Risk Factors for Abdominal Aortic Aneurysms
A 7-Year Prospective Study: The Tromsø Study, 1994–2001

Signe Helene Forsdahl, MD; Kulbir Singh, MD, PhD;
Steinar Solberg, MD, PhD; Bjarne K. Jacobsen, PhD

**Background**—Abdominal aortic aneurysm is an asymptomatic condition with a high mortality rate related to rupture. The incidence of AAA may have increased during the past 2 decades. This can be explained in part by longer life expectancy and by the fact that some AAAs have been diagnosed and treated owing to the introduction of screening programs and improved diagnostic tools.

**Methods and Results**—In a cohort of 2035 men and 2310 women in Tromsø, Norway, who were 25 to 82 years old in 1994, the authors identified risk factors for incident abdominal aortic aneurysm over the next 7 years. The impact of smoking was studied in particular. Ultrasound examination was performed initially in 1994/1995 and repeated in 2001. There were 119 incident cases of abdominal aortic aneurysms (an incidence of 0.4% per year). Male sex and increasing age were strong risk factors. In addition, the following variables were significantly associated with increased abdominal aortic aneurysm incidence: Smoking (OR = 13.72, 95% CI 6.12 to 30.78), hypertension (OR = 1.54, 95% CI 1.03 to 2.30), hypercholesterolemia (OR = 2.11, 95% CI 1.23 to 3.64), comparing subjects with serum total cholesterol ≥ 7.55 mmol/L with those with total cholesterol < 5.85 mmol/L, and low high-density lipoprotein cholesterol (OR = 3.25, 95% CI 1.68 to 6.27), comparing subjects with high-density lipoprotein cholesterol < 1.25 mmol/L with those with high-density lipoprotein ≥ 1.83 mmol/L. In addition, use of statins was associated with increased risk of abdominal aortic aneurysm (OR = 3.77, 95% CI 1.45 to 9.81), but this was probably a marker of high risk of cardiovascular diseases.

**Conclusions**—The results demonstrate strong associations between traditional atherosclerosis risk factors and the risk of incident abdominal aortic aneurysms. 

**Key Words:** aneurysm ■ aorta ■ cholesterol ■ epidemiology ■ smoking

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**Editorial p 2134**

**Clinical Perspective p 2208**

Approximately 50% of those with a ruptured AAA die before they reach the hospital. The operative (30 days) mortality rate in acute surgery for ruptured AAA is 30% to 70%. The overall mortality rate if the AAA ruptures is therefore as high as 65% to 85%. In contrast, operative mortality in elective surgery of AAAs is reported to be 2% to 6%. Hence, it is important to establish risk factors for AAA to identify patients at risk and candidates for screening for AAAs.

Several studies have found a strong coexistence of atherosclerosis and AAA, but there are also indications of an underlying disturbed connective tissue metabolism. The classic risk factors for atherosclerosis, such as tobacco smoking, male sex, age, hypertension, and hyperlipidemia, have all been found to also be risk factors for AAA, although the evidence for the role of lipids and hypertension is still controversial. Recently, Wong et al reported an increased risk for AAA with increasing alcohol consumption.

In a previous study, Singh and coworkers reported the prevalence of and risk factors for AAA on the basis of a cross-sectional population survey conducted in 1994/1995 in Tromsø, Norway. Here, we present results from follow-up of the same population. A total of 119 new cases of AAA were identified in 2001 in subjects who did not have an AAA in 1994. Several recently published studies have investigated the incidence of AAAs in different populations. The present study aims to increase our knowledge concerning predictors for an incident AAA.

**Methods**

The Tromsø Study started in 1974 as a population-based, prospective study of inhabitants in the municipality of Tromsø, Norway. The purpose of the study is to investigate the determinants of chronic
ultrasound examination of the abdominal aorta. The ultrasound examination was conducted in 4699 subjects. A total of 63 subjects did not give complete informed consent. In the remaining 4636 men and women, the examination did not give sufficient data to conclude whether an AAA (as defined below) was present or not in 127 individuals (3% of the subjects). Because we were investigating predictors for incident AAA, we excluded from the follow-up the 151 subjects with an AAA and the 11 subjects with unknown AAA status at baseline (1994/1995). We also excluded 2 subjects who according to the examination in 1994/1995 previously had been subject to surgery to insert a graft in the abdominal aorta. Thus, 4345 subjects (2035 men and 2310 women) 25 to 82 years of age in 1994 were included in the present study of incident cases of AAA.

