Excess of visceral adipose tissue with or without aortic elongation leads to a steeper heart position

S. Petteri Kauhanen, MD, PhD[1,2], Petri Saari MD, PhD[2], Tarmo Korpela BM[1,2], Timo Liimatainen, PhD[3,4], Ritva Vanninen, MD, PhD[1,2], Marja Hedman, MD, PhD[2,5,6]

1. School of Medicine, Clinical Radiology, University of Eastern Finland, Kuopio, Finland

2. Department of Clinical Radiology, Kuopio University Hospital, Clinical Imaging Center, Finland

3. Research Unit of Medical Imaging, Physics and Technology, University of Oulu, Oulu, Finland

4. Department of Diagnostic Radiology, Oulu University Hospital, Oulu, Finland

5. Department of Cardiothoracic Surgery, Heart Center, Kuopio University Hospital, Kuopio, Finland

6. Institute of Clinical Medicine, University of Eastern Finland

Corresponding author: S. Petteri Kauhanen MD, PhD

E-mail: petkau@student.uef.fi

PO Box 100, Puijonlaaksontie 2

70029 KYS, Finland

Abstract

Background

The heart's position determined as the heart-aorta-angle (HAA) has been demonstrated to associate with ascending aortic (AA) dilatation. Visceral adipose tissue (VAT) and aortic elongation may shift the heart to the steeper position.

Purpose

To investigate whether VAT and aortic length influence the HAA.

Materials and Methods

We examined 346 consecutive patients who underwent aortic CT angiography (CTA). HAA was measured as the angle between the long axis of the heart and AA midline. The amount of VAT was measured at the level of middle L4 vertebra from a single axial CT slice. Aortic length was measured by combining four anatomical segments in different CTA images. The amount of VAT and aortic length were determined as mild with values in the lowest quartile and as excessive with values in the other three quartiles.

Results

The patients' mean age was 67.0±14.1 years (58.4% were males); 191 patients (55.2%) had no history of aortic diseases, 134 (38.7%) displayed ascending aortic (AA) dilatation, 8 (2.3%) patients had abdominal aortic aneurysm (AAA), and 13 (3.8%) patients had both AA dilatation and AAA.

There was a strong nonlinear regression between smaller HAA and VAT/height, and HAA and aortic length/height. Median HAA was 124.2° (119.0–130.8) in patients with a mild amount of VAT vs. 120.5° (115.4°–124.7°) in patients with excessive VAT, p<0.001.

Conclusions

An excessive amount of VAT and aortic elongation led to a steeper heart position. These aspects may possess clinical value when evaluating aortic diseases in obese patients.

Keywords

Adipose tissue; Aorta; Dilatation; Obesity; Tomography, X-Ray Computed

Introduction

The heart-aorta-angle (HAA) measured as an angle between the long axis of the heart and ascending aortic (AA) midline describes the relation of the heart's position to the AA. A small HAA has been demonstrated to shift the aortic flow from the centerline and increase wall shear stress in the outer curve of the AA; this has been speculated to induce AA dilatation (1). Nonetheless, further studies are needed to establish the clinical significance of the HAA.

The presence of excessive visceral adipose tissue (VAT) associates with the risk of death (2) e.g. an excess of VAT has been linked to the development of several cardiovascular diseases and risk factors including ischemic heart disease and arterial hypertension, impaired glucose and lipid metabolism, and insulin resistance. It is also known to associate with prolonged hospitalization and increased mortality in hospitals. The amount of VAT can be measured accurately and easily with computed tomography (CT) (3). It has been speculated that an increased amount of VAT may push the diaphragm upwards, which can alter the

orientation of the heart and thus exert an influence on the HAA. According to our best knowledge, the association between VAT and HAA has not been studied earlier.

Aortic elongation has been demonstrated to be a part of the normal ageing process (4,5). However, aortic elongation has been postulated also to be an independent risk factor for A-type aortic dissection. An elongated aorta may push the heart into a deeper angle in relation to the AA which in turn can increase wall shear stress in the outer curve of AA. This may at least partly explain the detected association with A-type dissection (6,7). As far as we are aware, the association between aortic length and HAA has not been previously evaluated.

