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Predictor of residual false lumen remodelling of thoracic aorta after acute type A aortic dissection

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Abstract

Objectives

Some patients achieve complete recovery through false lumen remodelling in the descending aorta after surgery for acute type A aortic dissection. We quantitatively analysed true lumen shape in early postoperative stages to investigate its relationship with false lumen remodelling in later stages.

Methods

We examined 90 surgical patients between January 2007 and December 2016. Seven points of the descending aorta were assessed from the sixth (T6) to the twelfth (T12) vertebral levels. True lumen shape was evaluated at early stages, and false lumen remodelling at 1 year after surgery as the endpoint. The parameters of shape evaluation comprised the first principal components of elliptic Fourier analysis , minor diameter ratio and area ratio of the true lumen to the descending aorta, and number of contact points on the true lumen wall at early stages.

Results

Univariate analysis detected significant differences in the first principal components, minor diameter ratio and area ratio at the all thoracic vertebral levels ($p < 0.001$). The number of contact points displayed significant differences at the T6–T11 levels ($p < 0.05$). Multivariate logistic analysis revealed the first principal components was the most significant predictor at the T6–T9 levels.

Conclusions

The quantitative evaluation of true lumen shapes in early postoperative stages after surgery for acute type A aortic dissection can serve as a viable predictor for false lumen remodelling in later stages. Furthermore, the first principal components could serve as a more astute predictor than other quantitative parameters according to multivariate analysis.

Keywords: acute type A aortic dissection, elliptic Fourier analysis, false lumen remodelling

Introduction

Acute type A aortic dissection (ATAAD) has a high mortality rate of 10%–35% following central repair operations (1), which are primarily performed for saving lives. In addition, some patients whose lives have been saved can experience an enlargement of a residual false lumen in the descending aorta in late postoperative stages and require a re-operation (2–5). Conversely, approximately 30% of cases achieve complete recovery of dissection through false lumen remodelling, including enlargement of the true lumen and shrinkage of the false lumen (6). After surgery for ATAAD, the primary tear is resected, which can greatly alter the haemodynamics of the blood flow within the false lumen. With the re-entry serving as the main influx pathway of blood into the false lumen, the blood flow becomes retrograde towards the central side of the false lumen beyond the re-entry (7). However, it remains unclear as to how the blood flow from the re-entry in the false lumen affects false lumen remodelling in the late postoperative stages. Therefore, we considered it necessary to establish an index for early prediction of the actual process of false lumen remodelling in the late postoperative stages.

Previous studies have reported the following factors to be causes of enlarged aneurysms after surgery for ATAAD: patent false lumen, large initial aortic diameter, large false lumen relative to the true lumen, involvement of the supra-aortic branches and combination with malperfusion syndrome, Marfan syndrome and young age (6–9). Moreover, the true lumen shape has recently attracted attention as a predictor of late-stage enlarged aneurysms (10, 11). In a previous study, we used computed tomography (CT) in early postoperative stages to clinically demonstrate that a circular-type true lumen can cause thrombosis in the false lumen in late postoperative stages, thereby advancing false lumen remodelling. In contrast, a dent-type true lumen keeps the false lumen open in late postoperative stages and thus does not induce false lumen remodelling. These clinical and empirical risks of aneurysm enlargement and rupture in late postoperative stages have also been reported in the literature (10).

Elliptic Fourier analysis is a quantitative shape evaluation technique utilised in diverse fields (12, 13), and we substantiated its usefulness in a previous study focusing on acute type B aortic dissection (ATBAD) (14).

In the present study, we performed an elliptic Fourier analysis of the true lumen shape in early stages following ATAAD surgery. The subjects were divided into two groups depending on the presence/absence of false lumen remodelling and were compared to determine the first primary component value (PC1) for the true lumen in early postoperative stages. Other parameters of quantitative shape analysis such as the minor diameter ratio of the true lumen to the descending aorta (DTL), area ratio of the true lumen to the descending aorta (ATL) and number of contact points in the true lumen wall (CP) were also evaluated in the early postoperative stage. Finally, we compared the data of these evaluative parameters.

