Comparing Venous Reconstructions and Antimicrobial Graft Reconstructions in Mycotic Abdominal Aortic Aneurysms and Aortic Graft Infections

Ipema, Jetty; Schreve, Michiel A.; van de Mortel, Rob H. W.; de Vries, Jean-Paul P. M.; Unlu, Cagdas

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Comparing Venous Reconstructions and Antimicrobial Graft Reconstructions in Mycotic Abdominal Aortic Aneurysms and Aortic Graft Infections

Jetty Ipema,[1,2] Michiel A. Schreve,[1] Rob H.W. van de Mortel,[2] Jean-Paul P.M. de Vries,[3] and Çağdaş Ünlü,[1] Alkmaar, Nieuwegein, and Groningen, The Netherlands

Background: The perioperative mortality and morbidity rates of surgical repair of mycotic abdominal aortic aneurysms and aortic graft infections are high, and the appropriate treatment is debated. This retrospective study compared venous and antimicrobial prosthetic aortic graft reconstructions.

Methods: All patients of the Northwest Clinics and St. Antonius Hospital who were treated for mycotic abdominal aortic aneurysms or aortic graft infections between January 1, 2008, and January 1, 2018, were analyzed. Exclusion criterion was treatment other than venous or antimicrobial reconstructions. Primary end points were 30-day complications and mortality rates and 3-year overall survival. Secondary end points were reintervention-free survival, persistent infection and reinfection rates, and hospital length of stay.

Results: Fifty-one patients met the inclusion criteria, of whom 32 underwent venous reconstructions and 19 antimicrobial prosthetic aortic graft reconstructions. Baseline characteristics did not differ significantly between these groups, except for duration of surgical repair, which was longer in the venous group. The 30-day and 1-year mortality rates, reinfection rates, complication rates, and hospital length of stay did not significantly differ between the groups. The 3-year overall survival was 77% for venous reconstruction compared with 66% for antimicrobial reconstruction ($P = 0.781$). The 30-day reintervention rate was 19% for the venous group compared with 42% for the prosthetic group ($P = 0.071$). Reintervention-free survival at 3 years was 46% for the venous group compared with 52% for the prosthetic group ($P = 0.615$).

Conclusions: Venous reconstruction tends to have better 3-year overall survival and lower 30-day reintervention rates compared with antimicrobial prosthetic graft reconstruction in patients with mycotic abdominal aortic aneurysms or abdominal aortic graft infections. In the acute setting, antimicrobial prosthetic graft reconstruction is a valuable solution due to the shorter operation time and similar 30-day mortality and complication rates.

INTRODUCTION

Although the incidence of aortic graft infections is low, varying between 0.6% and 3%, perioperative mortality and morbidity rates are high, 30 to 60% and 40 to 60%, respectively.[1] Conservative treatment with antibiotics is associated with higher mortality rates compared with surgery and is

[1]*Department of Vascular Surgery, Alkmaar, The Netherlands.*

[2]*Department of Vascular Surgery, St. Antonius Hospital Nieuwegein, Nieuwegein, The Netherlands.*

[3]*Division of Vascular Surgery, Department of Surgery, University Medical Center Groningen, Groningen, The Netherlands.*

Correspondence to: Jetty Ipema, Departmant of Surgery, Northwest Clinics Alkmaar, Wilhelminalaan 12, 1815 JD Alkmaar, the Netherlands; E-mail: j.ipema@nwz.nl

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usually reserved only for patients with severe comorbidity.[1,2] Different surgical treatment options for in situ reconstruction are the use of venous autografts, cryopreserved allografts, or synthetic grafts. Synthetic grafts can be uncoated or coated with rifampicin, silver, or a combination of silver and triclosan (Intergard-Synergy, Maquet, Gothenburg, Sweden). Previous studies showed different results in outcomes of these treatment modalities.[3,4] Rifampicin-coated grafts were introduced after good results on *Staphylococcus* strains in canine models.[5,6] In vitro research of silver and triclosan grafts seemed promising, but no clinical studies have been published.[7]

