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Causes and consequences of mesenteric embolization after endovascular aorto-iliac intervention — a nested case control study

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Abstract

Background: Causes and consequences of mesenteric embolization after endovascular aorto-iliac procedures have not been studied adequately.

Methods: Consecutive patients with mesenteric embolization after endovascular aorto-iliac intervention between 2011 and 2015 (case-group, n = 9) were investigated and compared with age, gender and procedure-matched random controls (n = 36).

Results: Compared to the control group, a higher proportion of patients with mesenteric embolization were current smokers (89% vs. 53%; $P = 0.048$) and had renal insufficiency at admission (44% vs. 11%; $P = 0.019$). In patients treated for aorto-iliac occlusive disease, aortic irregularity (shagginess) was more severe ($P = 0.015$), visceral thrombus volume was larger ($P = 0.004$) and operation-time was longer ($P = 0.009$) among the case-group. However, no differences were found between cases with mesenteric embolization caused by endovascular aortic aneurysm repair versus controls. Myoglobin, arterial blood lactate, aspartate aminotransferase, alanine aminotransferase and pancreatic amylase levels were elevated in 100%, 67%, 89%, 89%, 89% and 56% of patients with mesenteric embolization, respectively. Overall in-hospital mortality among cases was 33% (3/9). The in-hospital mortality was 17% (1/6) in patients treated with open abdomen therapy, of whom five were managed with stomas.

Conclusion: Smoking cessation, careful patient selection and procedure planning with identification of severe shaggy aortas might prevent mesenteric embolization during aorto-iliac procedures. In suspected cases of mesenteric embolization, elevated myoglobin and arterial blood lactate may be indicative of this complication. Aspartate and alanine aminotranferases, as well as pancreatic amylase, are also relevant tests to assess the extent of organ ischaemia. Damage control with open abdomen therapy and the creation of stomas seem justifiable in order to improve survival in this complex situation.

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Key words: mesenteric embolization; aortic aneurysm, endovascular therapy, endovascular aneurysm repair; iliac occlusion; shaggy aorta

Mesenteric embolization after vascular or endovascular surgery is very likely an under-reported complication. Microembolization may occur more often than is thought after both open and endovascular aneurysm repair (EVAR) [1]. There are very few reported clinical series in the literature of trash embolization after open aortic surgery to the mesenteric [2] or lower limb [3] arterial circulation. However, morbidity and mortality are high in these patients. In a single-

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centre study of 1,159 patients undergoing open repair of the descending and thoracoabdominal aorta, 2.5% developed intestinal ischaemia with 62% mortality. Intestinal ischaemia was the most frequent gastrointestinal complication in this series; it was mainly caused by embolization due to aortic manipulation and aortic cross-clamping, and was associated with atherosclerotic disease of the visceral arteries [2]. The current enthusiastic implementation and reporting of outcomes of endovascular therapy in aortic disease has not been accompanied by corresponding reporting of all possible complications. Few vascular centres have reported the incidence, morbidity, and mortality of mesenteric embolization after endovascular aorto-iliac intervention [4]. A recent case-control study in patients undergoing elective fenestrated endovascular aneurysm repair (FEVAR) showed that the incidence of mesenteric embolization after FEVAR was as high as 5% and it was associated with 80% mortality [5]. Interestingly, this study demonstrated an association of aortic irregularity (i.e., 'shagginess') and paravisceral thrombus volume with increased risk of mesenteric embolization.

The main aim of the present study was to evaluate, in a nested case-control design, the causes and the consequences of mesenteric embolization after endovascular aorto-iliac intervention in a Scandinavian endovascular-first strategy centre.

METHODS

This clinical study was deemed a quality assurance project for the department, and as such, not considered as research that needs ethical approval. The study was conducted at a tertiary vascular unit with a catchment population of 2.5 million inhabitants (www.scb.se). Consecutive patients with mesenteric embolization after endovascular aorto-iliac intervention between 1st of January 2011 and 31st of December 2015 were identified and retrieved from the operation planning program (ORBIT). During this time, 1,128 patients underwent an explorative laparotomy with or without a bowel resection; 216 underwent an endovascular aorto-iliac procedure for aorto-iliac occlusive disease; 294 underwent EVAR; while 90 patients underwent endovascular intervention of the superior mesenteric artery. From the entire cohort of aorto-iliac procedures, four age, gender and procedure-matched controls were randomly retrieved per case by a random number generator within SPSS (Statistical Package for the Social Sciences). The endovascular interventions were performed at the operating theatre under general anaesthesia by vascular surgeons. Patients with non-complex iliac occlusive lesions (without aortic involvement) who had undergone treatment at the endovascular laboratory under local anaesthesia were excluded from this study. Patient records were reviewed retrospectively. All patients were monitored from the day of the endovascular intervention until the day of death or 31st of July 2016. Mortality data were retrieved from the Swedish Population Registry.

