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Outcomes of Surgical Explantation of Infected Aortic Grafts After Endovascular and Open Abdominal Aneurysm Repair

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WHAT THIS PAPER ADDS

Aortic graft infection is a life threatening complication after open and endovascular aortic repair. This retrospective study reports on early outcomes after open repair for infected aortic graft using rifampicin soaked synthetic grafts and points out differences in surgical repair for infected conventional and endovascular aortic grafts. A higher mortality and morbidity after removal of infected endografts was observed.

Objectives: Infection of the vascular graft represents one of the most threatening complications after aortic repair. It is rare and associated with high morbidity and mortality rates. The aim of this study was to present short-term outcomes after surgical treatment of infected aortic grafts after endovascular and open repair of abdominal aortic aneurysms (AAAs).

Methods: Data of all patients affected by aortic graft infection after aneurysm repair who underwent an explantation of a conventional or endovascular aortic graft between January 2008 and December 2016 were retrospectively reviewed. All patients underwent in situ reconstruction using a rifampicin soaked synthetic graft. The primary endpoint of this study was 30 day mortality; secondary endpoints were major post-operative complications.

Results: Twenty-six patients were included in the cohort, 16 with an infected endograft (iEVAR) and 10 patients with an infected conventional graft (iOAR). Thirty-day mortality was 23.1% overall, 37.5% for iEVAR and 0% ($p = .027$) for iOAR. Post-operative major complications occurred in eight (50%) patients from the iEVAR group and in four (40%) patients from the iOAR group ($p = .619$). The supravisceral clamping rate was higher in patients with infected iEVAR (93.8 vs. 20%, $p = .001$), furthermore a greater incidence of post-operative acute kidney injury was observed (50 vs. 0%, $p = .009$).

Conclusions: Explantation of the graft and in situ reconstruction for aortic graft infection is accepted as the therapy of choice. However, re-operation for iEVAR is related to significantly higher mortality and morbidity rates. The need for suprarenal aortic clamping seems to be a possible explanation for worse outcomes in iEVAR.

Keywords: Abdominal aortic aneurysm repair, Vascular graft infection, EVAR explantation, Failed EVAR
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INTRODUCTION

Complications after endovascular aneurysm repair (EVAR) or open aortic repair (OAR) can be challenging. In particular endograft (iEVAR) or conventional aortic graft infection (iOAR) represents one of the most serious complications after aortic aneurysm treatment.[1,2] Reported rates of iEVAR ranges from 0.2% to 0.7% and up to 2% for conventional grafts.[3,4] A cumulative incidence of aortic graft infection of 0.44% has been reported in population based studies.[5] The overall mortality for aortic graft infection ranges from 10 to 40% in published reports.[1,6–10]

The treatment spectrum for aortic graft infection diversifies into conservative, namely long-term or lifelong antibiotic therapy, or invasive including drainage or coverage of the infected graft without explantation of the same, in situ or extra-anatomical reconstruction.[11–13]

Thus, multiple reports for different techniques exist but current literature lacks knowledge regarding the comparison between iOAR and iEVAR.

The aim of this study was to compare the outcomes of patients treated surgically at the institution for infection

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after standard EVAR (iEVAR) and open repair (iOAR) for infrarenal aortic reconstructions.

METHODS

Inclusion criteria and definitions

The institutional database was analysed to identify patients presenting with aortic graft infection who underwent a surgical in situ reconstruction and local debridement for iEVAR or iOAR. The patients were all over 18 years of age and gave, where possible, consent to the procedure and the protocol and consent was approved by the Institutional Review Board.

Clinical charts were reviewed to collect pre-, peri-, and post-operative data concerning the explantation. Follow up data were analysed.

