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ORIGINAL ARTICLE

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Thoracic aortic vascular graft infection: outcome after conservative treatment without graft removal

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Key question

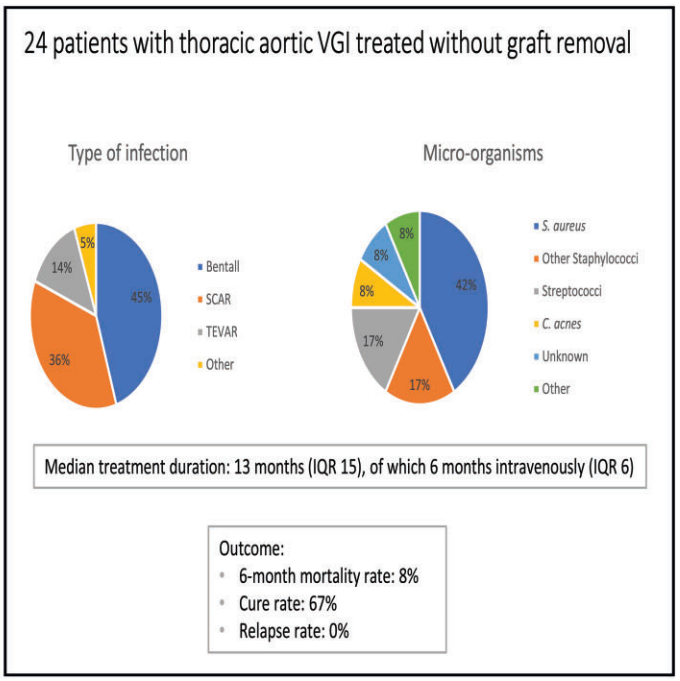
What is the outcome in patients with thoracic aortic VGI who were treated without graft removal?

Key finding(s)

Mortality rate 6 months after VGI diagnosis was 8% and no relapses occurred after 24 months (IQR 32) follow-up.

Take-home message

Intensive antibiotic treatment may be a non-inferior option in patients with thoracic aortic VGI who are not considered for surgery.



Abstract

OBJECTIVES: Surgical debridement with aortic graft removal is considered the preferred treatment for thoracic aortic vascular graft infection (VGI). Conservative treatment with antibiotics only is usually reserved for inoperable patients. Due to Outpatient Parenteral Antimicrobial Therapy (OPAT) and better understanding of the antibiotic impact on biofilms, long-term targeted antibiotic therapy without graft removal may be an alternative treatment option for selected thoracic aortic VGI patients. The aim of this case series was to evaluate the outcome in patients with thoracic aortic VGI who were treated without graft removal.

METHODS: This single-centre retrospective cohort study evaluated patients with a thoracic aortic VGI diagnosed between 2008 and 2021 and who were treated without graft removal. The primary outcome parameter was the 6-month mortality rate after VGI diagnosis. Secondary outcome parameters were cure rates and relapse of infection.

RESULTS: Twenty-four patients with thoracic aortic VGI who were managed without graft removal were identified. The mortality rate 6 months after VGI diagnosis was 8% (2/24); one of these deaths was infection related. The median antibiotic treatment duration was 13 months (interquartile range 15). A total of 16 patients (67%) were cured. No relapses occurred after a median of 24-month (interquartile range 32) follow-up.

CONCLUSIONS: Intensive antibiotic treatment, without graft removal, may be a non-inferior option in patients with a thoracic aortic VGI who are not considered for surgery.

