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ORIGINAL ARTICLE
Valvular heart disease

Prevalence and determinants of dilated ascending aorta in a Swedish population: a case–control study

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Aims Dilation of the ascending aorta (AA) is often asymptomatic until a life-threatening dissection or rupture occurs. An overall increase in the use of thoracic imaging has enabled early and sometimes incidental identification of AA dilation. Still, the prevalence and determinants of AA dilation remain to be clarified. The aim was to identify and characterize persons with AA dilation in a middle-aged Swedish population.

Methods and results We used the Swedish CardioPulmonary BioImage Study Linköping ($n = 5058$, age 50–65 years) to identify cases with AA diameter ≥ 40 mm on coronary computed tomography angiography (CCTA) or chest computed tomography. Age- and gender-matched individuals with AA diameter < 40 mm served as controls. Echocardiography, blood pressure (BP) measurements (office and home), pulse wave velocity (PWV), coronary artery calcification (CAC), CCTA-detected coronary atherosclerosis, and carotid ultrasound were used to characterize these subjects. We identified 70 cases (mean AA diameter 44 mm, 77% men) and matched these to 146 controls (mean AA diameter 34 mm). Bicuspid aortic valve and aortic valve dysfunction were more common in cases than in controls (8% vs. 0% and 39% vs. 11%, respectively). Both office and home BP levels were significantly higher among cases. Also, high PWV (>10 m/s) levels were more common in cases (33% vs. 17%). Neither CAC scores nor prevalence or burden of atherosclerosis in coronary and carotid arteries differed between groups.

Conclusion The prevalence of dilated AA was 1.4% and showed positive associations with male gender, aortic valve pathology, and diastolic BP, though not with subclinical atherosclerosis.

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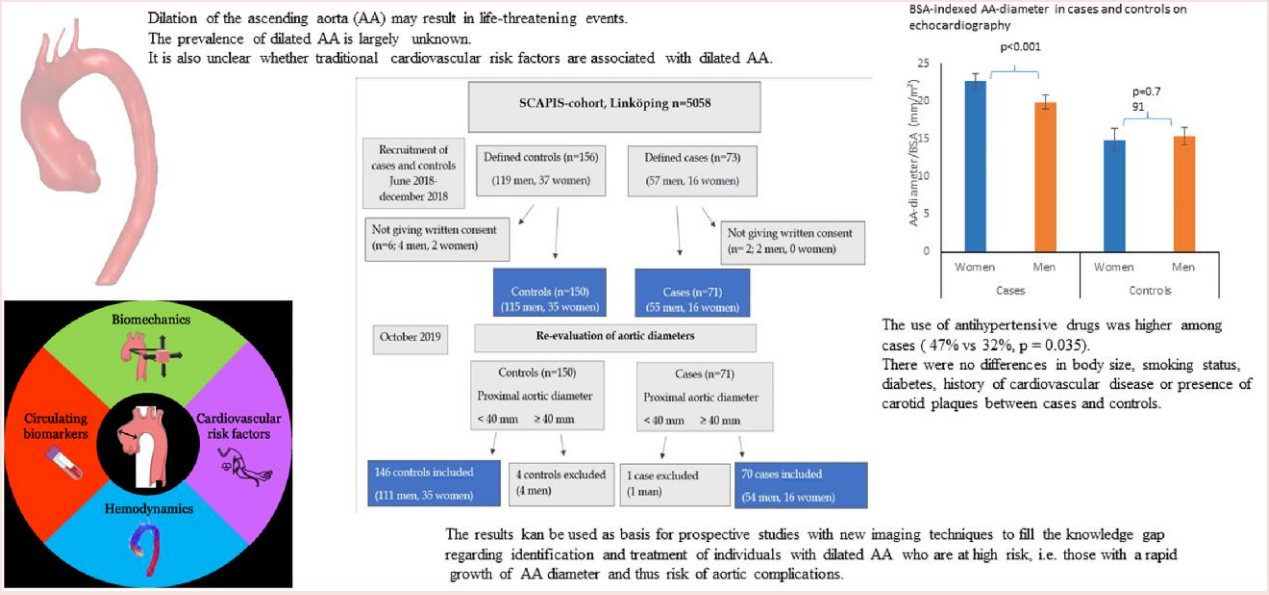
Graphical Abstract



