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# Systematic review of native and graft-related aortic infection outcome managed with orthotopic xenopericardial grafts

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## ABSTRACT

**Objective:** Limited data are available on the use of xenopericardium in the treatment of native and graft-related aortic infections. The aim of this review was to assess outcomes of neo-aortic reconstruction using xenopericardium in this challenging group of patients.

**Methods:** Studies involving xenopericardial graft reconstruction to treat native and aortic graft infections were systematically searched and reviewed (Embase, Medline, and Cochrane databases) for the period of January 2007 to December 2017.

**Results:** A total of 4 studies describing 71 patients treated for aortic graft ( $n = 54$ ) and native aortic ( $n = 17$ ) infections were included; 25 patients (35%) were operated on in an acute setting. The technical success rate was 100%. The mean 30-day mortality was 25% (range, 7.7%-31%). Only one death (1.4%) was linked to the operator-made pericardial tube graft (acute postoperative bleeding from proximal anastomosis). Septic multiorgan failure was the most common cause of perioperative death (72% [13/18]). Among the 53 patients who survived, only 3 presented with recurrent infection (5.7%), so 70.4% of patients were alive after intervention without evidence of infection (50/71). During follow-up, two false aneurysms (3.7% [2/53]), one early rupture (1.4% [1/71]), and two cases (3.7% [2/53]) of late rupture were reported. Other causes of late deaths unrelated to the aortic xenopericardial repair were not reported in the different series. The early reintervention rate was 1.4% (1/71), treated by open repair for rupture. The late reintervention rate was 7.5% (4/53) with thoracic endovascular aortic repair in three patients (one false aneurysm and two ruptures) and open repair in one patient (one false aneurysm). There were no cases of early or late graft thrombosis. One-year mortality rate was 38% but only 4.2% were related to the aortic repair using orthotopic xenopericardium (one early and two late ruptures).

**Conclusions:** These data confirm the high morbidity of native and graft-related aortic infections and provide insight into the results of orthotopic xenografts as a treatment alternative. Larger series and longer follow-up will be required to compare the role of operator-made pericardial tube graft with other treatment options in infected fields.

**Keywords:** Native aortic infection; Graft aortic infection; Xenopericardial graft

Infections of both the native and grafted aorta remain challenging no matter what the location. The diagnosis is suggested after clinical examination, analysis of a blood sample for inflammatory markers, computed tomography scan, and positron emission tomography scan. Unfortunately, the rate of aortic infection treated in each institution is unknown.

The classic approach is to combine long-term antibiotics with complete excision of infected tissues and material. Today, in situ reconstruction is preferred to extra-anatomic reconstruction.<sup>1</sup> Different vascular

substitutes can be used, such as rifampicin-soaked Dacron graft, cryopreserved arterial homograft,<sup>2</sup> and autologous vein.<sup>3</sup>

Biologic grafts are considered to have resistance to infection superior to that of rifampicin-soaked Dacron grafts.<sup>4</sup> The use of autologous vein, such as superficial femoral vein, is time-consuming, thereby increasing the morbidity of the procedure in already fragile patients. Moreover, in emergent patients, evaluation of deep vein patency by duplex ultrasound can be difficult to achieve.<sup>5</sup>

Cryopreserved arterial allografts have been demonstrated, both experimentally and clinically, to offer a high degree of resistance to infection. Their disadvantage is that of unpredictable availability and possible degenerative change.<sup>6</sup>

The use of xenopericardium as a vascular substitute is widespread in cardiac surgery.<sup>7</sup> Equine or bovine pericardium can achieve good results in an infected field.<sup>8</sup> As a consequence of the experience acquired from cardiac surgery, with good results in infected fields, excellent long-term outcomes in replacement of the ascending aorta, and easy availability, reconstruction of the infected

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aorta with operator-made tube grafts of xenopericardium has been proposed by various surgical teams.<sup>9-12</sup>

The aim of this study was to provide a systematic review of the literature detailing the feasibility and the outcomes of self-made pericardial tube grafts and patches used in the treatment of both native and graft aortic infections.

