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# Self Made Bovine Pericardial Tube Grafts in Aortic Infection: A European Multicentre Study

Short Title: Bovine Pericardial Tube Grafts in Aortic Infection

Salome Weiss <sup>a,\*</sup>, Maria Hugas Mallorqui <sup>a</sup>, Martin Czerny <sup>b,c</sup>, Tim Walter <sup>b,c</sup>, Gabor Biro <sup>d</sup>, Ilaria Puttini <sup>d</sup>, Veronika Almasi-Sperling <sup>e</sup>, Werner Lang <sup>e</sup>, Jürg Schmidli <sup>a</sup>, Thomas R. Wyss <sup>a,f</sup>

<sup>a</sup> Department of Vascular Surgery, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

<sup>b</sup> Clinic for Cardiovascular Surgery, University Heart Centre Freiburg – Bad Krozingen, Freiburg University Hospital, Freiburg, Germany

<sup>c</sup> Faculty of Medicine, Albert Ludwig's University of Freiburg, Freiburg, Germany

<sup>d</sup> Department for Vascular and Endovascular Surgery, Klinikum rechts der Isar, Technical University Munich, Munich, Germany

<sup>e</sup> Department of Vascular Surgery, University Hospital Erlangen, Erlangen, Germany

<sup>f</sup> Department of Vascular Surgery, Kantonsspital Winterthur, Winterthur, Switzerland

\* Corresponding author. Department of Vascular Surgery, Kantonsspital Winterthur, Winterthur, Switzerland.

thomas.wyss@ksw.ch (Thomas R. Wyss).

**Objective:** This study examines outcome and durability of self made bovine pericardial tube grafts in aortic infections of all anatomic locations.

**Methods:** This was a retrospective and prospective international multicentre study. Perioperative and long term outcomes of patients undergoing aortic *in situ* reconstruction for native or graft infections with self made bovine pericardial tube grafts between January 2008 and December 2020 in four European tertiary referral centres were analysed. The primary endpoint was recurrent aortic infection. Secondary endpoints were persistent infection, aortic re-operation for infection, graft related complications, and mortality.

**Results:** One hundred and sixty eight patients (77% male, mean age  $67 \pm 11$  years) were identified: 38 (23%) with native and 130 (77%) with aortic graft infection. Thirty day mortality was 15% ( $n = 26$ ) overall, 11% ( $n = 4$ ), and 17% ( $n = 22$ ) for native and aortic graft infections, respectively ( $p = .45$ ). Median follow up was 26 months (interquartile range [IQR] 10, 51). Estimated survival at one, two, three, and five years was 64%, 60%, 57%, and 50%, and significantly better for native (81%, 77%, 77%, and 69%) than for graft infections (58%, 55%, 51%, and 44%;  $p = .011$ ). Nine patients (5.3%) had persistent infection and 10 patients (6%) had aortic re-infection after a median of 10 months (IQR 5, 22), resulting in an estimated freedom from re-infection at one, two, three, and five years of 94%, 92%, 90%, and 86%. Estimated freedom from graft complications at one, two, three, and five years was 91%, 89%, 87%, and 87%.

**Conclusion:** This multicentre study demonstrates low re-infection rates when using self made bovine pericardial grafts, comparable to those of other biological grafts. The rate of graft complications, mainly anastomotic aneurysms and stenoses, was low, while graft degeneration was absent. Self made bovine pericardial tube grafts are an excellent tool for *in situ* reconstruction in the setting of native aortic infection or aortic graft infection.

### WHAT THIS PAPER ADDS

This paper adds multicentre and longer term evidence for the use of self made bovine pericardial grafts in aortic infection, demonstrating low re-infection and graft complication rates in a cohort of 168 patients with native and graft infections of all aortic segments.

**Keywords:** Infective native aortic aneurysm (INAA), *In situ* reconstruction, Mycotic aneurysm, Pericardial tube grafts, Vascular (endo-) graft infection (VGEI)

### INTRODUCTION

Infections of the native aorta and aortic grafts are a relatively rare but potentially life threatening pathology. When diagnosed or suspected, transfer of the patient to a specialised, multidisciplinary centre is recommended.<sup>1</sup> Conservative treatment is reserved for patients unfit

for surgery, as it is not curative and is associated with excessive mortality.<sup>1,2</sup> The current consensus on definitive treatment involves complete surgical removal of the infected aortic tissue or aortic graft, extensive local debridement, and *in situ* aortic reconstruction, combined with adequate antimicrobial treatment.<sup>1</sup> Nevertheless, early mortality remains high due to the severity of the disease, the invasiveness and complexity of the procedure, and complications like sepsis and consecutive multi-organ failure.

For *in situ* aortic reconstruction, current guidelines recommend biological materials such as autologous veins for abdominal graft infections and cryopreserved allografts for thoracic graft infections as the first choice of graft material to avoid the implantation of synthetic grafts into an infected field.<sup>1,3,4</sup> As alternative biological grafts, the use of xenopericardial grafts has emerged during the past decade and several centres have reported promising results.<sup>5-7</sup> These grafts are self made (on a back table) using a bovine pericardial patch and offer multiple benefits such as off the shelf availability, easy handling, and the possibility to be customised to individual anatomy. They have shown a freedom from re-infection of up to 100% while other early and late graft related complication rates were low.<sup>5-8</sup> However, the evidence supporting the use of these grafts is limited by the small sample size, short follow up, and the single centre and retrospective nature of the available studies. Concerns regarding graft durability have been raised. The aim of this European multicentre study is to provide more and much needed outcome data for the use of self made bovine pericardial tube grafts for *in situ* aortic reconstruction in native aortic and aortic graft infection.

## **MATERIALS AND METHODS**

The study was initiated in 2016 by the Department of Vascular Surgery at Bern University Hospital. The local ethics committee approved the study (project number 2016-00178). Four European centres contributed patient data – one centre in Switzerland (Bern) and three centres in Germany (Erlangen, Freiburg, and Munich). Some of these data may already have been published in single centre reports of the respective centres, but with shorter follow up.<sup>5-7,9</sup>

All patients who underwent *in situ* aortic reconstruction using self constructed bovine pericardial grafts for native or aortic graft infection from 2008 to 2020 were included. No other grafts were used for aortic infections during this period. Aortic reconstruction was defined as at least one aortic anastomosis. Data were collected retrospectively from 2008 to 2016 and prospectively from 2017 to 2020. The data were manually extracted from medical records by each centre and entered into a REDCap (Research Electronic Data Capture) database, hosted at the Clinical Trials Unit of the Faculty of Medicine at the University of Bern, Switzerland. The study team at the centre in Switzerland examined all submitted data for completeness and plausibility and queried each centre if necessary.