The suspected infection was confirmed by clinical, laboratory, and imaging findings as proposed in previous publications.[14] Diagnostic criteria for aortic graft infection included positive blood/graft cultures, leukocytosis or elevated C-reactive protein, oesophago-gastro-duodenoscopy with bleeding or melaena, radiological findings of perigraft fluid collection or periaortic abscess with gas collections surrounding the endograft on contrast enhanced computed tomography, a positive FDG-18 PET-CT. Additionally, intraoperative diagnosis of fistula involving the graft with or without pus surrounding the prosthesis could confirm the diagnosis. Patients treated by graft explantation for other indications such as endoleaks and anastomotic non-infectious aneurysms were not included. Patients deemed not fit for a surgical repair were also not included.

Acute kidney injury was defined as either a doubling or more of post-operative creatinine values relative to the pre-operative creatinine, oliguria with urine output $<$0.5 mL/kg/h ($>$12 h), anuria or acute need for dialysis post-operatively.[15] Multi-organ dysfunction was defined as the presence of altered organ function where homeostasis cannot be maintained without intervention, in this case involving two or more organ systems. Major cardio- and cerebrovascular events (MACCE) were defined as all cause mortality, stroke or transient ischaemic attack, and acute coronary syndrome (including unstable angina).

Endpoints

The primary endpoint of the study was 30 day mortality.

The secondary outcomes encompassed major post-operative complications including acute kidney injury or failure (AKIN 2 and 3),[15] septic multi-organ dysfunction syndrome (MODS), MACCE, the length of intensive care unit (ICU), and hospital stay.

Diagnostic routine and operative approach

All patients suspected of having aortic graft infection received a CT angiogram of the entire aorta; moreover, multiple blood cultures or microbial smears in the case of open wounds and laboratory testing were sampled (leukocytosis, white blood cell count $>$ 12,000/μL; elevated C-reactive protein level, $>$ 0.5 mg/dL at the laboratory; relevant anaemia requiring transfusion, haemoglobin level below 8 g/dL). In the case of upper gastrointestinal bleeding and stable haemodynamic conditions an upper endoscopy was performed to back up the diagnosis.

In selected cases in which a CT scan did not clearly confirm the diagnosis, a whole body ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) was performed. A CT scan with typical signs as mentioned above is shown in Fig. 1.