Besides aortic graft infections, mycotic abdominal aortic aneurysms, defined as infected aneurysms based on radiologic imaging, perioperative findings, and positive blood or tissue cultures, are also rare and associated with high morbidity.[8] They often exist in patients with severe comorbidity. Surgical treatment has the advantage of infection control, but perioperative morbidity and mortality rates are high.[9]

Despite the variety of treatment options, the best method for the treatment of aortic graft infections and mycotic abdominal aortic aneurysms remains unclear. In this study, we compared venous reconstruction with antimicrobial prosthetic reconstruction, consisting of grafts with silver and triclosan coating and rifampicin-coated grafts. Primary study end points were 30-day complications, 30-day mortality rates, and 3-year survival rates. Secondary objectives were reintervention-free survival, persistent infection or reinfection rate, and hospital length of stay.

MATERIALS AND METHODS

Study Population

All patients treated for aortic graft infection or mycotic aortic aneurysm from January 1, 2008, until January 1, 2018, in the Northwest Clinics Alkmaar and St. Antonius Hospital, Nieuwegein, were analyzed. Aortic graft infection was defined as a combination of clinical, radiological, and laboratory findings, according to the definition of the Management of Aortic Graft Infection Collaboration.[10] Mycotic abdominal aortic aneurysm was diagnosed based on clinical evidence of infection (fever, localized pain, leukocytosis, and elevated C-reactive protein levels), characteristic imaging (aortic diameter at least 150% of normal, saccular aneurysm, para-aortic soft tissue infiltration, and/or adjacent accumulation of blood, fluid, or gas), and intraoperative findings of periaortic inflammation or purulence.[11–13] Although [^{18F}]fluoro-2-deoxy-2-D-glucose positron emission tomography/computed tomography seems to be favorable to diagnose vascular graft infections, this was only performed when results of other radiologic modalities were doubtful.[14]

Inclusion criteria were aortic graft infection or mycotic abdominal aortic aneurysm treated with superficial femoral vein reconstruction (venous group) or reconstruction with silver and triclosan or rifampicin-coated grafts (prosthetic group). Exclusion criteria were other types of surgical or nonsurgical treatment modalities, such as debridement or conservative treatment.

Study Data

Data collected were demographic characteristics, procedure information, hospital and intensive care length of stay, additional tests, and medication use. Also collected was information about the end points, including mortality, reinfection or persistent infection, reinterventions, complications, and hospital length of stay. Reinfection or persistent infection was defined according to the definition of the Management of Aortic Graft Infection Collaboration for aortic graft infection, occurring at any moment after the initial treatment for the infection. Readmission was defined as new hospital admission within 30 days after discharge. Reintervention included every treatment-related and infection-related intervention at any moment after treatment for the aortic graft infection or mycotic aortic aneurysm; for example, correction of incisional hernia, percutaneous transluminal angioplasty for graft occlusion, or abscess drainage.

Study Procedures

All patients underwent treatment according to the standard of care. Clinical standard treatment in the Northwest Clinics was venous reconstruction by using the superficial femoral vein. The deep femoral vein was left intact to prevent postoperative complications such as deep venous thrombosis and leg complaints. Harvesting of the vein was performed before, simultaneously, or after abdominal exposure, but at least during the same procedure, depending on the certainty of the diagnosis preprocedural and the number of vascular surgeons present at the operation. Different treatment options were used in the St. Antonius Hospital according to the individual patient and preference of the surgeon. Prosthetic reconstruction was always accompanied by omental coverage. Because this was a retrospective study, no procedures or tests were required in addition to those that were

performed as standard of care. The study did not fall under the Medical Research Involving Human Subjects Act as accorded by the Medical research Ethics Committees United.

Periprocedural Medications and Follow-Up

Both institutions did not have general antibiotic guidelines for these diseases. Antibiotic treatment differed between the individual patients and was adapted to the result in case of positive bacteria cultures in consultation with the microbiologist. Commonly used antibiotics in different combinations were benzylpenicillin, amoxicillin, cefuroxime, ceftazidime, meropenem, vancomycin, metronidazole, ciprofloxacin, and clindamycin. The duration differed from a few weeks to lifelong. In many cases, the exact duration and type of antibiotics administered could not be traced.

