

Predictors of false lumen thrombosis in type B aortic dissection treated with TEVAR

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Background: Thoracic endovascular aortic repair (TEVAR) offers a less invasive treatment option in type B aortic dissection (TBAD) patients and its value has been demonstrated in acute and chronic dissection patients. Total false lumen thrombosis (FLT) is associated with better long-term outcome in these patients, however, this is not obtained in all patients. The purpose of this study was to investigate predictors of FLT.

Methods: We retrospectively investigated patients who underwent TEVAR for a type B dissection in a large referral center between 2005 and 2012. All patients with a CT angiogram (CTA) obtained preoperatively, postoperatively and after one year of follow-up were selected for analysis. Volume measurements and several morphologic characteristics were analyzed for all scans using Aquarius iNtuition software (TeraRecon, San Mateo, Calif, USA). Multivariate logistic regression analyses were used to study the influence of these characteristics on FLT.

Results: Of 132 patients that received TEVAR for an aortic dissection, 43 patients (mean age, 60.3±14.2; 30 male) met our inclusion criteria, of whom 16 (37%) developed full FLT after 1 yr of follow-up. Multivariate logistic regression showed that side branch involvement [odds ratio (OR), 0.03; 95% confidence interval (CI), 0.00-0.92; P=0.045] and a total patent false lumen (FL) at presentation (OR, 0.01; 95% CI, 0.00-0.58; P=0.027) were associated with decreased complete FLT. Volumetric data showed significantly more reduction of the thoracic false lumen in FLT patients compared with non-FLT (-52.3% vs. -32.4%; P=0.043) and also a tendency of less volume increase in the abdominal segment (-5.0±37.5 vs. 21.8±44.3; P=0.052).

Conclusions: Patients admitted with type B dissection and branch vessel involvement or a patent entry tear after TEVAR are less likely to develop FLT and aortic remodeling during follow-up. These findings suggest that these patients may require a more extensive procedure and more intensive follow-up to prevent long-term complications.

Keywords: Type B aortic dissection; TEVAR; endovascular; false lumen thrombosis



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Introduction

Type B aortic dissection (TBAD) is a potentially life threatening cardiovascular event, which is associated with significant morbidity and mortality (1,2). Uncomplicated TBAD patients have traditionally been managed medically, while complications like aortic rupture, mesenteric ischemia, limb ischemia, uncontrolled hypertension and

refractory pain mandate direct surgical intervention (3,4). Thoracic endovascular aortic repair (TEVAR) has replaced conventional open surgery as it is associated with lower morbidity and mortality, and it is currently the first-line treatment option in many acute and chronic dissections (5-7). During these procedures, the proximal tear is covered by a stent graft to re-establish normal antegrade blood flow

in the true lumen (TL). By excluding perfusion of the false lumen (FL), thrombosis is induced and regression of the thrombus will eventually result in aortic remodeling (8-10).

Recent studies have shown that FL thrombosis (FLT) and aortic remodeling are associated with better long-term outcomes and is considered as one of the primary outcome measures for TEVAR (8-10). A patent FL after TEVAR, comparable to those treated medically, can lead to aneurysmal dilatation and potential rupture. The clinical significance of FLT and aortic remodeling has recently been emphasized, as it is associated with better five-year survival (11). Despite these promising results, the primary mortality and the number of reinterventions remains high in TEVAR patients, which can be mainly attributed to periprocedural complications (4,7). By enhancing the understanding regarding which subset of patients are most likely to benefit from such procedures, a better assessment can be made not only to decide on which patient we should intervene, but also to determine the type and extent of the procedure. In this study, we sought to identify pre- and postoperative morphologic characteristics that are associated with FLT, in order to predict outcomes in patients who undergo TEVAR for TBAD.

