American Journal of Epidemiology
Vol. 169, No. 3
DOI: 10.1093/aje/kwn346
Advance Access publication December 9, 2008

Original Contribution

Relation of Common Carotid Artery Lumen Diameter to General Arterial Dilating Diathesis and Abdominal Aortic Aneurysms

The Tromsø Study

Stein Harald Johnsen, Oddmund Joakimsen, Kulbir Singh, Eva Stensland, Signe Helene Forsdahl, and Bjarne Koster Jacobsen

Initially submitted May 27, 2008; accepted for publication October 3, 2008.

In a cross-sectional, population-based study in Tromsø, Norway, the authors investigated correlations between lumen diameter in the right common carotid artery (CCA) and the diameters of the femoral artery and abdominal aorta and whether CCA lumen diameter was a risk factor for abdominal aortic aneurysm (AAA). Ultrasonography was performed in 6,400 men and women aged 25–84 years during 1994–1995. An AAA was considered present if the aortic diameter at the level of renal arteries was greater than or equal to 35 mm, the infrarenal aortic diameter was greater than or equal to 5 mm larger than the diameter of the level of renal arteries, or a localized dilation of the aorta was present. CCA lumen diameter was positively correlated with abdominal aortic diameter ($r = 0.3$, $P < 0.01$) and femoral artery diameter ($r = 0.2$, $P < 0.01$). In a multivariable adjusted model, CCA lumen diameter was a significant predictor of AAA in both men and women (for the fifth quintile vs. the third, odds ratios were 1.9 (95% confidence interval: 1.2, 2.9) and 4.1 (95% confidence interval: 1.5, 10.8), respectively). Thus, CCA lumen diameter was positively correlated with femoral and abdominal aortic artery diameter and was an independent risk factor for AAA.

aorta, abdominal; aneurysm; blood vessels; carotid arteries; ultrasonography

Abbreviations: AAA, abdominal aortic aneurysm; CCA, common carotid artery; CI, confidence interval.

Abdominal aortic aneurysm (AAA) is a relatively common, potentially life-threatening condition accounting for approximately 1% of all deaths in the Western world (1). AAAs are usually asymptomatic until they rupture. Most AAAs are discovered incidentally upon routine physical examination or in imaging studies ordered for other indications. The risk of rupture increases with increasing diameter of the aneurysm. In persons suffering a ruptured AAA, case fatality is 60%–80% (2).

The development of an AAA involves changes in the mechanical properties of the arterial wall. Reduction of elastin (elastolysis), defects in collagen, cystic degeneration of the smooth muscle layer (media), and atherosclerosis in the subendothelial space (intima) are important histologic features of AAAs. The degeneration ultimately leads to widening of the vessel lumen and loss of structural integrity (3). Current research suggests that genetic, environmental, hemodynamic, and immunologic factors all contribute to the development of AAA. Even though the majority of persons with atherosclerosis will never develop AAA, most aneurysms are associated with advanced atherosclerosis. AAA and atherosclerosis share some common risk factors such as hypertension and smoking (4–6), but not diabetes, which is reported to be protective against the development of an AAA (6). For hypercholesterolemia, reports have been inconsistent (4, 6, 7).

Men are 10 times more likely than women to have an AAA greater than or equal to 4 cm in size (8). In addition, the familial aggregation of AAAs suggests that genetic susceptibility may play a role in their pathogenesis (9–11). An

Correspondence to Dr. Stein Harald Johnsen, Department of Neurology, University Hospital of North Norway, N-9038 Tromsø, Norway (e-mail: stein.harald.johnsen@unn.no).

increased prevalence of AAA has been reported in patients with pulmonary emphysema (12), inguinal hernia (13, 14), and incisional hernia (15) and may be attributable to degeneration of systemic elastin and collagen fiber (16).

It has been proposed that aneurysm formation results from altered systemic connective tissue metabolism (17), which can change the mechanical compliance and diameter not only of the aorta but of the rest of the arterial tree as well. It has further been hypothesized that there exists a generalized dilating diathesis in these persons, but data supporting such a hypothesis are scarce (18–20).

In the Tromsø Study, we measured the lumen diameter of the common carotid artery (CCA), the external diameter of the common femoral artery, and the external diameter of the abdominal aorta in 6,400 men and women from the general population. In the present study, we investigated how lumen diameter in the CCA correlated with the diameters of the femoral artery and abdominal aorta and whether CCA lumen diameter was an independent risk factor for AAA.

MATERIALS AND METHODS

Subjects

The Tromsø Study is a population-based prospective study involving repeated health surveys of the inhabitants of Tromsø, Norway. As part of the fourth survey, carried out in 1994–1995, all subjects aged 55–74 years and a random 5%–10% sample of the other age groups over 24 years were invited to undergo ultrasound scanning of the carotid artery and the aorta. In all, 6,892 subjects (79% of the eligible population) attended ultrasound screening for AAA, as detailed elsewhere (21). Of these persons, ultrasonography of the right carotid artery was performed in 6,727 subjects. The Regional Committee for Research Ethics approved the study, and informed consent for research was obtained from 6,645 of the participants who underwent ultrasound scanning. Measurements of right CCA lumen diameter, right common femoral artery diameter, and abdominal aortic diameter were carried out in 6,411 persons. An abdominal Y-graft was present in 11 persons, who were subsequently excluded; thus, the present study comprised 6,400 persons (3,151 men and 3,249 women) aged 25–84 years.