This study aimed to investigate the effects of VAT and aortic length on the position of the heart as determined by the HAA in a consecutive population who were imaged with aortic computed tomography angiography (CTA).

Materials and Methods

The study was approved by the *BLINDED* and it follows the rules of Declaration of Helsinki. Aortic CTA was performed on the basis of a clinical indication; thus, the patients were not exposed to any additional radiation and their clinical treatment was unaffected by this retrospective study.

Study population

The study examined 346 consecutive patients of Finnish origin who had been imaged with aortic CTA between January 2014 and December 2020 in *BLINDED*. Typical indications for imaging were suspicion of aortic dissection, preoperative examination before elective aortic valve or some other heart surgery, or recently (< 1 month) diagnosed aortic dilatation or aneurysm. Patients were excluded if they had had a prior aortic or other heart operation, genetic syndromes predisposing for aortic diseases, previously (≥ 1 month) diagnosed aortic dilatation or aneurysm, aortic trauma, vasculitis, or if the information about the patient's height and weight was lacking. Risk factors for cardiovascular diseases as well as other baseline characteristics were collected from the medical records. Overweight was

determined as BMI greater than 25 kg/m^2, and obesity was determined as BMI greater than or equal to 30 kg/m^2.

CTA data acquisition

Aortic CTA imaging was performed during peak systole according to the routine clinical practice using four different CT scanners (Siemens Definition Flash, Siemens Definition Edge, Siemens Biograph Vision 600 Edge and Siemens Biograph mCT; Siemens Medical Solutions, Erlangen, Germany) with 128x0.6 slice collimation at a rotation time of 0.28 seconds. The imaging was performed with electrocardiogram (ECG)-gating and iodinated contrast agent (Omnipaque, GE healthcare). The tube voltage, varying between 80 and 120 kV, was adjusted semiautomatically according to the patient's size. The patients were scanned in the supine position with their hands above their head. The image area extended from the base of the skull to the groin.

Data analysis

A single observer (*BLINDED*) retrospectively performed the data analysis (measurements of aortic diameter and length, HAA and amount of VAT) and collection of the characteristics of the patients. In the measurement of intraobserver reproducibility, the data analysis was repeated for the last 50 patients. In order to calculate interobserver reproducibility, the data analysis of the last 50 patients was performed independently by another investigator (*BLINDED*) who was blinded to the previous measurements. All data analysis was conducted with a slice thickness of 3 mm.

Aortic diameters were measured with the IDS7 diagnostic workstation (Sectra Imtec, Linköping, Sweden) in six planes: aortic root, mid-AA, mid-arch, mid-descending aorta, coeliac trunk and the greatest diameter of the infrarenal abdominal aorta (Figure 1A). The AA was defined to include both sinus valsalva and mid-AA planes. The diameters were measured from the outer-to-outer vascular wall perpendicular to the centerline of the vessel. The greatest diameter of each plane was registered. Thoracic aorta was considered to be dilated if its diameter exceeded 40 mm and abdominal aortic aneurysm (AAA) was defined

as an aortic diameter greater than or equal to 30 mm (8). Healthy controls consisted of patients whose aorta was not dilated according to the above-mentioned criteria. The HAA was measured as the angle between the long axis of the heart and AA midline (1).

CTA images were loaded into a postprocessing workstation (Syngo.via, Siemens, Erlangen, Germany) for VAT and aortic length measurements. Adipose tissues were identified at the level of the middle fourth lumbar vertebra in single axial slice. The VAT area was calculated by delineating the abdominal cavity from muscle and bone tissues. The subcutaneous adipose tissue (SAT) area was calculated by drawing a line between the skin and the outer muscle wall (Figure 1B). Then the surface areas of adipose tissues were semiautomatically computed by using an attenuation range from −30 to −190 Hounsfield units (HU) (9).

