

The use of bovine pericardium for the treatment of aortic infection

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Abstract:

Introduction: Aortic graft infection is a rare yet devastating complication of aortic surgery, for the treatment of which several in situ and extraanatomic surgical options have been proposed. The aim of our study was to collect and meta-analyze all studies reporting on the safety and efficacy of bovine pericardium for the treatment of both native and aortic graft infection.

Methods: We used the PRISMA guidelines as a guide for this meta-analysis. Medical literature was searched until the end of 2021. The outcomes studied were the early and late all-cause mortality, graft-related complications, primary patency, and reinfection-free rate.

Results: Fifteen studies reporting on 290 patients were included in the meta-analysis. Pooled early all-cause mortality was estimated at 14.5% (95%CI: 9.1-20.7%), while late all-cause mortality was 33.5% (95%CI: 26.1-41.2). Graft-related complications occurred in 11.8% (95%CI: 3.9-22.3). Primary patency at the end of follow-up was as high as 99% (95%CI: 97-100), whereas reinfection-free rate was 98.6% (95%CI: 95.3-100).

Conclusion: The use of bovine pericardium for the treatment of both native and prosthetic graft infection is safe and effective, with low graft-related complications and acceptable mortality.

Key words: bovine, patch, pericardium, infection, aorta

Although infectious aortic disease is uncommon, it has been associated with high mortality and morbidity rates. These figures are expected to further increase due to both aging population and increase in the number of aortic operations performed among the elderly¹. Currently, there is still an ongoing debate regarding the best surgical treatment strategy for the patients who are diagnosed with aortic infection. Standard and well-described surgical operations include surgical resection, debridement and in-situ graft replacement or extra-anatomical bypass. Rifampicin-soaked Dacron grafts and cryopreserved arterial homografts have been also used with various reported results in the literature².

Biologic grafts have been reported as more resistant to infection, compared to rifampicin-soaked Dacron grafts. Among these, the use of bovine pericardial grafts has been sporadically reported in the literature with various conflicting results. The

aim of our study was to collect and meta-analyze all relevant published literature on the safety and efficacy of bovine pericardium for the treatment of both native and aortic graft infection.

MATERIALS AND METHODS

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines as a guide for this meta-analysis. The medical literature databases which were systematically searched were MEDLINE, Scopus, Embase, Google Scholar, Ovid, and the Cochrane Library. We also applied a snowball process in the reference lists of the eligible articles in order to perform a more extensive search among the initially eligible studies. We used Medical Subject Headings, including the terms “bovine”, “patch” “pericardium”, “infection”. We included all studies, without gender or language restriction, published up to the end of 2021. Our focus was on studies evaluating the safety and effectiveness of bovine pericardium after aortic infection. Two authors independently extracted and analyzed the data and in case of conflict, the final decision was reached after discussion with a third reviewer. Among the eligible studies we extracted data concerning the first author’s name, study year, country of origin, total number of patients and other relevant information. We also extracted the number of patients with the outcomes of interest. The outcomes studied were the early and late all-cause mortality, graft-related complications, primary patency, and the reinfection-free rate.

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The outcome rates were estimated for each study and reported as the proportion of patients with the corresponding outcome among all patients treated with bovine pericardium for aortic infection. All values of the studied outcomes were subsequently appropriately calculated, expressed as proportions and 95% confidence intervals (CIs), and thereafter transformed into quantities according to the Freeman-Tukey variant of the arcsine square root transformed proportion. The pooled effect estimates were calculated as the back-transformation of the weighted mean of the transformed proportions, using Der Simonian-Laird weights of random-effects model and expressed as percentage proportions. Heterogeneity was expressed as I^2 and a formal statistical test for heterogeneity using the I^2 test was performed. We used Stata statistical software version 14 (StataCorp LP, College Station, Tex) for the analyses.

RESULTS

The initial search revealed 837 studies. Among them and after screening of the titles and abstracts, 15 studies (Table) were finally deemed eligible for inclusion in the meta-analysis¹⁻¹⁵. The studies included a total of 290 patients. All but one study¹⁵ were retrospective in design. The largest study included 48 patients¹⁴, while the oldest study was published in 2011 by Czerny et al.¹⁵. Our meta-analysis showed that native aortic infection occurred in 29.2% (95%CI: 11.4 - 50.5; Figure 1) of the patients among the eligible studies, compared to 70.8% (95%CI: 49.51-88.60; Figure 2) who were treated for previous graft infection.