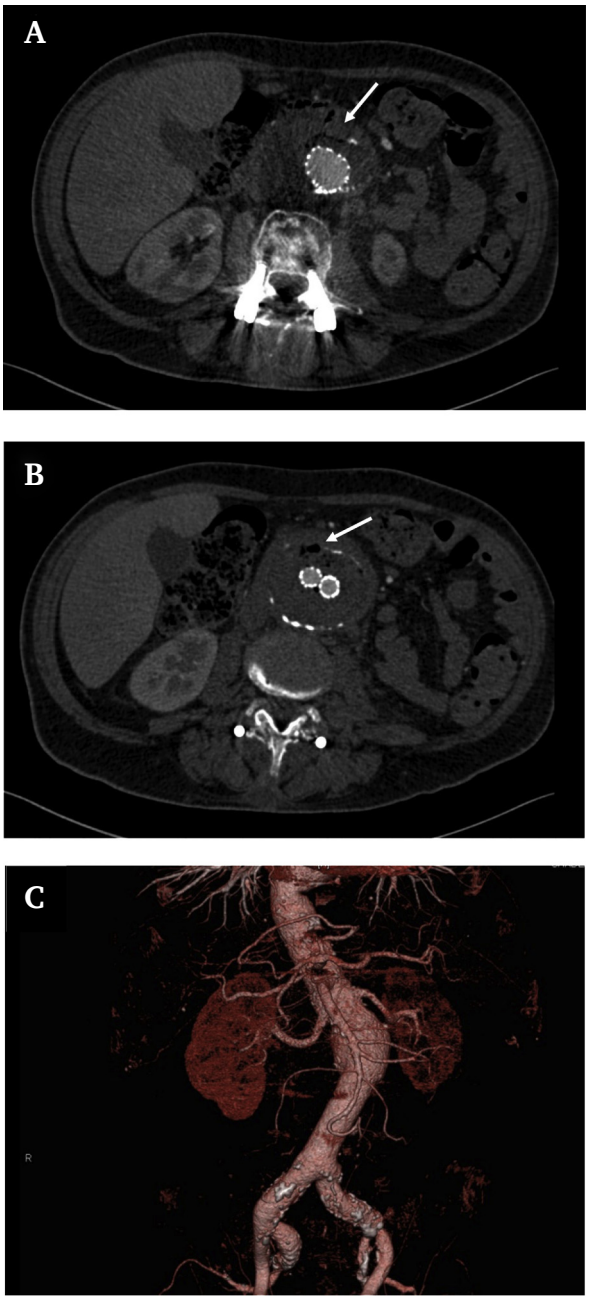

Figure 1. Pre-operative (A, B) and post-operative (C) CT imaging of one iEVAR patient. (A) Aorto-enteric fistula (arrow) after EVAR. (B) Gas collection (arrow) in the sac around the endograft. (C) 3D reconstruction of post-operative result.

Table 1. Patient demographics and comorbidities

	Overall (n = 26)	iEVAR (n = 16)	iOAR (n = 10)	p
Age, years	69.92 (55–90)	72.31 (55–90)	66.10 (56–79)	.097
Male gender	20 (77%)	14 (87%)	6 (60%)	.163
Hypertension	20 (77%)	13 (81%)	7 (70%)	.644
Diabetes	6 (23%)	5 (31%)	1 (10%)	.352
Coronary heart disease	13 (50%)	9 (56%)	4 (40%)	.688
Renal insufficiency	9 (35%)	5 (31%)	4 (40%)	.692
On haemodialysis	1 (4%)	1 (6%)	0 (0%)	1.000
Peripheral arterial disease	4 (15%)	3 (19%)	1 (10%)	1.000
COPD	8 (31%)	3 (19%)	5 (50%)	.189

Data are presented as mean (range) or as absolute number (percentage). COPD = chronic obstructive pulmonary disease.

Based on the operation timing, the procedures were defined as urgent when performed within 6 h, or elective if longer than 6 h after the patient presented at the hospital.

Different surgical accesses were employed (midline laparotomy, retroperitoneal, or thoraco-abdominal approach) based on the graft extension and operator's preferences. Clamping level was based on the extent of the disease and the graft to provide enough native tissue for a safe proximal anastomosis and was categorised in two groups: above and below the renal, superior mesenteric artery, and coeliac trunk segment (supravisceral clamping).

All procedures were conducted with the same technique including complete graft removal and an extended debridement of peri-aortal tissue. An in situ reconstruction was performed with rifampicin (Eremfat i.v., Riemser Pharma GmbH, Greifswald, Germany) soaked polyester graft (Uni-graft K DV, B. Braun Melsungen AG, Melsungen, Germany), which was sutured to healthy native tissue.

When enough greater omentum was available, an omental flap transposition was performed to cover and protect the new polyester graft. When there was a co-existing aorto-enteric fistula, the bowel defect was treated by direct suture, excision or resection.

Based on the microbial samples empiric or targeted antibiotic therapy was initiated.

Statistics

Data were collected and maintained in an Excel 16. database (Microsoft Corp, Redmond, WA, USA). Statistical analysis was performed with SPSS Statistics 24 software (IBM Corp, Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation unless noted otherwise. Differences between the groups in continuous variables were analysed using Mann–Whitney U test and analysis of variance test. Differences between the groups of non-continuous variables were analysed using the chi-square test or the Fisher exact test. A value of $p < .05$ was considered significant for all comparative analyses.

Table 2. Type of endograft implanted at the index procedure in the iEVAR group (n = 16)

Initial endograft	Suprarenal fixation	n (%)
Anaconda (Vascutek)	No	1 (6%)
Endurant (Medtronic)	Yes	4 (25%)
Excluder (Gore)	No	1 (6%)
Zenith (COOK)	Yes	5 (31%)
Treovance (Bolton)	Yes	1 (6%)
Vanguard (Boston Scientific)	Yes	1 (6%)
Unknown	1 of 3	3 (19%)

RESULTS

During a period of 8 years (January 2008 to January 2016) overall 26 of 30 patients met the inclusion criteria of the present study. Three patients could not be operated on because of ongoing septic shock and another one because of free intra-abdominal rupture of an aorto-duodenal fistula and haemorrhagic shock. From this cohort, three belonged to the iEVAR group and one to the iOAR group.

