Aortic elongation part II

ORIGINAL RESEARCH ARTICLE

Aortic elongation part II: the risk of acute type A aortic dissection

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ABSTRACT

Objectives Prophylactic surgery for prevention of acute type A aortic dissection (ATAAD) is reserved for patients with an ascending aortic aneurysm ≥55 mm. Identification of additional risk predictors is warranted since over 70% of patients presenting with ATAAD have a non-dilated aorta or an aneurysm that would not have met the diameter criterion for preventative surgery. Aim of the study was to evaluate ascending aortic elongation as a risk factor for ATAAD and to compare aortic lengths between ATAAD patients and healthy controls.

Methods Aortic lengths and diameters of ATAAD patients were measured on three-dimensional modelled computed tomography and adjusted to predissection dimensions in this cross-sectional single-centre study. Logistic regression was used to evaluate the relation between ATAAD and aortic dimensions. Lengths of different aortic segments were compared with a healthy control group using propensity score matching.

Results Two-hundred and fifty patients were included in the study (ATAAD, n=40; controls, n=210). Ascending aortic length and diameter proved to be independent predictors for ATAAD (OR=5.3, CI 2.5 to 11.4, p<0.001 and OR=8.6, CI 2.4 to 31.0, p=0.001). Eighty patients were matched based on propensity scores (ATAAD n=40, controls n=40). The ascending aorta was longer and more dilated in ATAAD patients compared with healthy controls (78.6±8.8 mm vs 68.9±7.2 mm, p<0.001, 34.4 mm ±3.2. vs 39.4 mm ±5.7, p<0.001, respectively). No differences were found in lengths of the aortic arch and descending aorta.

Conclusions Ascending aortic length could serve as an independent predictor for ATAAD. Future studies addressing indications for prophylactic surgery should also investigate aortic length.

INTRODUCTION

Acute type A aortic dissection (ATAAD) is a life-threatening cardiovascular disease with an annual incidence of approximately 10 per 100 000 per year.[1 2] Mortality rates are high and range from 27% in surgically treated patients to 56% in those who undergo conservative therapy.[3] Aortic dilatation is the only recognised anatomical risk factor for development of ATAAD and ascending aortic replacement is considered in patients with aortic aneurysms to prevent the occurrence of dissection and rupture.[4] Current guidelines recommend preventative surgical intervention in aneurysms≥55 mm, as these carry an annual complication risk that exceeds the current surgical mortality rates.[5–7] However, the sole use of aortic diameters in the risk prediction for ATAAD is questionable, since multiple studies have shown that the majority of dissected aortas exhibit diameters below this cut-off.[8 9] Modelling of dissected aortas to predissection dimensions even demonstrated that 97% of ATAAD patients would fail to meet the criterion for preventative aortic repair.[10] Therefore, the identification of additional risk factors is warranted in order to reduce the incidence of ATAAD. We hypothesise that excessive aortic elongation, like dilatation, could carry the risk of dissection. In part I of this two-part article, we have investigated the normal ageing process of the thoracic aorta and shown that its length gradually increases with age. In daily clinical practice, the dissected aorta often appears abnormally elongated and tortuous in its course. Moreover, a transverse intimal entry tear is often observed on inspection of the vessel wall, whereas a longitudinal burst would be expected as a consequence of severe aortic dilatation.[11 12] In our hypothesis, the transverse entry tear reflects disruptive stretch in the longitudinal direction, which may result from excessive aortic lengthening. Aim of the current study was to evaluate the potential role of elongation in the occurrence of ATAAD using three-dimensional (3D) modelled computed tomography (CT) and to compare the aortic lengths of ATAAD patients with those of propensity-matched healthy controls.

MATERIALS AND METHODS

Study population

We retrospectively evaluated all consecutive adult patients who were diagnosed with ATAAD at the Maastricht University Medical Center between January 2010 and December 2016 and who underwent contrast-enhanced CT angiography (CTA). Exclusion criteria were prior aortic surgery, iatrogenic dissection, connective tissue disease (Marfan's disease, Loeys-Dietz syndrome or Ehlers-Danlos syndrome), bicuspid aortic valve and familial thoracic aneurysm and dissection. Results were compared with those of an apparently healthy control group, which was presented in part I of this two-part article. In brief, the control group consisted of apparently healthy adult patients who were referred for contrast-enhanced chest CT between December 2015 and December 2016. The study protocol was reviewed and approved by the