All patients received lifelong aspirin 80 mg daily or carbasalate calcium 100 mg daily, unless there was an indication for another type of antiplatelet or anticoagulation therapy. During hospitalization, all patients received thrombosis prophylaxis with low molecular weight heparin adapted to the patients' weight.

Annual outpatient visit with duplex scan was performed up to 3 years after the operation and thereafter biannually in the Northwest Clinics. In the St. Antonius Hospital, outpatient visit was performed 6 weeks after discharge without standard additional examination. In case of the continuation of antibiotic treatment after discharge, outpatient visits took place more frequently with control of infection parameters until antibiotics were discontinued. No routine examination was performed for deep venous thrombosis, only in case of complaints.

Statistical Analysis

The different variables of baseline characteristics and data at presentation of treatment between the venous group and prosthetic group were compared. Continuous variables are expressed as means with the standard deviation if normally distributed and were compared using the Student's *t*-test, as appropriate. Categorical variables are expressed as medians with interquartile ranges and were compared using the Fisher's exact test, χ^2 test, or Mann-Whitney *U* test, as appropriate. Multivariate logistic regression was performed to assess the factors for mortality and secondary outcomes. Baseline characteristics were analyzed in univariate analysis. Variables with a univariate $P < 0.1$ and variables of known clinical importance were entered in a multivariate regression model. The Kaplan-Meier analysis was performed for survival and reintervention-free survival analyses. Statistical significance was defined as $P < 0.05$. Statistical analysis was performed using SPSS 20.0 software (IBM, Armonk, NY, USA).

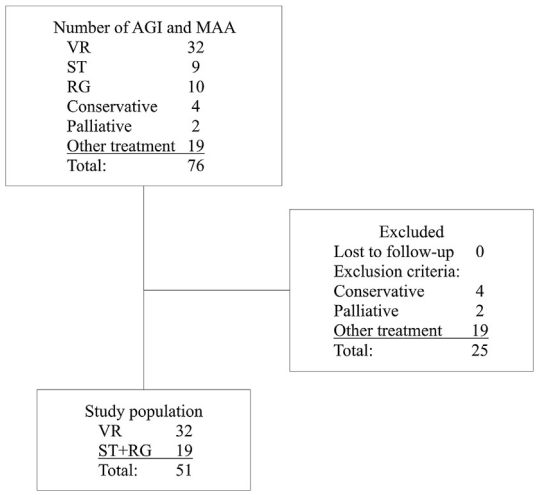

Fig. 1. Study population. AGI, aortic graft infection; MAA, mycotic aortic aneurysm; RG, rifampicin-coated graft; ST, silver and triclosan-coated graft; VR, venous reconstruction.

RESULTS

Study Population

Between January 1, 2008, and January 1, 2018, a total of 76 patients presented to the Northwest Clinics Alkmaar and St. Antonius Hospital Nieuwegein with a mycotic abdominal aortic aneurysm or aortic graft infection. No patients were lost to follow-up. Venous reconstruction was performed in 32 patients, 9 underwent reconstruction with silver and triclosan graft (Intergard-Synergy), 10 underwent reconstruction with rifampicin-coated graft (Gelsoft, Vascutek, Renfrewshire, Scotland, United Kingdom), 19 underwent other treatment (4 debridement of the aorta without explantation of the endograft, 3 with biological graft reconstruction, 11 with standard prosthetic graft, and 1 with endograft reconstruction), 3 were treated conservatively with antibiotics, 1 with abscess drainage, and 2 in a palliative setting. Fifty-one patients met the inclusion criteria (Fig. 1). The 32 patients in the venous group were of a median age of 70 years and comprised 20 men (63%). The prosthetic group also was a median age of 70 years and comprised 15 men (79%). Both groups were comparable, and basic characteristics

