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## How does descending aorta geometry change when it dissects?

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### Abstract

**OBJECTIVES:** Thoracic endovascular aortic repair is the treatment of choice in complicated acute type B aortic dissection. How to infer predissection aortic diameter is not well understood. Our aim was to delineate changes in descending aortic geometry due to dissection.

**METHODS:** Five tertiary centres reviewed their acute aortic dissection type B databases containing 802 patients. All patients who had undergone computed tomography angiography less than 2 years before and immediately after aortic dissection onset were included. We compared the aortic geometry before and after the dissection onset.

**RESULTS:** Altogether 25 patients were included [median age 60 (first quartile 52, third quartile 72) years; 60% men]. In all except 1 patient, the maximum descending aortic diameter was less than 45 mm before aortic dissection onset. The largest increase in diameter induced by the dissection was observed in the proximal descending aorta 28.2 (25.1, 32.1) vs 34.6 (31.3, 39.1) mm (+6.4 mm; +23%;  $P < 0.001$ ). The thoracic descending aortic length increased after the dissection onset [253.3 (229.3, 271.9) vs 261.3 (247.9, 285.4) mm;  $P = 0.003$ ]. The pre-dissection aortic diameter of the proximal thoracic descending aorta was 7.9 (5.2, 10.7) mm larger ( $P < 0.001$ ) than the post-dissection area-derived true-lumen diameter and 2.5 (1.3, 6.1) mm larger than the maximum true-lumen diameter ( $P < 0.001$ ).

**CONCLUSIONS:** Type B aortic dissection increases the diameter, length and volume of the descending thoracic aorta. The predissection aortic diameter most closely resembles the post-dissection maximum diameter of the true lumen.

**Keywords:** Aorta • Aortic dissection • Thoracic endovascular aortic repair • Aortic surgery

### INTRODUCTION

Thoracic endovascular aortic repair (TEVAR) is the treatment of choice in patients presenting with a complicated acute aortic dissection starting distal to the left subclavian artery (Stanford type B dissection) [1]. The aim of the endovascular approach is closing the primary entry tear, directing blood flow to the aortic true lumen and inducing false-lumen thrombosis.

TEVAR has revolutionized aortic surgery in the last 2 decades [1–3]. Despite its many obvious advantages, such as less invasiveness, rapid treatment and availability, it may lead to serious complications such as retrograde type A dissection [4, 5], true-lumen rupture [6] or late fistulas between the aorta and the adjacent organs [7]. Choosing the correct size of the stent graft prosthesis plays a key role in preventing such adverse events. There is a

general agreement that, in the context of acute dissection, the oversizing factor, namely the difference in diameter between the aorta and the stent graft, should not exceed 5% or that the oversizing should be avoided [1]. However, what remains unclear is how to measure the diameter of a dissected descending aorta prior to selecting the stent graft size, because the dissection itself destabilizes the aortic wall architecture and can change its diameter immediately. There have been no data on humans delineating the aortic geometry change due to the onset of acute type B dissection.

We have already reported that acute dissection of the ascending aorta leads to an average increase in diameter of 30% [8]. The aim of this study was first to evaluate the aortic geometry changes induced by the dissection starting distal to the left subclavian artery and second, to suggest how to retrospectively

assess the predissection aortic diameter according to the diameter measured in the freshly dissected aorta. This retrospective, multicentric study was carried out by referring to computed tomography angiographs (CTAs) taken before and after the onset of acute aortic dissection type B.

## MATERIALS AND METHODS

### Study population

Five tertiary centres in Germany and Switzerland reviewed their acute aortic dissection type B databases constituting a total of 802 patients admitted due to acute dissection between 2001 and 2015. Inclusion criterion was CTA examinations available and done within 2 years before and immediately (up to 6 h) after the aortic dissection onset. Patients with dissection components in the aortic arch, known in the literature as non-A non-B aortic dissection or type B dissection with arch involvement [9] were also included. This retrospective study was approved by all the institutional review committees, and the need for informed consent was waived.