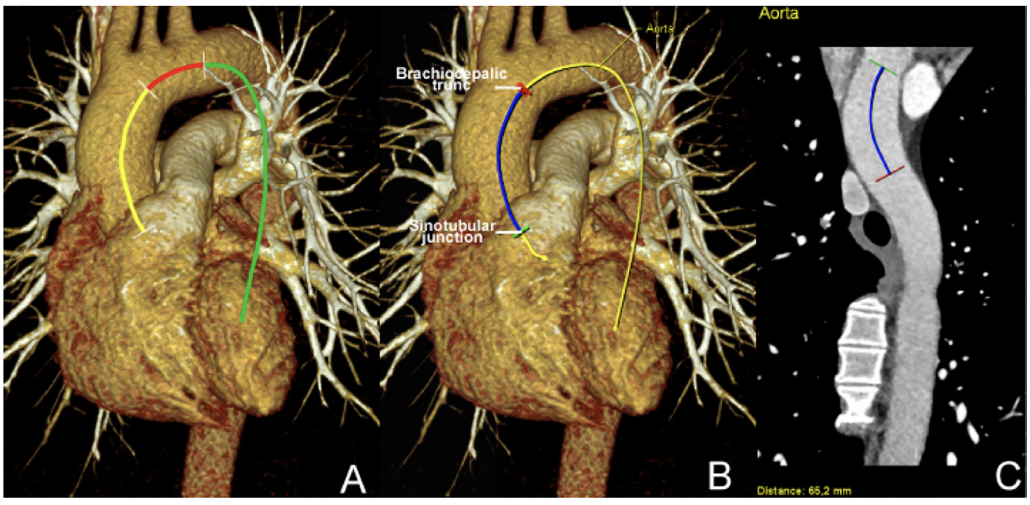

Figure 1 Length measurements of different aortic segments. (A) Segmental division of the aorta (yellow: ascending aorta, red: aortic arch, green: descending aorta). (B) Three-dimensional length measurement of the ascending aorta. (C) Multiplanar reformatted image of the thoracic aorta.

local ethics committee. The need for written patient consent was waived because of the observational character of this study.

Image acquisition

The CT protocol for control patients was described in part I of this study. In the ATAAD group, scans were performed on a second-generation dual source CT scanner (Somatom Flash, Siemens Healthineers, Forchheim, Germany) with 128×0.6 slice collimation at a rotation time of 0.28 seconds. The scan protocol consisted of a non-contrast-enhanced CT of the aorta, a retrospective electrocardiogram (ECG)-triggered helical CTA of the aortic root and ascending aorta followed by a high-pitch spiral CTA from the aortic arch to the femoral bifurcation. Tube voltage and tube current were semiautomatically adapted in all examinations (CARE kV, CARE Dose4D, Siemens) based on patient habitus. Iopromide (300 mg iodine/mL, Ultravist, Bayer, Berlin, Germany) was used as a contrast medium in all subjects, using an individualised approach (Contrast Dose Management, Certegra, Bayer). Image reconstruction was performed to achieve the same reconstruction parameters (slice thickness and increment) as in the control group.

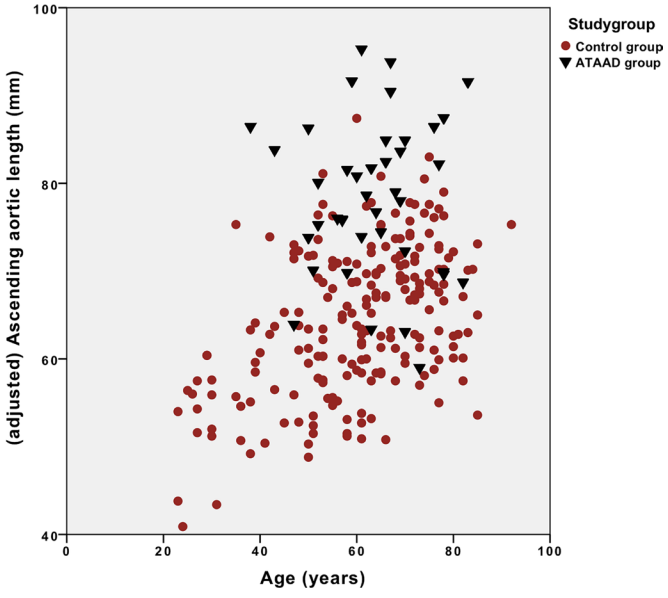

Figure 2 Modelled ascending aortic length of ATAAD patients and healthy controls. Scatter plot depicting the modelled length of the ascending aorta in healthy controls (red) and ATAAD patients (black). ATAAD, acute type A aortic dissection.