The primary endpoint of the study was recurrent aortic (pericardial graft) infection. Secondary endpoints were persistent infection, aortic reoperation for infection, graft related complications (aneurysm/pseudoaneurysm formation and graft stenosis/occlusion) as well as peri-operative and long term mortality.

### ***Diagnosis***

Diagnosis of native aortic or graft infection relied on the evaluation of clinical presentation, microbiological (blood cultures, pre-operative or intra-operative specimens), laboratory (C-reactive protein, white blood cell count), and radiological findings. In those with aortic graft infection, the MAGIC criteria had to be met for study inclusion.<sup>10</sup> Due to the lack of diagnostic criteria for native aortic infections at the time of the study, the diagnosis relied on the assessment of the specialists at the treating centre.

### ***Surgical treatment***

The surgical access and the use of adjuncts such as cardiopulmonary bypass, left heart bypass, hypothermia, circulatory arrest, passive aorto-visceral shunting, or selective renal and visceral perfusion was performed according to the standard practice for open aortic interventions at each centre. For graft infections, the treatment strategy was complete removal of all prosthetic graft material whenever possible. In selected cases, where complete graft removal was not deemed

feasible, macroscopically non-infected, well incorporated graft material was left *in situ* at the discretion of the surgeon. In both native and aortic graft infection, radical local debridement was performed. Multiple biopsies of the explanted graft material and/or the aorta as well as the surrounding tissues were taken for microbiological and histopathological examination.

*In situ* reconstruction was performed with a pericardial graft, self made during surgery using a bovine pericardial patch. The standard patch was the Supple Peri-Guard Patch (Synovis Life Technologies, St. Paul, MN, USA). The width of the patch needed was determined by multiplying the desired tube diameter by  $\pi$  and adding 2 – 3 mm for the suture line. A non-absorbable 3-0 or 4-0 polypropylene running suture (no stapler) was used to construct the pericardial patch into a tube. For longer segments, two tubes were sewn together. If needed, tapered or bifurcated grafts were constructed in the same manner (Fig. 1). From experience, the time required to suture the graft is negligible (approximately 10 minutes for a tube graft, 20 – 30 minutes for a bifurcated graft), especially when done during anaesthesia induction of the patient or when working in two teams.

In some thoracoabdominal infections, branches to the reno-visceral arteries were also reconstructed using pericardial tubes. Alternatively, additional graft materials were used at the discretion of the surgeon for the reno-visceral branches as well as in some cases for extension to the ilio-femoral vessels. Separation of the new graft from the surrounding organs was achieved by pedicled omentoplasty in the abdominal area when possible. Adjunct procedures, usually for the treatment of fistulae, were performed as needed.

### ***Antimicrobial therapy***

Antimicrobial therapy was administered after infectious disease consultation and adapted according to pre-operative blood cultures and the cultures of pre-operative or intra-operative specimens. In the presence of an enteric, bronchial, or oesophageal fistula, early antifungal treatment was established. The minimum post-operative duration of antimicrobial therapy was six weeks, but often longer, as determined on an individual basis.

### ***Follow up***

Follow up was performed according to centre specific practice. At each available follow up, imaging modality (computed tomography [CT], magnet resonance imaging [MRI],  $^{18}\text{F}$ -fludeoxyglucose positron emission CT [PET-CT], or sonography) and laboratory parameters were documented. Assessment for persistent or recurrent infection, aortic re-operation for infection, (pseudo-) aneurysm formation (defined as  $\geq 50\%$  diameter increase) and graft occlusion or stenosis (defined as  $\geq 50\%$  lumen reduction) was performed based on imaging, laboratory, and clinical presentation. An infection was considered to be persistent in patients without full infection control after pericardial graft replacement as judged by the treating physicians. Recurrent infection was defined as the resurgence of an infectious process after the infection had been considered controlled and at least 30 days after pericardial graft replacement, even if still under antibiotic therapy.

### ***Data analysis and statistics***

Continuous data are presented as mean values  $\pm$  standard deviation, or median values and interquartile range (IQR) where appropriate. Categorical variables are presented as absolute numbers and percentages. Differences between native aortic infections and aortic graft infections were analysed using the Student's t-test (continuous variables) or Fisher's exact test (categorical variables). Time to event data were analysed using the Kaplan–Meier method, using the log rank test for differences between groups. Statistical analyses were performed using Stata (StataCorp. 2019. Stata Statistical Software: Release 16; College Station, TX, US) and R-Studio (RStudio Inc., Boston, MA, USA).

## **RESULTS**

One hundred and sixty eight patients (77% male, mean age  $67 \pm 11$  years) underwent *in situ* aortic reconstruction using a self made bovine pericardial graft for aortic infection (Bern University Hospital  $n = 67$ ; Heart Centre Freiburg University  $n = 47$ ; Technical University Munich  $n = 46$ ; University Hospital Erlangen  $n = 8$ ; a total of 77 patients from 2008 to 2016

and 91 patients from 2017 to 2020). Thirty eight (23%) had native aortic infections and 130 (77%) had aortic graft infection. Comorbidities and risk factors are summarised in Table 1. Of those with graft infection, 42 (32%) had previous endovascular and 80 (62%) had previous open surgery, while eight (6.2%) had previously had both, open and endovascular surgeries, of the affected aortic segment. Mean time from previous surgery to pericardial graft implantation was  $46 \pm 60$  months.

### ***Patient presentation and diagnosis***

Only the percentage of patients with an American Society of Anesthesiologists (ASA) class  $\geq 4$  and those with pain at presentation differed significantly between native aortic and graft infection (Table 1). CT angiography was the most common imaging modality at diagnosis and available in 92% of patients pre-operatively. PET-CT and MRI were used as sole or additional imaging modality in 26% and 4.8%, respectively. PET-CT was more often used in graft infections than in native infections (32% vs. 7.9%,  $p = .003$ ; Table 1).