### Image analysis

Anonymized Digital Imaging and Communications in Medicine (DICOM) data on eligible patients were transferred to a core laboratory for further analysis. One observer blinded to patient-identifying information performed the image analysis using 3mensio Vascular Version 7.2 (3mensio Pie Medical Imaging BV, Maastricht, Netherlands).

A centre line was created from the aortic valve annulus to the aortic bifurcation. The thoracic descending aorta was divided into 4 segments by appropriate planes perpendicular to the centre line. Planimetric measurements yielding luminal area and maximum and minimum diameters via semi-automated polygonal border tracing were obtained by contour tracking at the following planes perpendicular to the centre line: the midascending aorta, the aortic arch at the innominate artery, between the left carotid and the subclavian arteries, at the left subclavian artery, the thoracic descending aorta at the 1st, 2nd and 3rd quartiles, at the celiac trunk and abdominal aorta at the renal arteries (proximal), the aortic bifurcation (distal) and between them (middle).

All reported diameters are diameters calculated according to the cross-sectional areas if not indicated otherwise. Minimum and maximum diameters were obtained to calculate the aortic ellipticity index, defined as the maximum diameter divided by minimal diameter, which was calculated for each plane. Circularity was defined as an ellipticity index  $\leq 1.1$ .

Length and volume were assessed in each aortic segment as follows: (i) the ascending aorta beginning at the aortic valve annulus and extending to the plane immediately proximal to the origin of the innominate artery; (ii) the aortic arch beginning immediately proximal to the origin of the innominate artery and extending to the plane immediately distal to the origin of the left subclavian artery; (iii) the proximal descending thoracic aorta beginning at the plane immediately distal to the left subclavian artery's origin and extending to the plane immediately proximal to the celiac trunk and (iv) the abdominal aorta beginning at the plane immediately proximal to the celiac trunk and extending to the aortic bifurcation. The length was defined as the centre line

distance between the aforementioned planes. Volumetric measurements were taken semi-automatically by marking the aorta's outer border every 22.5° in craniocaudal direction starting at the corresponding proximal and ending at the distal plane defining the analysed aortic segment. The total volume of each segment included the true lumen and the false lumen and was computed in reference to the aortic wall's outer surface.

We considered only segments involved in the dissection process to analyse the geometric changes due to type B dissection onset.

### Statistical analysis

Continuous data are reported as median (first quartile, third quartile), and categorical variables are reported as counts and percentages. To compare the continuous predissection versus post-dissection variables, the paired *t*-test was applied. When normality test failed, the signed rank test was employed. The statistical tests were 2-sided. A *P*-value of  $<0.05$  was considered statistically significant. All statistical calculations were performed using SigmaPlot 12 (Systat Software, San Jose, CA, USA).

## RESULTS

Of the 802 patients, we identified a total of 25 eligible patients. The median time interval between predissection and post-dissection CTAs was 12 (3, 21) months (14 patients with  $<1$  year). Clinical and demographic characteristics are summarized in Table 1. The descending thoracic aorta was dissected from the left subclavian artery to the celiac trunk in 21 (84%) patients and from the left subclavian to the aortic bifurcation in 11 (44%) patients. The most proximal entry was located in the 1st and the 2nd descending thoracic aorta quartiles in 17 (68%) patients. Figure 1 illustrates in detail the location of entries and the extent of dissection.

### Aortic diameters prior to type B dissection onset

Aortic diameters prior to type B dissection onset are presented in Supplementary Material, Table S1. Prior to dissection, the largest aortic dimensions were observed at the level of the ascending aorta with a median diameter of 37.7 (33.2, 41.2) mm. Median diameter of the descending thoracic aorta ranged between 27.2 (25.7, 31.1) mm and 30.5 (28.6, 34.0) mm measured in distal and proximal segments, respectively. The maximum descending aortic diameter measured 55.9 mm in 1 patient, and in all others, the descending aorta measured  $<45$  mm.

