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Calcification of Thoracic and Abdominal Aneurysms is Associated with Mortality and Morbidity

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WHAT THIS PAPER ADDS

This is the first study to investigate the role of calcium scoring in aneurysmal aortic disease. A well validated assessment of arterial calcium scoring is described and demonstrates excellent reproducibility of score assessments within the arterial segments described. These data show high scores are associated with poor outcomes and lend weight to the possibility of calcium scoring in clinical practice as a predictive tool of poor cardiovascular outcomes in patients with aneurysmal disease.

Introduction: Cardiovascular events are common in people with aortic aneurysms. Arterial calcification is a recognised predictor of cardiovascular outcomes in coronary artery disease. Whether calcification within abdominal and thoracic aneurysm walls is correlated with poor cardiovascular outcomes is not known.
Patients and methods: Calcium scores were derived from computed tomography (CT) scans of consecutive patients with either infrarenal (AAA) or descending thoracic aneurysms (TAA) using the modified Agatston score. The primary outcome was subsequent all cause mortality during follow-up. Secondary outcomes were cardiovascular mortality and morbidity.
Results: A total of 319 patients (123 TAA and 196 AAA; median age 77 [71—84] years, 72% male) were included with a median follow-up of 30 months. The primary outcome occurred in 120 (37.6%) patients. In the abdominal aortic aneurysm group, the calcium score was significantly related to both all cause mortality and cardiac mortality (odds ratios (OR) of 2.246 (95% CI 1.591—9.476; $p < 0.001$) and 1.321 (1.076—2.762; $p = 0.003$)) respectively. In the thoracic aneurysm group, calcium score was significantly related to all cause mortality (OR 6.444; 95% CI 2.574—6.137; $p < 0.001$), cardiac mortality (OR 3.456; 95% CI 1.765—4.654; $p = 0.042$) and cardiac morbidity (OR 2.128; 95% CI 1.973—4.342; $p = 0.002$).
Conclusions: Aortic aneurysm calcification, in either the thoracic or the abdominal territory, is significantly associated with both higher overall and cardiovascular mortality. Calcium scoring, rapidly derived from routine CT scans, may help identify high risk patients for treatment to reduce risk.

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INTRODUCTION

Arterial calcification is now recognised as a significant marker of poor cardiovascular outcome. This is most evident within the coronary circulation. Coronary artery calcification can be quantified using the Agatston score; an independent predictor of future coronary events.[1] Furthermore, the process atherosclerosis is a systemic inflammatory condition not only exclusive to the coronary or aortic circulation.

Arterial calcification is a systemic pathological process and as such can affect other arterial beds. Traditionally, calcification of both the abdominal and thoracic aorta has not been studied in the same detail as the coronary arterial circulation. Non-aneurysmal abdominal aortic calcification is strongly associated with both mortality and cardiovascular events rates with similar associations seen when considering the calcific burden of the thoracic aorta.[2,3]

Both the abdominal and descending thoracic aorta are prone to aneurysmal degeneration. Abdominal aortic aneurysms are the most common form of aortic aneurysm, affecting 5% of the males aged 65—74.[4] Thoracic aortic aneurysms have a more heterogeneous aetiology including atherosclerosis alongside less common genetic influences.

The emergence of endovascular intervention has revolutionised the management of aneurysmal disease,

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reducing the short-term risks associated with intervention.[5] Such conditions however are still associated with significant long-term risk, specifically the risk of major cardiovascular events.[6] As such, there is a continuing need for robust methods to predict such longer-term outcomes.

The evidence base for the predictive value of arterial calcification in aortic disease is limited, with only a small number of studies and no assessment in aneurysmal disease.[2,7] As such, and given the increasing use of CT based imaging modalities in the assessment of aneurysmal aortic disease, more in depth analysis of potential associations is both timely and warranted.

The primary aim of this study was to determine whether aortic aneurysmal calcification (the AAC score) could predict (a) all cause mortality and (b) cardiovascular related outcomes in a large, consecutive, well characterised cohort of patients with either thoracic and abdominal aortic aneurysms.

