



Observational Study

# Association of dissected ascending aorta diameter with preoperative adverse events in patients with acute type A aortic dissection

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## Abstract

### BACKGROUND

Acute type A aortic dissection (ATAAD) is a life-threatening disease associated with high morbidity and mortality.

### AIM

To evaluate the diameter of dissected ascending aorta in patients diagnosed with ATAAD and whether the aortic diameter is associated with preoperative adverse events.

### METHODS

A total of 108 patients diagnosed with ATAAD who underwent emergency operation under hypothermic circulatory arrest were enrolled in this study. Demographic characteristics and perioperative data were recorded. In all patients, preoperative chest and abdomen computed tomography (CT) scans were performed.

### RESULTS

Median age of the patients was 61.5 (52.5-70.5) years and median body mass index (BMI) was 28.2 (25.1-32.6) cm<sup>2</sup>. The number of female patients was 37 (25%). Median diameter of the ascending aorta was 5.0 (4.5-6) cm and 53.8% of the patients had an aortic diameter < 5.0 cm, while 32.3% of the patients had an aortic diameter of 4.5cm and 72.0% had an ascending aorta diameter < 5.5 cm. The diameter of the ascending aorta did not differ in patients with *vs* without preoperative adverse events: Preoperative neurological dysfunction ( $P = 0.53$ ) and hemodynamic instability ( $P = 0.43$ ). Median age of patients with preoperative hemodynamic instability was 65 (57.5-74) years, while it was 60 (51-68) years in patients without ( $P = 0.04$ ).

## CONCLUSION

Although current guidelines suggest replacing the ascending aorta with a diameter > 5.5 cm, most of the patients with ATAAD had an aortic diameter of less than 5.5 cm. The diameter of the ascending aorta in patients diagnosed with ATAAD is not associated with preoperative adverse events.

**Key Words:** Acute; Aortic dissection; Type A; Ascending aorta; Diameter

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**Core Tip:** Do patients with an ascending aorta diameter < 5.5 cm undergo more aggressive surgery for prevention of acute type A aortic dissection (ATAAD)? Most of the patients (72.0%) with ATAAD had an ascending aorta diameter < 5.5 cm. An international taskforce should adapt the new data extracted from the most recent scientific evidence in the surgical treatment of the ascending aortic aneurysm.

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## INTRODUCTION

Acute type A aortic dissection (ATAAD) is a life-threatening condition with excessive mortality and morbidity if not operated, reaching approximately 50% during the first 24 h and 70%-90% days and weeks after diagnosis[1-3]. Emergency surgical correction with replacement of the ascending aorta with or without aortic arch, despite being the treatment of choice, also carries a significant mortality and morbidity burden. Nowadays, emergency surgical correction of ATAAD under hypothermic circulatory arrest remains the treatment of choice[4-6]. On the other hand, the mortality rate of patients who underwent ATAAD repair is high at approximately 15%-25%[7-9].

The most common clinical manifestation of thoracic aorta dissection is acute chest pain. Due to the much commoner incidence of acute coronary syndrome (ACS), pulmonary embolism (PE), and other thoracic pathology, accurate diagnosis is frequently hindered or delayed. The sudden and insidious onset of symptoms, the delay in diagnosis, and the time required to transport of patients to cardiac surgery centers for treatment negatively affect the outcomes of these patients[10-12]. Replacement of the ascending aorta in patients with an enlarged aortic diameter is considered as an option for preventing acute aortic dissection. Existing and current guidelines recommend replacing the ascending aorta if the size reaches 5.5 cm in patients without Marfan syndrome[6,13]. On the other hand, the exact threshold of aortic size (< 5.5 cm) for early (preventive) operation remains a grey zone in current indications and guidelines, because in most patients with acute aortic dissection, the maximum aortic diameter is approximately 5 cm or less[14-17].

The present study evaluated the diameter of dissected ascending aorta in patients diagnosed with ATAAD and whether the aortic diameter is associated with preoperative adverse events.