Materials and Methods

We analysed retrospectively the CT scan data of patients with acute type A aortic dissection admitted at six referral medical institutions between January 2007 and December 2016.

Contrast-enhanced CT images obtained at early postoperative stages and at 1 year after surgery were used for evaluation. The study involved ATAAD patients with an open false lumen in whom early postoperative CT images showed the dissection extending all the way below the diaphragm and it was possible to capture new CT images 1 year later.

The analysis was conducted at seven points between the sixth thoracic vertebral level (T6) and the twelfth thoracic vertebral level (T12).

Contrast-enhanced CT images obtained at early postoperative stages were used to evaluate the true lumen shape.

91

92 **Preparation of images used for the quantitative evaluation of the true lumen shape**

A central line was drawn on the descending aorta based on early postoperative contrast-enhanced CT images. A stretch view was created so that the true lumen could be extracted perpendicularly (15), and this image was then used to analyse true lumen shape (Figure 1A).

93

94 **Elliptic Fourier analysis**

95 Images obtained from the stretch view were delineated using two-dimensional image analysis
96 software and then projected onto an x–y plane to be subjected to Fourier series development.
97 With the harmonic divisor number of the standardised elliptic Fourier descriptor set at 20, the
98 true lumen shape was represented by 80 numerical sequences. This signifies that as opposed to
99 univariate indices such as true lumen thickness and wall curvature, shape evaluation using the
100 standardised elliptic Fourier descriptor provides 80 times more information. The larger is the
101 harmonic divisor number, the more precise a shape is reproduced; however, the shape
102 contribution ratio of each descriptor diminishes, making it difficult to interpret the significance

(12–14). Hence, we focused on a few significant evaluation indices and performed principal component analysis (PCA), which is a technique for multivariate analysis. PCA is a technique based on the covariance matrix, with the eigenvector in the figure representing an index that characteristically retains the algebraic structure of the vector space in the multivariate PCA.

The data of the extracted true lumen shapes were collected and analysed using the elliptic Fourier analysis software SHAPE (16) and subjected to PCA.

PCA was performed until the fifth principal component wherein the contribution rate became approximately 80% at the respective vertebral levels. The correlation between each principal component value calculated based on elliptic Fourier analysis and the presence/absence of false lumen remodelling was assessed.

Measurement of length and area

The length and area of each specimen were measured using Osirix MD v.9.0 software.

The length was represented as the minor diameter ratio of the true lumen to the descending aorta (DTL) at the corresponding level. DTL was calculated as the minor diameter of the true lumen divided by the descending aorta diameter at the same thoracic vertebral level.

The area ratio of the true lumen at each thoracic vertebral level to the descending aorta (ATL) at the corresponding level was calculated. ATL was calculated as the area of the true lumen divided by the descending aorta area at the same thoracic vertebral level. (Figure 2A, B).

Evaluation of the number of contact points on the true lumen wall

To quantitatively evaluate the circular- and dent-type lumens reported in previous literature, true lumen specimens were divided into groups depending on whether the number of contact points with the line segment drawn on the true lumen wall was one or two. The specimens with one contact point were classified as circular type and those with two contact points as dent type (Figure 2C-1, C-2).

Definition of false lumen remodelling

CT images taken at 1 year after surgery were compared with those taken immediately after surgery.

The criteria for false lumen remodelling were as follows: (i) thrombosis and shrinkage of the false lumen by ≥3 mm compared with that immediately after surgery and (ii) disappearance of the false lumen if the CT image taken immediately after surgery showed a false lumen diameter of ≤3 mm.

Computerised tomography examination

The early postoperative contrast-enhanced CT images used in the analysis were taken within 14 days after surgery and captured the area between the aortic arch and aortic bifurcation. The slice thickness of horizontal sections ranged from 2.5 to 5.0 mm. A non-ionic contrast agent was used.