Keywords: Thoracic aortic vascular graft infection • Conservative treatment • Outcome

ABBREVIATIONS

IQR	Interquartile range
VGI	Vascular graft infection

INTRODUCTION

Vascular graft infection (VGI) is a serious complication with reported mortality rates up to 66% [1–3]. Thoracic aortic VGI is a difficult diagnosis and is based on the combination of clinical features, laboratory findings and the result of imaging techniques and microbiological examinations [4–6]. The current guidelines on diagnosis and management of thoracic aortic VGI lack data from randomized controlled trials [2, 7]. Surgical graft removal with prolonged antibiotic treatment is considered the preferred management strategy. However, this type of surgery is associated with considerable morbidity and mortality [1, 3, 8]. Conservative therapy with chronic suppressive antibiotic treatment is usually reserved for inoperable patients [9, 10]. Debridement without graft removal is proposed as an alternative option in selected patients [11, 12]. To date, limited data are available regarding conservative management without graft removal and with prolonged intensive antibiotic treatment. Outpatient Parenteral Antimicrobial Therapy (OPAT) and better understanding of the antibiotic impact on biofilms [13] have increased options for prolonged targeted antibiotic treatment in patients with VGI.

At our institute, conservative treatment with prolonged intensive antibiotic treatment is considered one of the treatment options for thoracic aortic VGI for patients who are considered to have an unacceptable high operation risk or in case of favourable setting for long-term targeted antibiotic therapy. The aim of this case series was to evaluate the outcome in patients with thoracic aortic VGI managed with antibiotic treatment without graft removal.

MATERIALS AND METHODS

Ethical statement

According to the Dutch law and in consultation with the Ethics Committee of the Radboudumc, this study was exempt from approval by an ethics committee and waived from informed consent, because of the retrospective character of this study and the anonymous storage of data.

Patients and design

In this retrospective cohort study, adult patients with a diagnosis of thoracic aortic VGI between January 2008 and December 2021 were included if the vascular graft was not completely explanted. Exclusion criteria were surgical treatment with total graft removal, abdominal and peripheral VGI and VGI due to *Coxiella burnetii* infection, as in these patients prolonged treatment is necessary independently of surgical treatment. The study was performed at the Radboud University Medical Center in Nijmegen, the Netherlands, a tertiary referral centre for cardio-thoracic surgery. Thoracic aortic VGI is treated in close collaboration with the department of infectious diseases. The regional institutional ethics committee approved this study and waived the requirement to obtain informed consent.

Data collection

The following variables were collected from the electronic medical charts: demographic characteristics, comorbidity, onset of signs and symptoms, characteristics of the initial placement of the thoracic (endo)vascular graft, clinical diagnosis of infection, microbiological diagnosis, antibiotic treatment and outcome measures.

Outcome parameters

The primary outcome of this study was 6-month mortality after diagnosis of thoracic aortic VGI. Secondary outcomes were cure rates, relapse of infection and complications.

Definitions

Diagnoses of VGI were classified as 'suspected' or 'diagnosed' according to the MAGIC criteria based on a combination of different clinical, radiological and laboratory findings [6]. Fever was defined as a body temperature of >38.0°C. The Charlson comorbidity index was used for the classification of comorbidity [14]. The exact date of the diagnosis was defined as the date of the diagnosis documented in the patients' record. When the time between implantation of the graft and the clinical infection exceeded 2 months, VGI was considered a late infection [15]. The registered date of start of treatment was defined as the first day on which the patient was administered antibiotic treatment. Decisions on treatment, including conservative treatment without graft removal, were made in the multidisciplinary heart team or endocarditis team. Conservative treatment was considered in patients with severe comorbidity, technically high-risk surgery or in case of favourable setting with haematogenous source of infection after bacteraemia and early start of targeted antibiotic treatment. Patients were considered to be cured when no relapse occurred after discontinuation of antibiotic therapy with a follow-up of at least 3 months. Relapse of infection was defined as a second episode of VGI with the same causative organism

after the completion of antibiotic treatment. Re-infection was defined as a second episode of VGI with a different causative microorganism, after the completion of adequate antibiotic treatment.

Statistics

SPSS (version 25.0; SPSS, Inc.) was used to perform statistical tests on the retrieved anonymized data. For the representation of continuous data, medians were used, including interquartile ranges (IQRs). Kaplan–Meier curves for infection-free survival were added.

