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Decreased biventricular function following thoracic endovascular aortic repair

Maximilian Kreibich *, Julia Morlock, Friedhelm Beyersdorf , Tim Berger, Stephan Allweier, Stoyan Kondov, Clarence Pingpoh, Martin Czerny, Matthias Siepe and Bartosz Rylski

Department of Cardiovascular Surgery, Faculty of Medicine, University Heart Center Freiburg, Albert-Ludwigs-University of Freiburg, Freiburg, Germany

* Corresponding author. Department of Cardiovascular Surgery, Faculty of Medicine, University Heart Center Freiburg, Albert-Ludwigs-University of Freiburg, Hugstetter Strasse 55, 79106 Freiburg, Germany. Tel: +49-761-27028180; fax: +49-761-27025500; e-mail: maximilian.kreibich@universitaets-herzzentrum.de (M. Kreibich).

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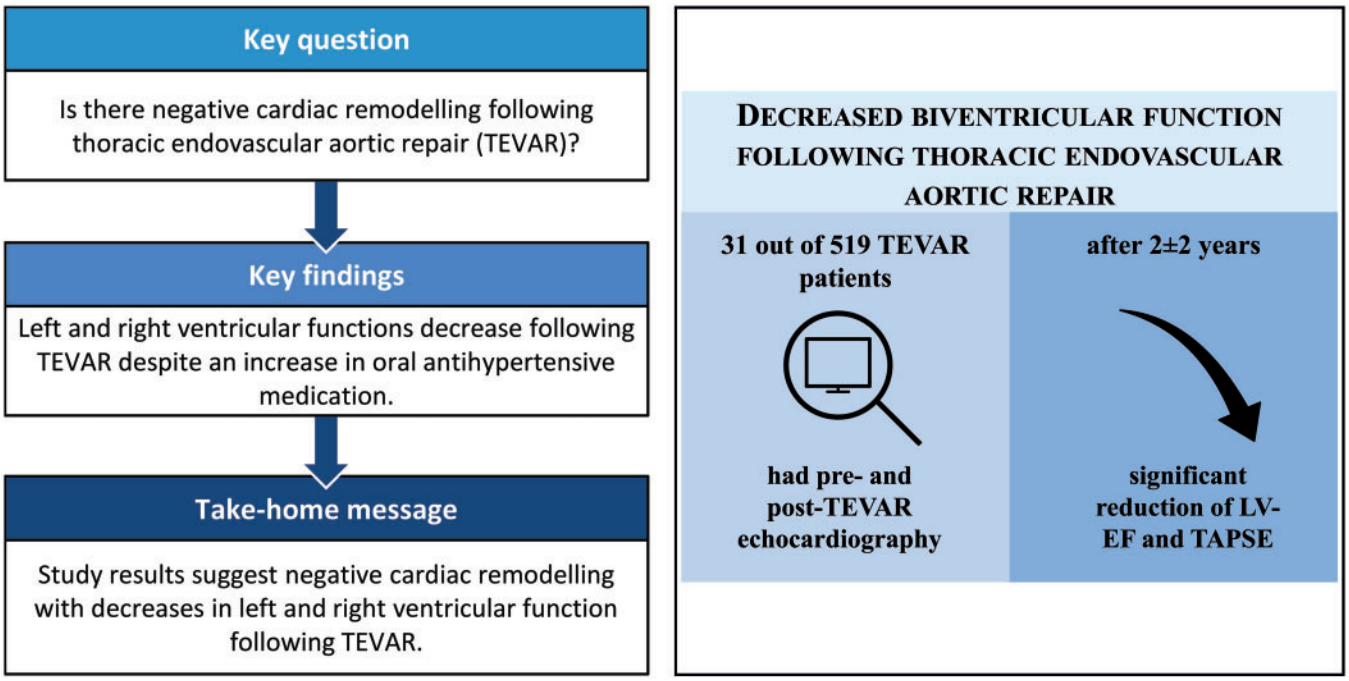

Abstract

OBJECTIVES: Preclinical studies have suggested acute stiffening of the aorta following experimental thoracic endovascular aortic repair (TEVAR), resulting in acute elevated pulse pressure, hypertension and possibly heart failure. The aim of this study was to evaluate cardiac remodelling following TEVAR.