The stretch view of the descending aorta was prepared using a workstation (Ziostation2, Ziosoft, Tokyo, Japan) (Figure 1A). Early postoperative CT data were extracted from seven points at each thoracic vertebral level. We selected smaller DTL images of the early phase and the delayed phase for analysis.

Contrast-enhanced CT or non-contrast CT images were taken at 1 year after surgery.

All CT images were evaluated and assessed based on the consensus between two investigators.

Statistical analysis

Continuous variables and the presence/absence of false lumen remodelling were assessed using the t-test and discrete variables and the presence/absence of false lumen remodelling using chi-squared test. The t-test was used to compare the presence/absence of false lumen remodelling for continuous variables, and chi-squared test was used for discrete variables. A multiple logistic regression analysis with the presence/absence of false lumen as dependent variable was performed to determine significant false lumen remodelling factors. The continuous variables as independent variables were divided into two groups based on a cut-off point that provided the maximum sum of sensitivity and specificity in a receiver operating characteristic (ROC) area under the curve (AUC). All analyses were performed using IBM® SPSS® Statistics Version 22 software.

Results

Of the 314 patients who had undergone surgery for ATAAD at the six medical institutions between January 2007 and December 2016, the study assessed 90 patients who had an open false lumen with a dissection that extended all the way to the diaphragm according to CT images taken immediately after surgery and in whom it was possible to capture CT images at 1 year after surgery. Supplementary Table 1 shows the patients' backgrounds. The average age was 64.1 ± 12.5 years, with men accounting for 46.7% of patients.

PC1 had the highest mean contribution rate at 58.6%, followed by PC2 at 11.7%, PC3 at 6.5%, PC4 at 5.0% and PC5 at 3.5%. Accordingly, PC1, which had the highest contribution rate, was used in the analysis.

Supplementary Table 2 lists the cases divided into two groups depending on the presence/absence of false lumen remodelling. The PC1, DTL, ATL and single CP were noted in these cases. PC1, DTL and ATL exhibited a correlation with false lumen remodelling at every thoracic vertebral level. Regarding the DTL and ATL, significantly higher values were reached at remodelled areas. In PC1, remodelled areas exhibited significantly higher values at the T6, 7, 9 and 11 levels and significantly lower values at the T8, 10 and 12 levels. Figure 3 shows the visualisation of PC1 evaluation in the present study. The true lumen wall was arcuate in the remodelled areas but convexed towards the aortic wall in the non-remodelled areas. When the number of CP was one, significant false lumen remodelling was observed between T6 and T11. The consecutive variables PC1, DTL and ATL were subjected to ROC analysis to calculate the AUC and cut-off point (Supplementary Table 3). The cut-off point was 0.01–0.05 for PC1, 0.52–0.6 for the DTL and 0.39–0.55 for the ATL. The AUC was 0.733–0.837 for PC1, 0.778–0.873 for the DTL and 0.778–0.837 for the ATL. The specimens were divided into two groups based on the cut-off point and subjected to multivariate logistic regression analysis.

Supplementary Table 4 shows the results of the multivariate analysis. It indicates that PC1 is a significant predictor for false lumen remodelling compared with the other factors [T6: odds ratio (OR), 13.8; 95% confidence interval (CI), 2.7–71.3; p = 0.002; T7: OR, 7.0; 95% CI, 1.8–27.9; p = 0.006; T8: OR, 5.2; 95% CI, 1.5–17.9; p = 0.009; and T9: OR, 7.3; 95% CI, 1.9–27.7; p = 0.003].

Discussion

In the present study, PC1 calculated using elliptic Fourier analysis, DTL, ATL and single CP were factors that correlated with late postoperative false lumen remodelling after ATAAD surgery at almost all areas in the descending aorta. In particular, PC1 was demonstrated to be the most relevant factor for late postoperative false lumen remodelling in the proximal and median thoracic descending aorta regions. This finding proves that shape evaluation of the true lumen at an early postoperative stage after ATAAD surgery can serve as a predictor for the fate of the false lumen at a later stage.