Ultrasonography of the abdominal aorta, femoral artery, and carotid artery

The ultrasonographic measurements and the reproducibility of data on the abdominal aorta have been described previously (22). Both the inter- and intraobserver mean absolute differences for measurements in the transversal and anterior-posterior plane were less than 4 mm, calculated as 2 standard deviations from the mean arithmetic difference (the limits of agreement) according to the method of Bland and Altman (23). Mean intraobserver arithmetic differences ranged between −1.0 mm and 0.2 mm. The corresponding range for mean interobserver arithmetic differences was −2.7 mm to 1.0 mm.

The measurements were taken on the monitor screen of the ultrasonograph from true orthogonal axial images frozen in systole (R-triggered). The external diameter of the right common femoral artery was measured. The external aortic diameter was measured with electronic callipers in both the anterior-posterior and transverse planes. An AAA was present if 1 or more of the following criteria were met: 1) the aortic diameter at the level of renal arteries was greater than or equal to 35 mm in either the anterior-posterior or the transverse plane; 2) the infrarenal aortic diameter in either plane was greater than or equal to 5 mm larger than the diameter of the level of renal arteries; or 3) a localized dilation of the aorta was present upon ultrasound. If the presence of an AAA was suspected, the patient was examined by computed tomography and referred to the Department of Cardiovascular Surgery at University Hospital of North Norway (Tromsø) for clinical evaluation and follow-up.

Automated R-triggered measurement of the right carotid intima-media thickness frozen in systole was performed in the near and far walls of the CCA and the far wall of the bulb (24–26). Measurements of intima-media thickness and CCA lumen diameter were analyzed off-line by means of an automated computerized edge-detection program developed by the Wallenberg Laboratory for Cardiovascular Research (Sahlgrenska University Hospital, Gothenburg University, Gothenburg, Sweden) (27). The computer program estimated the mean intima-media thickness and lumen diameter from 100 measurements taken along a 10-mm segment of the CCA. In the analyses, we used the average of the mean intima-media thicknesses of the 3 locations. The lumen diameter of the CCA was measured on longitudinal images and was defined as the distance between the leading edge of the near-wall intima-lumen interface and the leading edge of the far-wall lumen-intima interface (24). The mean inter- and intraobserver absolute differences were 0.21 mm and 0.22 mm, respectively. If carotid stenosis was suspected or occlusion was found, the subject was referred to the Department of Neurology at University Hospital of North Norway.

Cardiovascular risk factors

Information about smoking habits, self-reported prevalent diabetes mellitus, coronary heart disease, myocardial infarction, stroke, and use of antihypertensive and lipid-lowering drugs was collected from self-administered questionnaires. Standardized measurements of height and weight were carried out. Specially trained personnel recorded blood pressure with an automatic device (Dinamap Vital Signs Monitor; Dinamap, Tampa, Florida). Nonfasting serum total cholesterol and triglyceride levels were analyzed by enzymatic colorimetric methods with commercial kits (CHOD-PAP for cholesterol and GPO-PAP for triglycerides; Boehringer-Mannheim, Mannheim, Germany). Serum high density lipoprotein cholesterol was measured after the precipitation of low density lipoprotein with heparin and manganese chloride. We measured fibrinogen with the PT-Fibrinogen reagent (Instrumentation Laboratory, Milan, Italy). Monocytes and white blood cells were counted with automated cell counters using standard techniques. Blood analyses were carried out in the Department of Clinical Chemistry at University Hospital of North Norway.

Statistical analyses

The maximal abdominal aortic diameter and AAA, respectively, were the dependent variables in the regression models. Normal distribution assumptions were satisfied for maximal abdominal aortic dimensions. CCA lumen and external femoral artery diameter were the main explanatory variables. Known risk factors for atherosclerosis and AAA were introduced as covariates. First, we assessed the age-adjusted mean values for maximal aortic diameter according to quartiles of CCA lumen and external femoral artery diameter and quartiles of possible confounders, using analysis of covariance (the GLM procedure in SAS statistical software (SAS Institute Inc., Cary, North Carolina)). Linear trends across quartiles were tested by linear regression. Similarly, the age-adjusted prevalence of AAA was estimated in each quartile of CCA lumen and external femoral artery diameter as well as in quartiles of possible confounders. Linear trends across quartiles were tested by logistic regression. An assessment of the independent relation between CCA lumen diameter and the prevalence of AAA was obtained by multiple logistic regression, in which AAA was the dependent variable and CCA lumen diameter in quintiles was the main independent variable. Other cardiovascular risk factors were included as continuous or binary variables in the model in order to adjust for confounding. All analyses were sex-specific. Two-sided P values less than 0.05 were considered statistically significant. SAS software, version 9, was used for all statistical analyses.

RESULTS

Baseline characteristics of the study population are displayed in Table 1. Men had larger arterial lumens than women in the carotid artery, femoral artery, and abdominal aorta ($P < 0.01$). In men, CCA lumen diameter ranged between 3.95 mm and 11.89 mm. In women, the range was 4.02–10.69 mm. At least 1 carotid plaque was present in 53% of men and 45% of women ($P < 0.01$). Men also had higher intima-media thickness, more carotid plaques, and larger total plaque areas than women ($P < 0.01$). AAA was present in 254 of the men (8.1%) and 66 of the women (2.0%). There were no sex differences in systolic blood pressure, body mass index (weight (kg)/height $(m)^2$), or use of lipid-lowering or antihypertensive medication.