Methods

All patients treated at our institution between December 2005 and July 2012 for a TBAD with TEVAR were considered eligible for this study. Patients were included based on the availability of preoperative, postoperative and a CT angiogram (CTA) at 1-year follow-up. Type A aortic dissections, intramural hematomas, penetrating aortic ulcers and previous descending aortic replacement were considered exclusion criteria. Demographic information, operative details and follow-up data were retrospectively obtained. Institutional review board (IRB) approval was obtained (IRB # 12020).

Data collection

CT scan data were transferred to a workstation with Aquarius iNtuition (TeraRecon, San Mateo, Calif, USA) for semiautomatic volume measurement with a center lumen line method. Automated segmentation, which determines boundaries around voxels with a similar intensity, was used and manually adjusted in order to select the TL and total aortic lumen. Subsequently, the TL and overall aortic volume were calculated automatically. All volumes were analyzed for both the descending aorta, from the left subclavian

artery (LSA) to the celiac artery, and abdominal aorta, from the celiac trunk to the aortic bifurcation. FL volume was obtained by subtracting the TL volume from the total aortic volume on both the abdominal and thoracic levels. Changes in volumes were calculated by the following formula: [(volume at 1-year follow-up – volume postoperative)/volume postoperative] ×100. All diameter measurements were performed perpendicular to the center lumen line.

Pre-operative and post-operative morphologic predictors

The configuration of the dissection was classified as straight or spiral, with a spiral dissection defined as a dissection where the middle of the FL changed position at least 90 degrees, compared to the TL, at any level between the LSA and the aortic bifurcation. The LSA, celiac artery, superior mesenteric artery, left and right renal artery, inferior mesenteric artery and both iliac arteries were investigated with the use of transverse, coronal, sagittal and multiplanar reconstructions, whether side branches of the aorta were involved on the baseline CTA scan. Side branch involvement was considered when the FL partially or completely vascularized one or more of these branches. The location of the FL was classified as present in the inner or outer curve of the aortic arch. The aortic diameter at the level of the proximal and distal landing zone, the maximum diameter of the descending aorta, length of the dissection and distance from the beginning of the dissection to the LSA were measured.

On the postoperative scan, we quantified the following measurements and predictors: total treatment length, distance from proximal stentgraft to the LSA, distance from distal landing zone and the celiac artery, the presence of patent entry tears, FL patency, retrograde perfusion of the FL, and the presence of endoleaks.

Study end-points

Full FLT, defined as the absence of contrast in the FL, was objectified on CTA obtained after 1-year of follow-up.

Analysis

Descriptive statistics are reported as mean ± standard deviation (SD) or median and interquartile range (IQR). Statistical analyses were performed using the χ^2 -test for categorical variables and t-test for continuous variables. Predictors of FLT were explored using univariate logistic

Table 1 Baseline characteristics of 43 TEVAR patients

	Full lumen thrombosis (n=16)	No full lumen thrombosis (n=27)	P value
Gender (male)	9 (56.2)	21 (77.8)	0.137
Age (mean \pm SD; years)	66.3 \pm 8.9	56.7 \pm 15.5	0.008
Acute dissection (<14 days)	10 (62.5)	16 (59.3)	0.834
Hypertension	16 (100.0)	21 (77.8)	0.042
Diabetes	1 (6.2)	3 (11.1)	0.569
Ever smoked	9 (56.3)	21 (77.8)	0.137
Hyperlipidemia	7 (43.8)	8 (29.6)	0.348
Renal insufficiency	0 (0)	3 (11.1)	0.167
Obesity	5 (31.2)	8 (29.6)	0.911
COPD	1 (6.2)	1 (3.7)	1.000
Peripheral vascular occlusive disease	2 (12.5)	4 (14.8)	0.832
Cerebrovascular disease	2 (12.5)	6 (22.2)	0.688
Congestive heart failure	1 (6.2)	1 (3.7)	1.000
Previous aortic surgery	4 (2.5)	11 (40.7)	0.342
Medication			
Beta blocker	9 (56.2)	18 (66.7)	0.495
ACE-inhibitors	5 (31.2)	6 (22.2)	0.512
Aspirin	9 (56.2)	15 (55.6)	0.965
Clopidogrel	1 (6.7)	3 (11.1)	1.000

Values are expressed as n (%), unless otherwise indicated. TEVAR, Thoracic endovascular aortic repair.

regression analysis. Variables with a P value<0.1 were included for multivariate logistic regression to investigate independent predictors. Statistical analysis was conducted with SPSS software version 20.0 (SPSS Inc, Chicago, III, USA).