After the primary entry is resected, blood flow into the false lumen is dependent on the blood flow from the re-entry and is affected by multiple factors such as the entry size and number as well as the number of branches extending from the false lumen (11, 17, 18). Therefore, any single factor alone is not sufficient as a predictor for the prognosis of the false lumen in late postoperative stages. Meanwhile, the true lumen shape is determined by the pressure gap relative to the false lumen, with the crushed shape of the true lumen indicating a higher pressure within the false lumen than that within the true lumen. A report suggested that a pressure increase in the false lumen is a factor for late postoperative enlargement of the false lumen (19); thus, the true lumen shape may be a viable predictor for false lumen remodelling in late postoperative stages. Tolenaar et al. demonstrated that a dent-type true lumen in ATBAD precedes the enlargement of the false lumen in late postoperative stages (10). Moreover, Sato et al. quantified the actual degrees of dents in the true lumen using elliptic Fourier analysis and reported that the more dented the true lumen is the more likely it is that the false lumen will become enlarged at later stages (14).

In the present study, we measured DTL and ATL based on CT images and assessed the correlation with false lumen remodelling in late postoperative stages. This study was planned because a large false lumen relative to the true lumen has been suggested to be a factor for false lumen enlargement in late postoperative stages following ATAAD surgery (7). The number of CP was contrived as a means to easily and specifically represent the abstract concept of ‘dent-type’ of the true lumen. Either parameter was shown to significantly correlate with false lumen remodelling in the univariate analysis.

Elliptic Fourier analysis was reported by Kuhl (20) and is a technique capable of representing all closed curves of any shape. The coefficient matrix obtained from this analysis as multidimensional data is subjected to multivariate analyses such as PCA to downscale the dimension. By doing so, one can interpret shapes more simply and in greater detail. The fact that shapes can be reconstructed from data through inverse analysis signifies the abundance of inherent shape-related information involved in this technique. This analysis technique has enabled the quantification of shapes themselves, thus enabling the comparative evaluation of factors such as DTL, ATL and the number of CP. These findings should aid in determining the most relevant factors for false lumen remodelling in late postoperative stages.

The calculated PC1 values exhibited significant differences in the univariate analysis. Multivariate analysis proved that PC1 was more significantly involved in false lumen remodelling in the proximal and median descending aorta regions than other factors in the late postoperative stages.

However, elliptic Fourier analysis is associated with several issues such as its complexity, the time-consuming nature of shape analysis and the fact that the calculated principal component values are relative values. Hence, the values themselves are altered when the population is changed. In this evaluation, the values represented different conditions depending on the thoracic vertebral levels. Because the analytic values observed at our hospital were dissimilar to those at other institutions, the cut-off values listed in this report are not applicable to other institutions as is.

In that sense, the DTL, ATL and number of CP are more useful as simple and easy clinical indicators, which serve as significant parameters in univariate analyses.

Based on the cut-off point calculated in this analysis, DTL of ≥0.65 and the ATL of ≥0.55 should be good for predicting false lumen remodelling in late postoperative stages.

Very few attempts have been made to evaluate the prognosis of a residual false lumen after ATAAD surgery. This is mainly because only approximately 6.8%–14.8% of cases require a re-operation due to enlargement of the peripheral false lumen below the descending aorta following ATAAD surgery (2–5), implying that it is not a significant clinical problem. Compared with ATBAD, ATAAD has a better prognosis because the primary entry is resected through surgery and blood flow into the false lumen is reduced. Focusing on this pathological condition, we propose that these parameters should be used as indices for predicting the effects of stent graft treatment, which covers primary entry for ATBAD (21).

In recent years, the use of stent graft treatment for ATBAD has been gaining ground, with its superiority over medical management having been demonstrated for complicated cases. Consequently, this treatment modality has become the primary choice (22). In particular, the rate of aortic remodelling is exceptionally high following thoracic endovascular aortic repair

(TEVAR) (23, 24). The INSTEAD-XL trial revealed a significantly higher 5-year survival rate in the stent graft group (25). In aortic dissection, stent graft treatment is performed to cover the entry, with the covered areas highly likely to become thrombotic (26).