Keywords Ascending aortic dilatation • Bicuspid aortic valve disease • Hypertension • Atherosclerosis

Introduction

Aneurysmal dilation of the ascending aorta (AA) is often asymptomatic until life-threatening complications occur such as aortic dissection or rupture.[1] New imaging tools for assessment of cardiopulmonary diseases have brought management of incidental findings of mild to modest AA dilation into the spotlight.[2] In recent studies, the prevalence of AA dilation has been high: ~23% in patients scheduled for coronary angiography,[2,3] while an earlier study reported a prevalence of 2.7%.[4] The risk of complication is considered to be low, but some individuals develop rapidly expanding aneurysms.[5,6] Therefore, long-term monitoring of all individuals with incidentally found AA dilation is recommended.[7]Prophylactic surgery may be considered necessary when the AA diameter reaches 50–55 mm.[7]

Age, gender, and body size are known determinants of AA diameter.[8] Also, bicuspid aortic valve (BAV) disease and some other hereditary conditions have been associated with AA dilation.[9,10] There is consistent evidence that hypertension is a leading predisposing factor for AA dilation.[11] Although less documented, other lifestyle-related factors, such as smoking and obesity, have also been associated with AA dilation.[2] On the other hand, studies investigating the association between AA diameter and atherosclerosis have been largely contradictory. Several studies have shown that coronary artery calcification (CAC) score is associated with AA diameter,[12] while others have shown the opposite.[13] Moreover, a study by Jackson *et al.*[14] reported that the combination of clinically significant coronary artery disease (CAD) and AA dilation was rare in surgical patients with aortic valve and/or AA pathology. To study subclinical atherosclerotic disease in patients with AA dilation using coronary computed tomography angiography (CCTA) is a gap in the current knowledge.

The aim of this study was to identify those incidentally found with a dilated AA on computed tomography (CT) and thereafter match these to non-dilated controls assessed in the same study cohort. Participants were extensively characterized including transthoracic echocardiography (TTE) to examine aortic valve pathology, measurements of office and home blood pressures, and pulse wave velocity (PWV) and atherosclerosis imaging to assess CAC score and the presence of plaques in coronary and carotid arteries.

Methods

Study population

Data were derived from the Swedish CardioPulmonary BioImage Study (SCAPIS) cohort in Linköping ($n = 5058$), referred to as SCAPIS Linköping. SCAPIS is a nationwide population-based cohort including 30 000 men and women aged 50–65 years as previously described.[15]

All participants in SCAPIS Linköping with dilated AA, defined as AA diameter ≥ 40 mm according to current guidelines of European Society of Cardiology,[7] visualized on CCTA or chest CT between October 2015 and June 2018 were identified (*Figure 1*). A control group with AA diameter < 40 mm was selected from the same population, matched for age and gender. Upon re-evaluation, AA diameter ≥ 40 mm was confirmed on chest CT in all cases whereas five cases and all controls had < 40 mm in diameter on chest CT.

Radiologic diagnosis of the ascending aorta dilation

Imaging was performed using a dedicated CT scanner (Somatom Definition Flash scanner, Stellar detector, Siemens Healthcare, Forchheim, West Germany). The CT chest images were acquired using spiral imaging. Details regarding image acquisition in the SCAPIS cohort have previously been described.[15] Aortic measures were obtained on CT scans by one trained observer after testing reproducibility. Measures of the widest part of the AA were obtained from the non-contrast non–electrocardiogram (ECG)-gated CT chest images of 1 mm slice thickness on a IDS7 workstation. The width of two diameters measured perpendicular to each other was used after multiplanar reconstruction. Intrarater reliability of AA