Table I. Baseline characteristics of the 51 patients

Characteristic[a]	Total ($n = 51$)	Venous group ($n = 32$)	Prosthetic group ($n = 19$)	P value[b]
Male sex	35 (69)	20 (63)	15 (79)	0.221
Age, median (IQR), years	70 (11)	70 (12)	70 (7)	0.696
Smoking status	($n = 42$)	($n = 26$)	($n = 16$)	0.234
Never	6 (14)	2 (8)	4 (25)	
Former	15 (36)	11 (42)	4 (25)	
Current	21 (50)	13 (50)	8 (50)	
Diabetes mellitus	13 (26)	10 (31)	3 (16)	0.323[c]
COPD	10 (20)	5 (16)	5 (26)	0.470[c]
Hypertension	29 (57)	21 (66)	8 (42)	0.101
Hyperlipidemia	13 (26)	11 (34)	2 (11)	0.096[c]
Other cardiovascular disease	19 (37)	12 (38)	7 (37)	0.963
ASA class				0.146
I	1 (2)	0 (0)	1 (5)	
II	25 (49)	19 (59)	6 (32)	
III	24 (47)	13 (41)	11 (58)	
IV	1 (2)	0 (0)	1 (5)	
ASA				0.120
I + II	26 (51)	19 (59)	7 (37)	
III + IV	25 (49)	13 (41)	12 (63)	
Type of infection (mycotic of total mycotic + AGI)	12 (24)	6 (19)	6 (32)	0.325[c]
Duration of surgical repair, median (IQR), minutes	248 (154)	305 (132)	200 (60)	**0.001**
Rupture[d]	5 (10)	2 (6)	3 (16)	0.348[c]
Leukocyte count, median (IQR), $\times 10^9$/L	($n = 43$) 13.4 (7.6)	($n = 25$) 13.8 (9.1)	($n = 18$) 13.1 (4.7)	0.961
CRP, median (IQR), mg/L	($n = 41$) 130 (196)	($n = 24$) 79 (178)	($n = 17$) 162 (159)	0.177

AGI, aortic graft infection; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; IQR, interquartile range.
[a]Data are presented as number (%), unless stated otherwise.
[b]Significant ($P < 0.05$) data are highlighted in bold.
[c]The Fisher's exact test was used.
[d]Rupture before surgical treatment of the aortic graft infection or mycotic aortic abdominal aneurysm.

showed no significant differences except for duration of surgical repair ($P = 0.001$), as summarized in Table I. Nine patients underwent positron emission tomography-computed tomography scans, in addition to the conventional computed tomography scans, because of uncertainty about the diagnosis. In all cases, the results confirmed the suspicion of infection. 31 of 51 patients (61%) had positive tissue and/or blood cultures. In the group of patients with positive cultures, mortality, complications, and reinterventions were higher compared with the group with negative cultures, but there were no statistical differences.

Primary End Points

Treatment-associated 30-day and 1-year mortality rates were not significantly different between the venous group and prosthetic group ($P = 1.000$). Multivariate analysis was performed, including age, American Society of Anesthesiologists Physical Status Classification, and duration of surgical repair, and was also not significantly different for treatment-related 30-day mortality ($P = 0.155$) and for treatment-related 1-year mortality ($P = 0.143$). Treatment-related mortality included 6 patients who died within 1 year postoperatively. Four patients of the venous group died. Three patients died within 30 days postoperatively, one of sepsis and multiorgan failure and 2 of intestinal ischemia. One patient died of asystole, presumably based on abdominal sepsis, 125 days postoperatively. Two patients with silver and triclosan grafts died of sepsis within 30 days postoperatively. One of these patients had a ruptured aneurysm before the surgical repair.