### ***Surgical details***

Eighty four patients (50%) required urgent aortic replacement (within 24 hours). Treated aortic segments are listed in Table 2. In many patients, more than one segment was affected. A rupture was intra-operatively found in 11 (6.5%) and a fistula to the bowel, oesophagus, or bronchi in 43 (26%). In those with aortic graft infection, complete synthetic graft removal was achieved in 119 (92%). Debridement was deemed complete in 148 (88%) of all patients (Table 2).

### ***Microbiology***

Pre-operative blood cultures were positive in 65 (39%) patients. Fifty two (31%) had other positive pre-operative cultures, such as cultures from percutaneous drainage of a perigraft collection. Intra-operatively acquired microbiological samples were positive in 133 (79%) and the most common pathogens were from the *Staphylococcus* species (Table 3).

### ***Peri-operative outcomes***



Median length of hospital stay was 22 days (IQR 14, 40): 14 days (IQR 10, 22) for native and 27 (IQR 17, 45) for graft infections ( $p < .001$ ). Thirty day mortality was 15% ( $n = 26$ ) overall, 11% ( $n = 4$ ) and 17% ( $n = 22$ ) for native and aortic graft infections, respectively ( $p = .45$ ). Thirteen patients died post-operatively due to multi-organ failure as a consequence of the infection and/or the procedure. One patient died intra-operatively due to fulminant sepsis after prolonged but unsuccessful resuscitation. Three patients died due to cerebral, three due to cardiac, three due to respiratory, and one due to bleeding complications. In two patients, the cause of their sudden post-operative death remained unclear. Non-fatal peri-operative complications are listed in Table 4.

### ***Follow up***

Median duration of antibiotic therapy was 12 weeks (IQR 6, 15) with no significant difference between those with native and those with aortic graft infection (Table 4). During follow up ( $> 30$  days after surgery), 44 patients (five with native and 39 with graft infections) died after a median of eight months (IQR 3, 6). For the remaining patients, median follow up was 26 months (IQR 10, 51). Estimated survival at one, two, three, and five years was 64%, 60%, 57%, and 50%, and significantly better for those with native (81%, 77%, 77%, and 69%) than for those with graft infections (58%, 55%, 51%, and 44%;  $p=0.011$ ; Fig. 2). Eight deaths were related to persistent ( $n = 5$ ) or recurrent ( $n = 3$ ) aortic infection and occurred after a median of five months (IQR 1, 9), all in patients who initially had graft infections. One death was aortic/graft related, due to a ruptured anastomotic aneurysm and one death was due to aortic rupture unrelated to the graft or the infection (thoracic rupture after successful treatment of an infrarenal graft infection). Other causes of death during follow up were cardiac ( $n = 5$ ), pulmonary ( $n = 3$ ) or cerebral disease ( $n = 2$ ), cancer ( $n = 3$ ), and other ( $n = 6$ ). In 15 patients, cause of death remained unknown.

### ***Persistent and recurrent infection***

Nine patients (5.3%) were deemed to have persistent infection after pericardial graft reconstruction. All were patients who initially had aortic graft infection, five of them with an enteric fistula and one with faecal peritonitis due to colon perforation. Complete prosthetic graft removal had not been feasible in one patient but was performed in the other eight.

Ten patients (6%) had aortic (pericardial graft) re-infection after a median of 10 months (IQR 5, 22); of those, nine were patients who initially had aortic graft infection (one with an enteric fistula) and one had native aortic infection with an enteric fistula. All but one patient with graft infection had undergone complete graft prosthetic graft removal. Nine re-infections were located in the abdominal aorta and one in the ascending aorta. Six out of the 10 patients were under ongoing antimicrobial therapy when re-infection was diagnosed. Eight patients underwent aortic reoperation while one refused re-operation and one was deemed inoperable. Estimated freedom from recurrent aortic infection at one, two, three, and five years was 94%, 92%, 90%, and 86% (Fig. 3).

### ***Graft complications***

Eight anastomotic aneurysms (4.8%) occurred after a median of nine months (IQR 7, 28). Thereof, three were associated with persistent or recurrent aortic infection. All others were treated by stent graft implantation. In one patient with anastomotic aneurysm, rupture occurred, resulting in the abovementioned graft related death of the patient.

Occlusive graft complications occurred in seven patients after a median of 11 months (IQR 2, 12). Thereof, two patients (1.2%) suffered occlusion of an iliac limb of a bifurcated abdominal graft, treated by crossover bypass in one patient and conservatively in another patient. Five patients (3%) had anastomotic stenoses of the pericardial to native vessel anastomosis. Thereof three were located at the iliac level and two at the visceral level, where an additional small calibre pericardial branch had been used for revascularisation of the renal or visceral arteries. Three of the anastomotic stenoses were treated by stent implantation and two were treated conservatively, as both patients were asymptomatic.

Estimated freedom from graft complications (anastomotic aneurysm, graft limb occlusion, or anastomotic stenosis) at one, two, three, and five years was 91%, 89%, 87%, and 87% (Fig. 4). No aneurysmatic or stenotic graft degeneration occurred unrelated to an anastomosis.

## DISCUSSION

In this multicentre, combined retrospective and prospective study, data of 168 patients from four specialised European centres over a period of 13 years have been analysed. In this cohort, including patients with native or graft infections from the aortic root to the bifurcation, a 30 day mortality of 15% and an estimated five year mortality of 50% was noted. The aortic (pericardial graft) re-infection rate was 6%, resulting in a high freedom from re-infection. Graft complications, mainly anastomotic aneurysm and anastomotic stenosis, were rare.

It has to be kept in mind that aortic infection is a life threatening pathology *per se*. The severity of this condition combined with the surgical trauma necessary to achieve complete graft removal and/or debridement result in a high peri-operative mortality that is not related to the graft material used for reconstruction.<sup>11</sup> Patients were included with infections of all aortic segments, including the thoracic and thoracoabdominal aorta, where open surgery is inherently considered high risk, even in the elective, non-infectious setting. Previous single centre studies with similar (anatomically mixed) patient collectives found in hospital mortalities of 32% and 25%,<sup>8,12</sup> or a 30 day mortality of 17%, respectively,<sup>13</sup> comparable to the 30 day mortality of 15%. As for long term mortality, comparable data are lacking, owing to the short follow up in available studies.