Aortic length was measured by combining the result of four separate anatomical segments (Figure 2). The length of the AA was defined as the part of the aorta between the aortic valve and the origin of the brachiocephalic trunk. The aortic arch was defined as the segment between the origin of brachiocephalic trunk and the left subclavian artery. The descending thoracic aorta was designated as the segment between the left subclavian artery and the twelfth thoracic vertebra. The abdominal aorta was defined as the segment between the twelfth thoracic vertebra and the femoral bifurcation.

Both adipose tissue area measurements and aortic length measurements were adjusted for the patient's height in meters to obtain body size specific values for further analysis.

Statistical analysis

The normality of the aortic diameter data was analyzed by using the Kolmogorov-Smirnov test. Since the values displayed a normal distribution, diameters are presented as mean ± standard deviation and tested with independent-samples T-test. Those parameters with a skewed distribution (different subgroups) were tested with the Mann-Whitney test and the results are presented as median values with interquartile range (IQR).

Correlations between the HAA, adipose tissues and aortic length were tested by the Spearman correlation test. Linear regression was used to estimate the effects of VAT and aortic length on HAA.

The nonlinear regression of VAT and aortic length with HAA was tested by creating four new classes according to VAT and aortic length quartiles: I) 0–24.9%, II) 25.0–49.9%, III) 50.0–74.9%, and IV) 75.0–100%. Differences between the classes were tested with Mann-Whitney U-test. The amount of VAT was determined as mild for those values in the lowest quartile and as excessive with values in the other three quartiles. Aortic elongation was determined as mild with values in the lowest quartile and as excessive with values in the other three quartiles.

Multivariate logistic regression analysis was used to test the relationship between the HAA and factors which alone associated with the smaller HAA.

Paired samples t-test was used to test the systematic error in intra-and interobserver analysis. Intraclass correlation coefficients (ICC) using a two-way mixed effects model with absolute agreement were used to calculate intra- and interobserver reproducibility.
Statistical significance was set to $p<0.05$ and high statistical significance to $p<0.001$. All statistical analyses were performed by using SPSS Statistics 27 (IBM, Chicago, USA).

Results

The study population

The mean age of the patients was 67.0±14.1 years and 58.4% of the patients were male (n=202). Most of the patients (93.6%) had at least one cardiovascular risk factor (diabetes, hypercholesterolemia, hypertension, positive family history or smoking).

AA dilatation was found in 134 patients (38.7%), 8 patients (2.3%) had AAA, and 13 patients (3.8%) had both AA dilatation and AAA (Table 1). Thus, 191 patients (55.2%) had no dilatation in the aorta and were regarded as healthy controls. The mean age of the healthy controls was 65.0±16.0 years and 42.9% were males (n=82). In the overall study population,

the mean diameter of the mid-AA was 37.0±5.5 mm and 21.2±10.6 mm in the infrarenal abdominal aorta. The corresponding diameters in the healthy controls were 33.9±3.3 mm, and 18.1±2.8 mm. The detailed characteristics of the study population are shown in Table 1.

Nonlinear regression of VAT and aortic length to the HAA

A nonlinear regression between the HAA and VAT was found as well as between the HAA and the aortic length (both AA and whole aortic length). The HAA was significantly smaller when comparing the patients with values in the first quartiles indicating a mild amount of VAT / height and the AA length / height with the patients with values in the other three quartiles indicating that an excessive amount of VAT / height and the AA length / height, both in the overall study population and in the healthy controls, $p<0.05$ (Table 2). Either obesity or overweight alone was not associated with HAA ($p>0.05$). Illustrative images of HAA in severely obese patients with different body types are shown in Figure 3.

In multivariate logistic regression analysis, association between the HAA and VAT / height, AA length / height, diabetes, hypertension, hypercholesterolemia, bicuspid aortic valve, obesity, coronary artery disease and aortic dilatation or aneurysms were tested. As result, both VAT / height ($B=-4.1°$, $p<0.001$) and AA / length ($B=-2.4°$, $p=0.01$) associated independently with the smaller HAA.