Among the studies outcomes, the pooled early all-cause mortality was estimated at 14.5% (95%CI: 9.1-20.7%; Figure 3). The pooled late all-cause mortality was 33.5% (95%CI: 26.1-41.2; Figure 4). The graft-related complications were calculated with a pooled rate of 11.8% (95%CI: 3.9-22.3, Figure 5). Primary patency at the end of follow-up was high at 99% (95%CI: 97-100, Figure 6). Finally, pooling of the data from the eligible studies for reinfection-free rate at the end of follow-up derived a rate of 98.6% (95%CI: 95.3-100; Figure 7).

DISCUSSION

Our meta-analysis has shown excellent results concerning the use of bovine pericardium for the treatment of native and prosthetic graft aortic infection. More specifically, we estimated patency of 99% and reinfection free rate of 98% during follow-up. Early mortality was acceptable at 14%, while it doubled at 33% at the end of follow-up. However, it represented all-cause mortality, while graft related mortality was not possible to be accurately estimated. Our study has also shown low rates of graft-related complications, providing strong evidence for the use of pericardium in aortic infections.

The selection of an ideal vascular conduit for an aortic infection has always been a field of controversy. Variables such as resistance to reinfection, early or late complications, cost and availability must be considered before making a decision. The use of cryopreserved arterial allografts, rifampicin-soaked dacron grafts or the reconstruction of a neo-aortoiliac system

Table 1. Eligible studies characteristics

Study	Year	No	Study type	Follow-up (months)	Age (years)	Male/Female	Native infection	Prosthetic infection	Early mortality	Late mortality	Patency	Reinfection-free rate	Complication rate
Weiss et al	2017	35	Retrospective	48 (26-74)	69 (38-84)	30/5	12/35	23/35	11/35	17/35	35/35	35/35	9/35
Kubota et al	2015	6	Retrospective	31 (13-61)	70 (55-80)		2/6	4/6	2/6	2/6	6/6	6/6	2/6
Czerny et al	2011	15	Prospective	24 (5-85)	72 (62-82)	13/2	0	15	4/15	5/15	15/15	15/15	
Lutz et al	2016	11	Retrospective	9 (1-27)	70 (53-84)	9/2	1/11	10/11	1/11	6/11	11/11	9/11	2/11
Almasi et al	2020	19	Retrospective	6 (1-47)	70 (56-84)	16/3	0	19	10.5	32	89%	100%	53
Kreibich et al	2021	45	Retrospective	11 (2,26)	65 (54-74)	35/15	9/45	36/45	7/45	16/45		44/45	3/45
Zientara et al	2016	2	Retrospective	11.74	54 (37+71)		1/2	1/2	0/2	0/2	2/2	1/2	1/2
McMillan et al	2012	48	Retrospective	25 (3-48)						17		98%	
Anibueze et al	2017	6	Retrospective	13 (2-23)	69,5 (67-75)		4	2	0		6/6	6/6	0/6
Belkorissat et al	2020	12	Retrospective	12 (3-70)	68	9/3	12/12	0/12	2/12	2/12	12/12	12/12	6/12
Heinola et al	2018	12	Retrospective	26					5	29		100%	
Burghuber et al	2021	21	Retrospective	21.6 (6-34.6)	63 (55-71)	16/5	8/21	13/21	2/21	5/21	20/21	19/21	4/21
Gagnon et al	2020	31	Retrospective		69 (46-88)	22/9	16	15	3/31		29/31	28/31	
Terlecki et al	2019	6	Retrospective	9 (3-32)	67 (60-78)	5/1	0	6	0/6	2/6	6/6	5/6	2/6
Alonso et al	2021	21	Retrospective	14 (1-26)	69 (57-84)	20/1	4	17	1/21	4/21	20/21	20/21	4/21

