Usefulness of Calcium Scoring as a Screening Examination in Patients With a History of Kawasaki Disease

Andrew M. Kahn, MD, PhD[a,*], Matthew J. Budoff, MD[b], Lori B. Daniels, MD, MAS[a], Jun Oyamada, MD[c], John B. Gordon, MD[d], and Jane C. Burns, MD[c]

Subsets of patients with a remote history of Kawasaki disease (KD) have coronary artery aneurysms with associated risks of late morbidity. In a pilot study, we previously showed that computed tomography (CT) coronary artery calcium (CAC) scoring detects late CAC in patients with aneurysms and a remote history of KD. We performed CT calcium volume scoring in 166 subjects (median age 19.5 years) with a remote history of KD (median interval from KD to CT 15.1 years). Coronary arteries were classified as normal (n = 100), transiently dilated (n = 23), persistently dilated (n = 10), remodeled aneurysm (n = 9), or aneurysm (n = 24) based on echocardiography. All subjects with coronary arteries classified as normal, persistently dilated, or remodeled aneurysm had zero CAC. Of the 24 subjects with coronary aneurysms, all but 5 had CAC (median volume 542 mm^3; range 17 to 8,218 mm^3). For subjects imaged ≥9 years after their acute KD (n = 144), the presence of CAC had a sensitivity of 95% and a specificity of 100% for detecting coronary artery abnormalities (defined as coronary artery aneurysm and/or stenosis). In conclusion, coronary calcification was not observed in subjects with a history of KD who had normal coronary arteries by echocardiography during the acute phase. Coronary calcification, which may be severe, occurs late in patients with coronary aneurysms. Therefore, CAC scanning may be a useful tool to screen patients with a remote history of KD or suspected KD and unknown coronary artery status. **© 2017 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2017;■:■−■)**

Computed tomography (CT) coronary artery calcium (CAC) scoring requires no contrast and relatively little radiation. This test is widely used to detect plaque due to atherosclerotic coronary artery disease.[1] In a pilot study, we previously showed that CAC scoring also detects calcium in patients with coronary artery aneurysms (CAA) and a remote history of Kawasaki disease (KD).[2] Here, we present the results of a larger follow-up study evaluating the utility of CAC scoring by CT to detect coronary artery abnormalities in patients with a history of KD.

Methods

We recruited subjects of age ≥10 years from 2 cohorts. Cohort 1 (n = 90) consisted of patients with a history of KD diagnosed, treated, and followed by the KD Research Center at UCSD Medical Center and Rady Children's Hospital San Diego. Cohort 2 (n = 76) were self-referred, had a remote history of KD, and were originally diagnosed at another center. In 3 subjects in cohort 2, the diagnosis of KD was based on a history of a KD-compatible illness and the presence of proximal CAAs diagnosed by CT or coronary angiography independently reviewed by 2 cardiologists. This study was approved by the Institutional Review Board of the University of California, and all subjects provided informed consent or assent with parental consent as appropriate.

Coronary artery status was determined based on initial echocardiograms performed during the acute and subacute phases of KD. Subjects with a coronary artery z score (standard deviation from the mean for the internal diameter of the coronary artery normalized for body surface area) for the right coronary artery (RCA) or left anterior descending coronary artery (LAD) <2.0 on serial echocardiograms during the acute and subacute illness were designated as normal. Subjects with a CA z score of >2.0 and <3.0 that returned to normal within 6 weeks of fever onset were designated as transiently dilated. Subjects with a z score ≥3.0 but <10.0 were designated as aneurysm, and subjects with z ≥10.0 or CA internal diameter ≥8 mm were designated as giant aneurysm. For subjects with dilated or aneurysmal coronary artery abnormalities or unknown initial coronary artery status, the most recent CTA or invasive coronary angiogram was used when available. Subjects were classified into 5 categories by coronary status: (1) no history of coronary artery dilation (American Heart Association [AHA] risk level I), (2) transient (<6 weeks)

[a]Department of Medicine, University of California San Diego School of Medicine, La Jolla, California; [b]Department of Medicine, Harbor-UCLA Medical Center, Torrance, California; [c]Department of Pediatrics, University of California San Diego School of Medicine, La Jolla, California and Rady Children's Hospital San Diego, San Diego, California; and [d]San Diego Cardiac Center and Sharp Memorial Hospital, San Diego, California. Manuscript received August 17, 2016; revised manuscript received and accepted November 29, 2016.

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See page 5 for disclosure information.

*Corresponding author: Tel: (858) 657-5372; fax: (858) 657-5028.
E-mail address: akahn@ucsd.edu (A.M. Kahn).