The survey included questionnaires regarding inter alia smoking habits, physical activity in leisure, and use of antihypertensive medication. Information about present use of statins was based on interviews. We defined persons as physically inactive if they reported that they were never so active during their leisure time that they were sweating or out of breath and if they reported that they had been only lightly active (not sweating or out of breath) for fewer than 3 hours per week during the past year.

Smoking was categorized into 7 groups: Never-smokers, ex-smokers (stopped smoking ≥20 years ago, stopped smoking 10 to 19 years ago, and stopped smoking <10 years ago), and current smokers (<10 cigarettes/d, 10 to 19 cigarettes/d, and ≥20 cigarettes/d). Furthermore, smoking duration was categorized into 4 groups (never-smokers and 0 to 19, 20 to 29, and ≥30 years of smoking). Height and weight were measured in light clothing without shoes. Body mass index was calculated as the weight in kilograms divided by the square of height in meters (kg/m²). The waist-to-hip ratio was calculated as the waist circumference divided by the maximal hip circumference.

Blood pressure was recorded before blood sampling in a separate, quiet room with only a nurse present. An automatic device (Dinamap Vital Signs Monitor 1846; Criticon, Inc, Tampa, Fla) was used. After the participant had been seated for 2 minutes, 3 recordings were made at 2-minute intervals. The mean of the 2 last values of blood pressure was used in the analyses. Hypertension was defined as systolic blood pressure >160 mm Hg, diastolic blood pressure >95 mm Hg, or ever use of antihypertensive medication.

A venipuncture was performed with the subject seated. A brief venous stasis applied to the upper arm was released before blood sampling. Serum total cholesterol and triglycerides were analyzed by enzymatic colorimetric methods with commercial kits (CHOD-PAP for cholesterol and GPO-PAP for triglycerides; Boehringer-Mannheim, Indianapolis, Ind). Serum creatinine was measured by the HiCo creatinine Jaffé method with a commercial kit (Unimate 5 HBA1C; Roche Diagnostics Corp, Indianapolis, Ind). The analyses were done at the Department of Clinical Chemistry, University Hospital of North Norway. Glomerular filtration rate was estimated with the abbreviated (4-variable) Modification of Diet in Renal Disease equation. The interobserver and intraobserver variability of the ultrasound examination performed in 1994/1995 have been reported previously. The difference between 2 measurements (both interobserver and intraobserver agreement) of the maximal aortic diameters was ±4 mm in width of the pairs. In the 2001 survey, the corresponding interobserver and intraobserver agreements were 87% and 96%, respectively.

AAAs were defined as an abdominal aortic aneurysm with a maximal diameter ≥30 mm. When we applied this definition of an AAA, 140 subjects had developed an AAA. The concordance between the classification of an AAA according to the 2 definitions of an AAA was good, however, because the kappa (k) was 0.67.

**Statistical Analysis**

The age-adjusted associations between a number of possible predictors of AAA and the risk of an incident AAA were analyzed in men and women separately with logistic regression analysis. Furthermore, the age- and sex-adjusted relationships were assessed with men and women merged into 1 group. Age by December, 31, 1994, was included in the analysis as age at the baseline ultrasound examination. The considered risk factors were age, sex, height, body mass index (kg/m²), waist-to-hip ratio, smoking, alcohol consumption, prevalent diabetes mellitus, diastolic and systolic blood pressure, hypertension, inactive in leisure time, light and hard physical activity in leisure time, use of statins, serum total cholesterol, HDL cholesterol, triglycerides, creatinine, estimated glomerular filtration rate, glycohemoglobin (HbA1c), blood platelet count, hemoglobin, white blood cell count, and fibrinogen. Variables found to be associated with AAA incidence with P≤0.10 in 1 or both sexes or in the age-and sex-adjusted analyses were included in a logistic regression model, and the model was further simplified by the inclusion of only variables with P≤0.10 in the multivariate analysis in the final model of variables associated with an incident AAA in this prospective study. In separate analyses, relationships between smoking and the risk of a new AAA were examined in more detail in a logistic regression model.
All statistical analyses were performed with SPSS software. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written. The Regional Committee for Research Ethics approved the study.

