Replanting the inferior mesentery artery during infrarenal aortic aneurysm repair: Influence on postoperative colon ischemia

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Background: **Replanting the inferior mesentery artery (IMA) to prevent ischemic colitis (IC) has been discussed for many years; yet, to our knowledge, no prospective studies have been conducted to compare the incidence of histologically proven IC in patients with and without IMA revascularization. The aim of this prospective study, with histologic evaluation of the sigmoid colon mucosa, was to assess the influence of replanting the IMA on IC and mortality.**
Methods: **From January 1999 to December 2003, 160 consecutive patients who were operated on for a symptomatic (n = 21) or asymptomatic (n = 139) infrarenal aortic aneurysm were prospectively assessed and randomly assigned either to replanting or ligating the IMA. Sigmoidoscopy with biopsy was performed on day 4 or 5 after surgery; an autopsy was performed on patients not surviving to day 5 after surgery. All patients gave written informed consent.**
Results: **Of the 160 randomized patients, 128 had a confirmed patent IMA and formed the basis of this study. Their age was 70 ± 8 years (men, 70 ± 8 years; women, 73 ± 7 years). The IMA was replanted in 67 patients (52%) and ligated in 61 (48%) intraoperatively. IC developed in six patients with a replanted IMA and in 10 with a ligated IMA (relative risk [RR], 0.55; 95% confidence interval [CI], 0.21 to 1.41; $\chi^2 = 1.62$; $P = .203$). Blood loss in the two cohorts did not differ significantly ($P = .788$); however, patients with IC had a significantly higher blood loss compared with the cohort without IC ($P = .012$) and were older ($P = .017$). Age, sex distribution, clamping time, the use of tube or bifurcated grafts, and intraoperative hypotension did not differ between patients with ligated or replanted IMA.**
Conclusion: **Although replanting the IMA did not confer a statistically significant reduction of perioperative morbidity or mortality in this study, it appears that older patients and patients with increased intraoperative blood loss might benefit from IMA replantation, because this maneuver does not increase perioperative morbidity or substantially increase operation time. (J Vasc Surg 2006;43:689-94.)**

The observed incidence of colon ischemia after open aneurysm repair of the infrarenal aorta varies between 3% and 35%.[1-4] Many different factors have been associated with unapparent and symptomatic colon ischemia after aneurysm repair that predominantly affects the sigmoid colon. One of the presumed causes for the development of ischemic colitis (IC) includes the ligation of the inferior mesentery artery (IMA).[5] Replanting the IMA has been discussed for many years; yet, to our knowledge, no prospective studies have been conducted to compare the incidence of histologically proven IC in patients with and without IMA revascularization.

During the last decade, endovascular aortic surgery, in which this artery is always sacrificed by over-stenting, has challenged the concept of compulsory IMA replant. Nevertheless, because IC after infrarenal aortic aneurysm repair has multiple causes,[6-8] a certain proportion of patients could still have a benefit from IMA replant. Therefore, the possibility of patient selection for elective IMA replant to avoid postoperative IC, a complication with considerable morbidity and mortality, remains an unsolved problem in open aneurysm surgery. The aim of this prospective study, which used histologic evaluation of the sigmoid colon mucosa, was to assess the influence of replanting the IMA on IC and mortality compared with IMA ligation.

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PATIENTS AND METHODS

Patients. The study included 160 consecutive patients with symptomatic (n = 21) and asymptomatic (n = 139) infrarenal aortic aneurysm confirmed by computed tomography (CT) at 3-mm slices who were operated on from January 1999 to December 2003. Patients with bilaterally occluded hypogastric arteries, endovascular aneurysm repair, previous colon resection, inflammatory bowel disease, and a clinical condition indicating surgery ≤24 hours were excluded from the study. The cohort comprised 139 men (87%) and 21 women (13%). The mean age of patients was 77 ± 8 years (men, 76 ± 8 years; women, 81 ± 7 years).

All patients gave written informed consent. The study was conducted in accordance with the Declaration of Helsinki.