METHODS: From 2005 to 2018, 519 TEVAR procedures were performed at a single centre. Transthoracic echocardiography was performed pre- and post-TEVAR in 31 patients without previous replacement of the thoracic aorta. Patient characteristics, drug information, radiographic and follow-up data were evaluated. Aortic details were measured in multiplanar reconstruction.

RESULTS: Transthoracic echocardiography was performed 2 ± 2 years after TEVAR. At this time, patients received significantly more antihypertensive drugs compared to the pre-TEVAR intake (beta-blocker therapy: $P = 0.037$; calcium channel blocker: $P = 0.022$). Compared to

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pre-TEVAR, there was a significant reduction in the left ventricular ejection fraction ($P = 0.008$) and tricuspid annular plane systolic excursion ($P = 0.013$) post-TEVAR. A significant increase in the left ventricular mass was not detected in this study ($P = 0.95$). The mean distance of 163 ± 66 mm of the descending aorta was covered.

CONCLUSIONS: This study suggests negative cardiac remodelling with a decrease in the left and right ventricular function following TEVAR despite an increase in oral antihypertensive medication. The impact of stiffer endovascular grafts compared with the native aortic wall should be considered by endovascular specialists and manufacturers.

Keywords: Thoracic endovascular aortic repair • Cardiac remodelling • Cardiac function • Aorta

ABBREVIATIONS

SD	Standard deviation
TEVAR	Thoracic endovascular aortic repair
TTE	Transthoracic echocardiography

INTRODUCTION

Thoracic endovascular aortic repair (TEVAR) has become the treatment of choice for descending thoracic aortic pathologies [1, 2]. Compared to conventional surgery, TEVAR is more minimally invasive and is associated with significantly fewer perioperative complications [2, 3]. Hence, TEVAR has been increasingly offered to more patients with higher burdens of comorbidities and acute disease [2, 3].

Nevertheless, preclinical studies have detected acute stiffening of the aorta following TEVAR, resulting in acute elevated pulse pressure, hypertension and possibly heart failure [4–6]. Clinically, an increase in aortic stiffness has been associated with negative cardiac remodelling and a detrimental long-term outcome [7]. Indeed, one recent study including eight patients has shown a significant increase in left ventricular stroke work and mass post-TEVAR [8].

The aim of this study was to evaluate cardiac remodelling following TEVAR through transthoracic echocardiography (TTE).

PATIENTS AND METHODS

Patients and follow-up protocol

Between January 2005 and December 2018, 519 TEVAR procedures were performed at a single institution. Pre- and post-TEVAR echocardiography was not performed in 462 patients who were excluded from this study. Another 26 patients were excluded because previous replacement of the ascending aorta and/or the aortic arch and/or the descending aorta was performed. Hence, the study population consists of 31 patients (Fig. 1) who underwent TEVAR treatment either for thoracic aortic aneurysm ($n = 19$) or thoracic aortic dissection ($n = 12$). The follow-up data were available for all 31 patients after TEVAR implantation (100%). Patients were followed-up for a total of 76 patient-years, with a mean follow-up of 29 [standard deviation (SD): 28] months. TTE was performed after 24 (SD: 29) months. The institutional review committee approved this retrospective study and the need for informed consent was waived.

Imaging analysis

Pre- and post-TEVAR echocardiography images were performed by different, experienced cardiologists in our centre's department of cardiology. No external echocardiography images were available or included. Measurements and calculations were routinely performed as recommended by the European Association of Cardiovascular Imaging [9, 10]. Data were collected from clinical records and compared. Aortic measurements were taken in multiplanar reconstruction always in the plane perpendicular to the manually corrected local aortic centreline as previously described [11]. Proximal TEVAR landing zones were defined as previously published [12].

Outcome measures

Clinical data and information on antihypertensive medications were collected retrospectively from clinical records.

