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## a DANCAVAS substudy

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**Individual, expected diameters of the ascending aorta and prevalence of dilations in a study-population aged 60-74 years - a DANCAVAS substudy**

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All authors mentioned above take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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## Abstract

**Aims**: To determine individual, expected normal diameters of the ascending aorta (AAo) and prevalence of dilations based upon an absolute cut-off point (≥40 mm) and individual cut-off point (≥25% than expected normal).

**Methods:** Non-contrast computed tomography (CT) scans were obtained in 14,993 individuals (95.0% male, mean age 67.8±3.8). A sub-group (n=291) had AAo diameter measured by transthoracic echocardiography. A prediction formula for AAo diameters was created from multivariate linear regression analysis based upon gender, age, and body surface area. An index was made by dividing observed diameters with predicted diameters. A size-index ≥1.25 was defined as dilated.

**Results:** Prevalence of AAo dilations among males and females using 40 mm as cut-off point were 10.6% and 2.1% ($p<0.001$), respectively, while 3.3% and 2.6% ($p=0.305$) using the size-index ≥1.25, respectively. Proportion of agreement between cases of AAo dilations from the size-index and 40 mm was 93.0%. Using the size-index as 'golden standard' for dilation, the sensitivity and specificity using 40 mm as cut-off point for males were 100.0% and 92.4%, respectively, while 75.0% and 99.9%, respectively, for females. For males and females, the positive predicted values were 31.3% and 93.8%, respectively; the negative predicted values were 100.0% and 99.3%, respectively.

**Conclusions**: An absolute echocardiographic size-criterion of 40 mm entails a significant number of females with missed AAo dilation, and a large number of males are mistaken to have dilated AAo. Thus, AAo diameters should be evaluated in relation to gender, age and BSA. This study provides a formula for potential clinical implementation.

**Key words**: ascending aortic size, ascending aortic dilation, prevalence, general population

**Abbreviations:**

Ascending aorta (AAo)

Computed tomography (CT)

Transthoracic echocardiography (TTE)

Body surface area (BSA)

Body mass index (BMI)

BSA calculated with Du Bois' formula (BSA(d))

BSA calculated with Mosteller's equation (BSA(m))

Electrocardiography-gated (ECG)

The Danish Cardiovascular Multicenter Study I+II (DANCAVAS I+II)

## Introduction

An ectatic or aneurysmal (dilated) ascending aorta (AAo) is a potentially lethal condition in which there is a risk of dissection or rupture (1, 2). Early identification and appropriate surveillance in patients with a dilated AAo are therefore important. There are various options for imaging assessment of AAo dimensions, including computed tomography (CT), magnetic resonance imaging, and transthoracic echocardiography (TTE) (3-5). CT and magnetic resonance imaging are widely acknowledged as golden standards for exact measurement of AAo dimensions due to high reproducibility and accurate three-dimensional representation. However, compared to TTE, CT is a potentially harmful procedure as it exposes patients to radiation, and magnetic resonance imaging is often time consuming and more expensive. Thus, TTE is regularly preferred in clinical cardiology practice for assessment and surveillance of AAo dilations (2, 5, 6). Nevertheless, the agreement between TTE and the golden standards has only been sparsely investigated in the context of evaluating the AAo (7-9).

Furthermore, a clear definition of thoracic aortic dilations is lacking (2). A fully developed aneurysm is defined as an aneurysm with a diameter that exceeds normal size by ≥50% (10), while an artery in general is considered dilated if its diameter is ≥25% larger than normal. However, this definition makes sense only if we have knowledge of the individual patient's normal diameter, which rarely is available.

Previous studies have sought to establish cut-off values for normal AAo diameters stratified by gender, age and body surface area (BSA) (11-13). Nevertheless, individualized cut-off values have not been successfully implemented in the clinicians' everyday practice or in current guidelines. As the healthy aorta should not exceed 40 mm in diameter according to the ESC guideline from 2014 (2), a 40 mm cut-off point is commonly used in clinical echocardiographic practice for AAo dilations for both males and females.

The aims of this study were 1) to assess the agreement between AAo diameters measured by non-contrast CT and TTE, 2) to develop a prediction formula providing an individual reference diameter for normal AAo diameter, 3) to determine the prevalence of AAo dilations based upon an absolute cut-off point at 40 mm in diameter, and 4) to assess the prevalence of a ≥25% increase in AAo dimension using the prediction formula.

## Methods

*Patient population*

All data used in this study was prospectively collected in the comprehensive CT-based screening trials, the Danish Cardiovascular Multicenter Study I+II (DANCAVAS I+II), where men aged 60-74 years were randomly selected from the Danish national civil registry (14). Females at similar age were enrolled in a pilot phase, but as females were unlikely to benefit sufficiently from screening for cardiovascular disease cost-beneficially, only males have been recruited since May 2015 (15). The study was conducted in accordance with the Declaration of Helsinki. Written and verbally informed consent was obtained from each participant. The DANCAVAS trials were approved by the Danish Research Ethics Committee.

Besides screening for cardiovascular risk, the screening examinations included an electrocardiography-gated (ECG), non-contrast CT scan. Examinations were performed in the period from September 2014 to February 2018. Eighteen participants were excluded from this study due to missing measurements of height, weight, or AAo diameter on the CT scan. The final study population consisted of 14,237 males and 756 females. From February 2017 to March 2017, participants in the ongoing screening trials were consecutively recruited, and had a TTE recorded with the only purpose of measuring their AAo diameter (291 males).