Surgical procedure. All operations were done with deep intubation and Th10 spinal anesthesia, and a retroperitoneal (90.4%) or transperitoneal (9.6%) access was used. Before aortic clamping, heparin (5000 IU) was administered intraoperatively. A tube graft was used in 52 patients (33%), and a bifurcated graft was used in 108

Table I. Baseline characteristics and continuous variables of patients randomized to replantation or ligation of the inferior mesenteric artery

	IMA replantation (n = 71)		*IMA ligation (n = 86)*		
	Range	*Mean ± SD*	*Range*	*Mean ± SD*	P
Age (y)	52-85	69 ± 8	49-86	69 ± 11	.922
Aneurysm size (mm)	38-100	57 ± 12	40-100	63 ± 15	.017*
Clamping time (min)	21-120	52 ± 26	20-140	51 ± 24	.917
Operation time (min)	115-560	216 ± 125	82-440	185 ± 71	.080
Blood loss (mL)	300-4500	1404 ± 927	250-4000	1272 ± 993	.462
Diastole (mm Hg)	30-120	63 ± 26	35-160	66 ± 27	.591
Systole (mm Hg)	140-200	171 ± 18	100-210	171 ± 22	.936
MAP (mm Hg)	85-160	117 ± 21	75-160	119 ± 15	.659

IMA, Inferior mesenteric artery; *SD,* standard deviation; *MAP,* mean arterial pressure.
*Indicates statistical significance.

patients (67%). The decision on the type of graft was determined by the extent of iliac artery involvement.

To reduce aortic cross-clamping time for patients who received a bifurcated graft, the right peripheral anastomosis to the common iliac artery was completed first, then the aorta was cross-clamped and the central anastomosis was sutured to the aorta. After this procedure, the left bifurcation axis was clamped and the aortic and right iliac clamps were removed. Finally, the left axis was sutured to the iliac artery. Therefore, in patients with bifurcated grafts, the time from clamping the aorta until release of the bloodstream from the aorta to the right iliac arteries was counted as cross-clamping time.

Before this study was conducted, all of the surgeons at our department were routinely replanting the IMA. The technique for replanting the IMA was universally the same. The IMA was ligated at the aorta with a nonresorbable suture and transfixed before cross-clamping. Next, the IMA was cross-clamped about 1 cm distal to the aortic origin and divided. The lumen was then inspected and endarterectomy performed, if necessary. Then the artery was incised 2 to 3 mm to augment the anastomotic region and to preclude anastomotic stenosis. Finally, the IMA was replanted after completion of the aortic anastomoses (tube or bifurcated graft) with 6-0 nonresorbable sutures into the graft.

Patients were randomly assigned to replanting or ligating the IMA during the study period. Intraoperative blood loss, operation time, aortic cross-clamping time, and mean arterial blood pressures were charted.

Histologic evaluation. A sigmoidoscopy (flexible colonoscope, CF-401, Olympus, Tokyo, Japan) with biopsy was performed on day 4 or 5 after surgery. A single dose of a second-generation cephalosporin was given before the procedure. Biopsy specimens were taken at 20, 30, and 40 cm from the anal verge. All specimens were immediately stored in a 5% formaldehyde solution for consecutive histopathologic examination. Biopsy specimens were taken from all patients, even if no pathologies were present at inspection. Visible mucosal abnormalities were also biopsied in addition to the standard specimens. Autopsies were performed on patients not surviving to day 5 after surgery; specimens of all organs were histologically examined.

The sigmoid mucosa was assessed as normal (no pathologic changes), with stroma edema/erythema (grade I changes due to ischemia), with fibrin deposits (mild colitis, grade II), and mucosal necrosis (grade III).

Statistical analysis. Continuous variables were compared using a two-sided Student's *t* test. Categoric variables were compared by using the χ^2 test or Fisher's exact test, where appropriate. Relative risks (RR) together with 95% confidence intervals (CI) and two-sided *P* values were calculated with the Epi-Info 2002 software package (Centers for Disease Control and Prevention, Atlanta, Ga). Values of $P < .05$ were considered to indicate statistical significant difference.

