Original communication

Aortic stiffness and related complications after endovascular repair of blunt thoracic aortic injury in young patients

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Summary: *Background*: This study aimed to evaluate the changes in aortic stiffness in young patients undergoing thoracic endovascular aortic repair (TEVAR) after blunt thoracic aortic injury (TBAI) and to examine the associated cardiovascular complications during follow-up. *Patients and methods*: We included survivors of TBAI who underwent stent graft placement between November 2009 and November 2019 and gave their consent to participate. Patients with relevant cardiovascular risk factors, comorbidities with potential impact on arterial stiffness, and prior aortic surgical or endovascular interventions were excluded. Fourteen TEVAR patients prospectively underwent clinical and noninvasive examinations and morphological imaging (mean time of follow-up and duration of implanted stent graft: 5.3 ± 1.8 years; mean age: 35.1 ± 8.7 years) and were compared to 14 healthy controls (matched for sex, age, height, and body mass index) in order to evaluate aortic stiffness. During the follow-up examinations, we assessed the pulse wave velocity (PWV; m/s) and development of arterial hypertension or heart failure, as indicated by N-terminal pro-brain natriuretic peptide (NT-proBNP; pg/mL) levels and performed echocardiography. *Results*: A significant increase in PWV values was recorded in the TEVAR group (median = 10.1; interquartile range [IQR] = 8.9–11.6) compared to the healthy controls (median = 7.3; IQR = 6.7–8.4), with an increase in the rank mean PWV (+ 3.8; Mann-Whitney U test $p < .001$). NT-proBNP levels of patients after TEVAR did not vary significantly compared to those of healthy controls (Mann-Whitney U test, $p = .154$). After TEVAR, five patients developed arterial hypertension during the follow-up, and three of them exhibited diastolic dysfunction. *Conclusions*: In young patients, TEVAR after TBAI may cause adverse cardiovascular complications due to increased aortic stiffness; therefore, screening for arterial hypertension during follow-up is recommended.

Keywords: Aortic stiffness, blunt thoracic aortic injury, thoracic endovascular aortic repair, stent graft

Introduction

In the last two decades, management strategies for blunt thoracic aortic injury treated by thoracic endovascular aortic repair (TEVAR) have evolved significantly because of improvements in vascular imaging and advancements in endovascular grafting techniques. The spectrum of injury to the thoracic aorta ranges from a mild intimal injury, which will spontaneously heal with no adverse sequelae, to an aortic rupture, which is universally fatal. This injury is most commonly caused by motor vehicle crashes, and mortality is high with only up to 15 % of patients surviving to hospital admission.

Limited data exist concerning biomechanical changes induced by the implanted stent graft on related cardiovascular remodeling, especially with regard to the development of arterial hypertension and cardiac impairment due to stent graft-induced aortic stiffness [1–3]. Pulse wave velocity (PWV) is an effective marker of arterial stiffness for the timely detection of hemodynamic changes related

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Table I. Demographics and risk factors of TEVAR and healthy control groups.

Mean	TEVAR group (n = 14)	Healthy control group (n = 14)	p-value
Age (years) at follow-up	35.1 ± 8.7	35.3 ± 9.4	n.s., p = .951
Age (years) at the time of TEVAR	29.8 ± 8.8	–	
Gender (male/female)	12/2	12/2	
Height (cm)	180.4 ± 12.0	180.8 ± 10.7	n.s., p = .921
Body weight (kg)	87.4 ± 13.0	85.4 ± 13.5	n.s., p = .693
Body mass index (kg/m^2)	26.9 ± 3.5	26.0 ± 3.0	n.s., p = .500
Body surface area (m^2)	2.1 ± 0.2	2.1 ± 0.2	n.s., p = .787

None of the participants in either group had a history of aortic surgery/intervention, history of or current smoking status, diabetes mellitus, pre-existing/history of arterial hypertension (before TEVAR), hyperlipidemia, manifest atherosclerosis, chronic obstructive pulmonary disease, or chronic kidney disease. n.s.: not significant; TEVAR: thoracic endovascular aortic repair.

to cardiovascular morbidity and mortality [4]. Additionally, circulating serum N-terminal pro-brain natriuretic peptide (NT-proBNP) levels are associated with increased arterial stiffness, which reduces ejection fraction in patients with heart failure [5, 6]. In such cases, significant increases in both arterial stiffness and serum NT-proBNP levels can be associated with the implantation of thoracic stent grafts.

