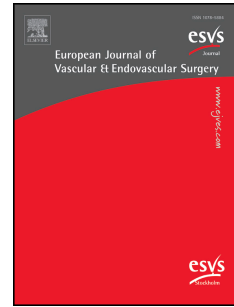


# Journal Pre-proof

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

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1 **Self Made Bovine Pericardial Tube Grafts in Aortic Infection: A European Multicentre**  
2 **Study**

3 Short Title: Bovine Pericardial Tube Grafts in Aortic Infection

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

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

27 **Results:** One hundred and sixty eight patients (77% male, mean age  $67 \pm 11$  years) were  
28 identified: 38 (23%) with native and 130 (77%) with aortic graft infection. Thirty day mortality  
29 was 15% ( $n = 26$ ) overall, 11% ( $n = 4$ ), and 17% ( $n = 22$ ) for native and aortic graft infections,  
30 respectively ( $p = .45$ ). Median follow up was 26 months (interquartile range [IQR] 10, 51).  
31 Estimated survival at one, two, three, and five years was 64%, 60%, 57%, and 50%, and  
32 significantly better for native (81%, 77%, 77%, and 69%) than for graft infections (58%, 55%,  
33 51%, and 44%;  $p = .011$ ). Nine patients (5.3%) had persistent infection and 10 patients (6%)  
34 had aortic re-infection after a median of 10 months (IQR 5, 22), resulting in an estimated  
35 freedom from re-infection at one, two, three, and five years of 94%, 92%, 90%, and 86%.  
36 Estimated freedom from graft complications at one, two, three, and five years was 91%, 89%,  
37 87%, and 87%.

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

#### 43 **WHAT THIS PAPER ADDS**

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

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

#### 49 **INTRODUCTION**

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

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

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

### 73 **MATERIALS AND METHODS**

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

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

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

### 92 ***Diagnosis***

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

### 99 ***Surgical treatment***

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

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

109 *In situ* reconstruction was performed with a pericardial graft, self made during surgery  
110 using a bovine pericardial patch. The standard patch was the Supple Peri-Guard Patch (Synovis  
111 Life Technologies, St. Paul, MN, USA). The width of the patch needed was determined by  
112 multiplying the desired tube diameter by  $\pi$  and adding 2 – 3 mm for the suture line. A non-  
113 absorbable 3-0 or 4-0 polypropylene running suture (no stapler) was used to construct the  
114 pericardial patch into a tube. For longer segments, two tubes were sewn together. If needed,  
115 tapered or bifurcated grafts were constructed in the same manner (Fig. 1). From experience, the  
116 time required to suture the graft is negligible (approximately 10 minutes for a tube graft, 20 –  
117 30 minutes for a bifurcated graft), especially when done during anaesthesia induction of the  
118 patient or when working in two teams.

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

### 125 ***Antimicrobial therapy***

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

**131 Follow up**

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

**143 Data analysis and statistics**

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

**152 RESULTS**

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

157 and 91 patients from 2017 to 2020). Thirty eight (23%) had native aortic infections and 130  
158 (77%) had aortic graft infection. Comorbidities and risk factors are summarised in Table 1. Of  
159 those with graft infection, 42 (32%) had previous endovascular and 80 (62%) had previous open  
160 surgery, while eight (6.2%) had previously had both, open and endovascular surgeries, of the  
161 affected aortic segment. Mean time from previous surgery to pericardial graft implantation was  
162  $46 \pm 60$  months.

### 163 *Patient presentation and diagnosis*

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

### 170 *Surgical details*

171 Eighty four patients (50%) required urgent aortic replacement (within 24 hours). Treated aortic  
172 segments are listed in Table 2. In many patients, more than one segment was affected. A rupture  
173 was intra-operatively found in 11 (6.5%) and a fistula to the bowel, oesophagus, or bronchi in  
174 43 (26%). In those with aortic graft infection, complete synthetic graft removal was achieved  
175 in 119 (92%). Debridement was deemed complete in 148 (88%) of all patients (Table 2).