RESULTS

Histologic samples of the sigmoid colon were obtained from 157 (98%) of 160 study patients. Three patients could not undergo postoperative sigmoidoscopy and were excluded from further analysis. After conventional surgical repair for infrarenal aortic aneurysm, histologically proven ischemic colitis was detected in 23 (15%) of the 157 patients, of whom nine had clinically apparent IC and 14 had asymptomatic IC. Seven of the symptomatic patients had a histologic grade III IC, and two had grade II IC. Two of the 14 asymptomatic patients had grade III IC, five had grade II, and seven had grade I IC.

Of 157 patients, 71 (45%) were randomized to IMA replant and 86 (55%) to ligating the IMA intraoperatively (baseline characteristics of the 157 patients are presented in Table I, and outcome variables are in Table II). Of the 71 patients in the replanted group, 42 had a primary patent IMA; in 25 patients, the main trunk was occluded or stenosed (thrombus or atherosclerotic plaque) and endarterectomy was performed. In four patients, the IMA was totally obliterated and hence not replanted. Thus, the IMA was successfully replanted in 67 patients. Of 86 patients randomized to IMA ligation, 61 patients had either angiographic evidence of a patent IMA or good backflow from the IMA.

Of the 128 patients that were further evaluated, six died perioperatively during a 30-day observation period, accounting for a 4.7% mortality rate. Four of the six patients

Table II. Baseline characteristics and outcome variables patients randomized to replantation or ligation of the inferior mesenteric artery

	IMA replantation (n = 71)		*IMA ligation (n = 86)*				
	n	*%*	*n*	*%*	*RR*	*95% CI*	P
Male	64	90.1	74	86.0	1.05	0.93-1.17	.433
Symptomatic patients	7	9.9	12	14.0	0.71	0.29-1.70	.433
Operation technique							
Bifurcated graft	48	67.7	58	67.4	1.00	0.81-1.25	.982
Tube graft	23	32.3	28	32.6	0.99	0.63-1.57	.982
Reptoperitoneal	66	93.0	76	88.4	1.05	0.95-1.16	.330
Transperitoneal	5	7.0	10	11.6	0.61	0.22-1.69	.330
Outcome							
Ischemic colitis	7	10.0	16	18.6	0.53	0.23-1.22	.122
Death	3	4.2	6	6.9	0.60	0.15-2.30	.511

IMA, Inferior mesenteric artery; *RR,* relative risk; *CI,* confidence interval.

Table III. Baseline characteristics and continuous variables of patients with replantation of the inferior mesenteric artery compared with ligation

	IMA replantation (n = 67)		*IMA ligation (n = 61)*		
	Range	*Mean ± SD*	*Range*	*Mean ± SD*	P
Age (y)	52-85	70 ± 9	50-87	71 ± 8	.494
Aneurysm size (mm)	38-100	56 ± 11	40-100	61 ± 13	.032*
Clamping time (min)	21-120	48 ± 25	27-140	56 ± 25	.071
Operation time (min)	110-560	214 ± 119	95-440	197 ± 72	.333
Blood loss (mL)	300-4500	1317 ± 853	500-4000	1358 ± 897	.788
Diastole (mm Hg)	30-110	66 ± 23	40-100	64 ± 16	.436
Systole (mm Hg)	130-200	167 ± 18	100-210	160 ± 23	.091
MAP (mm Hg)	90-143	116 ± 14	78-138	112 ± 13	.059

IMA, Inferior mesenteric artery; *SD,* standard deviation; *MAP,* mean arterial pressure.
*Indicates statistical significance.

(three in the ligation group and one in the replant group) had histologically proven IC, and two (both randomized to IMA ligation) died of cardiovascular complications without histologic evidence of IC. Patients with IC had a statistically significant elevated relative risk of perioperative mortality (RR, 14.00; 95% CI, 2.79 to 70.36; $P = .002$, two-tailed Fisher's exact test). The mortality rate of elective patients alone was 3.5% (4/115).

Of patients with a replanted IMA, 61 were men (91%) and six were women (9%); of those with a ligated IMA, 52 were men (85%) and nine were women (15%) ($P = .308$). Baseline characteristics and differences of continuous variables are listed in Tables III and IV.