The correlation coefficients for correlation between CCA lumen diameter and abdominal aortic transversal diameter and anterior-posterior diameter were both 0.3 ($P < 0.01$). The coefficients for correlation between external femoral artery diameter and abdominal aortic transversal diameter and anterior-posterior diameter were both 0.2 ($P < 0.01$). The coefficient for correlation between CCA lumen and external femoral artery diameter was 0.2 ($P < 0.01$).

Table 2 presents the age-adjusted aortic transversal and anterior-posterior diameters in quartiles of carotid lumen and external femoral artery diameter atherosclerotic measures, physical measures, systolic blood pressure, and total cholesterol. For both men and women, abdominal aortic diameter increased linearly with increasing CCA lumen and external femoral artery diameter ($P < 0.01$). There were also significant linear trends across strata of height, weight, and body mass index. Systolic blood pressure was correlated with anterior-posterior diameter in both sexes and with transversal diameter in women. We found no significant correlations between serum total cholesterol and abdominal diameters. For smoking, there were highly significant correlations with both transversal and anterior-posterior diameter in both men and women (all P's < 0.01) (not shown in table). Men with diabetes mellitus had a nonsignificantly lower abdominal diameter than men without diabetes. For plaque area, the relations were U-shaped. In a multivariate model including age, body mass index, systolic blood pressure, smoking status, total cholesterol, high density lipoprotein cholesterol, monocyte count, white blood cell count, fibrinogen, and use of antihypertensive and lipid-lowering medication, a 1-mm larger CCA lumen diameter was associated with 0.97-mm (in men) and 0.67-mm (in women) larger maximal abdominal transversal diameters (both P's < 0.01). Thus, a relatively large change in CCA lumen diameter (15% of the mean diameter) was associated with a relatively small (4% of the mean diameter) change in maximal aortic infrarenal diameter.

Table 3 shows the prevalence of AAA according to quartiles of risk factor levels. In both sexes, the prevalence of AAA increased with increasing CCA lumen diameter, but prevalence was particularly high in the fourth quartile (14.9% for men and 4.9% in women)—more than twice that in the third quartile. Men and women in the fourth quartile had CCA lumen diameters of >7.20 mm and 6.55 mm, respectively. In men, there was a direct relation between femoral artery diameter and AAA prevalence, whereas in women, no statistically significant relation was found. High systolic blood pressure was borderline-correlated with AAA in women only ($P = 0.07$), whereas serum total cholesterol was correlated only in men ($P = 0.004$). In men, 6.1% of nonsmokers had AAA as compared with 11.8% of smokers ($P < 0.01$). In women, the corresponding prevalences of AAA were 1.0% and 4.4%. No correlation between diabetes and AAA was observed in this study.

The prevalence of AAA increased with increasing CCA diameter (Table 4). Because of the very low prevalence of AAA in the lower strata among women, the first and second quintiles were merged and the third quintile was used as the reference category. In men, the unadjusted odds ratio for AAA was 3 times higher in the top quintile than in the reference group, whereas in women, this risk increased 7-fold. The age-adjusted odds ratio was 2.3 (95% confidence interval (CI): 1.6, 3.4) in men and 5.2 (95% CI: 2.2, 12.4) in women. In the fully adjusted analyses, CCA lumen diameter was still a significant predictor in both men and women (for the fifth quintile vs. the third quintile, odds ratios were 1.9 (95% CI: 1.2, 2.9) and 4.1 (95% CI: 1.5, 10.8), respectively). We also adjusted for height instead of body mass index, and the results were essentially the same. In men, the odds ratio for the fifth quintile versus the third quintile was now 2.0 (95% CI: 1.3, 3.1), whereas in women it was 4.0 (95% CI: 1.5, 10.7). In order to investigate whether the association between CCA lumen diameter and AAA was limited to subjects with established atherosclerosis only, we repeated the logistic regression analysis after excluding persons with

Table 1. Baseline Characteristics of Participants Who Underwent Ultrasound Screening as Part of the Fourth Tromsø Study Survey, Tromsø, Norway, 1994–1995[a]

Risk Factor	Men (n = 3,151)	Women (n = 3,249)	P Value
Age, years	59.5 (10.1)	60.6 (10.3)	<0.01
Weight, kg	80.0 (11.8)	67.6 (11.7)	<0.01
Height, cm	175.2 (6.8)	161.5 (6.3)	<0.01
Body mass index[b]	26.0 (3.3)	25.9 (4.4)	0.3
Systolic blood pressure, mm Hg	145.0 (20.4)	144.9 (24.3)	1.0
Diastolic blood pressure, mm Hg	85.0 (12.2)	81.6 (13.4)	<0.01
Current smoker, %	34.2	31.2	0.01
Ex-smoker, %	47.9	25.8	<0.01
Total cholesterol, mmol/L	6.56 (1.21)	6.93 (1.35)	<0.01
High density lipoprotein cholesterol, mmol/L	1.39 (0.39)	1.68 (0.43)	<0.01
Triglycerides, mmol/L	1.65 (1.0)	1.46 (0.87)	<0.01
Plasma glucosis, mmol/L	4.94 (1.37)	4.87 (1.31)	0.004
Monocyte count, 10^9 cells/L	0.63 (0.19)	0.55 (0.17)	<0.01
White blood cell count, 10^9 cells/L	7.10 (1.92)	6.81 (1.78)	<0.01
Fibrinogen, mmol/L	3.32 (0.88)	3.44 (0.80)	<0.01
Diabetes mellitus, %	2.8	3.0	0.7
Coronary heart disease, %	15.2	8.9	<0.01
Use of lipid-lowering drugs, %	2.2	1.8	0.3
Use of antihypertensive medication, %	13.2	13.4	0.8
Carotid artery lumen diameter, mm	6.7 (0.9)	6.2 (0.7)	<0.01
Presence of carotid plaque, %	52.8	45.4	<0.01
Total plaque area, mm^2	12.8 (20.4)	8.3 (13.9)	<0.01
Intima-media thickness, mm	0.89 (0.20)	0.83 (0.17)	<0.01
Femoral artery diameter, mm	14.9 (2.3)	13.4 (2.4)	<0.01
Maximal transversal abdominal diameter, mm	23.5 (5.5)	20.1 (3.4)	<0.01
Maximal anterior-posterior abdominal diameter, mm	22.3 (5.2)	19.1 (3.2)	<0.01
Presence of abdominal aortic aneurysm, %	8.1	2.0	<0.01