### Dissections change the aortic dimensions

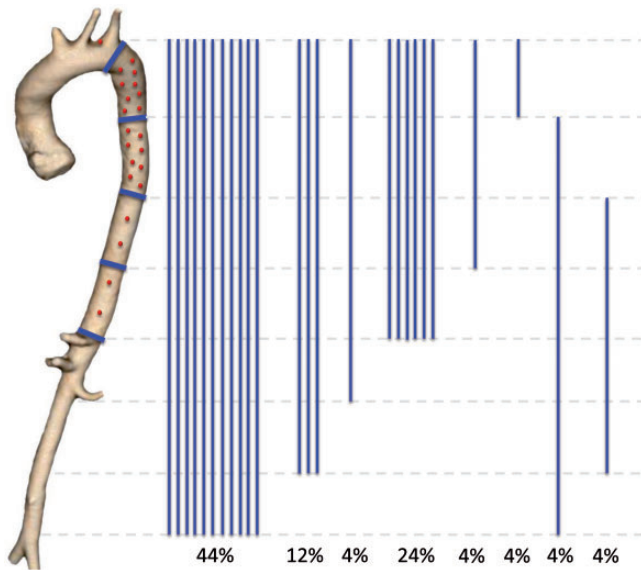
Thoracic aortic dimensions of primarily non-dissected segments were generally larger after type B dissection onset. The most pronounced increases in diameter and volume were observed in the proximal descending thoracic aorta (Fig. 2, Table 2). The ascending aorta was not affected by the dissection process, and its diameter [37.7 (33.2, 41.2) vs 36.7 (32.5, 41.4) mm;  $P=0.596$ ], length [99.6 (89.9, 108.1) vs 94.1 (85.6, 102.6) mm;  $P=0.202$ ] and volumes [105.2 (73.7, 140.6) vs 82.3 (63.1, 135.4) cm<sup>3</sup>;  $P=0.515$ ] were unchanged after type B dissection onset.

**Table 1:** Demographics and cardiovascular risk factors in patients with predissection aortic imaging

	(n = 25)
Demographics	
Age (years)	60.3 (51.5, 72.3)
Male gender	15 (60)
Race	
Caucasian	24 (96)
Black	1 (4)
Asian	0
Hispanic	0
Cardiovascular risk factors	
Hypertension	18 (72)
Dyslipidaemia	4 (16)
Diabetes	0
COPD	2 (8)
Renal failure	3 (12)
Current smoking	6 (24)
CAD	2 (8)
Family history of aneurysm or dissection	1 (4)
BAV	1 (4)

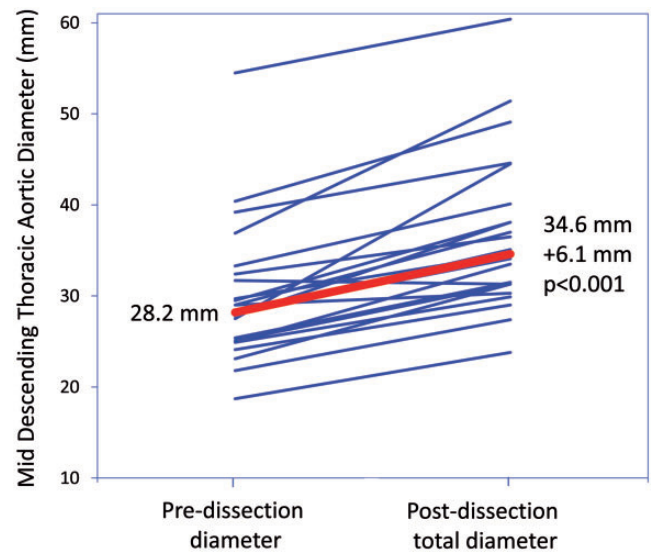
Continuous values are medians (first quartile, third quartile) and categorical values are n (%).

BAV: bicuspid aortic valve; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease.



**Figure 1:** The proximal entry location (red dots) and the extent of dissection (blue vertical lines). The descending thoracic aorta was dissected from the left subclavian artery to the celiac trunk in 84% of patients. The most proximal entry was located in the 1st and 2nd descending thoracic aorta quartiles in 68% of patients.

