosis simply is technically more demanding because of thick mesenteries and epiploic appendices. A

possible solution might be to lower the threshold for construction of a diverting stoma in this population [31]. However, since construction of a stoma is difficult in patients with high BMI, sensibilization and a higher alert for anastomotic leakage in these patients on the ward is a more logical consequence of this finding.

Patients operated upon after-hours had more than a twofold increased risk of anastomotic leakage. This finding was independent of the urgency of the operation, which may be explained by the fact that urgent operations were also performed during-hours and elective operations were performed after-hours (Table 4). The latter occurs regularly due to incoming trauma- or transplantation patients that require immediate operation (Table 4).

Possible explanations could be found in the fact that significantly more anastomoses were constructed by residents after-hours (95%) than during-hours (81%;  $p<0.001$ ) and that after-hours, obviously, significantly more urgent operations were performed (86%) than during-hours (10%;  $p<0.001$ ). However, these factors were no independent risk factors in multivariate analysis.

Since many potential confounders have been accounted for and are not significant (Table 1), it is reasonable to assume a decreased technical performance of the operating team has contributed to a higher leakage rate at night. This assumption is supported by several studies that have shown medical errors to occur more often at night [24, 34]. In addition, physicians appear to be less proficient at night, which leads to more errors at night than during daytime [25–27].

Decreased non-technical skills of the operating team at night, like teamwork- and management skills and situational awareness, could have contributed to higher leakage rates as well. Situational awareness (SA), defined as the ability of the surgeon to observe, understand and predict events in the operating room (OR), appears to be closely related to technical error rates [35]. In addition, the situational awareness, teamwork- and management skills of the anesthetists and nurses may have an important impact on the outcome of surgical patients as well [27]. Based upon these results, it should be considered to construct a diverting stoma when after-hours construction of a colorectal anastomosis is required.

**Table 4** Distribution of urgent and elective operations

Urgent vs. Elective		
Time of surgery	Urgent	Elective
During hours	64 (10%)	569 (90%)
After-hours	92 (87%)	14 (13%)

Most studies addressing the problem of anastomotic leakage focus on the urgency of the operation. However, few studies report on the time of surgery in relationship to leakage rate. Higher leakage rates at night may be caused by a decreased technical and/or non-technical performance of the entire operating team. Given the current focus of society on medical errors and its prevention, more research should be done on this aspect of colorectal surgery.

Prophylactic drainage (PD) appeared to be associated with anastomotic leakage, suggesting that it is a risk factor. However, statistical analysis shows that significantly more drains are placed after LAR (54% of all drains;  $p=0,001$ ) and that the duration of surgery on average is 70 min longer in the group that received a drain (219 min) than in the group without (148 min;  $p=0,001$ ). The latter is most likely caused by difficulty of operation and adverse events occurring during operation. This shows that the significant association between drainage and anastomotic leakage reflects the prophylactic drain-policy in our hospital. Additionally, since no significant differences in leakage rates between groups with and without drainage were reported in literature [11], PD cannot be considered as a risk factor for anastomotic leakage.

#### Patient outcome

Mortality rate due to leakage was 14.1%, which is comparable to mortality rates reported in literature [4, 29].

The aforementioned 33-day increase in mean hospital stay in case of anastomotic leakage was to be expected and is indicative for the enormous increase in costs that is accompanied by this complication.

Concerning the postoperative complications, abdominal wound dehiscence (AWD) occurred significantly more often in patients with anastomotic leakage. In literature, several factors associated with abdominal wound dehiscence, being advanced age, obesity, diabetes mellitus, and steroid use [36], are reported. In this population BMI ( $p=0.06$ ), presence of diabetes mellitus ( $p=0.99$ ) and use of steroids ( $p=0.07$ ) were not associated with AWD. The average age of surgery in the group without AWD was 57 years and in the group with AWD 67 years ( $p=0.010$ ). However, since age is not a factor associated with anastomotic leakage this finding cannot explain the correlation between AWD and leakage. Another possible explanation may be found in connective tissue disorders. To date, a substantial body of evidence exists correlating aortic aneurysms to incisional hernia, both caused by connective tissue disorders [37]. In addition, Stumpf et al. have shown colorectal anastomotic leakage is associated with disturbances of the extracellular matrix [38]. These findings suggest that a patient population exists that has a higher risk for developing aortic aneurysms, hernia and

anastomotic leakage. In addition, this concept may contribute to the previously mentioned misunderstanding and lack of consensus on the matter of anastomotic leakage.

#### Conclusion

Anastomotic leakage after colorectal surgery remains a major complication. In our hospital, overall leakage rate is 8.7% and mortality rate is 14.1% in patients with anastomotic leakage. BMI greater than 30 kg/m<sup>2</sup> and “after hours” construction of the anastomosis were independent risk factors for anastomotic leakage.

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