[a] Values are unadjusted means (with standard deviations in parentheses) or percentages.
[b] Weight (kg)/height $(m)^2$.

carotid plaque (3,153 men and women). Subjects in the merged first and second quintiles were used as the reference group. In a model including both sexes, with adjustment for age, sex, and body mass index, the odds ratio for AAA among subjects in the upper quintile of CCA lumen diameter was nearly 3 times higher than that among subjects in the 2 lower quintiles (odds ratio = 2.9, 95% CI: 1.6, 5.2). In the fully adjusted model, this risk remained significant (odds ratio = 2.5, 95% CI: 1.3, 4.8).

Seventy-five men (mean age = 66.5 years) had CCA lumen diameters greater than 9.0 mm. Twenty of them (27%) had an AAA (Figure 1). In contrast, the prevalence of AAA in men with CCA lumen diameters less than or equal to 9.0 mm (n = 3,076) was 7.6% (n = 234). The adjusted odds ratio for AAA with a CCA lumen diameter above 9.0 mm versus less than or equal to 9.0 mm was 2.3 (95% CI: 1.2, 4.2; P = 0.008). Only 9 women (mean age = 68.1 years) had CCA lumen diameters greater than 9.0 mm, but 4 (44%) of them had an AAA. In comparison, only 1.9% (n = 62) of women with CCA lumen diameters less than or equal to 9.0 mm had an AAA. After adjustment for all of the other risk factors, the odds ratio for having an AAA above this cutoff versus less than or equal to it was 6.1 (95% CI: 1.1, 34.4; P = 0.04).

DISCUSSION

In these Tromsø Study participants, CCA lumen and external femoral artery diameter increased linearly with abdominal aortic diameter. The association was stronger (in terms of both correlation and regression coefficient) for the CCA. Moreover, CCA lumen diameter was an independent risk factor for AAA. The association remained significant after adjustment for body size and atherosclerosis (intima-

Table 2. Maximal Diameter of the Abdominal Aorta by Sex and Quartile of Risk Factor Level, Tromsø Study, Tromsø, Norway, 1994–1995[a]

	Maximal Aortic Diameter, mm				*P* for Trend
	Q1	Q2	Q3	Q4	
Transversal abdominal diameter					
Men ($n = 3,151$)					
Carotid artery lumen diameter, mm (4.0–11.9)[b]	22.6	22.9	23.3	25.1	<0.01
Femoral artery diameter, mm (9.1–29.5)	22.7	23.4	23.9	24.0	<0.01
Carotid intima-media thickness, mm (0.36–2.09)	23.5	23.2	23.5	23.7	0.2
Carotid total plaque area, mm^2 (0.0–206.8)	23.3	22.6	23.4	23.9	0.05
Height, cm (151.0–199.0)	22.7	23.4	23.5	24.3	<0.01
Weight, kg (43.0–130.0)	22.4	23.1	23.6	24.8	<0.01
Body mass index[c] (16.2–39.3)	22.7	23.1	23.8	24.4	<0.01
Systolic blood pressure, mm Hg (91.0–234.0)	23.4	23.2	23.5	23.8	0.1
Total cholesterol, mmol/L (2.70–11.60)	23.3	23.4	23.5	23.7	0.1
Women ($n = 3,249$)					
Carotid artery lumen diameter, mm (4.0–10.7)	19.6	19.9	20.2	20.9	<0.01
Femoral artery diameter, mm (5.2–28.4)	19.7	20.0	20.4	20.5	<0.01
Carotid intima-media thickness, mm (0.46–1.79)	20.0	20.1	20.3	20.1	0.5
Carotid total plaque area, mm^2 (0.0–129.7)	20.2	20.2	19.9	20.3	0.8
Height, cm (133.0–199.0)	19.4	20.1	20.4	20.7	<0.01
Weight, kg (33.0–143.5)	19.2	19.8	20.5	21.1	<0.01
Body mass index (11.9–54.7)	19.5	19.8	20.4	20.9	<0.01
Systolic blood pressure, mm Hg (90.0–239.0)	19.8	20.1	20.1	20.5	<0.01
Total cholesterol, mmol/L (2.90–15.13)	20.1	20.3	20.1	20.1	0.5
Anterior-posterior abdominal diameter					
Men ($n = 3,151$)					
Carotid artery lumen diameter, mm (4.0–11.9)	21.4	21.7	22.2	23.9	<0.01
Femoral artery diameter, mm (9.1–29.5)	21.7	22.2	22.6	22.8	<0.01
Carotid intima-media thickness, mm (0.36–2.09)	22.2	22.1	22.3	22.6	0.1
Carotid total plaque area, mm^2 (0.0–206.8)	22.2	21.6	22.3	22.7	0.03
Height, cm (151.0–199.0)	21.5	22.2	22.3	23.2	<0.01
Weight, kg (43.0–130.0)	21.3	22.0	22.5	23.6	<0.01
Body mass index (16.2–39.3)	21.6	22.0	22.7	23.1	<0.01
Systolic blood pressure, mm Hg (91.0–234.0)	22.2	22.0	22.4	22.7	0.04
Total cholesterol, mmol/L (2.70–11.60)	22.1	22.3	22.3	22.6	0.08
Women ($n = 3,249$)					
Carotid artery lumen diameter, mm (4.0–10.7)	18.5	18.8	19.1	19.9	<0.01
Femoral artery diameter, mm (5.2–28.4)	18.6	19.1	19.3	19.3	<0.01
Carotid intima-media thickness, mm (0.46–1.79)	18.9	19.0	19.2	19.1	0.2
Carotid total plaque area, mm^2 (0.0–129.7)	19.1	19.1	18.8	19.3	0.2
Height, cm (133.0–199.0)	18.4	19.0	19.3	19.6	<0.01
Weight, kg (33.0–143.5)	18.2	18.8	19.4	19.9	<0.01
Body mass index (11.9–54.7)	18.5	18.7	19.4	19.7	<0.01
Systolic blood pressure, mm Hg (90.0–239.0)	18.7	19.1	19.0	19.4	<0.01
Total cholesterol, mmol/L (2.90–15.13)	19.1	19.1	19.0	19.1	0.6