DEFINITIONS

A current smoker was defined as active smoker or documentation of smoking within the last year. The maximal abdominal aortic aneurysm (AAA) diameter was specified as the shortest diameter at the widest portion of the aneurysm. The glomerular filtration rate (GFR) was calculated as a simplified variant of Modification of Diet in Renal Disease Study Group [6]. Renal insufficiency was present if GFR was < 60 mL min^{-1} in patients aged 50–65 years and < 50 mL min^{-1} in patients aged 65 years. Anaemia was defined as haemoglobin < 134 g L^{-1} in men and < 117 g L^{-1} in women.

AORTO-ILIAC MORPHOLOGY

Shagginess of the paravisceral aortic segment was assessed from the coeliac trunk to the lowest renal artery using preoperative computed tomography (CT) angiographies in each patient. The shagginess index was defined as degree of aortic irregularity and atheromatous plaque, where index 3 represented the most severe atheromatous disease with diffuse ulcers, and index 0 represented a clean, non-atheromatous aorta. The aortic thrombus volume between the coeliac artery and the lowest renal artery, and aorto-iliac tortuosity index was assessed using 3D software (TeraRecon; TeraRecon, Foster City, United States). After establishing a centre line of flow and defining the paravisceral segment to be measured, a vessel view was achieved in the stretched curved multiplanar reconstruction mode. External wall-to-external-wall volume, luminal volume, and non-luminal or thrombus volume were automatically measured. The aorto-iliac tortuosity index was defined as the ratio of length from the coeliac artery to the bifurcation of the common femoral artery in a centre line divided by the direct point-to-point length from the coeliac artery to the bifurcation of the femoral artery on 3D coronal view [7]. The TransAtlantic Inter-Society Consensus (TASC) guidelines were used for grading the extent of aorto-iliac occlusive disease.

OPEN ABDOMEN THERAPY

The vacuum assisted wound closure and mesh-mediated fascial traction technique (Fig. 1) was used when open abdomen therapy was anticipated to last longer than five days. The visceral protective layer was placed above the entire viscera (Acelity/KCI, San Antonio, United States). A polypropylene mesh was divided into two halves and sutured with a 0 running polypropylene suture with narrow bites to the fascial edges on each side. The mesh halves were sutured together with a 0 running polypropylene suture in the midline, keeping the viscera from protruding. The polyurethane foam outer layer was placed on top between the abdominal wall edges, after which the wound was sealed by occlusive self-adhesive polyethylene films. The suction device was connected to a calibrated negative pressure source. A continuous negative pressure of 125 mm Hg was the standard set-

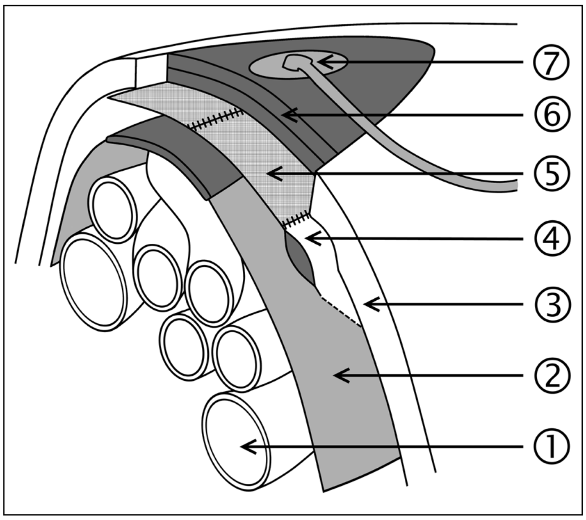

Figure 1. Vacuum-assisted wound closure and mesh-mediated fascial traction technique: 1. Bowel; 2. Visceral protective layer; 3 Abdominal wall; 4. Abdominal wall fascia; 5. Polypropylene mesh; 6. Two pieces of polyurethane foam placed on top of the mesh and subcutaneously between the wound edges; 7. Tubing set with an interface pad attached to an opening in the self-adhesive drapes and connected to the vacuum source

