Original Article

Are dilated ascending aortas of Chinese patients more likely to dissect?

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Background: Ascending aortic aneurysm is a disease requiring surgical intervention. However, the timing of operation is still controversial. The purpose of this study is to compare the ascending aortic diameter and postoperative outcomes in hospital between patients with simple ascending aortic dissection and patients with simple ascending aortic dilation in China, and to investigate the accuracy of the timing of operation determined by ascending aortic diameter alone.

Methods: We reviewed the data from 2,520 hospitalized patients of aortic aneurysm and aortic dissection who underwent surgical treatment from January 2010 to June 2017 in our hospital. A total of 139 simple ascending aortic dissection and simple ascending aortic aneurysm hospitalized patients excluding Marfan syndrome and heart valve diseases etc. (56 in the aortic dilatation group and 83 in the aortic dissection group) were enrolled. The t-test and univariable analysis were used to compare the differences between two groups.

Results: For the aortic diameter, the group of aneurysm has greater ascending aortic diameter and the index of ascending aortic diameter compared with the group of dissection (P<0.001, P<0.001). For male patients, the result is the same (P<0.001, P<0.001). But for female patients, there was no significant statistical significance between the two groups (P=0.631, P=0.288). For the postoperative outcomes, the dissection group had higher mortality, incidence of tracheotomy and postoperative re-exploration for hemorrhage (P=0.040, P=0.011, P=0.028).

Conclusions: The majority of patients with simple ascending aortic dissection present with aortic diameters <5.5 cm and this is not consistent with the current operation indications of aortic aneurysm. It is far from enough to predict aortic dissection with aortic diameter alone. More indicators are needed to do this.

Keywords: Ascending aortic dilation; ascending aortic dissection; surgical indication

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Introduction

The natural evolution of ascending aortic aneurysm without treatment might lead to aortic dissection or rupture, even death (1,2). According to Laplace's law, as the diameter of the aneurysm increases, the tension of the arterial wall increases. Therefore, it is commonly known that dilated aortas are more likely to dissect (3). Regardless of etiology, surgery should be performed in patients with simple aortic dilation who have a maximal aortic diameter larger than 5.5 cm according to 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases (4). In our usual consciousness, dissection often occurs when the diameter of the aneurysm increases to a certain extent and the diameter of aortic dissection is always larger than the diameter of aortic aneurysm. However, the average diameter of ascending aorta when the aortic dissection occurred is always controversial worldwide (5-7). It makes us begin to examine the correctness of the aortic diameter alone as a surgical indication.

When is the best time to operate? Various surgeons have different opinions. In our study, we compared the ascending aortic diameter and the ascending aortic diameter index between simple ascending aortic dilation group and simple ascending aortic dissection group, and also compared male and female differences between the two groups respectively. The aim of our study was to investigate the accuracy of the timing of operation determined by ascending aortic diameter alone. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/cdt-20-313).

Methods

Patient's data

The trial was conducted in accordance with the Declaration of Helsinki. The present study was granted by the Ethics Committee of Beijing Anzhen Hospital (Institutional Review Board File 2014019), and informed consent was taken from all the patients. We collected 2,520 hospitalized patients of aortic dilation and aortic dissection who underwent surgical treatment from January 2010 to June 2017 in Beijing Anzhen Hospital of Capital Medical University. All the disorders only involved the ascending aorta. The diameters of ascending aorta and aortic sinus were determined by transthoracic echocardiography database of the Beijing Anzhen Hospital. In order to exclude some interference factors which are not related to this research, we only identified simple ascending aortic dissection (the simple aortic dissection means the dissection of the ascending aorta alone, and this kind of dissection had been verified through both the preoperative CTA scans and intraoperative detection) and simple ascending aortic dilation (the simple aortic dilation means the dilation of the ascending aorta alone). And the other exclusion criteria included: age <18, hereditary connective tissue diseases such as Marfan syndrome, Loeys-Dietz, and Ehlers-Danlos syndromes; inflammatory aortic diseases; heart valve diseases such as aortic stenosis or insufficiency and bicuspid aortic valve, and a history of ascending aortic surgery. In addition, patients with pseudoaneurysm, ulcer of the ascending aorta and intramural hematoma were also excluded. We finally identified 139 patients in the two groups, 83 in the aortic dissection group and 56 in the aortic dilation group (*Figure 1*). Since these patients had only ascending aortic disorder, they all had the ascending aortic replacement with the peripheral artery cannulation. The data collection was mainly from medical records of the patients in hospital. The clinical data included diameter of ascending aorta, diameter of aortic sinus, sex, age, height, weight, body surface area, preoperative EF, preoperative LVEDD, preoperative LVESD, left atrial diameter, operation related parameters and postoperative outcomes.