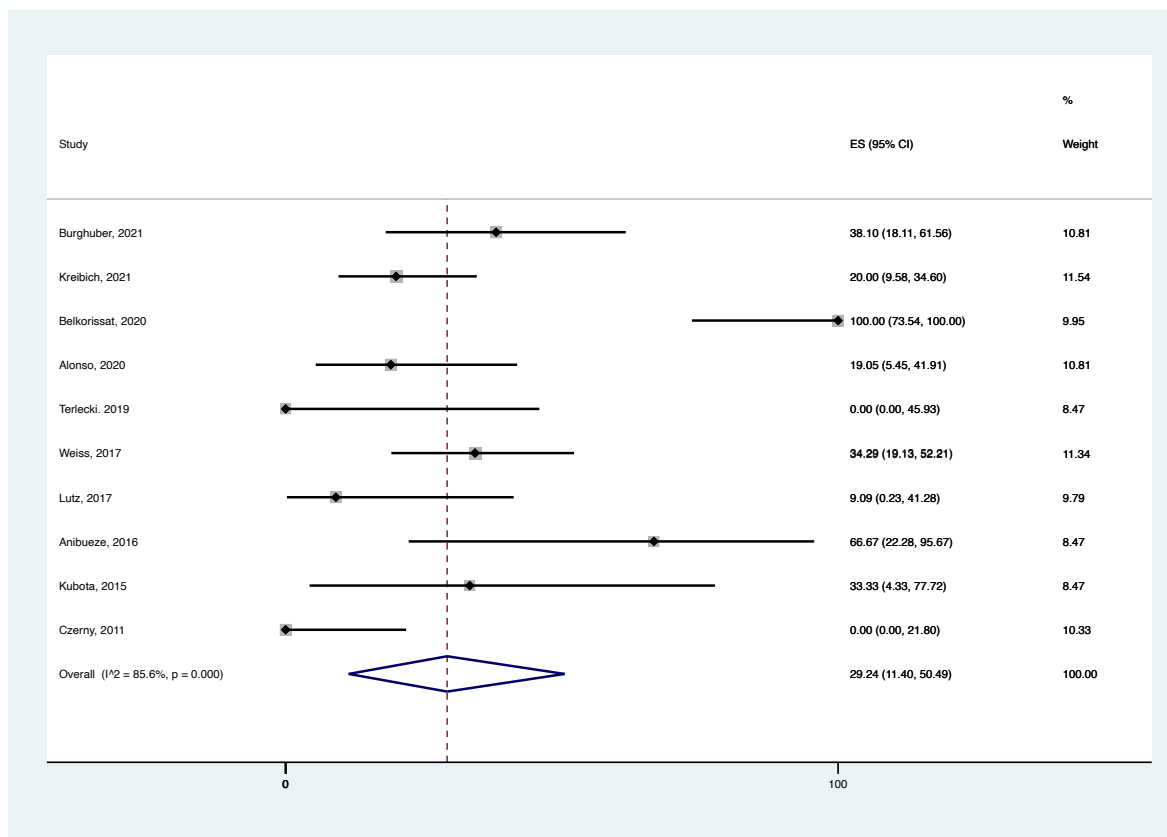


Figure 1.