The index procedure was EVAR in 16 (61.5%) cases, and 10 (38.5%) patients presented after initial open aneurysm repair. The mean time between the index procedure and the onset of the aortic graft infection was 58.7 months (range 1.0–251.6 months). Time to presentation was different in the two groups: 27.9 months for the iEVAR group and 107.8 months for the iOAR group ($p = .027$) (see Table 3).

Eleven (42.3%) patients were treated primarily at the institution; six (37.5%) of these were treated for iEVAR.

Demographic and baseline clinical features

Patients were classified in two groups based on the previous repair. Patient demographics and comorbidities of the entire cohort at the time of presentation with graft infection are summarised in Table 1, with no significant differences between the iEVAR and the iOAR groups.

In the iOAR group all implanted grafts at the primary procedure were polyester prosthesis. Table 2 presents an overview of endografts found in the iEVAR group.

Pre-operative presentation

The clinical presentation differed in the two groups, as summarised in Table 3. A higher rate of gastrointestinal bleeding was observed in the iOAR group (40% in iOAR vs. 0% in iEVAR, $p = .014$); however, in patients of the iEVAR group abdominal pain was the dominating clinical symptom (87.5% in iEVAR vs. 20% in iOAR, $p = .001$).

Leukocytosis was present in 14 individuals (53.8%), an elevated C-reactive protein level in 25 (96.2%), and a relevant anaemia requiring transfusion in one (3.8%) of the patients. Positive blood cultures with isolation of bacteria were present in six (23.1%) cases.

Active bleeding was found in seven (26.9%) patients, and 10 (38.5%) patients presented with a contained rupture; this feature was statistically significantly more common in the iEVAR group ($p = .037$). Details of imaging and laboratory findings are reported in Table 3.

Table 3. Time from index procedure to presentation and clinical, imaging and laboratory findings

	Overall (n = 26)	iEVAR (*n* = 16)	iOAR (*n* = 10)	*p*
Time from index procedure (months)	58.7 (1.0–251.6)	27.9 (1.1–144.9)	107.8 (1.0–251.6)	.027
Clinical presentation				
Pain	16 (61%)	14 (87%)	2 (20%)	.000
Abdominal	9 (35%)	7 (44%)	2 (20%)	
Flank	2 (8%)	2 (12%)	0 (0%)	
Back	6 (23%)	6 (37%)	0 (0%)	
Fever/chills	12 (46%)	7 (44%)	5 (50%)	1.000
SIRS	17 (65%)	12 (75%)	5 (50%)	.234
GI bleeding	4 (15%)	0 (0%)	4 (40%)	.014
Imaging findings				
Perigraft air	16 (61%)	9 (56%)	7 (70%)	.399
Graft perforation	7 (27%)	4 (25%)	3 (30%)	1.000
Contained rupture	10 (38%)	9 (56%)	1 (10%)	.037
Type I endoleak	n/a	2 (12%)	n/a	n/a
^{18}FDG PET pos. (performed in 16)	8 of 16 (50%)	5 of 6 (83%)	3 of 10 (30%)	.039
Laboratory findings				
Leukocytosis	14 (54%)	10 (62%)	4 (40%)	.069
Elevated CRP	25 (96%)	16 (100%)	9 (90%)	.385
Haemoglobin <8 g/dL	1 (4%)	0 (0%)	1 (10%)	.385
Positive blood culture	6 (23%)	6 (37%)	0 (0%)	.053
Microbial findings (intra-operative)				
Sterile	7 (27%)			
Bacteria				
Staphylococcus aureus (MSSA)	5 (19%)			
Staphylococcus epidermidis	1 (4%)			
Streptococcus spp.	6 (23%)			
Enterococcus spp.	4 (15%)			
Gram-negative	6 (23%)			
Candida spp.	4 (15%)			
Polymicrobial	6 (23%)			

Data are presented as mean (range), or as absolute number (percentage). SIRS = systemic inflammatory syndrome; GI = gastrointestinal; FDG PET = ^{18}F-fluorodeoxyglucose positron emission tomography; CRP = C-reactive protein.