## METHODS

**Search strategy.** The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A literature search was performed to identify all published studies within the past 10 years reporting the use of self-made pericardial tube graft to treat native and graft-related infections. Candidate studies were sought through a computerized search of the Embase, Medline, and Cochrane databases for the period of January 2007 to December 2017. Keywords entered in this search were “pericardial” or “pericardium” and “aortic graft infection” or “graft infection.” Articles were limited to those published in the English language. An additional manual evaluation of the reference lists of the retrieved articles and reviews was also performed.

**Study selection.** Studies reporting in situ reconstruction of native or aortic graft infection with the use of an operator-made xenopericardial graft, detailing clinical outcomes and follow-up, were considered for inclusion. Papers containing duplicate data were excluded by selecting the study with the most recent or the best documented material for use in the analysis.

**Data extraction.** Data were extracted on patients’ demographics and comorbidities. Case details included localization of infection, operative details, type of reconstruction, additional visceral reconstruction, technical success, perioperative mortality, freedom from reinfection, freedom from reintervention, and patency.

## RESULTS

### Search results

Four studies were integrated after the literature search (Table I).<sup>9-12</sup>

### Case selection

A total of 4 studies describing 71 patients treated for infected aortic grafts (n = 54) and native aortic infections (n = 17) were included. Patients’ demographic characteristics, presenting features, and comorbidities are shown in Tables I and II. The mean age was 70 years (range, 38-84), and 83% of the patients were male. The most common comorbidity was hypertension (92%). Reconstructions were reported for the ascending aorta and aortic arch in 14 patients (20%), descending thoracic aorta in 18 patients (25%), thoracoabdominal aorta in 8 patients (11%), and infrarenal aorta in 31 patients (43%).

When aortic reconstruction involved the ascending aorta and the aortic arch, cardiopulmonary bypass and hypothermic circulatory arrest were performed. Left-sided heart bypass was used when the reconstruction involved the descending thoracic aorta.

Additional surgical reconstruction was needed in the same sitting for five tracheobronchial fistulas (7%), five duodenal fistulas (7%), and eight esophageal fistulas (11%).

**Technical success.** All authors reported that the preparation of the xenopericardial vessel substitute was synchronous with the main operative dissection. The pericardial sheet was trimmed to form an appropriately sized tube with a running 4-0 polypropylene suture (Ethicon, Summerville, NJ). Preparation of the neoaorta is usually rapidly performed on a back table by a surgeon with one assistant; 69 (97%) were bovine pericardium sheets and 2 (2.8%) were equine pericardium sheets. The exact size and shape of the neoaorta are designed on the basis of the patient’s anatomy and the anticipated reconstruction configuration. For flexibility, some authors reported knotting the running suture every 2 to 7 cm, thereby allowing the use of a shorter reconstruction, by trimming the graft, if the intraoperative findings were less extensive than anticipated. Bifurcated grafts were constructed in a similar manner. One author<sup>11</sup> fashioned a fenestration in the rolled pericardial sheet to reimplant a branch if required. The graft configuration did not influence outcome. There were 60 (84%) self-made tubes implanted, and 9 (12%) self-made bifurcated tubes or tubes with at least one branch were implanted. Two patients with infected endovascular aneurysm repairs were treated by simple patch reconstruction of the ventral aorta and common iliac because the residual native vessel was thought to be sufficiently strong and not significantly damaged by the infective process. One patient with an infected aortobifemoral bypass, implanted because of aortoiliac occlusive disease and severe claudication, underwent explantation. It was possible to establish flow in the native vessels by thromboendarterectomy, and a patch was used to reconstruct the site of the previous proximal anastomosis. A second patient with a mycotic aneurysm due to a pancreatic fistula underwent débridement of inflammatory aortic wall tissue with reconstruction with a pericardial patch. Technical success rate was 100%. Antibiotic therapy was initially empirical, then guided by sensitivities. No consensus regarding the duration of antimicrobial therapy was evident in the synthesized papers.

