Detection of Abdominal Aortic Calcification with IVA

By Kevin E. Wilson, PhD

The Scope of the Problem

Heart disease and stroke are the first and third leading causes of death in the United States.[1] Atherosclerosis is the common pathological process underlying myocardial infarction, stroke and other occlusive vascular diseases. Atherosclerosis has a long latent period between early phases of the disease and the manifestation of clinical symptoms. Thus there is an opportunity for primary prevention if patients can be identified before the first clinical event. Unfortunately, for many asymptomatic individuals, the first manifestation of underlying disease is often an unexpected acute myocardial infarction or sudden death.[2, 3] Additionally, there is evidence that in women, coronary heart disease often presents atypically, making clinical recognition difficult.[4] Two-thirds of women who die of cardiovascular events had no prior sign of the disease.[5]

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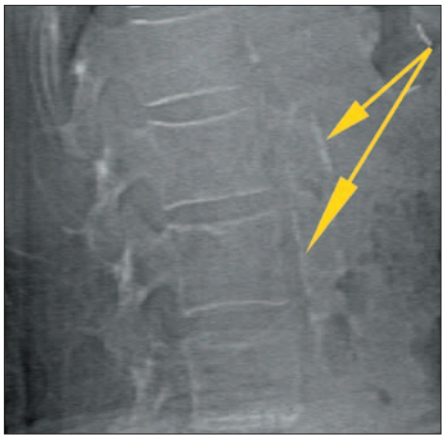
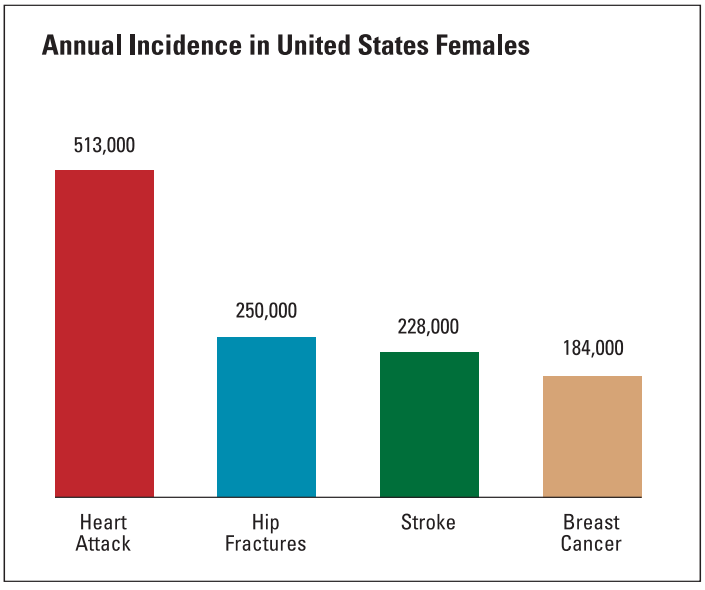
Traditionally, cardiovascular disease risk stratification has been conducted using risk factors such as cigarette use, diabetes mellitus, systolic blood pressure, dyslipidemia, etc. However, 60% of cardiovascular disease events occur in the population that is at low to intermediate risk by these traditional risk factors.[6] There is thus an urgent need for identifying patients at high risk of cardiovascular events using risk factors that are both strong and independent of the traditional cardiovascular risk factors, and this need is particularly acute in women.



An example of an AAC-8 score of 4. Two each on the anterior and posterior walls of the aorta.

Abdominal aortic calcification (AAC), an indication of atherosclerosis, is significantly associated with both cardiovascular heart disease and stroke even after adjustment for the traditional risk factors of age, cigarette use, diabetes mellitus, systolic blood pressure, left ventricular hypertrophy, body mass index, cholesterol, and HDL cholesterol.[7-10] The increased risk of cardiovascular disease mortality associated with moderate to severe AAC is similar to the increased risk of hip fracture in the presence of a moderate to severe vertebral fracture.

The prevalence of AAC in the population has a similar size and age related trend to that of prevalent vertebral fractures, though AAC is less well studied. In a study in the Netherlands the incidence of radiographically detectable AAC in women was approximately 30% at age 67, rising to 75% by age 82.[11] In the Framingham Heart study, the prevalence of AAC in the studied cohort (mean age 61) was 68% in men and 57% in women.[10] While this prevalence is quite high, it is in keeping with the high incidence of cardiovascular disease. Moreover, the studies



indicate a graded increase of risk with more severe AAC scores being associated with a higher risk of morbidity and mortality.

Detection of Abdominal Aortic Calcification with IVA

Instant Vertebral Assessment (IVA) has become a valuable and increasingly utilized tool to assess patients at risk of osteoporosis for the presence of vertebral fractures. Prevalent vertebral fractures predict future fractures independently of other risk factors such as age and BMD. This fact, along with IVA's low radiation dose and 10s exam time has contributed to its increasing utilization.