Statistical analysis

Data are presented as absolute and relative frequency or as mean (±SD). The paired *T*-test or the Wilcoxon signed-rank test was used to compare continuous variables as appropriate. Categorical variables were compared using the McNemar test. The Kaplan–Meier method was used to analyse survival during follow-up. The statistical analysis was performed using IBM SPSS Statistic 21.0.

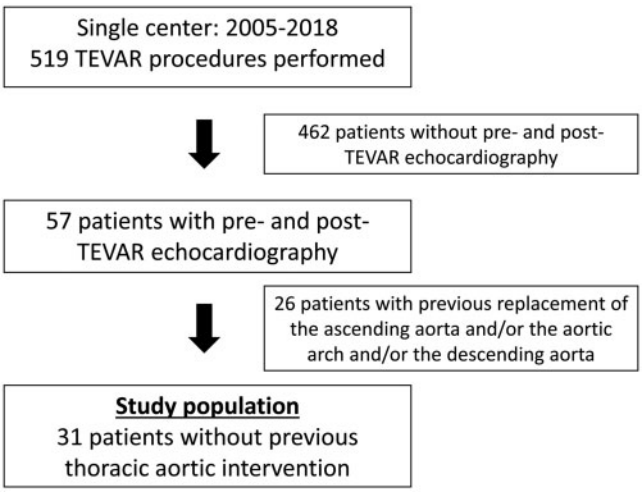

Figure 1: Flow chart of patient inclusion and exclusion criteria. TEVAR: thoracic endovascular aortic repair.

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Table 1: Patient characteristics

	N = 31
Age (years)	69 (SD: 9)
Male gender	22 (71)
History of smoking	14 (45)
Hyperlipidaemia	15 (48)
Hypertension	26 (74)
IDDM2	7 (23)
COPD	2 (6)
History of stroke	2 (6)
Coronary artery disease	11 (35)
Chronic renal impairment	5 (16)

Values are *n* (%) or mean (SD).
COPD: chronic obstructive pulmonary disease; IDDM2: insulin-dependent diabetes mellitus type 2; SD: standard deviation.

Table 2: TEVAR details

	N = 31
Number of stent grafts used	1 (SD: 1)
1 stent graft	22 (71)
2 stent grafts	7 (23)
3 stent grafts	2 (6)
Proximal landing zone	
Zone 1	2 (6)
Zone 2	7 (23)
Zone 3	12 (39)
Zone 4	10 (32)
Proximal stent graft diameter (mm)	29 (SD: 4)
Most distal stent graft diameter (mm)	27 (SD: 7)
Distance covered (mm)	163 (SD: 66)

Values are *n* (%) or mean (SD).
SD: standard deviation; TEVAR: thoracic endovascular aortic repair.

RESULTS

Patient characteristics

The mean age of the 22 male and 9 female patients was 69 (SD: 9) years. Hypertension was the most common risk factor in this cohort. All patient demographics and risk factors are summarized in Table 1.

Aortic characteristics

Most patients (*n* = 22, 71%) were treated with a single stent graft in the descending thoracic aorta. Zone 3 was the most common proximal landing zone in 12 patients (39%) and a distance of 163 (SD: 66) mm of the aorta was covered. All TEVAR details are summarized in Table 2.

Outcome characteristics

Post-TEVAR, 1 patient developed a stroke, 3 patients developed a temporary spinal cord injury and 1 patient developed a permanent spinal cord injury. Acute renal injury was diagnosed in 1 patient as well. During follow-up, 4 patients expired after 23, 26, 35 and 78 months, respectively (Supplementary Material, Fig. S1).