When a longer stent is placed, the thrombotic lesion becomes wider. Qing et al. reported that grafts longer than 162 mm induced significantly more aortic remodelling in the late postoperative stages than the ones shorter than 162 mm (27).

However, although longer grafts are more likely to induce aortic remodelling, an increased risk of paraplegia has also been pointed out. Matsuda et al. observed paraplegia in 6% of TEVAR cases, including dissecting aortic aneurysms, and attributed this percentage to the long length of stent grafts placed in these patients (28). To shorten the placement length of stent grafts as much as possible, we attempted to obstruct the primary entry in ATBAD using a stent graft and then immediately evaluate the true lumen shape at the periphery of the placed stent graft to predict the range of false lumen remodelling in the late postoperative stages. In this study, CT was performed to evaluate the true lumen shape at 1 week after surgery. By performing true lumen shape evaluation in the descending aorta using transesophageal echocardiography during the surgery, it might be possible to determine the need for additional treatment based on evaluation of the true lumen shape immediately after the placement of a stent graft that covers the primary entry.

Limitations

The sample size of this study was small so it can be affected by the effects of selection bias.

The aortic wall is soft and the shape of the true lumen changes over time during the acute phase of aortic dissection.

We captured images on two or more occasion after injecting a contrast agent and selected specimens with a lower minor diameter ratio to minimise the impact of chronological mismatch. However, the difficulty in completely matching chronological phases with this analysis might have influenced the results.

Conclusions

The quantitative evaluation of the true lumen shape in early stages after ATAAD surgery was shown to correlate strongly with false lumen remodelling in late postoperative stages in terms of the PC1, DTL, ATL and number of CP. In multivariate analysis, PC1 could serve as a more astute predictor of false lumen remodelling compared with other quantitative parameters.

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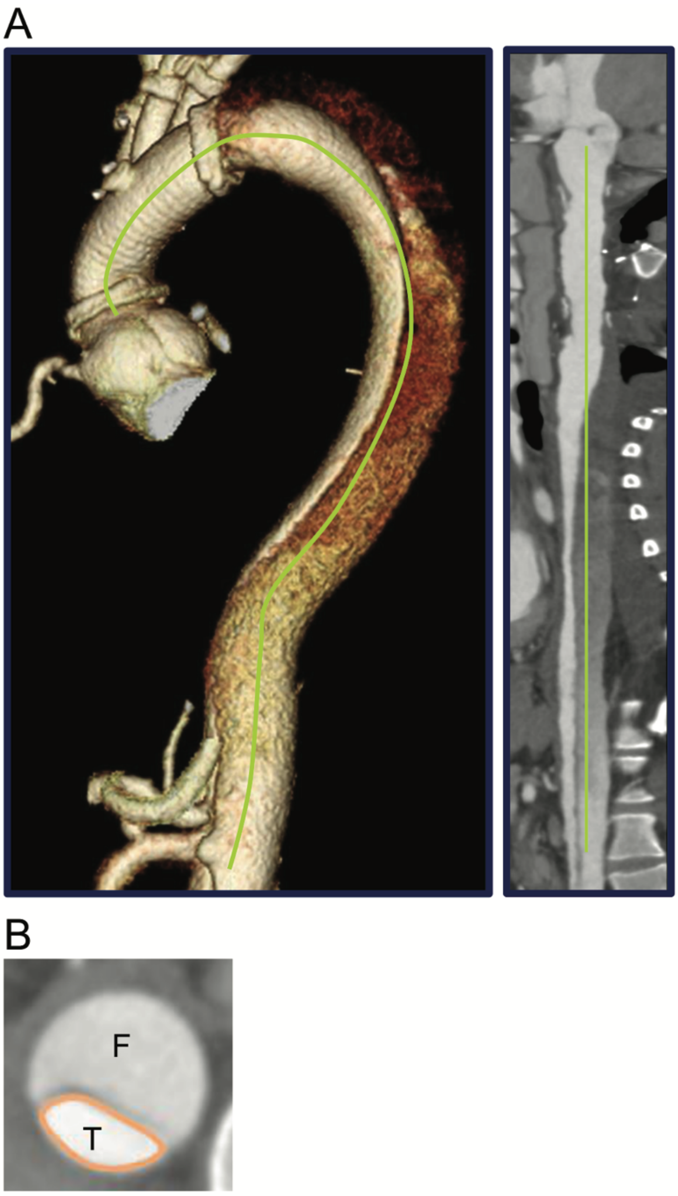
Figure 1

