Ascending Thoracic Aneurysms Are Associated With Decreased Systemic Atherosclerosis*

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Study objectives: **We noted clinically that patients with aortic root aneurysms and dissections seemed to have little systemic atherosclerosis. It is our objective to determine whether there is a negative association between ascending thoracic aneurysms and systemic atherosclerosis.**

Design: **Atherosclerosis was quantified by evaluating noncontrast CT images of the chest and scoring the degree of calcifications as a marker for atherosclerosis in the coronary arteries and aorta.**

Patients: **The degree of calcification was compared in 64 patients with aortic root aneurysm (annuloaortic ectasia, 31 patients; type A dissection, 33 patients) vs 86 control subjects. Multivariable analysis was applied to test for an association between aortic root aneurysms and systemic calcification independent of risk factors for atherosclerosis.**

Results: **Multivariable analysis revealed that patients with ascending aortic aneurysms of the annuloaortic ectasia type and patients with type A dissections had significantly lower overall calcification scores in their arterial vessels compared to patients in the control group ($p = 0.03$ and $p < 0.0001$, respectively). These results were independent of all other risk factors for atherosclerosis. Smoking, dyslipidemia, diabetes, and age were all found to increase the degree of atherosclerosis ($p < 0.01$ to 0.05).**

Conclusions: **Aortic root pathology (annuloaortic ectasia or type A dissection) is associated with decreased systemic atherosclerosis. It is possible that a mechanism exists whereby the same genetic mutations predisposing patients to ascending aortic aneurysms also exert a protective effect against systemic atherosclerosis.** ***(CHEST 2005; 128:1580–1586)***

Key words: aneurysm; aorta; atherosclerosis; dissection

Abbreviations: LAD = left anterior descending coronary artery; LCA = left circumflex coronary artery; MMP = matrix metalloproteinase; RCA = right coronary artery

It has been a clinical observation at our institution that patients with annuloaortic ectasia who are undergoing aortic root replacement have a noteworthy absence of atherosclerosis of the aorta and coronary arteries. Often, no atheromas at all are visible in any segment of the aorta, much of which is exposed to direct inspection when the aortic arch is opened under deep hypothermic circulatory arrest. At times, not even a single fatty streak, which are nearly ubiquitous in our cardiac surgical population, can be found. The femoral artery, which is exposed for cannulation in patients undergoing ascending aortic surgery, is also commonly soft and pliable, like that in a young person.

We have previously demonstrated the heritable nature of ascending aortic aneurysms and dissection.[1] It is conceivable that the mutations inherent in the aortic diathesis also play a role in the atherosclerotic process. If patients with certain inheritable aortic pathologies exhibit decreased systemic atherosclerosis, this finding would be important by virtue of providing new insights into the pathophysiology of the most common cause of death in the Western world, heart and blood vessel disease due to atherosclerosis.[2]

Our study compares two patient populations with

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disease of the ascending aorta, patients with annuloaortic ectasia and patients with type A dissection, to a control group that is representative of the general population (without any aortic pathology). Calcification in the coronary arteries and aorta was used as a marker for atherosclerosis and was quantified by evaluating CT scans of the chest without or prior to IV contrast medium administration.[3]

Materials and Methods

Patient Population

Patients who had undergone surgical repair of the aortic root aneurysm (annuloaortic ectasia or type A dissection) and nonsurgical patients who had undergone aortic root dilatation were extracted from the Yale Center for Thoracic Aortic Disease database[4] for study from the period covering 1997 to 2004. Our study population consisted of 31 patients with an aortic root dilatation of the annuloaortic ectasia type and 33 patients with type A dissection, either acute (27 patients) or chronic (6 patients) who were between the ages of 36 and 82 years. Of the patients with annuloaortic ectasia, 25 patients had undergone repair of the aortic root utilizing a composite graft to replace the valve and aorta with reimplantation of the coronary arteries (modified Bentall operation[5]) prior to the date of their CT scans. Of the patients with type A dissection, 19 were evaluated by reading postoperative CT scans. The CT scans of all other patients were performed preoperatively.