IC developed in 16 patients (6 replanted IMA, 10 ligated IMA), of whom seven had clinically apparent IC and nine had asymptomatic IC. Symptoms in these seven patients were abdominal cramps and bloody diarrhea in three patients (2 replanted, 1 ligated IMA), bloody diarrhea and clinical decline in two patients (both with ligated IMA), and clinical decline in two patients (1 replanted, 1 ligated IMA). Three of four patients who died with IC (2 from multiple organ failure) had laparotomy between days 2 and 4 postoperatively. In none of these patients, the attempt of IMA revascularization (2 ligated IMA, 1 replanted IMA) was made because the descending/sigmoid colon was necrotic. In one patient, a Hartman procedure was performed; however, the patient died 24 hours postoperatively.

Six of the symptomatic patients had histologic grade III (3 with replanted and 3 with ligated IMA) IC, and one had grade II (ligated IMA). One of the nine asymptomatic patients with IC had grade III (ligated IMA), four had grade II (2 ligated and 2 replanted IMA), and one (ligated IMA) had grade I.

Replanting the IMA did not account for a statistically significant reduction of risk of developing perioperative IC (RR, 0.55; 95% CI, 0.21 to 1.41; $\chi^2 = 1.62$; $P = .203$). Also, replanting the IMA did not have an influence on mortality. Of the six patients who died perioperatively, one had the IMA replanted, and five had the IMA ligated (RR, 0.17; 95% CI, 0.01 to 1.57; two-sided Fisher's exact test, $P = .102$).

Analyzed risk factors for the development of IC are summarized in Table V. Seven of 15 female patients

Table IV. Baseline characteristics and outcome variables of patients with replantation of the inferior mesenteric artery compared with ligation

	IMA replantation (n = 67)		*IMA ligation (n = 61)*				
	n	*%*	*n*	*%*	*RR*	*95% CI*	P
Male	61	90.0	52	85.2	1.07	0.94-1.21	.308
Symptomatic patients	6	9.0	7	11.5	0.78	0.28-2.19	.637
Operation technique							
Bifurcated graft	45	67.2	38	62.3	1.08	0.83-1.39	.564
Tube graft	22	32.8	23	37.7	0.87	0.54-1.39	.564
Retroperitoneal	64	95.5	53	86.9	1.10	0.98-1.23	.081
Transperitoneal	3	4.5	8	13.1	0.34	0.09-1.23	.081
Outcome							
Ischemic colitis	6	9.0	10	16.4	0.55	0.21-1.41	.203
Death	1	1.5	5	8.2	0.17	0.01-1.57	.102

IMA, Inferior mesenteric artery; *RR,* relative risk, *CI,* confidence interval.

Table V. Analyzed risk factors for developing ischemic colitis in 128 evaluated patients

Risk factor	*IC (n = 16)*	*No IC (n = 112)*	*RR*	*95% CI*	P
Male	9	104	0.17	0.07-0.39	<.0001*
Female	7	8	5.86	2.56-13.41	<.0001*
Age	75 ± 4	70 ± 8	n.a.	n.a.	.017*
Aneurysm size (mm)	55 ± 9	59 ± 13	n.a.	n.a.	.787
Blood loss (mL)	1844 ± 1243	1264 ± 785	n.a.	n.a.	.012*
Intraoperative hypotension (mm Hg)	1	24	0.27	0.04-1.98	.194
MAP (mm HG)	113 ± 12	115 ± 14	n.a.	n.a.	.658
Bifurcated graft	11	72	1.19	0.44-3.22	.726
Tube graft	5	40	0.84	0.31-2.26	.726
Symptomatic aneurysm	3	10	2.04	0.67-6.24	.208
Elective aneurysm repair	13	102	0.42	0.16-1.50	.208
Retroperitoneal access	15	101	1.55	0.22-10.74	.999
Transperitoneal access	1	11	0.64	0.09-4.46	.999
IMA replantation	6	61	0.55	0.21-1.41	.203
IMA ligation	10	51	1.83	0.71-4.74	.203
Clamping time (min)	63 ± 19	50 ± 25	n.a.	n.a.	.063
Operation time (min)	181 ± 57	209 ± 104	n.a.	n.a.	.286

IC, Ischemic colitis; *MAP,* mean arterial pressure; *IMA,* inferior mesenteric artery.
*Statistically significant.

developed perioperatively an IC compared with nine of 113 male patients (RR, 5.88; 95% CI, 2.56 to 13.41; $\chi^2 = 18.13$; $P < .0001$).