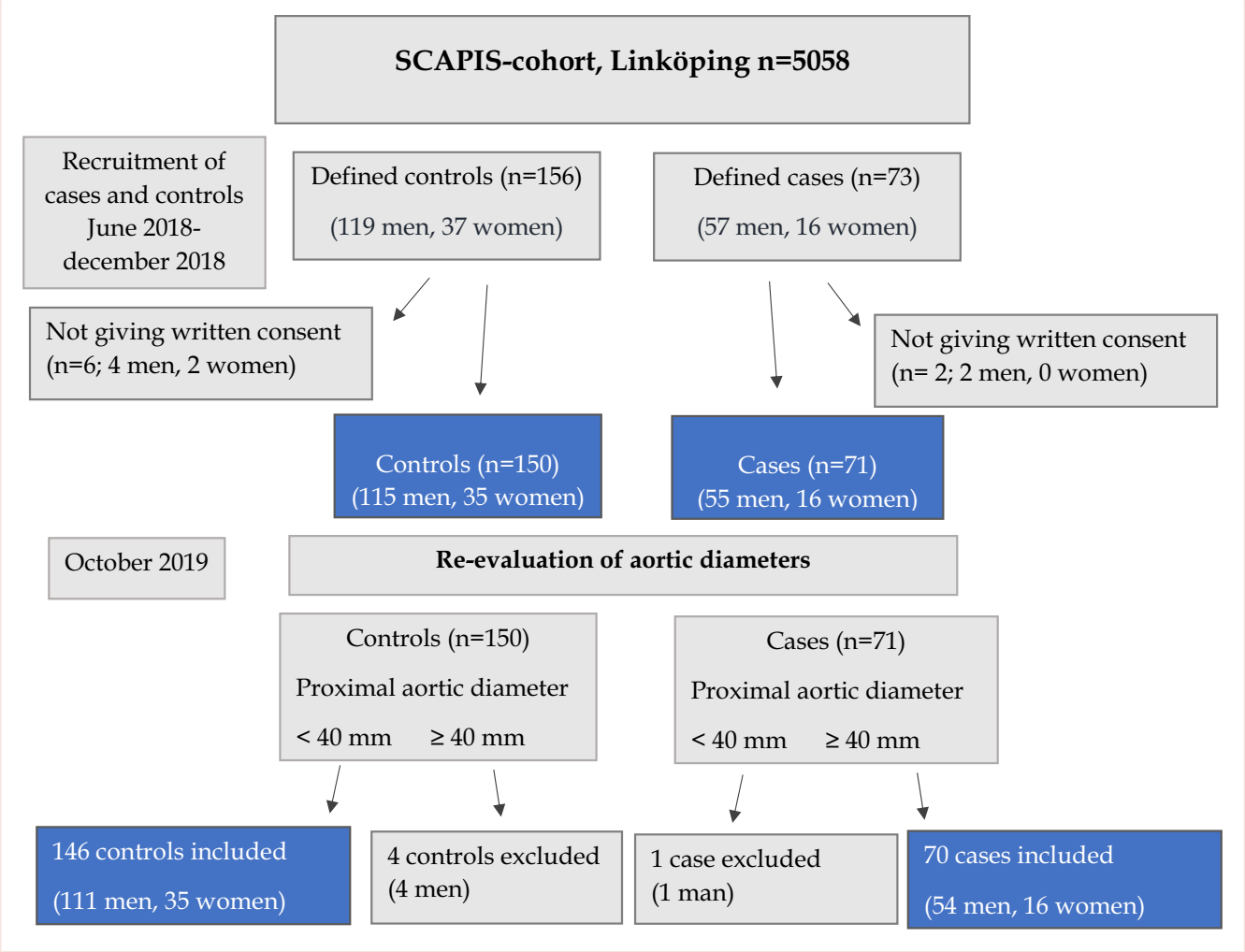


Figure 1 Flow chart.

diameter measurements on CT scans showed an intraclass correlation of 0.964 (0.906–0.985) and 0.97 (0.938–0.985) before and after confirmatory measurements were performed, respectively.

Evaluation of aortic valve morphology and function

Aortic valve morphology and function was also evaluated with TTE by an independent trained observer. The presence of BAV was assessed in short-axis views at the level of the aortic valve. Aortic jet velocity was measured by continuous-wave Doppler in the apical three-chamber view to screen for aortic stenosis, and an average of three measurements acquired by automated tracking was used. Grading of stenosis was based on peak velocity (m/s) in accordance with current guidelines.[16] The presence of aortic insufficiency was evaluated in the three-chamber view and/or in the parasternal long-axis view. In addition, we evaluated the AA diameter by the TTE trailing-to-leading-edge technique at the largest diameter of the visually accessible AA. The mean diameter out of three measurements was used.