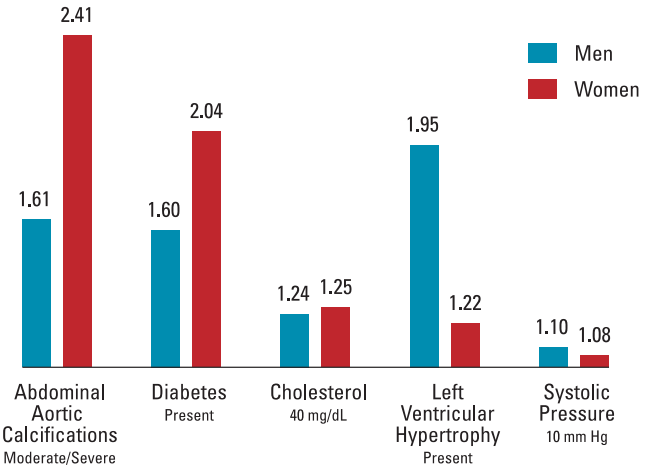
Because of expected prevalence of vertebral fractures, IVA exams are most typically performed in women age 65 or older. This is an important period in which to more accurately assess cardiovascular risk in women, since the average age of first myocardial infarction in women is 70.4 years.[5]

During an IVA scan, sufficient soft tissue anterior to the lumbar spine can be included to allow for the detection of calcified plaques in the abdominal aorta. There is good agreement between IVA and lateral radiographs for the detection of AAC,[12] similar to the agreement between the two modalities for vertebral fracture detection.[13, 14] Thus, the same diagnostic test can be used to measure strong risk factors for two highly prevalent public health problems, osteoporosis and cardiovascular disease.

There are several methods available for the quantization of AAC.[12, 15, 16] One quick and simple method was developed by Schousboe, Wilson, and Kiel[12, 17] and is called AAC-8. The AAC-8 scale estimates the total length of calcification of the anterior and posterior aortic walls in front of vertebrae L1 to L4. Abdominal aortic calcification is typically seen as a linear stippling at the anterior or posterior wall of the aorta or alternatively there is a "ground glass" appearance seen instead of a linear calcification. To be considered a calcification, this ground glass appearance needs a definite linear edge corresponding to the aortic wall. Both linear calcifications and "ground glass" are considered part of the aggregate length of the calcification. The anterior and posterior aortic walls are assigned a score between 0-4 as shown in the table (below).

The sum of the two scores for the anterior and posterior walls gives the AAC-8 score. An AAC-8 score greater than two is considered moderate to severe AAC on this scale.

Multi-variate Adjusted Relative Risk for Cardiovascular Disease Mortality, adapted from Wilson *et. al.*[5]



The Clinical Significance of Abdominal Aortic Calcification

The multivariate-adjusted relative risk for cardiovascular disease mortality for those with AAC in the upper one third of the population was 2.4 and 2.2 for women and men, respectively.[10] On the AAC-8 scale, this is roughly equivalent to a score greater than two. The fact that the AAC risk is independent of other typically assessed cardiovascular risk factors gives this measure particular strength. In fact, for the prediction of stroke, "Carotids IMT and aortic calcifications predict the risk of stroke independently of each other."[7] Similar independence of the predictive power of AAC and carotids IMT was seen for the prediction of incident myocardial infarction.[8]

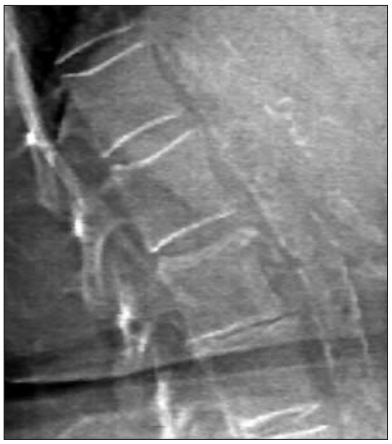
One way to understand the strength of the AAC risk factor is to compare it to the risk from total cholesterol. Each 40 mg/dL increase in total cholesterol above baseline (243 mg/dL in the Framingham study) has a RR of 1.25 in women.[10] The RR associated with moderate/severe AAC is 2.4, or equivalent to the relative risk a women would have with a total cholesterol of 400 mg/dL.