RESULTS

Characteristics of study population

Twenty-four patients with thoracic aortic VGI who matched the inclusion criteria were identified (Table 1). The primary indication for aortic replacement with a vascular graft was asymptomatic aneurysm (11 patients, 46%), acute type A aortic dissection (7 patients, 29%) and symptomatic aneurysm (3 patients, 13%), and in 3 patients (13%), a thoracic endovascular aortic repair was placed in an infected aneurysm. According to the MAGIC criteria [6], VGI was diagnosed in 17 patients (71%) and VGI was suspected in 7 patients (29%). A late infection occurred in 14 patients (58%) after a median of 37 months (IQR 36) after placement. Causative microorganisms were found in 22 patients (92%). Nineteen patients (79%) suffered from a bacteraemia at the diagnosis of VGI. Information on cultured microorganisms is shown in Table 1. At presentation of VGI, 18 patients (75%) had fever, 1 patient had backpain (4%), 3 patients (13%) had unexplained weight loss and 2 patients (8%) had night sweats. Two patients (8%) had a pseudoaneurysm at presentation (patients 10 and 13). None of the patients were lost to follow-up.

Outcome measures

Six-month mortality rate was 8% (2 of 24 patients) (Table 1). One death was directly related to the graft infection (patient 4 who developed an aorto-oesophageal fistula). The other patient died after a complicated admission on the intensive care unit 6 months after VGI diagnosis due to an abdominal sepsis. In patients who survived the first 6 months, mortality rates during follow-up after VGI diagnosis were 4% (1 patient). A total of 16 patients (67%) were cured. This complete recovery occurred after a median of 13 months (IQR 14) of antibiotic treatment. The median follow-up after discontinuation of antibiotic treatment in all cured patients was 24 months (IQR 32) (Fig. 1). Of all 19 patients with bacteraemia, 14 patients (74%) were cured. Chronic suppressive antibiotic treatment was started in 8 patients (33%) and finally discontinued in 3 patients (13%). None of the patients experienced relapse of infection. One patient with infected Bentall prosthesis with *Streptococcus mutans* had a re-infection with *Streptococcus mitis* 5 months after the discontinuation of antibiotic treatment (patient 17).

Of all patients, 7 patients (29%) experienced a total of 8 adverse events. Most adverse events were related to antibiotic treatment (2 patients with rash and 3 patients with tubulointerstitial nephritis). Other adverse events were aorto-oesophageal fistula (1), wound problem (1) and problem with peripherally inserted central catheter (1).

Antibiotic treatment with or without debridement

Reasons for receiving conservative treatment without graft removal were doctors' choice to retain the prosthesis because of favourable setting due to haematogenous cause of infection with early start of targeted antibiotic treatment (9 patients, 38%), technically high-risk surgery (4 patients, 17%), considered inoperable based on clinical condition (10 patients, 42%) or patients' refusal for surgery (1 patient, 4%). In 5 patients (21%), an open debridement was performed (patients 1, 10, 13, 16 and 21); patient 1 underwent debridement because of a mediastinitis, patient 10 underwent a pseudoaneurysm repair without removal of the graft, patient 13 underwent a pseudoaneurysm repair with partial removal of the graft, patient 16 underwent debridement twice and patient 21 underwent debridement with omental wrapping. Omentum flap was only used in 1 patient (patient 21). The median duration of antibiotic treatment in all patients was 13 months (IQR 15). All patients started with intravenous antibiotic treatment. The median treatment duration of intravenous antibiotics was 6 months (IQR 6). Fifteen patients (63%) were on antibiotic treatment with biofilm activity: rifampicin (12 patients, 80%), a quinolone (2 patients, 13%) or fusidic acid (1 patient, 7%). During follow-up, 2-[18F]fluoro-2-deoxy-D-glucose positron emission tomography with combined computed tomography ([^{18}F]FDG-PET/CT) was performed in 16 patients (67%) and in 9 patients (56%), it was used for the decision to discontinue the antibiotic treatment (Table 1).