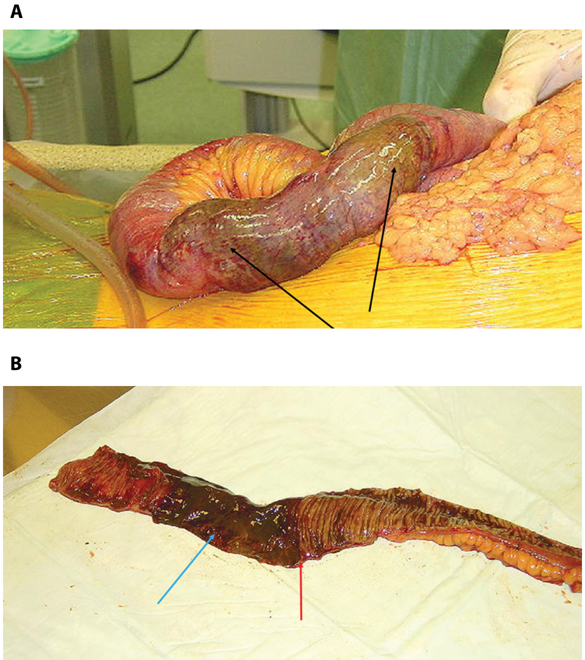

Figure 2. A — patient undergoing FEVAR complicated by mesenteric embolization and patchy signs of small bowel infarction with green discoloration of the serosa (arrows); **B** — Resected small bowel showing the necrosis of the small bowel mucosa (blue arrow). Note the abrupt margin to viable normal appearing mucosa (red arrow)

ting. Dressing changes were usually performed every three days under general anaesthesia. At each dressing change, the mesh was opened in the midline and the visceral protective layer was exchanged after inspection and/or exploration of the abdominal cavity. The mesh halves were re-sutured together with tightening of the mesh and re-approximation of the fascial edges. Thereafter, the outer polyurethane foam layer was applied. As the intra-abdominal swelling decreased, the abdominal wall edges were gradually brought together with each dressing change. Finally, the temporary mesh was removed and the fascia was closed with running polydioxanone sutures using the standardized suturing technique.

STATISTICS

Nominal data were expressed in proportions, and differences between groups were analysed with Fisher´s exact or chi-square test. Ordinal data was expressed in proportions and analysed with Kendall´s tau-b test. Continuous data were expressed in median and range, and differences between groups were analysed with the Mann-Whitney U test. All data were analyzed using SPSS version 22.0. *P*-values < 0.05 were considered significant.

RESULTS

CHARACTERISTICS OF PATIENTS WITH MESENTERIC EMBOLIZATION

Nine patients with mesenteric embolization (Fig. 2A,B) after aorto-iliac endovascular intervention were identified (eight elective, one acute). Six patients underwent endovascular aortic aneurysm repair (EVAR) (juxtarenal 3, thoracoabdominal 2, infrarenal 1) while three underwent endovascular intervention for aorto-iliac occlusive disease; the frequency of mesenteric embolization was 2.0% (6/294) and 1.4% (3/216), respectively. The overall frequency was 1.8% (9/510). The median age was 69 years (range 50–81) for patients with mesenteric embolization; five were men and four women.

RISK FACTORS FOR MESENTERIC EMBOLIZATION

In the EVAR group, one patient underwent quadruple- and four patients triple-fenestrated procedures with stent grafting of the target arteries. Stent grafting of the right renal artery failed in one case. The sixth patient in the EVAR group underwent infrarenal EVAR for ruptured AAA with balloon occlusion due to circulatory instability. Five out of the nine patients with mesenteric embolization had the most severe grade of shaggy visceral aorta; balloon occlusion of either the visceral aorta (Fig. 3) or the left renal artery (Fig. 4) was used as part of the procedure in two of these patients.