Correlations of HAA, adipose tissue and aortic length

The amount of VAT correlated strongly with BMI ($r=0.613$, $p<0.001$). However, it correlated only very weakly with the patient's height ($r=0.134$, $p<0.001$). A moderate correlation was detected with weight ($r=0.573$, $p<0.001$) and BSA ($r=0.505$, $p<0.001$). Furthermore, VAT was not correlated with age ($r=0.080$, $p>0.05$). A smaller HAA correlated weakly inversely with VAT and height-adjusted values (VAT / height) both in the overall study population and in healthy controls ($r= -0.191$ – -0.208, $p<0.05$).

The increased whole aortic length correlated very weakly with age ($r=0.168$, $p=0.002$), weakly with weight ($r=0.292$, $p<0.001$) and BSA ($r=0.369$, $p<0.001$) and moderately with

height (r=0.492, p<0.001). A smaller HAA correlated weakly with whole aortic length and its height-adjusted values in both study groups. The correlations are presented in Table 3.

Linear regression equations (p<0.05) were HAA = 126.4° - 0.035° x VAT / height and HAA = 155.9° - 0.117° x whole aortic length / height in the healthy controls.

Association between HAA and ascending aortic dilatation

In healthy controls, the HAA was 122.8° [118.0–127.3°]. The HAA was smaller in the patients with AA dilatation (119.8° [115.1–124.3°], p=0.001), and in the patients with both AA dilatation and AAA (115.7° [109.5–121.9°], p=0.001), but not in the patients with AAA only (120.3° [113.9–124.1°], p=0.199) compared with healthy controls (Figure 4).

Intra- and interobserver reproducibility

No systematic error was observed in the intraobserver measurements. Intraobserver reproducibility was very strong in the aortic diameter (ICC=0.942, p<0.001) and in the adipose tissue measurements (ICC=0.982, p<0.001), and strong in the aortic length (ICC=0.875, p<0.001) and the HAA measurements (ICC=0.886, p<0.001).

A systematic error was observed in the two planes of the aortic diameter measurements (mid-descending aorta and coeliac trunk). However, ICC was strong in the same planes (ICC=0.871 and 0.794). The overall interobserver reproducibility was also strong in the aortic diameter measurements (ICC=0.847). Mean VAT and SAT areas were smaller in the interobserver measurements than in the initial measurements (p<0.05). Interobserver reproducibility was still very strong in the adipose tissue measurements (ICC=0.930). No systematic error was observed in the aortic length measurements and ICC was very strong (0.861). Interobserver reproducibility was moderate in the HAA measurements (ICC=0.680).

Discussion

The smaller angle between the heart and AA has been previously shown to associate to AA dilatation. However, the clinical significance of this finding and the underlying mechanisms behind this phenomenon are unclear. The HAA may be exceptionally small already at birth,

but it has a tendency to change during the individual's lifetime. The current study demonstrated that both an excess amount of abdominal fat, especially VAT, and the severity of aortic elongation exert an influence in the position of the heart in adults. This has clinical value since in the previous studies it has been shown that the steeper heart position can lead to increased wall shear stress in the outer curvature of aorta. This, in terms, might expose the aorta for dilatation. VAT has recently arisen as an important independent risk factor for several new health problems, including atrial fibrillation and heart failure. The result of this study emphasizes the role of VAT as a risk factor also for aortic diseases, at least for the susceptibility for aortic dilatation caused by an increased HAA.

One explanation of the influence of a smaller HAA to AA dilatation is that it increases the wall shear stress in the outer curve of AA (1). It is possible that the smaller HAA alters the direction of blood flow towards the outer curve of AA which can predispose to aortic dilatation. Similar results have been demonstrated in an abstract published by Hardikar et al. (10). They also found an association between the HAA and aortic dissection. A smaller HAA has been detected also in the patients with hypertrophic obstructive cardiomyopathy which indicates that myocardial morphology has an effect on the HAA (11). It has also been demonstrated that the HAA increased aortic regurgitation and paravalvular leakage after a transcatheter aortic valve replacement (12,13). In addition, in the present study, the smaller HAA was associated with AA dilatation and also in the patients with both AA dilatation and AAA. As a novel finding, a smaller HAA did not associate to a sole AAA. This is logical, since the effects of the HAA on blood flow probably do not extend to the abdominal aorta.