Results

Of 132 patients that received TEVAR for TBAD, 43 patients (mean age 60.3 \pm 14.2; 30 male) met our inclusion criteria, of which 16 (37%) developed FLT after 1 year of follow-up. Demographics showed that FLT-patients tended to be older (66.3 \pm 8.9 *vs.* 56.7 \pm 15.5; P=0.008) and had more frequently a history of hypertension (100% *vs.* 77.8%; P=0.042) while no differences were observed among acute TBAD (62.5% *vs.* 59.3%; P=0.834. *Table 1*).

Preoperative images showed that FLT patients presented more often with a dissection situated in the outer curvature of the aorta compared with non-FLT patients (56.2% *vs.* 88.9%; P=0.048; *Table 2*). FL status differed between groups, with 6.2% of the FLT-patient had a patent FL at presentation compared to 63% of the non-FLT patients

(P<0.001). Side-branch vessels were involved in 74.1% of the non-FLT patients compared to 31.2% of the FLT group (P value=0.006). Landing zone diameter, length of dissection, and total length of aorta were not predictive of FLT.

Operative indications and characteristics are summarized in *Table 3*. Aneurysmal dilatation or an aortic diameter >5.5 cm was most often the indication for TEVAR in both the acute and chronic setting. Only refractory pain was more frequently observed in FLT-patients. Coverage of the LSA was necessary in 12 patients (12.5% in FLT *vs.* 44.4% in non-FLT; P=0.031), with eight patients undergoing prior LSA revascularization. Other revascularization procedures included a stent in a visceral or iliac artery in eight patients and a fenestration between the true and FL in one patient.

Postoperative imaging showed that two-thirds of the FLT patients did not have a patent entry tear after the initial procedure, while almost 90% of the non-FT patients had one or more patent entry tears (P<0.001; *Table 4*). Complete lumen thrombosis was present in 62.5% of the FT patients at the post-operative scan. Endoleaks were more often present in non-FT patients, with two third of the non-FT patients presenting with retrograde filling of the FL. In

Table 2 Pre-operative morphologic predictors of 43 TEVAR patients

	Full lumen thrombosis (n=16)	No full lumen thrombosis (n=27)	P value
Inner curvature	9 (56.2)	24 (88.9)	0.048
Spiral dissection	6 (37.5)	12 (44.4)	0.655
Total patent false lumen at presentation	1 (6.2)	17 (63.0)	<0.001
Partial thrombosis	13 (81.2)	10 (37.0)	0.005
Saccular formation	2 (12.5)	3 (11.1)	1.000
Side branch involvement	5 (31.2)	20 (74.1)	0.006
Diameter proximal landing zone	34.4±3.7	33.6±4.1	0.424
Diameter distal landing zone	33.8±5.8	34.6±8.6	0.698
Max. diameter descending aorta	48.4±11.3	48.0±10.2	0.908
Length of aorta (mm)	385±44.9	407±39.4	0.117

Values are expressed as n (%), unless otherwise indicated. TEVAR, thoracic endovascular aortic repair.