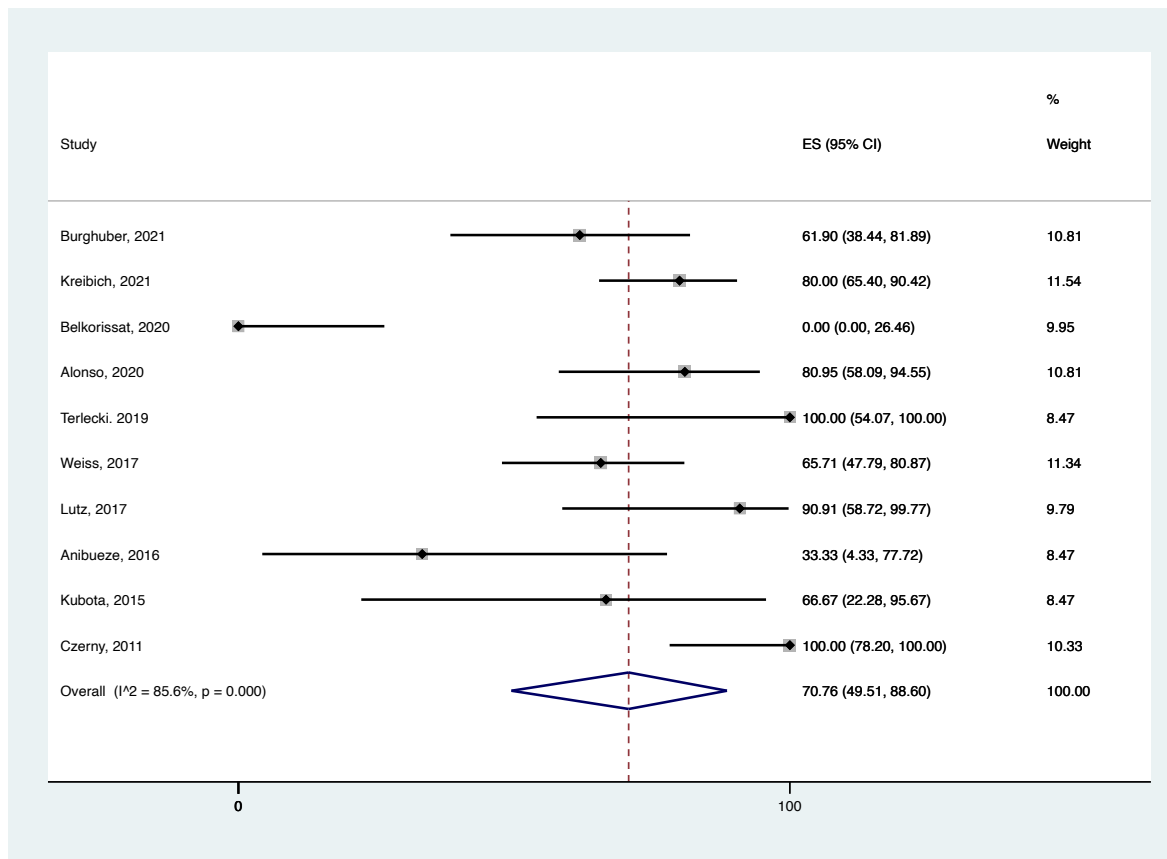


Figure 2.

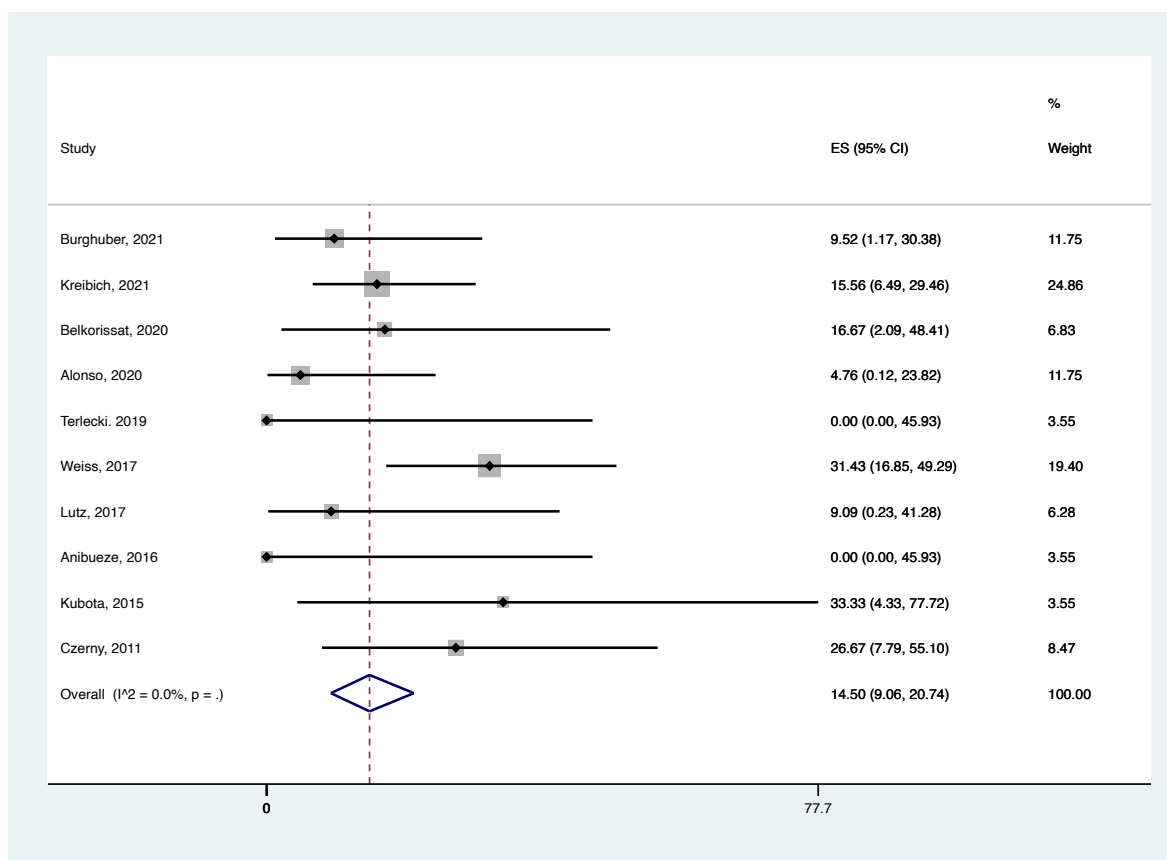


Figure 3.

