

Abstracts

Gregory L. Moneta, MD, Section Editor

Evidence for a Strong Genetic Influence on Carotid Plaque Characteristics: An International Twin Study

Tamoki AD, Baracchini C, Tamoki DL, et al. *Stroke* 2012;43:3168-72.

Conclusion: Heritability of ultrasound plaque characteristics is high.

Summary: Only a few studies have even partially investigated genetic determinants of carotid plaque characteristics. The San Antonio Family Heart Study found moderate (23%-28%) heritability of the presence of carotid plaques (Hunt KJ et al, *Stroke* 2002;33:2775-80). The Erasmus Rucphen Family (ERF) study used a carotid plaque score to quantify common carotid artery carotid bifurcation and internal carotid artery plaque and found 28% heritability of the carotid plaque (Sayed-Tabatabaei FA et al, *Stroke* 2005;36:2351-6). It is also known that underlying atherosclerotic phenotypes associated with carotid plaque formation (intima-media thickness, arterial stiffness) can also exhibit moderate heritability. However, genetic determinants related directly to carotid plaque characteristics are not clear. The authors sought to study the heritability of carotid plaque characteristics in a twin population. Twin studies more reliably estimate relative contribution of genes to phenotypic traits than can be determined with a "family study" design. There were 192 monozygotic and 83 dizygotic adult twin pairs (age 49 ± 15 years) from Italy, Hungary, and the United States who underwent B-mode and color Doppler ultrasound imaging of their bilateral common, internal, and external carotid arteries. Age-, sex-, and country-adjusted heritability was 78% for the presence of carotid plaque (95% confidence interval [CI] 55%-90%), 74% for plaque echogenicity (95% CI, 38%-87%), and 69% for plaque size (area in mm^2 in longitudinal plane; <50 percentile or >50 percentile; 95% CI, 16%-86%). Adjusted heritability for plaque sidedness was 74% (95% CI, 25%-90%). Heritability was 74% for plaque numerosity (95% CI, 26%-86%) and 68% (95% CI, 40%-84%) and 66% (95% CI, 32%-90%), respectively, for presence of plaque in the carotid bulb and proximal internal carotid artery. No role for shared environmental factors was found. The remaining variants (22%-34%) were attributed to unique environmental factors. Controlling for relative covariates did not change the results of the study significantly.

Comment: This is the first international twin population study to investigate heritability of carotid plaque characteristics. Heritability of the carotid plaque in this study is considerably higher than in previous studies, with the inevitable corollary that the influence of unique environmental factors on development of carotid plaque is actually moderate. Because unshared environmental factors accounted for only a modest portion of variability in carotid plaque, the authors' findings should stimulate a search for genes responsible for the variability of carotid plaque in response to atherosclerotic risk factors.

Current Prevalence of Abdominal Aortic Aneurysm in 70-Year-Old Women

Svensjo S, Bjorck M, Wanhainen A. *Br J Surg* 2013;100:367-72.

Conclusion: Screening 70-year-old women who do not smoke is likely to be ineffective in discovering abdominal aortic aneurysm (AAA).

Summary: Ultrasound screening of older men for AAA is an evidence-based method to reduce aneurysm-related and all-cause mortality. The only randomized study including women, however, demonstrated no reduction in mortality with aortic aneurysm screening (Scott RA et al, *Br J Surg* 2005;89:283-5). A modeling study, however, suggests screening woman could be cost-effective given the observed higher rupture rates of AAA in women and increased longevity among women compared with men (Wanhainen A et al, *J Vasc Surg* 2006;43:908-14). The Society for Vascular Surgery recommends aneurysm screening among older women with a family history of AAA or who have smoked (Chaikof EL et al, *J Vasc Surg* 2009;50(Suppl):S2-49). The U.S. Preventative Services Task Force, however, found no evidence of benefit in screening women, regardless of risk factors (U.S. Preventative Task Force, *Ann Intern Med* 2005;142:198-202). However, people also may be healthier now, and with delayed aneurysm development, than at the time screening for AAAs was first evaluated. The aim of this study was therefore to determine the prevalence of AAA and risk factors in a contemporary well-defined population of 70-year-old women. The study targeted 70-year-old women because previous investigations suggested AAAs present later in life in women than