Overall, 10 patients were treated urgently (38.5%); the remaining patients underwent elective surgery.

Operative approach and intra-operative findings

Midline laparotomy was the most common surgical access (15, 57.7%) followed by the thoraco-abdominal approach (10, 38.5%); only one (3.8%) patient was treated through an isolated retroperitoneal approach. Supravisceral clamping was needed in 17 (65.4%) cases, with a significantly higher rate in patients treated for infected EVAR (15 vs. 2, 93.8% vs. 20%, $p = .004$). After completion of the proximal anastomosis and leak testing the clamp was moved on the graft. Suprarenal fixation of the endograft in iEVAR was present in 12 of these 15 cases when supravisceral clamping was performed. The presence of suprarenal fixation did not lead to a significantly higher rate of supravisceral clamping (92.3% for suprarenal fixation vs. 100% for infrarenal fixation, $p = .620$).

The mean supravisceral clamping time differed significantly between iEVAR and iOAR with 30.5 min in iEVAR and 5.0 min in iOAR ($p = .005$). The average volume of perioperatively (within 24 h of the operation) transfused packed red blood cell units was significantly higher in the iEVAR group (4.55 for iEVAR vs. 1.69 for iOAR, $p < .0001$).

The revascularisation technique was mainly aorto-bi-iliac in iOAR (9/10) and for iEVAR a tube graft in most cases (11 tube grafts and 5 aorto-bi-iliac grafts). Additionally, in iEVAR in 11 cases at least one renal artery revascularisation was needed (7 left, 1 right and 3 both renal arteries).

An aorto-enteric fistula was found in nine patients (34.6%); however, with no significant difference between iOAR and iEVAR groups (40.0% vs. 31.3%, $p = .692$). Other concomitant findings were a spondylodiscitis in three patients and one aorto-ureteral fistula. All surgical and intra-operative findings are summarised in Table 4.

The intra-operative microbial pathogens were mostly *staphylococci*, *streptococci*, and Gram negative organisms (23.1% respectively) but also polymicrobial (23.1%). In four (15.4%) patients, *Candida* spp. were isolated. Seven samples (26.9%) showed no bacterial or fungal growth (Table 3).

Post-operative course and 30 day mortality

The overall in hospital or 30 day mortality was 23.1% (6 of 26). All these events occurred in the iEVAR group; for the same cohort, the in hospital mortality rate was 37.5% (6 of 16) and 0% (0 of 10) after iOAR ($p = .027$). A contained rupture at presentation was associated with a higher 30 day mortality rate than non-ruptured presentation (50% vs. 6.25%, $p = .018$). The presence of shock ($p = 1.000$) or gastrointestinal bleeding ($p = .542$) was not associated with a higher 30 day mortality.

Table 4. Surgical access and intra-operative findings

	Overall (n = 26)	iEVAR (n = 16)	iOAR (n = 10)	p
Midline laparotomy	15 (58%)	7 (44%)	8 (80%)	.109
Retroperitoneal	1 (4%)	1 (6%)	0 (0%)	.508
Thoraco-abdominal	10 (38%)	8 (50%)	2 (20%)	.218
Supravisceral clamp	17 (65%)	15 (94%)	2 (20%)	.000
Supravisceral clamping time (min)	20.69 ± 20.21	30.50 ± 18.55	5.0 ± 10.80	.005
No of PRBCs transfused within 24 h	4.96 ± 3.74	5.25 ± 4.55	3.80 ± 1.69	<.0001
Aorto-enteric fistula	9 (35%)	5 (31%)	4 (40%)	.692
Spondylodiscitis	3 (11%)	3 (19%)	0 (0%)	.262
Aorto-ureteral fistula	1 (4%)	1 (6%)	0 (0%)	.508

PRBCs = packed red blood cells.

