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EDITORIAL

Colonic Ischaemia – A Devastating Complication of Abdominal Aortic Aneurysm Repair

Colonic ischaemia (CI) has haunted abdominal aortic aneurysm (AAA) surgery ever since the beginning in the 1950s. In this edition of *EJVES* two systematic reviews are published, addressing this complication. The first paper, by Williamson et al.,[1] is a systematic review of the literature with the aim of identifying the contemporary incidence after elective AAA repair, be it open repair (OR) or EVAR. Interestingly, the authors excluded reports on ruptured AAA, despite the fact that CI is 5–10 times more common after ruptured aortic aneurysm repair. The main finding was that CI is more common after OR, with a relative risk of 2.7 after OR in a meta-analysis of the only three (out of 13) studies that attempted to address confounders.

This conclusion is most certainly correct, but multiple confounding factors exist that may be related to the disease, and the choice of treatment, rather than to the treatment as such. One such potential confounder is the anatomy of the aneurysm, patients undergoing EVAR are likely to have more favourable aortic neck anatomy. Furthermore, patients who present with common iliac aneurysms, in addition to the AAA, and may not be suitable for EVAR without sacrifice of the internal iliac arteries, and are therefore potentially more likely to undergo open repair.

The reported incidence of CI for both EVAR (0.5–1%) and OR (2.1–3.6%) relates to the definition of CI that the authors have chosen. They used a clinical definition of CI based on clinically detectable features of ischaemic colitis, abdominal pain, and bloody diarrhoea with or without endoscopic confirmation. It is inevitable that different authors use different definitions, making meta-analysis more difficult. The importance of the definition used can be clearly seen by comparing the low rates of CI reported in the study by Williamson et al.[1] when they are contrasted with those reported by von Meijenfeldt et al.[2] (in the second review in this edition of the journal) of 20.8% diagnosed by endoscopy, although the latter study included ruptured AAAs and mainly open repairs. The incidence of severe Grade 3 ischaemia in the latter study was 6.5%.

A significant factor, not touched on by Williamson et al.,[1] is intra-abdominal hypertension (IAH) and the abdominal compartment syndrome (ACS). The correlation between CI and IAH/ACS was shown in a prospective study on patients with ruptured AAA.[3] The evidence reported in the recently published ESVS Mesenteric Guidelines,[4] suggested that acute CI after AAA repair is most commonly associated with a hypoperfusion syndrome and often associated with IAH/ACS. This issue will be further elucidated in the revised ESVS AAA Guidelines, to be e-published and presented at the ESVS meeting in Valencia, in September 2018.

In a nationwide study from Sweden 2008–2013, the risk of developing ACS after intact AAA repair was 1.6% after OR versus 0.5% after EVAR ($p < .001$).[5] The figures are very similar to those reported on CI in this paper, and among those who developed ACS, 25% underwent bowel resection, compared with only 0.7% among those who did not develop ACS, underlining the important association between the two complications.

A further aim of this paper was to elucidate the interval between the primary operation and the complication. Approximately half the patients were diagnosed with CI within the first 24 h, and the other half within a week. Few patients developed CI more than a week after surgery. Unfortunately the authors were unable to demonstrate any difference in the timing of the CI diagnosis between patients undergoing EVAR and OR.

Despite the lower incidence of CI after elective EVAR in the largest study comparing outcomes of CI after open repair and EVAR, they also reported a significantly higher mortality following colectomy in the EVAR group (73% vs. 51%).[6] This interesting finding may suggest that a low index of suspicion of CI after elective EVAR, may result in diagnostic delay and in turn a poorer outcome. Many elective EVAR patients have very short hospital stays and it is important that vascular surgeons are aware of this devastating complication in order to improve the outcomes among the few patients that are affected.

The authors used the GRADE methodology to assess the quality of the evidence of the studies. They found the strength of the evidence to be very low for all outcomes. The probable reasons include the lack of a standard definition of CI and under reporting in large clinical studies on AAA repair. Even when CI is reported it is often done for the entire cohort, without sub-categorisation by type of repair or mode of presentation. It is vital that future publications provide accurate data on CI rates for elective and emergency AAA repair and for EVAR and OR.

In the second paper on CI von Meijenfeldt et al. performed a systematic review of the literature with the aim of evaluating the diagnostic test accuracy of routine endoscopy in diagnosing CI after treatment for both

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elective and acute AAA.[2] The authors identified 12 prospective studies that were included in the review, and the main conclusions were that colonoscopy has a strong negative predictive value, and thus is accurate in ruling out CI. In keeping with a previous review, it is not possible to distinguish mucosal from transmural ischaemia with colonoscopy.[7] However, the evidence suggests it is safe, as none of the studies reported serious adverse events associated with colonoscopy.

This paper is commended for reminding us about these "old truths" from the time prior to the widespread adoption of EVAR, when the majority of AAA patients underwent open repair. At this time there was limited knowledge of IAH/ACS, and no massive transfusion protocols. CI is less common today because of the lower incidence associated with EVAR, but remains a very serious complication with high mortality. The main limitation of this study is that the majority of the data are historical and only one study included patients treated by EVAR ($n = 44$).

Although colonoscopy appears to be safe, it may be uncomfortable for the patient, in particular during the insufflation of air. The authors also comment on the fact that endoscopy may contribute to IAH, and possibly ACS although there is no evidence to support this. Most of the studies included in the review were performed before the pathophysiology of IAH was well understood.

In conclusion, both these papers remind us of the devastating outcomes of colonic ischaemia following AAA surgery. The risk of CI appears lower after EVAR and is definitely lower following elective AAA repair. However, we must remain vigilant and have a high index of suspicion in order to allow early diagnosis and treatment when CI occurs. Endoscopic examination of the colon is safe and can reliably exclude CI and should be used when the suspicion of CI arises.

CI is still a complication with a very high mortality. The old surgical truth "It is better to look and see, than to wait and see" is still valid in the twenty first century when CI is suspected.

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REVIEW

Accuracy of Routine Endoscopy Diagnosing Colonic Ischaemia After Abdominal Aortic Aneurysm Repair: A Meta-analysis

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WHAT THIS PAPER ADDS

This paper presents a comprehensive overview of the diagnostic value of endoscopy in colonic ischaemia (CI) after aneurysm surgery. The 12 prospective studies included in this review showed that endoscopy is an accurate tool in ruling out CI rather than diagnosing the presence of the clinically relevant transmural CI. Endoscopy is a safe diagnostic test as none of the studies reported adverse events. The decision whether an exploratory laparotomy is necessary should also include the presence of pre- and post-operative risk factors of patients suspected of CI.

Background: Colonic ischaemia (CI) is a devastating complication after abdominal aortic aneurysm (AAA) surgery. The aim of this review was to evaluate the diagnostic test accuracy of routine endoscopy in diagnosing CI after treatment for elective and acute AAA.

Patients and methods: The Pubmed and Embase database searches resulted in 1188 articles. Prospective studies describing routine post-operative colonoscopy or sigmoidoscopy after elective or emergency AAA repair were included. The study quality was assessed with the QUADAS-2 tool. Sensitivity and specificity forest plots were drawn. Diagnostic odds ratios were calculated by a random effect model.

Results: Twelve articles were included consisting of 718 AAA patients of whom 44% were treated electively, 56% ruptured and, 6% by endovascular repair. Of all patients, 20.8% were identified with CI (all grades), and 6.5% of patients had Grade 3 CI. The pooled diagnostic odds ratio for all grades of CI on endoscopy was 26.60 (95% CI 8.86–79.88). The sensitivity and specificity of endoscopy for detection of Grade 3 CI after AAA repair was 0.52 (95% CI, 0.31–0.73) and 0.97 (95% CI 0.95–0.99) respectively. The positive post-test probability is up to 60% in all kinds of AAA patients and 68% in ruptured AAA patients.

Conclusion: Routine endoscopy is highly accurate for ruling out CI after AAA repair. Clinicians should be aware that endoscopy is less accurate in diagnosing the presence of the clinically relevant transmural CI. Endoscopy is a safe diagnostic test to use routinely as none of the studies reported adverse events.

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INTRODUCTION

Colonic ischaemia (CI) is a rare but severe and potentially fatal complication after abdominal aortic aneurysm (AAA) repair. Recent reports have shown an incidence of clinically significant CI of 1.4–2.8% after elective repair of an AAA and even higher after ruptured AAA.[1–4] CI can raise the mortality more than sevenfold after emergency repair compared with elective repair.[5] Open repair, emergency repair, peri-operative hypotension, abdominal compartment syndrome, and female sex are known risk factors for developing CI after AAA repair.

To lower the mortality after AAA repair, the early diagnosis of CI is important to allow for prompt and timely treatment of CI.[6] Different tests have been studied to determine the presence of CI but most lack specificity.[7–10] Bloody diarrhoea or early passage of stool occurred only in just over half of patients with transmural CI which makes

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clinical assessment very challenging. Moreover, measuring intra-abdominal pressure or sigmoid intramural pH did not correlate sufficiently with the occurrence of CI.

The diagnostic test most frequently used for diagnosing CI is sigmoidoscopy or colonoscopy. The majority of CI diagnosed on endoscopy will not involve transmural CI and will resolve with supportive care. However, full thickness CI may lead to colonic perforation and associated increased mortality and thus necessitates immediate diagnosis and treatment.

The aim of this review was to evaluate the diagnostic test accuracy of routine endoscopy in diagnosing CI after treatment for AAA, in both the elective and emergency setting.