### Results

The study population consisted of 4345 subjects (2035 men and 2310 women) who were 25 to 82 years old in 1994. Mean age at the start of follow-up was 60.1 years in women and 58.7 years in men. Table 1 gives selected characteristics in the study population. There were 119 incident cases of AAA in this prospective study, which is equivalent to 2.7% over 7 years, or a mean annual incidence of 0.4%.

Both sex and age were significantly ($P<0.001$) associated with the risk of AAA. In addition, a number of the considered possible risk factors for AAA, all measured at baseline in 1994/1995, were associated ($P\leq0.10$) with the risk of a new AAA in sex-specific analyses adjusted for age or in analysis adjusted for sex and age. Hypertension, systolic blood pressure, use of statins, smoking, serum total cholesterol, triglycerides, glucose, body mass index, waist-to-hip-ratio, plasma fibrinogen, hemoglobin, and white blood cell count were positively associated with the risk of an AAA, whereas high HDL cholesterol and hard physical activity in leisure, as well as alcohol use, reduced the risk of developing an AAA.

These variables were included in multiple logistic regression analyses. Because of the high correlation between hypertension and systolic blood pressure, only hypertension was included in the model. Sex, age, hypertension, use of statins, smoking, serum total cholesterol, and HDL cholesterol remained significantly associated with the risk of an incident AAA (Table 2). Because of missing values for some variables, a total of 4262 subjects, including 118 men and women with an AAA, were included in these multivariate analyses.

The risk of incident AAA increased significantly with age ($P<0.001$) in both men and women. Subjects who were $\geq$75 years old had nearly 8 times the risk of AAA of subjects 65 to 69 years of age. Men had a 2.7-times increased risk for an AAA compared with women ($P<0.001$). High serum total cholesterol and low HDL cholesterol were significantly ($P\leq0.004$) associated with the risk of

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### Table 1. Means, SDs, and Proportions of Selected Baseline Characteristics of the Study Population: Tromsø, Norway, 1994–2001

<table>
<thead>
<tr>
<th></th>
<th>Men ($n=2035^*$)</th>
<th>Women ($n=2310^*$)</th>
<th>Both Sexes ($n=4345^*$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Age, y</td>
<td>58.7</td>
<td>9.2</td>
<td>60.1</td>
</tr>
<tr>
<td>Height, cm</td>
<td>175.5</td>
<td>6.7</td>
<td>161.8</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>80.2</td>
<td>11.4</td>
<td>67.8</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.0</td>
<td>3.1</td>
<td>25.9</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.91</td>
<td>0.06</td>
<td>0.82</td>
</tr>
<tr>
<td>Serum total cholesterol, mmol/L</td>
<td>6.54</td>
<td>1.17</td>
<td>6.89</td>
</tr>
<tr>
<td>Serum HDL cholesterol, mmol/L</td>
<td>1.40</td>
<td>0.39</td>
<td>1.69</td>
</tr>
<tr>
<td>Serum triglycerides, mmol/L</td>
<td>1.77</td>
<td>1.13</td>
<td>1.54</td>
</tr>
<tr>
<td>Serum creatinine, μmol/L</td>
<td>75.2</td>
<td>15.3</td>
<td>60.9</td>
</tr>
<tr>
<td>GFR</td>
<td>95.8</td>
<td>18.0</td>
<td>90.4</td>
</tr>
<tr>
<td>Plasma fibrinogen, mmol/L</td>
<td>3.23</td>
<td>0.84</td>
<td>3.39</td>
</tr>
<tr>
<td>White blood cell count, 10⁹/L</td>
<td>7.00</td>
<td>1.93</td>
<td>6.70</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>84.6</td>
<td>11.6</td>
<td>81.2</td>
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<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>143.5</td>
<td>19.4</td>
<td>143.1</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>31.0</td>
<td>...</td>
<td>32.2</td>
</tr>
<tr>
<td>HbA1C, %</td>
<td>5.42</td>
<td>0.62</td>
<td>5.47</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>14.75</td>
<td>0.96</td>
<td>13.58</td>
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<tr>
<td>Inactivity, %</td>
<td>31.2</td>
<td>...</td>
<td>44.4</td>
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<tr>
<td>Statin use, %</td>
<td>1.4</td>
<td>...</td>
<td>1.6</td>
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<tr>
<td>Current smoker, %</td>
<td>29.3</td>
<td>...</td>
<td>27.7</td>
</tr>
<tr>
<td>Ever-smoker, %</td>
<td>49.4</td>
<td>...</td>
<td>25.4</td>
</tr>
<tr>
<td>Never-smoker, %</td>
<td>21.3</td>
<td>...</td>
<td>46.9</td>
</tr>
<tr>
<td>Alcohol consumption, times/mo</td>
<td>3.2</td>
<td>4.6</td>
<td>1.6</td>
</tr>
<tr>
<td>Cardiovascular disease, %</td>
<td>13.8</td>
<td>...</td>
<td>8.0</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>2.0</td>
<td>...</td>
<td>2.0</td>
</tr>
<tr>
<td>Family history of AAA, %</td>
<td>6.3</td>
<td>...</td>
<td>8.5</td>
</tr>
</tbody>
</table>