Image analysis and modelling of aortic dimensions

Image analysis of ATAAD patients was performed by a single observer. After image acquisition, CT datasets were loaded onto a workstation for postprocessing (Syngo.via, Siemens). A 3D model of the thoracic aorta was created and divided into three anatomical segments following current guidelines (figure 1).[13] The ascending aorta was measured as the centreline distance between the sinotubular junction (STJ) and the origin of the brachiocephalic trunk. The aortic arch was defined as the segment that comprised the three branch vessels. The descending aorta was defined as the part of the aorta from the left subclavian artery to the aortic hiatus in the diaphragm. Luminal diameters were measured using the inner edge to inner edge approach at different levels of the aorta (STJ, halfway the ascending aorta and maximal diameter). All diameter measurements were performed on multiplanar reformatted images perpendicular to the automatically detected vessel centreline.

To evaluate aortic diameter and length as a potential risk factor for ATAAD, we performed retrospective modelling of the aorta to obtain adjusted predissection dimensions. Rylski *et al* demonstrated the dimensions of the ascending aorta to increase on average with 30% (diameter) and 10% (length) after the occurrence of dissection, while the lengths of the aortic arch and descending aorta did not increase.[14] Like in their study, we modelled the aorta of ATAAD patients to predissection dimensions by deducting 30% and 10% of the measured aortic diameter and length, respectively.[10]

Statistical analysis

The distribution of continuous variables was assessed for normality using the Shapiro-Wilk test and assessed visually by inspection of histograms and standardised normal probability (P-P) plots. Continuous variables are presented as mean± standard deviation(SD) or median and interquartile range (IQR) in the presence of skewness. Categorical variables are presented as frequencies and percentages. Differences between groups were

Table 1 Ascending aortic diameters in ATAAD patients

	Non-adjusted diameters	Adjusted diameters
Mean max. diameter (mm, ±SD)	51.2±7.5	39. 4±5.7
Stratified max. diameter		
<50 mm	17 (43%)	39 (97%)
50–55 mm	10 (25%)	1 (3%)
>55 mm	13 (32%)	0

ATAAD, acute type A aortic dissection.

assessed using the Student's t-test or the Mann-Whitney U test (for continuous variables) or the χ^2 test (categorical variables). Binary logistic regression was performed to assess independent predictors for occurrence of ATAAD.

Covariates for aortic length, used for calculation of propensity scores, were identified using multivariable regression analysis. Variables with p<0.20 were considered to be important covariates and were used to calculate propensity scores. Differences in baseline characteristics were added to this model for balancing purposes. Propensity scores were matched using nearest neighbour matching on a 1:1 ratio. Replacement was not allowed. Calliper distance was set at 0.10. Baseline characteristics were presented both before and after propensity-score matching. All statistical analyses were performed using commercially available software (SPSS V.24, IBM, Armonk, New York, USA and R Statistics, the R Foundation, Vienna, Austria).

RESULTS

Study population

As described in part I of this two-part article, 210 patients were included in the control group. Between January 2010 and December 2016, a total of 48 patients were diagnosed with ATAAD at our institution based on findings at CT examination. Two patients were excluded because of the iatrogenic origin of their dissection. Six patients were excluded because of concomitant diagnosis of connective tissue disease or bicuspid aortic valve. The remaining 40 patients were included in the study group. Baseline characteristics of both groups before propensity score matching are presented in the online supplementary data 1. The ATAAD group comprised significantly more males than the control group (63% vs 39%, p=0.01). Furthermore, ATAAD patients had a larger body surface area (BSA) and were more likely to suffer from hypertension (both p<0.01).

Aortic length and diameters

As shown in part I, the length of the ascending aorta was significantly related to age in normal controls and increased by a mean of 3 mm/decade. Figure 2 depicts the adjusted predissection length of the ascending aorta of ATAAD patients when plotted against the aortic length of the healthy control group. Adjusted and non-adjusted ascending aortic diameters were presented in table 1. Binary logistic regression analysis was performed for evaluation of predictors for ATAAD. All variables with p<0.20 in univariable analysis were included in the multivariable model to assess independent predictors (table 2). Both ascending aortic length and diameter proved to be independently related to the occurrence of ATAAD (OR 5.3, CI 2.5 to 11.4, p<0.001 and OR 8.6, CI 2.3 to 31.0, p=0.001, respectively).

Propensity score matching

For covariate assessment, multivariable linear regression analysis was conducted in the control group with ascending aortic length as dependent variable. Age, gender and BSA showed to be independent predictors for ascending aortic length (table 3). These variables were therefore included in the model for calculation of propensity scores. Hypertension was also added to the model for balancing purposes. The propensity scores prematching and postmatching and their distribution are presented in the online supplementary data 2. Eventually, 40 pairs were matched. After matching, there were no persisting differences in baseline characteristics between the two groups (table 4).