Aneurysm size within the IC population (55 ± 9 mm) did not differ from patients without IC (59 ± 13 mm) ($P = .787$). Also, there was no significant difference in aneurysm size between men and women (men, 58 ± 12 mm; women, 55 ± 8 mm; $P = .835$).

The blood loss in the two cohorts with replanted and ligated IMA was 1317 ± 853 mL and 1358 ± 897 mL, respectively, and not statistically significant different ($P = .788$). The influence of blood loss in general, however, on the development of perioperative IC was of statistically significant relevance. Patients with IC had a perioperative blood loss of 1844 ± 1243 mL compared with 1264 ± 785 mL in the cohort without IC ($P = .012$).

Intraoperative hypotension, defined as mean arterial blood pressure of <65 mm Hg for >10 minutes occurred in one patient with IC compared with 24 patients without IC and was statistically not significant (RR, 0.27; 95% CI, 0.04 to 1.98; two-sided Fisher's exact test, $P = .194$).

Also, the use of a tube or bifurcated graft did not influence the outcome of IC or mortality. Eleven patients with a bifurcated graft (13% of all patients with a bifurcated graft) and five with a tube graft (11% of all patients with a tube graft) developed IC, implying that a bifurcated graft does not increase the risk for IC (RR, 1.19; 95% CI, 0.44 to 3.22; $\chi^2 = 0.12$; $P = .726$) or the risk of perioperative blood loss (bifurcated grafts, 1390 ± 897 mL; tube graft, 1238 ± 822 mL; $P = .347$). Aortic cross-clamping time in patients with bifurcated grafts was 53 ± 27 minutes and 50 ± 20 minutes for tube grafts ($P = .650$). Patients with a bifurcated graft had slightly longer operation times than those with tube grafts (218 ± 111 minutes vs 184 ± 68 minutes; $P = .0649$), although this was statistically not significant.

Patients with a symptomatic aneurysm operated on ≤4 days of admission were also not more likely to develop IC. Three symptomatic patients (23% of all symptomatic patients) developed perioperative IC compared with 13 elective patients (11% of all elective patients) (RR, 2.04; 95% CI, 0.67 to 6.24; two-sided Fisher's exact test, $P = .208$). Cardiovascular mortality within the symptomatic group was significantly higher, however, as both patients with cardiovascular mortality occurred within this patient population.

DISCUSSION

Many different causes for the postoperative development of IC after open aneurysm repair have been suggested. Because IC has the highest incidence among patients with ruptured abdominal aortic aneurysms, this population has been examined most extensively.[4,9] IC has been linked to preoperative shock, intraoperative blood loss,[10] or low cardiac output.[11]

The observed incidence of colon ischemia after elective open aneurysm repair of the infrarenal aorta varies between 3% and 35%.[1-4] Importantly, not all studies were conducted prospectively or included sigmoidoscopy and histologic evaluation of all patients, thus explaining the range of observed IC. Clinically relevant rates of IC causing diarrhea, systemic involvement, colon necrosis, and ultimately, death by multiple organ failure only affect a smaller proportion of patients, however.

The assessment of postoperative IC is ideally by sigmoidoscopy and histologic evaluation of the sigmoid mucosa, because the colonoscopic assessment alone may produce false positive and negative results.[4] Also, most ischemic lesions in the colon after aortic reconstructions are located at the sigmoid and rectosigmoid junction,[12] unless multiple embolization is the pathophysiologic cause. Obviously, both colonoscopy and colonoscopically yielded mucosa samples only allow for the assessment of mucosal ischemia and gangrene but not transmural ischemia. Nevertheless, histologically altered mucosa implies altered barrier function[13] and may be causative for the translocation of intraluminal contents into circulation.[14] Colonoscopy and histology evaluation therefore cannot be considered diagnostic for transmural ischemia, but they can help identify patients at increased risk.[15]

Replanting the IMA is an appealing concept for open aortic surgery to reduce IC rates, as this is not time consuming and is a factor the surgeon can control, other than embolization or intraoperative hypotension unless caused by bleeding. In our current study, replanting the IMA did not significantly increase operation time or blood loss. Some techniques have therefore been described to detect intestinal viability, possibly also indicating the need for replanting the IMA.[3,16-17] Intraoperative IMA stump pressures were also evaluated, and it has been suggested that they do correlate well with the safety of ligating the vessel.[18] Mean pressures of ≤40 mm Hg were associated with IC. During cross-clamping or shortly thereafter, however, patients are far away from the physiologic conditions of gut perfusion; therefore, these measurements may lead to a false assessment.