### 176 *Microbiology*

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

### 181 *Peri-operative outcomes*



182 Median length of hospital stay was 22 days (IQR 14, 40): 14 days (IQR 10, 22) for native and  
183 27 (IQR 17, 45) for graft infections ( $p < .001$ ). Thirty day mortality was 15% ( $n = 26$ ) overall,  
184 11% ( $n = 4$ ) and 17% ( $n = 22$ ) for native and aortic graft infections, respectively ( $p = .45$ ).  
185 Thirteen patients died post-operatively due to multi-organ failure as a consequence of the  
186 infection and/or the procedure. One patient died intra-operatively due to fulminant sepsis after  
187 prolonged but unsuccessful resuscitation. Three patients died due to cerebral, three due to  
188 cardiac, three due to respiratory, and one due to bleeding complications. In two patients, the  
189 cause of their sudden post-operative death remained unclear. Non-fatal peri-operative  
190 complications are listed in Table 4.

### 191 ***Follow up***

192 Median duration of antibiotic therapy was 12 weeks (IQR 6, 15) with no significant difference  
193 between those with native and those with aortic graft infection (Table 4). During follow up  
194 ( $> 30$  days after surgery), 44 patients (five with native and 39 with graft infections) died after a  
195 median of eight months (IQR 3, 6). For the remaining patients, median follow up was 26 months  
196 (IQR 10, 51). Estimated survival at one, two, three, and five years was 64%, 60%, 57%, and  
197 50%, and significantly better for those with native (81%, 77%, 77%, and 69%) than for those  
198 with graft infections (58%, 55%, 51%, and 44%;  $p=0.011$ ; Fig. 2). Eight deaths were related to  
199 persistent ( $n = 5$ ) or recurrent ( $n = 3$ ) aortic infection and occurred after a median of five months  
200 (IQR 1, 9), all in patients who initially had graft infections. One death was aortic/graft related,  
201 due to a ruptured anastomotic aneurysm and one death was due to aortic rupture unrelated to  
202 the graft or the infection (thoracic rupture after successful treatment of an infrarenal graft  
203 infection). Other causes of death during follow up were cardiac ( $n = 5$ ), pulmonary ( $n = 3$ ) or  
204 cerebral disease ( $n = 2$ ), cancer ( $n = 3$ ), and other ( $n = 6$ ). In 15 patients, cause of death  
205 remained unknown.

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

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

211 Ten patients (6%) had aortic (pericardial graft) re-infection after a median of 10 months  
212 (IQR 5, 22); of those, nine were patients who initially had aortic graft infection (one with an  
213 enteric fistula) and one had native aortic infection with an enteric fistula. All but one patient  
214 with graft infection had undergone complete graft prosthetic graft removal. Nine re-infections  
215 were located in the abdominal aorta and one in the ascending aorta. Six out of the 10 patients  
216 were under ongoing antimicrobial therapy when re-infection was diagnosed. Eight patients  
217 underwent aortic reoperation while one refused re-operation and one was deemed inoperable.  
218 Estimated freedom from recurrent aortic infection at one, two, three, and five years was 94%,  
219 92%, 90%, and 86% (Fig. 3).

#### 220 ***Graft complications***

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

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

233 Estimated freedom from graft complications (anastomotic aneurysm, graft limb  
234 occlusion, or anastomotic stenosis) at one, two, three, and five years was 91%, 89%, 87%, and  
235 87% (Fig. 4). No aneurysmatic or stenotic graft degeneration occurred unrelated to an  
236 anastomosis.

## 237 **DISCUSSION**

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

244 It has to be kept in mind that aortic infection is a life threatening pathology *per se*. The  
245 severity of this condition combined with the surgical trauma necessary to achieve complete  
246 graft removal and/or debridement result in a high peri-operative mortality that is not related to  
247 the graft material used for reconstruction.<sup>11</sup> Patients were included with infections of all aortic  
248 segments, including the thoracic and thoracoabdominal aorta, where open surgery is inherently  
249 considered high risk, even in the elective, non-infectious setting. Previous single centre studies  
250 with similar (anatomically mixed) patient collectives found in hospital mortalities of 32% and  
251 25%,<sup>8,12</sup> or a 30 day mortality of 17%, respectively,<sup>13</sup> comparable to the 30 day mortality of  
252 15%. As for long term mortality, comparable data are lacking, owing to the short follow up in  
253 available studies.