It is well known that an increased amount of VAT is linked to several cardiovascular diseases and stroke. The gold standard for quantitative assessment of VAT is based on CT- and MRI -imaging (3). CT and MRI are the most reproducible methods for the measurement of the VAT area (14,15) and accordingly, in the present study intra- and interobserver reproducibility with CT-based analysis of VAT was very strong according to ICCs.

An increased amount of VAT has been previously demonstrated to associate with impaired lung function by limiting the expansion of the lungs due to mechanical pressure of the

abdomen (16,17). In this study, we aimed to explore whether this above-mentioned phenomenon influence in heart position and the VAT measurement was for that reason chosen to be performed in the level of fourth vertebra. A parallel finding was that increased VAT led to a smaller HAA in obese patients. In other words, in obese patients, i.e. individuals who have an excessive amount of VAT, the diaphragm becomes elevated and this leads to a decreased HAA. On the contrary, overweight and obesity alone were not associated with a smaller HAA in the present study indicating that the distribution of the adipose tissue rather than obesity alone is a risk factor for the smaller HAA induced AA dilatation. This might have clinical significance when evaluating patients with newly diagnosed AA dilatation with respect to their future follow-up. In addition to the mechanical pressure, adults with visceral adiposity tend to manifest insulin resistance, hypertension and dyslipidemia more often when compared to those who are equally obese with lower levels of visceral fat. VAT is metabolically more active than SAT and it secretes pro- and anti-inflammatory factors that are shown to be associated with endothelial damage and modulate the inflammatory state (18). VAT also predisposes patients to atherosclerosis (19,20). As far as we are aware, the association between VAT and AA dilatation has not been studied.

Modern fast CT scanners with ECG-gating properties offer detailed information of the anatomy of the whole aorta, allowing also longitudinal measurements of aortic length. According to our best knowledge, the reproducibility of aortic length measurements has not been reported previously. We observed that these length measurements tend to have very strong reproducibility.

The clinical relevance of measuring aortic length is that it can be used for the evaluation of the severity of aortic elongation which has previously been postulated to be an independent risk factor for A-type aortic dissection (6,7). Aortic elongation makes the artery more tortuous and the increased arterial curvature may elevate wall shear stress and make the aorta susceptible to suffer a dissection (6,21,22). Our results indicate that the increased AA and whole aortic length affects the heart position when the elongation is large enough. The

observed connection between aortic dissection and aortic elongation might be at least partly explained by vascular tortuosity caused by aortic elongation.

The main limitations of this study were the small number of pure AAA patients, the high mean age of patients, and that most of the patients had at least one cardiovascular risk factor. However, the amount of VAT and AA length independently associated with steeper heart position when comparing other factors which affect to the HAA.

In conclusion, a smaller HAA associates strongly with AA dilatation. A high amount of VAT affects the heart position, but a similar effect is not related to subcutaneous abdominal fat. Similarly, the aortic length affects the heart's position. These relatively simple measurements of HAA, VAT and aortic length might be useful in the clinical evaluation of the patients with newly diagnosed AA dilatation.

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Table 1. Detailed characteristics of the study populations. Statistical differences are calculated between healthy controls and ascending aortic (AA) dilatation.

	Overall study population n=346	Healthy controls n=191	AA dilatation n=134	p-value
	mean±SD	mean±SD	mean±SD	
Age (years)	67.0±14.1	65.0±16.0	69.0±11.3	0.01
BMI (kg/m^2)	26.6±4.2	26.8±4.6	26.5±3.7	0.4
BSA (m^2)	1.9±0.2	1.9±0.2	1.9±0.2	<0.001
Height (cm)	170.1±9.3	167.5±8.9	173.1±8.8	<0.001
Infrarenal abdominal aorta (mm)	21.2±10.6	18.1±2.8	20.2±2.6	<0.001
Mid-AA (mm)	37.0±5.5	33.9±3.3	41.0±5.6	<0.001
Weight (kg)	77.2±14.4	75.5±15.2	79.4±13.1	0.01