## MATERIALS AND METHODS

### Study population

The study period was 2010-2017. This retrospective study included 108 patients with ATAAD who underwent an emergency operation under hypothermic circulatory arrest with antegrade or retrograde cerebral perfusion. Patients with a known diagnosis of connective tissue disorder or Marfan syndrome or iatrogenic dissection were excluded. All demographic characteristics and perioperative data were recorded. In all patients, preoperative chest and abdomen computed tomography (CT) scans were performed. The ascending aorta diameter was calculated based on preoperative chest CT or CT angiography. The maximum diameter of the ascending aorta was defined as the diameter which included the true and false lumen of the ascending aorta. The method for measuring the maximum aortic diameter was double oblique short axis. All preoperative neurological dysfunctions (including temporary and permanent neurological dysfunctions) on admission were included in our database. Temporary neurological dysfunctions (TND) were defined if the patients had transient ischemic attack (TIA) or delirium or disorientation, while permanent neurological dysfunctions (PND) if the patients

were admitted to hospital with hemiplegia or paraplegia or coma. Preoperative hemodynamic instability was defined as preoperative cardiac arrest or systolic blood pressure (< 80 mmHg) despite inotropic support or preoperatively diagnosed cardiac tamponade with hemodynamic consequences. The study was approved by the hospital's institutional review board (546/30-04-2015).

### Statistical analysis

Continuous variables are presented as the median (interquartile range), while categorical variables are presented as *n* (%). Normality of continuous variables was examined by Shapiro-Wilk test and Q-Q plot. Continuous variables were compared by Student's *t*-test for the normally distributed, while Mann-Whitney and Kruskal-Wallis tests for the non-normally distributed variables. Chi-square or Fisher's exact test was implemented for the rest variables (categorical variables). Correlation of ascending aorta diameter with continuous variables was evaluated by Spearman ( $r_s$ ) or Pearson ( $r$ ) correlation coefficient. Univariable linear regression model was used to identify the association of demographics and other factors with diameter of the ascending aorta. The effect size was expressed by linear regression coefficient " $\beta$ ". Binary univariable and multivariable logistic regression modeling was used to estimate the association of ascending aorta diameter with preoperative adverse events (neurological dysfunction and hemodynamic instability). Predictive ability is presented as odds ratio (OR). The Hosmer-Lemeshow goodness of fit test was performed for logistic regression analysis model. Confidence interval (CI) was set at 95% in all tests. Statistical significance was considered at  $P < 0.05$ . IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY, United States) was used in analysis.

## RESULTS

Median age of the patients was 61.5 (52.5-70.5) years and median body mass index (BMI) was 28.2 (25.1-32.6) cm<sup>2</sup>. Thirty-seven (25%) were female patients. Median diameter of the ascending aorta was 5.0 (4.5-6) cm and 53.8% of patients had an aortic diameter < 5.0 cm, while 32.3% of the patients had an aortic diameter of 4.5 cm. In addition, 72.0% of the patients had an ascending aorta diameter < 5.5 cm. Coexisting aortic regurgitation was recorded in 26.8% of the patients, while history of hypertension was observed in 86.1%. Other demographic characteristics and preoperative details are listed in [Table 1](#).

We tested the correlation of aortic diameter with age, BMI, LVEF, D-dimer, and NT-proBNP. No correlation was detected between aortic diameter and age ( $r = 0.13$ ,  $P = 0.20$ ), BMI ( $r = 0.05$ ,  $P = 0.67$ ), LVEF ( $r = 0.08$ ,  $P = 0.47$ ), D-dimer ( $r_s = -0.14$ ,  $P = 0.31$ ), or NT-proBNP ( $r_s = 0.19$ ,  $P = 0.14$ ). No difference in ascending aorta diameters was observed between males *vs* females ( $P = 0.83$ ), as well as between patients with *vs* without history of hypertension ( $P = 0.87$ ) and smoking *vs* no smoking ( $P = 0.90$ ). The BMI did not predict the diameter of the ascending aorta [ $\beta = 0.01$ , 95%CI: -0.05 to 0.08,  $P = 0.68$ ]. Preoperative plasma creatinine was not associated with the diameter of the ascending aorta ( $\beta = 0.09$ , 95%CI: -0.19-0.36,  $P = 0.53$ ).