DISCUSSION

In this retrospective study of 24 patients with thoracic aortic VGI and treatment without total graft removal, 6-month mortality was only 8%. Finally, 67% of patients were cured. No relapse of VGI after discontinuation of antibiotic treatment was reported.

For the treatment of VGI, surgery with graft removal followed by prolonged antibiotic treatment is considered the preferred management strategy. In general, conservative therapy without graft removal is usually reserved for patients considered inoperable. The results of our study show a reasonable outcome after conservative treatment in thoracic aortic VGI. Most previous studies on thoracic VGI show poor outcome after conservative treatment [3]. A recent study showed 14–36% in-hospital mortality rates for patients with thoracic VGI and graft-sparing procedures [11]. However, improved outcome was described by Erb *et al.* [16] who reported on 24 patients with thoracic aortic VGI of whom 12 were treated with debridement and antibiotic treatment and 6 patients were treated with antibiotic treatment only. After 1 year, 75% of the patients with debridement and 100% of the patients with antibiotic treatment only were cured. Overall, the conclusions on outcome of conservative treatment are based on studies with small number of conservatively treated patients [3, 16]. The favourable outcome of the VGI patients in our study may be explained by several aspects. First, no aortobronchial and only 1 aorto-oesophageal fistulae were reported in our study. Fistulae as complications of VGI are associated with high mortality rates [2]. Second, the majority of patients in our study (79%) had bacteraemia at the time of VGI diagnosis. A possible early

Table 1: Patients with thoracic aortic vascular graft infection and conservative treatment

Pt No.	G	Age (years)	CCI	Type of infection (graft or native aorta)	Time interval graft placement–diagnosis of infection (months)	Microorganism + type of culture	Antibiotic treatment duration after diagnosis (months)	Ongoing antibiotic treatment	6-Month mortality	Outcome	Follow-up after discontinuation of antibiotic treatment (months)	No. FDG-PET/CT scans in follow-up; end of AB based on FDG-PET/CT
1	F	78	3	Supracoronary ascending aortic replacement	0.5	*Staphylococcus aureus*, blood and tissue culture	19	No	No	Cured	48	4; yes
2	M	50	2	Aortic root replacement (Bentall)	4	*Staphylococcus aureus*, blood cultures	20	No	No	Cured	60	5; yes (although increased FDG uptake)
3	F	73	5	Aortic root replacement (Bentall)	6	*Enterococcus faecalis*, blood cultures	6	No	Yes	Death (other)	N.A.	0; N.A.
4	F	67	3	Thoracic endovascular aortic repair	0	*Streptococcus pneumoniae*, blood cultures	2	No	Yes	Death (infection)	N.A.	0; N.A.
5	F	63	2	Aortic root replacement (Bentall)	2	*Staphylococcus epidermidis*, blood and tissue cultures	96 (chronic suppressive)	No	No	Cured	60	6; yes (although increased FDG uptake)
6	M	67	2	Aortic root replacement (Bentall)	42	Unknown	13	No	No	Cured	120	3; yes (although increased FDG uptake)
7	M	71	2	Supracoronary ascending aortic replacement	1	*Staphylococcus aureus*, blood cultures	37 (chronic suppressive)	No	No	Cured	24	3; yes (although increased FDG uptake)
8	F	66	2	Aortic arch replacement	95	*Staphylococcus aureus*, blood cultures	27	No	No	Cured	36	5; yes
9	F	67	3	Thoracic endovascular aortic repair	0	Unknown	12	No	No	Cured	24	2; no
10	M	66	3	Supracoronary ascending aortic replacement	38	*C. acnes*, tissue cultures	8	No	No	Death (other)	N.A.	1; no
11	M	80	4	Thoracic endovascular aortic repair	0	*Salmonella paratyphi*, blood cultures	11	No	No	Cured	38	3; yes
12	M	27	0	Aortic root replacement (Bentall)	35	*Staphylococcus aureus*, blood cultures	19	No	No	Cured	28	4; yes (although increased FDG uptake)
13	M	57	1	Supracoronary ascending aortic replacement	25	*C. acnes*, tissue cultures	44 (chronic suppressive)	Yes	No	Ongoing treatment	N.A.	4; N.A.