The present study evaluated changes in aortic stiffness in young patients undergoing TEVAR after TBAI compared to well-matched healthy controls and examined the associated cardiovascular complications during follow-up.

Patients and methods

Ethical approval

This study was approved by the ethics committee of the Medical Faculty of Technische Universität Dresden (approval numbers: EK 317082014 for patients, EK 186042019 for healthy controls). Patients and healthy controls provided written informed consent.

Patient enrollment

Between November 2009 and November 2019, all survived patients with polytrauma as a cause of admission to the emergency department of a tertiary institution were retrospectively screened for study inclusion. Data were collected from an electronic data bank in the Technische Universität Dresden, Germany, which included all admitted patients.

Inclusion criteria comprised patients aged > 18 years and up to a maximum age of 50 years with polytrauma as a cause of admission and diagnosed aortic rupture as a blunt thoracic injury in the descending thoracic aorta, treated by TEVAR with the stent graft located in zone 2 (according to the classification proposed by Ishimaru) [7].

Patients with relevant cardiovascular risk factors (past or current smoking status, diabetes mellitus, arterial hypertension before treatment with TEVAR, and hypercholesterolemia), those with comorbidities (atherosclerotic or inflammatory cardiovascular disease and known connective tissue disease) with a potential impact on arterial stiffness, and those with prior aortic surgical or endovascular interventions were excluded (Table I). Indeed, all identified patients met the inclusion and exclusion criteria, so that none of them was excluded from the study.

Follow-up examinations

Fourteen surviving patients, with TBAI, met the inclusion criteria of the study and underwent clinical and noninvasive examinations and morphological imaging during the follow-up. Computed tomography angiography was performed at 3 months after TEVAR if there were no contraindications (e.g., severe renal insufficiency, allergies to contrast agents, and hyperthyroidism) to its use. When contraindications were present or an excellent result from aortic remodeling was approved, transesophageal echocardiography or magnetic resonance angiography in combination with chest radiography, to evaluate stent graft integrity was performed in further annual follow-up for up to an interval of 2 years to avoid radiation exposure in this young cohort.

Recruitment of matched healthy controls

Patients in the TEVAR group were matched with 14 healthy controls, according to the exclusion criteria. The matching criteria focused on sex, age (maximum age difference, 5 years), height (maximum difference, 10 cm), and body mass index (maximum difference, 10 kg) (Table I). Due to the retrospective design of the study pre-existing cardiovascular risk factors (past or current smoking status, diabetes mellitus, arterial hypertension and hypercholesterolemia) and already known and documented comorbidities (atherosclerotic or inflammatory cardiovascular disease and connective tissue disease) and prior aortic surgical or endovascular interventions were excluded and defined as healthy.

Study measurements

Due to the retrospective study design the measurement of Serum NT-proBNP levels, examination of pulse wave velocity and echocardiography were performed once at the latest presentation for follow-up after TEVAR.

Oscillometric measurement of PWV

Aortic stiffness indicated by PWV was determined using the AngE Pro8 software, version 1.18.36 (SOT Medical Systems, Maria Rain, Austria) and applying the Gesenius-Keller method of recording the echocardiogram-triggered pulse waves at different cuff pressures. Because of complete overstenting of the LSA by the stent graft, the arterial PWV between the right upper and both lower extremities at the height of the thigh was determined. The cuffs were placed according to the manufacturer's instructions. All participants were examined during the same conditions in the morning, after 10 minutes of rest in the supine position, and were kept in this position during the entire measurement process, which lasted approximately 10 minutes. The blood pressure was checked to be normal before beginning with the measurement of pulse wave velocity. The analysis focused on the central PWV calculated in m/sec.