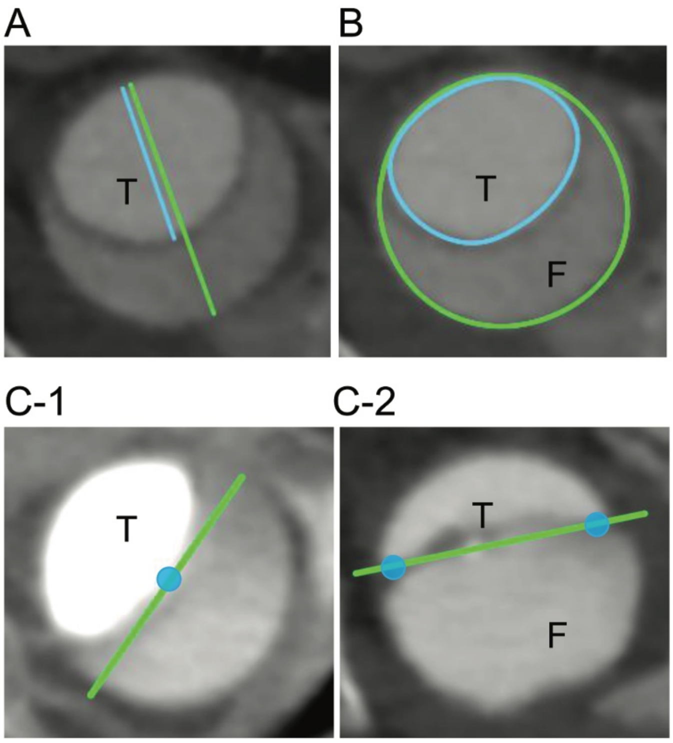


A. Stretched multiplanar reformation of the aorta was constructed by the ziostaton.(A)

B. Thoracic vertebral (T) 6, 7, 8, 9, 10, 11 and 12 levels were selected to extract the contour of the true lumen shape for the elliptic Fourier analysis.

T, true lumen; F, false lumen

Figure 2. Evaluation of the parameters used in shape analysis



A. Minor diameter ratio of the true lumen to the descending aorta (blue/green)

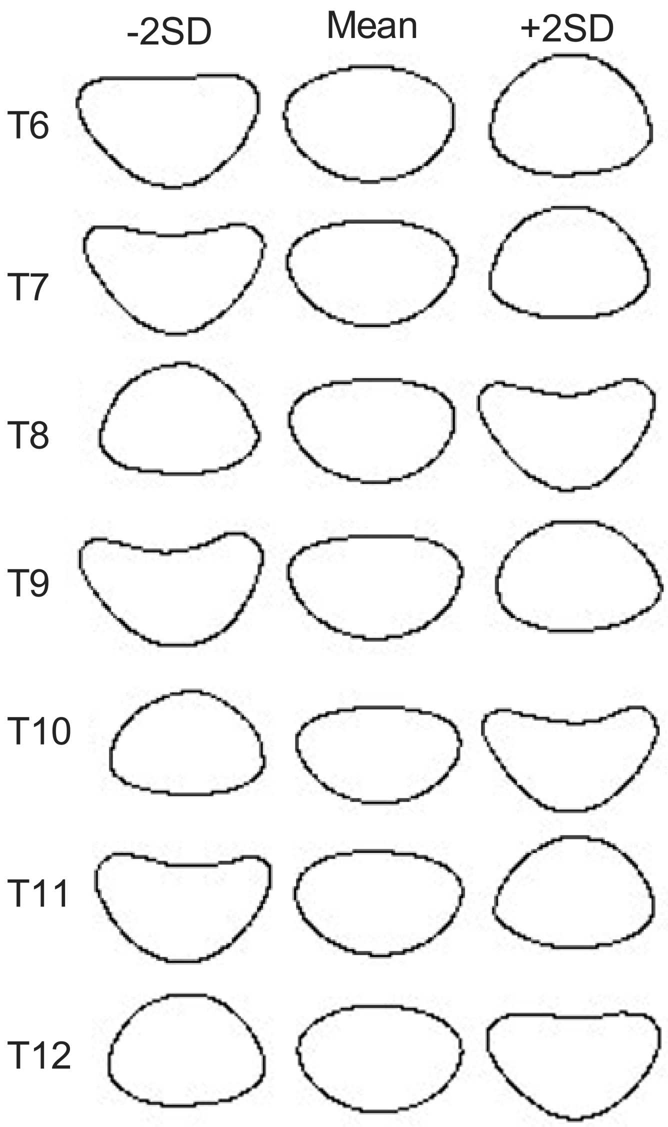
B. Area ratio of the true lumen to the descending aorta (blue/green)