	n (%)	n (%)	n (%)	
Bicuspid aortic valve	16 (4.6)	4 (2.1)	11 (8.2)	0.01
CAD	100 (28.9)	55 (28.8)	35 (26.1)	0.6
Diabetes	42 (12.1)	26 (13.6)	14 (10.4)	0.4
Males / females	202 (58.4) / 144 (41.6)	82 (42.9) / 109 (57.1)	101 (75.4) / 33 (24.6)	<0.001
Hypercholesterolemia	130 (37.6)	68 (35.6)	49 (36.6)	0.9
Hypertension	188 (54.3)	99 (51.8)	75 (56.0)	0.5
Obesity	63 (18.2)	40 (20.9)	20 (14.9)	0.2
Positive family history for aortic diseases	9 (2.6)	2 (1.0)	6 (4.5)	0.04
Smoking	62 (17.9)	31 (16.2)	25 (18.7)	0.6

AA; ascending aorta, CAD; coronary artery disease

Table 2. Associations between the heart-aorta-angle (HAA), height-adjusted visceral adipose tissue areas (VAT / height), and height-adjusted ascending aortic length (AA length / height) in the different quartiles representing nonlinear regression.

	First quartile (0–24.9%)	Other quartiles (25.0–100%)	p-value		First quartile (0–24.9%)	Other quartiles (25.0–100%)	p-value
Overall study population (n=346)				Healthy controls (n=191)			
VAT / height				VAT / height			
Range of quartile (cm^2/m)	0–60.6	60.7–348.5		Range of quartile (cm^2/m)	0–60.7	60.8–241.5	
HAA (degrees)	124.2 (119.0–130.8)	120.5 (115.4–124.7)	<0.001	HAA (degrees)	125.4 (119.7–133.1)	121.6 (117.1–125.8)	0.001
AA length / height				AA length / height			
Range of quartile (mm/m)	0–42.5	42.6–72.9		Range of quartile (mm/m)	0–42.6	42.7–58.9	
HAA (degrees)	123.6 (117.8–129.6)	120.6 (115.6–125.1)	0.001	HAA (degrees)	124.1 (118.3–130.3)	121.6 (117.8–126.6)	0.04

Table 3. Spearman correlations of the heart-aorta-angle with adipose tissue and the aortic length in the different subgroups. Statistical significances are shown as **<0.01 and *<0.05.

	VAT	VAT / height	SAT	SAT / height	AA length	AA length / height	Whole aortic length	Whole aortic length / height
Overall study population (n=346)	-0.204**	-0.191**	-0.107	-0.072	-0.243**	-0.184**	-0.348**	-0.273**
Healthy subgroup (n=191)	-0.204**	-0.208**	-0.084	-0.077	-0.125	-0.107	-0.286**	-0.277**
Pathological aorta (n=155)	-0.163*	-0.141	-0.142	-0.104	-0.207**	-0.112	-0.319**	-0.182*
AA dilatation (n=134)	-0.190*	-0.168	-0.194	-0.147	-0.239**	-0.151	-0.268**	-0.115
AAA (n=8)	-0.048	-0.095	-0.500	0.167	0.286	0.286	-0.667	-0.881**
Both AA dilatation and AAA (n=13)	-0.016	-0.016	-0.300	-0.700	-0.049	-0.038	-0.440	-0.269

AA; ascending aorta, AAA; abdominal aortic aneurysm, SAT; Subcutaneous adipose tissue, VAT; visceral adipose tissue cm^2