Statistical analysis

The continuous variable of normal distribution is expressed by mean ± standard deviation. The abnormal distribution data is represented by median (interquartile range), and the categorical variable is expressed as a percentage. The *t*-test and univariable analysis were used to compare the differences between two groups.

Results

Baseline characteristics

A total of 139 patients met the criteria for inclusion. The comparison of basic data is shown in *Table 1*. At baseline, The age of patients in the aortic dilation group was 57.27±10.96, the age of patients in the aortic dissection group was 56.93±10.74, the age and the proportion of women in the two groups was similar, in addition, there was no significant statistical difference between the two groups, such as height, weight, body surface area, body mass index,

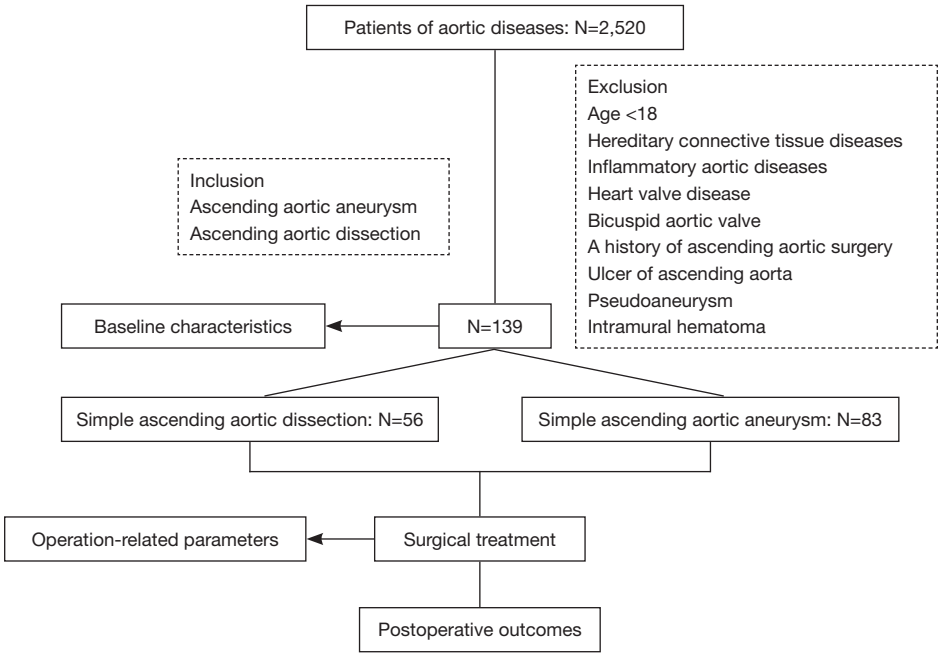

Figure 1 The study flow chart.

Table 1 Baseline patient characteristics

Variables	Aortic dissection (n=83)	Ascending aortic dilation (n=56)	P value
Age, yrs	56.93±10.74	57.27±10.96	0.856
Female	43 (51.8%)	31 (55.4%)	0.681
Height, cm	165.99±8.01	165.66±8.98	0.822
Weight, kg	72.08±15.90	68.79±12.70	0.197
BMI	26.02±4.69	24.91±3.17	0.123
Body surface area, m^2	1.90±0.23	1.85±0.20	0.261
Preoperative EF, %	63.53±6.36	65.12±5.79	0.168
Preoperative LVEDD, mm	47.31±5.21	48.21±4.49	0.336
Preoperative LVESD, mm	30.96±4.37	30.50±3.86	0.563
Left atrial diameter, mm	35.68±8.98	36.04±7.53	0.822

Data are expressed as mean ± standard deviation or number (percentage). BMI, body mass index; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end-systolic diameter.

preoperative EF, preoperative LVEDD, preoperative LVESD, left atrial diameter etc. before surgery.