METHODS

Patient identification

This was a retrospective, observational, single centre study consisting of consecutive asymptomatic patients undergoing CT angiography of either a thoracic aortic aneurysm (January 2008 to January 2012) or abdominal aortic aneurysm (January 2010 to January 2013), presenting to Addenbrooke's Hospital, Cambridge, UK. This study was registered with the local audit department to ensure all data collection was in line with local ethical standards. Radiology digital records were searched and all patients with a CT angiogram of the aorta identified. All CT scans were screened and an aneurysm diagnosis made when the largest single segment of the appropriate part of the aorta (infrarenal abdominal or thoracic) had an antero-posterior diameter of 3 cm or greater. Electronic patient records were reviewed to collect follow-up data, up to the final date of May 2015. Mortality and morbidity data were obtained from hospital medical records (cross-referenced with ONS data), hospital death certificates, and where further clarification was required general practitioners were contacted to access community medical notes, and community death certificates to ascertain the cause of death. Patients with a proven ruptured aneurysm or those imaged because of symptomatic aneurysms as well as patients with ascending or arch aneurysms were excluded (given the management of these patients in separate specialist cardiothoracic centre). Patients with aneurysms due to other causes (i.e., vasculitis) were also excluded. Patients with synchronous thoracic and abdominal aortic aneurysms were excluded to allow comparative analysis of calcification in these patients and to avoid confounding factors.

Patient demographics, medical history, and medication at the time of CT imaging were determined from the hospital electronic record system. Ischaemic heart disease (IHD) was defined as a clinical diagnosis of angina, a prescription of anti-anginal drugs, or a history of myocardial infarction or a coronary revascularisation procedure.

The primary endpoint was all cause mortality within the follow-up period with secondary endpoints of cardiac mortality and cardiac morbidity. Cardiac mortality was defined as death with documented evidence of acute myocardial infarction (MI). Cardiac morbidity was defined as a hospital admission with either (1) typical cardiac chest pain with ischaemic electrocardiogram (ECG) changes, or (2) typical chest pain with elevated cardiac enzymes, or (3) a discharge coding of a coronary event. Events were classified by the attending medical teams (in hospital event) or pathologists at post mortem (community event). Where hospital data were missing, data were sourced either from the primary care team or from the death certificate.

Measurement of arterial calcification using the AAC score

Patients underwent CT imaging on a 64 slice CT scanner (Somatom Definition AS, Siemens, Crawley, UK), using standard clinical protocols. Briefly, scans were performed using helical acquisition with kV = 120, mA = 200, and a field of view of 350–380 mm yielding typical spatial resolution $0.7 \times 0.7 \times 3.0$ mm^3. Images were read and reported by consultant interventional vascular radiologists and maximum diameter was calculated using both AP diameters as well as double oblique reformats to the centreline. Diagnosis was based on enhanced CT imaging. ECG gating was not used in the thorax scans. From acquired raw data, the scan was reconstructed in 3 mm slices. Image analysis was performed on an Apple Macintosh computer (Apple Inc, Cupertino, CA, USA) using the open source DICOM viewer (v4, OsiriX Imaging Software, Pixmeo SARL).

Calcification data were derived from unenhanced CT images. Patients without unenhanced CT images were excluded. Using the freely available "Calcium Scoring" plug-in, vascular calcification (based on an attenuation threshold of 130 Hounsfield Units in 3 contiguous voxels, after the method of Agatston[8]) was analysed on consecutive trans-axial slices along the length of the arterial segment, as previously described[9] (Fig. 1).

For the purposes of the thoracic aorta, the strict anatomical boundaries were from just distal to the left subclavian artery (proximal) to the proximal aspect of the coeliac axis (distal). For the abdominal aorta boundaries, analysis from the lowermost renal artery (proximal) down to the common iliac artery bifurcation on both limbs (distal) was performed. The AAC score was a cumulative score of each segment for both the thoracic aorta and the infrarenal abdominal aorta (including both aneurysmal and non-aneurysmal segments). No assessment of coronary calcium was made (inadequate and un-gated scans).

AAC scoring reproducibility

Inter-observer reproducibility of the AAC scores was determined in 10 patients by two experienced readers (M.M.C. and L.P.Z./J.J.S., for both thoracic (J.J.S.) and abdominal (L.P.Z.) scans, respectively). Intra-observer reproducibility was determined for the AAC scores by an expert reader blinded to patient demographics (M.M.C.) for both thoracic and abdominal aneurysms. Fifteen unenhanced CT scans were scored on two occasions 7 days apart.