Predictor of false lumen thrombosis after thoracic endovascular aortic repair for type B dissection

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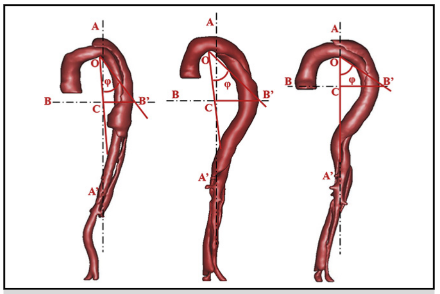
ABSTRACT

Objective: Thoracic endovascular aortic repair of type B aortic dissection initiates thrombosis in the false lumen, which eventually results in aortic remodeling. We aimed to determine whether the false lumen thrombosis rate (FLTR) after thoracic endovascular aortic repair can be accurately predicted by an index that expresses the degree of aortic arch angulation.

Methods: The geometry of 48 patients with acute type B aortic dissection (mean age, 48 years) after thoracic endovascular aortic repair was reconstructed from postoperative computed tomography images. We introduced a novel angle—the degree of question mark (φ)—to indicate the aortic morphology. Moreover, how aortic angulation influenced the FLTR was investigated based on hemodynamic parameters. Finally, a predicted mathematical model relating FLTR to aortic angulation was proposed, and 10 patients were chosen to validate the model.

Results: The degree of question mark shape was shown to negatively correlate with FLTR (n = 38; $P < .001$; $R = -0.661$), and the linear relationship model was created as follows: FLTR (%) $= -1.955 \times \varphi + 168.24$ ($R^2 = 0.437$; $P < .001$). In addition, the net flow rate to the false lumen significantly increased with the increase of the degree of the question mark shape of the aorta. Furthermore, the difference and concordance of the proposed prediction model were perfectly validated in the remaining 10 patients using paired-sample *t* test and the concordance correlation coefficient.

Conclusions: The size of the question mark shape may be a good predictor for FLTR of acute type B aortic dissection following thoracic endovascular aortic repair. The higher the degrees of the question mark, the less likely it was to form a complete thrombus. (J Thorac Cardiovasc Surg 2020;160:360-7)



A novel angle—the degree of question mark—to indicate aortic morphology.

Central Message

The false lumen thrombosis rate of type B aortic dissection after TEVAR can be predicted by the degree of the question mark shape, which accounts for the morphology of both the aortic arch and the descending aorta.

Perspective

There is a strong correlation between question mark degree and false lumen thrombosis rate. The application of the results is beneficial to stent design and clinical follow-up.

See Commentaries on pages 368 and 369.

Thoracic endovascular aortic repair (TEVAR) is an effective treatment option for patients with type B aortic dissection (TBAD)[1] who have undergone a systematic diagnostic modality for the selection of patients.[2] The primary aim of TEVAR is to cover the proximal tear, physically expand the true lumen while decreasing the size of the false lumen (FL), avoid perfusion of the FL, and induce thrombosis in the FL, which eventually results in aortic remodeling.[3-5] Moreover, it is suggested that complete thrombosis in the FL protects the patient from the ongoing risk of

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Supported by the Sichuan Province Science and Technology Support plan (grant No. 2016FZ0107), the National Natural Science Foundation of China (grant No. 81601462), and the Sichuan Provincial Health and Family Planning Commission Scientific Research Project (Key Research Projects) (grant No. 16ZD013).

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Received for publication March 18, 2019; revisions received July 6, 2019; accepted for publication July 14, 2019; available ahead of print Aug 25, 2019.

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0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2019.07.091

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Abbreviations and Acronyms

CCC	= concordance correlation coefficient
CFD	= computational fluid dynamics
CTA	= computed tomography angiography
FL	= false lumen
FLTR	= false lumen thrombosis rate
TBAD	= type B aortic dissection
TEVAR	= thoracic endovascular aortic repair

aneurysmal degeneration, leading to beneficial outcome.[5-8] Therefore, a predictive index for the development of late FL thrombosis rates (FLTR) may help in determining a therapeutic strategy for TBAD.

Until now, study on FLTR after TEVAR has mainly focused on the role of the remaining re-entry tears, but controversial findings have been reported. For example, a larger distance between remaining tears has been related to both unfavorable FLTR and the promotion of complete thrombosis in the FL following TEVAR,[9-11] which indicates that there are other contributing factors to FLTR.