C-1 Single contact point of true lumen flap (blue point)

C-2 Double contact points of true lumen flap (blue point)

T, true lumen; F, false lumen

Figure 3. Mean of the true lumen shape ± 2 SD variations along the first principal component at each thoracic vertebral level


-2SD
Mean
+2SD
T6
T7
T8
T9
T10
T11
T12

Supplementary Table1. Demographic and clinical characteristics of patients

Variables	**Mean ± SD** **No. (%) or (N = 90)**
Clinical background	
Age	64.1 ± 12.5
Male sex	42 (46.7)
Marfan syndrome	2 (2.2)
Hypertension	70 (77.8)
Diabetes	4 (4.4)
Chronic haemodialysis	1 (1.1)
Procedure	
Ascending aorta replacement	28 (31.1)
Total arch replacement	62 (68.9)
Concomitant procedure	
CABG	2 (2.2)
David procedure	3 (3.3)

CABG, coronary artery bypass grafting; SD, standard deviation

Supplementary Table 2. Relationships between the presence/absence of aortic remodelling at 1 year after surgery and various image evaluation parameters

T6	Presence	Absence	P-value
	N = 56	**N = 34**	
PC1	0.03 ± 0.03	−0.06 ± 0.07	<0.001
DTL	0.63 ± 0.2	0.40 ± 0.2	<0.001
ATL	0.56 ± 0.2	0.33 ± 0.2	<0.001
Single CP	53 (94.6)	22 (64.7)	<0.001
T7	**N = 51**	**N = 39**	
PC1	0.04 ± 0.05	−0.05 ± 0.08	<0.001
DTL	0.64 ± 0.2	0.37 ± 0.14	<0.001
ATL	0.57 ± 0.2	0.31 ± 0.1	<0.001
Single CP	46 (90.2)	21 (53.8)	<0.001
T8	**N = 49**	**N = 41**	
PC1	−0.04 ± 0.06	0.05 ± 0.08	<0.001
DTL	0.62 ± 0.2	0.40 ± 0.1	<0.001
ATL	0.55 ± 0.2	0.32 ± 0.1	<0.001
Single CP	44 (89.8)	22 (53.7)	<0.001
T9	**N = 44**	**N = 46**	
PC1	0.05 ± 0.04	−0.05 ± 0.09	<0.001