METHODS

This systematic review was written according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[11] and the Cochrane handbook for diagnostic test accuracy reviews.[12]

Objective

The study objective was divided in three key questions to improve full clinical comprehension.

> Key question 1: What is the value of endoscopy (all grades) to diagnose CI confirmed at positive laparotomy or CI related death in AAA patients?
> Key question 2: What is the value of Grade 3 CI (transmural) at first post-operative endoscopy confirmed at positive laparotomy or confirmation of CI on post-mortem in AAA patients?
> Key question 3: What is the value of Grade 3 CI (transmural) at first post-operative endoscopy confirmed at positive laparotomy or confirmation of CI on post-mortem in ruptured AAA patients?

Data sources

PubMed and Embase were searched up to March 1, 2017, identifying eligible studies. The search strategy was formulated with the assistance of a clinical librarian (see Supplementary material 1). Medical subject heading[13] terms and additional free entry terms for the patient groups (patients with an AAA, ruptured or elective, treated endovascular or with open surgery), the diagnostic test and result (endoscopy with CI), the reference standard (laparotomy), and outcome (sensitivity and specificity) were used. The references of the selected papers were reviewed for the completion of the list of articles eligible for full text assessment.

Study selection

Two investigators (G.v.M. and G.M.) individually reviewed 1188 titles and abstracts. Discrepancies were resolved through consensus and consultation with the last author. Pre-specified inclusion and exclusion criteria in the research protocol were used to select potentially eligible studies for full text analysis. Inclusion of a study followed if the study used prospective data and performed at least one mandatory (routine) endoscopy after AAA repair. Acute and electively treated AAA patients were included as well as open and endovascular treated AAA patients. Both colonoscopy and sigmoidoscopy based studies were included. The endoscopies had to be done in the same admission as the initial treatment of the AAA. The studies needed to include at least 10 patients. There was no restriction in the year of publication or language of the study. The process of study inclusion was summarised in a flow diagram with explanation of exclusion of studies mentioned.

Data extraction

The two investigators (G.v.M. and G.M.) independently extracted the necessary information from the eligible articles. The data were cross-checked, and any discrepancies were resolved by discussion between the two investigators. Some of the studies also reported on the grade of CI: Grade 1 was defined as mucosal ischaemia; Grade 2 was defined as mucosal ischaemia and involvement of the muscularis layer; and Grade 3 was defined as transmural ischaemia, gangrene, and perforations.[14] If any of the main variables were missing or not reported separately for AAA patients and aortic occlusive disease the authors of that particular study were contacted.

Quality assessment

The methodological quality of the included studies was independently assessed by two investigators (G.v.M. and G.M.). The quality assessment tool for diagnostic accuracy studies guidelines (QUADAS-2)[15] was used to judge the risk of bias and applicability of the studies for the research question. Patient selection, the index test, the reference standard, and flow and timing were included in this assessment.

Data synthesis and analysis

Sensitivity and specificity forest plots were drawn using RevMan version 5.3.3[16] per key question. Pooled sensitivities and specificities were calculated using 2 $\times$ 2 contingency tables and reported to show an estimation of the direction of the trend. Heterogeneity was investigated using the I^2 statistic and interpreted as follows: 0—40% was considered not to be important, 30—60% represented moderate heterogeneity, 50—90% represented substantial heterogeneity, 75—100% indicated considerable heterogeneity.[17] The heterogeneity of the included studies was also visually drawn for all analyses in hierarchical summary receiver operating characteristics (HSROC). Publication bias was tested using the linear regression method and funnel plot of Deeks et al.[18] A p value $<$ .05 in this linear regression model indicated potential publication bias.

For the three key questions the pooled odds ratios were calculated using a random effect model because there was moderate heterogeneity between studies. Weighted estimates for each study were calculated and illustrated in a

forest plot. To evaluate the meaning of a positive or negative test result the pre-test probability, and positive and negative post-test probability were calculated and shown in a bar chart. All tests were two sided with a $p < .05$ indicating statistical significance. Meta-analyses were performed using STATA version 13.0 (StataCorp, College Station, TX, USA).

RESULTS

The search strategy identified 1188 potential studies after excluding duplicate records. Twelve prospective cohort studies met the inclusion criteria for the final analysis (Fig. 1).[6,10,14,19–27] The studies included a total of 845 aortic surgery patients of which 718 were aneurysm patients (elective 44%, ruptured 56%). No randomised controlled trials were identified. The full overview of study variables is shown in Table 1. Included patients were 86.6% male with a mean age of 69.5 years. Only one study included patients treated exclusively endovascularly (44 patients). All patients underwent a routine sigmoidoscopy or colonoscopy postoperatively (median time 3 days, range 1–13 days). At endoscopy 20.8% patients were identified with CI (all grades); 6.5% of patients had Grade 3 CI. Sixty-eight percent of patients with Grade 3 CI underwent a laparotomy. A resection or confirmation of transmural CI was reported in 74% of all laparotomies performed. The reported CI related death rate was 3.7% (20/546, 9 studies). This accounts for 24.2% of the total 30 day mortality (16/66, 6 studies).

Quality assessment, heterogeneity, and publication bias

The quality assessment of all included studies is shown in Fig. 2. Some studies included not only patients with an aneurysm but also occlusive aortic disease, which accounts for the higher risk of bias assessment in patient selection. However, the results were mostly reported separately for both types of patients in these studies. The general risk of bias and applicability was deemed to be low in the included studies. The heterogeneity chi square statistic was 3.70 ($p = .079$) and the I^2 statistic was 46% (95% CI 0–100), which indicate moderate heterogeneity that is to be expected in a diagnostic accuracy test review.[12] In Fig. 3 the HSROC per key question is shown to visually interpret the heterogeneity as well. Significant evidence of publication bias was found ($p = .001$, Supplementary material 2) by using the linear regression method of Deeks et al.[18]

Key questions

In Fig. 4 the forest plots of sensitivities and specificities related to the three key questions is shown. These forest

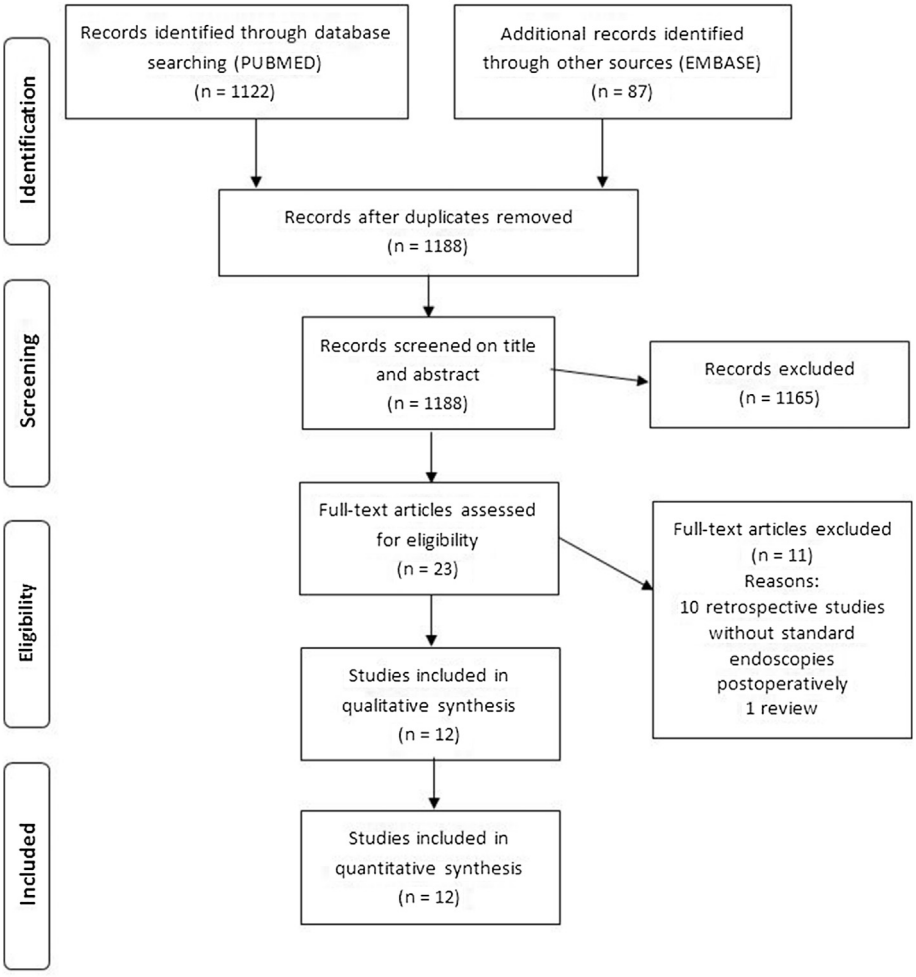


Figure 1. PRISMA flow diagram of study selection.

Table 1. Study characteristics and outcomes of the included studies.