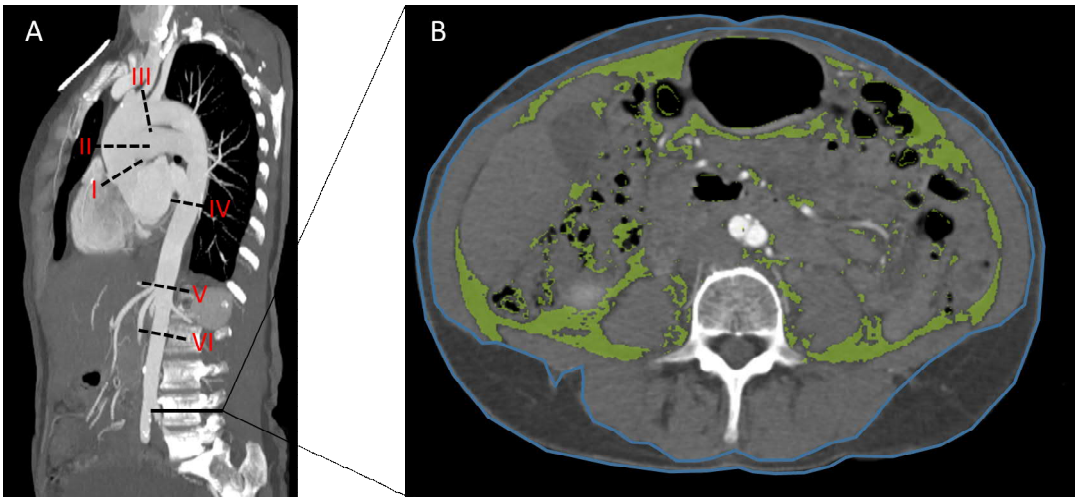

Figure 1. A) Diameters of aorta were measured in six planes (black broken line); I) aortic root, II) mid-ascending aorta, III) mid-arch, IV) mid-descending aorta, V) coeliac trunk, VI) and the greatest diameter of the infrarenal abdominal aorta. Areas of adipose tissue were measured at the level of the fourth lumbar vertebra in one axial slice using Syngo.via software (B); green areas represent an area of visceral adipose tissue, and blue lines represent the area of subcutaneous adipose tissue.

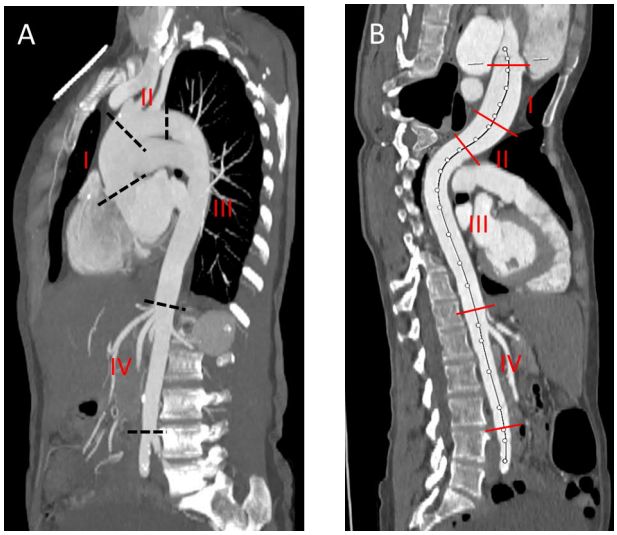

Figure 2. A) The length of aorta was measured by combining data of four separate segments (I–IV). B) The segment of ascending aorta (I) was defined as between the aortic valve and the origin of the brachiocephalic trunk. The segment of aortic arch (II) was defined to begin in the origin of brachiocephalic trunk and finish after the left subclavian artery. The segment of descending thoracic aorta (III) was defined to begin after the left subclavian artery and end at the level of the twelfth thoracic vertebra. The segment of abdominal aorta (IV) was designated as the region between the twelfth thoracic vertebra and the femoral bifurcation.