**Aortic arch.** The dissection process extended into the aortic arch in 10 patients (Table 3), in all of whom dissection components such as haematoma or dissection flap were identified in only the distal arch portion between the left carotid artery and the left subclavian artery. The proximal aortic arch diameter and aortic arch length did not change due to the dissection onset [33.5 (31.3, 39.0) vs 34.2 (31.8, 38.6) mm;  $P = 0.307$  and 41.6 (41.0,



**Figure 2:** Mid-descending thoracic aortic diameter change after acute Type B aortic dissection. Mid-descending thoracic aortic diameter increased 6.1 mm on average after dissection onset. Red indicates the overall change in median diameter.

44.0) vs 42.5 (38.3, 47.9) mm;  $P = 0.846$ ]. Aortic arch volume increased after the dissection onset [31.1 (29.3, 35.4) vs 39.1 (29.6, 51.5) cm<sup>3</sup>;  $P = 0.010$ ].

**Descending thoracic aorta.** The area and diameter of the mid-descending thoracic aorta increased from 640.6 (495.0, 837.4) to 938.1 (768.7, 1201.95) mm<sup>2</sup> (+46%;  $P < 0.001$ ) and from 28.2 (25.1, 32.1) to 34.6 (31.3, 39.1) mm (+23%;  $P < 0.001$ ), respectively (Figs 3 and 4, Table 2). After the onset of type B dissection, the descending aortic diameters equal to or exceeding 55 and 50 mm were observed in 4% (1 of 25) and 8% (2 of 63) of patients, respectively. We observed a similar although less pronounced increase in diameter in more distal aortic segments measured at the celiac trunk (+17%;  $P < 0.001$ ). The median aortic ellipticity ranged between 1.0 and 1.1 in all the descending thoracic aortic segments and was not influenced by the dissection onset.

The thoracic descending aortic volume increased [145.6 (122.5, 203.8) vs 244.4 (200.9, 303.3) cm<sup>3</sup>;  $P < 0.001$ , Supplementary Material, Fig. S1, Table 3] as did the length of the thoracic descending aorta [253.3 (229.3, 271.9) vs 261.3 (247.9, 285.4);  $P = 0.003$ , Table 3].

**Abdominal aorta.** The proximal, middle, and distal abdominal aorta diameter increased by medians +2.8 ( $P < 0.001$ ), +2.6 ( $P < 0.001$ ) and +3.2 ( $P < 0.001$ ) mm, respectively. The abdominal aortic length did not change significantly ( $P = 0.497$ , Table 3). The abdominal aortic volume increased on average by 19 cm<sup>3</sup> ( $P = 0.020$ ). The ellipticity ranged between 1.0 and 1.2 and did not change after the dissection onset.

## Predissection aortic diameter and post-dissection dimensions

**Predissection total versus post-dissection true-lumen diameter.** Predissection total aortic diameter measured at the left subclavian artery, 1st, 2nd and 3rd descending thoracic aortic

**Table 2:** Descending thoracic aortic diameter change after acute type B dissection onset

Aortic level	Predissection	Post-dissection	Δ	P-values
Left subclavian artery, n = 17	29.4 (27.8, 32.4)	32.8 (26.6, 40.1)	1.7 (0.3, 5.0)	0.012
Thoracic descending aorta				
1st quartile, n = 17	30.5 (28.6, 34.0)	36.6 (34.9, 43.3)	5.0 (3.7, 7.5)	<0.001
2nd quartile, n = 21	28.2 (25.1, 32.1)	34.6 (31.3, 39.1)	6.1 (5.1, 8.2)	<0.001
3rd quartile, n = 19	27.9 (24.5, 31.1)	32.4 (29.1, 33.5)	5.0 (2.8, 6.1)	<0.001
Celiac trunk, n = 22	27.2 (25.7, 32.5)	31.7 (29.7, 35.7)	3.8 (2.3, 5.3)	<0.001
Renal arteries, n = 21	22.9 (20.3, 25.3)	25.7 (22.9, 29.0)	3.0 (2.2, 4.3)	<0.001
Mid-abdominal aorta, n = 17	22.0 (18.8, 23.7)	24.6 (21.7, 27.4)	3.0 (2.0, 4.2)	<0.001
Aortic bifurcation, n = 15	22.1 (16.9, 24.6)	25.3 (21.0, 27.0)	3.2 (1.9, 4.3)	<0.001

Values are medians (first quartile, third quartile). Δ indicates pre- and post-dissection change.