*CT-imaging protocol*

Non-contrast ECG CT scans were performed from the jaw to the groin. Philips Brilliance was used at Nykoebing Falster Hospital, GE Revolution was used at Svendborg Hospital and Toshiba Aquillion One scanner at Silkeborg Hospital, while Siemens Somatom Definition Force/Flash was used at Odense University Hospital and Vejle Hospital. Common for all scanners was a slice thickness of 5 mm.

If a dilation of the AAo was detected, the largest measured diameter was used for further analysis; else, the anterior-posterior AAo diameter was measured on the first circular level above the sinotubular junction. The diameter was measured from the exterior-to-exterior surface of the aorta (*Figure 1A*). Experienced radiographers performed all measurements manually.

*TTE protocol*

Echocardiography was performed according to recommendations for TTE in adults (16). Images in the parasternal window were acquired to obtain long-axis views of the left ventricle. Images were optimized for optimal visualization of the AAo (*Figure 1B)*. When a frame with both the aortic valve and the AAo within the same window could not be produced, the transducer was moved one intercostal space up to optimize the sight of the AAo at the expense of loss of sight of the aortic valve (*Figure 1C*). The AAo diameter was measured end-diastolic from inner-edge to inner-edge from frozen 2D images (16). The largest detected diameter was used for further analysis. Three experienced cardiologists and a trainee performed all measurements blinded for measurements on CT scan.

*Definitions of ascending aortic dilations*

Two definitions of AAo dilations were used: 1) an echocardiographic, converted diameter ≥40 mm and 2) a diameter ≥25% of the individual, expected normal diameter. Both definitions are described in detail in the statistical paragraph.

*Statistical analyses*

Data distribution was assessed visually from probability plots and followed normal distributions. Descriptive statistics comprised means ± standard deviations (SDs) and frequencies with respective percentages. Accuracy measures (sensitivity, specificity, and predictive values) were evaluated with 95% confidence intervals (95% CIs). Differences between sexes were analyzed using the chi-squared test for dichotomous data and student's t-test for continuous data.

As TTE measurements of AAo are inner-edge to inner-edge and ECG-gated, non-contrast CT measurements are exterior-to-exterior surface, this will entail a difference. To estimate differences between these two modalities, TTE and CT were measured in the sub-group of 291 males. Correlation between measurements from TTE and CT scans was visualized in a scatterplot and examined using Pearson's r. Agreement between the two modalities was determined in a Bland Altman plot for which the average difference was estimated (17, 18). Hereafter, AAo diameters measured on CT scans were converted to their corresponding echocardiographic measurements by subtracting the observed mean difference between the two modalities. Further analyses and results are based upon these estimated echocardiographic measurements.

Correlations between AAo diameters and the physiological factors; age, height, weight, Body Mass Index (BMI), BSA calculated with Mosteller's equation (BSA(m)) and Du Bois' formula (BSA(d)) were assessed using Pearson's r (19, 20). A prediction formula providing expected normal AAo diameters was created through multivariate linear regression analyses based upon gender, age, and the strongest body size-related factor from participants with an AAo diameter <40 mm for exclusion of potentially dilated cases. By dividing the observed AAo diameter with the predicted AAo diameter, an index was created. An index ≥1.25 was defined as a dilated AAo, while an index <1.25 was considered normal (*Figure 2*) (21). Additionally, residual analyses from the prediction formula were performed. Proportion of agreement was calculated for AAo dilation using the size-index contra the 40 mm in diameter.(22, 23)

Furthermore, an exploratory backward variable selection model was performed using classical cardiovascular risk factors, to evaluate how extensive and precise a predictive formula for the AAo diameter could be, using a p-stay=0.20.

The reproducibility of measurements performed on non-contrast CT scans (n=291) was examined via inter-observer analyses using the Bland-Altman plot and Pearson's r. Inter-observer analyses on TTE (n=80) were equally assessed between sonographers in a Bland-Altman plot and Pearson's r. All analyses were performed with STATA/IC 16.1 (StataCorp LP).

## **Results**

*Baseline characteristics*

The study population consisted of 14,993 individuals (14,237 males, 756 females) with an average age of 67.8 ±3.8 years. Baseline characteristics stratified by gender are presented in Table 1. Male participants were statistically different from female participants on all parameters, except for self-reported prior stroke and known hypertension.

A table with clinical data from the sub-group undergoing TTE is presented in Appendix 1.

*Agreement between CT and TTE*

The correlation coefficient between CT and TTE (n=291) measurements of the AAo diameter was r = 0.81 (p<0.001) (*Figure 3A*). Regressing the differences on the means of measurements on CT and TTE in the Bland-Altman plot displayed no methodical difference if the AAo diameter was increased (Pearson's r = 0.09, p=0.117) (*Figure 3B*). The mean difference between CT and TTE was determined to be 2.3 mm (95% CI: 2.1-2.6) with 95% limits of agreement of -2.2 mm and 6.9 mm.

Regarding the CT measurements, the inter-observer variability showed a Pearson's r = 0.95 (p<0.001) and an average mean deviation of -0.1 ± 1.3 mm, while the inter-observer variability of the TTE measurements had a Pearson's r = 0.89 (p<0.001) with an average mean deviation of -0.1 ±1.8 mm.

*AAo diameter*

The mean echocardiographic converted diameter of the AAo was 35.2 ±4.1 mm among males and 31.9 ±3.6 mm among females (p<0.001). The average AAo diameter increase was 0.14 mm per year among males (p<0.001) and 0.09 mm per year among females (p=0.018).

