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Section II: Emerging Uses of Bone Densitometry

The Prevalence of Aortic Calcification on Vertebral Fracture Assessment Imaging Among Patients With Rheumatoid Arthritis

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Abstract

Patients with rheumatoid arthritis (RA) are at increased risk of osteoporosis (OP) and cardiovascular disease (CVD). Dual-energy X-ray absorptiometry scans have been validated for identifying patients with RA at risk for fracture. Reliable CVD risk stratification remains an unmet need in this population. Vertebral fracture assessment (VFA)−detected abdominal aortic calcification (AAC) has been validated as a marker of CVD in other populations, but the prevalence among patients with RA is unknown. In this study, we determined the prevalence and severity of AAC on VFA scans in a cohort of patients with RA. AAC was detected in 211 of the 603 (35%) eligible subjects; 24% were graded as severe. In multivariable analyses, the presence of AAC was significantly associated with longer disease duration and higher disease activity ($p < 0.05$). Further studies are needed on the relationship between AAC and CVD in patients with RA.

Key Words: Abdominal aortic calcification; cardiovascular disease; DXA; rheumatoid arthritis; VFA.

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting 1−2% of the population in the industrialized world *(1)*. Patients with RA are at significant risk of disability, osteoporosis (OP), and cardiovascular disease (CVD), and have increased cardiovascular mortality *(2−8)*. Although the mechanisms remain unclear, it is well established that the excess cardiovascular morbidity and mortality is predominantly attributable to an increased risk of atherosclerotic disease and myocardial infarction *(9−11)*. This CVD risk has not been fully explained by conventional cardiovascular risk factors *(2−4)*, appears to accumulate over time, and persists after adjustment for other cardiovascular risk factors *(4,9)*. This suggests that the presence of RA independently accentuates the risk of myocardial infarction and sudden cardiac death *(4,7,8)*. Identifying those at risk could help clinicians to decide when and whether to institute appropriate preventive measures, thereby reducing patient morbidity and mortality.

The Framingham risk index (FRI) is the generally accepted gold standard for predicting cardiovascular risk in the general population *(12)*. Although some studies have not shown differences in traditional cardiovascular risk factors between patients with RA and controls *(2,4)*, others show that the FRI as a prediction tool performs poorly in RA populations *(4,5,8)*. This may be owing to the importance of age and cholesterol in this tool because studies show that patients with RA experience CVD at a younger age *(4,5)*, and as serum cholesterol levels fall during inflammation, they may be lower in patients with active RA, who conversely may be at higher risk of CVD *(4,8)*. The addition of specific markers of CVD such as coronary calcification and carotid artery thickening to the FRI tool enhance the ability to identify RA populations at risk for CVD *(13)*.

Recent studies demonstrate that patients with RA have an increased prevalence and severity of coronary artery

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calcification compared with age-matched controls (14,15). Arterial calcification has long been recognized as a marker of prevalent CVD and is associated with the degree of atherosclerotic plaque, incident cardiovascular events, and cardiovascular mortality (16,17). An increased prevalence of abdominal aortic calcification (AAC) and carotid atherosclerosis has been noted in RA populations with coronary artery disease and ischemic stroke (18–21). AAC can be detected and quantified by several noninvasive methods including computed tomography (CT), ultrasonography, conventional radiography, and vertebral fracture assessment (VFA) technology (18,22–26).

Measurement of bone mineral density (BMD) and VFA by central dual-energy X-ray absorptiometry (DXA) is indicated in many patients with RA because their disease or treatment can result in rapid bone loss and increased propensity to fracture (27–30). Advances in DXA enable detection of prevalent vertebral fractures with VFA technology (31), which can also be used to measure AAC (22–26). The detection of AAC using such methods has been validated as a marker of CVD in non-RA populations (32), but there are no published studies in RA populations. Patients with RA regularly undergo VFA at the time of DXA scanning, which represents a potential opportunity to assess their cardiovascular risk and their fracture status without any additional testing.