Variables studies	Study duration	Number of patients	AAA surgery Total AAA surgery	Non-ruptured	Ruptured	Colonoscopy *N* (%)	AAA patients CI (*n*) with grades[a]	Time after surgery	Laparotomy AAA patients *N*	Positive laparotomy	30 day mortality AAA patients
Assadian 2008	Jan 1999—Dec 2003	100	100	N/A	N/A	100 (100%)	13 9 Gr 1—2 4 Gr 3	3—6 days	1	1	N/A
Bast 1990[e]	Jan 1986—Jul 1987	107	107	69	38	100 (100%)[b]	9 6 Gr 1—2 3 Gr 3	Days 2 and 4	3	1	N/A
Champagne 2004	Jul 1995—Sep 2002	88	88	0	88	62 (86%)[b]	24 18 Gr 1—2 6 Gr 3	<48 h	9	9	24% (21/88)
Champagne 2007	Jan 2002—Jan 2006	44	44 (all EVAR)	0	44	36 (92%)[b]	8 6 Gr 1—2 2 Gr 3	<24 h	3	3	N/A
Ernst 1976	N/A	50	27	25	2	27 (100%)	2	<4 days	0	0	3.7% (1/27)
Fanti 1997	May 1991—May 1994	105	105	88	17	105 (100%)	12	<3 days	0	0	N/A
Megalopoulos 2008	Mar 1999—Dec 2005	62	59	0	59	59 (100%)	19 16 Gr 1—2 3 Gr 3	<48 h + every 12 h	11	9	29.0% (18/62)
Scherpenisse and van Hees 1989[e]	'2 years'	48	48 (4 TAAA)	25 (2 TAAA)	23 (2 TAAA)	48 (100%)	24 15 Gr 1—2 9 Gr 3	<4 days	4	1	14.6% (7/48)
Schiedler 1987	May 1985—Feb 1986	34	20	16	4	20 (100%)	9	<13 days mean 3.2 days	3	3	N/A
Tottrup 2013	Jan 2010—Sep 2011	51	41	0	41	41 (100%)	9 5 Gr 1—2 4 Gr 3	<24 h	2	2	33.3% (17/51)
Welch 1998	N/A	56	28	28	0	28 (100%)	16[d]	<7 days	0	0	34% (19/56)
Zelenock 1989	1983—1986	100	58	N/A	N/A	58 (100%)	3	<48 h	3[c]	0[c]	2% (2/100)
Total	1976—2011	845 (12 studies)	718 (12 studies)	248/560 (44%, 10 studies)	312/560 (56%, 10 studies)	718 (12 studies)	148/718 (20.8%, 12 studies) Grade 3: 31/480 (6.5%, 7 studies)	Median 3 days (12 studies)	39/718 (5.4%, 12 studies)	29/718 (4.0%, 9 studies) 74.4% positive laparotomies	85/432 (19.7%, 7 studies)

AAA = abdominal aortic aneurysm; CI = colonic ischaemia; EVAR = endovascular aortic repair; TAAA = thoraco-abdominal aortic aneurysm.

[a] Grades of CI; Grade 1 was defined as mucosal ischaemia; Grade 2 was defined as mucosal ischaemia and involvement of the muscularis layers; and Grade 3 was defined as transmural ischaemia, gangrene, and perforations.

[b] Percentage of patients who survived long enough to be offered a colonoscopy, were not lost to follow up for other reasons.

[c] Data according to all patients included in the study not only AAA patients.

[d] The diagnosis of ischaemic colitis was determined by colonoscopy and histology.

[e] Studies from the same hospital in which the included patients might have overlapped.

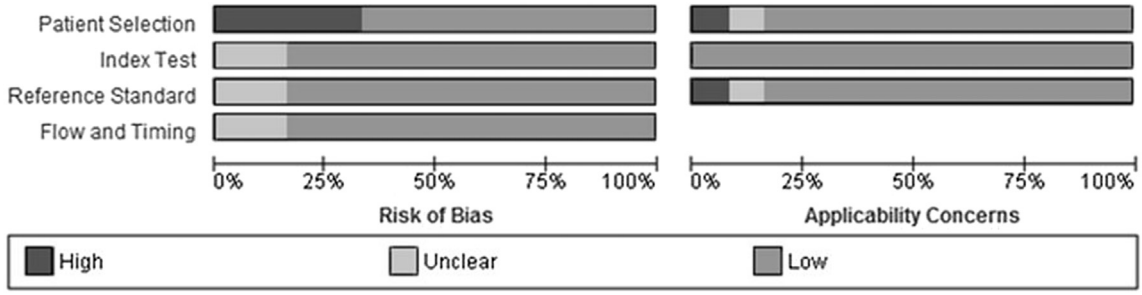


Figure 2. QUADAS-2 tool for quality assessment of the included studies for risk of bias and applicability concerns.

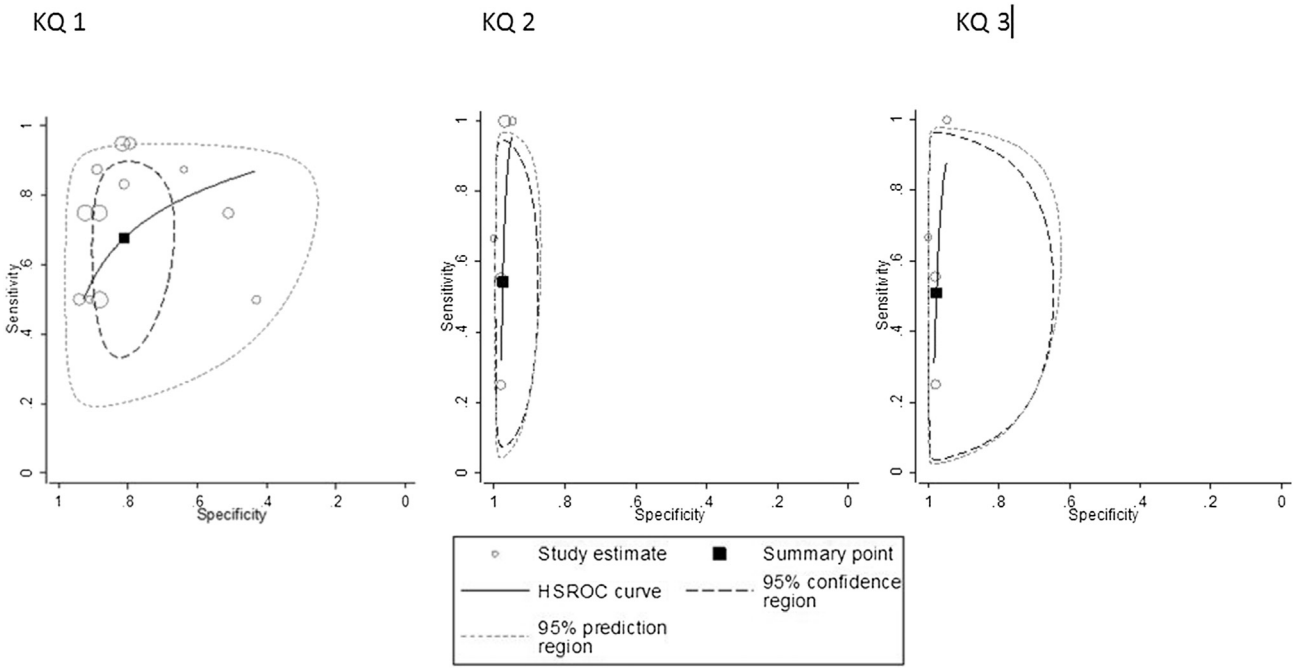


Figure 3. Hierarchical summary receiver operating characteristics (HSROC) per Key Question (KQ1—3). KQ1: all grades of CI on colonoscopy confirmed at positive laparotomy or confirmation of CI on postmortem in all AAA patients. KQ2: Grade 3 CI (transmural) on colonoscopy confirmed at positive laparotomy or confirmation of CI on postmortem in all AAA patients. KQ3: Grade 3 CI (transmural) on colonoscopy confirmed at positive laparotomy or confirmation of CI on postmortem in ruptured AAA patients. AAA = abdominal aortic aneurysm; CI = colonic ischaemia; HSROC = hierarchical summary receiver operating characteristics.

plots graphically show the differences in the sensitivities and specificities of the studies.

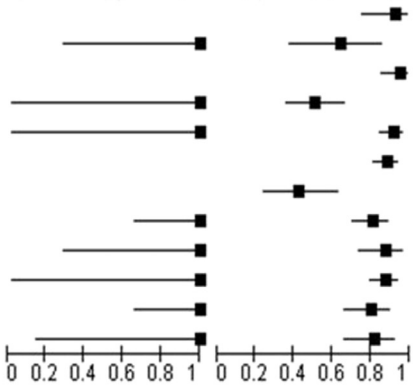
Key question 1: All grades of CI on colonoscopy confirmed at positive laparotomy or confirmation of CI on post-mortem in all AAA patients. To answer the first key question the estimated pooled sensitivity was 1.00 (95% CI 0.88—1.00) because no false negative test results were reported and the specificity was 0.83 (95% CI 0.80—0.86) (Fig. 4). The positive predictive value (PPV) for this test was 0.20 (95% CI 0.17—0.22) and the negative predictive value was 1.00. Some of the studies included only the final results of endoscopy since the endoscopy was repeated post-operatively. The pooled diagnostic odds ratio for all grades of CI on endoscopy was 26.60 (95% CI 8.86—79.88) as shown in Fig. 5. The diagnostic odds ratio reflects the diagnostic test accuracy of the index test and describes how many times higher the odds are of obtaining a positive test result in a diseased rather than a non-diseased person.[12]

Key question 2: Grade 3 CI (transmural) on colonoscopy confirmed at positive laparotomy or confirmation of CI on post-mortem in all AAA patients. The clinically more important second key question, to diagnose Grade 3 CI by endoscopy, showed an estimated pooled sensitivity of 0.52 (95% CI 0.31—0.73) and specificity of 0.97 (95% CI 0.95—0.99) (Fig. 4). The PPV was 0.63 (95% CI 0.43—0.80) and the NPV 0.96 (0.94—0.97). This corresponds with endoscopy being able to exclude CI reliably but in contrast, having a positive test result does not mean CI is definitely present in all cases. The pooled diagnostic odds ratio for Grade 3 CI on the first endoscopy was 50.40 (95% CI 13.89—182.89), which suggests good discriminative power of the test.