Assessment of atherosclerosis

Carotid arteries

A standardized scanning protocol was performed using a Siemens Acuson S2000 ultrasound scanner equipped with a 9L4 linear transducer (both from Siemens Healthcare, Forchheim, Germany) to evaluate the presence of carotid artery atherosclerosis, as previously described.[12] Images were reviewed to determine the number of plaques in the common carotid arteries, bulbs, or in the internal carotid arteries. Plaques were, in accordance with current consensus,[17] defined as focal structures intruding into the arterial lumen of at least 0.5 mm height or 50% of the surrounding intima–media thickness value or defined as a thickness > 1.5 mm as measured from the intima–lumen interface to the media–adventitia interface. The number of visually detected plaques in the carotid arteries was added to produce a total number of plaques. Significant carotid atherosclerosis was defined as more than one plaque in the carotid arteries, as previously described.[18]

Coronary arteries

The CCTA protocol in SCAPIS has been previously described.[15,19] Briefly, to assess coronary atherosclerosis, an 18-segment coronary model was used with focus on the 11 clinically most relevant segments. Per-segment status of the coronary vessel was defined as follows: no atherosclerosis, 1–49% stenosis, and ≥50% (i.e. significant) stenosis.

Each coronary artery was also assessed for calcium content reported as total CAC score, in accordance with international standards using electrocardiogram-gated non-contrast CT imaging at 120 kV.[15]

Cardiovascular risk factors and morbidity

Medical records were reviewed by one observer using a predefined template to evaluate the presence of comorbidity. Diabetes, hypertension,

Table 1 Baseline characteristics of cases with ascending aorta dilation (ascending aorta diameter > 40 mm) and age- and gender-matched controls with normal ascending aorta diameter (ascending aorta diameter < 40 mm)

	Cases $n = 70$	Controls $n = 146$	P
Age, years	59 ± 4	59 ± 4	0.642
Male sex, *n* (%)	54 (77)	111 (76)	0.857
BMI (kg/m^2)	28 ± 4,4	27 ± 4,6	0.070
BSA (m^2)	2.1 ± 0.2	2.0 ± 0.2	0.067
Smoking, *n* (%)	7 (10)	15 (10)	0.943
Diabetes, *n* (%)	6 (9)	13 (9)	0.936
Antihypertensive therapy, *n* (%)	33 (47)	44 (30)	0.015
Lipid-lowering therapy, *n* (%)	15 (21)	28 (19)	0.698
Manifest CVD[a], *n* (%)	5 (7)	12 (8)	0.783
Family history of premature CAD, *n* (%)	6 (9)	20 (14)	0.278
Laboratory variables			
White cell counts, 10^9/L	5.5 ± 1.5	5.9 ± 1.5	0.164
CRP, mg/L	0.9 (0.5–1.6)	1.2 (0.5–2.5)	0.226
Creatinine, μmol/L	82 ± 12	85 ± 17	0.148
Total cholesterol, mmol/L	5.3 ± 1.0	5.4 ± 1.1	0.633
LDL cholesterol, mmol/L	3.2 ± 0.9	3.3 ± 1.0	0.768
HDL cholesterol, mmol/L	1.6 (0.5)	1.6 (0.4)	0.646
Triglycerides, mmol/L	1.3 (0.8)	1.3 (0.8)	0.792

AA, ascending aorta; BMI, body mass index; BSA, body surface area; CVD, cardiovascular disease; CAD, coronary artery disease; CRP, C-reactive protein; LDL, low-density lipoprotein; HDL, high-density lipoprotein.
[a]Manifest cardiovascular disease including peripheral artery disease, occurrence of aneurysm or dissection, cerebrovascular disease, coronary artery disease (previous myocardial infarction or previous revascularization of coronary arteries), and heart failure.

lipid-lowering therapy, and manifest cardiovascular disease, including peripheral artery disease, occurrence of aneurysm or dissection, cerebrovascular disease, CAD (defined as previous myocardial infarction or previous revascularization of the coronary arteries), and heart failure, were noted.