Operation related parameters and postoperative outcomes

Among patients in the dissection group, more CPB time, more aortic cross-clamping time, less hospitalization days, more mechanical ventilation time and longer ICU stay were present which was shown in *Table 2*. There was no significant statistical difference between the two groups, such as postoperative hospital days, suspension red blood cells transfusion, plasma transfusion, postoperative ejection fraction and postoperative serum creatinine. For postoperative outcomes, the dissection group had higher mortality, incidence of tracheotomy and postoperative re-exploration for hemorrhage. The incidence of stroke, pulmonary infection and postoperative dialysis between the two groups were similar.

Ascending aortic diameters

We can find out in *Table 3*, among the 139 patients, that the mean ascending aortic diameter of the dissection group was 50.72±9.53 mm and the mean ascending aortic diameter

Table 2 Operation related parameters and postoperative outcomes

Variables	Aortic dissection (n=83)	Ascending aortic dilation (n=56)	P value
CPB time, min	147.00 (120.50–175.50)	92.00 (79.00–116.00)	<0.001
Aortic cross-clamping time, min	73.00 (55.00–99.50)	52.00 (36.75–60.75)	<0.001
Postoperative hospitalization days, d	10.00 (7.50–12.50)	9.00 (7.00–12.25)	0.767
Hospitalization days	14.00 (11.00–20.50)	17.50 (14.75–23.25)	0.005
Mechanical ventilation time, hours	39.00 (18.00–75.00)	19.00 (13.25–31.50)	<0.001
ICU stay, hours	42.00 (24.00–73.50)	23.50 (19.00–29.75)	<0.001
Suspension red blood cells transfusion, IU	6.00 (0.00–10.00)	4.00 (0.00– 7.00)	0.052
Plasma transfusion, mL	400.00 (0.00–800.00)	400.00 (0.00–800.00)	0.219
Postoperative ejection fraction, %	61.05±6.44	62.07±6.193	0.345
Postoperative serum creatinine, μmol/L	69.50 (53.00–94.25)	66.00 (53.00–75.00)	0.252
Death	6 (7.23%)	0 (0.00%)	0.040
Tracheotomy	9 (10.84%)	0 (0.00%)	0.011
Postoperative re-exploration for hemorrhage	1 (1.20%)	5 (8.93%)	0.028
Stroke	5 (6.02%)	3 (5.36%)	0.868
Pulmonary infection	4 (4.82%)	4 (7.14%)	0.564
Postoperative dialysis	6 (7.23%)	1 (1.79%)	0.150

Data is represented as the median (interquartile) or number (percentage). CPB, cardiopulmonary bypass; ICU, intensive care unit.

Table 3 Comparison of the aortic diameter

Variables	Aortic dissection (n=83)	Ascending aortic dilation (n=56)	P value
Aortic sinus diameter, mm	35.86±5.13	36.02±5.41	0.866
Ascending aortic diameter, mm	50.72±9.53	57.30±9.41	<0.001
Ascending aortic diameter index[a]	27.22±6.40	31.12±5.38	<0.001

[a], ascending aortic diameter index means the ratio of ascending aortic diameter divided by body surface area.