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

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

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

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

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

288 While previous series reported optimistically low re-infection rates of 0 – 2%,<sup>5,6,8,12,17,18</sup>  
289 this study found a re-infection rate of 6% (excluding persistent infections). This is comparable  
290 to the re-infection rates of autologous veins of 4 – 5%<sup>19,20</sup> and cryopreserved allografts of 4 –  
291 6%<sup>21,22</sup> in abdominal aortic infections. For a recently developed polyester graft coated with  
292 silver acetate and triclosan, a one year re-infection rate of 2.8% has been reported.<sup>23</sup> Another  
293 study examining the performance of a prefabricated bovine pericardial graft, the No-React non-  
294 valved conduit (Biointegral Surgical Inc., Mississauga, ON, Canada) reported a one year re-  
295 infection rate of 9%.<sup>24</sup> The extent and virulence of the initial infection (including the presence  
296 of a fistula), and the completeness of debridement probably also play a role in the development  
297 of re-infection. This again illustrates the difficulties to distinguish between persistent and  
298 recurrent infection. Although it is believed the choice of graft material for aortic reconstruction  
299 is relevant to prevent re-infection, other factors may be just as important. This includes an  
300 experienced multidisciplinary team, aggressive intra-operative debridement (balanced against  
301 the condition of the patient), the treatment of fistulas, the separation of the pericardial graft  
302 from surrounding organs, and the adequate type and duration of the antimicrobial therapy.

### 303 ***Graft complications***

304 Graft complications are a well known issue for biological grafts, in particular for cryopreserved  
305 allografts. In a meta-analysis of cryopreserved allograft reconstruction in aorto-iliac infections,  
306 anastomotic/allograft disruption was found in 5.9%, aneurysmal degeneration in 5.0%,  
307 anastomotic/pseudoaneurysm in 3.1%, and thrombotic/stenotic complications in 12.2%.<sup>4</sup> For  
308 autologous veins in abdominal aortic infections, Heinola *et al.* found a graft occlusion rate of  
309 3.6% and a graft rupture rate of 5%.<sup>3</sup> In the present study, besides two graft limb occlusions  
310 (1.2%), all graft complications were anastomotic aneurysms (4.8%) or stenoses (3%). Knowing

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

### 321 *Limitations*

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

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

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

#### 341 **Conclusion**

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

#### 348 **CONFLICT OF INTEREST**

349 None.

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

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

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

441 **Figure 4.** Cumulative Kaplan–Meier estimate of 168 patients treated with self constructed  
 442 bovine pericardial grafts showing freedom from graft complication (anastomotic aneurysm,  
 443 anastomotic stenosis, graft limb occlusion). The dotted lines represent the 95% confidential  
 444 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 ( <i>n</i> = 168)	Native aortic infections ( <i>n</i> = 38)	Graft infections ( <i>n</i> = 130)	<i>p</i> 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

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

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

450 <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.