COMPARISON OF PATIENTS WITH MESENTERIC EMBOLIZATION VERSUS CONTROL GROUP

Compared to the control group, a higher proportion of patients with mesenteric embolization were current smokers (89% vs. 53%; $P = 0.048$) and had renal insufficiency at admission (44% vs. 11%; $P = 0.019$) (Table 1). In the EVAR

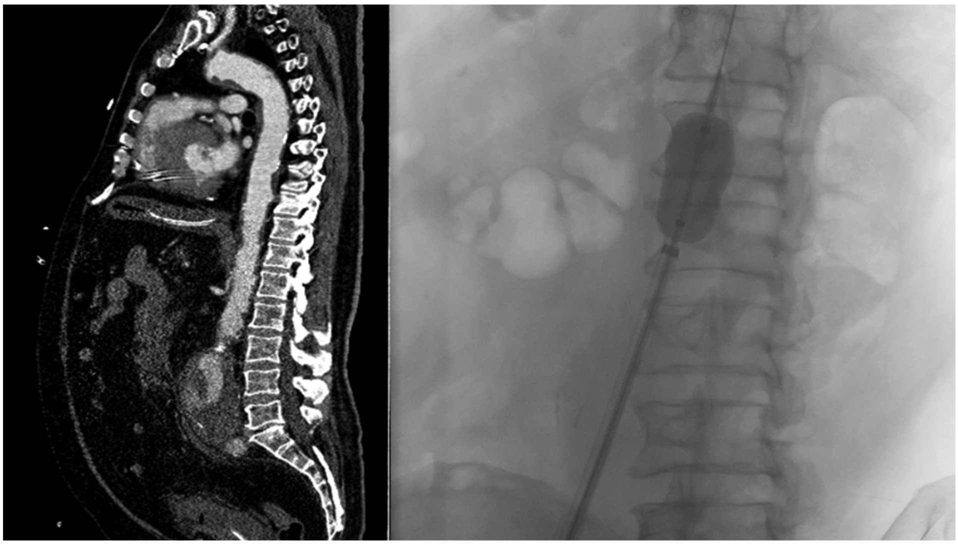

Figure 3. Patient with a ruptured AAA and hypotensive shock. The preoperative sagittal CT view shows that the entire thoracic and upper abdominal aorta is very shaggy. Emergency endovascular procedure was initiated by inflating a balloon to occlude the visceral aorta to achieve temporary blood pressure control. The balloon was placed unplanned in the visceral aortic segment at the level of L1 and L2 vertebrae resulting in embolization into the mesenteric and renal arteries. The patient died after 2 days

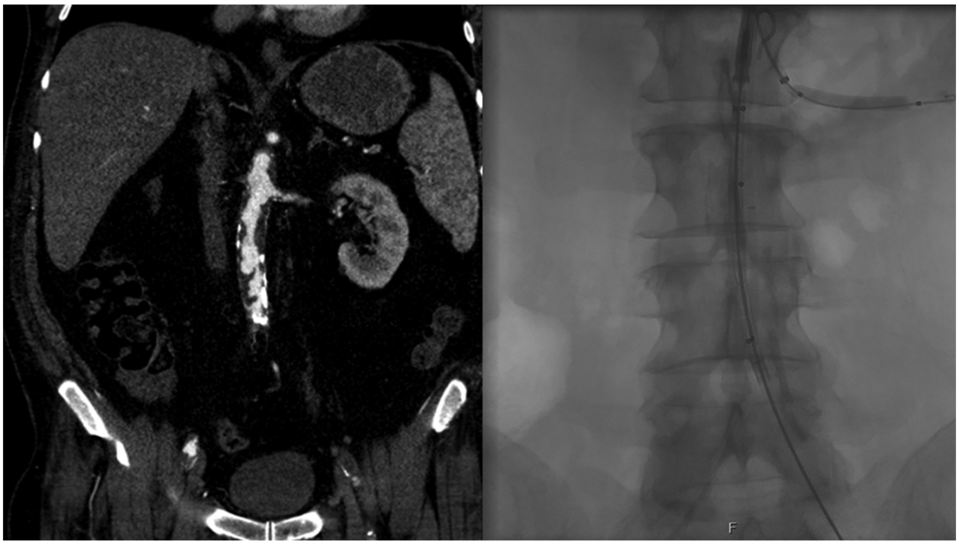

Figure 4. Patient with extensive aorto-iliac occlusive disease. The preoperative CT image in the coronal view shows a shaggy aorta. To protect the left renal artery from embolization while stenting the aorta, a protective balloon was inserted. Unfortunately, the result was massive embolization into the mesenteric arteries and left renal artery as well and the right profunda femoris. The patient survived with ileostomy, colonostomy, and right transfemoral amputation