Continued

Table 1: Continued

Pt No.	G	Age (years)	CCI	Type of infection (graft or native aorta)	Time interval graft placement–diagnosis of infection (months)	Microorganism + type of culture	Antibiotic treatment duration after diagnosis (months)	Ongoing antibiotic treatment	6-Month mortality	Outcome	Follow-up after discontinuation of antibiotic treatment (months)	No. FDG-PET/CT scans in follow-up; end of AB based on FDG-PET/CT
14	M	59	1	Aortic root replacement (Bentall)	0	*Staphylococcus epidermidis*, blood and tissue cultures	6	No	No	Cured	16	1; no
15	F	78	3	Supracoronary ascending aortic replacement	81	*Staphylococcus aureus*, blood cultures	36 (chronic suppressive)	No	No	Cured	12	2; no
16	M	50	1	Supracoronary ascending aortic replacement	1	*Staphylococcus aureus*, blood cultures	18	No	No	Cured	15	2; no
17	M	32	1	Aortic root replacement (Bentall)	47	*Streptococcus mutans*, blood cultures	12	No	No	Cured	10	2; yes
18	M	55	1	Aortic root replacement (Bentall)	0.5	*Staphylococcus lugdunensis*, blood and tissue cultures	13 (chronic suppressive)	Yes	No	Ongoing treatment	N.A.	0; N.A.
19	M	66	2	Total arch with frozen elephant trunk	0.5	*Staphylococcus aureus*, blood cultures	13 (chronic suppressive)	Yes	No	Ongoing treatment	N.A.	0; N.A.
20	M	53	1	Aortic root replacement (Bentall)	14	*Streptococcus mitis* group, blood cultures	1.5	No	No	Cured	7	0; N.A.
21	F	68	3	Supracoronary ascending and arch replacement	39	*Staphylococcus aureus*, blood and tissue culture	22 (chronic suppressive)	Yes	No	Ongoing treatment	N.A.	3; no
22	M	74	3	Aortic root replacement (Bentall)	21	*Streptococcus bovis* group, blood cultures	3	No	No	Cured	4	0; N.A.
23	M	57	1	Supracoronary ascending aortic replacement	78	*Staphylococcus aureus*, blood cultures	3	No	No	Cured	5	0; N.A.
24	M	60	4	Supracoronary ascending, arch replacement and elephant trunk	28	*Staphylococcus epidermidis, C. acnes*, tissue cultures	7 (chronic suppressive)	Yes	No	Ongoing treatment	N.A.	0; N.A

CCI: Charlson comorbidity index; F: female; M: male; N.A.: non-applicable.

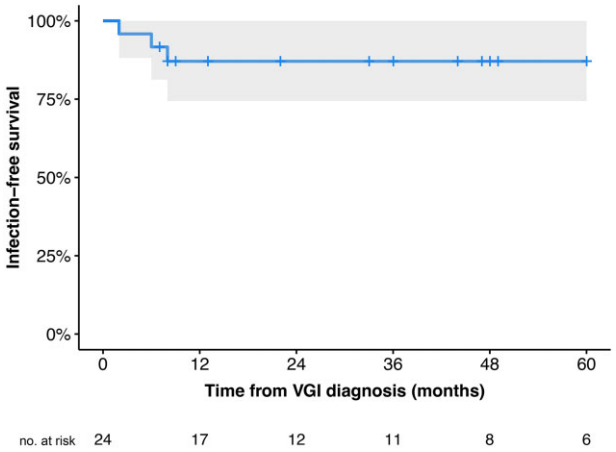


Figure 1: Kaplan–Meier survival curve showing infection-free survival in all patients with thoracic aortic vascular graft infection from the diagnosis of vascular graft infection until 60 months of follow-up (95% confidence interval included)

start of adequate treatment in the context of acute onset of illness and known causing microorganism may have contributed to the observed non-inferior outcome. This early start of adequate antibiotic treatment may also lead to less biofilm formation [17], which is difficult to treat. Third, aggressive targeted antibiotic treatment was started with a median duration of intravenous therapy of 6 months (IQR 6). Fourth, in 21% (5/24) of patients, a debridement without graft removal was performed.