Morphologic assessment of the aortic arch, particularly its angulation, has been widely adopted in the evaluation of the treatment outcome of aortic diseases, including TBAD. Bruse and colleagues[12] pointed out that the aortic arch shape after successful aortic coarctation repair correlates with left ventricular function. De and colleagues[13] suggested that abnormal morphology of the aortic arch in patients with Turner syndrome is a risk factor for hypertension. In addition, acute aortic curvature was suggested to be associated with endoleaks after stent-graft repair of complicated TBAD.[14]

Previous studies have used a number of definitions of arch morphology; however, these have only defined the curvature of the aortic arch.[15-18] In clinical practice, we observe that almost all TBAD patients following TEVAR not only have a tortuous aortic arch, but also a tortuous descending aorta that results in a question-mark-shaped aorta. In other words, the aorta in a TBAD patient takes the shape of a question mark, where the descending aorta is twisted below the apex of the aortic arch and the tail of the aortic arch is away from the apex of the aortic arch. In addition, the question mark degree of the aorta varies greatly from patient-to-patient, and an increase in the degree of question mark is indicative of a more distorted thoracic aorta. Therefore, we proposed a new definition of the angulation of the aortic arch using the degree of the question mark, which can be quickly and easily judged using computed tomography angiography (CTA) images. Moreover, it is well known that the geometry will decide the hemodynamic parameters, factors important to thrombosis formation in the FL.[19] Therefore, we considered that there might be a correlation between the thrombosis rate of the FL in TBAD patients following TEVAR and the well-known degree of angulation of the aortic arch (ie, the question mark shape).

The purpose of the present study was to evaluate the predictors of FLTR, and to determine whether the FLTR after TEVAR can be accurately predicted by an index that expresses the degree of aortic arch angulation.

METHODS

This study was conducted in accordance with the principles of the Declaration of Helsinki and met the requirements of the medical ethics. The Ethical Review Committee of the West China Hospital of Sichuan University (Chengdu, Sichuan, China) approved this research. Patient approval and informed consent were waived because the study was purely observational, retrospective in nature, and used anonymized data.

Study Population

The detailed CTA images of all patients with acute TBAD who underwent TEVAR at the West China Hospital, Sichuan University, between November 2014 and May 2017 were collected. Acute TBAD was defined as the onset of symptoms <2 weeks.[20] We excluded patients without re-entry tears and patients who only had 1 re-entry tear because this will result in either the rapid formation of a complete thrombus in the FL, or the immediate disappearance of FL after the operation.[21] Finally, this study included 48 patients with 2-year follow-up (Figure 1). The TEVAR procedures were performed in a hybrid operating room under general anesthesia

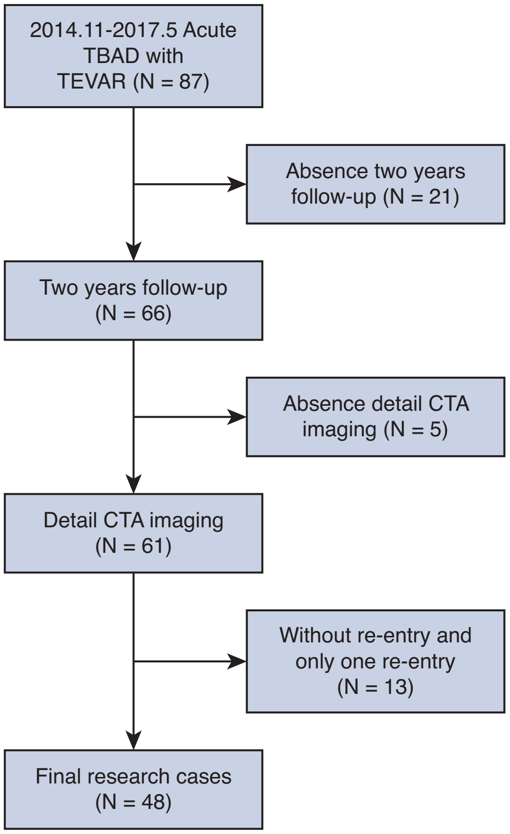


FIGURE 1. Flowchart for study inclusion. *TBAD*, Type B aortic dissection; *TEVAR*, thoracic endovascular aortic repair; *CTA*, computed tomography angiography.