*Prediction formula*

Age correlated modestly but significantly with the AAo diameter (r=0.12, p<0.001). The competing body size-relating factors; weight (r=0.26), height (r=0.22), BMI (r=0.17), BSA(m) (r=0.28), and BSA(d) (r=0.29) all correlated significantly with the AAo diameter (p-values <0.001). Gender, age, and BSA(d) were used in the prediction formula to calculate the individual, expected normal AAo diameter (*Figure 2*):

$$\mathrm{AAo}_{\mathrm{Estimated}} = 15.28 + (\mathrm{age} * 0.12) + (\mathrm{BSA} * 4.38) + 1.63(\text{if male})$$

All coefficients from the multivariate regression analyses had p-values <0.001. The mean of the residuals for the prediction of AAo diameter was 0.83 ±3.89 and showed little deviation from normal distribution. In a scatterplot between the residuals and the linear predicted values of AAo diameter, variance appeared to be acceptably homogeneous. The adjusted R-squared was 0.103.

Running an expanded backward exploratory selection analyses for prediction of normal AAo diameter led to the following formula:

$$AsAo_{estimated} = 14.87 + 1.65 \text{ (if male)} – 0.61 \text{ (if diabetic)} + 0.41 \text{ (if hypertensive)} – 0.16 \text{ (if previous stroke)} – 0.16 \text{ (if PAD)} + 0.40 \text{ (if AFLI)} – 0.30 \text{ (if statins)} – 0.13 \text{ (if platelet inhibitors)} – 0.22 \text{ (if CKD)} + (age*0.12) + (BSA*4.43)$$

The adjusted R-squared for the expanded prediction formula was 0.113.

Comparing the adjusted R-squared values for the prediction formulas for normal AAo diameter, gains are negligible by expanding the simple formula based upon age, gender and BSA – especially with the aspect of pathophysiological and clinical relevance. Thus, the simple formula was used in this study.

The proportion of agreement between cases of AAo dilations from the size-index and the cut-off value at 40 mm was 93.0% (92.5-93.4).(22, 23)

Based on the prediction formula, maximal diameter of the normal AAo can be calculated as

$$AAo_{Maximal} = 1.25 * AAo_{Estimated}$$

*Figure 4A and 4B* illustrates the maximal normal AAo stratified by gender, age and BSA.

Using a cut-off point at 40 mm, we found a prevalence of AAo dilations among males of 10.6% (95% CI: 10.1-11.2) and among females of 2.1% (95% CI: 1.2-3.4) ($p<0.001$). Using the prediction formula, we found a prevalence of AAo dilations at 3.3% (95% CI: 3.0-3.6) among males and 2.6% (95% CI: 1.6-4.1) among females (p=0.305).

Using the prediction formula as the 'golden standard', the sensitivity and specificity of the cut-off point at 40 mm for males were 100.0% (95% CI: 99.2-100.0) and 92.4% (95% CI: 92.0-92.9); for females they were 75.0% (95% CI: 50.9-91.3) and 99.9% (95% CI: 99.2-100), respectively. The positive and negative predicted values for males were 31.3% (95% CI: 29.0-33.7) and 100.0% (95% CI: 100.0-100.0); for females, they were 93.8% (95% CI: 69.8-99.8) and 99.3% (95% CI: 98.4-99.8), respectively (*Table 2*).

## **Discussion**

*Main findings*

In this large population-based cross-sectional study including randomly selected males and females aged 60-74 years, we developed a prediction formula offering individual, expected normal AAo diameters. We find that accepting a uniform definition of AAo dilations set at 40 mm in diameter may be problematic, as two out of three males with a large but healthy AAo risk being misdiagnosed as having ascending dilation, and one out of four females with dilated AAo will potentially be thought to have a normal AAo. Furthermore, the study confirms that TTE is useful for assessing AAo dimensions.

*Comparison of non-contrast CT and TTE*

We found that AAo diameters measured on non-contrast ECG CT and TTE are closely associated, and echocardiographic measurements are on average 2.3 mm smaller than the corresponding measurements on non-contrast CT scans. This difference between the two modalities is driven by the thickness of the aortic wall as different protocols for measurements were used for CT (exterior-to-exterior surface) and TTE (inner-edge to inner-edge). This observation is in agreement with prior studies (24-26). The strong correlation indicates that TTE nearly equals CT for evaluation of AAo diameters when assessing the first part of the AAo and when image quality is adequate.

*Individual, expected normal AAo diameter*

Males had a significant larger AAo diameter than females. This suggests that a unisex-shared cut-off point at 40 mm in diameter is not suitable as it may overlook dilated AAo among females. Additionally, we observed a surprisingly large number of dilated cases in males using the absolute cut-off point at 40 mm, suggesting that a threshold at 40 mm may be too low for males. There was a significant difference of AAo dilations using the absolute cut-off point, while no difference in prevalence was observed using the relative cut-off point.

The AAo diameter showed a constant age-related increase of 0.14 mm per year among males and 0.09 mm among females, which supports previous findings of an increase of approximately 1-2 mm per decade in adulthood (27-29). Finally, BSA was closely related to AAo diameter. In our formula, we used Du Bois' formula, as the correlation with the AAo diameter was slightly better than with Mosteller's equation, but the difference was not significant.

The observed proportion of agreement between dilations found from the size-index based on the prediction formula compared to the conventional definition of a diameter >40 mm was high.