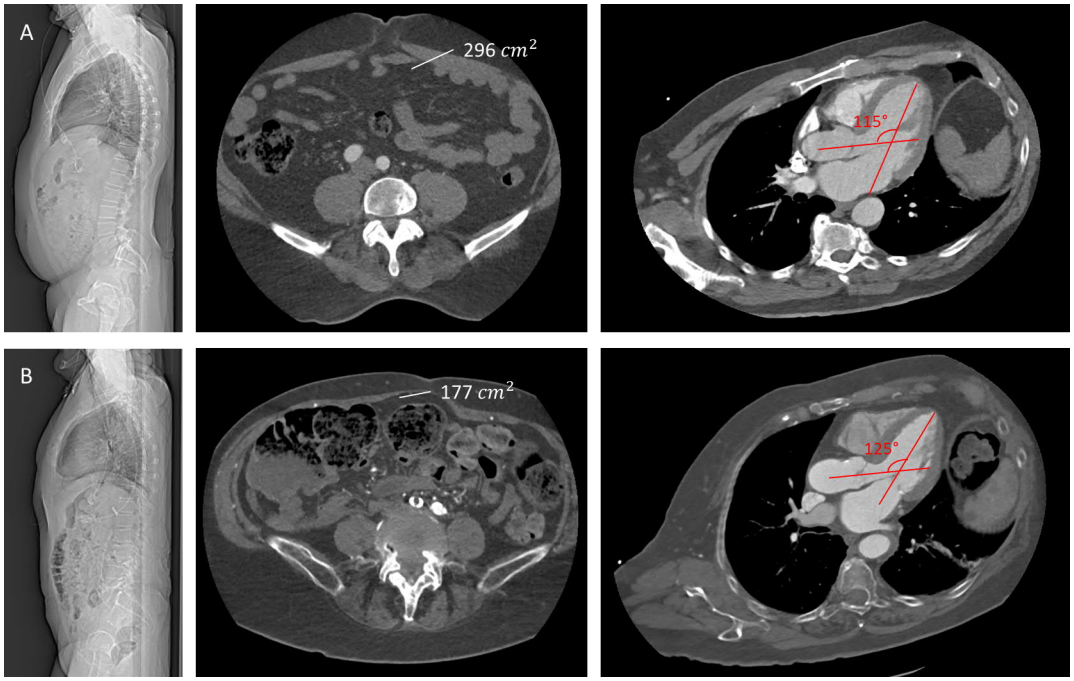

Figure 3. Illustrative images of two different body types. Body mass index was 36 kg/m^2 (severely obese) in both cases. A) A 55-year-old male with a dilated ascending aorta (AA). Visceral adipose tissue (VAT) area is 296 cm^2, and heart-aorta-angle is 115°. B) A 67-year-old female with a normal AA. VAT area is 177 cm^2, and heart-aorta-angle is 125°.

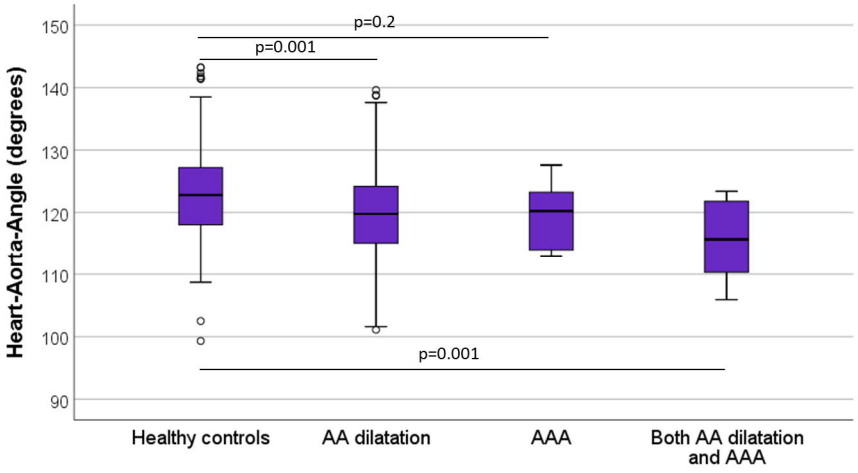

Figure 4. Boxplots of the heart-aorta-angle (HAA) in the different study subgroups. The HAA was statistically significantly smaller in the patients with ascending aortic (AA) dilatation, and with both AA dilatation and abdominal aortic aneurysms (AAA), but not in a subgroup of the patients with exclusively AAA as compared with healthy controls. Statistical differences were tested with Mann-Whitney U-test.