Coronary calcium scoring with electron beam CT (EBCT) or multislice CT has gained some acceptance for identifying those at high risk for heart disease. Strong and graded associations have been shown between coronary calcium score and AAC. In women, severe AAC was associated with a 20-fold increase in

Description	Score
No calcification seen	0
Aggregate length of calcification is ≤ to the height of one vertebra	1
Aggregate length of calcification is > one but ≤ two vertebra	2
Aggregate length of calcification is > two but ≤ three vertebra	3
Aggregate length of calcification is > three vertebra	4

coronary calcium score as assessed by EBCT,[16] and there was an 11-fold increase for men.

In summary, IVA's new indication for the detection of abdominal aortic calcifications[18] may have as much clinical significance as its previous indication for the detection of vertebral fractures.[19] Most patients at high risk for osteoporotic fracture are commonly also at high risk for cardiovascular disease.[20] A single IVA exam can assist in stratifying patients into high and low risk groups for two highly prevalent and significant health care problems.



An example AAC-8 score of 7, four and the posterior aortic wall and three on the anterior aortic wall.

References

[1] Kenneth D Kochanek, S.L.M., Robert N. Anderson, and Chester Scott., Deaths: Final Data for 2002. National Vital Statistics Report, Center for Disease Control. **53**(5).

[2] Myerburg, R.J., Scientific gaps in the prediction and prevention of sudden cardiac death. J Cardiovasc Electrophysiol, 2002. **13**(7): p. 709-23.

[3] Thaulow, E., et al., Initial clinical presentation of cardiac disease in asymptomatic men with silent myocardial ischemia and angiographically documented coronary artery disease (the Oslo Ischemia Study). Am J Cardiol, 1993. **72**(9): p. 629-33.

[4] Wenger, N.K., Coronary heart disease: the female heart is vulnerable. Prog Cardiovasc Dis, 2003. **46**(3): p. 199-229.

[5] Thom, T., et al., Heart disease and stroke statistics--2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation, 2006. **113**(6): p. e85-151.

[6] Greenland, P., S.C. Smith, Jr., and S.M. Grundy, Improving coronary heart disease risk assessment in asymptomatic people: role of traditional risk factors and noninvasive cardiovascular tests. Circulation, 2001. **104**(15): p. 1863-7.

[7] Hollander, M., et al., Comparison between measures of atherosclerosis and risk of stroke: the Rotterdam Study. Stroke, 2003. **34**(10): p. 2367-72.

[8] van der Meer, I.M., et al., Predictive value of noninvasive measures of atherosclerosis for incident myocardial infarction: the Rotterdam Study. Circulation, 2004. **109**(9): p. 1089-94.

[9] Walsh, C.R., et al., Abdominal aortic calcific deposits are associated with increased risk for congestive heart failure: the Framingham Heart Study. Am Heart J, 2002. **144**(4): p. 733-9.

[10] Wilson, P.W., et al., Abdominal aortic calcific deposits are an important predictor of vascular morbidity and mortality. Circulation, 2001. **103**(11): p. 1529-34.

[11] Witteman, J.C., et al., Aortic calcification as a predictor of cardiovascular mortality. Lancet, 1986. **2**(8516): p. 1120-2.

[12] Schousboe, J.T., K.E. Wilson, and D.P. Kiel, Detection of Abdominal Aortic Calcification with Lateral Spine Imaging Using Dual Energy X-Ray Absorptiometry. Accepted for publication in the Journal of Clinical Densitometry, 2006.

[13] Rea, J.A., et al., Visual assessment of vertebral deformity by X-ray absorptiometry: a highly predictive method to exclude vertebral deformity. Osteoporos Int, 2000. **11**(8): p. 660-8.

[14] Schousboe, J.T. and C.R. Debold, Reliability and accuracy of vertebral fracture assessment with densitometry compared to radiography in clinical practice. Osteoporos Int, 2006. **17**(2): p. 281-9.

[15] Kauppila, L.I., et al., New indices to classify location, severity and progression of calcific lesions in the abdominal aorta: a 25-year follow-up study. Atherosclerosis, 1997. **132**(2): p. 245-50.

[16] Oei, H.H., et al., The association between coronary calcification assessed by electron beam computed tomography and measures of extracoronary atherosclerosis: the Rotterdam Coronary Calcification Study. J Am Coll Cardiol, 2002. **39**(11): p. 1745-51.

[17] JT Schousboe, KE Wilson, and D. Kiel. Comparison of a Simplified 8-Point Scale (AAC-8) with a Previously Validated 24-Point Scale to Score Abdominal Aortic Calcification With Densitometry or Radiography. In ISCD 2006 Annual Meeting. 2006. San Diego, CA.

[18] FDA 510K Clearance K060111. April 24, 2006.

[19] FDA 510K Clearance K992775. October 1, 1999.

[20] Tanko, L.B., et al., Relationship between osteoporosis and cardiovascular disease in postmenopausal women. J Bone Miner Res, 2005. **20**(11): p. 1912-20.

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W-158 US/INTL May 06