Mean follow-up was 1,180 days (standard deviation, 1,099 days). The Kaplan-Meier survival analysis

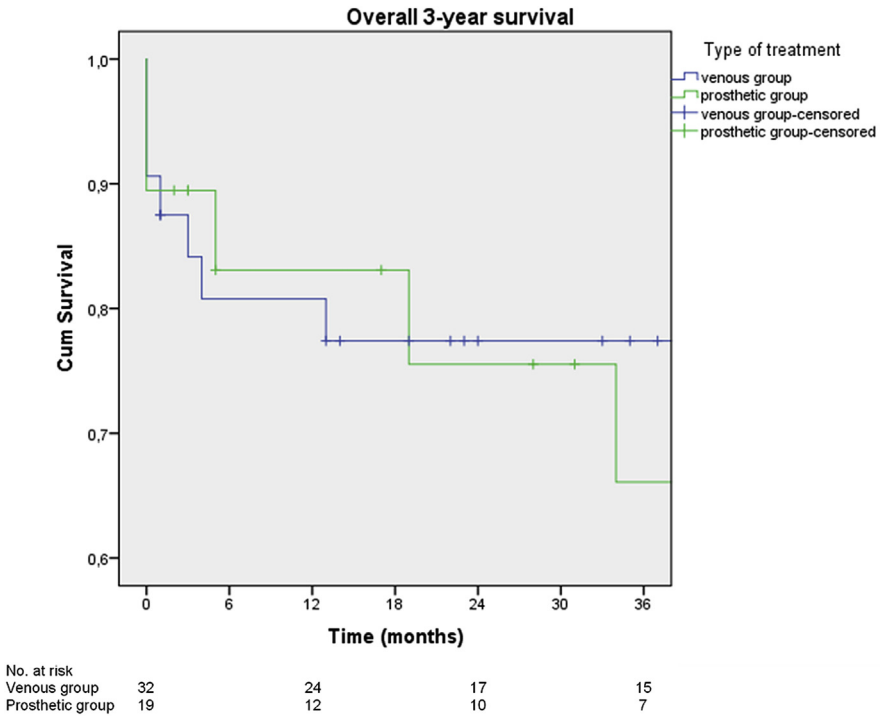

Fig. 2. Kaplan-Meier curves demonstrating survival.

showed significant differences for neither overall mortality ($P = 0.781$) nor for treatment-related mortality ($P = 0.846$). The overall survival rate after 3 years was 77% for the venous group compared with 66% for the prosthetic group (Fig. 2).

The 30-day complication rates were high, at 66% for the venous group and 58% for the prosthetic group, but this was not significant in univariate ($P = 0.581$) and multivariate ($P = 0.660$) analyses (Table II). There was one case of deep venous thrombosis, in the venous group, which was treated conservatively with a Vitamin K antagonist (Acenocoumarol) as per institutional protocol.

Secondary End Points

No significant differences were found for reinfection/persistent infection, readmission within 30 days, reintervention, hospital length of stay, and complications between venous reconstruction and antimicrobial reconstruction in univariate and multivariate analyses when corrected for age, American Society of Anesthesiologists class, and duration of surgical repair (Table II).

Only one of the patients with reinfection or persistent infection died of the infection. No difference in reinfection or persistent infection rate was observed based on bacterial species. All patients with reinfection or persistent infection suffered from different bacterial species.

Reintervention within 30 days was 19% for the venous group and 42% for the prosthetic group ($P = 0.071$). The Kaplan-Meier analysis of reintervention-free survival within 30 days was 81% in the venous group versus 58% in the prosthetic group and within 3 years was 46% vs. 52% ($P = 0.615$; Fig. 3).

Three of the 5 patients (60%) with a rupture before surgical repair underwent reintervention within 30 days. One of these was treated with venous reconstruction and 2 with prosthetic reconstruction. Reasons for reintervention were blowout of the proximal anastomosis, limb amputation, and recurrent mycotic inguinal bleeding.

DISCUSSION

Venous reconstruction and antimicrobial synthetic graft reconstruction in 51 patients with mycotic abdominal aortic aneurysms or aortic graft infections were compared in this study. When interpreting data, the present study shows no significant differences in 30-day complication and mortality rates. Baseline data are equal, except for longer operation time for the venous group. However, a closer look at the results shows the venous group had lower 30-day reintervention rates and tends

