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CHAPTER 5

The value of sigmoidoscopy to detect colonic ischemia after ruptured abdominal aortic aneurysm repair

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ABSTRACT

Objectives

Diagnosing colonic ischemia (CI) after ruptured abdominal aortic aneurysm (RAAA) repair is challenging. This study determined the diagnostic value of sigmoidoscopy in patients suspected of CI after RAAA repair.

Methods

This was a retrospective multicenter cohort study. Patients who underwent RAAA repair in three hospitals in Amsterdam, the Netherlands, between 2004 and 2011 (AJAX cohort) were included. Sigmoidoscopies were carried out based on clinical judgment. Endoscopy results were classified as “no ischemia”, “mild CI”, or “moderate to severe CI”. The surgical diagnosis was classified as “transmural” or “no transmural” CI. The value of sigmoidoscopy was assessed with calculation of positive and negative predictive values (PPV, NPV) with 95% CI for transmural CI. Logistic regression analysis was used to express the association of risk factors with CI as adjusted OR.

Results

Transmural CI was diagnosed in 23 of 351 patients (6.6%). Thirteen of sixteen patients (81%) who underwent direct laparotomy for high suspicion of CI indeed had transmural CI. Forty-six patients (13%) underwent sigmoidoscopy. The prevalence of transmural CI was 22% (10/46; 95% CI 12-36%) in these patients. The PPV for transmural CI of “moderate to severe CI” on sigmoidoscopy was 73% (8/11; 95% CI 43-90%). The PPV of “mild CI” on sigmoidoscopy was 11% (2/19; 95% CI 2.9-31%). The NPV of “no ischemia” on sigmoidoscopy was 100% (95% CI 78-100%). Cardiac comorbidity (OR 3.1, 95% CI 1.19-7.97), low first hemoglobin (OR 0.6, 95% CI 0.47-0.87), and high vasopressor administration (OR 9.4, 95% CI 1.99-44.46) were independently associated with CI.

Conclusions

Sigmoidoscopy increases the likelihood of correctly identifying the presence or absence of transmural CI, especially in patients with a moderate clinical suspicion for CI after RAAA repair.

INTRODUCTION

Colonic ischemia (CI) is one of the major complications after repair of ruptured abdominal aortic aneurysm (RAAA). CI can be mild and self-limiting, lead to prolonged sepsis, or progress to transmural ischemia with bowel perforation. The only meaningful treatment of transmural CI is operative resection of ischemic bowel segments.

The diagnosis of CI is challenging – especially in postoperative patients who are sedated and ventilated. Bloody stools, diarrhea, elevated markers of infection, or abdominal pain can indicate the presence of CI. It is also known that patients in shock are at increased risk of developing CI.¹ Yet, no symptoms are specific for CI, and the *a priori* chance of CI remains low after manifestation of symptoms. Previous trials have shown a prevalence of severe CI of approximately 6% after RAAA repair.^{2,3}

Clinicians often resort to sigmoidoscopy to ascertain the presence or absence of CI. The Society for Vascular Surgery suggests prompt endoscopy when CI is suspected after RAAA repair.⁴ Others have even suggested routine sigmoidoscopy after RAAA repair.^{5,6} However, evidence showing added value for sigmoidoscopy after RAAA repair is limited to few studies with relatively small cohorts.⁵⁻⁹ Therefore (routine) sigmoidoscopy is not widely established as common practice after RAAA repair.

The primary objective of this study was to determine the diagnostic value of sigmoidoscopy by calculating the positive predictive value (PPV) and negative predictive value (NPV) for transmural CI after RAAA repair. Other objectives were to determine risk factors for CI, to assess the consequences of CI, and to determine the difference in prevalence between open surgical repair (OSR) and endovascular aneurysm repair (EVAR).

METHODS

Study design and setting

This was a multicenter retrospective cohort study of patients who underwent repair of ruptured abdominal aortic aneurysm (RAAA) and were prospectively registered in the Amsterdam Acute Aneurysm (AJAX) cohort database. This database was part of a prospective cohort study which was carried out in parallel with the AJAX trial (ISRCTN: 66212637). Details of the AJAX trial and AJAX cohort have been reported previously.² The AJAX cohort consisted of all consecutive patients who presented with RAAA in three hospitals in Amsterdam (Academic Medical Center, VU Medical Center, and OLVG hospital) between 2004 and 2011. The institutional review board of OLVG hospital waived formal ethical approval for this retrospective study (reference WO 17.109) as it was not under the scope of the Dutch Act on Medical Scientific Research involving Human Subjects (WMO). This study was carried out in accordance with the STROBE statement.¹⁰

Participants and study size

All AJAX cohort patients who underwent RAAA repair and survived more than 6 h after arrival on the intensive care unit (ICU) were included in this study. Because this study focused on postoperative CI, patients with CI at RAAA repair were excluded, as well as those with ischemia of the small intestines.