451

**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

452 Dara are presented as *n* (%).

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

454

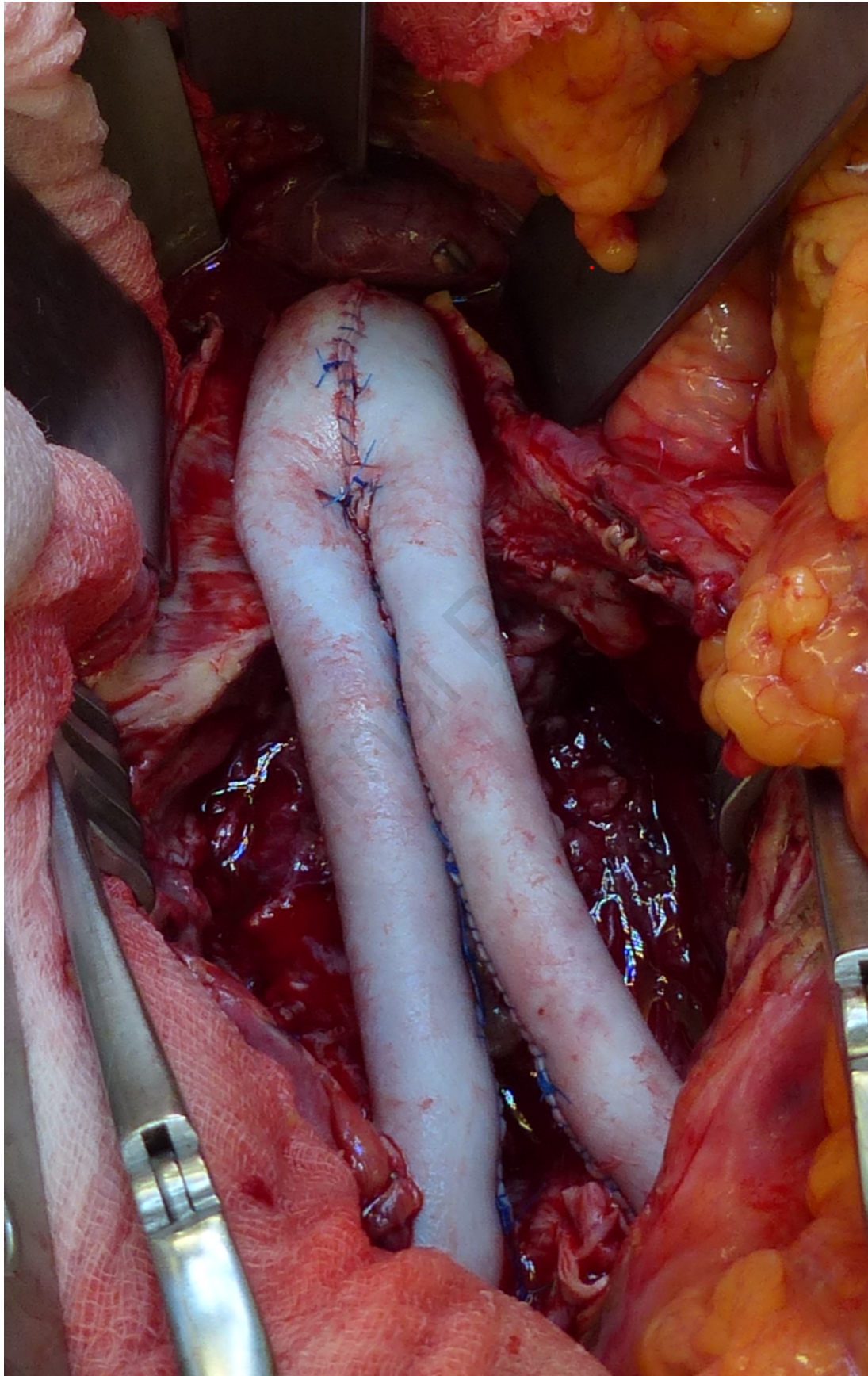
**Table 4. Post-operative outcomes of 168 patients treated with self constructed bovine pericardial grafts due to native and graft infections of the aorta.**

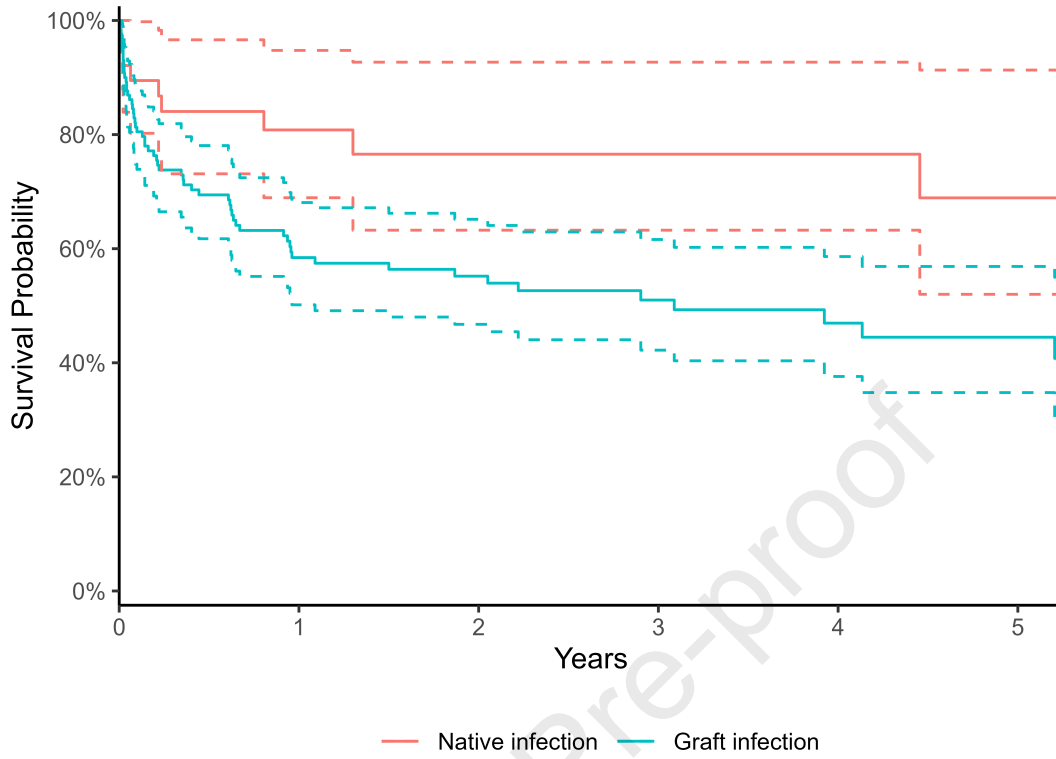
Characteristics	All ( <i>n</i> = 168)	Native aortic infections ( <i>n</i> = 38)	Graft infections ( <i>n</i> = 130)	<i>P</i> value
30 d mortality	26 (15)	4 (11)	22 (17)	.45
Length of hospital stay – d	22 (15, 41)	15 (11, 22)	28 (19, 45)	<.001
<i>Peri-operative complications</i>				
Stroke	9 (5.4)	1 (2.6)	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