of the dilation group was 57.30±9.41 mm. The dilation group had greater ascending aortic diameter compared with the dissection group. For the aortic sinus diameter, there was no significant statistical significance between the two groups (*Figure 2*). Nearly 73% of the patients of the dissection group had aortic diameters <5.5 cm, and 52% of the patients had aortic diameters <5 cm (*Figure 3*). If we considered the influence of body surface area, we used the index of ascending aortic diameter, which was equal to the diameter of ascending aorta/body surface area. We could conclude from *Table 3* that the dilation group had greater index of ascending aortic diameter compared with the group of dissection. This was consistent with the result of ascending aortic diameter. After that, we divided the two groups into male group and female group which were compared respectively. We found that male group and female group had different results which were shown in *Tables 4* and *5*. For male patients, the ascending aortic diameter and the index of ascending aortic diameter of the dilation group was greater compared with the dissection group. However, the aortic sinus diameter was similar between the two groups. But for female patients, there was no significant statistical significance between the two groups including the aortic sinus diameter, the ascending aortic diameter and the index of ascending aortic diameter. In order to eliminate interference from other confounding factors, we used univariable binary logistic regression analysis, which was shown in *Table 6*.

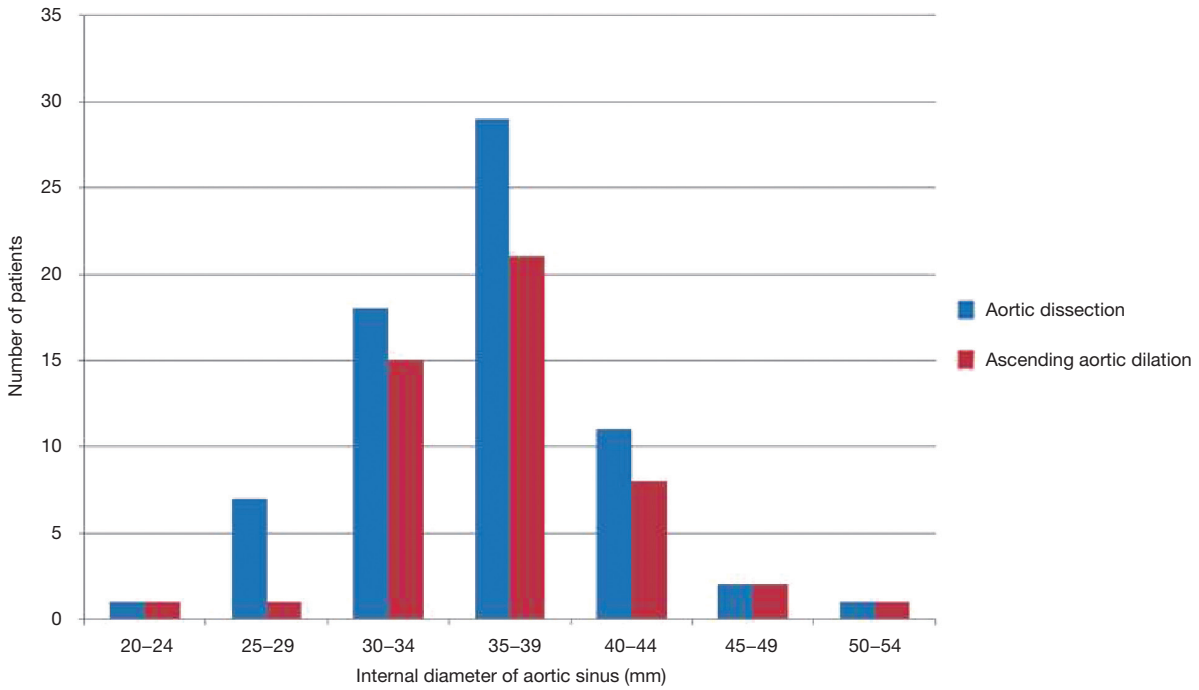

Figure 2 Population distribution of aortic sinus diameter stratified by patients with aortic dissection versus those with ascending aortic dilatation.