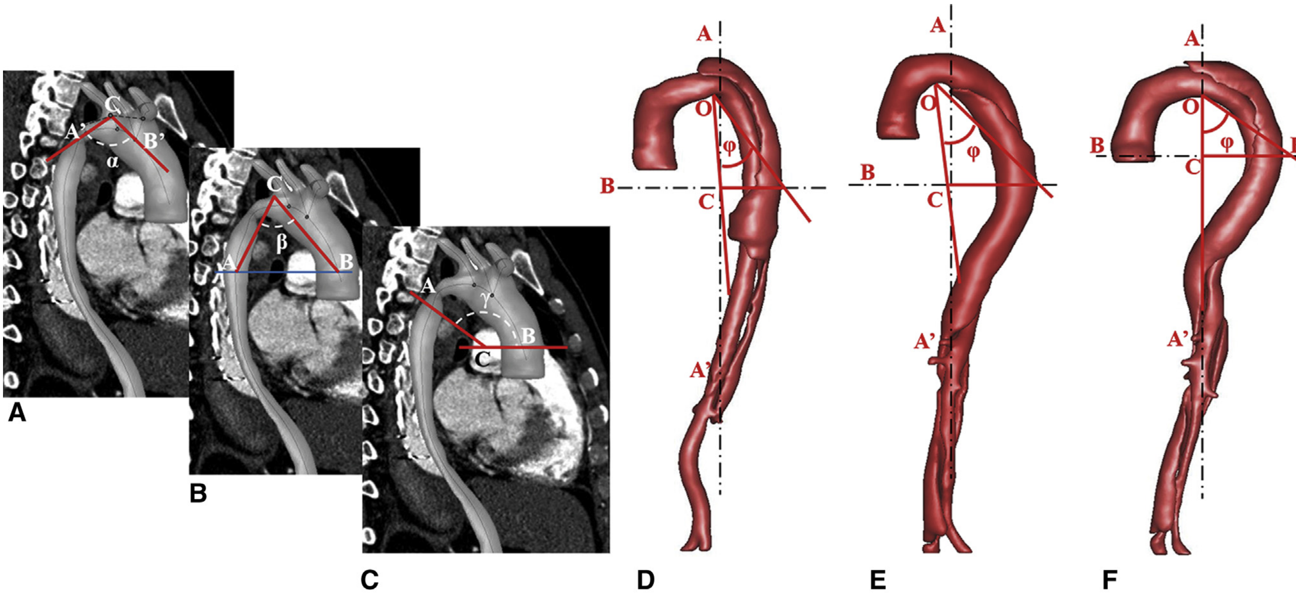


FIGURE 2. A description of the method used to measure different aortic arch angles. A, The angle α was defined as the angle between the left subclavian artery entrance to the left carotid artery and the same distance point at the descending aorta.[18] B, The aortic angle β was defined as the angle between the highest point of the transverse aorta and the descending and ascending aorta.[17] C, The angle γ was defined as the angle of the supra-aortic branches of the aortic arch or the curvature of the arch.[16] D through F, The angle φ is the degree of the question mark shape.

with open femoral access. Valiant (Medtronic, Minneapolis, Minn) aortic stent grafts were used in all patients, the length of which were all 200 mm. According to the preoperative assessment and intraoperative angiography, stent grafts were placed in the descending aorta with at least 2 cm of proximal, undissected landing zone to the primary entry tears. The stent graft oversize rate was routinely no more than 10%. Distal entry tears were regularly left behind for follow-up.[9]

Within 1 week postoperatively and at the 2-year follow-up, thin-slice CTA images of the aortic dissection were obtained using a second-generation dual-source CT scanner (Somatom Definition; Siemens Healthcare, Erlangen, Germany) with the following parameters: $512 \times 512 \times 700$, pixel spacing: 0.785/0.785 with a resolution of 1.274 pixels/mm and 1-mm slice thickness. The 3-dimensional aortic dissection geometries were then reconstructed from CTA images by the same investigator through a rigorous approach. The commercially available software Mimics (Materialise, Plymouth, Mich) was used for analysis.

The FLTR was defined as the ratio of the thrombus volume to the total volume of FL in the stented segment,[8,22] and the FLTRs of all patients were objectified on CTAs obtained after a 2-year follow-up.