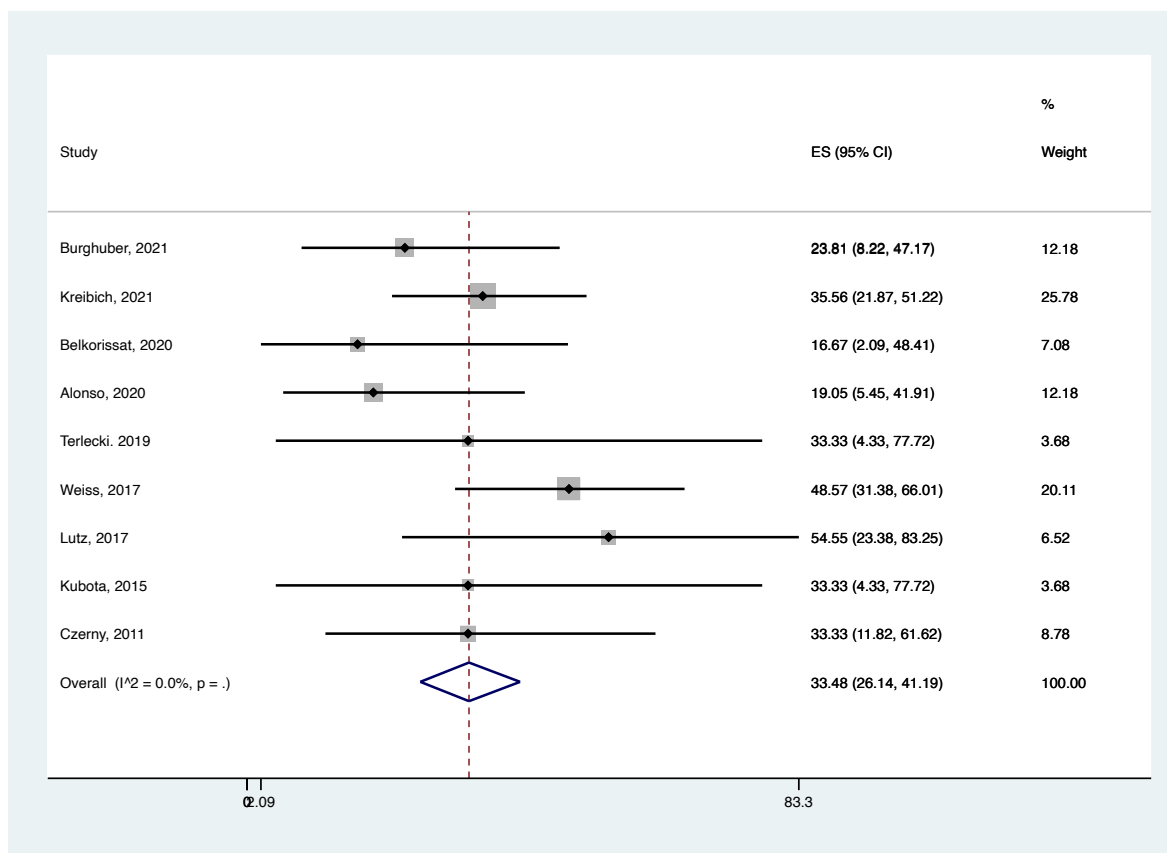


Figure 4.