Smoking status and heredity were obtained from the SCAPIS questionnaires. Family history of premature CAD was defined as parental myocardial infarction at <60 years of age and of stroke was defined as parental stroke at <65 years of age. Body surface area (BSA) was calculated according to the DuBois formula.[20]

Blood pressure and aortic stiffness

Office blood pressure was measured twice in each arm with an automatic device (Omron M10-IT, Omron Health care Co., Kyoto, Japan), and a mean value was recorded. The same device was used for home blood pressure twice daily for 1 week, as recently described.[21] In brief, all participants were asked to measure the blood pressure in the seated position in the morning and evening for 7 days except for the first day in which the morning was spent in the hospital outpatient department. Thus, a total of 13 home blood pressure recordings (mean of three each time) were measured by the participants.

Carotid–femoral PWV was measured with a cuff-based SphygmoCor device (Xcel) in 70% of participants. Pulse wave velocity was calculated from pulse transit distance from the carotid to the femoral artery, divided by pulse transit time. Pulse transit time was derived using a partially inflated femoral cuff together with carotid applanation tonometry. The distance between the carotid and femoral artery was acquired by using the direct method, measuring from the carotid artery to the femoral cuff and from the femoral artery to the thigh cuff multiplied by 0.8 as currently recommended.[22] The average of two PWV measures was used. As currently recommended, a cut-off of 10 m/s was set for the prediction of cardiovascular events.

Statistical analysis

Continuous variables are presented as means ± standard deviation when normally distributed, and differences between groups were calculated by independent samples Student's *t*-test. Non-normally distributed data are presented as median and interquartile range, and differences between groups were calculated by the Mann–Whitney *U* test. Categorical variables are presented as number and percentage. Differences between groups were calculated using the χ^2 test. Fisher's exact test was used when the χ^2 test was not applicable. Simple and multiple linear regression was used to showcase the relationship between AA dilation and other variables. Age and gender were not included in the multiple regression analysis since controls were age and gender matched. $P < 0.05$ was considered statistically significant. IBM SPSS statistics version 25 was used for statistical analyses.

Ethics

The study was approved by the regional Ethical Review Board in Linköping Sweden (Registration number 2018/24-31) and performed in accordance with the Declaration of Helsinki. All participants gave written informed consent.

Results

Baseline characteristics

Among 5058 individuals (50% women) in SCAPIS Linköping, 70 cases with AA dilation were identified representing a prevalence of 1.4% (77% men). As shown in *Table 1*, the use of antihypertensive therapy was more common in cases than in controls. Also, body mass index (BMI) and BSA values tended to be higher in cases.

Ascending aorta diameter and aortic valve characteristics

Ascending aorta diameters on CT scans showed a strong correlation with AA diameters on TTE ($r = 0.86$, $P < 0.001$). Bicuspid aortic valve was only found in cases ($n = 8$, 11%, five women and three men).

Table 2 Aortic and valvular characteristics in cases with ascending aorta dilation (ascending aorta diameter > 40 mm) and age- and gender-matched controls with normal ascending aorta diameter (ascending aorta diameter < 40 mm)

	Cases, $n = 70$	Controls, $n = 146$	P
CT measurements			
AA diameter[a], mm	44 ± 3	34 ± 3	<0.001
BSA-adjusted AA diameter, mm/m^2	21 ± 2.6	17 ± 2.0	<0.001
Echocardiographic measurements			
AA diameter[b], mm	41 ± 3	31 ± 4	<0.001
BSA-adjusted AA diameter, mm/m^2	20 ± 2	15 ± 2	<0.001
Bicuspid aortic valve, *n* (%)	8 (11)	0	<0.001
Mild aortic regurgitation, *n* (%)	21 (30)	15 (10)	<0.001
Moderate aortic regurgitation, *n* (%)	2 (3)	0	0.106
Mild aortic stenosis *n* (%)	4 (5.8)	1 (0.7)	0.026

CT, computed tomography; AA, ascending aorta; BSA, body surface area.
[a]CT measurements were available in all cases and controls.
[b]Echocardiographic measurements were available in 67 cases and 126 controls.