The median antibiotic treatment duration in our study was 13 months. Guidelines recommend prolonged antibiotic treatment after diagnosis of VGI and lifelong treatment should be considered in patients without surgical treatment [1]. In most studies, no exact antibiotic treatment duration is reported. Erb *et al.* [16] found a median of 92 days of total duration of antibiotic therapy in 24 patients with thoracic aortic VGI, including biofilm active antibiotic treatment in all patients (rifampicin in 67% and ciprofloxacin in 33% of patients). These data suggest that in case of conservative treatment without graft removal, targeted antibiotic therapy is not definitely life lasting.

As clear guidelines on conservative treatment in VGI are lacking, the decision to discontinue antibiotic treatment in these patients is made by the attending physician for each individual patient based on clinical signs, inflammation parameters and imaging. At our institute, [^{18}F]FDG-PET/CT is often used for the follow-up of VGI. Consecutive [^{18}F]FDG-PET/CT scans have shown encouraging results in therapy monitoring of VGI patients in combination with elevated inflammatory markers and/or clinical signs [18]. However, [^{18}F]FDG-PET/CT may show increased [^{18}F]FDG uptake around the graft due to sterile inflammation of the prosthetic material possibly leading to false-positive results and thereby unnecessary extension of antibiotic treatment [19]. In our study, multiple [^{18}F]FDG-PET/CT scans were made in many patients, and discontinuation of antibiotic treatment was not always based on [^{18}F]FDG-PET/CT results only. A recent study in 15 patients treated with open or endovascular repair because of infected native aortic aneurysms showed that [^{18}F]FDG-PET/CT showed large discrepancies between trends of CRP and metabolic activity or even opposed course [20]. Metabolic activity in the aneurysms remained slightly elevated after the end of antibiotic treatment in patients without any signs of infection at follow-up.

VGI includes multiple variables with different types of grafts, causative microorganisms and types of preferred antibiotics; therefore, VGI is a complex infection for large (randomized) studies on treatment duration. A multidisciplinary approach for the diagnosis and treatment of VGI patients is necessary, including cardio-thoracic surgeons, cardiologists, infectious disease specialists, clinical microbiologists, radiologists and nuclear medicine physicians. The final treatment plan should be made multidisciplinary based on specific patient characteristics and extent of the infection.

Limitations

One limitation of our study is its retrospective nature. Second, the number of patients included in this study is limited. Still, this study describes one of the largest cohorts of patients with thoracic aortic VGI treated without graft removal.

CONCLUSION

This study contributes to the current knowledge of treatment of thoracic aortic VGI and suggests that targeted antibiotic therapy without graft removal may be a non-inferior option in patients who are not considered for surgery.

Conflict of interest: none declared.

Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Author contributions

Ilse J.E. Kouijzer: Conceptualization; Formal analysis; Investigation; Methodology; Project administration; Validation; Writing—original draft; Writing—review & editing. **Celine T. Baranelli:** Data curation; Formal analysis; Investigation; Project administration; Writing—original draft. **Ianthe Maat:** Supervision; Writing—review & editing. **Frederik M.A. van den Heuvel:** Methodology; Writing—review & editing. **Erik H.J.G. Aarntzen:** Conceptualization; Formal analysis; Writing—review & editing. **Tim Smith:** Conceptualization; Methodology; Writing—review & editing. **Quirijn de Mast:** Conceptualization; Methodology; Supervision; Writing—review & editing. **Guillaume S.C. Geuzebroek:** Conceptualization; Formal analysis; Supervision; Writing—original draft.

Reviewer information

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