Using our formula as the 'golden standard', 25% dilated females were missed when the conventional definition of a 40 mm diameter was used, while nearly 70% of males with an AAo diameter exceeding 40 mm would have been mistaken as dilated.

When comparing results from the present study with results from similar previous studies, image modalities, placement of measurement of the aorta and measurement technique (leading-edge to leading edge, exterior to exterior surface or inner-edge to inner-edge) must be taken into account. (11-13)

This study confirms the significant correlation between gender, age and BSA with AAo diameter. The mean AAo size reported in this paper varies little from earlier findings in a population >60 years old. The novelty of this study is the comparison between the presently used absolute criteria for AAo dilations at 40 mm with a relative individualized age-, sex- and size-dependent criterion at a 25% increase in observed diameter from calculated normal diameter.

However, as age is a determinant of aortic size, it is questionable if data presented in this manuscript can be duplicated to other age groups than 60-74 years old.

All preventive issues such as surveillance of AAo dilations must balance harms and benefits. Numerous of papers have proven aortic aneurysm surveillance to cause fear and stigmatization. However, the proportion of patients with identified ectatic AAo qualifying for surveillance is many-fold higher than the proportion ending up having an operation-demanding dilation or dissection (30, 31). This over-diagnosing is only causing fear and impaired cost-effectiveness. The relative size assessment is an attempt to reduce these side effects, as it excludes the upper normal of biological variation from those who potentially may have started a pathological dilation. Upcoming progression studies will tell us the magnitude of achievement, as current cases >40 mm hardly progresses more than the age-related progression.

*Study limitations and strengths*

An important limitation is the lack of an internationally recognized definition of AAo dilations. Consequently, we chose to use an individual cut-off point set at an observed 25% increase in diameter of the calculated, expected normal AAo diameter. This definition was based upon the definition of an ectatic abdominal aorta being 25%, while aneurysms are 50% (32-35). Presently, we cannot support our formula with events as the present study is a cross-sectional study.

The strengths of this study are the general population-based setup in various Danish geographically and thus socioeconomically diverse areas, leaving the risk of selection bias low. We therefore believe that our results are quite generalizable. In addition, the standardized protocols of the various measurements combined with large numbers guarantee high internal validity. The inter-observer viabilities showed very strong correlations between sonographers and radiographers when measuring the AAo diameter from both TTE images and CT scans, respectively.

A very large number of males was included, but the number of females was relatively low as they were enrolled only in the pilot phase. Even so, the number of females studied here exceeds that of most other studies.

Furthermore, measuring the AAo diameter on non-contrast CT scans is associated with a risk of overestimation of the AAo size if the measuring angle is not perpendicular. We tried to avoid this by measuring on the first circular level above the sinotubular junction. Lastly, it has to be taken into account that a large majority of the CT scans were measured on a pre-determined location, while the largest detected TTE measurements were used. Additionally, the pre-determined location for CT-scans on the AAo hindered an evaluation between TTE and CT for other AAo levels, including the sinus of Valsalva.

*Conclusions*

In conclusion, this study suggests that using an absolute echocardiographic size criterion at 40 mm for AAo dilations is associated with high sensitivity and specificity. However, a significant number of females with dilated AAo may be missed, and more than 2 out of 3 males will be mistaken to have dilated AAo. Missing females with dilated AAo may have serious consequences, while overestimating the rate of dilated AAo in males is associated with psychological costs and impaired cost effectiveness. Thus, this study emphasizes the need for the use of individualized cut-off values, and we here provide a formula for clinical implementation. This should be validated in future studies.

*Conflict of interest:* The authors declare that they have no conflict of interest.

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*Table 1* – Baseline characteristics stratified by gender.

| ***Table 1*** | **All** | **Males** | **Females** | **P values** |
|---|---|---|---|---|
| **Number (N)** | 14,993 (100%) | 14,237 (95.0%) | 756 (5.0%) | |
| **Age** (yrs.) | 67.8 (±3.8) | 67.8 (±3.8) | 68.7 (±3.5) | <0.01 |
| **BMI** (kg/m$^2$) | 28.0 (±4.4) | 28.1 (±4.4) | 26.7 (±5.1) | <0.01 |
| **BSA** (m$^2$) | 2.0 (±0.2) | 2.1 (±0.2) | 1.8 (±0.2) | <0.01 |
| **Smoking** | | | | <0.01 |
| Current | 2,388 (16.0%) | 2,288 (16.1%) | 100 (13.3%) | |
| Former | 7,467 (50.0%) | 7,203 (50.8%) | 264 (35.1%) | |
| Never | 5,077 (34.0%) | 4,688 (33.1%) | 389 (51.7%) | |
| **Known hypertension** | 6,580 (43.9%) | 6,227 (43.7%) | 353 (46.7%) | 0.11 |
| **Known diabetes** | 1,642 (11.0%) | 1,592 (11.2%) | 50 (6.6%) | <0.01 |
| **Statin treatment** | 4,962 (33.1%) | 4,687 (32.9%) | 275 (36.4%) | 0.049 |
| **Prior cardiovascular disease** | | | | |
| AMI | 867 (5.8%) | 855 (6.0%) | 12 (1.6%) | <0.01 |
| Stroke | 958 (6.4%) | 898 (6.3%) | 60 (7.9%) | 0.07 |

Numbers are mean (±SD) or number of patients (% proportion)

*Abbreviations*: Body Mass Index (BMI); Body surface area (BSA); Acute myocardial infarction (AMI).