**Table 3:** Aortic geometry change after type B dissection onset

	Predissection	Post-dissection	Δ	P-values
Ascending aorta, n = 20				
Centre line length (mm)	99.6 (89.9, 108.1)	94.1 (85.6, 102.6)	-2.0	0.202
Total volume (cm <sup>3</sup> )	105.2 (73.7, 140.6)	82.3 (63.1, 135.4)	-0.1	0.515
Aortic arch, n = 10				
Centre line length (mm)	41.6 (41, 44)	42.5 (38.3, 47.9)	0	0.846
Total volume (cm <sup>3</sup> )	31.1 (29.3, 35.4)	39.1 (29.6, 51.5)	+5.7	0.010
True-lumen volume (cm <sup>3</sup> )		33.8 (27.0, 37.9)		
False-lumen volume (cm <sup>3</sup> )		4.75 (3.5, 8.6)		
Descending thoracic aorta, n = 19				
Centre line length (mm)	253.3 (229.3, 271.9)	261.3 (247.9, 285.4)	+7.4	0.003
Total volume (cm <sup>3</sup> )	145.6 (122.5, 203.8)	244.4 (200.9, 303.3)	+91.6	<0.001
True-lumen volume (cm <sup>3</sup> )		95.9 (68.3, 130.9)		
False-lumen volume (cm <sup>3</sup> )		157.2 (81.6, 176.9)		
Abdominal aorta, n = 14				
Centre line length (mm)	156.2 (135.8, 161.8)	155.2 (128.1, 167.1)	+2.8	0.497
Total volume (cm <sup>3</sup> )	62.2 (56.6, 75.4)	81.4 (61.4, 90.2)	+16.7	0.020
True-lumen volume (cm <sup>3</sup> )		36.7 (27.7, 50.2)		
False-lumen volume (cm <sup>3</sup> )		30.5 (14.5, 55.6)		

Values are medians (first quartile, third quartile). Δ indicates pre- and post-dissection change. Ascending aorta dimensions were evaluated in all patients with available computed tomography angiography allowing volumetric analysis. In all other segments, only patients with dissection process involving the analysed segment were included.

quartiles was on average 1.7 (0.0, 3.4 mm;  $P = 0.038$ ), 7.9 (5.2, 10.7 mm;  $P < 0.001$ , Fig. 4), 9.2 (3.1, 10.6 mm;  $P < 0.001$ ) and 8.0 (4.4, 10.0 mm;  $P < 0.001$ ) larger than the corresponding true lumen of the dissected aorta, respectively. Predissection total aortic diameter in the 1st quartile of the descending thoracic aorta differed by 2.5 (1.3, 6.1) mm compared with the maximum diameter of the post-dissection true lumen [30.5 (28.6, 34.0) vs 28.5 (23.8, 30.9);  $P < 0.001$ , Fig. 5].