Abbreviation: Q, quartile.
[a] All values were adjusted for age.
[b] Numbers in parentheses, range.
[c] Weight (kg)/height $(m)^2$.

Table 3. Prevalence of Abdominal Aortic Aneurysm by Sex and Quartile of Risk Factor Level, Tromsø Study, Tromsø, Norway, 1994–1995[a]

	Aneurysm Prevalence, %				*P* for Trend
	Q1	Q2	Q3	Q4	
Men ($n = 3,151$)					
Carotid artery lumen diameter, mm (4.0–11.9)[b]	5.0	5.4	7.0	14.9	<0.01
Femoral artery diameter, mm (9.1–29.5)	6.7	7.1	9.4	9.0	0.01
Carotid intima-media thickness, mm (0.36–2.09)	7.6	5.7	8.2	10.7	0.02
Carotid total plaque area, mm^2 (0.0–206.8)	6.0	4.2	7.9	12.4	<0.01
Height, cm (151.0–199.0)	7.2	9.1	7.8	8.1	0.6
Weight, kg (43.0–130.0)	6.7	7.6	8.6	9.5	0.009
Body mass index[c] (16.2–39.3)	7.0	6.8	9.4	9.0	0.02
Systolic blood pressure, mm Hg (91.0–234.0)	8.2	6.5	8.4	9.1	0.5
Total cholesterol, mmol/L (2.70–11.60)	7.0	7.6	7.7	10.1	0.004
Women ($n = 3,249$)					
Carotid artery lumen diameter, mm (4.0–10.7)	0.5	0.8	1.9	4.9	<0.01
Femoral artery diameter, mm (5.2–28.4)	2.1	2.6	1.2	2.1	0.8
Carotid intima-media thickness, mm (0.46–1.79)	1.9	0.7	2.2	3.4	0.01
Carotid total plaque area, mm^2 (0.0–129.7)	0.0	1.1	1.2	4.7	<0.01
Height, cm (133.0–199.0)	1.4	1.6	3.7	1.4	0.3
Weight, kg (33.0–143.5)	2.2	1.9	1.8	2.2	0.8
Body mass index (11.9–54.7)	2.3	1.8	1.3	2.7	0.7
Systolic blood pressure, mm Hg (90.0–239.0)	1.9	1.5	1.3	3.4	0.07
Total cholesterol, mmol/L (2.90–15.13)	2.5	1.9	0.9	2.8	0.4

Abbreviation: Q, quartile.
[a] All values were adjusted for age.
[b] Numbers in parentheses, range.
[c] Weight (kg)/height $(m)^2$.

media thickness) and also after exclusion of persons with atherosclerotic plaques, suggesting that the relation between carotid artery enlargement and AAA is independent of vascular remodeling secondary to atherosclerosis. Although there was a highly significant linear trend between CCA lumen diameter and AAA prevalence, it was particularly high in the highest quintile. This may indicate a threshold effect of artery enlargement more than a true linear relation. Above a CCA lumen diameter of 9.0 mm, the increase in AAA seemed to follow an exponential curve. Our findings strengthen the generalized dilating hypothesis, suggesting that carotid artery enlargement above a critical diameter implies a high risk of AAA.

In most patients, the development of an aneurysm is multicausal. Even if atherosclerosis is strongly associated with AAA and this association may be causal, there are epidemiologic and biochemical differences between occlusive atherosclerotic disease and aneurysmal disease of the aorta. Compared with aortic tissue in atherosclerotic occlusive disease, there are greater amounts of proteolytic activity (28, 29) and inflammation (30) in aneurysmal aortic tissue. There are data indicating that aneurysm formation is primarily due to structural changes in the arterial wall and that the atherosclerotic process may be a secondary event (31). The results of this study are in line with previous reports demonstrating that patients with AAA have dilated peripheral arteries (18, 19), and they support the hypothesis of a constitutional dilating arterial diathesis in predisposed persons. Knowledge of genetic defects associated with aortic diseases is incomplete. However, a hereditary predisposition to AAA seems obvious, since the risk is significantly increased among first-degree relatives (32). Genetic defects altering the quality of the collagen and elastin structures can change the mechanical properties in the vessel wall and contribute to the development of AAA (5). It is still unclear whether connective tissue alterations associated with AAA may also influence the connective tissue in other organs. If there is a generalized defect in connective tissue in these persons, this may also explain the predisposition to other conditions like hernias (14, 15), cerebral aneurysms (33), polycystic kidneys (34, 35), and pulmonary emphysema (12).