*Table 2* – Prevalence of dilated ascending aorta

| | **Dilated AAo** | **Normal AAo** | |
|---|---|---|---|
| **Total (N=14,993)** | *Index ≥ 1.25* | *Index < 1.25* | Total |
| Dilated AAo ≥ 40 mm | 489 | 1,042 | 1,531 |
| Normal AAo < 40 mm | 5 | 13,457 | 13,462 |
| Total | 494 | 14,499 | 14,993 |
| **Males (n=14,237)** | *Index ≥ 1.25* | *Index < 1.25* | |
| Dilated AAo ≥ 40 mm | 474 | 1,041 | 1,515 |
| Normal AAo < 40 mm | 0 | 12,722 | 12,722 |
| Total | 474 | 13,763 | 14,237 |
| **Females (n=756)** | *Index ≥ 1.25* | *Index < 1.25* | |
| Dilated AAo ≥ 40 mm | 15 | 1 | 16 |
| Normal AAo < 40 mm | 5 | 735 | 740 |
| Total | 20 | 736 | 756 |

Two times two tables with prevalence of dilated ascending aorta using the individualized, relative cut-off value at a 25% increase in diameter as the 'golden standard' versus the absolute echocardiographic cut-off value at 40 mm.

*Abbreviations*: AAo = Ascending aorta

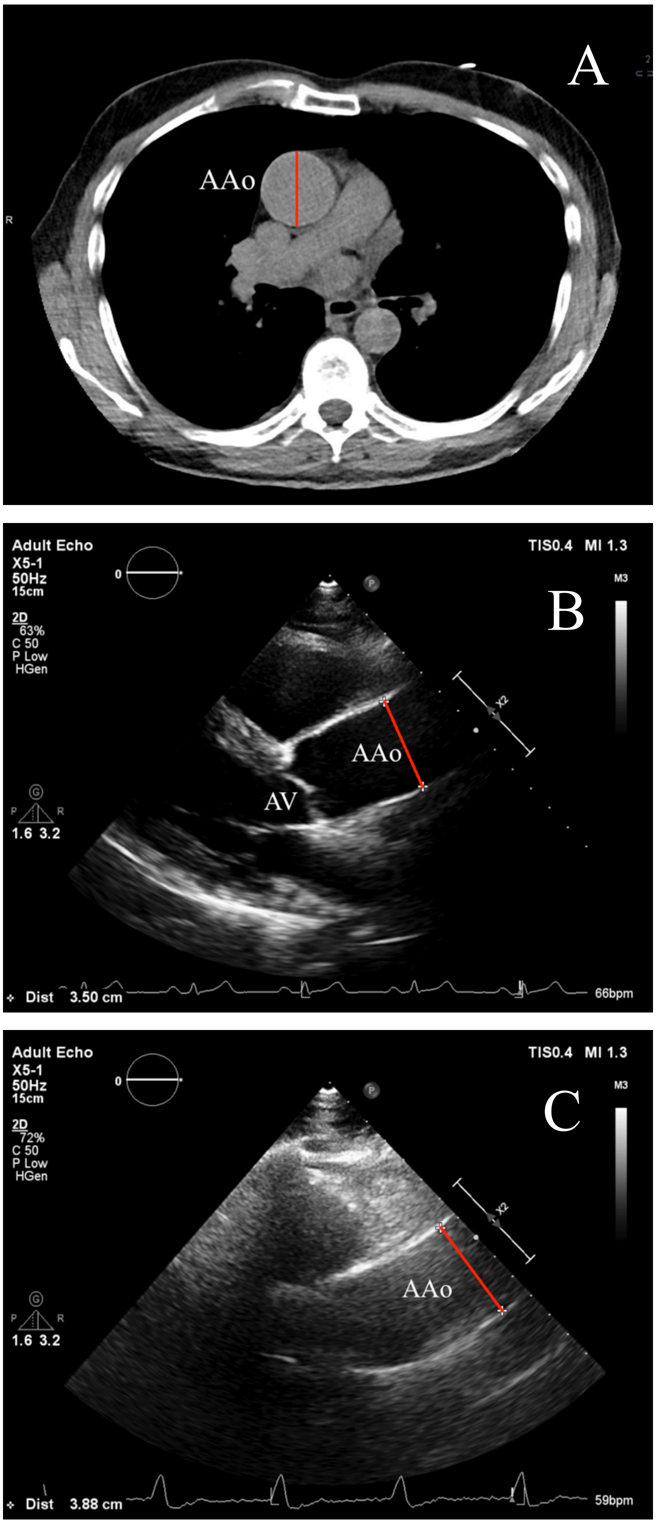



*Figure 1:* A) Non-contrast CT-scan with anterior-posterior measurement of the ascending aortic (AAo) diameter on the first circular level above the sinotubular junction from exterior-to-exterior surface. B) Transthoracic echocardiography measurement of the ascending aortic (AAo) diameter from inner-edge to inner-edge in the parasternal long-axis view with the aortic valve (AV) as reference point. C) Transthoracic echocardiography of the AAo from inner-edge to inner-edge in the parasternal long-axis view, one intercostal space higher than (*B)*