Key question 3: Grade 3 CI (transmural) on colonoscopy confirmed at positive laparotomy or confirmation of CI on post-mortem in ruptured AAA patients. For ruptured AAA patients (KQ3) the estimated pooled sensitivity of the first endoscopy after repair was 0.50 (95% CI 0.28—0.72) with a

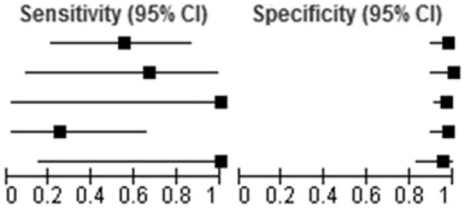
KQ1

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ernst 1976	0	2	0	25	Not estimable	0.93 [0.76, 0.99]
Schiedler 1987	3	6	0	11	1.00 [0.29, 1.00]	0.65 [0.38, 0.86]
Zelonock 1989	0	3	0	55	Not estimable	0.95 [0.86, 0.99]
Scherpenisse and van Hees 1989	1	23	0	24	1.00 [0.03, 1.00]	0.51 [0.36, 0.66]
Bast 1990	1	8	0	91	1.00 [0.03, 1.00]	0.92 [0.85, 0.96]
Fanti 1997	0	12	0	93	Not estimable	0.89 [0.81, 0.94]
Welch 1998	0	16	0	12	Not estimable	0.43 [0.24, 0.63]
Champagne 2004	9	15	0	64	1.00 [0.66, 1.00]	0.81 [0.71, 0.89]
Champagne 2007	3	5	0	36	1.00 [0.29, 1.00]	0.88 [0.74, 0.96]
Assadian 2008	1	12	0	87	1.00 [0.03, 1.00]	0.88 [0.80, 0.94]
Megalopoulos 2008	9	10	0	40	1.00 [0.66, 1.00]	0.80 [0.66, 0.90]
Tottrup 2013	2	7	0	32	1.00 [0.16, 1.00]	0.82 [0.66, 0.92]



KQ2

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Champagne 2004	5	1	4	52	0.56 [0.21, 0.86]	0.98 [0.90, 1.00]
Champagne 2007	2	0	1	33	0.67 [0.09, 0.99]	1.00 [0.89, 1.00]
Assadian 2008	1	3	0	97	1.00 [0.03, 1.00]	0.97 [0.91, 0.99]
Megalopoulos 2008	2	1	6	50	0.25 [0.03, 0.65]	0.98 [0.90, 1.00]
Tottrup 2013	2	2	0	37	1.00 [0.16, 1.00]	0.95 [0.83, 0.99]



KQ3

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Champagne 2004	5	1	4	52	0.56 [0.21, 0.86]	0.98 [0.90, 1.00]
Champagne 2007	2	0	1	33	0.67 [0.09, 0.99]	1.00 [0.89, 1.00]
Megalopoulos 2008	2	1	6	50	0.25 [0.03, 0.65]	0.98 [0.90, 1.00]
Tottrup 2013	2	2	0	37	1.00 [0.16, 1.00]	0.95 [0.83, 0.99]

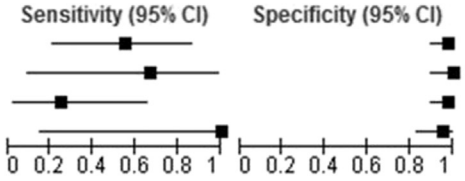


Figure 4. Forest plots of the sensitivities and specificities of the different key questions. KQ1: all grades of CI on colonoscopy confirmed at positive laparotomy or confirmation of CI on post-mortem in all AAA patients. KQ2: Grade 3 CI (transmural) on colonoscopy confirmed at positive laparotomy or confirmation of CI on postmortem in all AAA patients. KQ3: Grade 3 CI (transmural) on colonoscopy confirmed at positive laparotomy or confirmation of CI on postmortem in ruptured AAA patients. TP = true positives; FP = false positives; FN = false negatives; TN = true negatives.

specificity of 0.97 (95% CI 0.92—0.99) (Fig. 4). The PPV was 0.73 (95% CI 0.49—0.89) and the NPV 0.92 (95% CI 0.88—0.94). These results are quite similar to KQ2 as most studies included ruptured aneurysm patients. The pooled diagnostic odds ratio for Grade 3 CI on the first endoscopy in ruptured AAA patients was 47.78 (95% CI 12.09—188.81). There was no significant difference in the incidence of CI between patients treated endovascularly and those treated by open surgery for ruptured aneurysms (6.8% vs. 10.6% resp. $p = .58$). This non-significant difference could be explained by the small EVAR group that could be included in this review.

Pre- and post-test probabilities

To interpret the results of a positive or negative endoscopy after aneurysm repair the pre- and post-test probabilities were calculated (Fig. 6). This shows that having a positive endoscopy with any grade of CI, the chances of truly developing clinically relevant CI increase up to 22%. This is much higher if only Grade 3 is analysed, in which the positive post-test probability goes up to 60% in both elective and ruptured AAA patients and 68% in ruptured AAA patients. The chance of developing Grade 3 CI when the first endoscopy was negative, decreases to 5% post-endoscopy for all types of AAA patients, and to 7% for ruptured AAA patients.

DISCUSSION

This review evaluated the diagnostic accuracy of routine post-operative endoscopy in diagnosing CI after AAA repair. Endoscopy shows a high negative predictive value for diagnosing CI but a less sufficient positive predictive value. Therefore endoscopy has a place in clinical practice ruling out CI when the suspicion arises but does not necessarily allow the clinician to link a positive result to immediate laparotomy. The most ideal timing for the first endoscopy appears to be between days 2 and 3 after initial treatment as most patients were diagnosed around this time in the included studies. Particularly for patients treated for a ruptured AAA, in whom the incidence is highest (10% in this

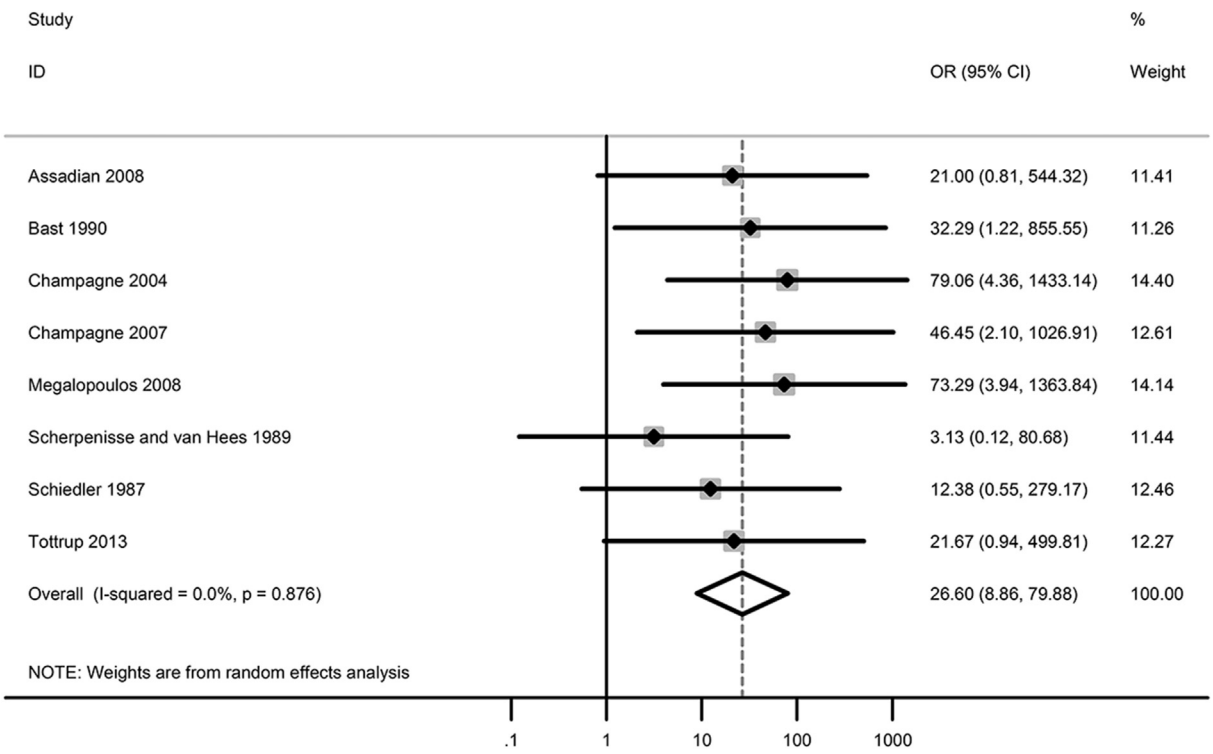


Figure 5. Pooled diagnostic odds ratios (OR) for Key Question 1: all grades of CI on colonoscopy confirmed at positive laparotomy or confirmation of CI on postmortem in all AAA patients. AAA = abdominal aortic aneurysm; CI = colonic ischaemia.