Table 3 Operative indications and operations characteristics of 43 TEVAR patients

	Full lumen thrombosis (n=16)	No full lumen thrombosis (n=27)	P value
Refractory pain	5 (31.2)	2 (7.4)	0.041
Uncontrolled hypertension	2 (12.5)	3 (11.1)	0.891
Visceral or distal ischemia	0 (0.0)	2 (7.4)	0.265
Aortic rupture/Hematoma/effusion	1 (6.2)	4 (14.8)	0.397
Aneurysmal growth/Large aortic diameter	5 (31.2)	7 (25.9)	0.707
Chronic aneurysmal growth	4 (25.0)	6 (22.2)	0.835
Refractory pain	2 (12.5)	1 (3.7)	0.545
Acute extension/rupture	3 (18.8)	5 (18.5)	1.000
Number of stents	1.81±0.7	1.78±0.7	0.128
Proximal diameter stent graft [med; range]	34.3 [26-40]	33.4 [26-40]	0.507
Distal diameter stent graft [med; range]	33.4 [26-40]	32.9 [20-40]	0.659
LSA covered	2 (12.5)	12 (44.4)	0.031
Prior LSA revascularization	2 (100.0)	6 (50%)	0.688
Revascularization procedures	5 (31.2)	11 (40.7)	0.534
Spinal cord drainage	13 (81.2)	17 (63)	0.207

Values are expressed as n (%), unless otherwise indicated. LSA, left subclavian artery; med, median; TEVAR, thoracic endovascular aortic repair.

addition, FT-patients tended to have an increased treatment length (202±67.0 mm *vs.* 186.9±54.6 mm; P=0.101), which probably also resulted in the distal portion of stent graft being deployed closer to the celiac artery (63.4±52.3 mm *vs.* 108.3±59.1 mm; P=0.014).

Outcome multivariate logistic regression model

Multivariate logistic regression showed that side-branch

involvement [odds ratio (OR), 0.03; 95% confidence interval (CI), 0.00-0.92; P=0.045] and a total patent FL at presentation (OR, 0.01; 95% CI, 0.00-0.58; P=0.027; *Table 5*) were associated with decreased full FLT.

Outcome volumetric data

Volumetric data analyses showed that both subsets of patients had an increase of the thoracic TL volume and

Table 4 Post-operative CT findings of 43 TEVAR patients

	Full lumen thrombosis (n=16)	No full lumen thrombosis (n=27)	P value
Patent entry tear(s)	6 (37.5)	24 (88.9)	0.001
Endoleak present	5 (31.2)	19 (70.4)	0.013
None	11 (68.6)	8 (29.6)	0.027
Type Ia	1 (6.2)	0 (0)	
Type Ib	4 (25.0)	18 (66.7)	
Type II	(0)	1 (3.7)	
Thrombosis total stent length	12 (75.0)	8 (29.6)	0.005
Total thrombosis	10 (62.5)	1 (3.7)	<0.001
Birdbeak configuration	4 (25)	8 (32)	0.631
Diameter distal landing zone (mm)	34.7±5.6	36.5±10.2	0.453
Min diameter TL distal landing zone (mm)	23.1±5.2	20.7±5.1	0.162
Max diameter TL distal landing zone (mm)	27.8±3.7	26.9±4.9	0.564
Distance to LSCA (mm)	13.4±17.3	10.6±10.0	0.555
Distance to Celiac (mm)	63.4±52.3	108.3±59.1	0.014
Total treatment length (mm)	225.1±67.0	186.4±54.6	0.101

Values are expressed as n (%), unless otherwise indicated. LSCA, left subclavian artery; NA, not available; TEVAR, thoracic endovascular aortic repair; TL, true lumen.

Table 5 Multivariate logistic regression for predictor of false lumen thrombosis

Variables	Odds ratio (95% CI)	P value
Distance to celiac artery	0.98 (0.95-1.01)	0.106
Branch vessel involvement	0.03 (0.01-0.92)	0.045
Age of presentation	0.96 (0.85-1.08)	0.955
Male gender	0.23 (0.02-2.34)	0.234
Post operative patent entry tear	0.29 (0.01-6.18)	0.429
Total patent false lumen at presentation	0.01 (0.00-0.57)	0.027
Left subclavian artery coverage	0.26 (0.11-3.36)	0.257

decrease in FL volume after stent graft placement and during follow-up (*Figure 1*). Changes in TL volume were comparable for both groups, but we found a more significant reduction of the thoracic FL in FLT patients compared with non-FLT (-52.3% vs. -32.4% ; $P=0.043$; *Tables 6,7*) There was a tendency towards less volume increase in the abdominal segment. (-5.0 ± 37.5 vs. 21.8 ± 44.3 ; $P=0.052$)