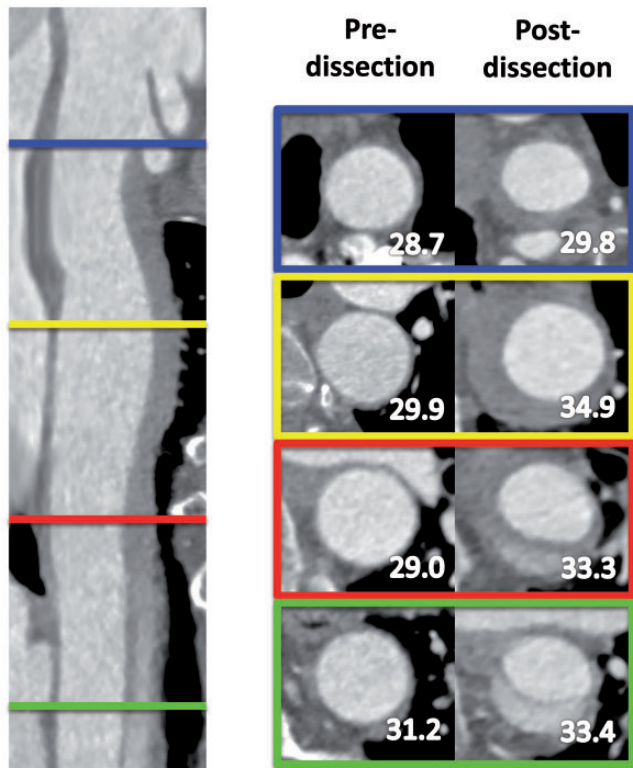
**Predissection thoracic descending versus post-dissection aortic arch diameter.** Predissection total aortic diameter measured at the left subclavian artery, 1st, 2nd and 3rd descending thoracic aortic quartiles was on average 4.3 (0.8, 5.7 mm;  $P < 0.001$ ), 3.4 (1.3, 5.1 mm;  $P = 0.709$ ), 5.4 (2.2, 6.9 mm;  $P = 0.017$ ) and 5.2 (3.3, 8.1 mm;  $P < 0.001$ ) smaller than the post-dissection total aortic diameter between the left carotid and the left subclavian arteries, respectively.

## DISCUSSION

TEVAR has radically changed the therapeutic strategies for pathologies of the descending thoracic aorta (e.g. aneurysms and aortic dissection). In patients presenting with a complicated acute type B aortic dissection, currently, TEVAR represents a valuable option to cover the entry tear and restore the flow into the true lumen [10]. The decision on the stent graft size in patients with acute type B dissection is critical to treatment outcomes. There is little consensus on how to assess the aortic diameter in the setting of acute dissection and whether the true lumen or the true-lumen and false-lumen diameters measured together represent the predissection true aortic diameter most accurately.

This study is the first to address the changes in aortic geometry after an acute onset of aortic dissection type B in humans by means of CTA. Our study findings can be summarized as follows:



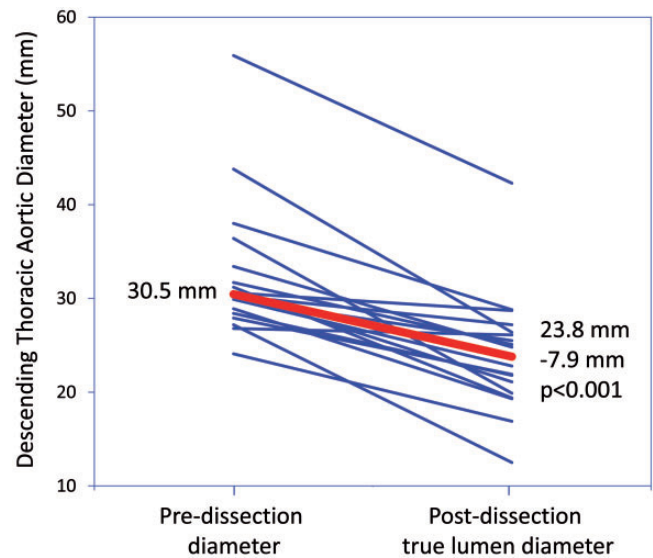


**Figure 3:** Descending thoracic aortic diameter change after acute type B aortic dissection. Pre- and post-dissection CT angiography of a 60-year-old female patient. Centerline rendered image of the dissected descending thoracic aorta and cross-sectional images in the distal aortic arch (blue), 1st (yellow), 2nd (red) and 3rd (green) quartiles of descending thoracic aorta. Area-derived diameters are provided.