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

456

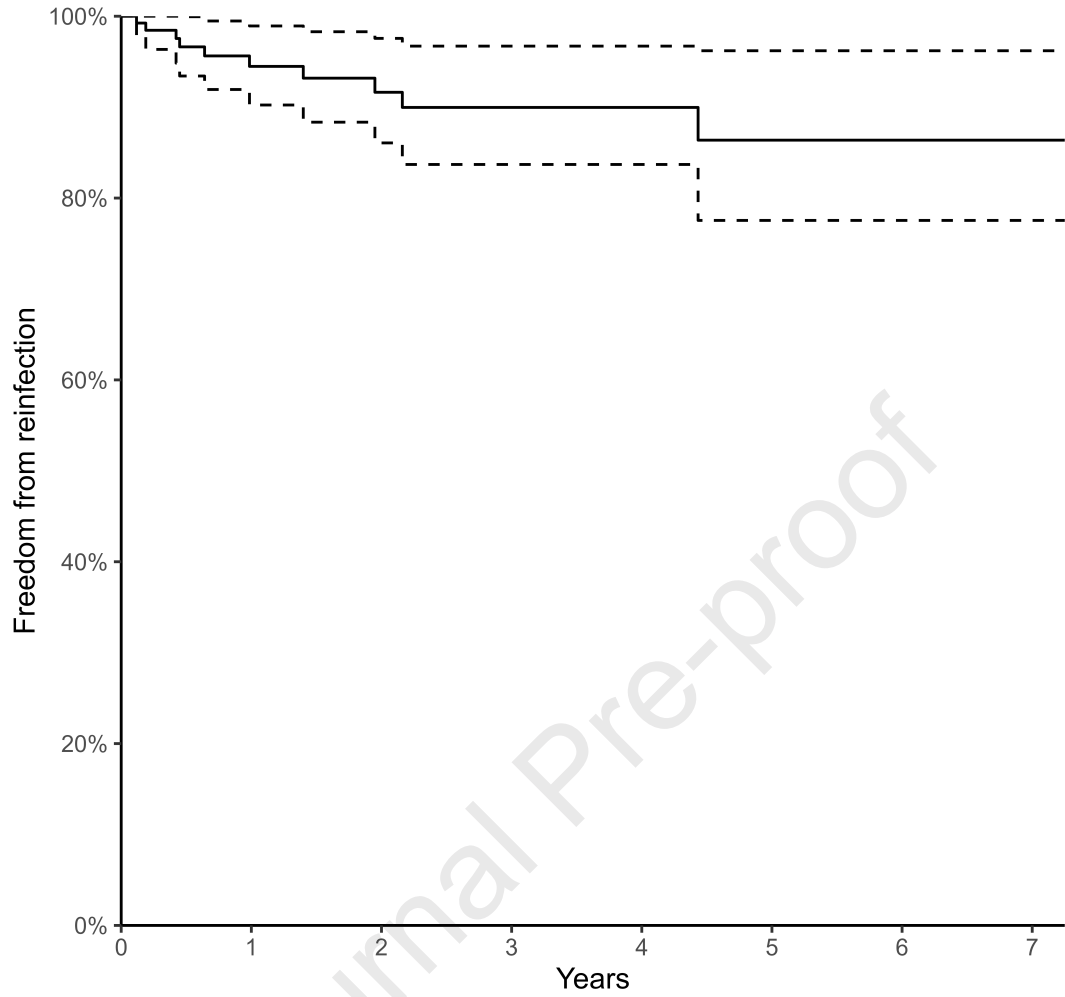




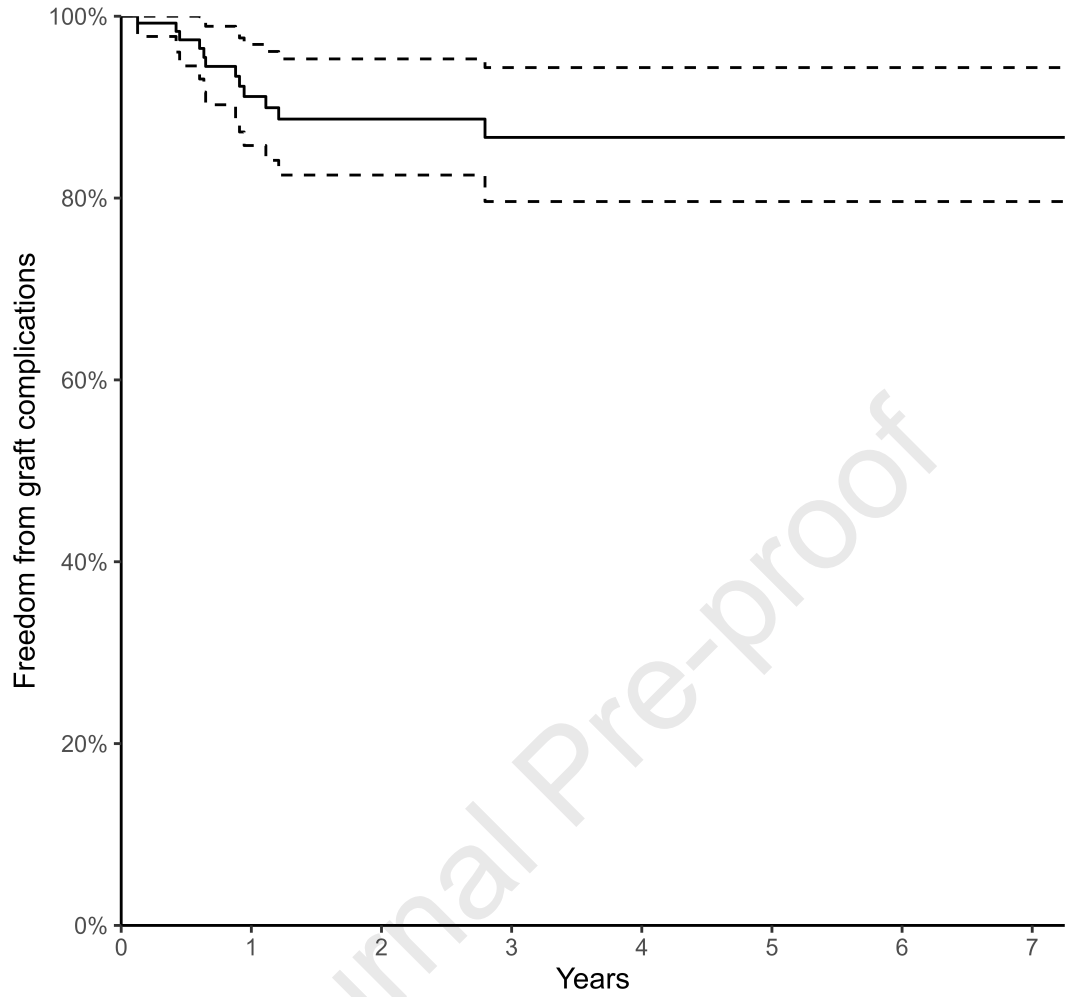


Native infection						
At Risk	38	22	17	14	10	9
Events	0	7	8	8	8	9
Graft infection						
At Risk	130	61	45	31	19	14
Events	0	50	53	56	58	59





At Risk	168	82	59	43	27	21	11	8
Events	0	6	8	9	9	10	10	10



At Risk	168	78	57	40	25	20	12	9
Events	0	9	11	12	12	12	12	12