Although a trend for lower peri-operative mortality in native aortic infections compared with graft infections has been reported,<sup>5</sup> a significant difference at 30 days was not observed. During follow up, however, better survival was observed for those with native than for those with graft infections. The treatment of patients with graft infections may be expected to be more complex than the treatment of native aortic infections. Although extensive atherosclerosis may

be a risk factor for native aortic infections,<sup>14</sup> it is almost always present in patients with graft infections, in whom the primary graft was implanted for either occlusive or dilative arteriopathy. In these patients, pericardial graft reconstruction is either redo surgery (after primary open surgery) or associated with often complex endograft explantation<sup>15</sup> in patients who may initially not have been considered good candidates for open surgery. Nevertheless, no significant differences were found between native and aortic graft infections regarding age and comorbidities. Interestingly, more patients with native aortic infection were deemed ASA class IV or higher ( $p < .001$ ) and 16% of them presented in circulatory shock, possibly representing a relatively sick cohort of native infections and maybe explaining the similar peri-operative mortality when compared to graft infections. In the longer term, persistence and recurrence of aortic infection probably plays the most important role in regards to the differences in mortality between both groups. Among 39 deaths of graft infections during follow up, eight (21%) were related to persistent or recurrent aortic infection, whereas no late deaths among those with native aortic infections were attributed to aortic (re-)infection.

### ***Persistent and recurrent infection***

There is currently no established definition of when an aortic infection should be considered cured and the differentiation between persistent and recurrent infection may be controversial.<sup>16</sup> As the primary aim of this study was to evaluate the performance of the bovine pericardial grafts, persistent und recurrent infection were reported separately. The classification into persistent or recurrent infection was difficult, especially since six out of 10 patients were still under antibiotic therapy when re-infection was reported by the centre. Therefore, some of the re-infections in this cohort may also have been persistent infections. Again, this is difficult to prove as repetitive aortic tissue sampling (comparable to repetitive blood cultures in bacteraemia) is not feasible in aortic infection. Persistent infection is not a graft failure but may rather reflect the extent of the infection, the virulence of the causative pathogen, and the completeness of intra-operative debridement, independently of the graft material used for

reconstruction. However, defined criteria for persistent and recurrent infection after surgical treatment of native aortic and graft infection would improve reporting and should be established in the future.

While previous series reported optimistically low re-infection rates of 0 – 2%,<sup>5,6,8,12,17,18</sup> this study found a re-infection rate of 6% (excluding persistent infections). This is comparable to the re-infection rates of autologous veins of 4 – 5%<sup>19,20</sup> and cryopreserved allografts of 4 – 6%<sup>21,22</sup> in abdominal aortic infections. For a recently developed polyester graft coated with silver acetate and triclosan, a one year re-infection rate of 2.8% has been reported.<sup>23</sup> Another study examining the performance of a prefabricated bovine pericardial graft, the No-React non-valved conduit (Biointegral Surgical Inc., Mississauga, ON, Canada) reported a one year re-infection rate of 9%.<sup>24</sup> The extent and virulence of the initial infection (including the presence of a fistula), and the completeness of debridement probably also play a role in the development of re-infection. This again illustrates the difficulties to distinguish between persistent and recurrent infection. Although it is believed the choice of graft material for aortic reconstruction is relevant to prevent re-infection, other factors may be just as important. This includes an experienced multidisciplinary team, aggressive intra-operative debridement (balanced against the condition of the patient), the treatment of fistulas, the separation of the pericardial graft from surrounding organs, and the adequate type and duration of the antimicrobial therapy.

### ***Graft complications***

Graft complications are a well known issue for biological grafts, in particular for cryopreserved allografts. In a meta-analysis of cryopreserved allograft reconstruction in aorto-iliac infections, anastomotic/allograft disruption was found in 5.9%, aneurysmal degeneration in 5.0%, anastomotic/pseudoaneurysm in 3.1%, and thrombotic/stenotic complications in 12.2%.<sup>4</sup> For autologous veins in abdominal aortic infections, Heinola *et al.* found a graft occlusion rate of 3.6% and a graft rupture rate of 5%.<sup>3</sup> In the present study, besides two graft limb occlusions (1.2%), all graft complications were anastomotic aneurysms (4.8%) or stenoses (3%). Knowing

this, outcomes may be further improved. This may include consequent reinforcement of the anastomoses with an additional bovine pericardial strip to prevent anastomotic aneurysms. As all anastomotic stenoses occurred either at the iliac or reno-visceral level, narrowing sutures must be avoided when performing these anastomoses. It remains unclear, whether pericardial graft should be used for small calibre vessels such as the reno-visceral arteries. In addition, consequent and regular follow up is mandatory in order to detect graft complications. Except for infection associated findings, anastomotic aneurysms or stenoses are easily treatable by endovascular means and fatal events, as it occurred in one patient (anastomotic aneurysm rupture), may be prevented. However, the impact of the radial force of an endovascular graft on the self constructed pericardial tube graft has not been studied so far.

### ***Limitations***

The inclusion of a heterogeneous patient collective in regards to anatomical localisation and pathology is a limitation of this study. As outlined, native and graft infections are two different entities with specific outcomes. However, since the aim was to evaluate the performance of the graft material, it is reasonable to include both pathologies as well as all aortic segments. Data of patients with conservative treatment or in whom alternative graft materials were used, were not available for comparison. Although the same surgical concept was used at all centres, treatment of aortic infection remains individual as well as surgeon and centre dependent. This includes antimicrobial regimen and follow up protocols. After some point, imaging studies were not routinely performed anymore, which seems justifiable in uneventful courses and to limit radiation exposure. Autopsies of deaths during follow up were not systematically performed and in a number of patients, cause of death remained unknown.