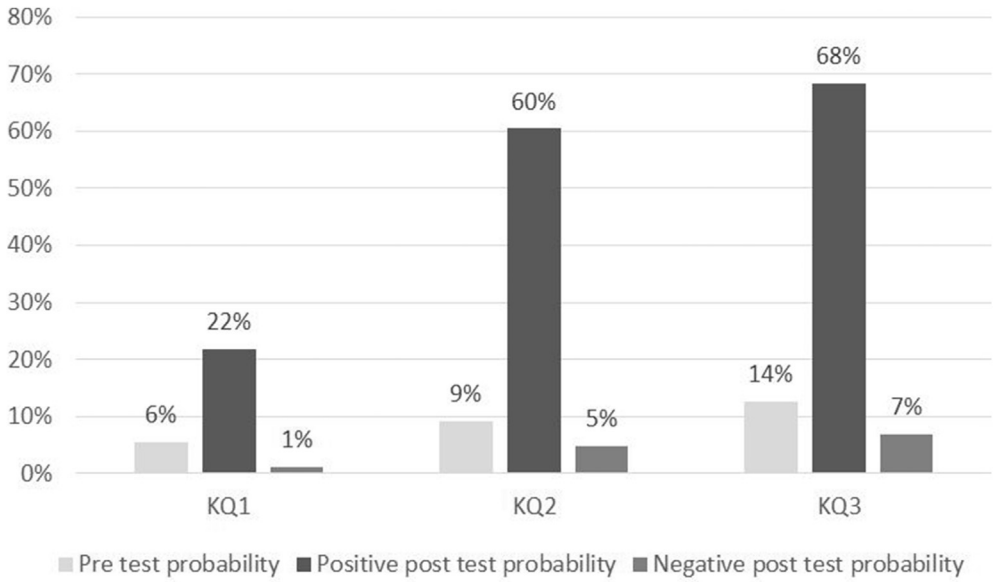


Figure 6. Pre- and post-test probabilities of the different Key Questions (KQ1—3). KQ1: all grades of CI on colonoscopy confirmed at laparotomy or confirmation of CI on postmortem in all AAA patients. KQ2: Grade 3 CI (transmural) on colonoscopy confirmed at positive laparotomy or confirmation of CI on postmortem in all AAA patients. KQ3: Grade 3 CI (transmural) on colonoscopy confirmed at positive laparotomy or confirmation of CI on postmortem in ruptured AAA patients. AAA = abdominal aortic aneurysm; CI = colonic ischaemia.

review), endoscopy has additional value to screen for CI. Additionally, none of the studies reported any adverse events due to the endoscopy. Therefore, the use of routine endoscopy, especially in ruptured AAA patients, could be a safe method to screen for CI after repair as presenting symptoms of CI are frequently unreliable and non specific.[7]

The reported overall pre-test probability in this review of 7% for CI is the combined incidence for elective and emergency AAA repair and therefore higher compared with most elective AAA studies.[4] Additionally, this reported incidence might be slightly higher than previously published cohorts because of the mandatory endoscopy protocol resulting in a overestimation of the clinically relevant transmural CI in whom intervention is necessary. Unfortunately, not enough data from the included studies were present to distinguish the value of endoscopy between

open and endovascularly treated patients reliably. Champagne et al.[14] was the only study including endovascularly treated AAAs and showed an incidence of CI of 6.8% in ruptured AAA patients against 10.6% in the ruptured AAA patients treated by open surgery but this was not significantly different. Previous cohorts did show that the incidence of CI was significantly higher in patients treated by open repair than endovascular repair. No difference in CI incidence was shown in the AJAX or IMPROVE trial between the two treatment modalities for ruptured AAAs[28,29] or elective endovascular and open AAA repair (DREAM trial; $n = 2$ after open vs. $n = 1$ after endo).[30]

As endoscopy also identifies clinically less important ischaemic lesions the sensitivity is relatively low. Endoscopy is insufficient to differentiate between severe mucosal ischaemia and clinically relevant transmural ischaemia.[31] Only a subsequent laparotomy can definitively confirm the presence of transmural ischaemia. A quarter of patients who underwent a laparotomy in this review had a negative laparotomy but it is unclear how this affected the morbidity and mortality in these patients.

It is important to realise the mechanism of developing CI after AAA repair is multifactorial and it is suggested to be caused by ligation of the inferior mesenteric artery (IMA) with occluded or stenotic internal iliac arteries,[9,22] hypoperfusion in the acute setting and during aortic clamping,[6,14,32] and abdominal compartment syndrome.[8] Endoscopy might cause an extra risk of increased intra-abdominal pressure (IAP) due to insufflation. If the patient has a borderline IAP, CI may develop as a complication of the investigation, although this cannot be corroborated with data.

Other means to identify patients with CI or who are likely to develop it have previously been studied. Variables such as age, hypotension, ligation of hypogastric artery, aortic clamping time, open repair, and many more have been described as potential risk factors.[4,6,9,27] A recent review including risk factors for CI could only identify open surgery and emergency repair as definite risk factors for CI.[5] Champagne et al.[14] showed that lactate was a good marker for CI, although this is contradicted by others.[32] Furthermore, there is evidence that if lactate is used, plasma D-lactate is more reliable than total blood lactate.[33,34] D-lactate is produced by colonic bacteria rather than the non specific L-lactate. The use of modalities like intramucosal pH and IMA stump pressure have not proven their additional worth.[10]

Diagnostic accuracy test reviews are generally affected by high heterogeneity and bias. In this review heterogeneity was attributable to different types of endoscopy, timing of the endoscopy after initial treatment (e.g., up to 13 days after AAA repair in the study of Schiedler et al.[10]) and the different thresholds for performing laparotomy. In addition to this, the publication date of the included studies was diverse. Also, according to the reported significant publication bias, studies that were not published due to negative results or other reasons could not be included in this review.[15] From two of the included studies it remains unclear if study cohorts overlap as they are from the same hospital. This would mean patients might have been included twice in this review.

As the incidence of CI is low, a large number of patients is necessary to reach sufficient statistical power. None of the included prospective studies mentioned a thorough power calculation to address this issue.

In conclusion, routine endoscopy has a high accuracy to rule out CI after AAA repair and is safe. Clinicians should be aware that endoscopy is less accurate in diagnosing the presence of clinically relevant transmural CI. The chance of truly having transmural CI after the diagnosis Grade 3 CI on endoscopy is 60% in contrast to only 5% when Grade 3 is not present on endoscopy. Endoscopy is a safe diagnostic test to use routinely as none of the studies reported adverse events. In future research a risk score might be developed to decide which patients would benefit most from endoscopy post-repair based on peri-operative risk factors. The decision whether a laparotomy is necessary should also include the presence of pre- and post-operative risk factors and comorbidities of patients suspected of CI.

CONFLICT OF INTEREST

None.

FUNDING

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ejvs.2018.02.008.

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Eur J Vasc Endovasc Surg (2018) 56, 31—39

REVIEW

Elective Repair of Abdominal Aortic Aneurysm and the Risk of Colonic Ischaemia: Systematic Review and Meta-Analysis

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WHAT THIS PAPER ADDS

This is the largest and most contemporary analysis that demonstrates colonic ischaemia (CI) occurs more frequently in open repair (2.1—3.6%) than in EVAR (0.5—1%) in the elective setting. The majority of cases present within 7 days. There is insufficient evidence to determine whether there is a difference in rates of re-operation for CI between the two techniques but when colectomy is required, the mortality rate is high. Most randomised trials of OR versus EVAR do not specifically report colonic ischaemia and its sequelae and this should be addressed by future trials given the high morbidity and mortality.

Introduction: Colon ischaemia (CI) is a significant complication of open (OR) and endovascular (EVAR) repair of abdominal aortic aneurysm (AAA). With a rapid increase in EVAR uptake, contemporary data demonstrating the differing rates and outcomes of CI between EVAR and OR, particularly in the elective setting, are lacking. The aim was to characterise the risk and consequences of CI in elective AAA repair comparing EVAR with OR.
Methods: A systematic review and meta-analysis of the literature was performed using the Cochrane collaboration protocol and reported according to the PRISMA guidelines. PubMed, MedLine, and EMBASE were searched for studies reporting CI rates after elective AAA repair. Ruptured AAAs were excluded from analysis.
Results: Thirteen studies reporting specific outcomes of CI after elective AAA repair, containing 162,750 evaluable patients (78,151 EVAR and 84,599 OR) were included. All studies found a higher risk of CI with OR than with EVAR. Three studies performed confounder adjustment with CI rates of 0.5—1% versus 2.1—3.6% (EVAR vs. OR) and combined odds ratio of 2.7 (2.0—3.5) for the development of CI with OR versus EVAR. The majority of cases of CI occurred within 30 days and were associated with variable mortality (0—73%) and re-intervention rates (27—54%). GRADE assessment of evidence strength was very low for all outcomes. There was a high degree of heterogeneity between studies both methodologically and in terms of CI rates, re-intervention, mortality, and time to development of CI.
Conclusions: EVAR is associated with a reduced incidence of CI compared with OR.