Data collection

Baseline patient characteristics (e.g. comorbidity) were extracted from the AJAX cohort database. Data regarding surgical characteristics (e.g. additional procedures) and CI (e.g. grading and treatment) were retrospectively retrieved from electronic patient files. The three main sources in the patient files were surgical reports, discharge letters and when applicable, sigmoidoscopy reports. Writing of these reports was mandatory for clinical staff.

Primary endpoint

The primary endpoint was CI, as diagnosed at laparotomy or sigmoidoscopy. All sigmoidoscopies were carried out by gastroenterologists, but were not performed routinely. The decision to perform sigmoidoscopy was based on the clinical judgment of the treating vascular surgeons or intensive care staff. The sigmoidoscopy reports were graded categorically by two researchers (HJ, JD; in consensus) to enable inclusion in the cross tabulation analysis, which is explained below. Sigmoidoscopy results were graded as “no ischemia”, “inconclusive” (when the gastroenterologist could not make a diagnosis, e.g. because of fecal contamination), “mild ischemia” (when reported as grade I or as mild CI) or as “moderate to severe ischemia” (when reported as grade II or III, or as moderate mucosal CI to severe CI with gangrene or perforations). Laparotomy for CI suspicion was categorized as “none performed”, “negative for transmural CI”, or “positive for transmural CI”. Patients were considered not to have transmural CI when there was no clinical suspicion of CI at time of discharge or death, and when no laparotomy or sigmoidoscopy was carried out for CI. This included patients who died without undergoing laparotomy or sigmoidoscopy. Laparotomies for CI were carried out by either vascular or gastrointestinal surgeons. The presence of transmural ischemia during laparotomy was considered as the reference standard for confirmation of severe CI. Laparotomies were not included in the analysis when they were carried out for purposes other than suspicion of CI and CI was not detected. When multiple sigmoidoscopies or re-operations were carried out in a patient, no distinction was made between CI detection at first, second or third sigmoidoscopy, or re-operation. However, sigmoidoscopies that were performed after CI related laparotomies were excluded. When autopsies were carried out, autopsy reports were searched for potential CI diagnosis.

Other endpoints

Other endpoints were the sequelae of CI – defined as bowel perforation, death, laparotomy, bowel resection, or stoma placement – as well as abdominal compartment syndrome (ACS), markers for shock, and the combined 30 day or in hospital death rate. Pre-operative shock was represented by the Glasgow Aneurysm Score (GAS). GAS includes age, shock, myocardial, cerebrovascular, or renal disease, and type of aneurysm repair.¹¹ Post-operative shock was represented by the Acute Physiology and Chronic Health Evaluation (APACHE) II score, and by vasopressor administration, and fluid balance. APACHE II score is a measure of disease severity – used to predict the risk of ICU mortality – and comprises body temperature, the Glasgow Coma Scale, and serum electrolyte levels. Fluid balance was distributed in tertiles and categorized as: <2 L, 2-5 L positive, or >5 L positive. Vasopressor administration was categorized as none (no ICU admission or no vasopressors administered), low dose (noradrenalin <2 mg/min, or dopamine <500 mg/min), or high dose (any adrenalin, noradrenalin >2 mg/min, or dopamine >500 mg/min). The first hemoglobin (Hb) after arrival in the hospital was expressed in mmol/L. ACS was a clinical diagnosis, as intra-abdominal pressure was not routinely measured.

Statistical analyses

Diagnostic value of sigmoidoscopy

The diagnostic value of sigmoidoscopy was assessed with a cross tabulation analysis that enabled calculation of the PPV and NPV with 95% CI of sigmoidoscopy for transmural CI. Sensitivity and specificity were not calculated as sigmoidoscopy was not performed routinely.

Analysis of risk factors for CI

A univariable and multivariable logistic regression analysis was carried out to assess the association between risk factors and transmural CI. Included factors were baseline characteristics and pre-operative, intra-operative and post-operative factors. Missing data were not imputed. The three variables with the smallest *p* value in the univariable analysis and with less than 50 missing values were included in the multivariable model. Possible interactions between included variables were tested by means of interaction terms, which were added to the multivariable model when significant. Subsequently, the model was reduced with backward elimination to only retain variables with a *p* value smaller than 0.05. The results were expressed in OR with 95% CI.

Prevalence after OSR and EVAR

The difference in CI prevalence between OSR and EVAR was tested with the Fisher's exact test. A *p* value of < 0.05 was considered to be statistically significant.

Categorical data are reported in numbers and percentages. Continuous data are described as mean \pm standard deviation (SD) or as median and interquartile range (IQR) depending on normality of the distribution. All analyses were carried out with SPSS Statistics version 24 (IBM Corp, Armonk, NY).

RESULTS

Participants

Of the 407 patients undergoing RAAA repair, 56 were excluded: 32 died during repair, nine died within six h, six had CI diagnosed at open RAAA repair, five had ischemia of the small intestines, and four had missing charts (Figure 1). Thus, 351 patients were included in this study.