The diameter of the ascending aorta did not differ in patients with *vs* without preoperative adverse events: Preoperative neurological dysfunction ( $P = 0.53$ ) and hemodynamic instability ( $P = 0.43$ ). In addition, univariable logistic regression analysis showed that aortic diameter did not predict the preoperative hemodynamic instability (OR = 1.2, 95%CI: 0.87-1.60,  $P = 0.29$ ) or preoperative neurological dysfunction (OR = 1.0, 95%CI: 0.72-1.51,  $P = 0.81$ ). Multivariable logistic regression analysis (adjusted for age, gender, and BMI) showed that aortic diameter did not predict preoperative neurological dysfunction (OR = 1.1, 95%CI: 0.68-1.74,  $P = 0.70$ ) ([Table 2](#)). Furthermore, multivariable logistic regression analysis (adjusted for age, gender, BMI, and aortic diameter) revealed that only age predicted the preoperative hemodynamic instability (OR = 1.05, 95%CI: 1.01-1.11,  $P = 0.02$ ), while diameter of the aorta did not (OR=1.1, 95%CI: 0.68-1.57,  $P = 0.86$ ) ([Table 3](#)). Median age of the patients with preoperative hemodynamic instability was 65 (57.5-74) years, while it was 60 (51-68) years in those without ( $P = 0.04$ ) ([Figure 1](#)). In conclusion, our analysis showed that no difference in dissected ascending aorta diameter was observed between patients who died in hospital *vs* who did not ( $P = 0.75$ ). In addition, the diameter of dissected ascending aorta was not correlated with postoperative ICU or hospital stay ( $r_s = -0.08$ ,  $P = 0.45$  and  $r_s = -0.02$ ,  $P = 0.85$ , respectively).

## DISCUSSION

Currently, American and European guidelines are in agreement regarding the main criterion for elective surgical aneurysm resection in the thoracic aorta: The size of the aortic diameter[6,13]. For non-syndromic, asymptomatic aortic aneurysmal disease, the indicative diameter threshold for elective replacement of the ascending aorta is 5.5 cm. However, these guidelines are relying on post-dissection diameter measurements, which are much larger than diameter size prior to dissection[6,13].

**Table 1 Demographic characteristics and preoperative details of patients**

Variable	Total number of patients (N = 108)
Age, yr, median (IQR)	61.5 (52.5-70.5)
Body mass index, cm <sup>2</sup> , median (IQR)	28.2 (25.1-32.6)
Female, n (%)	37 (25)
History of hypertension, n (%)	93 (86.1)
History of smoking, n (%)	65 (60.2)
Aortic regurgitation, n (%)	29 (26.8)
Left ventricle ejection fraction, %, median (IQR)	45 (40-50)
Diabetes mellitus, n (%)	11 (10.2)
Preoperative neurological dysfunction, n (%)	22 (16.1)
Temporary neurological dysfunction	14 (13.0)
Permanent neurological dysfunction	3 (2.7)
Preoperative hemodynamic instability, n (%)	35 (32.4)
Maximum diameter of ascending aorta, cm, median (IQR)	5.0 (4.5-6)
NT-proBNP, pg/mL, median (IQR)	377.5 (180-928)
D-Dimers, µg/L, median (IQR)	5256.5 (2477-10000)

NT-proBNP: N-terminal pro-brain natriuretic peptide; IQR: Interquartile range.

**Table 2 Multivariable logistic regression analysis of risk factors for preoperative neurological dysfunction**

Variable	P value	OR	95%CI
Age	0.28	1.1	0.97-1.09
Gender	0.46	1.7	0.38-8.12
Body mass index	0.42	1.1	0.92-1.19
Diameter of ascending aorta	0.70	1.1	0.68-1.74

OR: Odds ratio; CI: Confidence interval.

**Table 3 Multivariable logistic regression analysis of risk factors for preoperative hemodynamic instability**

Variable	P value	OR	95%CI
Age	0.02 <sup>1</sup>	1.05	1.01-1.11
Gender	0.76	0.81	0.21-3.11
Body mass index	0.56	0.97	0.86-1.08
Diameter of ascending aorta	0.86	1.1	0.68-1.57

<sup>1</sup>Statistical significance ( $P < 0.05$ ).

OR: Odds ratio; CI: Confidence interval.

There is evidence to suggest that the size of the aorta significantly increases post-dissection[18]. Mansour *et al*[18] from the Aortic Institute at Yale-New Haven Hospital demonstrated that the mean aortic diameter at ATAAD was 54.2 mm, whereas the mean aortic diameter prior to dissection was only 45.1 mm[18]. Wu *et al*[19] described an 18% increase in aortic diameter after an ATAAD. Therefore, the pre-dissection aortic diameter falls in several studies well below the current threshold for elective surgical replacement of the ascending aorta. Saade *et al*[20] introduced the term aortic size index in order to stratify patients into risk groups. It was calculated by dividing the aortic diameter by the body

