Journal of Indian College of Cardiology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Journal of Indian College of Cardiology

journal homepage: www.elsevier.com/locate/jicc

Original article

The role of multidetector computed tomography coronary angiography with calcium score and Framingham Risk Score in evaluation of rheumatoid arthritis patients with chest pain

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ARTICLE INFO

Article history:
Received 2 March 2017
Accepted 24 March 2017
Available online xxx

Keywords:
Rheumatoid arthritis
Coronary artery calcium scoring
Acute chest pain

ABSTRACT

Objectives: To evaluate diagnostic yield of coronary artery calcium (CAC) scoring using multidetector CT imaging in rheumatoid arthritis (RA) patients presented with chest pain.
Patients and methods: Seventy RA patients evaluated using the 28 joint disease activity (DAS-28) score, Disability Index (DI) and radiologically for Larsen–Dale index. Patients underwent assessment for coronary artery disease (CAD) risk factors and coronary risk stratification using the Framingham Risk Score (FRS). Patients were clinically categorized according to criteria for typical anginal pain (TAP) and were scanned using a 64-row spiral CT scanner for CAC scoring and were stratified according Agatston CAC scores for calculation of total Agatston score (TAS).
Results: Clinically, 32 patients had full criteria of TAP, 27 patients showed a picture of atypical anginal pain, while 11 patients had non-anginal chest pain. FRS predicted low, intermediate and high risk of CAD in 34, 18 and 18 patients, respectively. TAS defined no CAC in 4 patients, while mild, moderate and severe CAC was detected in 24, 36 and 6 patients, respectively. Regression analysis defined low HDL blood level, current smoking and high TAS, DAS-28 and FRS as significant predictor for TAP in decreasing order of significance. Receiver operating characteristic (ROC) curve analysis defined low HDL blood level and high TAS as the significant sensitive and specific tests, respectively. There was positive significant correlation between FRS and both of TAS scores and extent of coronary stenosis. However, FRS was the least significant predictor for TAP.
Conclusion: Screening of RA patients with combination of clinical scoring using FRS and CAC using non-invasive multidetector CT could allow early detection of patients at risk for acute cardiovascular events. However, TAS acts better for the prediction of TAP.

1. Introduction

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease in which the peripheral joints are the primary sites of inflammation, often leading to destruction of these joints. RA is characterized by symmetrical synovitis, progressive joint damage, pain, fatigue, and disability.[1]

The spectrum of RA ranges from benign remitting manifestations to rapidly progressive forms with increased mortality. About 10% of patients show an intractable rapidly progressive course associated with severe extra-articular manifestations. Within the first three years, 70% of the patients develop radiological erosions of the joints and 31% of patients had hand deformities.[2]

Cardiovascular disease (CVD) is also prevalent in patients with RA, with onset in early disease and subclinical involvement is higher than anticipated. Several disease-specific risk factors, like seropositivity, disease activity, and medications, are implicated in the pathogenesis of CVD in RA. Cardiovascular risk assessment in RA varies from the general population.[3]

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http://dx.doi.org/10.1016/j.jicc.2017.03.004
1561-8811/

RA can manifest in a variety of cardiac complications, including pericarditis, valvular disease, cardiomyopathy, and amyloidosis. There is an increased incidence of coronary artery disease (CAD) in RA. Patients with prevalent RA suffer more severe CAD compared to the general population and also have poorer outcomes[4] with an increased risk of cardiovascular (CV) mortality attributed to a higher incidence of heart failure and ischemic heart disease.[5]

The elevated risk of ischemic heart disease in patients with RA has been linked to immune-mediated mechanisms, chronic inflammation and disease severity as evidenced by the lower risk of CAD in RA patients treated with tumor necrosis factor inhibitors compared with biologic-naïve RA patients.[6]

Several imaging techniques may reveal vascular calcium deposits. Although calcifications may occur in small amounts in the earlier stages of atherosclerosis, they are usually seen in more advanced lesions. Vascular calcification is commonly used as a subclinical marker of atherosclerosis and has been linked to increased all-cause mortality, cardiovascular mortality and coronary events.[7]

Patients with RA are known to develop early-onset, diffuse calcification in various vascular beds compared to age and sex-matched controls, so they are at increased risk for morbidity and mortality from CVD.[8] This is consistent with the concept whereby inflammation promotes atherosclerosis and vascular calcification. However, specific mediators such as proinflammatory cytokines and not global inflammation could be involved.[9]

Recent meta-analyses of the relationship between calcification and cardiovascular risk have focused exclusively on coronary artery calcium (CAC) scores.[10] Thus, the current study aimed to evaluate the diagnostic yield of CAC scoring and CT coronary angiography using multidetector CT imaging in RA patients presented with chest pain.

2. Patients and methods

The present prospective study was conducted at Departments of Rheumatology and Rehabilitation, Cardiology and Internal Medicine, Dallah Hospital, Riyadh KSA from June 2014 to February 2016. The study protocol was approved by the Local Ethical Committee and patients' fully informed written consents were obtained prior to study participation.