Sixty-seven patients (19%) underwent EVAR and 284 underwent OSR. Aorto-iliac anatomy was unsuitable for EVAR in 205 patients. The combined 30 day or in hospital mortality was 26% (90/351). The mortality in the total cohort (with patients excluded for reasons mentioned above) was 34% (140/407). Of the patients, 286 (81%) were male and the mean age was 74 ± 8.4 years. Other patient characteristics are listed in Table 1.

Outcome data

Colonic ischemia prevalence

In 43 of 351 patients (12%) any grade of CI, as detected by sigmoidoscopy or laparotomy, was diagnosed. Twenty-one patients (6.0%) developed transmural ischemia as confirmed by laparotomy. Two others required laparotomy for CI (severe CI on sigmoidoscopy) but were inoperable because of severe comorbidity. They subsequently died and were considered as having transmural CI, leading to a total number of 23 cases of transmural CI in the study (prevalence 6.6%). Twenty of 284 patients undergoing OSR developed transmural CI (7.0%, 95% CI 4.6%-10.6%), and three of 67 patients undergoing EVAR developed transmural CI (4.5%, 95% CI 1.5%-12.4%). This difference was not statistically significant ($p = 0.589$). Autopsy was carried out in 17 of 90 patients who died. Autopsy revealed CI as cause of death in only one patient. This patient was previously diagnosed with CI at laparotomy. No signs of CI were observed in the other patients.

Diagnostic value of sigmoidoscopy

After exclusion of six patients because of missing data (Figure 1), 345 patients were included in the sigmoidoscopy analysis. In 16 patients (4.6%), suspicion for CI was high and immediate laparotomy without prior sigmoidoscopy was performed (Table 3). In

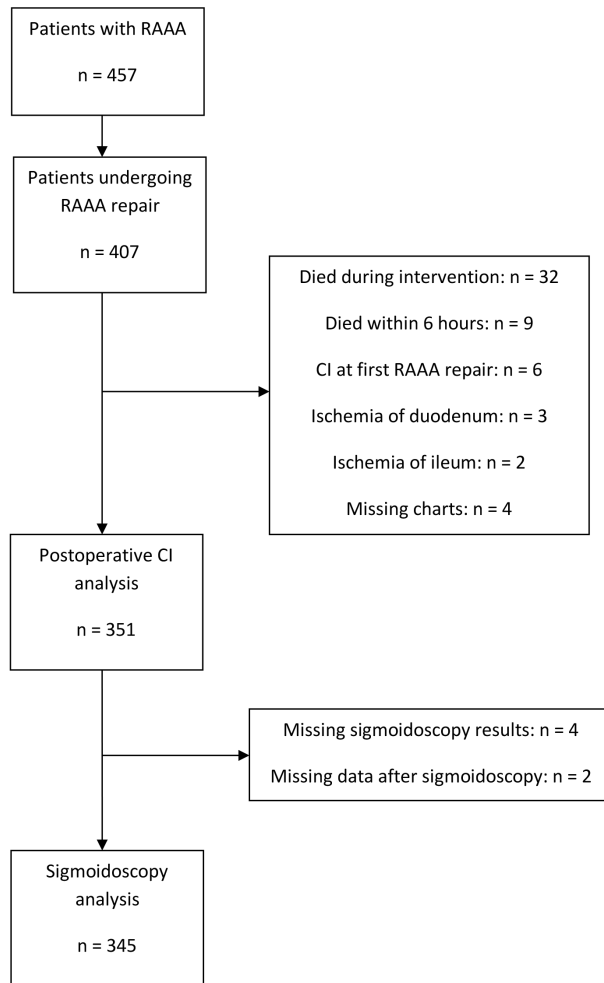


Figure 1. Flowchart of patient selection

four of them there was concomitant suspicion of other abdominal complications such as ACS or re-bleeding.

Forty-six patients (13%) underwent sigmoidoscopy, 40 after OSR and six after EVAR. Reasons for sigmoidoscopy were bloody stools in 21, increasing septic profile in 19, diarrhea in six, abdominal pain or distention in five, and unknown reasons in four patients. Ten patients had two or more symptoms leading to sigmoidoscopy.

Sigmoidoscopy results were “no ischemia” in 14, “inconclusive” in two, “mild CI” in 19 and “moderate to severe CI” in 11 patients (Table 3). The prevalence of transmural

Table 1. Baseline characteristics of 351 patients

Variable	Value	Missing
Age	74.2 ± 8.4	0
Sex: male/female	287/64	0
Cardiac comorbidity	42% (146/349)	2
Renal comorbidity	12% (41/348)	3
Cerebrovascular comorbidity	15% (54/349)	2
Body Mass Index	25.9 ± 3.9	44
Lowest preoperative in-hospital blood pressure	102 ± 13	13
Preoperative cardiopulmonary resuscitation	7.6% (26/340)	11
Repair: EVAR/OSR	67/284	0
Glasgow Aneurysm Score	92.2 ± 15.2	19
APACHE II score	20.0 ± 6.6	33
Vasopressor administration	None: 34% (119) Low dose: 44% (156) High dose: 21% (73)	3
Fluid balance	<2 L: 37% (129) 2 - 5 L: 36% (126) >5 L: 27% (93)	3

Continuous data are described as mean ± standard deviation

ischemia in patients who had undergone sigmoidoscopy was 22% (95% CI 12-36%), as confirmed by either laparotomy ($n = 8$) or as presumed cause of death ($n = 2$). Eight of ten had moderate to severe CI on sigmoidoscopy and two had mild ischemia. The scope reached into the sigmoid in 10 patients, to the descending colon in eight, to the splenic flexure in nine, to the transverse colon in seven, to the caecum in six, and to unknown distances in the others.