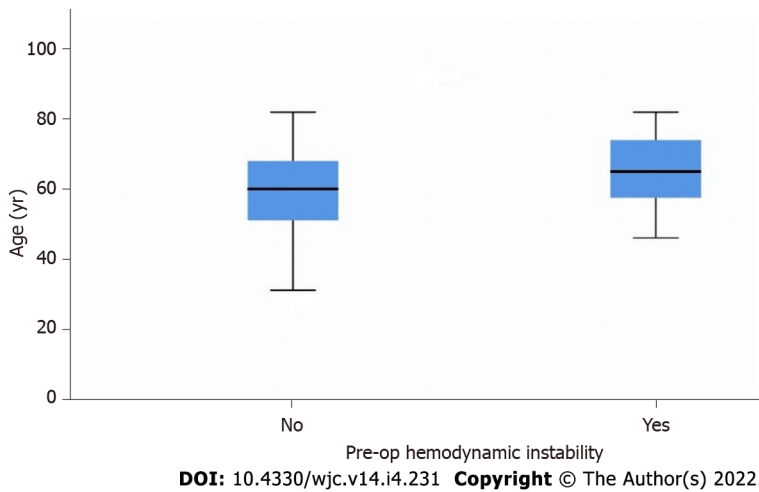


Figure 1 Boxplot graph for the age of patients with and without preoperative hemodynamic instability ( $P = 0.04$ ).

surface area. However, 10 years later, researchers from the same institution argued against that theory and concluded that body surface area should not be taken into consideration[21]. The same researchers focused on the importance of aortic height index, which is calculated by dividing the aortic diameter by the patient's height. An increased index is associated with an increased annual risk of aortic aneurysm complications[21]. Eliathamby *et al*[22] concluded that the aortic length (distance between the aortic valve and the innominate artery) was strongly correlated with the diameter of the ascending aorta. Wu *et al*[19] suggested the length-height index, which is calculated by dividing the aortic length by the patient's height. An index  $> 7.5$  cm/m was found to have an annual fivefold increased risk of aortic adverse events compared with patients with an index  $< 5.5$  cm/m. However, genetic susceptibility should always be taken into account as it plays an important role in identifying high risk patients[19,23].

ATAAD continues to carry a high peri-operative mortality risk with rates reaching as high as 25%[23, 24]. Many authors highlight the safety of preventive surgical replacement of the ascending aorta as published data on elective replacement of the ascending aorta is associated with mortality rates less than 3%[23,24]. For elective operations, postoperative stroke rates are also low with no more than 1.0% strokes noted when the operation takes place in a large volume aortic centre[25]. Moreover, emergency surgical operations show a 5-year survival rate of 37%, rather poorer than the rate ( $> 85\%$ ) related to elective surgical repair of the ascending aorta[25].

## CONCLUSION

Although current guidelines suggest replacing the ascending aorta with a diameter  $\geq 5.5$  cm, many of the patients with ATAAD have an aortic diameter of less than 5.5 cm. The diameter of the ascending aorta in patients diagnosed with ATAAD is not associated with preoperative adverse events. An international taskforce should adapt the new data extracted from the most recent scientific evidence for the surgical treatment of the ascending aortic aneurysm.

## ARTICLE HIGHLIGHTS

### Research background

Acute type A aortic dissection (ATAAD) is a life-threatening cardiovascular disease. Current guidelines recommend that ascending aortic replacement be performed when the ascending aorta is 5.5 cm in non-syndromic patients, while in syndromic patients, it should be replaced if the diameter reaches 4.5 cm in the sinus of Valsalva and 5.0 cm in the ascending aorta.

### Research motivation

New approach for ascending aorta aneurysm management should be considered for prevention of ATAAD.

### Research objectives

The objective of our study was to evaluate the correlation of the diameter of dissected ascending aorta in patients with ATAAD with preoperative adverse events, such as neurological dysfunctions and

hemodynamic instability.

### Research methods

A retrospective analysis was performed on patients who were admitted to our hospital for ATAAD treatment. In all patients, the diameter of dissected ascending aorta was measured and its association with adverse events was analyzed.

### Research results

The diameter of dissected ascending aorta was not associated with adverse events. Also, the diameter of the ascending aorta was not associated with 30-d mortality and ICU and hospital stay postoperatively.

### Research conclusions

Maybe the threshold of ascending aorta aneurysm should be revised for lower limits regarding the risk for late acute dissection

### Research perspectives

Randomized controlled studies including more patients should be performed to confirm our results and preventive ascending aorta replacement may be considered for prevention of ATAAD.

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## FOOTNOTES

**Author contributions:** All authors contributed equally in carrying out the research and writing the manuscript.

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