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Keywords: Ischaemia, Colon, Abdominal aortic aneurysm

INTRODUCTION

Despite recent advances in the treatment of abdominal aortic aneurysm (AAA) the post-operative risk of colonic ischaemia (CI) remains. Colonic ischaemia is a serious complication and a significant cause of post-operative mortality.[1—3]

Reported rates of colonic ischaemia after intervention for AAA vary between trials, as does its relationship with mortality. It is currently unclear whether CI is more common after open repair or EVAR, with overlapping rates quoted in different trials.[4—7] Colonic ischaemia has previously been considered to be more common after OR than EVAR and, looking explicitly at ruptured AAA, a Cochrane review found a decreased risk of CI after EVAR compared with OR (odds ratio 0.39, 95% confidence interval 0.07—2.11); however, much of the data were produced by a single trial with only 116 patients.[8] Furthermore, the acceptance of EVAR has increased significantly in the last few years[9,10] and so the rate of colonic ischaemia may have changed.

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Recent randomised controlled trials of EVAR versus OR were powered to detect differences in survival and all cause mortality;[11] however CI is relatively rare and there are therefore few high quality or powered data to reflect contemporary rates of colonic ischaemia. Furthermore, the incidence of CI may increase with time after EVAR, especially with Type 2 endoleak intervention and embolisation of the inferior mesenteric artery.

The aim of this meta-analysis was to compare and pool data from the literature to identify the contemporary incidence of post-operative colonic ischaemia after elective EVAR and open AAA repair, and to assess whether there is a relationship between the type of AAA intervention and the time when CI develops.

METHODS

Data sources, search strategy, and selection criteria

A systematic review was undertaken utilising the Cochrane collaboration specified protocol,[12] and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for the conduct of meta-analyses of interventional studies.[13] The following sources were searched without date restrictions: PubMed, Medline via OVID, Embase, the Cochrane Library Database, and the Current Controlled Trials register. Details of the protocol for this systematic review were registered on PROSPERO and can be accessed at www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017069624.

Studies reporting CI rates after elective AAA repair were included. Exclusion criteria included articles where ruptured aneurysms could not be analysed separately and aneurysms involving the suprarenal aorta. Definition of colonic ischaemia was based on clinically detectable features of ischaemic colitis including abdominal pain and bloody diarrhoea with or without endoscopic confirmation. There was no limitation on publication type or language in the initial search. An extensive search was also conducted using the "related articles" function in PubMed, of which the results were limited to human research, with review articles excluded. The last search date was June 10, 2017. Outcome events were captured when two or more papers presented extractable data. Non-English language papers were subsequently excluded, as were papers arising, or suspected of arising, from duplicate publications.

Data extraction and outcome measures

Data extraction and assessment of methodological quality were performed independently by two of the authors. For cases of disagreement a consensus was reached among all authors. Extracted data consisted of first author, year of study, study type, and design (including whether retrospective or prospective, single or multiple centres, whether consecutive patients were enrolled), number of participants, modality of treatment (EVAR or OR), numbers of patients experiencing colonic ischaemia, confounder corrected odds ratio, or relative risk of colonic ischaemia, number, nature, and timing of re-interventions for treatment of CI. Where available, data regarding the perioperative patency, embolisation and/or endoleak intervention to visceral arteries were extracted. Data were extracted at the 1 year follow up where available, or if not given at maximum follow up.

Outcome measures were defined as

1. CI rate
2. Mortality related to CI
3. Re-intervention rate for CI and any consequences
4. Time to CI.

Assessment of study quality and evidence rating

Study quality was assessed using the Downs and Black checklist, which assigns points depending on the quality of design (maximum 11 points), external validity (maximum 3 points), study bias (maximum 7 points), confounding and selection bias (maximum 6 points), and study power (maximum 5 points).[14] Studies with a score $\geq$ 17 were considered to be of higher quality.

Rating of the quality of evidence and strength of recommendation was undertaken using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system, according to Cochrane collaboration recommendations.[15] Quality was assessed and depended on risk of bias, indirectness of evidence, heterogeneity, imprecision of results, and publication bias. Cohort studies, by definition, have a "low" quality of evidence prior to further quality assessment. The presence of one or more serious limitations results in a "very low" grade of evidence. A serious effect on quality of evidence was considered to occur when >50% of included papers evidenced a risk of bias. Inconsistency was defined as an I^2 of greater than 50%. Indirectness was assumed not to occur in this setting. Imprecision was defined as fewer than 150 patients in either cohort. A serious effect on quality of evidence was considered to occur when greater than 50% of included papers evidenced a risk of imprecision.

Statistical analysis

Meta-analysis was undertaken in Review Manager version 5.3.5 (RevMan; Nordic Cochrane Centre, Copenhagen, Denmark). Meta-analysis was performed for dichotomous data where confounder corrected odds ratios or relative risks were available, using the odds ratio as the summary statistic, and reported with the 95% confidence interval, in line with the recommendations of the Cochrane Handbook.[12] Random effects models were used where significant heterogeneity between studies was detected. Heterogeneity was assessed using an I^2 calculation.[16]

The protocol specified that publication bias was to be assessed using funnel plots for outcomes with more than 10 studies,[17] although there were no outcomes which satisfied this criterion, so no funnel plots are presented.

RESULTS

Paper search and selection process

The initial search yielded 1190 results, and after initial screening for eligibility based on title and abstract 48 papers were retrieved for full evaluation. A total of 13 papers fulfilled the inclusion criteria and were included in the subsequent review[1,4–6,18–26] (Fig. 1). Excluded papers of note include five studies in which ruptured and elective AAA data could not be separated.[27–31] Also excluded were three randomised controlled trials[2,3,32] and four retrospective large case series[33–36] in which gastro-intestinal (GI) complications of AAA repair were reported but no specific data referring to ischaemic colitis were recorded. All included studies were case series reporting outcomes of ischaemic colitis after elective AAA repair either with EVAR, OR, or both. A total of 84,599 OR and 78,151 EVAR were available for evaluation.

Study design and baseline characteristics

Study characteristics are given in Table 1. There were six studies[1,4,5,24–26] comparing outcomes for patients treated by EVAR (76,520 patients) and OR (80,501). Three of these performed confounder adjustment, one by multivariate propensity matching of the cohorts[1] and the other two via multivariate modelling.[4,25] There were four studies reporting only EVAR[6,18,20,21] (1631 patients) and three studies reporting only OR outcomes[19,22,23] (4098 patients). Data for patients crossing over from EVAR to OR were not presented in any study. The diagnosis of colonic ischaemia was made on clinical grounds in all studies with endoscopic confirmation in four.[6,18,20,21]

There were three high quality papers as determined by the Downs and Black assessment presented in Table 1.[2,6,19] GRADE quality assessment was “very low” for all outcomes (Table 2).

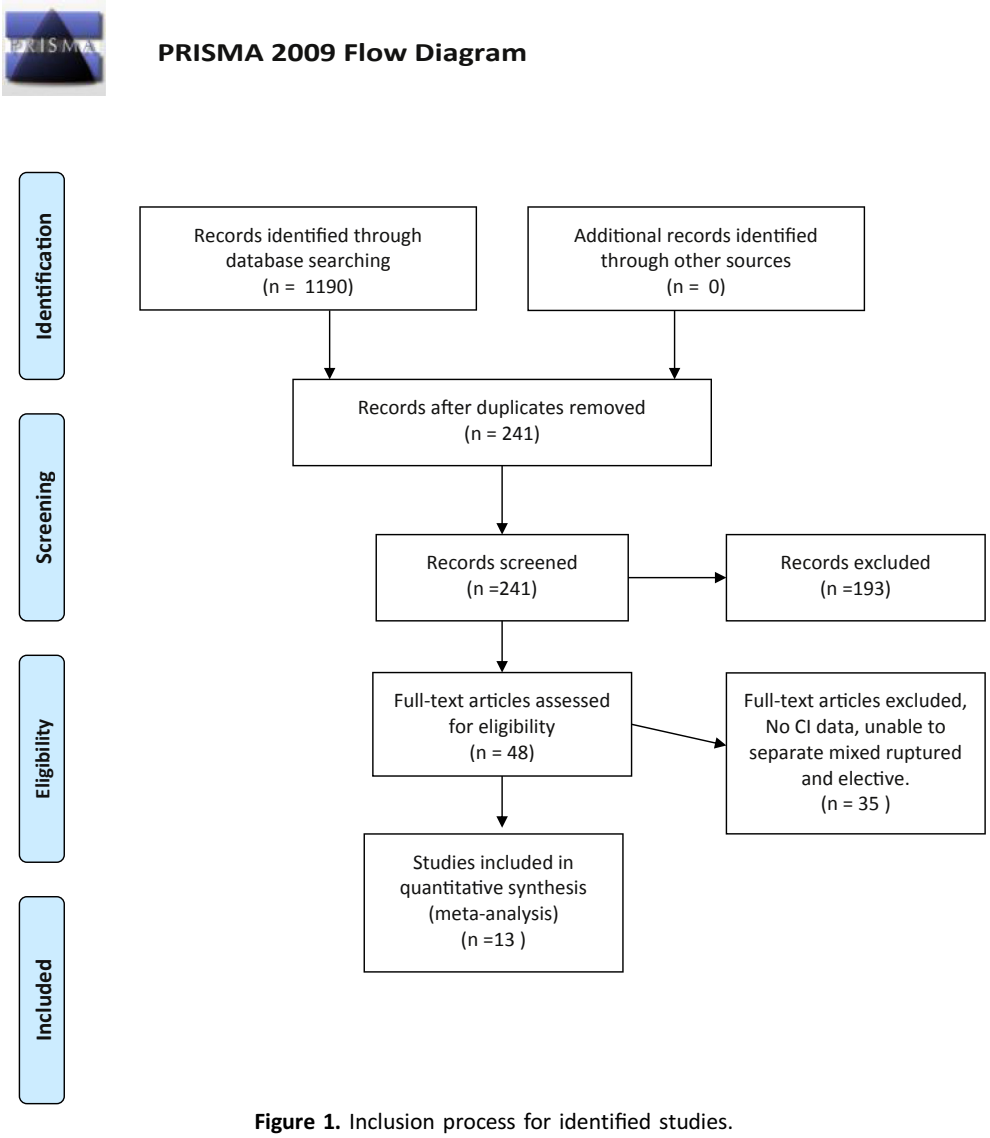

Figure 1. Inclusion process for identified studies.