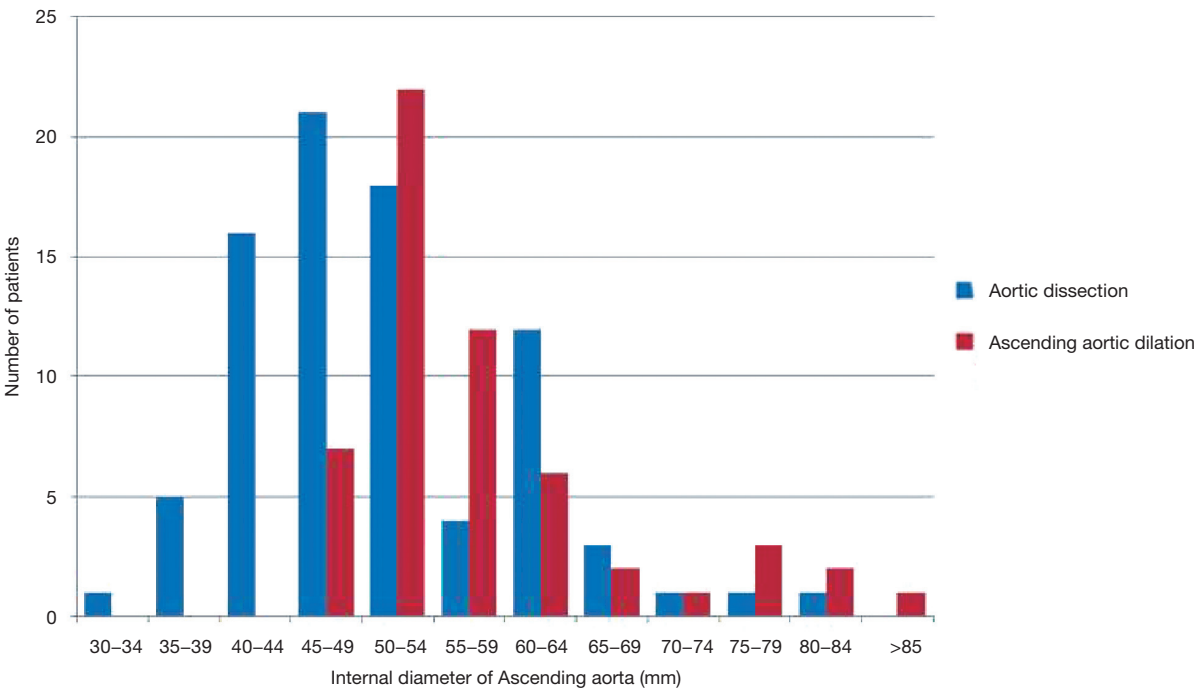

Figure 3 Population distribution of ascending aortic diameter stratified by patients with aortic dissection versus those with ascending aortic dilatation.

Table 4 Comparison of the aortic diameter of male patients

Variables	Aortic dissection (n=40)	Ascending aortic dilation (n=25)	P value
Aortic sinus diameter, mm	37.34±6.28	38.39±5.73	0.935
Ascending aortic diameter, mm	47.40±6.53	60.28±10.80	<0.001
Ascending aortic diameter index[a]	23.60±3.72	30.00±6.33	<0.001

[a], ascending aortic diameter index means the ratio of ascending aortic diameter divided by body surface area.

Table 5 Comparison of the aortic diameter of female patients

Variables	Aortic dissection (n=43)	Ascending aortic dilation (n=31)	P value
Aortic sinus diameter, mm	34.57±3.48	33.92±4.19	0.509
Ascending aortic diameter, mm	53.81±10.84	54.90±7.47	0.631
Ascending aortic diameter index[a]	30.58±6.56	32.03±4.37	0.288

[a], ascending aortic diameter index means the ratio of ascending aortic diameter divided by body surface area.

Table 6 Univariable analysis of aortic dissection

Variables	OR	95% CI	P value
Age (by 1 year increment)	1.00	0.97–1.04	0.8549
Female	1.15	0.58–2.28	0.6808
Aortic sinus diameter (by 1-mm increment)	1.01	0.94–1.08	0.8650
Ascending aortic diameter (by 1-mm increment)	1.08	1.03–1.12	0.0004
Height (by 1-cm increment)	1.00	0.96–1.04	0.8207
Weigh (by 1-kg increment)	0.98	0.96–1.01	0.1978
Portion of ascending aorta diameter divided by body surface area	1.11	1.05–1.18	0.0007
Preoperative EF (by 1% increment)	1.04	0.98–1.11	0.1680
Preoperative LVEDD (by 1-mm increment)	1.04	0.96–1.12	0.3332
Preoperative LVESD (by 1-mm increment)	0.97	0.89–1.07	0.5593

LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end-systolic diameter.