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Table 1
Patient characteristics

Variable	Cohort		
	1 (N=90)	2 (N=76)	Total (N=166)
Males (%)	60 (67)	44 (58)	104 (63)
Age at onset of KD (years):	2.4 (1.4-5.2)	4.0 (2.1-7.1)	3.5 (1.5-5.9)
Age at time of calcium score, (years):	16.7 (13.6-19.6)	24.9 (20.1-31.1)	19.7 (15.8-25.4)
Interval from onset of KD to calcium score (years):	13.2 (10.6-15.8)	20.0 (13.6-27.1)	15.1 (11.1-20.6)
Body mass index (kg/m^2):	22 (19-24)	23 (20-27)	22 (20-25)
Coronary artery status			
Normal:	51 (57%)	49 (64%)	100 (60%)
Transiently dilated:	22 (24%)	1 (1%)	23 (14%)
Persistently dilated:	6 (7%)	4 (5%)	10 (6%)
Remodeled aneurysm:	9 (10%)	0 (0%)	9 (5%)
Aneurysm:	2 (2%)	22 (29%)	24 (14%)
Atherosclerosis risk factors			
Hypertension:	1 (1%)	13 (17%)	14 (8%)
Diabetes mellitus:	1 (1%)	3 (4%)	4 (2%)
Tobacco use, ever:	8 (9%)	14 (18%)	22 (13%)
Hyperlipidemia:	5 (5%)	18 (24%)	23 (14%)
Family history of early CAD (< 55 years):	18 (19%)	17 (22%)	35 (21%)
Medications			
Statin:	1 (1%)	9 (12%)	10 (6%)
ACE-I or ARB:	2 (2%)	5 (7%)	7 (4%)
Beta blocker:	0	10 (13%)	10 (6%)
Calcium channel blocker:	0	3 (4%)	3 (2%)
Warfarin or NOAC:	1 (1%)	11 (14%)	12 (7%)
Aspirin:	3 (3%)	26 (34%)	29 (17%)
Clopidogrel:	0	5 (7%)	5 (3%)
MACE	1 (1%)	12 (16%)	13 (8%)
Myocardial infarction	1 (1%)	6 (8%)	7 (4%)
Coronary artery bypass graft surgery	0	5 (7%)	5 (3%)

Cohort 1: Patients originally diagnosed, treated, and followed by the Kawasaki Disease Research Center at the University of California, San Diego Medical Center and Rady Children's Hospital.

Cohort 2: All other patients.

Remodeled aneurysm: Artery that is acutely aneurysmal but undergoes myointimal proliferation with filling in of the aneurysm such that the lumen is no longer dilated on follow-up imaging.

Hyperlipidemia: Subject report of having this diagnosis.

Values for continuous variables are listed as median (IQR).

Values for discrete variables are listed as n (%).

ACE-I = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blocker; NOAC = novel oral anticoagulant (rivaroxaban, apixaban, edoxaban, dabigatran).

coronary artery dilation (AHA II), (3) persistent (≥6 weeks) coronary artery dilation, (4) remodeled aneurysm (AHA III/IV), and (5) aneurysm (AHA III/IV). Subjects completed a standardized questionnaire documenting medications, cardiac history, and risk factors for atherosclerotic coronary artery disease (physician-diagnosed hypertension, diabetes mellitus, hyperlipidemia, family history of early atherosclerotic coronary artery disease defined as disease diagnosed at age <55 years in a first-degree relative, and current smoking). Coronary artery abnormality was defined as the presence of CAA and/or stenosis on the most recent available imaging. Major adverse cardiac events (MACE) were defined as myocardial infarction, coronary artery bypass graft surgery, or percutaneous coronary intervention.

The CT scanning protocol has been previously described.[2] In brief, subjects were scanned during a single breath-hold on a 64-slice Discovery CT750 HD scanner (GE Healthcare, Milwaukee, Wisconsin) in gated axial mode with 2.5-mm slice thickness. For 3 of the subjects, the tube energy was set to 120 kVp, and for the remainder, the tube energy was set to 100 kVp (instead of the tube energy of 120 kVp traditionally used for calcium scoring) to minimize the radiation dose, and the tube current was chosen based on subjects' body mass index. The median radiation dose−length product was 43 mGy-cm, corresponding to a median effective radiation dose of 0.61 mSv. If clinically indicated, CT angiography was performed in selected patients using the scanner described previously with prospective gating.

Images for CAC scoring were reconstructed using a 512 × 512 matrix and analyzed offline using a Ziostation workstation (QI Imaging, Redwood City, California). Coronary calcium volume was measured using a minimum threshold of 130 Hounsfield units for the 3 patients imaged using 120 kVp and 147 Hounsfield units for the remainder imaged using 100 kVp, following the work of Nakazatu et al[3] to adjust for the lower tube energy and a minimum

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