It has to be underlined that the pericardial patch used in this study was the Synovis Supple Peri-Guard and that results cannot be generalised to other commercially available pericardial patches or prefabricated bovine pericardial grafts. Variations in the tissue processing and sterilisation may impact biocompatibility, mechanical strength, and durability of the

pericardial patch. Results of a currently available prefabricated graft were recently published with a one year re-infection and occlusion rate of 9% and 6%, respectively.<sup>24</sup> However, a similar graft has previously been used in cardiac surgery as an aortic valved conduit with a relatively high rate of re-operations in the mid-term.<sup>25</sup>

### **Conclusion**

Self- made bovine pericardial grafts offer many advantages over other biological grafts like allografts and autologous veins, such as availability, easy handling, customisation to the patient's anatomy, and avoidance of harvesting trauma. Evidence from this multicentre study supports the use of these grafts by demonstrating low re-infection and graft complications rates that compare well to those of other biological grafts. Graft degeneration was not observed. However, longer term surveillance is still necessary and should be the focus of future studies.

### **CONFLICT OF INTEREST**

None.

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### **References**

1. Chakfe N, Diener H, Lejay A, Assadian O, Berard X, Caillon J, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2020 clinical practice guidelines on the management of vascular graft and endograft infections. *Eur J Vasc Endovasc Surg* 2020;**59**:339–84.
2. Kahlberg A, Grandi A, Loschi D, Vermassen F, Moreels N, Chakfe N, et al. A systematic review of infected descending thoracic aortic grafts and endografts. *J Vasc Surg* 2019;**69**:1941–51.

- 363 3. Heinola I, Kantonen I, Jaroma M, Alback A, Vikatmaa P, Aho P, et al. Editor's Choice  
 364 – Treatment of aortic prosthesis infections by graft removal and in situ replacement with  
 365 autologous femoral veins and fascial strengthening. *Eur J Vasc Endovasc Surg* 2016;**51**:232–  
 366 9.
- 367 4. Antonopoulos CN, Papakonstantinou NA, Hardy D, Lyden SP. Editor's Choice –  
 368 Cryopreserved allografts for arterial reconstruction after aorto-iliac infection: a systematic  
 369 review and meta-analysis. *Eur J Vasc Endovasc Surg* 2019;**58**:120–8.
- 370 5. Weiss S, Tobler EL, von Tengg-Kobligk H, Makaloski V, Becker D, Carrel TP, et al.  
 371 Self made xeno-pericardial aortic tubes to treat native and aortic graft infections. *Eur J Vasc*  
 372 *Endovasc Surg* 2017;**54**:646–52.
- 373 6. Kreibich M, Siepe M, Berger T, Pingpoh C, Puiu P, Morlock J, et al. Treatment of  
 374 infectious aortic disease with bovine pericardial tube grafts. *Eur J Cardiothorac Surg*  
 375 2021;**60**:155–61.
- 376 7. Almasi-Sperling V, Heger D, Meyer A, Lang W, Rother U. Treatment of aortic and  
 377 peripheral prosthetic graft infections with bovine pericardium. *J Vasc Surg* 2020;**71**:592–8.
- 378 8. Keschenau PR, Gombert A, Barbat ME, Jalaie H, Kalder J, Jacobs MJ, et al.  
 379 Xenogeneic materials for the surgical treatment of aortic infections. *J Thorac Dis*  
 380 2021;**13**:3021–32.
- 381 9. Lutz B, Reeps C, Biro G, Knappich C, Zimmermann A, Eckstein HH. Bovine  
 382 pericardium as new technical option for in situ reconstruction of aortic graft infection. *Ann*  
 383 *Vasc Surg* 2017;**41**:118–26.
- 384 10. Lyons OT, Baguneid M, Barwick TD, Bell RE, Foster N, Homer-Vanniasinkam S, et  
 385 al. Diagnosis of aortic graft infection: a case definition by the Management of Aortic Graft  
 386 Infection Collaboration (MAGIC). *Eur J Vasc Endovasc Surg* 2016;**52**:758–63.
- 387 11. Schmidli J, Wyss TR. Self-made bovine pericardial tube grafts: maybe the best thing  
 388 since sliced bread. *Eur J Cardiothorac Surg* 2021;**60**:162–3.



- 389 12. Kubota H, Endo H, Noma M, Ishii H, Tsuchiya H, Yoshimoto A, et al.  
390 Xenopericardial roll graft replacement for infectious pseudoaneurysms and graft infections of  
391 the aorta. *J Cardiothorac Surg* 2015;10:133.
- 392 13. Belkorissat RA, Sadoul C, Bouziane Z, Saba C, Salomon C, Malikov S, et al. Tubular  
393 reconstruction with bovine pericardium xenografts to treat native aortic infections. *Ann Vasc*  
394 *Surg* 2020;64:27–32.
- 395 14. Sorelius K, Wyss TR, Academic Research Consortium of Infective Native Aortic A,  
396 Adam D, Beck AW, Berard X, et al. Editor's Choice – Infective native aortic aneurysms: a  
397 Delphi consensus document on terminology, definition, classification, diagnosis, and  
398 reporting standards. *Eur J Vasc Endovasc Surg* 2023;65:323–9.
- 399 15. Khalid W, Puges M, Stenson K, Cazanave C, Ducasse E, Caradu C, et al. Single centre  
400 experience with infected abdominal aortic endograft explantation. *J Vasc Surg* 2023;77:971–  
401 2.
- 402 16. Sorelius K, Lyons OT. Present need to improve the diagnosis and outcome measures  
403 for aortic vascular graft and endograft infection: a call to action. *Eur J Vasc Endovasc Surg*  
404 2023;66:292–4.
- 405 17. Czerny M, von Allmen R, Opfermann P, Sodeck G, Dick F, Stellmes A, et al. Self-  
406 made pericardial tube graft: a new surgical concept for treatment of graft infections after  
407 thoracic and abdominal aortic procedures. *Ann Thorac Surg* 2011;92:1657–62.
- 408 18. Anibueze C, Sankaran V, Sadat U, Tan K, Wilson YG, Brightwell RE, et al. Neo-aortic  
409 xenoprosthetic grafts for treatment of mycotic aneurysms and infected aortic grafts. *Ann Vasc*  
410 *Surg* 2017;44:419.
- 411 19. Heinola I, Kantonen I, Mattila I, Alback A, Venermo M. Cryopreserved venous  
412 allografts in supra-inguinal reconstructions: a single centre experience. *Eur J Vasc Endovasc*  
413 *Surg* 2019;58:912–9.