Patient outcome

Mean follow-up was 2.7 ± 1.6 years, during which 21 patients required reintervention. In the non-FLT group, two

patients required open arch repair, one ascending and total arch replacement for retrograde type A aorta dissection and four patients required open repair for thoracoabdominal aorta aneurysms. Other reinterventions included proximal extension for type I endoleak, coil embolization for type II endoleaks and EVAR for abdominal aneurysm (*Table 8*).

Discussion

Acute TBAD is a cardiovascular catastrophe associated with high morbidity and mortality (1,2). According to current guidelines, medical treatment should be offered to those presenting with uncomplicated aortic dissection, while

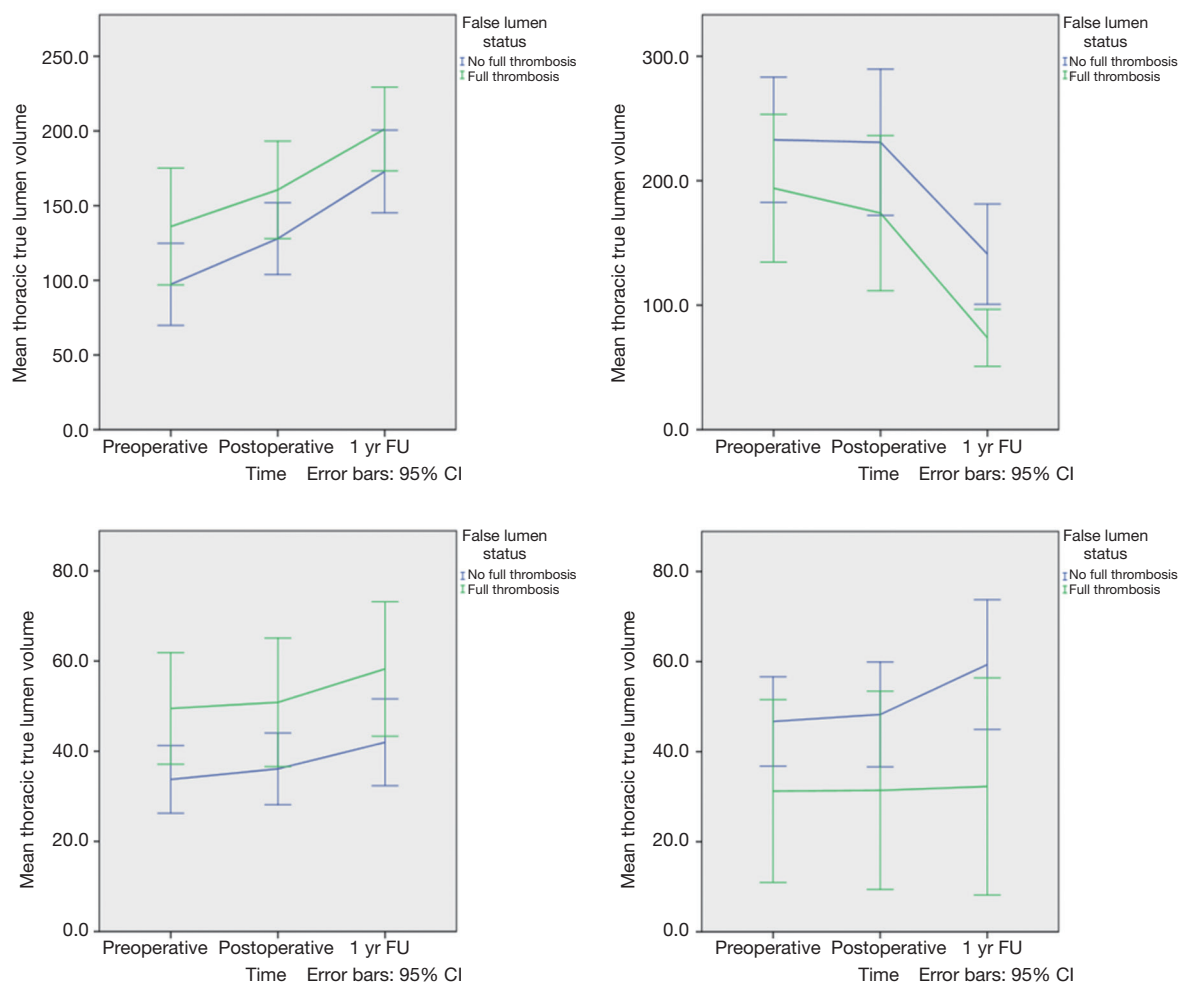


Figure 1 Volumetric measurement over time. FU, follow-up.

	Full thrombosis (n=16)			P value	No full thrombosis (n=27)			P value
	Preoperative	Post-operative	1-year		Preoperative	Post-operative	1-year	
TL volume thoracic	136.1±73.4	160.6±61.2	201.4±52.6	<0.001	97.3±69.4	127.9±60.8	172.9±69.9	<0.001
FL volume thoracic	193.9±111.5	174.0±116.1	73.8±43.0	<0.001	232.9±127.1	230.9±148.4	141.1±101.8	<0.001
TL volume abdominal	49.5±22.4	50.9±24.7	54.4±29.1	0.003	33.8±19.0	51.3±81.3	42.0±24.4	0.372
FL volume abdominal	31.2±36.7	31.4±38.1	30.1±41.1	0.657	46.7±25.0	48.3±28.8	59.3±36.4	0.006

TL, true lumen; FL, false lumen.

Table 7 Changes in volumes during follow-up calculated by the following formula (1 year follow-up data – postoperative/postoperative) ×100

	Full thrombosis (n=16)	No full thrombosis (n=27)	P value
TL volume thoracic	33.8±35.6	40.5±40.6	0.571
FL volume thoracic	-52.3±17.9	-32.4±43.4	0.043