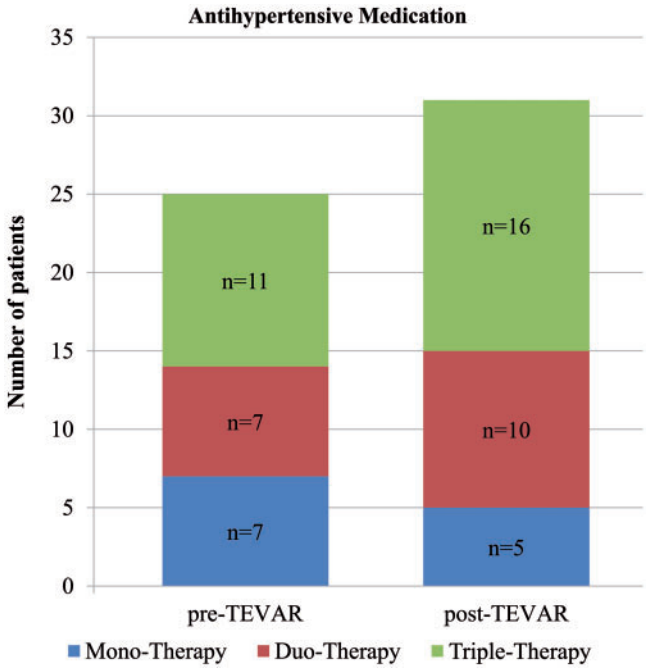

Figure 2: Number of patients receiving antihypertensive medication. TEVAR: thoracic endovascular aortic repair.

Table 3: Antihypertensive medication

	Pre-TEVAR	Post-TEVAR	*P*-value
ARBs	8 (26)	7 (23)	0.23
Beta blocker	19 (61)	27 (87)	0.027
ACE inhibitor	12 (39)	16 (52)	1.00
CCB	15 (48)	23 (74)	0.022
Mono-therapy	7 (23)	5 (16)	0.51
Duo-therapy	7 (23)	10 (32)	0.75
Triple-therapy	11 (35)	16 (52)	0.33

Values are *n* (%).
ACE: angiotensin-converting-enzyme; ARBs: angiotensin II receptor blockers; CCB: calcium channel blockers; TEVAR: thoracic endovascular aortic repair.

Antihypertensive medication

Post-TEVAR, 31 patients were treated with antihypertensive drugs compared with 25 patients pre-TEVAR ($P = 0.13$, Fig. 2) and more patients were treated with a duo-therapy ($P = 0.75$) or triple-therapy ($P = 0.33$) post-TEVAR (Table 3). Beta-blocker and calcium channel blocker therapies were the most frequent antihypertensive drugs used and a significant increase in beta-blocker ($P = 0.027$) and calcium channel blocker ($P = 0.022$) intake was observed post-TEVAR (Table 3).

Echocardiographic data

The left ventricular ejection fraction ($P = 0.008$) and tricuspid annular plane systolic excursion ($P = 0.013$) significantly decreased post-TEVAR (Fig. 3A and B). There was no statistically significant change in other TTE parameters (Table 4), including left ventricular mass ($P = 0.95$).

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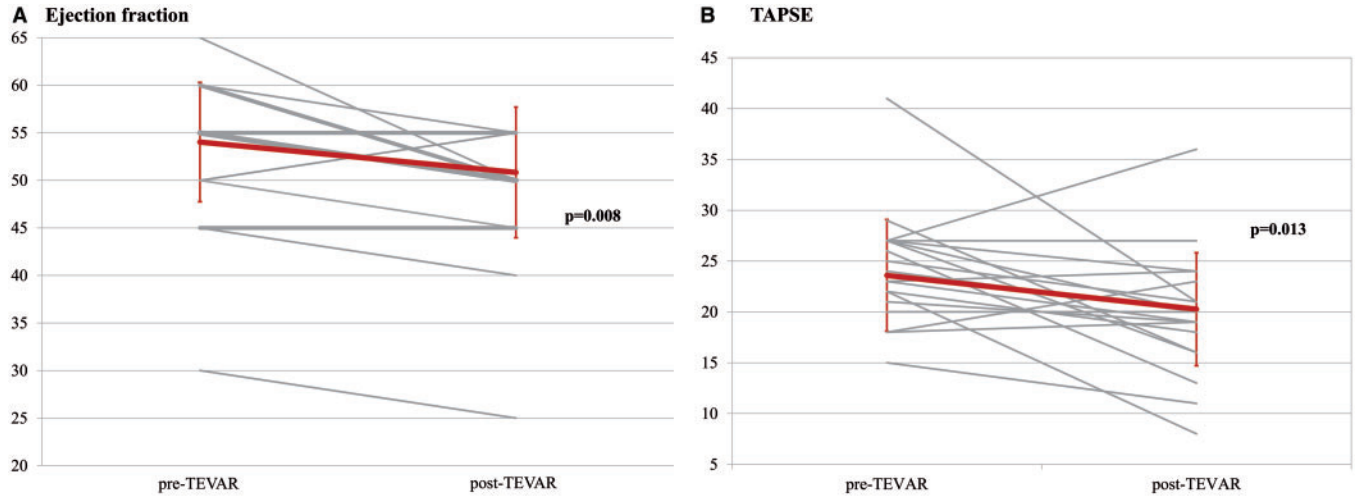