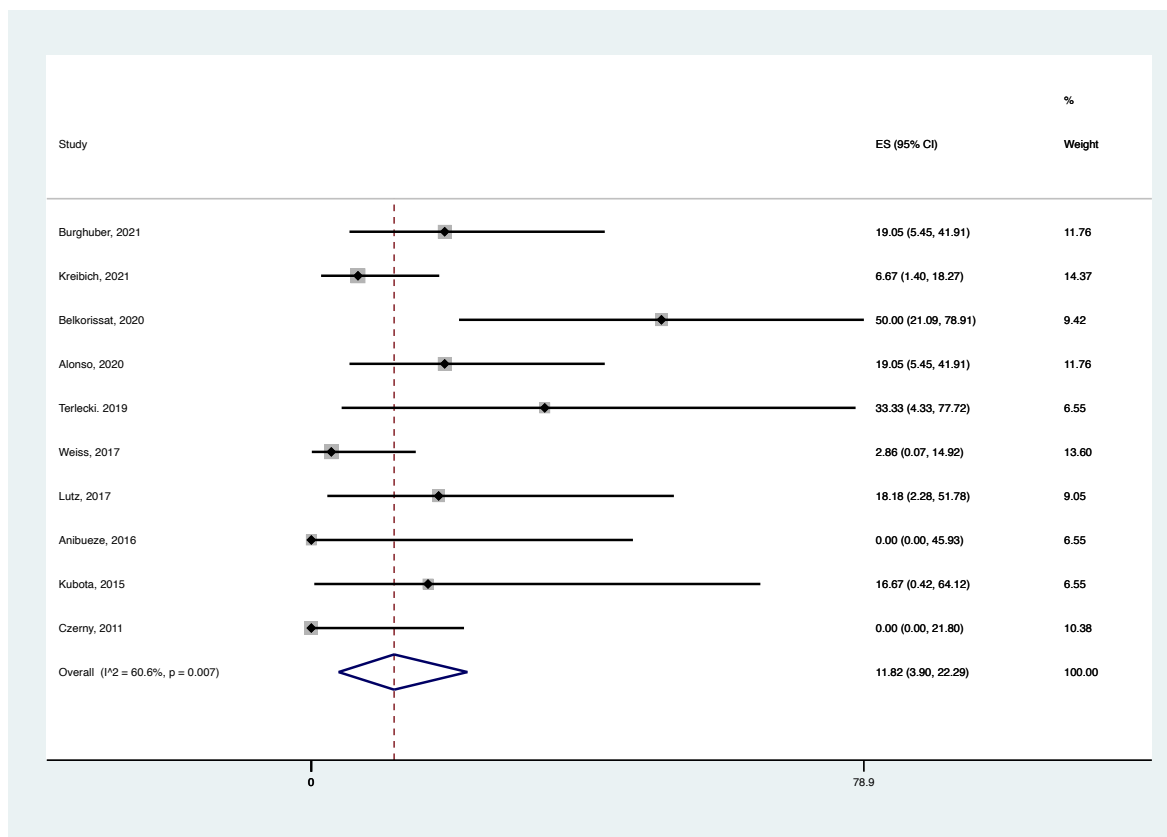


Figure 5.