The prevalence of AAA is 5% among men aged 65 years or more who are screened by ultrasound (36). In persons with a CCA lumen diameter greater than 9.0 mm, we found AAA in 25% of men and more than 40% of women. These persons represent a small group but carry a very high risk for AAA. Therefore, these findings have implications as to how to handle these cases in daily routine practice. The finding of an asymptomatic AAA may be of vital importance to the person concerned. According to investigators from

Table 4. Odds Ratio for Abdominal Aortic Aneurysm by Sex* and Quintile of Carotid Artery Lumen Diameter, Tromsø Study, Tromsø, Norway, 1994–1995

	Quintile				*P* for Trend
	1 + 2	3	4	5	
Men	(n = 1,259)	(n = 632)	(n = 631)	(n = 629)	
Carotid artery lumen diameter, mm	3.95–6.43	6.44–6.81	6.82–7.37	7.38–11.89	
No. (%) with abdominal aortic aneurysm	53 (4.2)	39 (6.2)	49 (7.8)	113 (18.0)	
Unadjusted OR (95% CI)	0.6 (0.4, 1.0)	1.0 (referent)	1.3 (0.8, 1.9)	3.3 (2.2, 4.8)	<0.01
Age-adjusted OR[a] (95% CI)	0.7 (0.4, 1.0)	1.0 (referent)	1.1 (0.7, 1.7)	2.3 (1.6, 3.4)	<0.01
Age- and body mass index[b]-adjusted OR[a] (95% CI)	0.7 (0.4, 1.0)	1.0 (referent)	1.0 (0.7, 1.6)	2.2 (1.5, 3.3)	<0.01
Multivariate-adjusted OR[a,c] (95% CI)	0.7 (0.5, 1.1)	1.0 (referent)	1.0 (0.6, 1.6)	1.9 (1.2, 2.9)	<0.01
Women	(n = 1,299)	(n = 648)	(n = 654)	(n = 648)	
Carotid artery lumen diameter, mm	4.02–5.91	5.92–6.24	6.25–6.70	6.71–10.69	
No. (%) with abdominal aortic aneurysm	3 (0.2)	6 (0.9)	17 (2.6)	40 (6.2)	
Unadjusted OR (95% CI)	0.3 (0.1, 1.0)	1.0 (referent)	2.9 (1.1, 7.9)	7.0 (3.0, 16.7)	<0.01
Age-adjusted OR[a] (95% CI)	0.3 (0.1, 1.3)	1.0 (referent)	2.5 (1.0, 6.3)	5.2 (2.2, 12.4)	<0.01
Age- and body mass index-adjusted OR[a] (95% CI)	0.3 (0.1, 1.3)	1.0 (referent)	2.5 (1.0, 6.3)	5.2 (2.2, 12.4)	<0.01
Multivariate-adjusted OR[a,c] (95% CI)	0.3 (0.1, 1.6)	1.0 (referent)	2.6 (0.9, 7.2)	4.1 (1.5, 10.8)	<0.01

Abbreviations: CI, confidence interval; OR, odds ratio.

* P for sex difference < 0.01.

[a] Adjusted with logistic regression.

[b] Weight (kg)/height (m)^2.

[c] Adjusted for age, body mass index, total cholesterol, high density lipoprotein cholesterol, smoking, systolic blood pressure, white blood cell count, monocyte count, fibrinogen, carotid intima-media thickness, and use of lipid-lowering and antihypertensive medication.

the Multicentre Aneurysm Screening Study—the largest population-based screening program ever undertaken for AAA—detection, follow-up, and correct timing of surgery (aneurysm diameter $\geq$ 5.5 cm) reduce the risk of aneurysm-related death by 42% (36). Ultrasonography of the abdominal aorta is cheap, mobile, and easily available and has practically no complications or side effects. It is well suited for use as a screening tool and plays a central role in the diagnosis and measurement of AAA. Based on our findings, we recommend that when carotid artery duplex imaging demonstrates a dilated carotid artery, the patient should be referred for abdominal ultrasonography. Screening of this high-risk group is cost-effective.

In the present study, the criteria for diagnosis of an AAA were set to produce high sensitivity for AAA identification. In spite of this, there were no persons with AAA under age 48 years. Some previous studies have used a threshold of maximal infrarenal diameter greater than 29.0 mm as the definition of AAA, since this represents a 50% increase in infrarenal aortic diameter over and above the normal mean suprarenal diameter of 20.0 mm (37, 38). When we applied this definition of AAA, the concordance with our classification of AAA was substantial, with a kappa value (39) of 0.80 (95% CI: 0.76, 0.83).