group, no differences in maximal AAA size, aortic shagginess, visceral thrombus volume, aorto-iliac tortuosity, or operation-time was found between patients with mesenteric embolization and controls (Table 2). In the aorto-iliac occlusive disease group, where stenting of the iliac arteries was extended into the aorta in the three patients, aortic shagginess was more severe (P = 0.015), visceral thrombus volume was larger (P = 0.004) while operation-time was longer (P = 0.009) in the mesenteric embolization group compared to the control group (Table 2). All three patients with aorto-iliac occlusive disease and mesenteric embolization after intervention had TASC D lesions. Eight out of twelve patients in the control group were classified as having TASC D lesions, whereas four patients had TASC C lesions.

CONSEQUENCES OF MESENTERIC EMBOLIZATION

Among the nine patients with mesenteric embolization, infarctions were diagnosed in the intestine (n = 7; 78%), liver (n = 6; 67%), pancreas (n = 5; 56%) and spleen (n = 3; 33%).

Table 1. Patient characteristics at admission in cases with mesenteric embolization after endovascular aorto-iliac intervention compared to age, gender and procedure-matched control group (4 controls per case)

	Mesenteric embolization (n = 9) (%)	Control group (n = 36) (%)	*P*
Current smoker (smoking ≤ 1 year)	8 (89)	19 (53)	0.048
Hypertension	9 (100)	27 (75)	0.17
Atrial fibrillation	1 (11)	1 (3)	0.36
Ischaemic heart disease	3 (33)	12 (33)	1.0
Diabetes mellitus	1 (11)	10 (28)	0.42
Peripheral arterial disease	2 (22)	19 (53)	0.14
TIA/Stroke	2 (22)	6 (17)	0.65
Previous vascular surgery	4 (44)	16 (44)	1.0
COPD	4 (44)	9 (25)	0.41
Renal insufficiency	4 (44)	4 (11)	0.019
Anaemia	2 (22)	9 (25)	0.86
Medication			
ASA	6 (67)	28 (78)	0.67
Clopidogrel	0 (0)	2 (6)	1.0
Vitamin K antagonist	2 (22)	1 (3)	0.097
Statin	6 (67)	29 (81)	0.39

TIA — transient ischemic attack; COPD — chronic obstructive pulmonary disease; ASA — acetylosalicylic acid

Table 2. Anatomic and operation-related variables in patients with mesenteric embolization after endovascular aorto-iliac intervention compared to age, gender and procedure-matched control group (4 controls per case)

	Mesenteric embolization	Control group	*P*
EVAR	6	24	
Maximal aneurysm size (cm; median [range])	5.8 (5.0–6.3)	5.8 (4.4–8.5)	0.94
Aortic irregularity (shagginess)			
Clean non-atheromatous visceral aorta	0	1	
Grade I (little)	2	12	
Grade II (modest)	1	6	
Grade III (severe)	3	5	0.22
Thrombus volume in the visceral aorta (cm^3; median [range])	18.4 (6.8–39.9)	11.8 (3.4–20.5)	0.57
Aorto-iliac tortuosity (index; median [range])	1.35 (1.3–1.4)	1.4 (1.2–1.7)	0.59
Acute/elective operation	1/5	2/22	0.50
Operation time (min; median [range])	385 (269–763)	273 (127–824)	0.13
Recanalization of aorto-iliac occlusive disease	3	12	
TASC D	3	8	0.52
Aortic irregularity (shagginess; median [range])			
Clean non atheromatous visceral aorta	0	1	
Grade I (little)	0	9	
Grade II (modest)	1	1	
Grade III (severe)	2	1	0.015
Thrombus volume in the visceral aorta (cm3; median [range])	11.9 (9.4–15.0)	2.6 (1.8–5.8)	0.004
Acute/elective operation	4/8	0/3	0.52
Operation time (min; median [range])	437 (307–519)	172 (71–433)	0.009