**Perioperative mortality.** The overall 30-day mortality was 25.4% (18/71). Only one death was directly linked to the xenopericardial tube with acute postoperative bleeding from the proximal anastomosis 3 weeks after implantation (5.5% [1/18]) without overt signs of infection based on findings during intraoperative exploration. The most common cause of postoperative death was sepsis-related multiorgan failure (72% [13/18]).



**Table I.** Studies reporting the use of orthotopic xenopericardial grafts to manage native or graft-related aortic infection

Study	Year	No.	Study type	Follow-up, months	Age, years	Sex	Native infection	Prosthetic infection
Weiss et al <sup>9</sup>	2017	35	Retrospective	48 (26-74)	69 (38-84)	30 M/5 F	12	23
Kubota et al <sup>11</sup>	2015	8	Retrospective	31 (13-61)	70 (55-80)	6 M/2 F	4	4
Czerny et al <sup>12</sup>	2011	15	Prospective	24 (5-85)	72 (62-82)	13 M/2 F	0	15
Lutz et al <sup>10</sup>	2017	13	Retrospective	9 (1-27)	70 (53-84)	10 M/3 F	1	12
Values are reported as mean (range).								

One patient died of excessive bleeding after deep hypothermia and prolonged cardiopulmonary bypass time after descending aorta replacement for infected thoracic endovascular aortic repair (TEVAR) with aorto-esophageal fistula (5.5% [1/18]). Three patients died of respiratory failure (16% [3/18]). Death within 30 days occurred in 3 of 14 ascending aorta or aortic arch, 5 of 18 descending aorta, 5 of 8 thoracoabdominal aorta, and 5 of 31 abdominal aorta reconstructions.

With regard to the reconstruction of patients with a graft fistula, Czerny et al<sup>12</sup> reported two cases of duodenal fistula, two cases of bronchial fistula, and two cases of esophageal fistula. One of the patients with bronchial reconstruction died postoperatively during the first 30 days. Kubota et al<sup>11</sup> reported two cases of esophageal fistula, with one early death. Lutz et al<sup>10</sup> did not report any early deaths among the four patients with enteric fistula and three with cutaneous fistula. Weiss et al<sup>9</sup> did not discuss the rate of postoperative complication in patients with and without fistula. No graft complications were associated with the presence of a concomitant fistula.

Only two authors reported perioperative morbidity. Weiss et al<sup>9</sup> reported renal failure leading to dialysis in 26%, heart failure in 9%, and pneumonia in 14% of patients. Lutz et al<sup>10</sup> reported renal failure leading to filtration in 30% (4/13) of patients, although only one individual required permanent dialysis (7.7%). In critical care, 38.5% (5/13) of patients had extended periods of ventilation.

**Micro-organisms from intraoperative sample.** *Staphylococcus aureus* was found in 20 patients (28%), enterococcus in 15%, and gram-negative bacteria in 25%, with *Escherichia coli* in 14%. Fungi were identified in 15%. Cultures were negative in 13% of patients.

Unfortunately, Weiss et al<sup>9</sup> did not report mortality by type of microorganism. Three other studies reported seven early deaths. Cultures were negative in three patients. In the remaining four patients, *Haemophilus influenzae*, *Salmonella* sp, methicillin-resistant *S. aureus*, and oral *Bacillus* were cultured.

**Follow-up.** The mean follow-up was 28 months (1-74 months). Follow-up was complete for all the patients in each study except for one, who was lost to follow-up after 3 years.