The PPV of “moderate to severe CI” on sigmoidoscopy was 73% for transmural CI (8/11; 95% CI 43-90%; Table 3, Figure 2). If the two non-operated patients were to be considered as false positives, PPV would be 55% (6/11; 95% CI 28-79%). The PPV of “mild CI” on sigmoidoscopy was 11% for transmural CI (2/19; 95% CI 2.9-31%). The NPV of “no ischemia” on sigmoidoscopy was 100% (14/14; 95% CI 78-100%). The small number of patients undergoing EVAR and sigmoidoscopy prevented the comparison of PPV or NPV between the OSR and EVAR group (Supplemental Table 1a and 1b). No adverse events occurred as a consequence of sigmoidoscopy.

Consequences of CI

Twenty-nine patients underwent laparotomy for suspicion of CI. Thirteen of them had previously undergone sigmoidoscopy (Table 3). CI was transmural in 21. In two of these

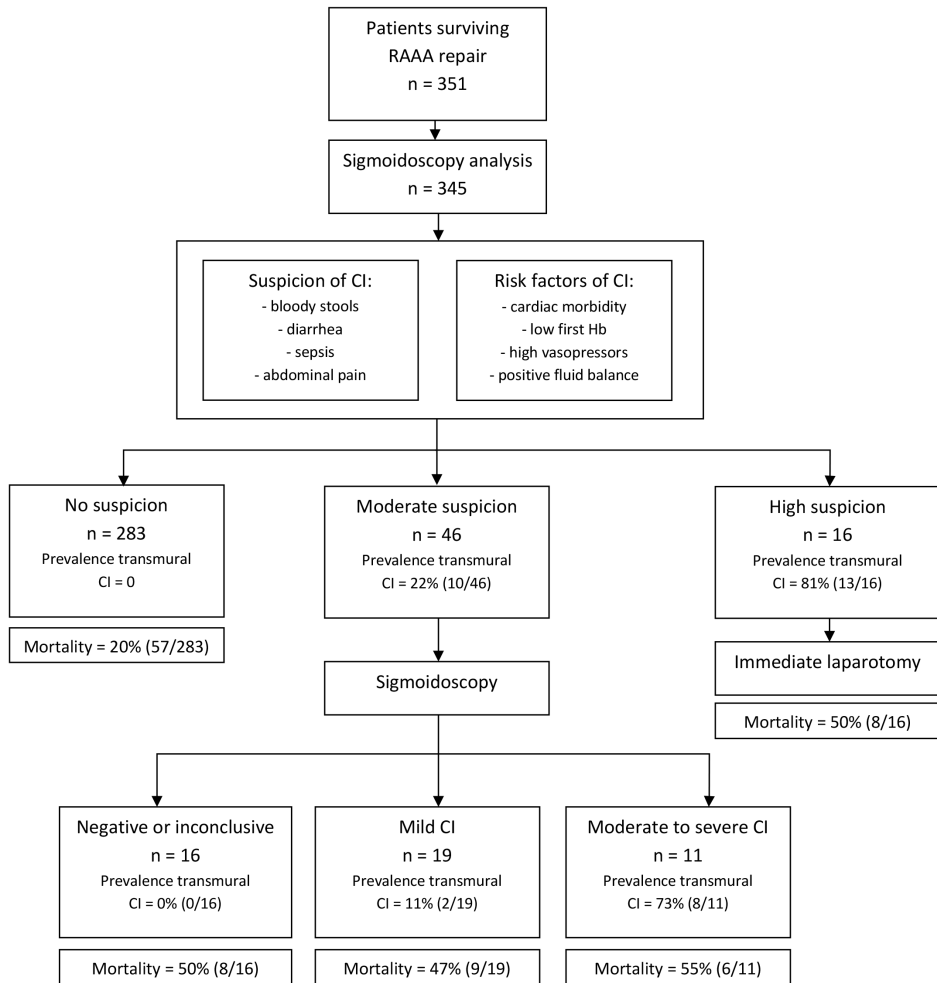


Figure 2. Flowchart of diagnostic process

patients extensive necrosis was found and palliative care was instigated. Sigmoidoscopy had previously revealed severe CI in one of them. The other 19 patients underwent bowel resection and received a stoma at laparotomy. The bowel was perforated in nine patients, three of whom had undergone previous sigmoidoscopy. There was no indication that the perforations were caused by sigmoidoscopy – they were present in severely ischemic segments. Laparotomy was negative (i.e. revealed no transmural ischemia) in eight patients (six had previously undergone OSR and two EVAR). Four of eight had previously undergone sigmoidoscopy (Table 3).