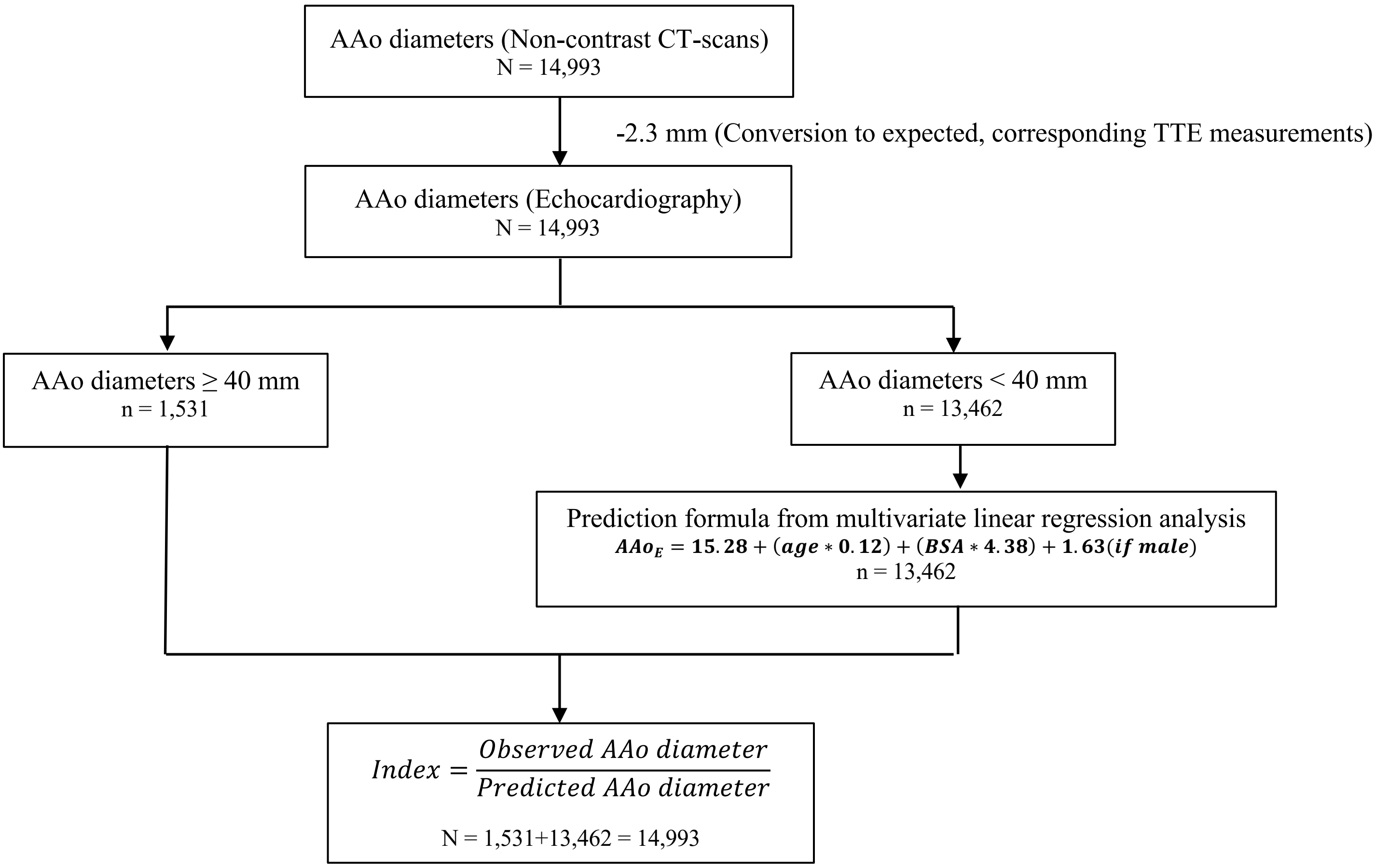



*Figure 2*: Flow chart with an illustration of the selection of participants prior the multivariate linear regression analyses. Hereafter a formula was generated to calculate the individual reference diameter for the normal ascending aortic (AAO) diameter. Finally, an index was created: observed / predicted diameter. An index ≥1.25 defined a dilated AAo.