Definition of Arch Angulation Index

The specific definition of the question mark is the vertical line AA' passes through the base point A, which is the upper end of the celiac trunk connected to the aorta. The horizontal line BB' passes through the point B, which is the furthest end of the descending aorta. Point C is the intersection of AA' and BB', and point O is the highest point of the aortic arch. The angle φ between line OB and line OC is defined as the degree of the question mark and has the unit "°."

In addition, we compared the arch angulations defined in previous research using different methodologies. The detailed definitions of 3 angles (ie, α, β, and γ) are shown in Figure 2.[16-18]

New Correlation Estimating FLTR

Two groups were created in 48 cases. These included the modeling group (n = 38) and the validation group (n = 10). First, morphology analysis was carried out for the modeling group and a new predictive formula for FLTR was proposed using regression analysis on the degree of question mark (angle φ) of the aortic arch. Then, the flow field within the idealized aortic dissection models with different FLTR were numerically investigated to explore the underlying mechanism for FLTR. To exclude other possible factors that might influence the FLTR after TEVAR, we choose 4 idealized models that were only different in terms of question mark (ie, 30°, 45°, 60°, and 75°), with the intention to indicate an increase in the degree of angulation as a result of the hemodynamic parameters within the aorta (Figure 3). The chosen angulations are within the range of real patients (ie, 32°-85°). Finally, the remaining 10 patients were chosen to validate the predicted correlation between the FLTR and the aortic angulation.

Hemodynamic Parameters Simulation

The evaluation of hemodynamic parameters and their links to anatomic features have been used extensively in clinical applications, including abdominal aortic aneurysms, cerebral aneurysms, and aortic dissection.[23-25] Image-based computational fluid dynamics (CFD) modeling can provide critical hemodynamic parameters information linked to thrombotic risk,[23,26] which is difficult or impossible to measure in vivo.[27] Previous CFD studies have demonstrated that net flow flux to the FL will increase the unobstructed area, make the blood flow more regular, and ultimately prevent thrombosis formation in the FL.[11]

Governing Equation

The blood flow was assumed isotropic, homogeneous, incompressible, and Newtonian, and the corresponding governing equations are given as follows:

$$\rho((\partial \vec{u})\,/\,\partial t+\vec{u}\cdot\nabla\vec{u})+\nabla p-\mu\nabla^{\wedge}2\;\vec{u}=0 \qquad (1)$$

$$\nabla\cdot\vec{u}=0 \qquad (2)$$

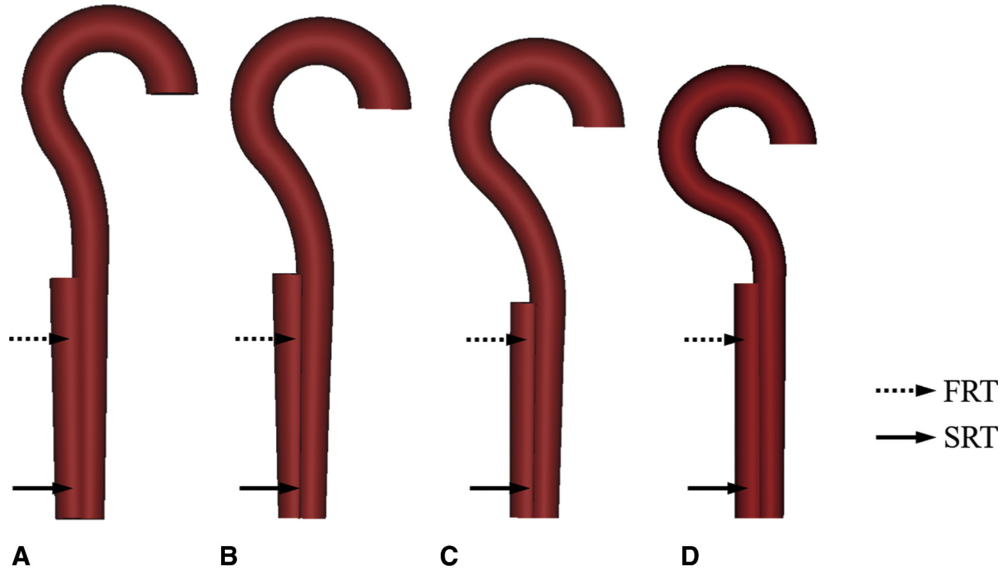


FIGURE 3. Idealized 3-dimensional models of aortic dissection with different degrees of the question mark shape. A, 30°. B, 45°. C, 60°. D, 75°. Each model has 2 re-entry tears; the first and second re-entry tears are 100 mm and 20 mm away from the common iliac artery, respectively. *FRT*, First re-entry tear; *SRT*, second re-entry tear.