Table 2. Patient outcomes per OSR and EVAR

	Total (n = 351)	OSR (n = 284)	EVAR (n = 67)
Colonic ischemia			
CI, of any grade	43	35	8
CI, confirmed transmural	23*	20*	3
- location	-	-	-
- sigmoid	25	20	5
- descending colon	10	8	2
- colon, other	4	4	0
- colon and small intestines	3	3	0
- unknown	1	1	0
Laparotomy for CI	29	24	5
- immediate laparotomy	16	12	4
- bowel resection	19	17	2
- stoma	19	17	2
- perforation	9	8	1
Conservative treatment of CI			
- after mild CI on sigmoidoscopy	15	11	4
- after severe CI on sigmoidoscopy	3*	3*	0
Mortality (combined 30 day and in hospital)	90	76	14

OSR = open surgical repair, EVAR = endovascular aneurysm repair, CI = colonic ischemia

* including two who were inoperable and died most likely as a consequence of CI.

Of the 21 patients with transmural CI at laparotomy, eight survived hospital stay and 13 died – predominantly because of sepsis and multi-organ failure. As mentioned previously, two other patients also required laparotomy for CI (severe CI detected on sigmoidoscopy), but they were inoperable and died. With these patients included as confirmed transmural CI, the mortality rate in patients with transmural CI was 15/23 (65%, 95% CI 45-81%). Two of the eight patients with “negative laparotomy” did not survive the hospital stay (because of cardiac arrest and sepsis). All three patients with a negative immediate laparotomy (without prior sigmoidoscopy) survived the hospital stay.

Abdominal Compartment Syndrome

Postoperative ACS was diagnosed in a total of 15 patients (12 after OSR, three after EVAR). In four of them CI was also suspected. Two of four underwent sigmoidoscopy (showing severe CI in one and mild CI in the other) prior to laparotomy. Transmural CI was found in one of them at laparotomy. In the other, only decompression was carried

Table 3. Sigmoidoscopy and laparotomy results

		Laparotomy			
		None performed	Laparotomy without transmural ischemia	Laparotomy with transmural ischemia	
Sigmoidoscopy	None performed	283	3	13	299
	Inconclusive	1	1	-	2
	Negative for CI	14	-	-	14
	Mild CI	15	2	2 ^a	19
	Moderate / severe CI	3 ^b	2	6	11
		316	8	21	345

Six patients were excluded for this sigmoidoscopy analysis because of missing sigmoidoscopy results (4) or missing data after sigmoidoscopy (2).

^a One patient underwent a CT scan one day after sigmoidoscopy. CT revealed a perforated bowel.

^b Two of three were inoperable and died most likely as a consequence of CI.

out. In the other two patients, sigmoidoscopy was not performed and immediate laparotomy revealed transmural CI and ACS.

Risk factors for CI

The univariable logistic regression analysis revealed the following risk factors for transmural CI: cardiac comorbidity (OR 3.4, 95% CI 1.38-8.61), first Hb after arrival in the hospital (OR 0.6, 95% CI 0.47-0.82), high vasopressor administration (OR 11.5, 95% CI 2.50-53.07) and high fluid administration (OR 5.6, 95% CI 1.53-20.81; Table 4). Surgery duration and blood loss were also significant factors (OR 1.01, 95% CI 1.00-1.01 per minute and OR 1.2 95% CI 1.06-1.33 per L respectively; Table 4). Independent risk factors associated with transmural CI were cardiac comorbidity (adjusted OR 3.1, 95% CI 1.19-7.97), first Hb (adjusted OR 0.6, 95% CI 0.47-0.87), and high vasopressor administration (adjusted OR 9.4, 95% CI 1.99-44.46; Table 4).

DISCUSSION

This study suggests that the diagnostic value of sigmoidoscopy to detect CI after RAAA repair is high in patients with a clinically moderate suspicion of CI. First, it is effective in ruling out the presence of CI. Second, when doubts exist about the presence of CI, the probability of identifying a patient with transmural ischemia increases from approximately 22% to 73% when moderate to severe CI is detected at sigmoidoscopy. Risk factors for transmural CI were cardiac comorbidity and shock related variables (low first Hb, high vasopressors administration, and high fluid administration).