20. Ali AT, Modrall JG, Hocking J, Valentine RJ, Spencer H, Eidt JF, et al. Long-term results of the treatment of aortic graft infection by in situ replacement with femoral popliteal vein grafts. *J Vasc Surg* 2009;**50**:30–9.
21. Weiss S, Bachofen B, Widmer MK, Makaloski V, Schmidli J, Wyss TR. Long-term results of cryopreserved allografts in aortoiliac graft infections. *J Vasc Surg* 2021;**74**:268–75.
22. Ben Ahmed S, Louvancourt A, Daniel G, Combe P, Duprey A, Albertini JN, et al. Cryopreserved arterial allografts for in situ reconstruction of abdominal aortic native or secondary graft infection. *J Vasc Surg* 2018;**67**:468–77.
23. Caradu C, Jolivet B, Puges M, Cazanave C, Ducasse E, Berard X. Reconstruction of primary and secondary aortic infections with an antimicrobial graft. *J Vasc Surg* 2023;**77**:1226–37.
24. Reinders Folmer EI, Verhofstad N, Zeebregts CJ, van Sambeek M, Saleem BR, VASC-REGAIN collaborators. Performance of the BioIntegral bovine pericardial graft in vascular infections: VASCular No-REact Graft Against Infection Study. *Ann Vasc Surg* 2023;**95**:116–24.
25. Reineke DC, Kaya A, Heinisch PP, Oezdemir B, Winkler B, Huber C, et al. Long-term follow-up after implantation of the Shelhigh® No-React® complete biological aortic valved conduit. *Eur J Cardiothorac Surg* 2016;**50**:98–104.

**Figure 1.** Example of a self constructed bovine pericardial graft, here as a bifurcated graft for an aorto-iliac *in situ* reconstruction.

**Figure 2.** Cumulative Kaplan–Meier estimate of survival of patients who had native aortic infection ( $n = 38$ ) vs. those who had aortic graft infection ( $n = 130$ ),  $p = .011$  (log rank test). The dotted lines represent the 95% confidential intervals for native and graft infections, respectively.

**Figure 3.** Cumulative Kaplan–Meier estimate of 168 patients treated with self constructed bovine pericardial grafts showing freedom from aortic (xenograft) re-infection. The dotted lines represent the 95% confidential interval.

**Figure 4.** Cumulative Kaplan–Meier estimate of 168 patients treated with self constructed bovine pericardial grafts showing freedom from graft complication (anastomotic aneurysm, anastomotic stenosis, graft limb occlusion). The dotted lines represent the 95% confidential interval.

**Table 1. Demographics, comorbidities, clinical presentation, and imaging of 168 patients treated with self constructed bovine pericardial grafts due to native and graft infections of the aorta.**

Characteristics	All (n = 168)	Native aortic infections (n = 38)	Graft infections (n = 130)	p value
Age – y	67 ± 11	68 ± 11	67 ± 11	.93
Male	130 (77)	28 (74)	102 (78)	.52
<i>Comorbidities</i>				
Cerebrovascular disease	14 (8.3)	3 (7.9)	11 (8.5)	1.00
Coronary heart disease	65 (39)	16 (42)	49 (38)	.71
Pulmonary disease	41 (24)	9 (24)	32 (25)	1.00
Renal insufficiency, eGFR <60 mL/min	47 (28)	6 (16)	41 (32)	.070
Peripheral artery disease	55 (33)	10 (26)	45 (35)	.43
Diabetes mellitus	37 (22)	11 (29)	26 (20)	.27
<i>Immunosuppression</i>				
Steroid medication	6 (3.6)	2 (5.3)	4 (3.1)	.62
Other immunosuppressive medication	2 (1.2)	1 (2.6)	1 (0.8)	.40
<i>Clinical presentation</i>				
ASA class ≥IV	91 (54)	31 (82)	60 (46)	<.001
Circulatory shock	21 (13)	6 (16)	15 (12)	.58
Lower limb ischaemia	13 (7.7)	1 (2.6)	12 (9.2)	.30
Pain	84 (50)	29 (76)	55 (42)	<.001
Fever	112 (67)	21 (55)	91 (70)	.12
<i>Suspected focus of infection</i>				
No	73 (43)	25 (66)	48 (37)	
Yes	95 (57)*	13 (34)*	82 (63)*	

Organ fistulation <sup>†</sup>	21 (12.5)	2 (5.3)	19 (15)	.17
Soft tissue infection	17 (10)	1 (2.6)	16 (12)	.12
Endocarditis	13 (7.7)	0 (0)	13 (10)	.040
Intravascular catheter infection	5 (3.0)	3 (7.9)	2 (1.5)	0.08
Septic arthritis or prosthetic joint infection	4 (2.4)	1 (2.6)	3 (2.3)	1.00
Urinary tract infection	4 (2.4)	1 (2.6)	3 (2.3)	1.00
Pneumonia	3 (1.8)	0 (0)	3 (2.3)	1.00
Gastroenteritis	3 (1.8)	1 (2.6)	2 (1.5)	.54
Other	28 (17)	5 (13)	23 (18)	.63
<i>Laboratory</i>				
C-reactive protein – mg/L	80 (26, 152)	128 (30, 228)	80 (27, 144)	.12
White blood cell count – G/L	11 ± 5.7	11 ± 4.0	12 ± 6.1	.56
<i>Imaging findings</i>				
Air	46 (27)	0 (0)	46 (35)	<.001
Collection/abscess/soft tissue mass	128 (76)	25 (66)	103 (79)	.13
Fistula	36 (21)	3 (7.9)	33 (25)	.024
Rupture	9 (5.4)	4 (11)	5 (3.8)	.12

Data are presented as *n* (%), median (interquartile range), or mean ± standard deviation. ASA = American Society of Anaesthesiologists classification; eGFR = estimated glomerular filtration rate.

\*Three patients had two documented suspected focuses of infection each: one with native and two with aortic graft infection, therefore, the numbers below add up to more than 95.