Where $\vec{u}$ and p represent the fluid velocity vector and the pressure, respectively. ρ and μ are the density and dynamic viscosity of blood given to 1050 kg/m^3 and 3.5×10^{-3} $kg/m \cdot s$, respectively.

Boundary Conditions

A fixed flow rate of 0.2 m/sec was set at the inlet, and the average Re number, that was based on the inlet aortic diameter (in millimeters), was 1258 in all models. The outlet was set to 0 pressure and rigid vessel walls were assumed.

Numerical Simulation

The flow visualization and analysis were completed using the CFD software Ansys FLUENT (Ansys Inc, Canonsburg, Pa), based on the finite volume method. A default implicit 3-dimensional solver was applied. Discretization of the equations involved a second order upwind differencing scheme; SIMPLEC was adopted for the pressure velocity correction and the residual error convergence threshold was set as 10e-7.

Statistical Analysis

Data were expressed as mean ± standard deviation or as median (range) depending on the distribution. Comparisons of continuous variables were performed with the Student *t* test and 1-way analysis of variance test. The χ^2 test was used to compare categorical variables as appropriate. For the correlation of 2 variables, the correlation of the continuous variable was tested by Pearson test, and that of the categorical variable was performed by Spearman test. Linear regression was performed to generate the concomitant regression expression of the thrombosis rate and the geometry of the aortic arch. The estimated FLTR was compared with the actual FLTR by a 2-sided paired-samples *t* test. All statistical analyses were performed using SPSS for Windows 18.0 (IBS-SPSS Inc, Armonk, NY).

The concordance correlation coefficient (CCC), as introduced by Lin[28] was used to measure the concordance between the actual FLTR and the estimated FLTR. The Landis and Koch benchmark[29] was used to determine the strength of agreement as follows: poor agreement = 0.00, slight agreement = 0.01 to 0.02, fair agreement = 0.21 to 0.40, moderate agreement = 0.41 to 0.60, substantial agreement = 0.61 to 0.80, and almost perfect agreement = 0.81 to 1.00.

RESULTS

A total of 48 patients presenting with TBAD underwent analysis at the West China Hospital, Sichuan University. Among them, an emergency operation was performed in 6 patients, and the preoperative clinical characteristics are illustrated in Table 1. There were no significant correlations among FLTR and the variables, including age, sex, blood pressure, ascending aortic diameter, maximum diameter of the true lumen, maximum diameter of the FL, and the maximum diameter of the descending aorta (all P values > .05).

Angulation of the Aortic Arch

The angulations of the postoperative and 2-year follow-up geometrical configurations of 38 patients are shown in Table 2. The angulations at postoperative week 1 were performed by correlation and regression analysis. The aortic arch angles α, β, and γ (defined previously) showed no correlation with FLTR (all P values > .05). However, the degree of the question mark shape (φ) was highly negatively correlated to FLTR (Pearson $R = -0.661$; $P < .001$). The linear relationship between the FLTR and φ (Figure 4) was used to create a regression model for the FLTR following TEVAR as follows: FLTR (%) $= -1.955 \times \varphi + 168.24$ ($R^2 = 0.437$; $P < .001$).

CFD Simulation

Figure 5 presents the streamlines inside the aortic dissection after TEVAR, where the velocity magnitudes are

TABLE 1. The preoperative clinical characteristics and postoperative aortic diameters of 2 groups in all patients (N = 48)

Variable	Modeling group (n = 38)	Validation group (n = 10)
Age (y)	48 ± 9.0	49.2 ± 7.8
Sex		
Male	28	5
Female	10	5
Smoking	2 (5.3)	1 (10)
Hypertension	30 (78.9)	7 (70)
Diabetes	1 (2.6)	0
Chronic obstructive pulmonary disease	4 (10.5)	1 (10)
Atherosclerosis	3 (7.9)	2 (20)
Peripheral vascular disease	3 (7.9)	1 (10)
Coronary artery disease	2 (5.1)	1 (10)
Emergency	5 (13.1)	1 (20)
Length of stay (d)	11 ± 2	13 ± 2
Postoperative diameter (mm)		
Ascending aorta	35.7 ± 4.5	33.2 ± 3.7
Maximum of descending aorta	40.6 ± 9.4	41.4 ± 9.2
Maximum of true lumen	22.9 ± 6.7	21.4 ± 3.4
Maximum of false lumen	17.8 ± 9.9	18.0 ± 8.4
False lumen thrombosis rate (%)	67.9 ± 30.9	61.9 ± 37.3