Table 1. Study characteristics, demographic data, and Downs and Black scores for each paper.

Author (year)	Study period	Retro/prospective	No. of centres	Consecutive	Confounder correction	Intervention	Follow up (mo)	Patients (EVAR)	Patients (OR)	Diagnosis of CI	Outcomes	DB
Schermerhorn 2008	2001–2004	Retrospective	Multiple	N	Y	Both	48	29,542	32,056	CC	1, 2	17
Miller 2009	1996–2007	Retrospective	Single	Y	N	EVAR	12–120	809		E or C	1, 2, 3, 4	14
Valentine 1998	1994–1997	Prospective	Single	Y	N	Open	NS		120	C	1, 2, 3, 4	14
Dadian 2001	1992–2001	Retrospective	Single	Y	N	EVAR	12–108	278		E	1, 2, 3, 4	14
Geraghty 2004	2002–2004	Retrospective	Single	Y	N	EVAR	12	233		E	1, 2, 3, 4	14
Maldonado 2004	1994–2003	Retrospective	Single	Y	N	EVAR	22.5	311		E or C	1, 2, 3, 4	17
Perry 2008	2003–2004	Retrospective	Multiple	N	Y	Both	12	37,172	44,184	CC	1, 2, 3	21
Chiesa 2012	1993–2010	Retrospective	Single	Y	N	OR	Up to 17 years		3857	NS	1	9
Cruz 2001	1995–1998	Retrospective	Single	Y	N	OR	NS		121	NS	1, 2	12
Bonardelli 2012	2008–2011	Retrospective	Single	N	N	Both	36	12	303	NS	1, 2, 3, 4	7
Mehta 2005	2001–2003	Prospective	Single	Y	N	Both	18	175	232	NS	1, 3	9
Ultee 2016	2003–2014	Retrospective	Multiple	Y	Y	Both	1	4472	2196	E or C	1, 2, 3	15
Hynes 2017	2007–2013	Retrospective	Multiple	N	N	Both	48	5147	1530	NS	1, 3, 4	14

Note. Outcomes: 1, colon ischaemia (CI) rate; 2, CI mortality rate; 3, re-intervention rate; 4, time to CI. Mo = months; NS = not stated in the manuscript; DB = Downs and Black score. Diagnosis of CI: CC (clinical ICD code), E (endoscopic diagnosis), C (clinical diagnosis).

Outcomes

Outcome data for each study are presented in Table 3.

Colonic ischaemia rate

Thirteen studies reporting specific outcomes of CI after elective AAA repair, containing 162,750 patients (78,151 EVAR and 84,599 OR) were included. No randomised controlled studies reported specific CI outcomes. Six retrospective case studies directly compared CI in elective AAA between EVAR and OR. Confounder correction was performed in three of these studies, making them suitable for formal meta-analysis (Fig. 2). Colonic ischaemia rates in these three studies for EVAR (71,186 patients) versus OR (78,436 patients) were 0.5% versus 2.2%,[4] 1% versus 2.1%,[1] and 0.6% versus 3.6%.[25]

Odds ratios (95% confidence intervals) for the development of CI with OR versus EVAR were 2.19 (1.87–2.56),[1] 3.1 (2.7–3.7),[4] and 2.9 (1.8–4.7)[25] in the three studies which employed methods to correct for confounding, giving a combined odds ratio of 2.7 (2.0–3.5).

There was significant heterogeneity between these three studies, both methodologically and in terms of rates (I^2 = 80%). In the three studies which did not employ confounder correction, odds ratios were 1.003 (0.997–1.010),[5] 4.59 (0.55–38.5),[24] and 3.07 (1.17–7.98).[26]

A further seven retrospective case series were included in which three[19,22,23] reported CI rates in a total of 4098 elective open repairs and four[6,18,20,21] reported CI rates in a total of 1631 elective EVAR. Studies considering open repairs consistently published rates of CI which were higher than those studies considering EVAR.

CI mortality

There were three studies comparing EVAR to OR and of these, one reported no CI related mortality[5] and two reported significant mortality rates in the CI group: 25 out of 107 (23%) in one study[25] and 370 out of 1941 (19%) in the other.[4] In this latter paper, mortality associated with colectomy was significantly higher following EVAR than OR (73% vs. 51%, $p < .05$); however, conservative management was associated with increased survival following EVAR compared with OR (84% vs. 78%, $p < .05$). There were four studies reporting CI mortality in EVAR only patients[6,18,20,21] and of 27 cases of CI in these four papers, 11 patients (41%) died. There were two studies reporting CI mortality in OR only patients[19,23] and none of the three patients with CI died. See Table 3 for individual study mortality rates.

Re-intervention rate for CI

Re-intervention data were available in 11 papers (Table 3). Six papers reported re-intervention rates for patients undergoing both EVAR and OR and none demonstrated a significant difference in colectomy rates following EVAR compared with OR. Reported colectomy rates were variable between 27% and 100%. In one,[1] specific re-intervention rates for colonic ischaemia were not available. However,

Table 2. GRADE analysis and assessment of quality of evidence.

Outcome	EVAR (studies)	OR (studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
Colonic ischhaemia rate	78,151 (10)	84,599 (9)	No	Serious	Some	Serious	N/A	Very low
CI mortality	43,287 (7)	46,924 (5)	Serious	Serious	Serious	Serious	N/A	Very low
Re-intervention rate	78,151 (10)	80,412 (7)	Serious	Serious	Serious	Serious	N/A	Very low
Timing to CI	6790 (6)	1953 (3)	Serious	Serious	Serious	Serious	N/A	Very low

Risk of bias was assessed for each included paper, and was assumed to be present when a non-consecutive, or non-propensity matched cohort was analysed, or follow up did not reach 12 months.

rates of bowel resection as a complication of surgery were available and patients undergoing EVAR were less likely to undergo a small bowel resection than those undergoing OR in the first 4 years after aneurysm repair (3% vs. 3.4%, $p < .05$). In four papers reporting re-intervention rates in 1631 patients undergoing EVAR only,[6,18,20,21] 11 out of 27 with CI (41%) underwent emergency colectomy. A single paper[19] containing 120 patients reporting on OR only reported a single patient with CI treated surgically.

Time to colonic ischaemia

Seven studies reported the timing of initial signs and symptoms of colonic ischaemia. Hynes et al.[26] looked at the timing of re-operations within the first 30 days, finding that five out of 10 patients requiring intervention for CI following OR did so within the first 24 h and the remainder required intervention within the first week. Rates were similar following EVAR, with four of 14 in the first 24 h, 13 of 14 in the first week, and only one patient requiring re-intervention between 7 and 30 days. Four papers contained data on timing of development of CI after EVAR without comparison with OR.[6,18,20,21] Eighty-one per cent (22/27) of these cases occurred within 30 days and 19% (5/27) occurred after 30 days. Limited data were available for CI in OR without comparison with EVAR, with only two studies reporting on 423 patients undergoing OR. These reported two cases of CI, one of which was at 11 days and one was after 30 days.[5,19]

Peri-operative visceral arterial status

There was a single study reporting the effect of endoleak on CI and it found colonic ischaemia was associated with Type 3 but not Type 2 endoleak at the end of the procedure.[25] It was not possible to determine whether re-intervention was performed in these cases. Four studies recorded pre-procedure inferior mesenteric artery (IMA) patency and whether IMA embolisation had been performed.[6,18,21,25] It was not possible to extract data to draw specific comparisons of the effect of IMA embolisation on CI; however, in one paper, all patients who went on to develop CI following EVAR had a patent IMA pre-operatively[21] whereas the others reported between 62% and 91% of those who developed CI following EVAR had pre-existing IMA occlusions. Six studies reported on the effect of internal iliac artery (IIA) embolisation on CI. Of these, two reported a higher risk of CI with unilateral IIA embolisation,[18,25] whereas four studies reported no difference in risk of CI with either uni- or bilateral IIA embolisation.[6,20,21,24]

DISCUSSION

This analysis has identified several case series, which have compared CI rates between elective EVAR and OR. These studies are of variable quality, GRADE assessment was very low for all outcomes and only three performed any type of confounder adjustment. Meta-analysis of results from these studies suggests CI rates may be significantly higher for OR than EVAR. Outcome data for over 150,000 patients in 11 studies also demonstrated an advantage for EVAR in terms of reduced incidence of CI. It was not possible to consider comorbidities or patency of the IMA; however, in general EVAR demonstrates a lower risk of CI.