Figure 3: Changes in left ventricular ejection fraction (%, **A**) and TAPSE (mm, **B**) pre- and post-TEVAR. Grey lines indicate individual patient changes in ejection fraction or TAPSE, respectively. Thicker lines indicate multiple patients with identical change. Red line indicates the overall mean decrease with standard deviation. The paired *T*-test or the Wilcoxon Signed Rank test was used as appropriate. TAPSE: tricuspid annular plane systolic excursion; TEVAR: thoracic endovascular aortic repair.

Table 4: Transthoracic echocardiography

N = 31	Pre-TEVAR	Post-TEVAR	*P*-value
Ejection fraction (%)	55 (55–55)	55 (50–55)	0.008
TAPSE (mm)	24 (SD: 6)	20 (SD: 6)	0.013
Aortic root diameter	34 (32–39)	35 (33–41)	0.91
E/E′ medial	11 (SD: 5)	11 (SD: 4)	0.42
E/E′ lateral	9 (SD: 5)	8 (SD: 3)	0.87
LVPWd (mm)	11 (SD: 2)	11 (SD: 2)	0.88
LVSd (mm)	11 (SD: 3)	12 (SD: 2)	0.89
LVEDD (mm)	49 (SD: 11)	51 (SD: 9)	0.66
LV mass (g)	219 (SD: 84)	237 (SD: 102)	0.95

Values are *n* (%), mean (SD) or median (first quartile–third quartile).
LV: left ventricular; LVEDD: LV end-diastolic dimension; LVPWd: LV posterior wall thickness at end-diastole; LVSd: interventricular septal thickness at end-diastole; SD: standard deviation; TAPSE: tricuspid annular plane systolic excursion; TEVAR: thoracic endovascular aortic repair.

DISCUSSION

The most important findings of this study can be summarized as follows: (i) this exploratory study suggests negative cardiac remodelling with a decrease in the left and right ventricular function following TEVAR, (ii) a significant increase in the left ventricular mass was not detected in this study and (iii) cardiac remodelling occurred despite an increase in oral antihypertensive medication.

Even though TEVAR is associated with excellent short term results in the treatment of thoracic aortic disease [2], this study aimed to evaluate the detrimental effects of TEVAR on cardiac function. A large clinical database was screened for this study, but only 31 patients were eligible for inclusion. In our centre, it is a common policy to perform a routine preoperative cardiovascular examination before surgery and TEVAR including a left heart catheterization, TTE, duplex ultrasound scanning of the carotid arteries and/or the access vessels, and computed tomography angiography of the complete aorta in all elective cases. Before this study, postoperative completion TTE was not performed on a routine basis. Hence, the findings of this study have to be interpreted carefully. Nevertheless, this heterogeneous patient cohort is a representative of the general TEVAR population as chronic health conditions and risk factors in this cohort were comparable to those noted in other TEVAR reports.