Echocardiography

Echocardiography was performed to assess the left ventricular systolic and diastolic functions and to evaluate hypertrophy (Philips iU22 Ultrasound Machine, Philips Ultrasound Inc., Reedsville, PA). The collected parameters included the left ventricular diameters (left ventricular end-systolic and end-diastolic diameters) and ejection fraction (%), and the wall thickness of the interventricular septum and posterior left ventricular wall (mm) to exclude asymmetric hypertrophy. The diastolic function of the left ventricle was assessed by measuring the left E/E' ratio (the ratio between early mitral inflow velocity and mitral annular early diastolic velocity) and E/A ratio (the ratio of peak velocity blood flow from gravity in early diastole to peak velocity flow in late diastole caused by atrial contraction).

Laboratory examination

Serum NT-proBNP levels were measured as a biomarker for heart failure with an age-related (< 50 years) cut-off value of 14.75 pmol/l.

Statistical analysis

Descriptive statistics of binary data are reported as absolute values, whereas continuous variables are expressed as mean ± standard deviation. Two-tailed t-test was used to compare continuous variables, and Bonferroni correction was applied to prevent alpha error accumulation. The Mann-Whitney U test was used to compare categorical variables. A p-value < .05 was considered statistically significant. The Spearman correlation was used to determine the correlation between PWV and the length or duration of the implanted stent graft. All statistical tests were performed using SPSS software (IBM SPSS Statistics 26, IBM Corp., Armonk, NY, USA).

Results

Fourteen patients (TEVAR group; mean age: 35.1 ± 8.7 years, age at the time of TEVAR: 29.8 ± 8.8 years; 12 men/2 women) with TBAI, with aortic rupture in zone 2 of the descending thoracic aorta in all cases, underwent TEVAR with 10–20 % oversizing of stent graft and complete overstenting of the LSA. In patients with aortic rupture, the rupture was completely covered by the stent graft (GORE or Medtronic, length: 100–250 mm), and the left subclavian artery (LSA) showed no persistent aortic pathology after this procedure (Table II). All investigated patients survived the follow-up and had no stent graft-related complications or need for reinterventions. The patients of the TEVAR group were once evaluated for pulse wave velocity, echocardiography and NT-proBNP serum levels at the latest follow-up examination (at mean 5.3 ± 1.8 years after implanted stent grafts) of pulse wave velocity, echocardiography and NT-proBNP serum levels and matched according to sex, age, height, and weight to comparable healthy controls (n = 14). The demographics (age, height, weight and the calculated body mass index), risk factors, and comorbidities did not vary significantly between the TEVAR and control groups.

Figure 1A, 1B shows the median and interquartile range (IQR) of the PWV (m/sec) of patients in the TEVAR group after a mean follow-up of 5.3 ± 1.8 years compared to those of matched healthy controls. An increase in the PWV value was recorded in the TEVAR group (median = 10.1; IQR = 8.9–11.6) compared to the healthy controls (median = 7.3; IQR = 6.7–8.4), and this was statistically significant (p < .001; Mann-Whitney U test), with an increase in the rank mean PWV (+ 3.8). There was no statistically significant correlation between the length of the stent grafts (variation in the length of aortic coverage, 100–250 mm; Spearman-Rho p = .596) or duration of implantation (time of follow-up: 5.3 ± 1.8 years) and related aortic stiffness.

During the follow-up period, only two patients in the TEVAR group displayed elevated serum NT-proBNP levels. Serum NT-proBNP levels of patients after TEVAR did not vary significantly from those of the healthy controls (Mann-Whitney U test, p = .154) (Figure 2). In addition, five patients in the TEVAR group developed arterial hypertension and required medical treatment, and three of these patients showed diastolic dysfunction grade I without aortic insufficiency. Chamber sizes left ventricular mass and systolic wall function did not differ significantly in TBAI in comparison to healthy group (electronic supplementary material [ESM], Table).