Table 3 Blood pressure levels and pulse wave velocity in cases with ascending aorta dilation (ascending aorta diameter > 40 mm) and age- and gender-matched controls with normal ascending aorta diameter (ascending aorta diameter < 40 mm)

	Cases $n = 70$	Controls $n = 146$	P
Office systolic blood pressure (mmHg)	138 ± 15	132 ± 17	0.017
Office diastolic blood pressure (mmHg)	87 ± 9	82 ± 10	<0.001
7-day mean home systolic blood pressure (mmHg)			
Morning	126 ± 13	120 ± 15	0.011
Evening	126 ± 13	123 ± 14	0.096
7-day mean home diastolic blood pressure (mmHg)			
Morning	83 ± 8	78 ± 9	<0.001
Evening	82 ± 8	77 ± 8	<0.001
PWV[a] (m/s)	9.4 ± 1.5	8.9 ± 1.4	0.064
PWV > 10 m/s, *n* (%)	17 (33)	17 (17)	0.025

AA, ascending aorta; PWV, pulse wave velocity.
[a]PWV was available in 51 cases and 99 controls.

After adjustment for BAV, AA dilation remained significantly associated with mild aortic regurgitation ($P < 0.001$; *Table 2*).

Blood pressure levels and arterial stiffness

Systolic and diastolic blood pressure levels were significantly higher in cases than in controls, both office blood pressure levels and 7-day home blood pressure levels (except for systolic levels in the evening). Data on arterial stiffness were available in 51 cases (mean age 59 years, 24% women) and 99 controls (mean age 59 years, 28% women). Overall, PWV levels tended to be generally higher in cases than in controls. Pulse wave velocity levels > 10 m/s were significantly more common in the case group (*Table 3*). There were significant associations between PWV and mean systolic morning levels ($r = 0.511$), evening levels ($r = 0.474$), mean diastolic morning levels ($r = 0.373$), and evening levels ($r = 0.301$), all $P < 0.001$.

In multivariate linear regression analysis, AA dilation was associated with the use of antihypertensive therapy, office as well as home blood pressure levels during 7 days (except for systolic levels in the evening), and high PWV levels > 10 m/s. After adjustment for BSA, these correlations remained significant. After adjustment for BSA, BAV, and aortic valve dysfunction, only diastolic blood pressure levels remained significantly associated with AA dilation, office diastolic blood pressure $P = 0.006$, home diastolic blood pressure in the morning $P = 0.000$, and in the evening $P = 0.001$ (see Supplementary material online, *Table S1*).

Atherosclerotic burden

The CAC score, the presence of any CCTA-detected atherosclerosis, and the prevalence of obstructive CAD (≥50% significant stenosis) were similar in both groups. Obstructive multivessel disease (≥2 coronary vessels) was not observed in any participant. The prevalence of carotid plaques did not differ between groups (*Table 4*).

Sex differences

The sex difference in prevalence was 2.1 and 0.6% in men and women, respectively. However, BSA-adjusted aortic diameters > 2.1 cm/m^2[27] were more common among women (88 and 44% in women and men, respectively), while aortic valve dysfunction did not differ between sexes. Women cases were less likely than men to have any form of coronary obstructive disease. Absolute PWV levels were lower in women compared with men. No woman with dilated AA exhibited PWV > 10 m/s (see Supplementary material online, *Table S2*).

Discussion

We found the prevalence of AA dilation in a middle-aged Swedish population to be 1.4%. Previous studies using the same threshold of AA dilation (≥40 mm) on cardiac CT have shown disparate results. In a study by Benedetti and Hope,[4] the prevalence of incidental AA dilation in a sample of 24 992 individuals, 55–80 years old, with routine CT scans was 2.7%. However, in two other recent studies, the prevalence was much higher.[3] In the Rotterdam Study (48% men, mean age 69 years, mean BSA 1.9 m^2, smoking 17%, hypertension 42%), 2505 participants were examined and showed 12.2% prevalence of aortic dilation.[18] Kauhanen *et al.*[2] showed an even higher prevalence of 23% in 1000 consecutive subjects (34% men, mean age 53 years, mean BSA 1.9 m^2, smoking 25%, hypertension 46%) scheduled for diagnostic CCTA. Apart from potential methodological issues related to CCTA, differences in the prevalence of dilated AA among populations might be due to factors such as age, sex distribution, BSA, smoking, and hypertension. Compared with our study population, smoking was more common in the populations described by Kauhanen *et al.* and Bons *et al.*,[2,3] where the latter also included more elderly people.