GFR indicates glomerular filtration rate.$^{21}$

*Number may vary somewhat due to missing information.
developing an AAA. For serum total cholesterol, the results may suggest that only subjects with rather high readings (≥7.55 mmol/L) were at increased risk; however, a second-order term for serum cholesterol was not statistically significant, and a linear relationship is the most likely one. Both use of statins (P = 0.003) and hypertension (P = 0.03) increased the risk of AAA. The association with statin use (OR = 3.77, 95% CI 1.45 to 9.81) was somewhat weaker when adjusted
The mean annual incidence of AAA in the study population was ≈0.4%. A similar incidence was found in England, in the Veteran Affairs Cooperative Study in the United States, and in the Chichester study. A lower incidence of AAA was found in an Asian population. The present findings with regard to male sex and advancing age as risk factors are in accordance with previous findings.

Blood lipid levels have also been found to be related to AAA incidence or prevalence in previous studies. Some but not all studies have indicated that increasing blood pressure and diagnosed hypertension are both significant risk factors for AAA. In the sex-specific and age- and sex-adjusted analyses, we found indications that increasing systolic blood pressure and hypertension were risk factors for the development of an AAA. In the multivariate analyses, however, only hypertension (defined as a systolic
blood pressure >160 mm Hg, a diastolic blood pressure >95 mm Hg, or ever use of antihypertensive medication) was significantly associated with AAA risk, and only in women.

Some studies have indicated that use of statins may reduce the risk and growth of AAA.\textsuperscript{35–37} Surprisingly, the present study indicates that use of statins increases the risk of AAA. The prevalence of use of statins in the baseline population screened in 1994 was low (1.5%), and in 1994, statins were probably only used by patients with a high risk of cardiovascular disease. This was reflected in the much higher prevalence of statin use in subjects with self-reported cardiovascular disease or diabetes (7.5%) than in other subjects (0.7%). Adjustment for self-reported cardiovascular disease or diabetes did not explain the association between use of statins and AAA incidence; however, residual confounding is likely, and we cannot conclude from the present study whether statin use influences the incidence of AAA.

We confirm that smoking is a very strong risk factor for AAA.\textsuperscript{6,12,23,28,33,38–40} The results suggest that both duration of smoking and the number of cigarettes smoked per day in ever-smokers are important for AAA risk; however, the cross-sectional study\textsuperscript{6} that forms the basis for the present study indicates that smoking duration was more important.