Values are presented as mean ± standard deviation, n, or n (%).

differentiated by color. It shows that a partial true lumen flow enters the FL through the first re-entry tear, which is obstructed and diverted, spreading out over the FL walls and then returning to the true lumen through the second re-entry tear. As the degree of question mark shape increases, the blood flow entering from the first re-entry tear gradually changes from a smooth flow to a jet flow, which results in increased flow from the true lumen to the FL, and a more active region with blood in the FL.

Figure 6 shows that the net flow rate to the FL increases with the increase in the degree of the question mark shape of the aortic arch. To be more specific, when the question mark shape was 30°, 45°, 60°, and 75°, the corresponding net flow into the FL was 0.05 mL/sec, 0.11 mL/sec, 0.22 mL/sec, and 0.35 mL/sec, respectively; this indicates that the increase in the net flow is exponential to the increase of the degree. For example, when the degree increased from 30° to 45°, the percentage increase was only 120%, but when the degree reached 75°, the percentage increase was as high as 600%.

Evaluation of the Difference and Concordance of the Novel Prediction Model

Detailed predicted data are shown in Table 3, and all 10 patients demonstrated a matched result. There was no significant difference between the actual FLTR and the predicated FLTR using a 2-sided paired-samples *t* test ($P = .234$). Based on the results, the CCC further identified the degree of concordance between the actual FLTR and the predicated FLTR; the CCC value was 0.895, the Pearson value of precision was 0.915, and the bias correction factor of accuracy was 0.975. The Landis and Koch benchmark showed an almost perfect agreement between the actual FLTR and the predicated FLTR, for which the CCC was between 0.81 and 1.00. Six patients were within the 95% confidence interval after the 2-year follow-up, and all 10 patients were within the 95% predictive interval after the 2-year follow-up. In Figure 7, the solid line represents the Pearson correlation line and the dashed line represents the 45° line through the origin. The CCC was 0.895, and *R* was the Pearson correlation coefficient, which was a measure of the precision compared with the golden measure ($R = 0.915$). The correction bias factor (0.975) was a measure of the accuracy compared with the golden measure. In this study, the golden measure was the actual FLTR.

DISCUSSION

The thrombosis rate in the FL is decisive to the restoration of true lumen flow and aortic remodeling for patients with aortic dissection, and has been identified as a key parameter in which to evaluate TEVAR treatment outcomes.[5-8,11] An index to predict FL thrombosis after TEVAR could help to identify the anatomic features that would favor complete FL thrombosis to guide the initial treatment plans and improve stent graft design.[30-32] The aim of the current research was to demonstrate the

TABLE 2. Pearson correlation coefficient between false lumen thrombosis rate (FLTR) and the angulations of aortic arch (n = 38)

Angulation of aortic arch*	Postoperative value (°) 1 wk	2 y	*P* value†	FLTR (%)	*P* value‡
α	135.90 ± 20.00	136.24 ± 18.85	.563	67.9 ± 30.9	.350
β	59.09 ± 9.25	60.44 ± 10.95	.140		.399
γ	136.35 ± 20.89	137.33 ± 21.40	.412		.403
φ	51.35 ± 10.44	51.77 ± 10.46	.454		.000

FLTR, False lumen thrombosis rate. *Angulations of aortic arch defined by previous literature; φ presents the degree of question mark. †Change of angles between after-thoracic endovascular aortic repair and 2 years. ‡The *P* value refers to the Pearson correlation coefficient between FLTR and the angulations of aortic arch after thoracic endovascular aortic repair.