Discussion

The surgical indication for simple aortic dilation was set in 5.5 cm, which comes from the guideline of American College of Cardiology (ACC), American Heart Association (AHA), Society of Thoracic Surgery (STS) and the American Association for Thoracic Surgery (AATS) in the year of 2010 (8). Coady *et al.* (9) also put forward a lot of clinical evidence in 1997 to support this surgical indication. The guideline was mainly based on the experience accumulated by clinicians and surgeons, and lacked sufficient evidence support and theoretical basis (10-13). At the same time, the guideline implied that these indications were not absolute, and the influence of many other factors should be considered. The surgical indication for patients with Marfan syndrome was 5 cm, and for patients with additional risk factors, consisting of family history of dissection and severe aortic regurgitation, the indication could be reduced to 4.5 cm (8). As seen from the guidelines, genetic factors, valve disorders and so on had a great influence on surgical indications. So in our study, we excluded the interference caused by genetic factors, inflammation, valve disorders, etc., and chose simple ascending aortic dilation and simple

ascending aortic dissection as the subjects for our study. This allowed us to focus on the effect of aortic diameter on indications for ascending aortic dilation and the two groups of patients were more comparable.

Our clinical data from Anzhen Hospital showed that in 83 aortic dissection patients, nearly 73% of the patients were less than 5.5 cm in diameter, and nearly 52% were less than 5 cm. Pape *et al.* (14) showed similar data in his article in 2007. This article enrolled 591 type A dissection patients (mean age, 60.8 years) from International Registry of Acute Aortic Dissection (IRAD) between 1996 and 2005. It was found that 59% of the patients were less than 5.5 cm in diameter and 40% were less than 5 cm, which was similar to our article. According to our data, most patients in dissection group had diameters <5.5 cm. If current indications were applied, these patients would face the risk of death. For some patients, the diameter of ascending aorta when aortic dissection occurrence was even normal. In clinical practice, we do find that some patients had suffered aortic dissection, although they have a "small aorta" or even less than 3.5 cm. On the contrary, in some patients of aortic dilation, the diameter of ascending aorta sometimes even reaches 8–9 cm and it was still "safe", so, for these "small aorta" patients, it seems to be necessary to use more radical surgical indications to avoid disastrous aortic diseases, but for some "big aorta" patients, 5.5 cm appears too radical. This fact indicates that it is not enough to rely solely on diameter of the aorta to decide whether or not to operate. It is necessary to find more accurate evaluation indexes for the surgery.

Traditionally, we believed that the diameter of ascending aortic dilation was less than the diameter of ascending aortic dissection. With the increase of the diameter of the aorta, the risk of dissection increases, which means that the diameter of the aorta is "large enough", causing the occurrence of aortic dissection under this diameter. However, our research was different from this. Many doctors believed that aortic diameter was still interfered by many factors, gender and body surface area are two important factors. Davies *et al.* (15) reviewed 805 patients of aortic aneurysm and found that the incidence of dissection in female was higher and the 5-year survival rate was lower. Cheung *et al.* (16,17) found that aortic diameter increased faster in women patients of aortic aneurysm. In order to exclude the interference of sex factors, we divided the patients into two groups, male and female, and it had different results. The diameter of the ascending aorta in female patients appeared to be thicker than that in male patients. We also recognized the effect of body surface area on the diameter of the aorta. Kälsch *et al.* (18) found out that BSA is an independent factor associated with increased aortic diameter. In order to exclude the interference of this factor, we compared the parameter of the ascending aortic diameter/body surface area between two groups, which was called the aortic diameter index, and found it was consistent with the results of aortic diameter. Davies *et al.* (15) believed that surgical treatment should be performed in patients of aortic aneurysm when the aortic diameter index reaches 2.75 cm/m.