**Table II.** Patients' comorbidities

Study	Weiss <sup>9</sup>	Kubota <sup>11</sup>	Czerny <sup>12</sup>	Lutz <sup>10</sup>
Hypertension	34 (97)	NA	13 (87)	11 (85)
Smoking	24 (69)	NA	NA	7 (53)
Dyslipidemia	24 (69)	NA	NA	7 (53)
Ischemic heart disease	NA	NA	3 (20)	6 (46)
COPD	10 (29)	NA	5 (33)	5 (38)
Renal impairment	9 (26)	NA	7 (47)	4 (30)
Diabetes	9 (26)	NA	3 (20)	5 (38)
ASA score				
1	NA	NA	NA	0
2	NA	NA	NA	2 (15)
3	NA	NA	NA	3 (23)
4	29 (83)	NA	NA	7 (53)
ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; NA, not applicable. Values are reported as number (%).				

One early rupture occurred 3 weeks after graft implantation, leading to the death of the patient after thoracoabdominal reconstruction. This rupture was the only case of orthotopic xenopericardial graft-related 30-day mortality among the 71 patients operated on (1.4%). During the follow-up, among the 53 patients who survived, two other ruptures occurred at 4 and 7 months after implantation. Both led to the death of the patient even after endovascular exclusion (3.7% late rupture). The first rupture was localized to the left iliac limb pericardial reconstruction and the second to a reimplanted renal artery, both after abdominal aortic reconstruction. Both these ruptures were associated with infection. Two false aneurysms (3.7%) were reported. A false aneurysm of the proximal anastomosis and of the suture line forming the pericardial tube was treated by TEVAR. There was no evidence of local infection recurrence and no antibiotic treatment was required. The second patient had a false aneurysm of the native vessel caused by pancreatitis, treated by open repair with a new pericardial patch. The author reported that after only 3 months, the original pericardial graft was well incorporated at the time of revision surgery.

There were no cases of early or late graft thrombosis with no readmissions for occlusion.



One-year mortality rate was 38%, but only 4.2% (3/71) was linked to the pericardial patch (one early rupture treated by open repair and two late ruptures treated by endovascular aneurysm repair). During the follow up, three patients died of respiratory complications, one patient died of digestive complication (stomach roll), and two patients died of lung cancer.

**Reintervention rate.** The early reintervention rate was 1.4% (1/71), treatment by open repair for rupture. The late reintervention rate was 7.5% (4/53) with TEVAR in three patients (one false aneurysm and two ruptures) and open repair in one patient (one false aneurysm).

Whereas there was one false aneurysm associated with a reimplanted renal artery, there were no reported complications, such as false aneurysm, occlusion, stenosis, or rupture, in those with bifurcated or branched grafts.

**Freedom from reinfection.** Among the 53 patients who survived, 3 patients (5.6%) suffered from a recurrent infection, leading to the death of two of them by rupture at 4 and 7 months after implantation of the self-made tube graft. Except for those three patients, all others who survived to the first postoperative month were considered healed of infection (94%).

## DISCUSSION

The standard procedure for treating aortic graft and native aortic infections is complete removal of the infected graft or infected aortic aneurysm, extensive débridement, and in situ replacement with a Dacron graft, rifampicin-soaked Dacron graft, or cryopreserved homograft combined with antibiotic treatment. Whereas extra-anatomic grafts were state of the art some decades ago, in situ reconstruction, with its superior patency, is clearly favored today. Extra-anatomic bypass grafting for infected infrarenal abdominal aneurysm resection has a similar long-term survival rate and should be considered in patients who are unsuitable for in situ graft revascularization with heavy comorbidities such as cardiac or respiratory failure; however, the late postoperative complication rate is higher.<sup>13</sup>

The most suitable graft material for reconstructing infected aorta remains a matter of controversy. Cryopreserved arterial allograft is the most common vascular substitute<sup>2,8</sup>; autologous femoral vein or rifampicin-soaked Dacron grafts are also used.