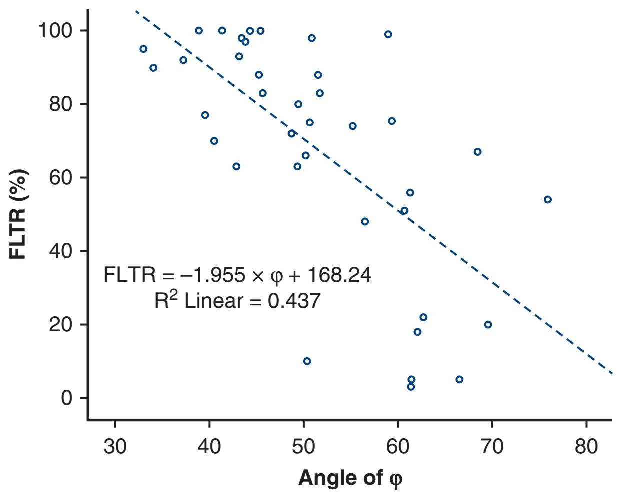


FIGURE 4. The regression line of the prediction model. *φ*, Degree of the question mark; *FLTR*, false lumen thrombosis rate.

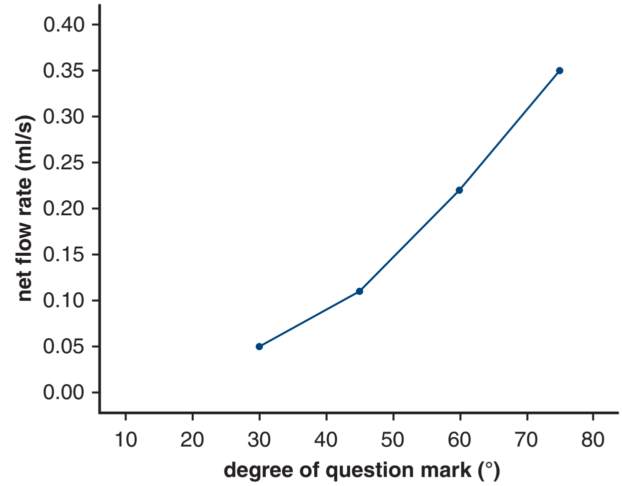


FIGURE 6. The net flow rate into the false lumen with respect to the degree of the question mark shape of the aorta. False lumen net flow rate is equal to the inlet flow rate to the false lumen minus the outlet flow rate from the false lumen.

potential applicability of aortic angulation in the prediction of FL thrombosis following TEVAR.

This study revealed that due to the aortic remodeling, the geometrical configuration of the descending aorta in the dissection segment changed with time after TEVAR. However, the angle of the aortic arch of patients with aortic dissection remained almost unchanged following TEVAR, which suggests that it is a potential predictor of the FLTR after TEVAR. In addition, only the new proposed definition of aortic angulation (the degree of question mark shape) was observed to be related to the FLTR in TBAD patients following TEVAR, and a predicted model of FLTR based on the degree of question mark shape of the aortic arch was given and validated using paired-samples *t* test and the CCC. Moreover, the degree of question mark shape of the aortic arch was found to gradually decrease as the FLTR gradually increased. Namely, a small question mark implicates a high thrombosis rate in the FL after TEVAR. Furthermore, as the question mark got bigger, the jet flow at the first re-entry tear became stronger, which resulted in a significant increase in the net blood flow into the FL. It is known that increased net flow inside the FL will reduce the slow and stagnant blood flow zones and ultimately prevent FL thrombosis formation.[11,33,34]

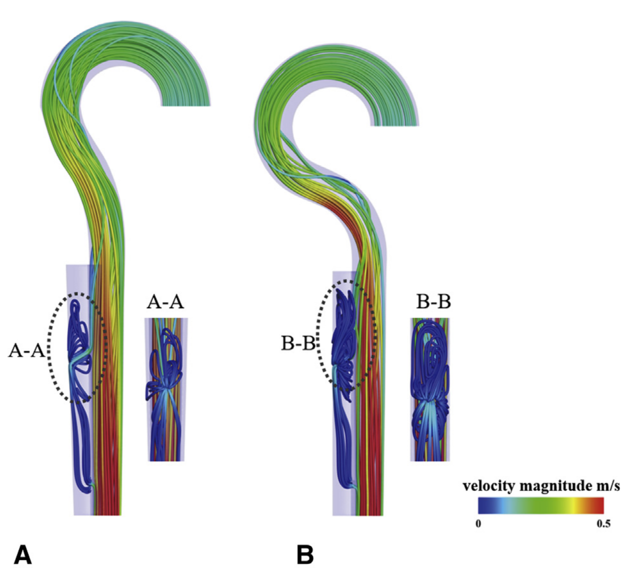


FIGURE 5. Velocity contour map superimposed with streamlines inside the virtual aortic dissection following thoracic endovascular aortic repair. A, The question mark shape is 30°. B, The question mark shape is 75°.