Discussion

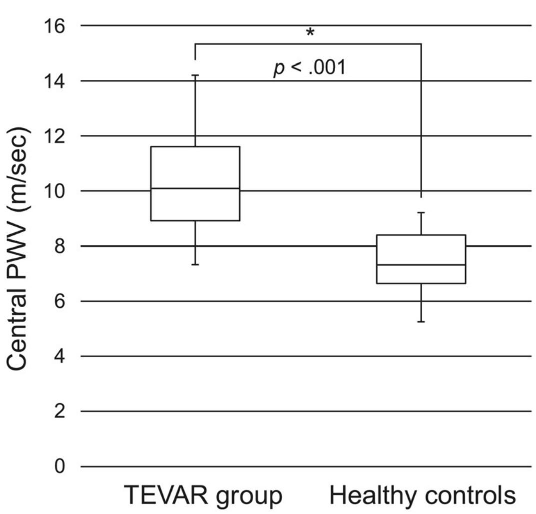
TEVAR is the preferred treatment for saving the lives of patients with polytrauma and rupture of the descending thoracic aorta. Our young patient cohort, with no relevant comorbidities or cardiovascular risk factors, showed no

Table II. Detailed procedures and results in the TEVAR group.

Patient no.	Age (years) at the time of TEVAR	Gender (m/f)	Trauma	Diagnosis	Stent type	Stent measurements proximal/distal/length (mm)
1	33	m	MCC	TAR	Medtronic Valiant	28/28/100
2	43	m	CC	TAR	Gore TAG	31/31/150
3	40	m	MCC	TAR	Gore TAG	26/26/100 and 28/28/150
4	17	m	CC	TAR	Gore TAG	26/21/100
5	21	m	MCC	TAR	Medtronic Endurant II	24/24/82
6	26	m	CC	TAR	Medtronic Valiant	24/24/150
7	19	m	MCC	TAR	Gore TAG	28/28/100 and 31/31/100
8	38	f	CC	TAR	Gore TAG	28/28/150
9	36	m	CC	TAR	Gore TAG	26/26/100
10	25	m	MCC	TAR	Gore TAG	22/22/150
11	36	m	CC	TAR	Gore TAG and Medtronic Valiant	28/28/100 and 31/31/100
12	27	m	MCC	TAR	Gore TAG	26/26/100
13	31	m	CC	TAR	Gore TAG	21/21/100
14	18	f	CC	TAR	Gore TAG	26/26/100

CC: car crash; f: female; m: male; MCC: motorcycle crash; no.: number; TAR: traumatic aortic rupture.

A



B

No.	Pulse wave velocity (m/sec) TEVAR group			Healthy controls		
1	11.21			6.77		
2	10.23			7.42		
3	9.52			5.26		
4	7.7			8.49		
5	7.33	Minimum	7.3	6.61	Minimum	5.3
6	9.38	Q1	8.9	7.28	Q1	6.7
7	8.62	Median	10.1	8.54	Median	7.3
8	8.72	Q3	11.6	7.40	Q3	8.4
9	11.98	Maximum	14.2	6.27	Maximum	9.2
10	10.69			9.23		
11	14.23			8.64		
12	11.76			8.15		
13	13.57			6.1		
14	10.00			6.78		

Figure 1. (A) Box plots of central pulse wave velocity (PWV) in patients after thoracic endovascular aortic repair (TEVAR) of blunt thoracic aortic injury and matched healthy controls without stent grafts. Aortic stiffness measured by PWV is significantly higher in the TEVAR group than in the healthy controls ($p < .001$). (B) Single values, means, and interquartile ranges.

indication for re-intervention following excellent results from morphological imaging at a mean duration of stent graft implant of 5.3 ± 1.8 years, although required oversizing of stent graft enhances the radial force and might lead to stent graft related complications [8, 9].