Table II. Secondary end points of the 51 patients

End point[a]	Total ($n = 51$)	Venous group ($n = 32$)	Antimicrobial group ($n = 19$)	*P* value univariate analysis	*P* value multivariate analysis
Reinfection or persistent infection	5 (10)	4 (13)	1 (5)	0.639[b]	0.997
Readmission	5 (10)	4 (13)	1 (5)	0.639[b]	0.246
Reintervention	25 (49)	15 (47)	10 (53)	0.691	0.735
Hospital length of stay, median (IQR), days	($n = 49$) 17 (13)	20 (18)	($n = 17$) 16 (11)	0.991	0.338
Complications[c]					
<30 days	32 (63)	21 (66)	11 (58)	0.581	0.660
>30 days	10 (20)	7 (22)	3 (16)	0.725[b]	0.175
Pneumonia	6 (12)	2 (6)	4 (21)	0.179[b]	0.148
Kidney failure	6 (12)	5 (16)	1 (5)	0.392[b]	0.317
Cardiac events	7 (14)	4 (13)	3 (16)	1.000[b]	0.692
Intestinal ischemia	2 (4)	2 (6)	0 (0)	0.523[b]	0.999
Limb amputation	3 (6)	2 (6)	1 (5)	1.000[b]	0.463
Ileus/gastroparesis	6 (12)	5 (16)	1 (5)	0.392[b]	0.306
Incisional hernia	5 (10)	4 (13)	1 (5)	0.639[b]	0.278
Deep venous thrombosis	1 (0)	1 (0)	0 (0)	1.000[b]	0.997
Bleeding[d]	8 (16)	6 (19)	2 (11)	0.694[b]	0.315
Wound infection	4 (8)	2 (6)	2 (11)	0.623[b]	0.630
Other infection	6 (12)	4 (13)	2 (11)	1.000[b]	0.711
Other type of complication	16 (31)	9 (28)	7 (37)	0.517	0.258

IQR, interquartile range.
[a]Data are presented as number (%), unless stated otherwise.
[b]The Fisher's exact test was used.
[c]Number of patients with complication, excluding reinfection, readmission, reintervention, and mortality.
[d]Sources of bleeding: at the level of the crus, inguinal (2), thigh, unknown source; evacuation of abdominal hematoma (2), unknown source; hemoglobin decrease and melena (1), unknown source; hemoglobin decrease and hypotension (1).

to have better 3-year overall survival. The 30-day reintervention rate for the venous group is 2 times lower compared with prosthetic treatment, and this might explain the differences in mortality.

A comparison of our results against the venous reconstruction literature showed similar outcomes, with a freedom from reintervention rates at 5 years of 91%.[15] The advantage of the prosthetic group is the shorter operation time, although this did not affect the outcomes in multivariate analysis. Prosthetic reconstruction might therefore be preferable in acute settings and it can be performed directly, whereas venous reconstruction is often performed as a staged procedure.

Treatment-related mortality seems to be similar between the venous and prosthetic group, which is supported by the literature.[3] Overall, the results of the present study suggest that the risk of dying as a result of treatment-related causes is very unlikely after 4 months (125 days) with the treatment methods used in this study. A 2018 study by Heinola et al.[16] showed treatment-related mortality in 5 of 56 patients (9%) treated with biological grafts for mycotic abdominal aortic aneurysms, of which the last treatment-related death was also after 4 months (120 days) in a patient with venous reconstruction. A 2018 study by Schaefers et al.[17] showed 30-day mortality was 0% for infected conventional grafts in 26 patients with rifampicin-coated graft reconstruction, which also corresponds to our results. Another study showed no late mortality (>30 days) for rifampicin-coated grafts.[18] We showed that silver and triclosan grafts also seem to have low late mortality rates.

Although treatment-related mortality seems comparable, the venous group tends to have better overall survival at 3 years postoperatively; namely, 77% vs. 66% for the prosthetic group, although this was not significant. Smeds et al.[19] showed the same tendency for reconstruction of infected endografts. The 3-year survival rates for venous reconstruction in our cohort are in line with studies of Heinola et al.[20] (±78%) and Ali et al.[21] (63.8%).