in men (Katz DJ et al, *J Vasc Surg* 1997;25:561-8). The 70-year-old women were identified through the Swedish National Population Registry in two neighboring counties of Uppsala and Dalarna and were invited to a free ultrasound examination of the abdominal aorta. An aorta >30 mm in diameter was defined as an AAA. Of the 6925 women who were invited, 5140 (74.2%) accepted the invitation for screening and 19 AAAs (0.4%) were detected (95% confidence interval [CI], 0.2%-0.5%). In the invited cohort, 12 women (0.2%; 95% CI, 0.1%-0.3%) had undergone previous AAA repair (11) or had a known AAA under surveillance (one). The total prevalence of AAA was therefore estimated at 0.5% (0.4%-0.7%). Of 19 women with screen-detected AAAs, 18 (95%) had a history of smoking compared with a smoking history of 44.2% of those with a normal aorta (odds ratio, 20.29; 95% CI, 2.7-152.65). Prevalence of AAA was 0.03% (0%-0.1%) among never smokers, 0.4% (0.2%-0.8%) among former smokers, and 2.1% (1.0%-3.7%) among current smokers.

Comment: People are getting healthier and engaging in less risky behavior. In the current study, smoking was the only independent risk factor for AAA. Previous studies have indicated higher rates among women for smoking history, hypertension, elevated cholesterol, and coronary disease than were found in the current study (Derubertis BG et al, *J Vasc Surg* 2007;46:630-7 and Lederle FA et al, *J Vasc Surg* 2001;34:122-6). In Sweden, a 70-year-old woman is likely to live another 17 years. We also know that at least in men, some people who initially screen negatively will eventually die of a ruptured AAA. Therefore, although the data certainly indicate screening for AAA among nonsmoking woman at age 70 is of no benefit, the value of targeted screening of an older woman who is still smoking is potentially an open question. Given the low prevalence of aneurysm in women, this question is unlikely to be answered without a study randomizing at least 100,000 elderly women; a study so ponderous as to be a logistic impossibility.

Final Follow-up of the Multicentre Aneurysm Screening Study (MASS) Randomized Trial of Abdominal Aortic Aneurysm Screening

Thompson SG, Ashton HA, Gao L, et al, on behalf of the Multicentre Aneurysm Screening Study (MASS) Group. *Br J Surg* 2012;99:1649-56.

Conclusion: Screening for abdominal aortic aneurysms (AAA) results in a reduction of all-cause mortality out to 13 years of follow-up.

Summary: The UK Multicenter Aneurysm Screening Study (MASS) is the largest randomized trial of screening vs no screening of AAAs to reduce aneurysm and all-cause mortality. Previous results from MASS were published after 10 years of follow-up (Thompson SG et al, *BMJ* 2009;338:b2307). At that time, there was some increase in rupture of AAA among those initially screened as normal. However, this increase had no impact on overall proportionate AAA-related mortality. The 15-year results of the UK Chichester trial suggested a possible substantial increase in ruptured AAAs during follow-up (Ashton HA et al, *Br J Surg* 2007;94:696-701). Significant numbers of AAA ruptures in those initially screened as normal could result in a long-term reduction of benefits in AAA mortality implied by a normal initial screening study. This latest publication from the MASS trial investigators examined further follow-up in the MASS trial participants with respect to potential benefits of all-cause mortality and late AAA rupture in those initially screened as normal. The MASS trial was a population-based sample of men aged 65 to 74 years who were randomized to an invitation for ultrasound screening (invited group) for AAA or to a control group that was not offered screening. Patients with an abdominal aorta >3 cm detected at the initial study underwent surveillance and were offered surgery after predefined criteria had been met. Cause-specific mortality data were analyzed using Cox regression techniques. The study enrolled 67,770 men. Over 13 years, 224 AAA-related deaths occurred in the invited group and 381 in the control group. This was a relative risk reduction of 42% in the invited group compared with the control group (hazard ratio, 0.58; 95% confidence interval, 0.49-0.69). Relative risk reduction did not vary by baseline age or center, and there was no evidence of an effect on other causes of death. There was an overall reduction in all-cause mortality of 3% (1%-5%). Benefit was greater in earlier years of follow-up and decreased with longer follow-up, with a risk reduction of 48% from randomization to 10 years and 20% from 10 to 14 years. During the 13-year interval, nonfatal AAA ruptures were halved