In contrast to Wong et al,\textsuperscript{17} we did not find any significant positive association between alcohol consumption and AAA risk. Thus, the present results are in accordance with those of Törnwall et al.\textsuperscript{31} However, mean alcohol consumption in the present study population was low (the mean frequency of alcohol consumption was 2.3 times per month), much lower than in the cohort studies by Wong et al.\textsuperscript{17} This may have hampered our investigation of the relationship between alcohol consumption and the risk of AAA in the present study population.

We found no association between estimated glomerular filtration rate and the risk of AAA. This is in variance with the findings of Iribarren et al.\textsuperscript{33} One reason for this may be that we included incident cases of AAA in our analyses, whereas Iribarren et al\textsuperscript{33} analyzed the risk of clinically diagnosed AAA. Thus, a substantial number of the cases included in their analysis may have had a small AAA at baseline when the glomerular filtration rate was measured, and the reduced glomerular filtration rate may be the result rather than the cause of the AAA.

One weakness of the present study is that we were not able to estimate the incidence of AAAs exactly (eg, as 4 cases per 1000 person-years) because we did not know when during follow-up the subjects developed the AAA, only that they had an AAA in 2001 and had not registered with one in 1994. In addition, the diagnosis of small AAAs may not be easy to make, and it is possible that a few AAAs were overlooked in 1994, thus not being truly incident in the present study population. We may also have missed a few small AAAs in 2001. The latter is the most important for our analyses, because it would reduce the statistical power. From an analytical point of view, it would have been an advantage if there had been more incident cases of AAA in the population. In particular, there were few cases in women, and it was not feasible to perform sex-specific analysis.

The strength of the study is that it is a population-based prospective study over a time period of 7 years. Effects of an AAA on risk factor level (eg, on blood platelet count) may therefore be excluded to a large extent. The attendance rate at the baseline study was high (79% of the eligible population). Furthermore, 78% of the individuals who had their aortas examined in 1994 and were alive and living in Tromsø in 2001 had a follow-up ultrasound examination the same year. To influence our findings, the association between the different risk factors considered and the incidence of AAAs must differ considerably in the included men and women and in individuals who died, moved out of Tromsø, or did not want to take part in the follow-up study in 2001. We do not consider this to be likely.

In summary, we found that both smoking and low HDL cholesterol significantly increased the risk of a new AAA during a 7-year follow-up of 4345 Norwegian men and women. Our results underscore the importance of cardiovascular risk factors and smoking in the origin of AAA.

Acknowledgments

The study was conducted in cooperation with the Norwegian Health Screening Services, Oslo, Norway.

Sources of Funding

This study was supported by grants from the Norwegian Research Council and the Norwegian Council on Cardiovascular Diseases, Oslo, Norway.

Disclosures

None.

References


Abdominal aortic aneurysms (AAAs) have no or few symptoms until a possible rupture. In rupture, the mortality rate is 65% to 85%. Death due to ruptured AAA accounts for 1% of all deaths in the Western world. Screening of risk groups has been suggested to reduce the frequency of ruptured AAAs. In this population-based study, 4345 persons with normal-sized abdominal aortas in 1994/1995 were rescanned by ultrasound 7 years later. The aim was to identify risk factors for developing an AAA. There were 119 incident cases of AAA, which yielded an incidence of 0.4% per year. Risk factors for developing an AAA were increasing age, male sex, smoking, high serum total cholesterol, low serum high-density lipoprotein cholesterol, and hypertension. Smoking, both the number of years and the number of daily cigarettes, influenced the risk for AAA strongly. Thus, the risk factors for AAA are the same as those for developing atherosclerosis. These results may be helpful both to identify patients at risk for developing an AAA (eg, smokers with low high-density lipoprotein cholesterol) and to clarify which groups should be offered a possible screening program. Both smoking reduction and (ideally) complete smoking cessation for reducing the risk for AAA are supported by the present results.
Signe Helene Forsdahl, Kulbir Singh, Steinar Solberg and Bjarne K. Jacobsen

Circulation, 2009;119:2202-2208; originally published online April 13, 2009; doi: 10.1161/CIRCULATIONAHA.108.817619
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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