Not unexpectedly, aortic valve dysfunction, in particular mild aortic regurgitation, was more common among those with dilated AA. Also, eight (11%) of them exhibited BAV whereas none of the controls did. The results are in agreement with a previous study by Kim *et al.* who reported that the prevalence of BAV was 12.6% in a large echocardiographic data set of 4654 adults with dilated AA.

Table 4 Measurements of atherosclerosis in cases with ascending aorta dilation (ascending aorta diameter > 40 mm) and age- and gender-matched controls with normal ascending aorta diameter (ascending aorta diameter < 40 mm)

	Cases $n = 70$	Controls $n = 146$	P
CAC score[a]			
0, *n* (%)	29 (42)	69 (50)	0.279
1–10, *n* (%)	9 (13)	18 (13)	1.000
11–100, *n* (%)	16 (23)	29 (21)	0.721
101–400, *n* (%)	8 (12)	12 (9)	0.506
>400, *n* (%)	7 (10)	10 (7)	0.474
Coronary plaques on CCTA[b]			
Any form of atherosclerosis	30 (44)	38 (56)	0.204
Any stenosis >50%, *n* (%)	4 (6)	12 (8)	0.557
Carotid plaques on ultrasound[c]			
Plaque in any carotid artery, *n* (%)	39 (56)	93 (64)	0.260
>1 plaque in any carotid artery, *n* (%)	20 (29)	51 (35)	0.352

CAC, coronary artery calcification; AA, ascending aorta; CCTA, computed tomography coronary angiography.
[a]CAC score was available in 69 cases and 138 controls.
[b]CCTA data were available in 68 cases and 144 controls.
[c]Carotid ultrasound was performed on all cases and controls.

When it comes to cardiovascular risk factors, there were no significant associations between dilated AA and obesity, smoking, or diabetes. On the other hand, hypertension was a significant determinant of dilated AA even after adjustment for BSA. In addition, higher PWV rates were more common among those with dilated AA, indicating a higher degree of arterial stiffness and vascular aging. These results are congruent with several previous studies reporting that hypertension and PWV are determinants of AA diameter.[8,11,23–25] However, after multiple adjustments including BSA, BAV, and aortic valve dysfunction, we found that only the diastolic blood pressure level remained an independent determinant of AA dilation. Previous data on the association between AA dilation and blood pressure levels are sparse. Yet, an imaging substudy of the Framingham Heart Study ($n = 3431$, mean age 51 years) showed that AA diameter correlated with both systolic and diastolic blood pressures after adjustment for age and gender. In line with our findings, a multivariate linear regression analysis revealed that only diastolic blood pressure remained significantly associated with AA diameter.[26]

Finally, we investigated the association between dilated AA and atherosclerosis using a variety of atherosclerosis imaging modalities. Neither CAC score nor the burden of atherosclerotic plaques in coronary or carotid arteries differed between groups. Concerning markers of atherosclerosis and their relationships with AA diameter, a number of studies have presented contradictory results. In an echocardiographic data set of 373 subjects, mean age 68 years, there were no associations between the prevalence of aortic atherosclerotic plaques and AA diameter[27] whereas another study of 345 subjects, mean age 53 years, showed that AA diameter was positively associated with both CAC score and ultrasound-detected extra-coronary atherosclerosis.[10] In the large MESA study, Turkbey *et al.*[8] reported that CAC score was associated with AA diameter, while other surrogate markers of atherosclerosis, such as carotid intimal–media thickness, were not. Recently, the relationship between diameters of various segments of the aorta and CAC score was evaluated in 2678 individuals in the Copenhagen General Population Study. After adjustment for risk factors, individuals with CAC score >400 had larger diameters in all aortic segments, including AA.[12] Noteworthy, these studies have included the whole spectrum of AA diameters, i.e. the majority of individuals had AA diameters within the normal range, while we have focused on a subgroup with pathological AA dilation (≥40 mm) within a much larger cohort. A few studies have investigated the presence of atherosclerotic disease in surgical patients with pathologically dilated AA with varying results. In a cohort of 702 Swedish surgical patients with aortic valve and/or AA pathology, Jackson *et al.*[14] reported that AA dilation and CAD rarely coexisted regardless of valve phenotype. On the other hand, Albini *et al.*[28] performed a histological analysis of AA tissue from 68 patients with non-familial AA aneurysms, mean age 63 years, and found that the majority exhibited advanced atherosclerosis combined with severe medial degeneration, thus suggesting a role for atherosclerosis in the progression of AA aneurysms.

