Carotid Atherosclerosis and Relation to Growth of Infrarenal Aortic Diameter and Follow-up Diameter: The Tromsø Study CME

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WHAT THIS PAPER ADDS?

Even strongly cross-sectional associated the role of atherosclerosis in abdominal aortic dilatation and aneurysm formation has been questioned. Prospective data in this area are spare. The new prospective data presented in this study demonstrate an independent linear dose—response relationship between carotid plaque growth and growth of abdominal aortic diameter. These observations suggest that atherosclerosis may explain some of the variance in dilatation of the abdominal aorta and aneurysm formation. Identification and aggressive treatment of risk factors for atherosclerosis are recommended in patients with dilatation of the abdominal aorta.

Objectives: This research aims to study how carotid atherosclerosis is related to growth of infrarenal aortic diameter and aneurysmal formation.

Design: Population-based follow-up study.

Materials and methods: At baseline, ultrasound examination of the carotid artery and the abdominal aorta was performed in 4241 persons from a general population with no evidence of abdominal aortic aneurysm (AAA). The burden of atherosclerosis was assessed as carotid total plaque area (TPA). After a mean follow-up of 6.3 years, a new ultrasound examination was performed and measurements of the aortic diameter and carotid TPA were repeated. The effects on aortic diameter progression, follow-up diameter and risk for AAA were assessed in multiple linear and logistic regression models according to carotid TPA, adjusted for known risk factors.

Results: When analysing AAA as a dichotomous variable, a borderline association between atherosclerosis and AAA could be demonstrated. When modelling aortic diameter as a continuous variable, a 1-SD increase in 5 years' carotid plaque area (ΔTPA) was associated with a 0.12-mm growth in infrarenal aortic diameter (standard error (SE) 0.04) and a 0.20-mm wider aorta at follow-up (SE 0.06). No independent relation was seen for baseline atherosclerosis.

Conclusions: Carotid plaque progression was positively related to growth in infrarenal aortic diameter and aortic diameter at follow-up. Whether this co-variation between plaque growth and aortic diameter growth is causally related or independent events is still an open question.

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The formation of an abdominal aortic aneurysm (AAA) has historically been considered to be a focal manifestation of advanced atherosclerosis as the presence of atherosclerosis in the aneurysmal wall and in other circulatory beds is a common finding in AAA patients.[1,2] However, the aetiological role of atherosclerosis in AAA has been questioned.[3,4] The strong association between atherosclerosis and AAA may be confounded by several shared risk factors, smoking in particular, and also hypertension and hyperlipidaemia, although the strength of these associations differs between the two diseases.[5—12]

Recent case—control studies did not find evidence for more carotid, coronary or peripheral atherosclerosis in AAA patients.[13,14] In a previous cross-sectional population-based study, we could not find any consistent relationship between total carotid plaque area (TPA) and maximal

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infrarenal aortic diameter, in aortic diameter <27 mm. Neither were we able to demonstrate any correlation between TPA and aneurysmal diameter in those with AAA. However, an aortic diameter beyond 27 mm was associated with increased burden of both carotid atherosclerosis and coronary heart disease (CHD).[15] Due to the cross-sectional design of that study, no inferences could be made whether atherosclerosis precedes aortic dilatation or vice versa. In the present study of 4241 persons without AAA, we prospectively examined how baseline carotid TPA and carotid plaque growth (ΔTPA) were related to increase in infrarenal aortic diameter, follow-up diameter and incident AAA.