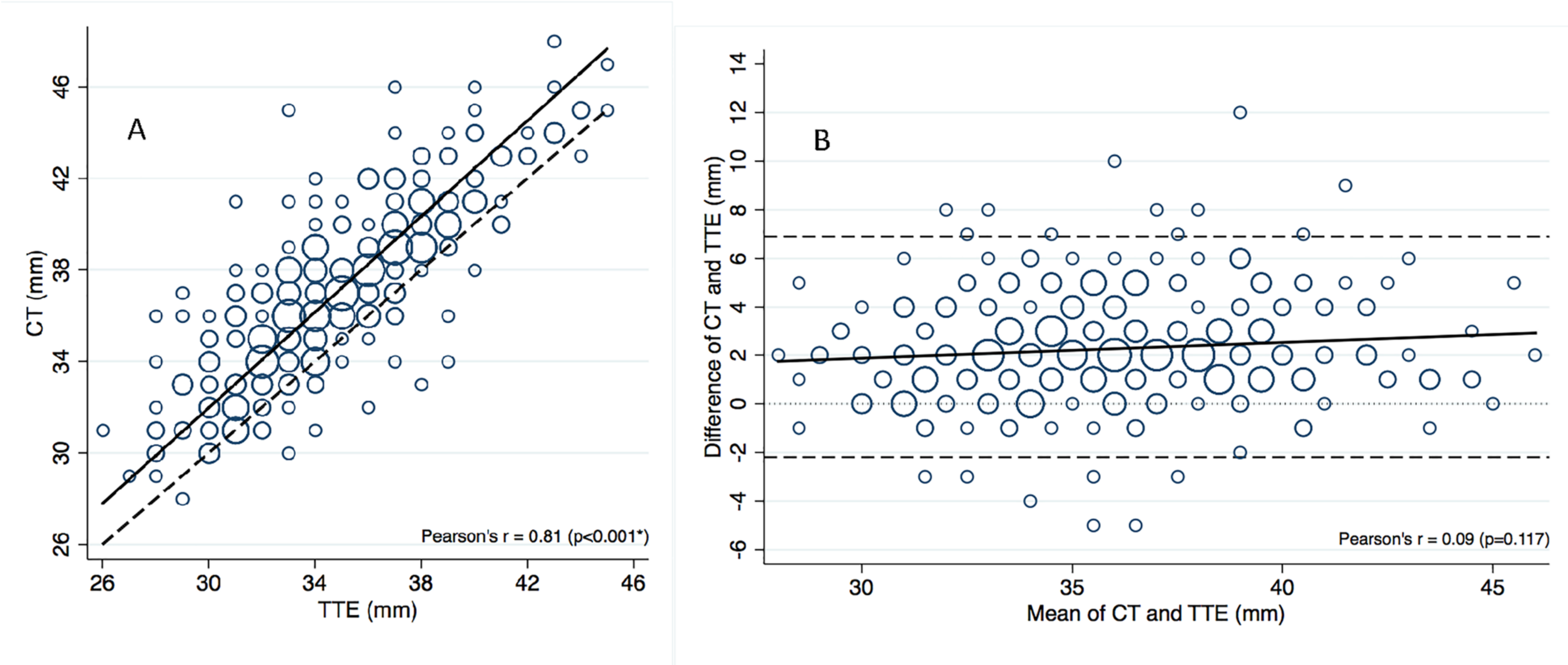
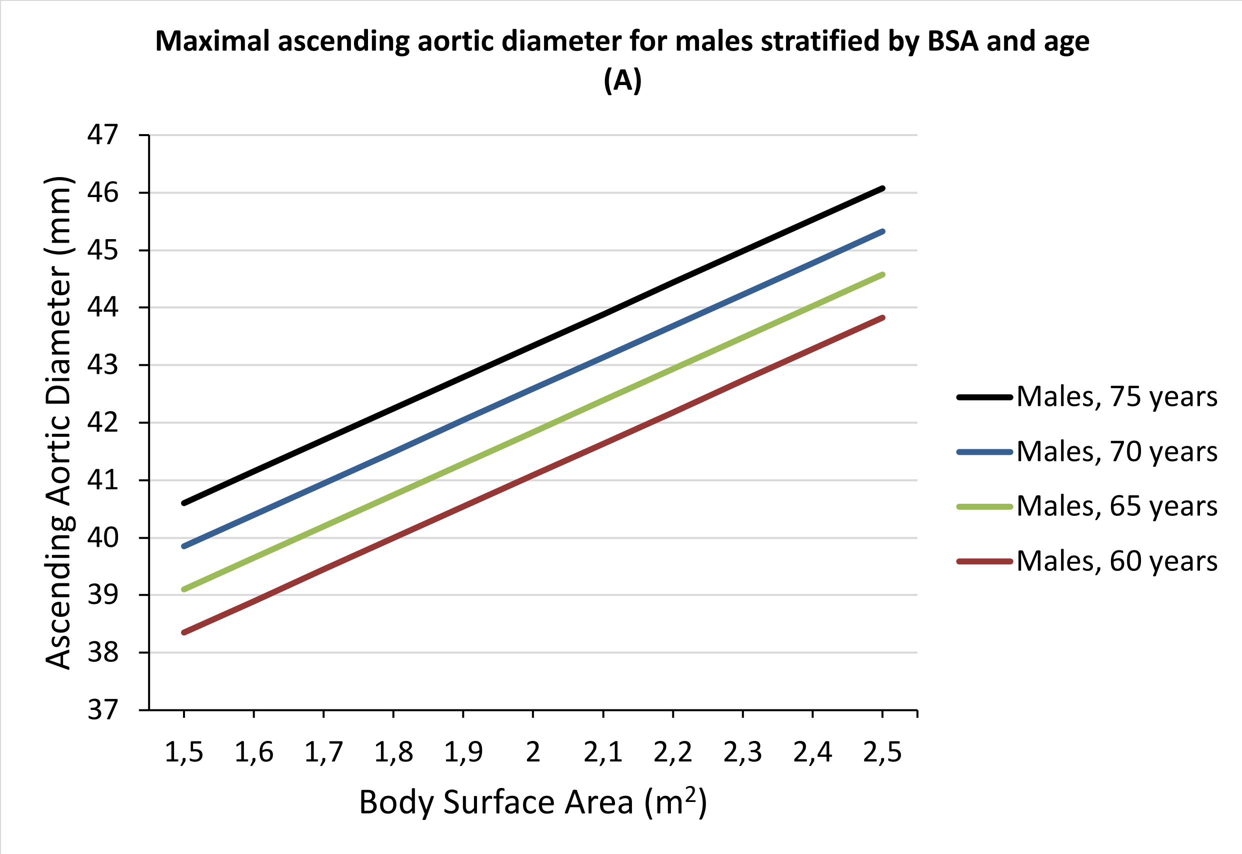



*Figure 3: Scatter and Bland-Altman plot of measurements of the ascending aortic diameter from CT and TTE.*
The size of the circles illustrates the number at patients at a given point. A) The dashed line displays the line of perfect correlation. The solid line displays the observed correlation. B) The dashed lines represent the 95% limits of agreement [-2.2 ; 6.9]. The solid line displays a regression line between the observed differences and means from ascending aortic diameters measured on CT and TTE. The displayed Pearson's r belongs to the regression line.