Table 4. Logistic regression analysis assessing the association between baseline and peri-operative characteristics and transmurals CI (n = 23/351)

Variable	Univariable		Multivariable		Missing
	Odds Ratio	95% CI	Odds Ratio	95% CI	
Baseline					
Glasgow Aneurysm Score	1.02	0.99 - 1.05			19
Age	1.00	0.95 - 1.05			0
Female sex	0.41	0.09 - 1.79			0
Cardiac comorbidity*	3.45	1.38 - 8.61	3.08	1.19 - 7.97	2
Pulmonary comorbidity	1.81	0.74 - 4.43			3
Renal comorbidity	2.23	0.78 - 6.37			3
Cerebrovascular comorbidity	0.23	0.03 - 1.78			2
Body Mass Index	1.04	0.94 - 1.15			44
Preoperative					
First Hb	0.62	0.47 - 0.82	0.64	0.47 - 0.87	2
First systolic blood pressure	0.99	0.98 - 1.00			15
Lowest systolic blood pressure	0.99	0.98 - 1.00			13
Cardiopulmonary resuscitation	2.03	0.56 - 7.35			11
Glasgow Coma Scale	0.73	0.16 - 3.26			44
Intraoperative					
Open surgical repair	1.62	0.46 - 5.61			0
Surgery duration (per minute)	1.01	1.00 - 1.01			15
Blood loss (per liter)	1.18	1.06 - 1.33			145
Hypogastric (All) coverage	Reference	Reference			22
- unilateral	2.74	0.85 - 8.78			
- bilateral	0.00	-			
Additional procedures	1.71	0.70 - 4.19			4
Postoperative					
APACHE II score	1.06	0.99 - 1.12			33
Vasopressor administration					
- None	Reference	Reference	Reference	Reference	3
- Low dose	3.58	0.76 - 16.90	3.46	0.72 - 16.63	
- High dose	11.51	2.50 - 53.07	9.41	1.99 - 44.46	
Fluid balance					
- <2 L	Reference	Reference			3
- 2 - 5 L	3.23	0.85 - 12.22			
- >5 L	5.63	1.53 - 20.81			

* Cardiac comorbidity was defined as the presence of cardiac arrhythmias or ischemic heart disease (either with symptoms or requiring intervention).

Some authors have recommended routine sigmoidoscopy in all patients after RAAA repair.^{5,6} As demonstrated in a recent meta-analysis, routine sigmoidoscopy is accurate for ruling out CI after AAA repair, but is less accurate in diagnosing the presence of clinically relevant transmural CI.⁹ Therefore, other authors have recommended sigmoidoscopy in patients with specific risk factors.^{7,12} It remains unclear whether sigmoidoscopy has actually improved, or possibly worsened, the clinical outcome of patients in the present study. Performing sigmoidoscopy carries the risk of delaying the time to bowel resection, and possible worsening of CI. In two patients, CI was too extensive at laparotomy to allow for curative bowel resection. One of them had undergone immediate laparotomy, but the other had undergone prior sigmoidoscopy which had revealed severe CI. It is unclear whether the latter would have had a better outcome if sigmoidoscopy had been carried out, and the surgeon had immediately proceeded to laparotomy. In contrast, sigmoidoscopy could have the ability to advance the decision to perform laparotomy. As previously mentioned, nine patients had bowel perforation at laparotomy. This indicates a delay before laparotomy. Only three of nine patients had undergone previous sigmoidoscopy. Their outcome might have been improved if the decision for laparotomy had been brought forward by positive findings at prior sigmoidoscopy.

The results show a low rate of negative immediate laparotomies (3/16). Surgeons appear to adequately withhold from unnecessary laparotomies – and only proceed to immediate laparotomy when CI suspicion is very high. The negative laparotomies did not appear to worsen the outcome of patients. They were mainly performed because of laboratory findings (infectious parameters, liver enzymes, lactate acidosis). The majority of patients with a negative laparotomy survived hospital stay (6/8). The two patients who died after a negative laparotomy had both undergone prior sigmoidoscopy – one with inconclusive results because of fecal contamination, and one showing mild ischemia. Unfortunately, sigmoidoscopy could not prevent the unnecessary laparotomy in these two patients. This underscores the necessity for other diagnostic methods for early CI detection. Previous studies have shown that computed tomography (CT) can diagnose acute mesenteric ischemia with high sensitivity and specificity,¹³ but its value for CI detection after RAAA repair is unclear. Therefore, recent AAA guidelines do not advise CT for CI detection.⁴ Other studies have shown promising results for colonic perfusion monitoring through intramucosal or intraluminal tonometry.^{14,15} Unfortunately the findings have not been replicated, and sigmoidoscopy has remained the most common method for CI detection in clinical practice. Future studies are therefore needed to assess the diagnostic value of CT and other modalities for CI after RAAA repair.

The risk factor analysis showed cardiac comorbidity and low first Hb as pre-operative risk factors for CI, and high vasopressor and fluid administration as post-operative risk factors. These findings are similar to the results of other studies.^{6,7,12,16,17} In contrast to

Ultee et al., hypogastric artery occlusion and additional procedures were not associated with transmural CI in the present study.¹⁶ Other predictive factors such as pH, transfusions, and temperature could not be validated in the present study as these were not registered in the patient files.