EVAR — endovascular aneurysm repair; TASC — TransAtlantic Inter-Society Consensus

Table 3. Consequences of mesenteric embolization

	Event (n = 9) (%)
Extent of infarction	
Peritonitis	5 (56)
Small bowel infarction	5 (56)
Colonic infarction	5 (56)
Liver infarction	6 (67)
Pancreatic infarction	5 (56)
Spleen infarction	3 (33)
Renal infarction	3 (33) bilateral 3 (33) unilateral
Leg ischaemia	1 (11) bilateral 1 (11) unilateral
Laboratory values after embolization	Lab (median [range])
Myoglobin (maximal; µkat L^{-1}; ref 25–58)	26293 (1838–79022); n = 5
Arterial blood lactate (first sample after endovascular intervention)	4.2 (0.8–10.0)
Arterial blood lactate (maximal; mmol L^{-1}; ref 0.5–2.2)	7.3 (2.2–12.8)
C-reactive protein (maximal; mg L^{-1}; ref ≤ 3)	314 (114–492)
ASAT (maximal; µkat L^{-1}; 0.25–0.60)	6.3 (0.2–31.0)
ALAT (maximal; µkat L^{-1}; 0.15–0.75)	1.4 (0.2–31.0)
Amylase (maximal; µkat L^{-1}; 0.15–1.1)	8.1 (0.4–32.0)
Management and outcome	
Explorative laparotomy at index operation	1 (11)
Damage control and open abdomen	6 (67)
Non-operative management	2 (22)
Bowel resection	5 (56)
Ileostomy	4 (44)
Colonostomy	3 (33)
Any stoma	5 (56)
Cholecystectomy	1 (11)
Spinal cord ischaemia	1 (11)
Transfemoral amputation	1 (11)
Renal replacement therapy	5 (56)
Tracheostomy	3 (33)
In-hospital mortality	3 (33)

Renal infarctions were detected bilaterally in three patients and unilaterally in another three patients (Table 3).

Laboratory values after mesenteric embolization are shown in Table 3. The share of pathologic laboratory results among patients with mesenteric embolization was the following: myoglobin (5/5; 100%); leukocytes (9/9; 100%); first arterial blood lactate after the endovascular intervention (6/9; 67%); maximal arterial blood lactate after the endovascular intervention (8/9; 89%); aspartate amino transferase (AST; 8/9; 89%); alanine amino transferase (ALT; 8/9; 89%); and pancreatic amylase (5/9; 56%). The median maximal creatinine kinase MB isoform (CK-MB) concentration was 41 µg L^{-1} (range 7–299; n = 5). The median maximal troponin T concentration was 44 ng L^{-1} (range 25–360; n = 7). All measured CK-MB and troponin T levels were elevated.

The management, morbidity and mortality are shown in Table 3. Two patients, both with pancreatic infarction, were managed non-operatively while the other seven underwent laparotomy. A damage control strategy and open abdomen therapy (up to 22 days) was used in six patients. An ileostomy and colostomy was created in four and three patients, respectively while a tracheostomy was performed in three patients. Overall in-hospital mortality was 33% (3/9). After damage-control and open abdomen therapy, five patients were managed with stomas and the in-hospital mortality was 17% (1/6). The causes of death were ruptured AAA together with extensive visceral embolization (n = 1), cerebral infarction of both hemispheres (due to guidewire-induced embolization from the aortic arch) together with extensive visceral infarction (n = 1), and massive pancreatic infarction (n = 1).

DISCUSSION

This study demonstrates that mesenteric embolization is one of the most severe complications of endovascular aorto-iliac procedures and that it results in high morbidity and mortality. All study patients who suffered from mesenteric embolization had undergone advanced time-consuming endovascular procedures, prior to the embolic event, where manipulation of numerous guidewires, sheaths, and stent grafts within atherosclerotic aorta and visceral arteries lined with a thrombus very likely contributed to this adverse outcome. In view of a recent report on carotid interventions where an alarming 85% of all endovascular carotid artery stenting procedures resulted in new microemboli [8], it seems probable that microembolization occurs much more often [9] after complex endovascular aorto-iliac procedures than the reported macroembolization rate of 1.8% in the present study.