TL volume abdominal	18.2±55.9	19.2±33.2	0.945
FL volume abdominal	-5.0±37.5	21.8±44.3	0.052

TL, true lumen; FL, false lumen.

Table 8 Early and midterm outcomes of 43 TEVAR patients

	Full lumen thrombosis (n=16)	No full lumen thrombosis (n=27)	P value
Early outcomes			
30-day mortality	0 (0)	0 (0)	1.000
Spinal cord ischemia	0 (0)	0 (0)	1.000
Stroke	2 (12.5)	1 (3.7)	0.545
Duration follow-up (years)	3.2±1.9	2.3±1.4	0.113
Endoleak	8 (50)	16 (59.3)	0.555
Reintervention	7 (43.8)	14 (51.9)	0.607
Late mortality	2 (12.5)	3 (11.1)	1.000

Values expressed as n (%), unless otherwise indicated. TEVAR, thoracic endovascular aortic repair.

TEVAR should be reserved for those patients presenting with malperfusion or aortic rupture (3,4). The recent long-term outcomes of the INSTEAD-xl trial have shown that TEVAR in uncomplicated acute TBAD is associated with better aortic remodeling and improved long-term aorta-specific survival compared to medical therapy alone (11). However, the drawbacks of TEVAR are not isolated to early mortality, but also include the number of reinterventions, which is relative high in TBAD compared to TEVAR in thoracic aortic aneurysms (5,7). FLT portends a better outcome in these patients, as persistent pressurization of the FL is associated with aortic related events like aortic dilatation and rupture. Via coverage of the entry tear and directing blood-flow to the TL, stent graft placement can induce FLT, promoting remodeling of the aorta and preventing late expansion and malperfusion (8,9). Our analyses showed that patients with a patent FL at presentation and branch vessel involvement are less likely to develop FLT and potential have a worse outcome.