MATERIALS AND METHODS

Study population

The Tromsø Study was initiated in 1974 and is a population-based, prospective study with six repeated health surveys including total birth cohorts and random samples of the inhabitants of the municipality of Tromsø, Norway.[16] The study has been approved by The Regional Committee for Medical and Health Research Ethics and informed consent was obtained from all participants. As a part of the fourth survey in 1994/1995, a total of 6892 men and women, aged 25–84 years, underwent ultrasound scanning of the abdominal aorta in order to measure the maximal diameter of the infrarenal aorta. The attendance rate was 79%.[17] Ultrasound of the carotid artery was also performed. In the fifth survey, conducted in 2001, 5087 (85%) of these subjects attended the part of the study that included ultrasound examination of the abdominal aorta. Persons with a Y-graft were excluded ($n = 37$). Baseline carotid TPA and baseline and follow-up maximal infrarenal transversal and anterior–posterior aortic diameters were available in 4326 persons. However, an AAA (defined as the maximal infrarenal aortic diameter ≥30 mm) was present at baseline in 85 persons. They were excluded from this follow-up. Thus, 4241 subjects (1995 men and 2246 women) aged 25–82 years in 1994 were included in the present study.

Cardiovascular risk factors

Information about smoking habits, angina pectoris, myocardial infarction and use of anti-hypertensive drug was collected from self-administered questionnaires. Information about the use of lipid-lowering drugs (mainly statins) was collected at the screening examination. The participants were asked the following questions: “Do you have or did you ever have angina pectoris (heart cramp)?” and “Do you have or did you ever have a heart attack (myocardial infarction)?” If the answer to either question was yes, the participant was classified to have CHD. Standardised measurements of height, weight, blood pressure and non-fasting serum total cholesterol, high-density lipoprotein (HDL)-cholesterol and triglycerides were performed as described previously.[11]

Ultrasonography of the abdominal aorta and carotid artery

The ultrasonographic measurements of the abdominal aorta have been described in detail previously.[11,17] The maximal infrarenal aortic diameter was in the present analyses defined as the mean of the maximal transversal and anterior–posterior diameters. The difference between inter- and intra-observer variability of the maximal aortic diameter in the ultrasound examination at baseline was ≤4 mm in 95% of the pairs.[17] At follow-up in 2001, the corresponding figures were 87% and 96%.[12] An incident AAA was defined as follow-up maximal infrarenal aortic diameter ≥30 mm or as gone through surgery on the abdominal aorta due to aneurysm between baseline and follow-up screening.

The carotid ultrasound examination was carried out as detailed elsewhere.[18,19] A plaque was defined as a localised protrusion of the vessel wall into the lumen of at least 50% compared to the adjacent intima–media thickness. In each subject, a maximum of six plaques were registered in the near and far walls of the common carotid artery (CCA), bifurcation and internal carotid artery (ICA), respectively. Digitalised longitudinal plaque images were transferred to and standardised in Adobe Photoshop, to calculate the plaque area.[20] In subjects with more than one plaque, the areas of all plaques were summarised to give the TPA.

Statistical analyses

As the follow-up differed somewhat between the individuals, we calculated the estimated change per 5 years and included this variable in the analysis instead of the change without adjustment for follow-up period. The maximal infrarenal aortic diameter at follow-up, the estimated change per 5 years in aortic diameter and incident AAA were the dependent variables in the regression models. Carotid TPA and the estimated change in this variable per 5 years (ΔTPA) were the main explanatory variables. Change was assessed as 2001 readings − 1994 readings. Known risk factors for atherosclerosis and AAA were introduced as covariates. We assessed the effect of atherosclerosis and risk factors using a general linear model and logistic regression (the GLM and LOGISTIC procedures in the SAS statistical software). First, the age- and sex-adjusted mean levels of cardiovascular risk factors and measures of atherosclerosis at baseline were calculated in six categories of maximal infrarenal aortic diameter at follow-up: <18, 18–20, 21–23, 24–26, 27–29 and ≥30 mm (see Table 2). Linear trends across strata were tested by logistic regression for categorical variables and by linear regression for continuous variables (Tables 2 and 4). Linear and logistic regression models were used to model the independent relation between carotid atherosclerosis and aortic diameter and AAA (Tables 3 and 5). In these models, baseline TPA and ΔTPA were the main explanatory variables. Other vascular risk factors were introduced as continuous or binary variables in the model in order to adjust for confounding. We used the SAS statistical software package