The mean time from the operation for aortic graft infection to in hospital death was 13.83 days (range 1—35 days). Three patients died because of persistent sepsis with multiple organ dysfunction syndrome (post-operative days 9, 24, and 35). Two patients developed fatal bowel ischaemia (on post-operative days 6 and 8), and one patient died of haemorrhagic shock caused by bleeding at the proximal anastomosis the night after surgery.

Post-operative major complications occurred in eight (50%) patients of the iEVAR group and in four (40%) patients of the iOAR group; detailed information is shown in Table 5. A significantly higher rate of post-operative acute renal deterioration was observed in eight (50%) patients in the iEVAR cohort, whereas no patients in the iOAR group developed this complication (p = .007).

Supravisceral clamping led to significantly higher rates of post-operative renal failure (47.1% vs. 0%, p = .013) and post-operative death (35.3% vs. 0%, p = .042). Renal artery reconstruction was not associated with post-operative renal failure (45.5% vs. 60%, p = .589).

In the iEVAR cohort the presence of suprarenal fixation of the endograft did not contribute to a higher rate of post-operative kidney injury (46.2% vs. 66.7%, p = .522), post-operative major complications in general (46.2% vs. 66.7%, p = .522), or death (38.5% vs. 33.3%, p = .869).

The mean ICU and hospital stay and the duration of administration of antibiotics did not differ between the iEVAR and iOAR group (Table 5).

Follow up

The mean follow up was 13.6 (1—35) months for the iEVAR group and 27.25 (1—46) months for iOAR. In this follow up period, no patient presented with signs of re-infection.

DISCUSSION

This is the first single centre study comparing the outcome of patients affected by iOAR and iEVAR. Overall mortality rates are similar to the reports of the current literature, with post-operative mortality (23.1% overall, 37.5% for iEVAR, and 0% for iOAR) after aortic graft infection.[2,9,16]

The study showed that explantation of an infected conventional graft was related to significant lower 30 day mortality rates and peri-operative complications than the iEVAR group. The clinical presentation probably plays a crucial role on the outcome; of note in the series gastrointestinal bleeding was the dominant presentation in the iOAR group; however, contained rupture and abdominal pain were the dominating clinical symptoms in the iEVAR cohort. This suggests a difference in development, initial presentation, and course of aortic graft infection after OAR and EVAR.

These findings are possibly due to the more extensive surgical approach and more frequent supravisceral aortic clamping applied in repair for iEVAR. Furthermore, in cases of suprarenal fixation for EVAR, a more invasive approach for aortic exposure and clamping was preferred in the series

Table 5. Early mortality, severe post-operative complications and post-operative course

	Overall (n = 26)	iEVAR (n = 16)	iOAR (n = 10)	p
30 day mortality	6 (23%)	6 (37%)	0 (0%)	.027
Any complication	12 (46%)	8 (50%)	4 (40%)	.619
AKI 2 and 3	8 (31%)	8 (50%)	0 (0%)	.009
MODS	2 (8%)	2 (12%)	0 (0%)	.508
MACCE	8 (31%)	6 (37%)	0 (0%)	.420
Wound infection	3 (11)	0 (0%)	3 (30%)	.046
Paralysis	1 (4%)	0 (0%)	1 (10%)	.385
ICU stay (days)	11.00 ± 10.30	12.06 ± 12.04	9.30 ± 6.90	.561
Hospital stay (days)	22.96 ± 13.35	19.87 ± 12.82	27.90 ± 13.32	.090
Antibiotics duration (weeks)	6.31 ± 5.80	6.19 ± 5.56	6.50 ± 6.49	.915

Data are presented as mean (range), or as absolute number (percentage). AKI = acute kidney injury; MODS = multi-organ dysfunction syndrome; MACCE = major adverse cardiac and cerebrovascular events; ICU = intensive care unit.

to achieve secure clamping above the barbs of the endograft. However, the supravisceral clamping rate was not significantly higher in cases with suprarenal fixation (only three cases without suprarenal fixation).