DTL	0.63 ± 0.2	0.38 ± 0.1	<0.001
ATL	0.55 ± 0.2	0.32 ± 0.1	<0.001
Single CP	40 (90.9)	23 (50.0)	<0.001
T10	**N = 41**	**N = 49**	
PC1	−0.05 ± 0.05	0.04 ± 0.09	<0.001
DTL	0.64 ± 0.2	0.41 ± 0.2	<0.001
ATL	0.58 ± 0.2	0.31 ± 0.1	<0.001
Single CP	36 (87.8)	27 (55.1)	0.001
T11	**N = 36**	**N = 54**	
PC1	0.05 ± 0.03	−0.03 ± 0.09	<0.001
DTL	0.69 ± 0.2	0.44 ± 0.1	<0.001
ATL	0.59 ± 0.2	0.33 ± 0.1	<0.001
Single CP	33 (91.7)	37 (68.5)	0.018
T12	**N = 32**	**N = 58**	
PC1	−0.03 ± 0.03	0.02 ± 0.07	<0.001
DTL	0.70 ± 0.2	0.47 ± 0.1	<0.001
ATL	0.63 ± 0.2	0.37 ± 0.1	<0.001
Single CP	29 (90.6)	46 (79.3)	0.24

T, thoracic vertebral level

DTL, minor diameter ratio of the true lumen to the descending aorta

ATL, area ratio of the true lumen to the descending aorta

CP, contact point on the true lumen wall

Supplementary Table 3. Cut-off points and AUC for PC1, area ratio and minor diameter ratio at each level

	PC 1		DTL		ATL	
vertebral level	Cut-off point	AUC	Cut-off point	AUC	Cut-off point	AUC
T6	0.01	0.837	0.58	0.821	0.45	0.826
T7	0.02	0.812	0.55	0.873	0.48	0.837
T8	0.03	0.811	0.58	0.806	0.54	0.778
T9	0.02	0.816	0.55	0.825	0.55	0.78
T10	0.03	0.766	0.64	0.778	0.39	0.817
T11	0.05	0.741	0.52	0.819	0.44	0.828
T12	0.04	0.733	0.61	0.804	0.48	0.836

T, thoracic vertebral level

AUC, area under curve; PC, principal component

DTL, minor diameter ratio of the true lumen to the descending aorta

ATL, area ratio of the true lumen to the descending aorta

Supplementary Table 4 Multivariate analyses comparing aortic remodelling based on morphological parameters at 1 year postoperatively

T6	B	Odds ratio	95% CI	P-value
PC1	2.625	13.8	2.7–71.3	0.002
DTL	1.535	0.2	0.0–1.3	0.101
ATL	1.445	4.2	0.9–19.6	0.064
Single CP	−0.059	0.9	0.1–7.2	0.954
Th7				
PC1	1.948	7	1.8–27.9	0.006
DTL	3.007	20.2	2.9–141.9	0.002
ATL	0.335	1.4	0.2–8.2	0.71
Single CP	−0.246	0.8	0.2–3.6	0.751
T8				
PC1	1.65	5.2	1.5–17.9	0.009
DTL	0.967	2.6	0.4–17.5	0.318
ATL	1.122	3.1	0.4–25.5	0.298

Single CP	0.724	2.1	0.6–7.7	0.283
T9				
PC1	1.994	7.3	1.9–27.7	0.003
DTL	0.64	1.9	0.4–9.7	0.441
ATL	1.796	6	0.8–44.4	0.078
Single CP	0.777	2.2	0.5–9.9	0.315
T10				
PC1	0.994	2.7	0.7–10.7	0.156
DTL	2.807	16.6	1.8–155.1	0.014
ATL	0.99	2.7	0.7–9.9	0.137
Single CP	-0.04	1	0.2–4.2	0.957
T11				
PC1	0.817	2.3	0.6–8.9	0.243
DTL	0.904	2.5	0.5–11.6	0.252
ATL	2.023	7.6	1.8–31.9	0.006
Single CP	0.147	1.2	0.2–6.3	0.865
T12				
PC1	1.226	3.4	0.9–	0.064

			12.5	
DTL	2.321	10.2	2.3–46.0	0.003
ATL	2.091	8.1	2.2–29.2	0.001
Single CP	−0.553	0.6	0.1–3.6	0.553

B, regression coefficient; CI, confidence interval

T, thoracic vertebral level

DTL, minor diameter ratio of the true lumen to the descending aorta

ATL, area ratio of the true lumen to the descending aorta

CP, contact point on the true lumen wall

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