As a control group, we retrospectively evaluated 128 trauma patients who had presented to our emergency department and had undergone a CT scan without IV contrast medium as part of a trauma workup between 1997 and 2004. We excluded 21 patients because they were deemed too young to show calcification on their CT scan (using age > 35 years as the criterion for study inclusion). Furthermore, 6 control patients were excluded because of incidental aortic pathology (aortic aneurysms and aortic stenosis), 10 control patients were excluded because they carried the diagnosis of chronic renal failure (which alters calcium metabolism), and 5 control patients were excluded because of unobtainable cardiac risk factor profiles. A total of 86 patients remained in the control group.

Patients with Marfan syndrome were excluded from this investigation. This investigation looked specifically at patients with non-Marfan annuloaortic ectasia. Our study was approved by the Human Investigation Committee at Yale University School of Medicine.

Risk Factor Analysis

All patients were evaluated for the presence or absence of the following risk factors for atherosclerosis and calcification, which were included as multiple dichotomous independent variables in our analysis:

1. Hypertension, as documented in the chart or defined by antihypertensive treatment;
2. Diabetes mellitus, as documented in the chart or defined by hypoglycemic treatment;
3. Tobacco use (past or present);
4. Illicit drug use (past or present);
5. Dyslipidemia, defined by history or by a fasting LDL level of > 160, an HDL level of < 40, a triglyceride level of > 150, or a total cholesterol value of > 200;
6. Gender; and
7. Obesity, defined as a calculated body mass index of > 30.

The two study groups were encoded as multiple dichotomous variables as well. Age at the time of the CT scan was included as an interval-independent variable.

Calcification Scoring

CT scans of the chest performed without IV contrast in all patients were read by an experienced chest radiologist in a blinded fashion and were analyzed for the degree of calcification in the coronary arteries and aorta. The three coronary arteries, the right coronary artery (RCA), left anterior descending (LAD) artery, and the left circumflex coronary artery (LCA), were analyzed separately. Similarly, the aorta was divided into four segments, and each segment was evaluated separately, as follows:

1. Ascending aorta, defined by the aortic annulus proximally and the brachiocephalic artery distally;
2. Aortic arch, defined as the segment between the brachiocephalic artery proximally and the left subclavian artery distally;
3. Descending thoracic aorta, defined by the left subclavian artery proximally and the diaphragm distally; and
4. Abdominal aorta, defined by the diaphragm proximally and the renal arteries distally.

A calcification score was allocated to each coronary artery and aortic segment, with 0 points to denote the absence of calcium, 1 point to denote a small number (three or fewer) of minimal flecks (flecks were < 1 mm in greatest dimension), 2 points for more than three minimal flecks or larger noncircumferential calcification ranging from 1 to 3 mm in its greatest extent, and 3 points for any calcification > 3 mm in greatest extent or circumferential calcification.

The total score for a given patient could therefore range from 0 points for no calcifications to 21 points for a 3-point calcium score in each of the seven segments of vasculature that were analyzed. Patients who had received a prosthetic graft in place of their ascending aorta (as was the case in all patients operated on) or whose CT scan did not include the abdominal aorta were not scored for those specific parts. Since almost all patients in the annuloaortic ectasia study group had undergone a Bentall operation, we decided to disregard all calcification scores of the ascending aorta for all patients in our statistical analysis.

Statistical Analysis

We used χ^2 statistics for categoric variables and t tests for continuous variables. Multivariate linear regression analysis was performed for the overall degree of calcification, and logistic regression analysis was applied for the individual arterial segments evaluated. We used a statistical software package (SAS, version 8.2; SAS Institute; Cary, NC). The p values were two-tailed, and a p value of < 0.05 was considered to be significant.

Because the majority of the individual artery segments that were positive for calcification had a score of 3, we decided to convert each outcome score to a dichotomous variable for the calcification that was present (calcification scores 1, 2, and 3) or absent (calcification score 0). χ^2 analysis was performed to test for significant differences in the patients' baseline characteristics using the Mantel-Haenszel χ^2 test. For observations with calcification scores ≤ 3, we used the Fisher exact test. There were no statistically significant differences between the groups for the independent variables obesity and illicit drug use. Moreover, preliminary statistical analyses did not suggest that either factor