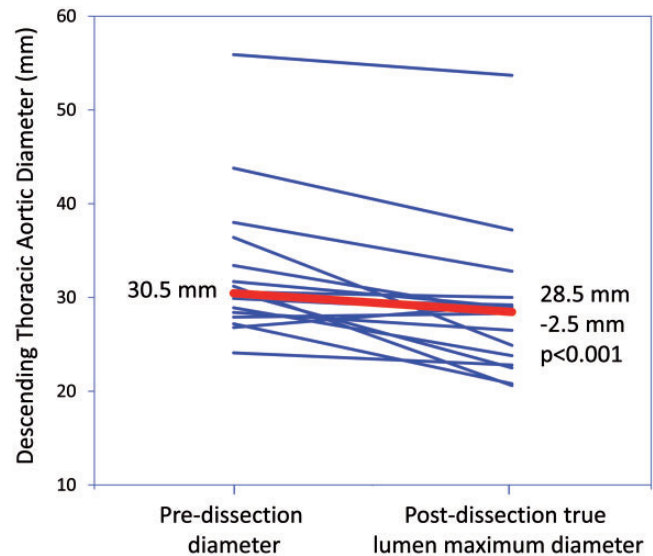
- i. Acute aortic dissection leads to an immediate, significant, mid-descending thoracic aortic diameter increase of 6 mm (+23%).
- ii. Predissection aortic diameter of the proximal thoracic descending aorta is on average 7 mm larger than the post-dissection area-derived true-lumen diameter and 2 mm larger than the maximum true-lumen diameter.

### Relationship with previous studies

To the best of our knowledge, no research had been conducted in humans to quantify the aortic geometry changes occurring immediately after the onset of a type B aortic dissection. Okuno *et al.* [11] observed a trend towards an increase in the descending aortic diameter after an induced dissection in a porcine model (from  $10.9 \pm 2.9$  mm to  $12.9 \pm 3.8$  mm). Neri *et al.* [12] measured the perimeter of the intimal flap in type A dissection patients and calculated the predissection aortic diameter by assuming that the circumference of the true lumen resembles the predissection total diameter. Our group assessed the diameter change in the ascending aorta due to dissection onset in a study of 63 patients via predissection and post-dissection imaging [8]; we observed the greatest diameter increase in the ascending aorta, whereas a dissected sinus of Valsalva did not lead to major geometric changes. The acute changes in the descending thoracic aorta due to dissection in humans have not been addressed until now.



**Figure 4:** First quartile descending thoracic aortic diameter: pre-dissection total vs post-dissection true lumen diameter. Pre-dissection total aortic diameter measured at the 1st descending thoracic aortic quartile was on average 7.9 mm larger than corresponding true lumen of dissected aorta. Red indicates the overall change in median diameter.



**Figure 5:** First quartile descending thoracic aortic diameter: pre-dissection total vs post-dissection true lumen maximal diameter. The pre-dissection aortic diameter resembles most closely the true lumen's post-dissection maximum diameter. Red indicates the overall change in median diameter.

### Aortic diameter in patients developing acute dissection type B

Aortic dilation and aneurysms are well-described risk factors for developing an acute aortic dissection [13, 14]. However, the rate of predissection aneurysm is lower than generally believed. In a study of 343 consecutive acute ascending aortic dissection patients, we modelled the predissection diameter and demonstrated that more than 60% had had non-dilated aortas before the onset of dissection and that only 3% would have fulfilled the criteria for elective ascending replacement to

prevent aortic dissection [15]. In this investigation, we observed that only 1 patient with a descending aortic aneurysm (maximum diameter 56 mm) developed an acute type B dissection. The median diameter in all other patients measured 30 mm; there was just 1 descending aorta measuring over 45 mm. The normal proximal descending aortic diameter ranges between 24 mm and 30 mm [16]. These findings highlight the fact that the dissection process may occur in aortas of normal diameter. However, this study was not designed to determine the incidence of normal size versus large aortas in patients developing acute type B dissection. The very low number of patients with aortic aneurysm prior to type B dissection onset may result from the fact that patients with larger aortas on initial computed tomography scan would have undergone aortic repair, which would have eliminated their risk of acute type B dissection and automatically excluded them from this study.