The prevalence of CI in this cohort was in line with the prevalence reported in other retrospective studies.^{16,18,19} Studies with routine sigmoidoscopy have revealed higher prevalences ranging between 14 and 32%.⁵⁻⁷ Therefore it is likely that the present study underestimated actual CI prevalence – especially regarding cases of grade I or II CI. Patients with a mild clinical course of CI who were treated conservatively might be missed in this study. This is also the case for patients who died without undergoing sigmoidoscopy or laparotomy for suspicion of CI. The cause of death was reported as multi-organ failure or sepsis in more than 20 patients who were classified as having no CI. It cannot be ruled out that some of them also suffered from CI. Unfortunately, the small number of autopsies could not provide more information regarding undetected CI cases.

Recent meta-analyses demonstrated a higher prevalence of CI after OSR compared with EVAR, both after elective and ruptured AAA repair.^{20,21} Contrary to the other studies, the present study did not highlight a significant difference in CI prevalence after EVAR compared to OSR (4.5% vs. 7.0%). The most likely reason for this was the low absolute rate of CI, particularly in the EVAR group in our study (n = 3). Another reason could be the changed and improved EVAR techniques of recent years. The inclusion period comprised the first years that EVAR was introduced for RAAA. Uni-iliac devices with femoro-femoral crossover bypass were used in the majority of EVARs. However, it is unlikely that the development of CI is related to different devices, as they all cover the inferior mesenteric artery and generally do not cover the hypogastric arteries.

Strengths and Limitations

Using a prospective cohort of consecutive patients, selection bias was reduced. One drawback of this study was that sigmoidoscopy was not performed routinely. This could have introduced detection bias because clinicians had different reasons and thresholds for performing or refraining from sigmoidoscopy. In addition, this prevented the estimation of the sensitivity and specificity of sigmoidoscopy. However, it was possible to estimate the PPV and NPV in patients with a suspicion of CI. Furthermore, the mere fact that sigmoidoscopy was not performed routinely enabled the estimation of the accuracy of immediate laparotomy for CI – which appeared to be very high. This would not have been possible if all patients had received routine sigmoidoscopy. Because sigmoidoscopy was not carried out routinely, it needs emphasizing that the estimated PPVs and NPVs only represent scenarios where CI suspicion is already present. The found PPVs and NPVs are not applicable to routine sigmoidoscopy – and probably overestimate the value of

routine sigmoidoscopy. However, a recent meta-analysis demonstrated a very similar PPV of 68% for grade 3 CI at routine sigmoidoscopy after RAAA repair.⁹

Furthermore, this study could not determine the time period between first CI suspicion and subsequent sigmoidoscopy or laparotomy. Possible delays caused by sigmoidoscopy or prolonged conservative management could not be analyzed. Another limitation was the fact that the cohort consisted of patients who presented with RAAA more than 6 years ago. It is possible that the prevalence of CI, especially after EVAR, could have changed since then. However, sigmoidoscopic techniques have largely remained the same, and the diagnostic value for determining CI should still be applicable today. Moreover, the absolute numbers of patients with mild or severe CI remained relatively small despite the large size of the cohort. As a consequence, the number of variables in the multivariable risk factor analysis was limited. The low numbers also resulted in relatively wide confidence intervals for PPV and NPV, which therefore need validation in other studies.

In addition, the categorization of endoscopically diagnosed CI in either “mild” or “moderate to severe” CI in this study was subjective. This categorization was chosen because the sigmoidoscopy reports allowed for a stricter division between mild and moderate CI, than between moderate and severe. Moreover, as mentioned in the Methods section, the detection of CI at sigmoidoscopy or laparotomy needed to be categorized and simplified to allow for clear distributions in the cross tabulation analysis.

Conclusion

Some 13% of patients underwent sigmoidoscopy for suspicion of CI after RAAA repair. Sigmoidoscopy increases the likelihood of correctly identifying the presence or absence of transmural CI, especially in patients with moderate clinical suspicion for CI after RAAA repair. Transmural CI was diagnosed in 6.6% of patients, but this is likely to be an underestimate of actual CI prevalence.