This approach is related to higher mortality rates and increased incidence of severe post-operative complications because of bowel and renal ischaemia during clamping and the extent of the exposure. A significantly higher rate of post-operative acute kidney injury was recorded in the iEVAR group. Additionally, the more complex revascularisation technique, the longer supravisceral clamping time and the greater volume of blood transfusion certainly contributed to increased morbidity and mortality in iEVAR.

Moreover, owing to increased post-operative chest pain, airway infections and mechanical mismatch negatively influences the ventilation and clinical course. To achieve sufficient exposure of the vessel and guarantee an appropriate debridement, supravisceral clamping is mandatory in cases of aorto-enteric fistula, as already described by other groups.[17,18] However, in this study the presence of an aorto-enteric fistula did not lead to higher mortality rates; in contrast other authors found this to be a risk factor for post-operative mortality.[18]

Different grafts have been used for reconstructions after aortic graft infection; rifampicin soaked grafts have been well described and evaluated in large series as the preferred treatment option.[16] However, since rifampicin soaked polyester grafts are associated with re-infection rates up to 12%, other graft materials (allografts, deep femoral vein, bovine pericardium) have also been proposed, especially since immediate re-infection islikely to be fatal.[10,11,19–21]

Lavigne et al.[22] compared two asynchronous series of patients presenting with aortic graft infection, including a minority of aorto-esophageal fistula. In the first series there was an inhomogeneous treatment spectrum with the majority treated by explantation and extra-anatomical reconstructions, whereas in the second series patients were treated by in situ reconstructions using cryopreserved allografts. They concluded that compared with conventional treatment, the incidence of re-operations and length of hospital stay are significantly decreased after cryopreserved allograft implantation. However, this comparison could not be applied to the current state of the art, since extra-anatomical reconstruction are only offered to those patients who are not deemed fit for an in situ reconstruction.[22] Furthermore, Touma et al.[23] reported an unsatisfactory 30 day survival rate and a substantial early graft related complication rate. A recent meta-analysis comparing different types of graft for in situ reconstructions for aortic graft infection failed two show any convincing advantage of any type of graft (autogenous veins, cryopreserved allografts, and synthetic prosthesis either standard, rifampicin of silver polyesters). But they concluded that silver polyesters appear to be most appropriate for older patients, and in order to limit re-infection, autogenous veins are probably the most suitable conduit.[24] However, in the current study no re-infections of the new implanted polyester grafts were recorded.

As an alternative solution, graft explantation and extra-anatomic axillo-femoral reconstruction was proposed, albeit related to higher mortality, morbidity, and lower patency rates; in particular, there was a high risk of aortic stump blow out and limb amputation after graft occlusion.[1,11,16]

The use of different peri-operative antibiotic therapy regimens has been reported, but without consensus statements regarding class of drug, titration, and duration of therapy.[25] Cultures and intra-operative strains mostly showed Gram positive bacteria. But there were Gram negative, fungal and sterile strains as well. Consequently, empirical antibiotic treatment should cover all these possible specimens and the absence of positive microbial findings or even repetitive sterile strains cannot rule out a life threatening aortic graft infection. The patients were treated for at least 6 weeks post-operatively with antibiotics. Other authors have proposed a lifelong antibiotic therapy.[26]

Standardised medical and surgical strategies would improve the outcomes of such demanding situations.

Limitations

There are limitations that need to be stated. The retrospective setting of this study should be considered in the statistical power of the analysis. Also, there is a possible selection bias regarding the patients referred to the university hospital. Randomised trials are lacking and difficult to report because of the overall small number of cases.

CONCLUSIONS

In situ surgical reconstruction represents a therapeutic option for this lethal entity with encouraging results in patients fit for surgery. Extended surgical access with supracoeliac clamping is often necessary for iEVAR and seems to be accompanied by a higher mortality and acute kidney injury rates.

CONFLICTS OF INTEREST

None.

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None.

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