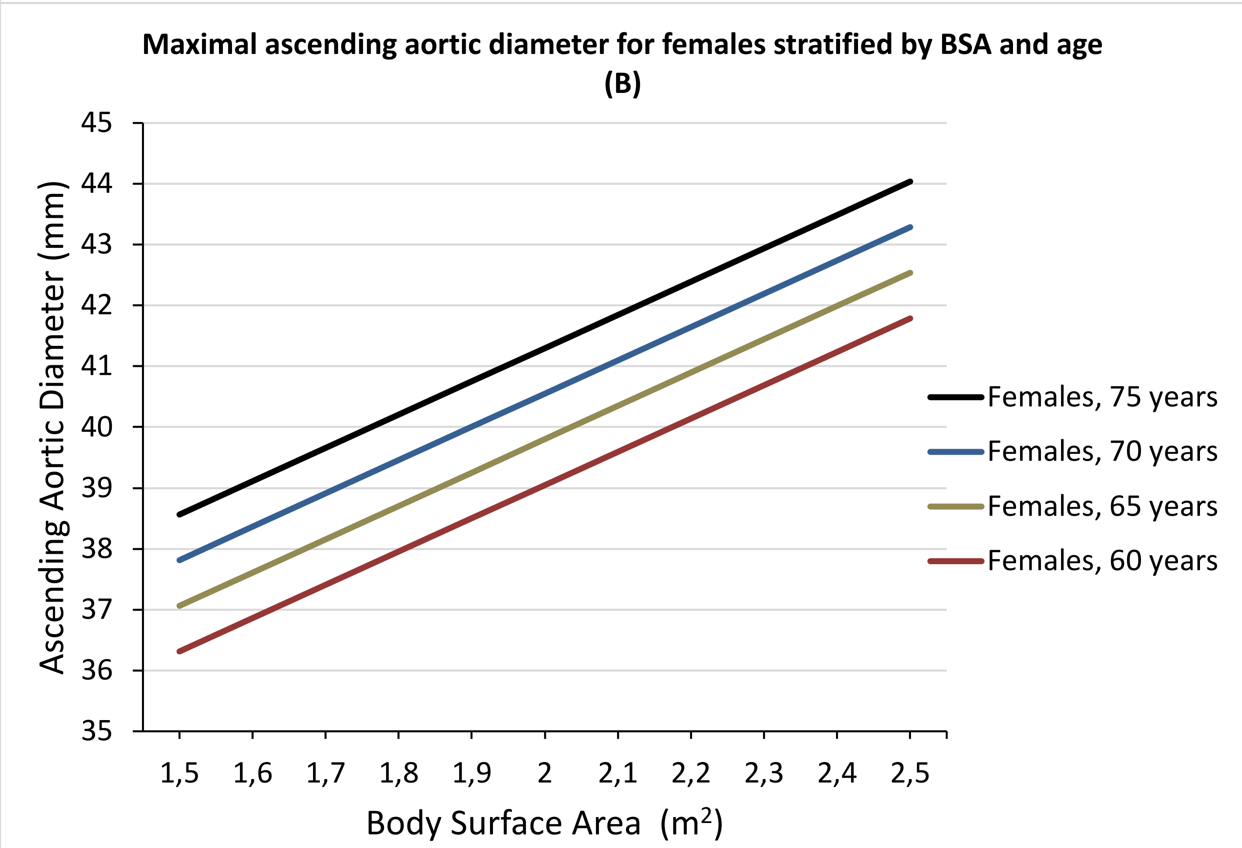




*Figure 4A and 4B:* Based on a prediction formula and stratified by gender, age, and body surface area, the maximal ascending aortic diameter is illustrated.

*Appendix 1* – Baseline characteristics stratified by the population not having TTE performed and the study population undergoing TTE.

| ***Appendix 1*** | **Study population not undergoing TTE** | **Males undergoing TTE** | **P values** |
|---|---|---|---|
| **Number (N)** | 14,702 | 291 | |
| **Male gender** | 14,237 (94.9%) | 291 (100.0%) | <0.01 |
| **Age** (yrs.) | 67.8 (±3.8) | 68.5 (±2.6) | <0.01 |
| **BMI** (kg/m$^2$) | 28.0 (±4.4) | 28.4 (±4.0) | 0.19 |
| **BSA** (m$^2$) | 2.04 (±0.2) | 2.07 (±0.2) | <0.01 |
| **Smoking** | | | 0.58 |
| Current | 2,337 (16.0%) | 51 (17.7%) | |
| Former | 7,320 (50.0%) | 147 (50.9%) | |
| Never | 4,986 (34.1%) | 91 (31.5%) | |
| **Known hypertension** | 6,455 (43.9%) | 125 (43.0%) | 0.79 |
| **Known diabetes** | 1,613 (11.0%) | 29 (10.0%) | 0.60 |
| **Statin treatment** | 4,862 (33.1%) | 100 (34.4%) | 0.61 |
| **Prior cardiovascular disease** | | | |
| AMI | 849 (5.8%) | 18 (6.2%) | 0.76 |
| Stroke | 943 (6.4%) | 15 (5.2%) | 0.39 |

Numbers are mean (±SD) or number of patients (% proportion)

*Abbreviations*: Body Mass Index (BMI); Body surface area (BSA); Acute myocardial infarction (AMI).