Although the cryopreserved arterial homograft is an excellent material for the treatment of infected aortas, supply is inadequate, and it can be difficult to obtain in sufficient time for an urgent operation.<sup>6,14</sup> Cryopreserved or fresh allografts are also prone to rupture of the graft body as well as anastomotic dehiscence and bleeding and therefore need urgent revision in one-third of patients. Kieffer et al<sup>2</sup> reported 22% 30-day mortality (39/179) in their series of in situ reconstruction with arterial allograft.<sup>2</sup> Touma et al<sup>6</sup> reported 28% 30-day mortality (7% graft related) in 52 cases of abdominal aorta

infection and 2 cases of thoracic aorta infection.<sup>8</sup> In addition, no grafts used have demonstrated complete resistance to reinfection.<sup>6</sup> Furthermore, depending on the type of reconstruction, the preparation of the allograft on the back table with oversewing of all collaterals and anastomosis of all required branches can be arduous.

Silver-coated or silver-impregnated grafts are easy to use and readily available but have not demonstrated the desired resistance to infection.<sup>15</sup> Subsequently, patients have considerable reinfection rates (20%) with the incumbent risk of secondary rupture.

The use of autologous deep femoral vein graft is associated with good result with regard to prevention of reinfection. The diameter mismatch between the deep vein and aorta, morbidity, and time-consuming nature of harvest are problematic.<sup>7</sup> Furthermore, this approach is suitable only for reconstruction of the infrarenal segment of the aorta.

In this systematic review, treatment of native or graft-related infections of the thoracic, thoracoabdominal, and abdominal aorta by complete removal of the infected material or tissue, extensive débridement, and orthotopic vascular reconstruction using xenopericardial grafts as neoaortic segments achieved encouraging results regarding durability and freedom from reinfection and reoperation. In this review, 30-day mortality was 25.4%, with only one death directly linked to a rupture of the reconstruction (1.4%). The reported cases include patients with infection of all aortic segments, including those requiring hypothermic circulatory arrest and cardiopulmonary bypass (20%) and left-sided heart bypass (25%). These procedures increase the mortality in patients already vulnerable because of both infection and comorbidities.

During the mean follow-up of 28 months, the reinfection rate was just 5.6% (3 patients among the 53 who survived the initial operation). The resistance to infection of pericardial patches is well established from cardiac surgery, with 80% freedom from reinfection at 5 years.<sup>4</sup> With no cases of early and late graft thrombosis, patency appears to be superior to that of allograft, with a 5% to 9% occlusion rate in published series.<sup>14,15</sup>

The early and late complication rates associated with pericardial grafts were 1.4% and 7.5%, whereas the arterial cryopreserved allograft literature suggests an early graft-related complication rate of 19% to 26%.<sup>14,16</sup> Another advantage of customized xenopericardial tissue is the availability, which is a problem with homografts. Accumulation of clinical cases and confirmation of the long-term durability of xenopericardial branched grafts may demonstrate their advantages as an option for the treatment for infected aortic aneurysms.

This review has several limitations. The pooled results are weakened because of lack of standardization in reporting of patient-specific data and end points.

Furthermore, we specifically focused the review on clinical outcomes. Unfortunately, we were not able to clearly compare the mortality in patients with and without aortoenteric or aortobronchial fistulas to determine the prognostic significance of the organism involved. Finally, some small studies were included, whereas a larger number of patients are needed to better understand the outcomes of this approach.

CONCLUSIONS

In this systematic review, data confirm the high morbidity of native and graft-related aortic infections and provide insight into the results of orthotopic xenografts as a treatment alternative by complete removal of the infected prosthetic material or of the infected aorta, extensive débridement, and orthotopic vascular reconstruction, with encouraging results regarding durability and freedom from reinfection and reoperation. Although this review included four retrospective studies and one prospective study, the small number of patients can lead to biases, such as selection bias. Long-term follow-up and controlled trials to eliminate bias, such as selection, are needed to compare the results with cryopreserved arterial allografts; this procedure can be considered a good option to treat these critical patients.

AUTHOR CONTRIBUTIONS

Conception and design: AH, BO, PA, LC  
Analysis and interpretation: AH, JS, LC  
Data collection: AH, LS, PA, LC  
Writing the article: AH, BO, LC  
Critical revision of the article: AH, JS, LS, PA, LC  
Final approval of the article: AH, BO, JS, LS, PA, LC  
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