<sup>†</sup>Aorto-pulmonary or bronchial, aorto-oesophageal, aorto-enteric fistulation.

**Table 2. Surgical details of 168 bovine pericardial tube graft implantations of the aorta.**

Characteristics	All ( <i>n</i> = 168)	Native aortic infections ( <i>n</i> = 38)	Graft infections ( <i>n</i> = 130)	<i>p</i> value
Urgent surgery, <24 h	84 (50)	28 (74)	56 (43)	.001
<i>Location of surgery*</i>				
Ascending aorta	27 (16)	1 (2.6)	26 (20)	.010
Aortic arch	12 (7.1)	1 (2.6)	11 (8.5)	.30
Descending aorta	36 (21)	8 (21)	28 (22)	1.0
Paravisceral/pararenal aorta	42 (25)	17 (45)	25 (19)	.003
Infrarenal aorta	109 (65)	27 (71)	82 (63)	.44
Iliac	44 (26)	4 (11)	40 (31)	.012
Complete synthetic graft removal			119 (92)	

Complete debridement	148 (88)	36 (95)	112 (86)	.25
Omental wrapping	33 (20)	12 (32)	21 (16)	.060
<i>Additional graft material</i>				
Vein	4 (2.4)	2 (5.3)	2 (1.5)	.22
Homograft	3 (1.8)	0 (0)	3 (2.3)	1.0
Biograft (e.g., Omniflow)	8 (4.8)	0 (0)	8 (6.2)	.20
<i>Intra-operative findings</i>				
Collection/abscess/soft tissue mass	132 (79)	24 (63)	108 (83)	.013
Fistula	43 (26)	5 (13)	38 (29)	.060
False aneurysm/anastomotic aneurysm	37 (22)	19 (50)	18 (14)	<.001
Rupture	11 (6.5)	4 (11)	7 (5.4)	.27
Other, e.g., infected soft tissue, gross contamination	18 (11)	7 (18)	11 (8.5)	.13

Data are presented as *n* (%).

\*In many patients, more than one segment was affected.

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**Table 3. Microbiology of 168 patients treated with self constructed bovine pericardial grafts due to native and graft infections of the aorta.**

Characteristics	All ( <i>n</i> = 168)	Native aortic infections ( <i>n</i> = 38)	Graft infections ( <i>n</i> = 130)	<i>p</i> value
No microbe identified	15 (8.9)	6 (16)	9 (6.9)	.17
<i>Pre-operative blood cultures</i>				
Not available	30 (18)	7 (18)	23 (18)	
Positive	65 (39)	19 (50)	46 (35)	.20
<i>Pre-operative other cultures, e.g., percutaneous biopsy</i>				
Not available	105 (63)	28 (74)	77 (59)	
Positive	52 (31)	8 (21)	44 (34)	.29
<i>Intra-operative cultures</i>				
Positive	133 (79)	27 (71)	106 (82)	.24
<i>Identified microbes, all cultures*</i>				
<i>Staphylococcus</i>	59 (35)	17 (45)	42 (32)	.20
<i>Streptococcus</i>	32 (19)	5 (13)	27 (21)	.40
<i>Enterococcus</i>	32 (19)	1 (2.6)	31 (24)	.002
<i>Escherichia coli</i>	21 (12)	2 (5.3)	19 (15)	.20
<i>Klebsiella</i>	11 (6.5)	0 (0)	11 (8.5)	.07
<i>Pseudomonas</i>	6 (3.6)	0 (0)	6 (4.6)	.30

<i>Salmonella</i>	8 (4.8)	4 (11)	4 (3.1)	.08
Fungus	37 (22)	3 (7.9)	34 (26)	.02
Other	55 (33)	6 (16)	49 (38)	.01

Dara are presented as *n* (%).

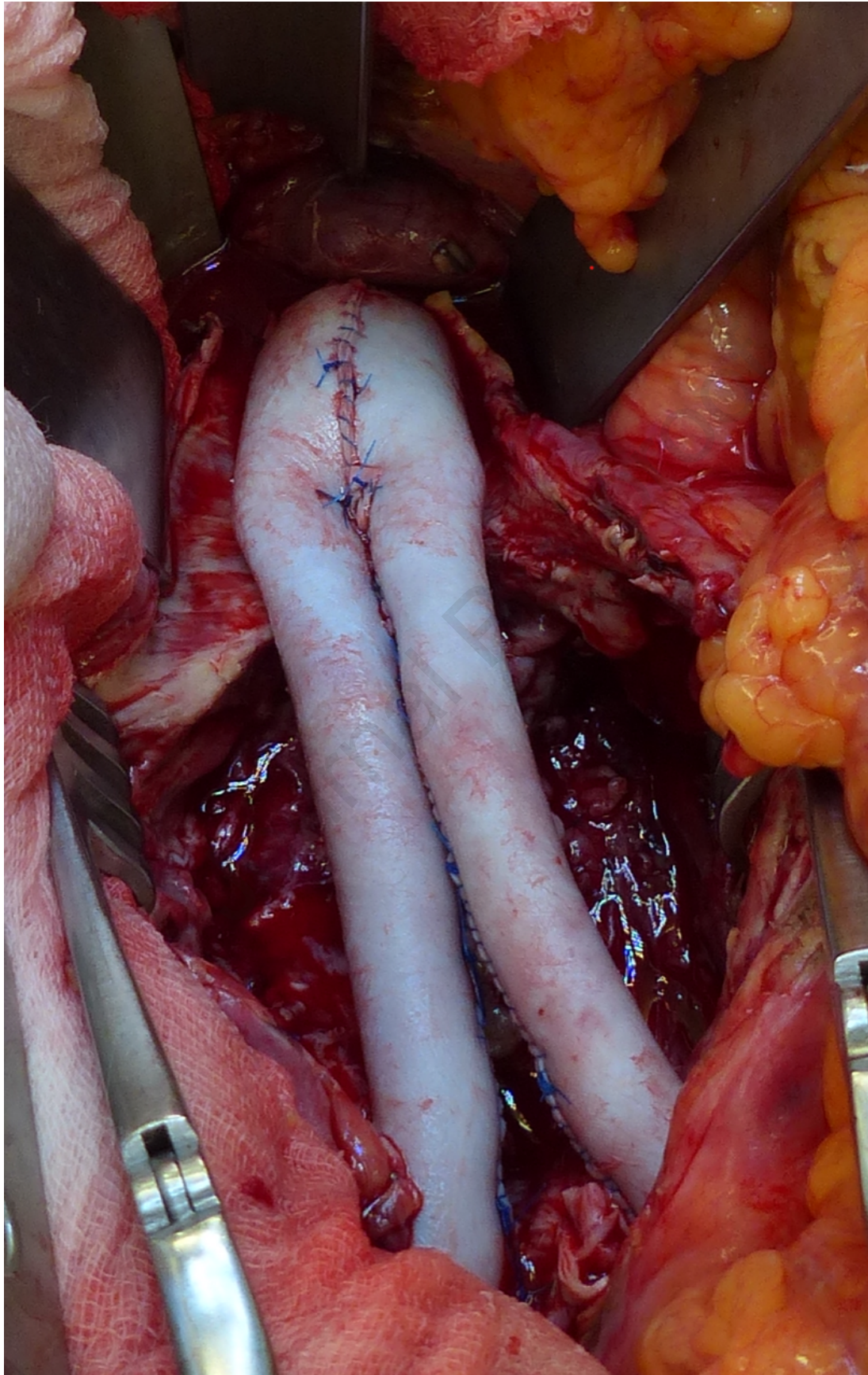
\*Or polymerase chain reaction analysis in case of negative cultures.