Limitations

Currently, the patients have been followed for only 2 years. The 5-year follow-up outcomes will be analyzed during the next 3 years for our points. Furthermore, this study only focused on the relationship between the aortic angulation and FLTR; other parameters, including the diameters, number, and localizations of entry tears; length of stent graft; absence of endoleaks or reentry tears; and anticoagulation status were not considered. A future study that includes those parameters is necessary. Because this was a primary study of the influence of the arch angulation on FL thrombosis, our sample size was not large. Additional studies will enlarge the number of patients and increase the validity of the results.

Finally, previous studies pointed out that there are 3 qualitative states of a FL, including the absence of thrombus, partial thrombosis, and complete thrombosis based on imaging results. In our current study, the quantitative FLTR was calculated—a value that cannot be properly classified into the qualitative status of an FL. Thus, the potential correlation will be analyzed between the qualitative FL status

TABLE 3. The prediction results of 10 patients

Question mark (°)	Actual false lumen thrombosis rate (%)	Predicted false lumen thrombosis rate (%)	*P* value*	Concordance correlation coefficient (95% confidence interval)
84.96	2	2.15	.234	0.895 (0.661-0.970)
79.84	7	12.15		
68.45	38	34.43		
58.38	48	54.10		
62.32	58	46.40		
43.42	81	83.35		
31.77	90	106.13		
48.58	96	73.27		
47.95	99	74.49		
49.12	100	72.20		

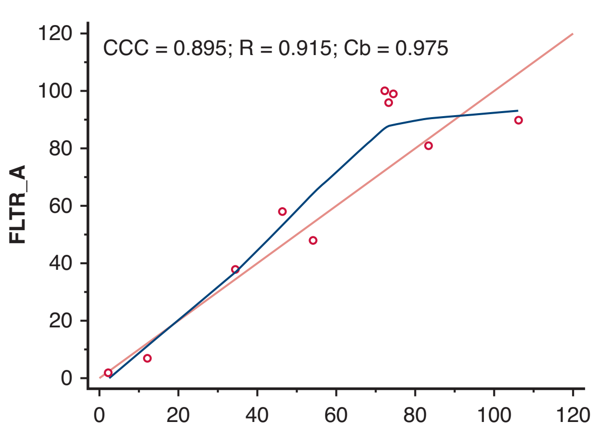
*P value of difference using paired-samples t test.

and the quantitative FLTR based on increased samples in the near future.

CONCLUSIONS

The degree of question mark shape marker we propose may be a good predictor for the FLTR of acute TBAD following TEVAR, which takes into account the geometry of the descending aorta and is negatively correlated with postoperative FLTR (Video 1). The larger the question mark shape, the less likely the FL is to form a complete thrombus. In general, the FL disappeared immediately after the operation if all the re-entry tears of the aortic dissection were covered. Generally, the Society for Vascular Surgery guidelines recommend contrast-enhanced CT scanning at 1 month, 6 months, 12 months, and then annually after TEVAR for thoracic aortic dissection.[35] Thus, we suggest that patients undergoing TEVAR who display a large question mark degree should have regular and more frequent follow-ups—at least every 6 months—for monitoring FLTR. Moreover, if a poor thrombosis rate in the FL is observed during follow-up, the remaining distal re-entry tears need to be treated as soon as possible to promote thrombus formation in the FL. Moreover, a multilayer flow modulating stent is reported to be good at reducing FL blood flow and eliminating local flow disturbances in TBAD patients[36]; this also appears to be a safe and feasible solution for type A[37] and type B aortic dissections[36] and aneurysms[38,39] in both early and midterm outcomes. We suggest that surgeons working with TBAD patients with a large question mark shape adopt multilayer flow modulating stents to promote FL thrombosis.

FIGURE 7. The concordance between the actual false lumen thrombosis rate (FLTR_A) and the predicted false lumen thrombosis rate (FLRT_P). *CCC*, Concordance correlation coefficient; *Cb*, correction bias factor.



VIDEO 1. The introduction of the question mark and the process of thoracic endovascular aortic repair. Video available at: https://www.jtcvs.org/article/S0022-5223(19)31645-9/fulltext.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: aortic dissection, morphology, aortic arch, thrombosis in false lumen, TEVAR