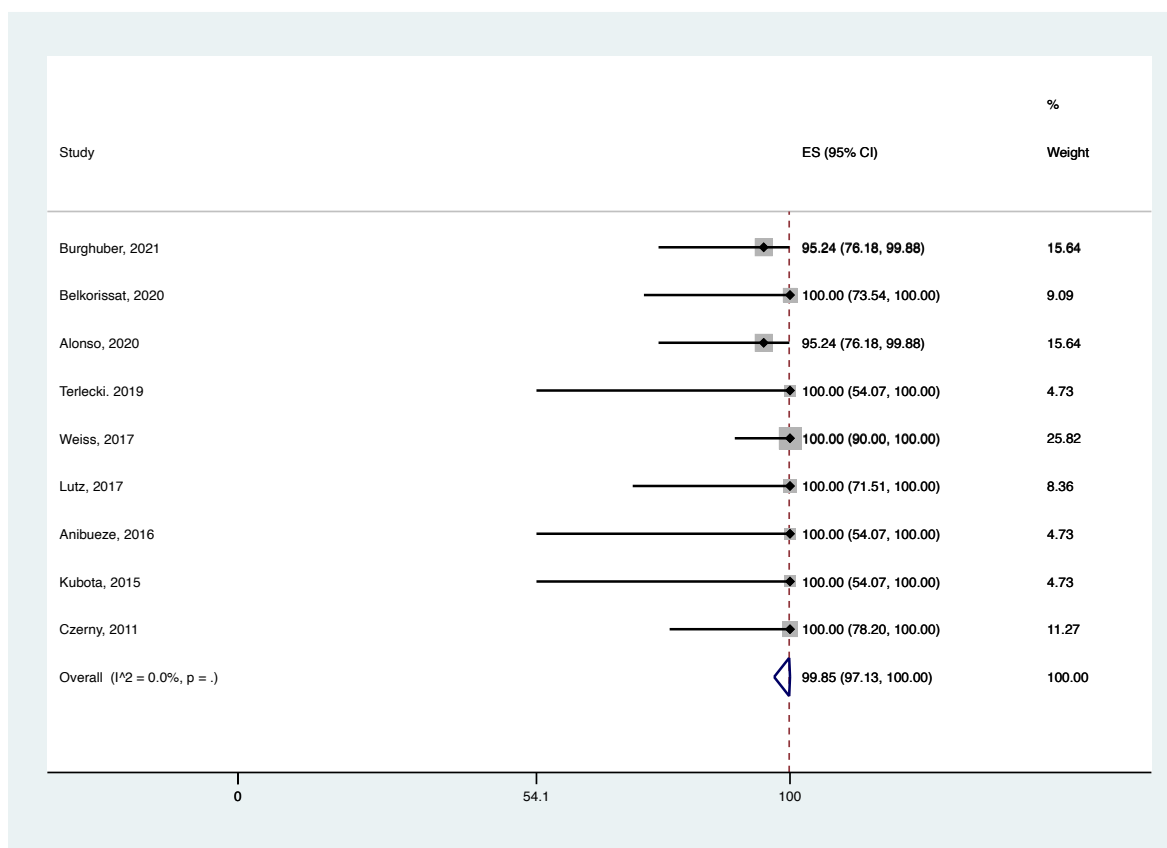


Figure 6.

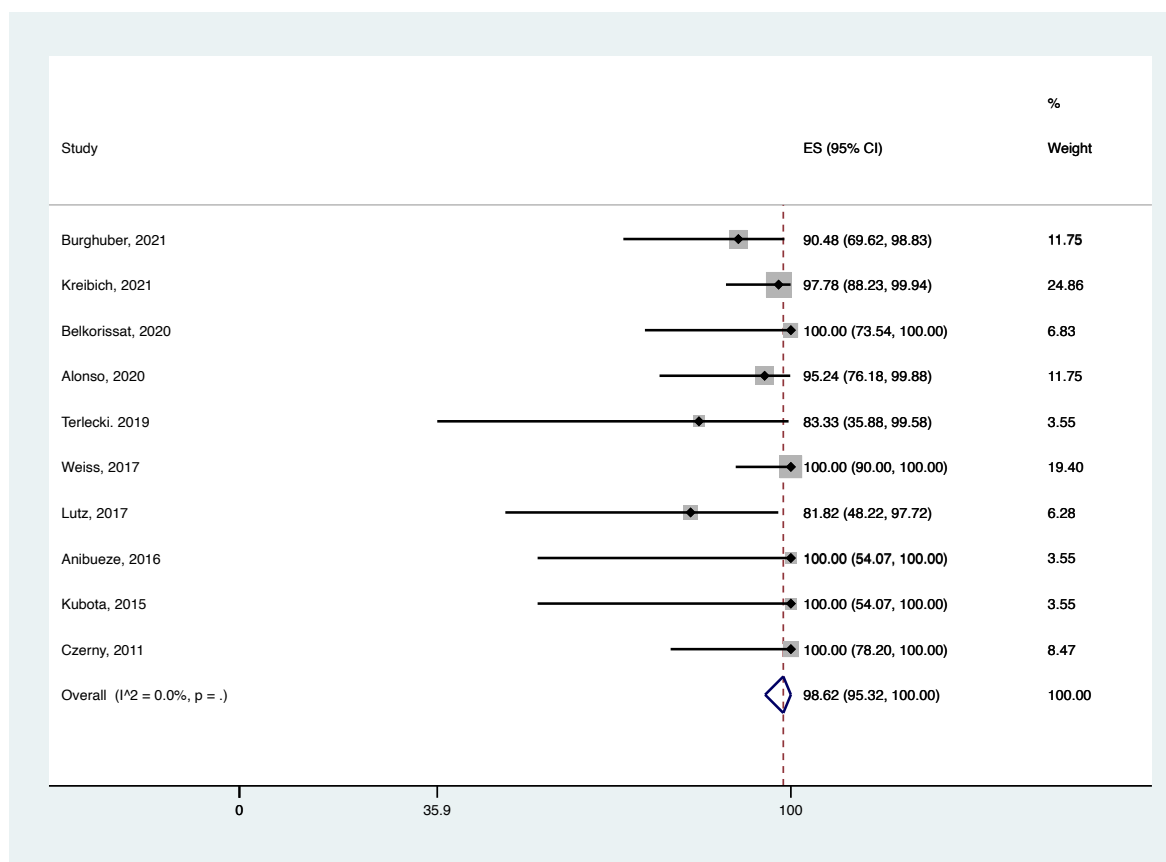


Figure 7.