Of 128 comparable patients by means of IMA patency who were randomized to ligation or replant, 16 had a histologically proven IC. The IMA was replanted in six and ligated in 10. Ligation of the IMA did not lead to a significantly elevated risk for developing IC ($P = .203$). It therefore appears that the role of the IMA is overrated. However, even in endovascular aneurysm repair, where the IMA is universally sacrificed by over-stenting, the incidence of clinically symptomatic IC is 1.4% to 2.9%.[8,19,20] This finding is in keeping with our results in this current study for open surgery.

Seven patients (5.5%) did have abdominal symptoms that were due to histologically verified colitis; however, three of our patients who died perioperatively with histologically proven IC had multiple organ failure. In this scenario, it is unclear whether IC caused multiple organ failure or, indeed, was induced by multiple organ failure. Nine patients (7%) did have microscopic evidence of colon ischemia without clinical symptoms. Of note, embolization seems to be the typical pathophysiologic mechanism of IC during endovascular interventions.[8,19,20] However, only one of our patients had histologic evidence of embolization (cholesterol emboli), and none of the other patients had any evidence of an embolic origin of IC.

In our patient population, aortic cross-clamping, which has been described as predictive for the development of IC,[4] did not demonstrate any difference between patients with a bifurcated or a tube graft ($P = .650$) and also no difference between patients with and without histologically proven IC ($P = .0.63$).

The relation of blood loss with the development of IC, however, was statistically significant ($P = .012$), indicating rather a nonocclusive, hemodynamic pathophysiology of IC in these patients. Importantly, no significant difference in blood loss was noted between patients with a replanted IMA and those with a sacrificed IMA ($P = .788$). The procedure itself does not, therefore, appear to be harmful to the patient. However, a significant difference was not demonstrated in intraoperative hypotension (mean arterial blood pressure <65 mm Hg for >10 minutes intraoperatively) between replanted and ligated IMA and patients who developed colitis or without colitis. On the other hand, this would indicate against a hemodynamic pathophysiology of IC in our patients. Yet, volume and drugs and their respective administration and timing intraoperatively were not recorded prospectively and may play an important role in flow dynamics of the intestine.

Finally, female sex appeared to have a statistically significant influence on the development of IC (RR, 5.86; 95% CI, 2.56 to 13.41; $\chi^2 = 18.13$; $P < .0001$). Yet, as sex distribution was very much in favor for male patients, this result may possibly be only by chance.

The major weakness of the study is that the final analysis revealed it was underpowered. Power calculations for a $P = .05$ with a two-tailed 90% CI under the assumption of histologically proven IC of 35%[4] in the ligated population

and 10% in the replanted population determined a sample size of <80 patients in each group. In this study, however, IC rates were 16.4% for the ligated and 9% for replanted IMA. Assuming that doubling the sample size would bear similar histologic IC rates for the respective groups, there would be a statistically significant difference in favor of replanting the IMA. Yet, current data do not demonstrate any difference. Importantly, seven of 16 patients with IC had clinically relevant IC, four in the ligated and three in the replanted group. Of these, three died with a ligated IMA and one with a replanted IMA, which is also not statistically significant.

CONCLUSION

In this study, replanting the IMA did not confer a statistically significant reduction of perioperative morbidity or mortality. However, it appears that older patients and patients with increased intraoperative blood loss might benefit from IMA replantation, because this maneuver does not increase perioperative morbidity or substantially increase operation time.

AUTHOR CONTRIBUTIONS

Analysis and interpretation: CS, OA, AA
Data collection: CS, AA, HP, HH
Writing the article: AA, CS
Critical revision of the article: GWH, HP, HH
Final approval of the article: CS, AA, OA, HH, HP, GWH
Statistical analysis: OA
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