Preclinical studies performed in experimental models have suggested an increase in aortic stiffness following TEVAR resulting in hypertension, reduced coronary blood flow and possibly heart failure [4–6]. The underlying cause seems to be a stiffer stent graft compared with the relatively elastic native aorta [8, 13]. In a clinical setting, an increase in the proximal aortic stiffness is associated with increased mortality and a higher incidence of cardiovascular events [14, 15]. In this patient collective, on average 163 mm of the thoracic aorta was covered with a comparably stiff stent graft causing decreased aortic distensibility and reduced aortic compliance. Of note, the area covered was different among the study groups and different stent grafts were used in these patients, so we are unable to investigate a correlation between the length of the stent grafts and the level of cardiac remodelling.

A significant reduction in cardiac function was observed post-TEVAR in this study suggesting negative remodelling following the chronic increase in aortic stiffness. Interestingly, not only the left ventricular function seemed to be impaired post-TEVAR, but also a significant reduction in right ventricular function was observed. This would suggest global negative remodelling following TEVAR, but the sample size of this study remains too small for this definite conclusion. Nevertheless, in preclinical studies, reduced aortic compliance caused a global increase in myocardial oxygen consumption and reduced coronary flow reserve [4, 16]. However, the effects diminished after three weeks [4]. Larger clinical series are required to draw definitive conclusions. In addition, this study did not detect a significant increase in the left ventricular mass even though other preclinical and clinical studies have observed cardiac hypertrophy following an increase in aortic stiffness [7, 8, 17]. The effects of a variable covered aortic distance with a decreased aortic distensibility and the location of the stent grafts warrant further clinical investigation.

Of note, the reduction in cardiac function occurred despite a significant increase in oral antihypertensive medication. Following TEVAR, 30 of the 31 patients were taking antihypertensive drugs and there was a substantial increase in the number of patients receiving dual- or triple-therapy. This might suggest that an even

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more aggressive drug regime may be necessary in order to prevent negative cardiac remodelling in patients following TEVAR since antihypertensive medication has been shown to decrease aortic stiffness in non-TEVAR populations [18]. Hence, the increase in antihypertensive medication might be one potential explanation for the stable left ventricular mass observed in this study, but it cannot explain the decrease in the left and right ventricular function. Therefore, the impact of comparably stiff stent grafts with a low distensibility compared with the native aorta should be considered by manufacturers and by endovascular specialists.

Limitations and strengths

The study is obviously limited by its small sample size as most patients treated at our institution were excluded due to a lack of TTE data. Hence, the exploratory nature of the study has to be stressed. In addition, this is an observational retrospective study with a relatively brief follow-up period and we are unable to provide data on lifestyle modification or target blood pressure goals. However, this study adds novel information and valuable knowledge on the high likelihood of detrimental cardiac remodelling and underlines the need for continuous medical follow-up of these patients.

CONCLUSIONS

This retrospective observational and exploratory study suggests negative cardiac remodelling with a decrease in the left and right ventricular function following TEVAR. A significant increase in the left ventricular mass was not detected in this study, but cardiac remodelling occurred despite an increase in oral antihypertensive medication. The impact of stiffer endovascular grafts compared to the native aortic wall should be considered by endovascular specialists and manufacturers.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

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Conflict of interest: none declared.

Author contributions

Maximilian Kreibich: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing–original draft. **Julia Morlock:** Data curation; Formal analysis; Visualization; Writing–review & editing. **Friedhelm Beyersdorf:** Conceptualization; Funding acquisition; Project administration; Resources; Supervision; Writing–review & editing. **Tim Berger:** Data curation; Formal analysis; Visualization; Writing–review & editing. **Stephan Allweier:** Data curation; Formal analysis; Writing–review & editing. **Stoyan Kondov:** Data curation; Formal analysis; Software; Visualization; Writing –review & editing. **Clarence Pingpoh:** Data curation; Formal analysis; Writing–review & editing. **Martin Czerny:** Conceptualization; Formal analysis; Funding acquisition; Methodology; Project administration; Supervision; Validation; Writing–review & editing. **Matthias Siepe:** Formal analysis; Methodology; Project administration; Resources; Supervision; Writing–review & editing. **Bartosz Rylski:** Conceptualization; Funding acquisition; Methodology; Project administration; Supervision; Writing–review & editing.

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