However, there was a significant increase in the PWV, a marker for aortic stiffness, compared to matched healthy controls without stent grafts. Experimental studies have shown that depending on the type of stent graft and extent of aortic coverage, stent grafts may affect aortic stiffness [10]. Moulakakis et al. reported a significant increase in the NT-proBNP levels and PWV between baseline and 6 months after elective TEVAR, most commonly due to atherosclerotic aneurysm in elderly patients (mean age: 68.8 ± 11.3 years) [11]. Although they claimed that further studies were required to ascertain the short- and long-term effects of TEVAR on cardiovascular outcomes, they concluded that TEVAR has adverse cardiac effects. Clinical

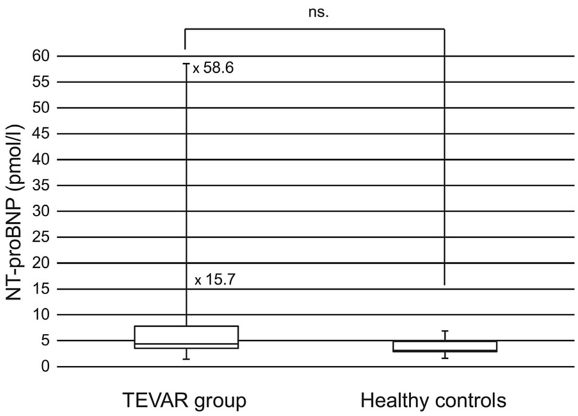


Figure 2. Box plots of serum N-terminal pro-brain natriuretic peptide (NT-proBNP) level in patients after thoracic endovascular aortic repair during the follow-up and in healthy controls without stent grafts. n.s.: not significant.

studies have demonstrated the association between arterial stiffness and atherosclerotic burden as well as incidence of adverse cardiovascular events [12, 13].

In the present study, we showed that TEVAR may lead to adverse cardiovascular problems due to increased aortic rigidity in young patients with TBAI. Therefore, these patients would require a follow-up examination to assess their blood pressure or cardiac insufficiency status.

Tzilalis et al. investigated younger patients (mean age: 26.9 years) with blunt injuries in the descending thoracic aorta (only two of 11 patients had an aortic rupture) for a shorter follow-up period (13–66 months) than our study and reported a significant increase in the PWV compared to healthy age- and sex-matched controls [1]. In the follow-up period of our study, only two patients in the TEVAR group showed elevated NT-proBNP levels, five developed arterial hypertension with an indication for medical treatment, and three exhibited grade I diastolic dysfunction. Because of the small number of patients in the cohort, a statistically significant calculation of group differences was unattainable. Recent clinical studies have shown the potential for adverse cardiac remodeling following TEVAR [14]. Hirotsu et al. concluded that TEVAR not only induces direct structural modifications of the stented aorta but also results in dynamic changes to the upward and stented aorta, for various reasons [15]. In their research, they showed that endograft and cardiac stretching became shortened by length stiffness, which was compensated by the stretching and changes of curvature in the aorta from diastole to systole compared to pre-TEVAR. In another study, researchers showed that TEVAR could increase cardiac stress during physical activity by reducing left ventricular contraction [16]. They analyzed echocardiograms of their study subjects and concluded that cardiac stress was generated because of the effect of TEVAR on the interaction between the heart and aorta. TEVAR has evolved as a safe and efficient treatment for multiple aortic pathologies and has resulted in promising long-term outcomes compared with OR. Changes in aortic length have been observed not only immediately but also within a year after the procedure [16]. New-onset of arterial hypertension after implanted stent graft was observed up to 35 % in previously nonhypertensive patients in other studies [17].

Limitations

This study was based on a small sample size with retrospective design, which may affect the generalizability of the results. Further multicenter studies with a larger cohort and precise algorithm of examination PWV, NT-proBNP-levels and echocardiography are needed to further investigate cardiovascular complications following TEVAR for TBAI.

Conclusions

Young patients with TBAI treated with TEVAR should be screened during the follow-up period for adverse cardiovascular complications caused by increased aortic stiffness. Measuring the PWV is a reliable, non-invasive method for early detection and risk stratification.

Electronic supplementary material

The electronic supplementary material (ESM) is available with the online version of the article at https://doi.org/10.1024/0301-1526/a000858

ESM 1. Echocardiographic parameters in the TEVAR and healthy control groups (Table).

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