The strength of this study was its size and the high attendance rate. Carotid, femoral, and aortic diameters were measured in 75% of the eligible population, where the majority of subjects were aged 55–74 years. The attendance rate in persons older than 74 years was only 58%, and this is of some concern, since this age group has the highest prevalence of AAA. However, we find it unlikely that the relation between carotid diameter and aortic diameter is much different in this age segment than in the rest of the population. Scanning of the carotid artery, femoral artery, and aorta was performed on the same day, which produced a true cross-sectional relation. The number of AAAs was relatively low in persons with the most enlarged carotid arteries, especially in women (only 9 cases); therefore, the results should be

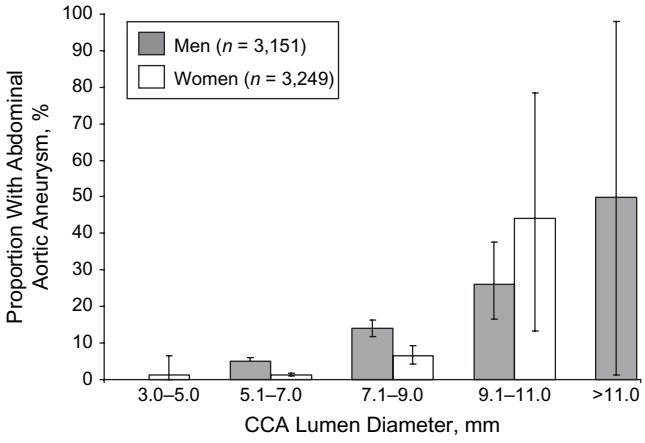

Figure 1. Proportion of participants with abdominal aortic aneurysm, by 2.0-mm increase in common carotid artery (CCA) lumen diameter, Tromsø Study, 1994–1995. Bars, 95% confidence interval.

interpreted with caution. Another possible shortcoming of this study is that only 1 carotid artery and 1 femoral artery were studied besides the aorta. Denarié et al. (40) measured CCA lumen diameter on both sides in 133 men and 216 women aged 17–65 years by B-mode ultrasound, using an automated computerized edge-detection program. They found that diameter was higher on the right side than on the left side in men and women aged 31–40 years and in women aged 41–50 years, but there was no difference in older subjects (40). However, because the majority of subjects in our study were older (86% of the study participants were over age 50 years), it is reasonable to assume that the correlation between lumen diameters in the 2 CCAs was high in our population. Inclusion of other arterial segments (left femoral artery, brachial artery) might have given better information regarding the propensity for general arterial dilation.

We conclude that in a general population, CCA lumen diameter is positively correlated with abdominal aortic and femoral artery diameter and the risk of AAA. Persons with markedly dilated carotid arteries upon duplex ultrasound scanning should also undergo ultrasonography of the abdominal aorta to be evaluated for asymptomatic AAA.

ACKNOWLEDGMENTS

Author affiliations: Department of Neurology, University Hospital of North Norway, Tromsø, Norway (Stein Harald Johnsen, Oddmund Joakimsen, Eva Stensland); Institute of Clinical Medicine, University of Tromsø, Tromsø, Norway (Stein Harald Johnsen, Oddmund Joakimsen, Eva Stensland); Department of Radiology, University Hospital of North Norway, Tromsø, Norway (Kulbir Singh); and Institute of Community Medicine, University of Tromsø, Tromsø, Norway (Signe Helene Forsdahl, Bjarne Koster Jacobsen).

This study was supported by grants from the Norwegian Research Council and the Norwegian Council on Cardiovascular Diseases and was conducted in collaboration with the Norwegian Health Screening Services, Oslo, Norway. The Regional Committee for Research Ethics approved the study, and informed consent was obtained from all participants.

Conflict of interest: none declared.