Previous reports showed that FLT can be obtained in 40-90% of TBAD patients treated with TEVAR, which is relative high compared to our results of 32% (8-10,12,13). Our analyses showed that FLT at 1 year was predominantly obtained in patients with (partial) FLT at presentation.

These findings suggest that patients with high flow in the FL, as a result from sufficient in and outflow, are less likely to benefit from TEVAR. This observation is supported by the fact that 90% of the non-FLT patients still had a patent entry tear after TEVAR. This confirmed previous findings of Kusagawa *et al.*, who showed that remaining intimal tears in the thoracic aorta hamper shrinkage of the thoracic FL (14). However, outflow or retrograde perfusion of the FL can also be constituted by perfusion through branch vessels, which was confirmed by our multivariate analyses. Our findings showed that branch vessel involvement indicates that the presence of re-entries is predictive of reduced FLT and aortic remodeling, thus warranting additional endovascular interventions or even potential conversion to open surgical repair. Therefore, patients where all vessels originate from the TL might present a favorable subgroup.

The extent of distal coverage remains controversial since the primary focus of TEVAR in TBAD focusses on coverage of the proximal entry tear. The drawback of this approach is that it overlooks additional problems encountered more distally, such as additional re-entry tears, branch vessel involvement, or a collapsed TL. While we routinely place a stent graft over the proximal entry tear and reserve

deployment of additional grafts to those presenting with a major endoleak or TL collapse, the use of two-component devices might address these issues in a better fashion (15). With this technique, standardized TEVAR is supplemented with placement of uncovered stent over the entire length of the dissection in order to appose the dissected segment to the aortic wall thereby stabilizing the lamella, while preserving blood-flow to the visceral vessels and spinal cord. Indications for this technique are currently dynamic malperfusion and distal TL collapse. Our findings suggest that this technique might be extended to those patients with an entry-tear near the branch vessels or involvement of one the branch vessels. Some groups demonstrated that the petticoat technique stabilized the abdominal segment and was beneficial maintaining the overall aortic volumes, although they did not observe remodeling of the abdominal aorta (15-17). Nevertheless, before such techniques are implemented in practice in the United States, further studies are mandatory.

We observed favorable TL expansion and FL reduction for both group over time. In our analysis, we found significant more reduction of the thoracic FL in FT patients compared with non-FT (-52.3% vs. -32.4% ; $P=0.043$), while there also was a tendency to significant reduction in the abdominal aorta for FT-patients as continuous perfusion of the FL in the abdominal aorta can lead to a significant increase in abdominal aortic diameter. In the non-FT group, four patients required open surgical repair for type IV aneurysms during follow-up, showing the clinical importance of FLT over the entire length of the aorta. Previous reports showed that smaller preoperative TL volumes and smaller maximum descending aorta diameter were independent predictors of postoperative FT, which could not be confirmed by our analyses (18). However, the post-operative reduction of the FL was significantly more distinct in FT-patients, suggesting that if there is a tendency to remodeling, this will become apparent directly after surgery.

There are several limitations in the present study, including its retrospective design, single-center site and a small number of patients, which limits the power of the study. The short follow-up time might have influenced the results, as the benefits of TEVAR will likely become more prominent after 2 years. In addition, static CTA does not provide the correct visualization of this dynamic disease process. Future studies using 4D PC-MRI, which can both visualize and quantify flow characteristics in relationship to aortic expansion, will allow us to better understand this

dynamic disease in the future (19).

Conclusions

This study was performed in order to better define those patients that would most likely benefit from TEVAR following TBAD. Our study showed that patients with a fully patent FL at presentation and branch vessel involvement are less likely to develop full FLT and thus benefit from standard TEVAR. These patients may require a more extensive procedure, with more aortic coverage and more aggressive stent grafting of end organ vessels, such as the mesenteric and renal, to prevent long-term complications.

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