These results are similar to a recent review by Lee et al.,[37] who confirmed a reduced likelihood of CI after EVAR compared with OR (relative risk 0.22, 0.12—0.39, $p < .001$). However this analysis included both ruptured and elective AAA and contained older studies with a smaller number of patients and did not employ confounder correction. For ruptured AAA, a recent Cochrane review found a decreased risk of CI after EVAR compared with OR (odds ratio 0.39, 95% confidence interval 0.07—2.11); however, this relied upon a single randomised trial with only 116 patients.[8,38]

Peri-operative mortality was significantly lower in a recent meta-analysis of four randomised trials comparing EVAR with OR.[11] However, this early survival advantage is lost by 3 years, principally due to aneurysm specific complications, although patients with low ankle brachial pressure index experienced worse long-term survival with EVAR than with OR. There were insufficient data to determine whether colonic ischaemia was a factor in this. From this analysis, when CI occurs, it is usually identified within 30 days and is associated with a significant mortality rate, particularly when colectomy is required.

In several large randomised controlled trials, there were no available data for CI rates. Instead the authors reported less specific complications such as the need for re-laparotomy or GI intervention.[2,3,32,39,40] In one large series, there was an increased risk of small bowel resection following OR compared with EVAR and although the cause was not identified there was an associated increased risk of adhesion and hernia related bowel obstruction after OR and this is likely to be related. There were insufficient data to determine whether re-intervention rates for treatment of CI differed between OR and EVAR and were broadly similar in the larger series. Future randomised controlled trials should specifically report CI outcomes when comparing both procedures. This is particularly relevant as more patients with prohibitive risk factors for surgery are being offered EVAR.[41]

Table 3. Outcome data for each study.

Author (year)	Intervention	CI rate % (EVAR)	CI rate % (OR)	CI mortality rate	Re-intervention rate EVAR	Re-intervention rate OR	Time to CI	Pre-operative visceral arterial status	IMA intervention	IIA intervention
Schermerhorn 2008	Both	1	2.1	NS	"bowel resection" 3% $p = .02$	Bowel resection 3.4% $p = .02$	NS	NS	NS	NS
Miller 2009	EVAR	1.4	NS	4 of 11	3 of 11	NS	7/11 within 30 days, 4/11 after 30 days	IMA and IIA patency	10/11 with CI had pre-existing IMA occlusion	Unilateral IIA embolisation increased risk of CI. No comparable IMA data
Valentine 1998	OR	NS	0.83	0 of 1	NS	1 of 1	11 days	CA and SMA not IMA, IIA	No difference in GI complications	NS
Dadian 2001	EVAR	2.9	NS	3 of 8	2 of 8	NS	7 of 8 within 30 days, 1 within 6 months	IMA and IIA patency/ embolisation	5/8 with CI had preop occluded IMA. No comparable data without CI	No effect on CI rates with uni- or bilateral IIA embolisation
Geraghty 2004	EVAR	1.7	NS	2 of 4	3 of 4	NS	2 ± 1.4 days	IMA not reported. IIA patency/ embolisation reported	NS	No effect on CI rates with uni- or bilateral IIA embolisation
Maldonado 2004	EVAR	1.2	NS	2 of 4	3 of 4	NS	$3 < 12$ h, $1 < 7$ days	IMA and IIA patency/ embolisation	All with CI had patent IMA preop	No effect on CI with preop uni- or bilateral IIA embolisation
Perry 2008	Both	0.5	2.2	37.8%	27% colectomy $p < .01$	31% colectomy $p < .01$	NS	NS	NS	NS
Chiesa 2012	OR	NS	3	NS	NS	NS	NS	NS	NS	NS
Cruz 2001	OR	NS	1.6	0 of 2	NS	NS	NS	NS	NS	NS
Bonardelli 2012	Both	0	0.3	0 of 1	0 of 0	0 of 1	After 30 days	NS	NS	NS
Mehta 2005	Both	0.6	2.6	NS	1 of 1	6 of 6	NS	Data could not be extracted	NS	No patients developed CI where bilateral IIA sacrifice performed
Utlee 2016	Both	0.6	3.6	25/107 (23%)	14/26 (54%)	37/78 (47%)	NS	IMA and IIA patency/ embolisation/ reimplantation	Higher risk of CI if IMA reimplantation performed in OR	Higher risk of CI if unilateral IIA ligation/ embolisation in OR and EVAR
Hynes 2017	Both	0.3%	0.7%	NS	11/13	10/11	$9/24 < 24$ h, $18/19 < 7$ days	NS	NS	NS

IMA = inferior mesenteric artery; IIA = internal iliac artery; NS = not stated in the manuscript; CI = colonic ischaemia; CA = coeliac artery; SMA = superior mesenteric artery.

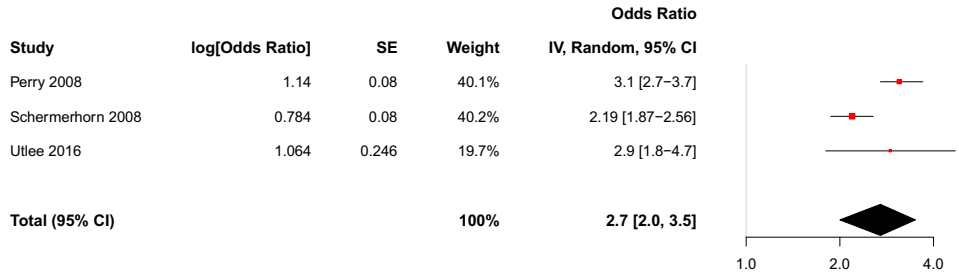

Figure 2. Forest plot comparing rates of colonic ishachemia between open repair (OR) and EVAR in studies employing techniques for multivariate confounder correction. Higher odds ratios imply higher rates among patients undergoing OR. Heterogeneity, tau-square = 0.05; chi-square = 10.06, d.f. = 2 ($p = .007$); $I^2 = 80\%$. Test for overall effect, $Z = 6.81$ ($p < .00001$).

The benefit of a selective approach to EVAR use in more frail patients is not clear[42] and the relative contributions of comorbidity and specific complications such as CI to survival and long-term outcomes from both EVAR and OR will be more difficult to interpret.

The physiological basis for CI after AAA repair is likely to be multifactorial and may explain the differences in CI rates. During open surgery a significant factor is aortic cross clamping causing ischaemia and reperfusion injury of the colon. One study found a threefold increase in colonic mucosal apoptosis in biopsies obtained immediately after surgery compared with EVAR. There were also significant rises in peripheral pro-inflammatory cytokines including tumour necrosis factor α compared with no evidence of apoptosis and much lower cytokine release following EVAR.[43] In the case of EVAR, a possible cause of CI is occlusion of the IMA. The effect of this on CI is unclear but is commonly performed in both EVAR and OR. One study attempted to address this by randomising 160 patients to IMA ligation or re-implantation during OR and found no difference in CI rates.[44] To perform EVAR, one and occasionally both internal iliac arteries need to be covered. A case control study demonstrated a tendency towards higher risk of CI after bilateral internal iliac artery ligation compared to unilateral ligation during open repair.[28] However, a review of 278 EVARs found that of eight developing CI, only one underwent internal iliac artery embolisation. The remaining 121 who underwent uni- or bilateral internal iliac embolisation showed no evidence of CI.[6] Furthermore, of the eight with CI, four had evidence of distal emboli within colonic arterioles because of embolisation from the aorta.

In the present analysis, data regarding the effect of peri-operative visceral arterial embolisation were limited and contradictory and no firm conclusions can be drawn from the available literature. Various techniques have been employed to improve detection and reduce the risk of CI including intra-operative intravenous fluorescein,[45] early post-operative sigmoidoscopy,[7] and intra-operative laser doppler flowmetry[46] although none is reliable for routine clinical practice.

Factors contributing to CI are emergency open repair for rupture and associated parameters such as blood loss, pre-existing renal and respiratory morbidity and length of surgery.[27,30,47]

The strengths of the analysis are that a large number of outcome parameters were available for analysis. All showed a higher rate of CI with OR. Unfortunately, most studies were poorly designed with limited or no evidence of cohort matching. Furthermore, the majority did not clearly describe how colonic ischaemia was diagnosed and definitions were largely based on clinical grounds with only limited descriptions of endoscopic confirmation.

It is notable many studies did not report the timing of onset of CI. Many studies did not use routine post-operative sigmoidoscopy and it is certainly possible minor and self limiting CI may not have been detected and only those with severe CI included in the analysis thereby increasing reported mortality and re-intervention rates. Several series reported onset of CI more than 30 days after initial treatment and may represent a different pathological process. Unfortunately, it was not possible to accurately confirm this from the data available. A sensitivity analysis was not possible due to the limited number of directly comparable studies. Furthermore, it was not possible to extract and meta-analyse data for confounding factors such as renal impairment, comorbidity, management of endoleaks, IMA ligation and/or re-implantation, transfusion requirements, length of stay, and operative time or technique including use of intra-operative Doppler monitoring of colonic perfusion or mesenteric artery re-implantation.

CONCLUSION

During elective procedures for treatment of AAAs, EVAR is associated with reduced frequency of CI compared with OR. When it occurs, CI is associated with significant mortality rates. Should emergency colonic resection be required mortality rises to over 50% in most studies. It is not clear if there is a difference in CI related mortality or colectomy rates between EVAR and OR; however, when it does occur, most cases present within 7 days for both procedures.

CONFLICT OF INTEREST

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