Small bowel ischaemia in non-complex, non-fenestrated infrarenal EVAR is very rare, whereas colonic ischaemia due to embolization to the inferior mesenteric artery occurs in 1.0–2.9% [4, 10]. The occurrence of colonic ischaemia has also been found to be unrelated to the presence of preoperative hypogastric artery occlusion [4].

The proportion of current smokers was high in this study, higher in patients with mesenteric embolization (89%) than in the control group (53%). This demonstrates that anti-smoking campaigns and programs need to be improved for patients with aorto-iliac disease. Furthermore, current smoking is associated with atherosclerotic plaque progression and destabilization [11], perhaps making these patients susceptible for embolization after endovascular aorto-iliac procedures. The finding that the proportion of patients with renal insufficiency at admission was higher for patients with mesenteric embolization compared to the control group might reflect more reflect an advanced stage of reno-vascular disease, i.e., more shaggy aortas prone to embolization during endovascular procedures in these patients. Hence, the results of our study, and one previous study, suggest that smoking and renal insufficiency are, indeed, risk factors for mesenteric embolization after aorto-iliac procedures [5]. Although diabetes was not found to increase the risk of mesenteric embolization in the present study, microembolism has been reported to be more likely in diabetics after carotid interventions [8].

From a diagnostic perspective, the laboratory workup in patients with suspicion of mesenteric embolization after aorto-iliac procedures seem to be very important for early diagnosis. Plasma biomarkers such as very elevated myoglobin, persistently elevated arterial blood lactate, AST, ALT and pancreatic amylase were all indicators of extensive mesenteric embolization. We suggest that these laboratory tests should be obtained selectively after the intervention from those patients who undergo an endovascular procedure with a high risk of mesenteric embolization. A contrast-enhanced biphasic CT of the abdomen should be performed as soon as possible in all circulatory stable patients upon suspicion of an embolic event to evaluate the extent of mesenteric embolization and organ infarction.

From a therapeutic perspective, the majority of patients with extensive mesenteric embolization, especially those with intestinal infarctions, were managed with explorative laparotomy, open abdomen therapy and damage control principles [12]. Stomas were used with a low threshold in order to minimize the risks of bowel leakage, the breakdown of an anastomosis, and late perforations. As the extent and severity of visceral embolization is unpredictable in these cases, careful repetitive clinical judgement and inspection of the abdomen via open abdomen management are warranted. The vacuum-assisted wound closure and mesh-mediated fascial traction technique as a temporary abdominal closure dressing has several advantages in handling the open abdomen: The airtight seal and suction facilitates controlled fluid drainage and wound care, while the mesh traction facilitates fascial closure in patients with a need of a longer time of open abdomen. In this study, the damage control strategy may have contributed to the low in-hospital mortality rate of 33% in these challenging cases.

The main findings of the anatomic assessments of the aorto-iliac segments were that patients undergoing recanalization of aorto-iliac occlusive disease complicated by mesenteric embolization had more shaggy aortas, larger thrombus volumes in the aortic visceral segment and longer operation times than the control group (Table 2). Despite the small sample size, it was possible to show these associations for the aorto-iliac occlusive group in a uni-variate analysis. However, a multi-variate analysis was not possible. The very long operation times in the three patients with mesenteric embolization after recanalization of the aorto-iliac segment was an indicator that these procedures, indeed, were very challenging and complex to perform.

In a recent report, shaggy aorta was defined as a nominal variable [13] and it appeared to be a prominent risk factor for multiple arterial thromboembolism, and for increased short- and long-term mortality after both open and endovascular AAA repair. However, a shaggy aorta was not found to be associated with mesenteric embolization in EVAR patients in the present study. Perhaps, this was due to the small sample size, and thus, a statistical type 2 error is possible. On the other hand, the nested case-control design with age, gender and procedure-matched control groups assured a high-quality control group in this study.

In conclusion, based on this study, smoking cessation, careful patient selection, and procedure planning with identification of severe shaggy aortas may prevent mesenteric embolization during aorto-iliac procedures. In suspected cases of mesenteric embolization, myoglobin and arterial blood lactate may be indicative of this complication, while ASAT, ALAT and pancreatic amylase are also relevant tests in order to assess the extent of organ ischaemia. In this particular group of patients with intestinal infarction, damage control, open abdomen therapy using a temporary abdominal closure device, and the creation of stomas seem to be a justified strategy in order to improve survival.

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