In another study, some scholars believed that the diameter of the aorta presented the so-called "normal distribution" in the population, and the number of the middle aorta was largest, which meant that the population of the "smaller diameter" aorta had a relatively larger population, so the number of aortic dissection was also larger than that of "larger diameter" aorta (19,20). They confirmed that although aortic dissections did occur at small sizes, patients with large aortas were at a 6,000-fold higher risk of experiencing aortic dissection. If we want to measure the risk of occurrence of aortic dissection, the number of patients with aortic dissection/the total population of that diameter should be measured. The result was that the risk of aortic dissection in the larger diameter was significantly larger than the smaller diameter, which explained why 5.5 cm was used as a surgical indication for ascending aortic dilation. However, in the actual situation, the data of the aorta diameter of the total population is difficult to collect. Therefore, whether diameter of the aorta in the general population is normally distributed still needs further evidence. Besides, although the risk of aortic dissection occurrence in small aortas is less than large aortas, the population of people with small aortas is quite large, so the absolute number of patients of aortic dissection in small aortas is very large too, which can't be ignored in clinical practice. In our study, the dissection group had higher mortality, incidence of tracheotomy and postoperative re-exploration for hemorrhage. It suggested that once aortic dilation developed into aortic dissection, the perioperative mortality and morbidity would be significantly increased, and the risk of surgical intervention for the patients with aortic dilation would be much lower before aortic dissection occurrence.

In China, there is no database platform like IRAD yet. It is difficult to summarize the experience of diagnosis and treatment of ascending aortic dilation and hard to get evidence-based medical researches. At present, cardiac

surgeons in China rely more on European and American guidelines to guide clinical work. Our existing indications for ascending aortic dilation are also based on these European and American guidelines. As everyone knows, there is a big difference between Chinese and European or American race, so it is necessary to establish an indication of surgery for ascending aortic dilation that belongs to the Chinese. This article is to investigate the diameter of the aorta and the risk of aortic dissection occurrence in Chinese, but there is still a lot of work to do before we have our own guidelines.

There were also some limitations in our article. We excluded the hereditary and inflammatory aortic diseases in the selection of cases, which may be a key to unlock the "silent killer" secrets of the aortic dilation. Besides, it should be noted that our research mostly included only ascending aortic diameters post-dissection, which was known to be roughly 13 mm larger compared to pre-dissection (21). And more than 60% of patients have non-dilated aortas prior to the dissection (22). But the pre-dissection diameter was the real diameter at risk. So, the actual diameter of aorta when aortic dissection occurred was smaller than expected. Did it mean that the current surgical indication was wrong? For ascending aortic dilation, should we adopt a more aggressive surgical strategy? Apart from these, Wu *et al.* referred that ascending aortic length could serve as a novel predictive factor to evaluate risk of aortic adverse events, which include aortic rupture, aortic dissection and death and raised that aortic elongation of 11 cm should be a new indication for aortic intervention. It is a completely new criterion for aortic surgery and needs to be further verified. We did not assess the quality of this factor in our research because we paid more attention to the existed criterion of surgery. But it certainly should be one of our next research interests to check its effectiveness (23).

In the future, we will further explore the pathogenesis of the aortic dilation. At the same time, the factors that affect the diameter of the aorta in this article only include gender and body surface area, and there are still some other factors that are not involved. This is the problem we need to further study in the future.

Conclusions

The majority of patients with aortic dissection present with aortic diameters <5.5 cm and this is not consistent with the current indications of aortic dilation. The group of aortic dilation has greater ascending aortic diameter and the index of ascending aortic diameter compared with the group of aortic dissection. And for male and female patients, it has different results. It is far from enough to predict the occurrence of aortic dissection with aortic diameter alone. We need better risk predictors to identify patients at risk and individualized surgical indications should be applied to different patients.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/cdt-20-313

Data Sharing Statement: Available at http://dx.doi.org/10.21037/cdt-20-313

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/cdt-20-313). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The trial was conducted in accordance with the Declaration of Helsinki. The study was approved by the Ethics Committee of Beijing Anzhen Hospital (Institutional Review Board File 2014019), and informed consent was taken from all the patients.

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