REFERENCES

1. Piotrowski JJ, Ripepi AJ, Yuhás JB, Alexander JJ, Brandt CP. Colonic ischaemia: the Achilles heel of ruptured aortic aneurysm repair. *Am Surg.* 1996;62:557-60; discussion 60-1.
2. Reimerink JJ, Hoornweg LL, Vahl AC, Wisselink W, van den Broek TA, Legemate DA, et al. Endovascular repair versus open repair of ruptured abdominal aortic aneurysms: a multicenter randomized controlled trial. *Ann Surg.* 2013;258:248-56.
3. Investigators IT, Powell JT, Sweeting MJ, Thompson MM, Ashleigh R, Bell R, et al. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. *BMJ.* 2014;348:f7661.
4. Chaikof EL, Dalman RL, Eskandari MK, Jackson BM, Lee WA, Mansour MA, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg.* 2018;67:2-77 e2.
5. Champagne BJ, Lee EC, Valerian B, Mulhotra N, Mehta M. Incidence of colonic ischaemia after repair of ruptured abdominal aortic aneurysm with endograft. *J Am Coll Surg.* 2007;204:597-602.
6. Tottrup M, Fedder AM, Jensen RH, Tottrup A, Laustsen J. The value of routine flexible sigmoidoscopy within 48 hours after surgical repair of ruptured abdominal aortic aneurysms. *Ann Vasc Surg.* 2013;27:714-8.
7. Megalopoulos A, Vasiliadis K, Tsalis K, Kapetanos D, Biztani M, Tsachalis T, et al. Reliability of selective surveillance colonoscopy in the early diagnosis of colonic ischaemia after successful ruptured abdominal aortic aneurysm repair. *Vasc Endovascular Surg.* 2007;41:509-15.
8. Champagne BJ, Darling RC, 3rd, Daneshmand M, Kreienberg PB, Lee EC, Mehta M, et al. Outcome of aggressive surveillance colonoscopy in ruptured abdominal aortic aneurysm. *J Vasc Surg.* 2004;39:792-6.
9. von Meijenfeldt GCI, Vainas T, Mistiotis GA, Gans SL, Zeebregts CJ, van der Laan MJ. Accuracy of Routine Endoscopy Diagnosing Colonic Ischaemia After Abdominal Aortic Aneurysm Repair: A Meta-analysis. *Eur J Vasc Endovasc Surg.* 2018;56:22-30.
10. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol.* 2008;61:344-9.
11. Samy AK, Murray G, MacBain G. Glasgow aneurysm score. *Cardiovasc Surg.* 1994;2(1):41-4.
12. Levison JA, Halpern VJ, Kline RG, Faust GR, Cohen JR. Perioperative predictors of colonic ischaemia after ruptured abdominal aortic aneurysm. *J Vasc Surg.* 1999;29:40-5; discussion 5-7.
13. Menke J. Diagnostic accuracy of multidetector CT in acute mesenteric ischaemia: systematic review and meta-analysis. *Radiology.* 2010;256:93-101.
14. Djavani K, Wanhainen A, Valtysson J, Björck M. Colonic ischaemia and intra-abdominal hypertension following open repair of ruptured abdominal aortic aneurysm. *Br J Surg.* 2009;96:621-7.
15. Djavani Gidlund K, Wanhainen A, Björck M. A comparative study of extra- and intraluminal sigmoid colonic tonometry to detect colonic hypoperfusion after operation for abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg.* 2011;42:302-8.
16. Ultee KH, Zettervall SL, Soden PA, Darling J, Bertges DJ, Verhagen HJ, et al. Incidence of and risk factors for bowel ischaemia after abdominal aortic aneurysm repair. *J Vasc Surg.* 2016;64:1384-91.
17. Björck M, Troeng T, Bergqvist D. Risk factors for intestinal ischaemia after aortoiliac surgery: a combined cohort and case-control study of 2824 operations. *Eur J Vasc Endovasc Surg.* 1997;13:531-9.

18. Becquemin JP, Majewski M, Fermani N, Marzelle J, Desgrandes P, Allaire E, et al. Colon ischaemia following abdominal aortic aneurysm repair in the era of endovascular abdominal aortic repair. *J Vasc Surg.* 2008;47:258-63; discussion 63.
19. Desikan SK, Singh N, Steele SR, Tran N, Quiroga E, Danaher P, et al. The Incidence of Ischaemic Colitis after Repair of Ruptured Abdominal Aortic Aneurysms Is Decreasing in the Endovascular Era. *Ann Vasc Surg.* 2017. *Ann Vasc Surg.* 2017;47:247-252.
20. Williamson JS, Ambler GK, Twine CP, Williams IM, Williams GL. Elective Repair of Abdominal Aortic Aneurysm and the Risk of Colonic Ischaemia: Systematic Review and Meta-Analysis. *Eur J Vasc Endovasc Surg.* 2018;56:31-39.
21. Jalalzadeh H, van Leeuwen CF, Indrakusuma R, Balm R, Koelemay MJW. Systematic review and meta-analysis of the risk of bowel ischaemia after ruptured abdominal aortic aneurysm repair. *Journal of Vascular Surgery.* 2018. doi: <https://doi.org/10.1016/j.jvs.2018.05.018>

SUPPLEMENTS

Supplemental table 1. Sigmoidoscopy and laparotomy results**a. Open surgical repair**

		Laparotomy for CI suspicion			
		None performed	Laparotomy without transmural ischemia	Laparotomy with transmural ischemia	
Sigmoidoscopy for CI suspicion	None performed	226	2	10	238
	Inconclusive	1	1	-	2
	Negative for CI	13	-	-	13
	Mild CI	11	2	2	15
	Moderate / severe CI	3 *	1	6	10
		254	6	18	278

* 2 of 3 were inoperable and died most likely as a consequence of CI

b. EVAR

		Laparotomy for CI suspicion			
		None performed	Laparotomy without transmural ischemia	Laparotomy with transmural ischemia	
Sigmoidoscopy for CI suspicion	None performed	57	1	3	61
	Inconclusive	-	-	-	0
	Negative for CI	1	-	-	1
	Mild CI	4	-	-	4
	Moderate / severe CI	-	1	-	1
		62	2	3	67