### Aortic geometry changes after dissection onset

Aortic dissection destabilizes the integrity of the aortic wall. Before a dissection occurs, all 3 aortic layers (intima, media and adventitia) contribute to aortic stability and distensibility. The aortic dissection begins with a tear in the inner layers. When a tear occurs, blood flows into the wall separating the adventitia from the media and the intima layers, or dividing the media into 2 layers, thereby weakening the aortic wall. From this moment on, the adventitia is the only layer resisting pulsatile blood pressure and preventing aortic rupture. A dissection in the ascending aorta leads to an immediate diameter increase of 30%, revealing the adventitia's remarkable elasticity. We hypothesized that a dissection in the descending aorta may lead to similar changes and noted an immediate diameter increase of 23% in the mid-descending thoracic aorta and 12% in the abdominal aorta. The greatest diameter increase in the proximal segments and the lowest one in the more distal segments might be due to an anatomical barrier such as visceral arteries, which may hinder the expansion of the total aortic diameter, and to less blood flow in the more distal aorta than in its proximal portion.

### Inferring predissection aortic diameter

The stent graft diameter used for acute type B dissection should be large enough to prevent stent graft migration, close the primary entry and/or expand the true aortic lumen. It should not be too large, because excessive oversizing can lead to serious complications. In a study on retrograde aortic dissection after TEVAR, both the indication of TEVAR for aortic dissection and the device oversizing (OR 1.14 per 1% increase in oversizing,  $P < 0.0001$ ) were significantly associated with the risk of retrograde aortic dissection [4]. Stent graft-induced new entries were associated with an oversizing ratio of 1.86 ( $P = 0.018$ ) [2], and there is a correlation between oversizing and secondary organ fistulation after TEVAR [7].

In our investigation, we made 2 critical observations that must be considered in type B dissection patients referred for TEVAR, namely that (i) the descending aortic diameter increases after the onset of dissection and (ii) the true lumen of the dissected aorta is smaller than the predissection total aortic diameter. To keep the dissection

flap from rupturing and creating a new entry, the stent graft size should not exceed the predissection aortic diameter. Following this rule, the true lumen can be restored to its former diameter without over-distension, resulting in a media-to-adventitia reapproximation but usually not reconnection. In this study, we suggest how the predissection descending aortic diameter can be inferred. One way is to add 8 (5, 11) mm to the true-lumen diameter measured in the 1st quartile of dissected aorta. Another way is to subtract 3 (1, 5) mm from the diameter measured between the left carotid artery and the left subclavian artery. Finally, the maximum diameter of the post-dissection true lumen is most similar to the predissection diameter. We suggest not to oversize more than 5–10% according to the predissection aortic diameter if landing in the acutely dissected aorta.

### Limitations

Median time between the 2 CTAs was 12 months. The aortic diameter increases slowly during life [17]. However, no change in the non-dissected ascending aortic diameter during this time indicates that the diameter increase measured in dissected aortic segments was due to dissection and not natural aortic growth. The suggestions on how to model the predissection total aortic diameter according to the post-dissection measurements should be carefully considered, because diameters vary greatly from 1 patient to another. Furthermore, patients with dissection components in the aortic arch (non-A non-B dissection) were also included. Because dissection components in non-A non-B dissection patients were found only in the distal aortic arch portion (between the left carotid artery and the left subclavian artery), the mechanism of dissection might be similar to the regular type B dissection. Finally, this study is limited by relatively small number of patients and potential selection bias.

### CONCLUSIONS

The aortic dissection type B changes the geometry of the descending thoracic aorta, increasing its diameter, length and volume. The diameter of the true lumen in the dissected aorta is less than the aortic diameter measured prior to the dissection onset. The predissection aortic diameter most closely resembles the true lumen's post-dissection maximum diameter.

### SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

### ACKNOWLEDGEMENTS

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**Conflict of interest:** none declared.

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