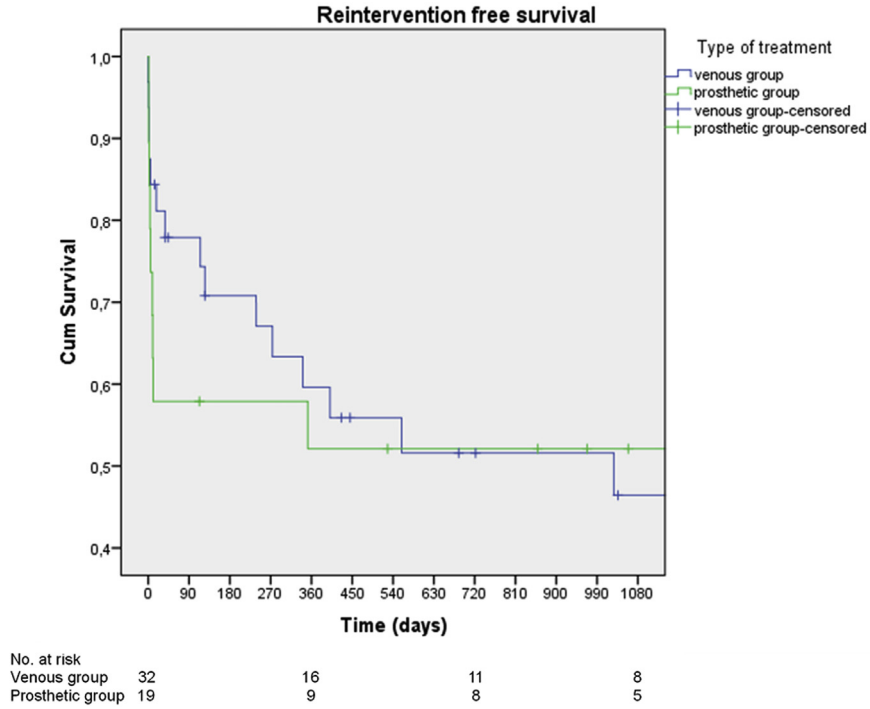

Fig. 3. Kaplan-Meier curves demonstrating reintervention-free survival.

A striking finding in this study is that limb amputation was low in both groups. Amputation rates reported in the literature vary considerably, but up to 40% is described, depending on the illness of the patients and the occurrence of graft occlusion.[3,22] Except for this, both for venous reconstruction and prosthetic graft reconstruction, reintervention and complication rates in our study were very high. Two patients with pneumonia stayed temporarily on the intensive care unit. Bleeding was a reason for reintervention in 6 of 8 patients. The foregoing shows that the treatment of mycotic aortic aneurysms and aortic graft infections still remains challenging because of high morbidity rates, especially within 30 days postoperatively.

The strength of this study is that it is the first including this number of patients with silver- and triclosan-coated grafts and comparing this with venous reconstruction. It brings new insights in the complex treatment of mycotic abdominal aortic aneurysms and aortic graft infections.

This study has some limitations. First, because this was a retrospective study, patients were obviously not randomized. However, baseline characteristics did not significantly differ between the groups, except for duration of operation, which would also differ in a randomized trial.

Second, rifampicin-coated grafts might be resistant to methicillin-resistant *Staphylococcus aureus*, although data are conflicting.[5,6,18] We did not take into account the type of microorganism that caused the infection or the duration and type of perioperative antibiotic treatment. However, the cases with proven *Staphylococcus aureus* in this cohort were not treated with rifampicin-coated grafts.

Third, long-term analysis was not possible because of small numbers of patients in both groups. Therefore, differences in long-term mortality and reintervention could not be observed.

Fourth, 2 different graft types, namely silver and triclosan next to rifampicin-bonded grafts, were used in the prosthetic group. No difference was seen in the analysis between the 2 groups, although the numbers in the groups were too small to make a distinction. Further research with larger series is needed to gain more knowledge about silver and triclosan grafts.

CONCLUSION

In patients with mycotic aortic aneurysms or aortic graft infections, venous reconstruction tends to have a better 3-year survival and a lower 30-day reintervention rate. In the acute setting,

antimicrobial prosthetic graft reconstruction is a valuable solution due to the significantly shorter operation time and similar 30-day mortality and complication rates.

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