Aortic dimensions in dissection patients

The adjusted length of the ascending aorta was significantly increased in the ATAAD group when compared to their propensity-matched healthy peers (78.6±8.8 vs 68.9±7.2 respectively, p<0.001). Adjusted maximum ascending aortic diameter was significantly increased as well (39.4±5.7 vs 34.4±3.2, p<0.001). Aortic arch length (36.2±7.0 vs 34.3±11.9, p=0.39) and descending aortic length (219.4±23.3 vs 210.4±28.1, p=0.13) did not differ significantly between the two matched groups (table 5).

DISCUSSION

Acute type A aortic dissection is a catastrophic cardiovascular disease that carries high morbidity and mortality rates.[15] Although aortic dilatation is a well-known risk factor for dissection, it can also occur in normal-sized aortas. Only 32% of dissection patients in the current study exhibited diameters on postdissection scans that would qualify for prophylactic surgery, which is in accordance with previous studies that stated that the sole use of aortic diameters is insufficient for adequate risk prediction for ATAAD.[8 9 14] In fact, when the acute diameter expansion after dissection onset is taken into account, 97% of patients would fail to meet the indication criterion of <55 mm, which is also in line with previously reported findings.[10] We hypothesised that, like dilatation, aortic elongation could also

Table 2 Binary logistic regression analysis for occurrence of ATAAD

	Univariable			Multivariable		
	OR	CI	P value	OR	CI	P value
Age	1.0	0.9 to 1.1	0.21			
Gender	0.4	0.2 to 0.8	0.01	1.9	0.6 to 6.0	0.25
BSA	9.0	1.9 to 44.2	0.01	1.2	0.1 to 14.5	0.89
Hypertension	3.4	1.7 to 6.8	<0.001	1.3	0.5 to 3.5	0.56
Diabetes	0.3	0.0 to 2.0	0.19	0.5	0.1 to 4.8	0.54
Adjusted ascending aortic diameter (cm)	7.8	4.1 to 14.6	<0.001	8.6	2.4 to 31.0	0.001
Adjusted ascending aortic length (cm)	31.8	11.1 to 90.9	<0.001	5.3	2.5 to 11.4	<0.001

ATAAD, acute type A aortic dissection; BSA, body surface area.

Table 3 Univariable and multivariable linear regression analyses for assessment of covariates for aortic length in healthy controls

	Univariable				Multivariable	
	R	P value	B	β	CI	P value
Age	0.47	<0.001	0.25	0.46	0.18 to 0.32	<0.001
Gender	0.44	<0.001	−4.63	−0.30	−6.72 to −2.55	<0.001
BSA	0.29	<0.001	9.22	0.25	4.62 to 13.83	<0.001
Hypertension	0.33	<0.001	1.09	0.08	−0.77 to 3.52	0.21
Diabetes	0.06	0.35	1.60	−0.05	−4.62 to 1.69	0.36

β, standardised regression coefficient; B, unstandardised regression coefficient; BSA, body surface area; R, correlation coefficient.

carry risk for dissection and used 3D modelled CT to show that the adjusted ascending aorta of ATAAD patients is significantly longer than would have been expected based on age, gender and body posture. Our conclusions concur with those of Krüger *et al*, who were the first to investigate aortic length and diameters in dissected aortas and proposed a new risk scoring system based on these two anatomical variables.[16 17] However, in their study, the normal age-related changes of longitudinal aortic dimensions were not accounted for, and non-ECG-gated scans were used for length and diameter measurements. Besides the differences in aortic dimensions between ATAAD patients and healthy controls, we additionally investigated the role of ascending aortic length and diameter in the occurrence of ATAAD using a regression model. This model also included predisposing factors like age, BSA, diabetes and hypertension. Length and diameter increase both proved to be significantly associated with an increased risk for ATAAD (with every centimetre increase of ascending aortic length carrying a 5-fold risk of ATAAD occurrence). A similar significant increase in risk was demonstrated for diameter expansion. We therefore endorse the vision of Krüger *et al* for a multifactorial risk scoring system for the prediction of ATAAD, which would include both aortic length and diameter.[17] Ideally, also factors like aortic curvature,[18] genetic predisposition,[19] and hemodynamics[20] would be included in this model.

Of note, the aortic arch and descending aorta were not elongated in ATAAD patients. In healthy controls however, elongation and tortuosity of these segments is not uncommon. The question arises if the aetiology of aortic elongation, like aneurysm formation, differs per anatomical segment. It has been well-described that aneurysm disease divides itself into two entities, one involving the ascending aorta and one involving the descending aorta.[21] The distinct embryological origin of the aorta's smooth muscle cells (the smooth muscle cells of the ascending aorta derive from the neural crest, while those of the descending aorta derive from somatic mesoderm) are thought to attribute to this segmental predisposition of aneurysm formation.[22] Likewise, and in accordance with the findings of the current study, it is conceivable that the extent of aortic elongation varies per segment and concentrates solely in the ascending aorta in patients suffering from ATAAD.