with autologous deep femoral veins are all viable options when it comes to in situ aortic reconstruction and there is always the option for an aortic stamp combined with an extra-anatomical bypass. In addition, experience with these multiple choices varies from one department to another as these procedures are somewhat uncommon and are usually combined with relatively high early mortality.

The ability of bovine pericardium to effectively resist infection has already been established as it is routinely used as an arterial patch. In the present study, the encouraging 98.62% re-infection free rate confirms that it is at the very least not inferior to its alternatives options. In a meta-analysis that was performed in 2019, Antonopoulos et al¹⁶ found arterial allografts to have a 3.32% reinfection rate, while another study by Batt et al¹⁷ found rifampicin or silver coated grafts to have a reinfection rate of 11%, while extra-anatomic bypasses with standard PTFE grafts had the worst results with reinfection rates being as high as 20%¹⁷. This is the reason why it would be sensible to offer this kind of treatment only to older patients, as age is the most important factor influencing early mortality in these cases¹⁸. In any case, these high recurrent infection numbers combined with high early and late mortality rates, underline the importance of prolonged use of post-operative antibiotic therapy with values ranging from 2 weeks after surgery to lifelong suppression therapy. Inflammatory biomarkers, diagnostic imaging or clinical signs of persisting infection all have to be taken into account before deciding to discontinue antibiotic treatment.

Bovine pericardium as an aortic graft also had a very high 99.85% late patency rate. Kieffer et al, in a series with 179 patients found arterial allografts to also having a high patency rate, reporting only 4 thrombotic events, but a high number of 42 occlusive lesions in late follow-up¹⁹. Autogenous vein and silver-coated dacron grafts also seem to be consistently patent grafts, with patency rates of 2% and 7% respectively¹⁷. Axillofemoral bypass still seems to be the option with the highest risk for thrombosis reporting a five-year patency of 83.6%²⁰. Graft-related complications, such as ruptures, bleeding from the anastomosis site, creation of pseudoaneurysms were found to be at 11.82% at the present study, which is a relatively good number considering the high mortality rates for patients with aortic graft or native aortic infections.

When comparing side by side conduits for in situ reconstruction of the aorta, self-made grafts made from bovine pericardial patches seem to have some promising characteristics. Even though arterial allografts are resistant to infections, they are expensive, they have limited availability and they often do have some late restenosis-occlusion cases leading to reinterventions. Rifampicin and silver coated dacron grafts on the other hand make the in-situ reconstruction simpler reducing surgery time and as a result early mortality is sufficiently low 11%¹⁷ comparing to the 14.5% found for bovine grafts in this study. Their main drawback nevertheless is high reinfection rate that can lead to potentially fatal complications such as aorto-enteric fistula or sepsis. The main disadvantage of autogenous femoral veins used for in situ reconstruction of the

aorta mostly come from the vein harvesting, as it is considerably time consuming, making for a longer procedure overall. Another potential issue with this technique is the possible complications such as venous morbidity post-surgery, deep venous thrombosis or persistent leg edema. Less, but still considerable amount of time is also needed for the construction of the aortic graft from the bovine patches, if it's not prefabricated as an aortic graft.

The main limitation of this meta-analysis is the low number of studies included. From these studies not all cases were included because we only analyzed data for aortic reconstruction and not just bovine pericardial use. The self-made bovine pericardium aortic graft still is not a widely used conduit, hence the low number of studies exploring it. Another potential issue with this study is the fact that there is some heterogeneity and as these procedures are very volume and experience dependent, there is always the chance for publication bias that could well affect our already small sample.

CONCLUSION

The use of bovine pericardium for the treatment of both native and prosthetic graft infection is safe and effective, with low graft-related complications and acceptable mortality. However, larger studies with unselected patient populations are needed before sound conclusions can be drawn.

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