REFERENCES

1. Collin J, Araujo L, Walton J, et al. Oxford screening programme for abdominal aortic aneurysm in men aged 65 to 74 years. *Lancet*. 1988;2(8611):613–615.
2. Basnyat PS, Biffin AH, Moseley LG, et al. Mortality from ruptured abdominal aortic aneurysm in Wales. *Br J Surg*. 1999;86(6):765–770.
3. Alexander JJ. The pathobiology of aortic aneurysms. *J Surg Res.* 2004;117(1):163–175.
4. Alcorn HG, Wolfson SK Jr, Sutton-Tyrrell K, et al. Risk factors for abdominal aortic aneurysms in older adults enrolled in the Cardiovascular Health Study. *Arterioscler Thromb Vasc Biol.* 1996;16(8):963–970.
5. van der Vliet JA, Boll AP. Abdominal aortic aneurysm. *Lancet*. 1997;349(9055):863–866.
6. Blanchard JF, Armenian HK, Friesen PP. Risk factors for abdominal aortic aneurysm: results of a case-control study. *Am J Epidemiol*. 2000;151(6):575–583.
7. Norrgård O, Angquist KA, Johnson O. Familial aortic aneurysms: serum concentrations of triglyceride, cholesterol, HDL-cholesterol and (VLDL + LDL)-cholesterol. *Br J Surg*. 1985; 72(2):113–116.
8. Lederle FA, Johnson GR, Wilson SE. Abdominal aortic aneurysm in women. *J Vasc Surg*. 2001;34(1):122–126.
9. Frydman G, Walker PJ, Summers K, et al. The value of screening in siblings of patients with abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg*. 2003;26(4):396–400.
10. Johansen K, Koepsell T. Familial tendency for abdominal aortic aneurysms. *JAMA*. 1986;256(14):1934–1936.
11. Darling RC III, Brewster DC, Darling RC, et al. Are familial abdominal aortic aneurysms different? *J Vasc Surg*. 1989; 10(1):39–43.
12. van Laarhoven CJ, Borstlap AC, Berge Henegouwen DP, et al. Chronic obstructive pulmonary disease and abdominal aortic aneurysms. *Eur J Vasc Surg*. 1993;7(4):386–390.
13. Lehnert B, Wadouh F. High coincidence of inguinal hernias and abdominal aortic aneurysms. *Ann Vasc Surg*. 1992;6(2): 134–137.
14. Pleumeekers HJ, De Gruijl A, Hofman A, et al. Prevalence of aortic aneurysm in men with a history of inguinal hernia repair. *Br J Surg*. 1999;86(9):1155–1158.
15. Augestad KM, Wilsgaard T, Solberg S. Incisional hernia after surgery for abdominal aortic aneurysm. *Tidsskr Nor Laegeforen*. 2002;122(1):22–24.
16. Wagh PV, Leverich AP, Sun CN, et al. Direct inguinal herniation in men: a disease of collagen. *J Surg Res.* 1974;17(6): 425–433.
17. Baxter BT, Davis VA, Minion DJ, et al. Abdominal aortic aneurysms are associated with altered matrix proteins of the nonaneurysmal aortic segments. *J Vasc Surg*. 1994;19(5): 797–802.
18. Tilson MD, Dang C. Generalized arteriomegaly. A possible predisposition to the formation of abdominal aortic aneurysms. *Arch Surg*. 1981;116(8):1030–1032.
19. Ward AS. Aortic aneurysmal disease. A generalized dilating diathesis. *Arch Surg*. 1992;127(8):990–991.
20. Sonesson B, Hansen F, Länne T. Abdominal aortic aneurysm: a general defect in the vasculature with focal manifestations in the abdominal aorta? *J Vasc Surg*. 1997;26(2):247–254.
21. Singh K, Bønaa KH, Jacobsen BK, et al. Prevalence of and risk factors for abdominal aortic aneurysms in a population-based study: The Tromsø Study. *Am J Epidemiol*. 2001;154(3): 236–244.
22. Singh K, Bønaa KH, Solberg S, et al. Intra- and interobserver variability in ultrasound measurements of abdominal aortic diameter. The Tromsø Study. *Eur J Vasc Endovasc Surg*. 1998; 15(6):497–504.
23. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986;1(8476):307–310.
24. Stensland-Bugge E, Bønaa KH, Joakimsen O. Reproducibility of ultrasonographically determined intima-media thickness is dependent on arterial wall thickness. The Tromsø Study. *Stroke*. 1997;28(10):1972–1980.
25. Joakimsen O, Bønaa KH, Stensland-Bugge E. Reproducibility of ultrasound assessment of carotid plaque occurrence, thickness, and morphology. The Tromsø Study. *Stroke*. 1997;28(11): 2201–2207.

26. Fosse E, Johnsen SH, Stensland-Bugge E, et al. Repeated visual and computer-assisted carotid plaque characterization in a longitudinal population-based ultrasound study: The Tromsø Study. *Ultrasound Med Biol.* 2006;32(1):3–11.
27. Wendelhag I, Liang Q, Gustavsson T, et al. A new automated computerized analyzing system simplifies readings and reduces the variability in ultrasound measurement of intima-media thickness. *Stroke*. 1997;28(11):2195–2200.
28. Cohen JR, Mandell C, Margolis I, et al. Altered aortic protease and antiprotease activity in patients with ruptured abdominal aortic aneurysms. *Surg Gynecol Obstet*. 1987; 164(4):355–358.
29. Cohen JR, Sarfati I, Danna D, et al. Smooth muscle cell elastase, atherosclerosis, and abdominal aortic aneurysms. *Ann Surg*. 1992;216(3):327–330.
30. Gregory AK, Yin NX, Capella J, et al. Features of autoimmunity in the abdominal aortic aneurysm. *Arch Surg*. 1996; 131(1):85–88.
31. Tilson MD. Atherosclerosis and aneurysm disease. *J Vasc Surg*. 1990;12(3):371–372.
32. Bengtsson H, Norrgård O, Angquist KA, et al. Ultrasonographic screening of the abdominal aorta among siblings of patients with abdominal aortic aneurysms. *Br J Surg*. 1989; 76(6):589–591.
33. Norrgård O, Angqvist KA, Fodstad H, et al. Co-existence of abdominal aortic aneurysms and intracranial aneurysms. *Acta Neurochir (Wein)*. 1987;87(1-2):34–39.
34. Chapman JR, Hilson AJ. Polycystic kidneys and abdominal aortic aneurysms. *Lancet*. 1980;1(8169):646–647.
35. Torra R, Nicolau C, Badenas C, et al. Abdominal aortic aneurysms and autosomal dominant polycystic kidney disease. *J Am Soc Nephrol*. 1996;7(11):2483–2486.
36. Multicentre Aneurysm Screening Study Group. Multicentre Aneurysm Screening Study (MASS): cost effectiveness analysis of screening for abdominal aortic aneurysms based on four year results from randomised controlled trial. *BMJ*. 2002; 325(7373):1135.
37. Sakalihasan N, Limet R, Defawe OD. Abdominal aortic aneurysm. *Lancet*. 2005;365(9470):1577–1589.
38. McGregor JC, Pollock JG, Anton HC. Ultrasonography and possible ruptured abdominal aortic aneurysms. *Br Med J*. 1975;3(5975):78–79.
39. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33(1):159–174.
40. Denarié N, Gariepy J, Chironi G, et al. Distribution of ultrasonographically-assessed dimensions of common carotid arteries in healthy adults of both sexes. *Atherosclerosis*. 2000; 148(2):297–302.