Table 4 Postmatching baseline characteristics

	Control group (n=40)	ATAAD group (n=40)	P value
Age (years)	65±13	63±11	0.65
Gender (male)	24 (60%)	25 (63%)	1.00
BSA (m^2)	1.95±0.20	1.97±0.18	0.80
Hypertension	26 (65%)	25 (63%)	1.00
Diabetes	1 (3%)	1 (3%)	1.00
Medication			
Beta blockers	11 (28%)	10 (25%)	1.00
ACE-inhibitors	14 (35%)	10 (25%)	0.46
Calcium blockers	10 (25%)	3 (8%)	0.07
Diuretics	9 (23%)	7 (18%)	1.00

ACE, angiotensin converting enzyme; ATAAD, acute type A aortic dissection; BSA, body surface area.

Limitations

Some limitations of the current study should be addressed. First, we used a cross-sectional study design. To evince a clear causal relationship between aortic elongation and dissection, a prospective and longitudinal study design should be conducted. However, given the low incidence rate of ATAAD and the time span that is required to investigate an ageing process like aortic elongation, it would be challenging to perform such a study. We therefore consider our study design combined with modelling of dimensions to be the best achievable alternative.

Second, we measured aortic diameters in the healthy control group using non-ECG-gated CT. The accuracy of diameter measurements in the control group could benefit from ECG-gating on CT.[23] However, reference values for aortic diameters are mostly based on non-triggered scans and in daily practice, the majority of diameter and circumferential measurements are performed on non-ECG-gated images.[6 24]

Finally, aortic modelling was performed using a generalised algorithm in all patients. However, the actual increase in diameter and length after dissection onset may differ between patients.

CONCLUSION

Ascending aortic diameter is an insufficient stand-alone predictor for the occurrence of ATAAD. The current study demonstrated ascending aortic diameter and length to contribute equally to the occurrence of dissection. Furthermore, we have shown that the ascending aorta of ATAAD patients is significantly longer compared with their propensity matched counterparts. No difference was found between the lengths of the aortic arch and descending aorta, implying ATAAD to have a specific pathophysiological origin in the ascending aorta.

Table 5 Dimensions per segment

	Control group (n=40)	ATAAD group (n=40)	P value
Adjusted ascending aortic length (mm)	68.9±7.2	78.6±8.8	<0.001
Adjusted max. ascending aortic diameter (mm)	34.4±3.2	39.4±5.7	<0.001
Aortic arch length (mm)	34.3±7.0	36.2±11.9	0.39
Descending aortic length (mm)	219.4±23.3	210.4±28.1	0.13

ATAAD, acute type A aortic dissection.

Key messages

What is already known on this subject?

- Aortic dilatation is known to be associated with an increased risk of aortic dissection. Nevertheless, only 30% of all patients with type A aortic dissection would have met the criteria for preventative aortic surgery. Therefore, there is urgent need for identification of other risk factors. In daily clinical practice, the dissected aorta often looks elongated and tortuous in its course. We hypothesise that longitudinal aortic dimensions (ie, aortic elongation) could also serve as a risk factor for the occurrence of dissection. Previous studies[16 25] have investigated aortic length in dissection patients and indeed found increased aortic length when compared with healthy controls. However, these studies used two-dimensional imaging[25] and did not account for the normal age-related changes of longitudinal aortic dimensions (both references). Moreover, no regression analysis was performed to show the influence of aortic length on the occurrence of dissection.

What might this study add?

- In the current study, we have demonstrated that ascending aortic length could serve as an independent predictor for aortic dissection. Furthermore, we have shown that the length of the ascending aorta is increased in dissection patients when compared with propensity-matched controls, whereas there is no difference in the lengths of the aortic arch and descending aorta.

How might this impact on clinical practice?

- Future studies need to focus on the inclusion of additional risk factors for dissection, including length, as demonstrated in the current study. This could eventually lead to alteration of the guidelines for prophylactic aortic replacement, in order to provide more patients a timely intervention.

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Competing interests None declared.

Patient consent Detail has been removed from this case description/these case descriptions to ensure anonymity. The editors and reviewers have seen the detailed information available and are satisfied that the information backs up the case the authors are making.

Ethics approval Medical Ethical Review Board, Maastricht University Medical Center.

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