2.1. Patient selection

All enrolled patients had RA and required evaluation because of symptoms of chest pain and carrying one or more cardiovascular risk factor. All patients were fulfilled the 2010 American college of Rheumatology criteria for diagnosis of RA.[11]

Patients' demographic data including gender, weight, height for calculation of body mass index (BMI) according to the equation: BMI = weight (kg)/height (m^2)[12] were determined. Patients with history of acute myocardial infarction (AMI), heart failure, coronary artery revascularization, stroke, peripheral vascular disease, abdominal aortic aneurysm, current atrial fibrillation, cardiomyopathy, valvular heart disease, congenital heart disease, weight exceeding 150 kg, inflammatory diseases other than RA were excluded from the study.

2.2. Assessment of RA disease activity and severity

RA disease activity was assessed using the 28 joint disease activity score (DAS-28) and was categorized as follows: DAS-28 $\leq$ 3.2 means inactive, >3.2–$\leq$5.1 means moderate activity and >5.1 means very active disease.[13] Pain was assessed by a 0–100 mm horizontal visual analog scale (VAS) with VAS score of 0–25 indicates mild pain, >25–50 indicates moderate pain, >50–75 indicates severe pain and >75 indicates intolerable pain.[14]

Functional disability was evaluated using the Swedish version of the Stanford health assessment questionnaire to calculate the Disability Index (DI). The eight categories assessed by DI are (1) dressing and grooming, (2) arising, (3) eating, (4) walking, (5) hygiene, (6) reach, (7) grip, and (8) common daily activities. The difficulty during each of these acts was assessed as follows: 0: without any difficulty, 1: with some difficulty, 2: with much difficulty and 3: unable to do, then the sum of the categories scores is calculated and divided by the number of categories. This gives a score in the 0–24 range.[15]

Laboratory assessment of RA disease activity included measurement of erythrocyte sedimentation rate (ESR; mm/h), C-reactive protein (mg/l) and ELISA quantitation of Rheumatoid factor IgM isotype using standard laboratory methods were performed at hospital laboratory.

Radiological assessment included postero-anterior radiographs of hands, wrists, and forefeet and joint destruction was classified by comparison with standard reference films according to the Larsen–Dale index.[16] For the scored 32 joints; each joint is graded where grade 0 indicates no abnormality; grade I indicates slight abnormality with one or more of the following criteria: soft tissue swelling, juxta-articular osteoporosis, slight narrowing of the joint space; grades II–V indicate erosion and narrowing of the joint space of increasing severity. The degree of erosive damage is the most decisive criterion in grading and patient was considered having erosive disease if at least one definite erosion, on any of the hands or feet radiographs, was detected.

2.3. CAD risk factors assessment

Patients were assessed for conventional coronary risk factors including obesity, cigarette smoking, hypertension, hypercholesterolemia, diabetes mellitus, and family history of CAD. Obesity was defined as BMI $\geq$ 30 kg/m^2. Smoking was defined as any cigarette smoking within the last year. Hypertension was defined as a previously established diagnosis with systolic blood pressure $\geq$ 140 mmHg, diastolic blood pressure $\geq$ 90 mmHg, or maintenance antihypertensive medication use. Hypercholesterolemia was defined according to the National Cholesterol Education Panel guidelines[17] or by the current use of lipid-lowering medication. Diabetes mellitus was defined as a previously established diagnosis, insulin or oral hypoglycemic therapy, fasting glucose of $\geq$126 mg/dl, or non-fasting glucose of $\geq$200 mg/dl. Family history of CAD was defined as MI, coronary revascularization, or sudden cardiac death for father <55 years-of-age or mother <65 years-of-age. Typical angina was defined as a combination of: (1) discomfort in the anterior chest, neck, shoulders, jaw, or arms; (2) precipitated by physical exertion or emotional stress; and (3) relieved by rest or nitroglycerin within minutes. Atypical angina was defined as chest pain with 2 of these 3 factors, and non-anginal chest pain was defined as chest pain with <2 of these 3 factors.[18]

2.4. Cardiac risk stratification

Coronary risk stratification was conducted using the Framingham Risk Score (FRS) calculated using age, sex, smoking status, serum total cholesterol and HDL cholesterol concentrations, blood pressure, and on antihypertensive therapy or not. FRS was used to assess the 10-year risk of developing heart disease or having a heart attack with low risk was defined as FRS < 10%, Moderate risk as FRS as 10–20% and sever risk as FRS > 20%.[19]

Please cite this article in press as: Gomaa AM, et al. The role of multidetector computed tomography coronary angiography with calcium score and Framingham Risk Score in evaluation of rheumatoid arthritis patients with chest pain, *J Indian Coll Cardiol.* (2017), http://dx.doi.org/10.1016/j.jicc.2017.03.004