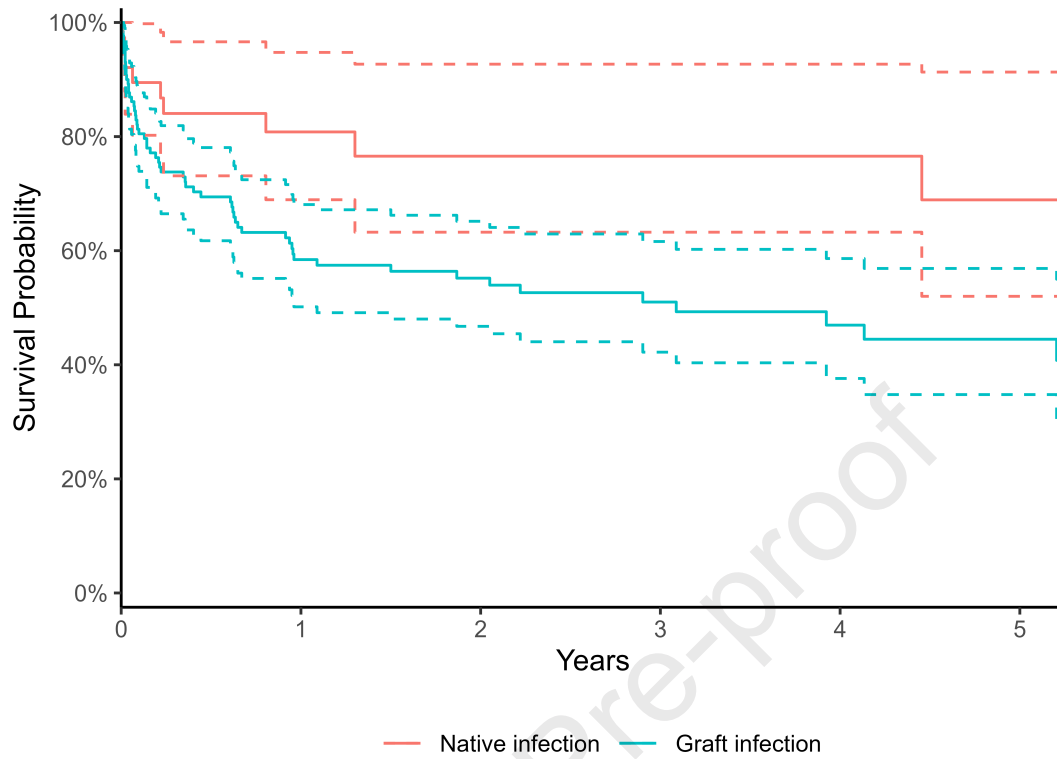
**Table 4. Post-operative outcomes of 168 patients treated with self constructed bovine pericardial grafts due to native and graft infections of the aorta.**

Characteristics	All ( <i>n</i> = 168)	Native aortic infections ( <i>n</i> = 38)	Graft infections ( <i>n</i> = 130)	<i>P</i> value
30 d mortality	26 (15)	4 (11)	22 (17)	.45
Length of hospital stay – d	22 (15, 41)	15 (11, 22)	28 (19, 45)	<.001
<i>Peri-operative complications</i>				
Stroke	9 (5.4)	1 (2.6)	8 (6.2)	.69
Permanent paraparesis/paraplegia	4 (2.4)	1 (2.6)	3 (2.3)	1.0
Other neurological	7 (4.2)	1 (2.6)	6 (4.6)	1.0
Cardiac	13 (7.7)	4 (11)	9 (6.9)	.49
Respiratory	18 (11)	1 (2.6)	17 (13)	.080
Pulmonary embolism	4 (2.4)	1 (2.6)	3 (2.3)	1.0
Gastrointestinal	24 (14)	6 (16)	18 (14)	.79
Acute kidney injury, >1.5 fold increase of serum creatinine	30 (18)	9 (24)	21 (16)	.34
Urinary tract	4 (2.4)	0 (0)	4 (3.1)	.58
Intravenous catheter infection	3 (1.8)	1 (2.6)	2 (1.5)	.54
Revision for bleeding	7 (4.2)	1 (2.6)	6 (4.6)	1.0
Wound revision	29 (17)	4 (11)	25 (19)	.33
Other	26 (15)	5 (13)	21 (16)	.80
Duration of post-operative antimicrobial therapy – wk	12.3 (6.4, 14.9)	12.6 (9.6, 16.3)	12.1 (6, 14)	.35

Dara are presented as *n* (%), or median (interquartile range).







Native infection						
At Risk	38	22	17	14	10	9
Events	0	7	8	8	8	9
Graft infection						
At Risk	130	61	45	31	19	14
Events	0	50	53	56	58	59