Sex differences

As in previous studies,[2–5] the majority of cases with dilated AA were men. Noteworthy, absolute AA diameter values were similar in male and female cases while BSA-adjusted values were significantly larger among female cases. According to the European Society of Cardiology definition, AA is dilated when the absolute diameter value exceeds 40 mm, regardless of sex.[7] However, like our study, others have reported higher BSA-adjusted AA diameters in women.[3,29] The question has thus been raised whether sex-specific cut-off values should replace the current 'one-size-fits-all' cut-off value. Even though AA dilation is more prevalent in men, the consequences of AA aneurysms have been shown to be worse for women including poorer surgical outcome and greater growth rate of the aneurysm.[30]

Strengths and limitations

The strength of our study is the identification of subjects with AA dilation in a large population-based cohort and its extensive characterization including TTE, home blood pressure monitoring, and atherosclerosis imaging. However, although selection of participants in SCAPIS was designed to minimize bias typically associated with studies of volunteers, it does not necessarily represent a random sample of the Swedish population aged 50–65 years. Also, importantly, the cross-sectional design of the study impairs the ability to establish the temporal and causal nature of the associations.

Conclusions

The prevalence of dilated AA in a middle-aged Swedish population was relatively low, 1.4%. Ascending aorta dilation showed association with male sex, aortic valve pathology, hypertension (in particular diastolic blood pressure), and arterial stiffness. There was however no association between dilated AA and subclinical atherosclerosis in coronary or carotid arteries, supporting the theory of AA dilation as part of a hypertensive acceleration of media degeneration that occurs independently of plaque formation. Prospective studies are needed to fill the knowledge gap regarding identification and treatment of individuals with dilated AA who are at high risk, i.e. those with a rapid growth of AA diameter and risk of aortic complications.

Clinical perspectives

Aneurysmal dilation of the AA is often asymptomatic until life-threatening complications occur such as aortic dissection or rupture. We found no association between dilated AA and subclinical atherosclerosis, neither in coronary nor in carotid arteries. On the other hand, blood pressure, in particular diastolic blood pressure, was a major determinant of AA dilation. The results can be used as a basis for

prospective studies to further investigate the association between dilated AA and blood pressure. Future preventive strategies may include systematic screening of AA diameter in individuals with high diastolic blood pressure levels.

Lead author biography

Eva Swahn, Professor, Department of Health, Medicine and Care, Division of Cardiology, Linköping University and Department of Cardiology, University Hospital, Linköping, Sweden. Her research interests are acute coronary syndromes, including the gender perspective, with early diagnosis, risk stratification, and management. Throughout her professional career, she has worked to promote excellence in science and equity in health care. An important underlying theme in the work concerns the pathophysiology of the ACS including the thrombotic state and also health economy and quality of life.

Supplementary material

Supplementary material is available at *European Heart Journal Open* online.

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Authors' contribution

E.S., H.L., J.E., and L.J. are responsible for the conception and design of the study, have full access to all data, analysed and interpreted the data, and drafted the manuscript. F.H.N. provided the 7-day HBP data, critically revised the manuscript, and added important intellectual content. E.S. is responsible for the overall content as guarantor.

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Conflict of interest: All authors declare that they have no conflicts of interest related to this study.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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