Therefore, we undertook a cross-sectional study with an aim to determine the prevalence and severity of calcification in the abdominal aorta by VFA technology in a cohort of RA patients. We also evaluated factors independently associated with AAC in this population.

Materials and Methods

Study Population

We conducted a cross-sectional study of a convenience cohort of subjects with RA at our University Hospital between October 2011 and May 2012. Eligible subjects included all patients aged 40 yr or older who met the American College of Rheumatology (ACR) classification criteria for RA (33), and had a DXA and VFA scan available for analysis. Patients' medical records were reviewed to access their medical histories, medications, and to confirm the diagnosis of RA. Demographics were obtained from their medical records and cross-checked with their DXA scan record. The study was approved by local institutional ethical review board. We excluded subjects with incomplete or missing medical records, and those with missing DXA and/or VFA images.

Study Protocol

Detailed data were collected from all subjects including baseline demographics such as age, gender, ethnicity, smoking status, and body mass index (BMI); RA clinical characteristics such as disease duration, extra-articular features, rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (aCCP) status, C-reactive protein (CRP), and the Westergren erythrocyte sedimentation rate; baseline cardiovascular risk factors including tobacco smoking, diabetes mellitus, hypercholesterolemia, hypertension, and family history of CVD; and medication use. We defined glucocorticoid use as "user" for RA subjects who were using 5 mg/d or more of glucocorticoids for more than 3 mo, and nonuser for those who appeared to have never used glucocorticoids or only 1 or 2 brief courses for the purpose of the study. Disease activity was measured using the most recent Disease Activity Score (DAS) (34), and ability to perform activities of daily living was measured using the modified Health Assessment Questionnaire (35). All the data were obtained by double-data entry by 1 reviewer (AM) excluding patient identifiers.

Scoring of Aortic Calcification

All DXA scans were performed using 1 of 2 DXA scanners, GE Lunar Prodigy Advance, Whole Body (software, version 13.50; Milwaukee, WI) and GE Lunar Prodigy Advance, Compact Body (software, version 13.60) by 1 of the 3 *International Society for Clinical Densitometry (*ISCD)-certified DXA radiographers. Scans are reported by ISCD-certified consultant physicians in radiology and rheumatology. The VFA images were assessed by 2 musculoskeletal radiologists (DL and DB) who were blinded to the patients' clinical details and scored for AAC using a previously validated 24-point scale (22). Briefly, the anterior and posterior aortic walls were divided into 4 segments, corresponding to the areas in front of the lumbar vertebrae L1–L4. Within each of these 8 segments, aortic calcification was recognized visually as either a diffuse white stippling of the aorta extending out to the anterior and/or posterior aortic walls, or as white linear calcification of the anterior and/or posterior walls. AAC was scored as 0 if there was no calcification, as 1 if one-third or less of the aortic wall in that segment was calcified, as 2 if more than one-third but two-thirds or less of the aortic wall was calcified, or as 3 if more than two-thirds of the aortic wall was calcified. The scores were obtained separately for the anterior and posterior aortic wall, resulting in a range from 0 to 6 for each vertebral level and 0 to 24 for the total score. Severity was assessed based on the 3 categories of the calcification score, namely 1–4 as mild, 5–12 moderate, and more than 12 as severe AAC (25,32).

Statistical Analysis

Baseline characteristics among patients with RA are expressed in mean and standard deviation or median values (interquartile range) for continuous variables and proportions for categorical variables. We examined AAC as a categorical variable (0, 1–4, 5–8, 9–12, and 13+) as well as a continuous, natural-log-transformed variable because of the skewed distribution. Patients with score 0, indicating the complete absence of AAC, were used as the reference group. Comparison between groups was performed by the independent samples *t*-test, Pearson χ^2, and Fisher exact test when appropriate. Correlation of AAC score to different variables was performed using Spearman's rank correlation test. The interobserver agreement for the presence of AAC was measured using