

Identification of Unexpected Nonatherosclerotic Cardiovascular Disease With Coronary CT Angiography

Thomas Knickelbine, MD,* John R. Lesser, MD,* Tammy S. Haas, RN,†
Eric R. Brandenburg, BS,* B. Kelly Gleason-Han, MD,‡ Björn Flygenring, MD,*
Terrence F. Longe, MD,* Robert S. Schwartz, MD,* Barry J. Maron, MD†

Minneapolis, Minnesota

OBJECTIVES The aim of this study was to assess, in a general cardiology cohort screened for obstructive coronary artery disease (CAD), the effectiveness and frequency with which multidetector computed tomography (MDCT) angiography unexpectedly imaged and identified other nonatherosclerotic cardiovascular diseases.

BACKGROUND MDCT angiography is a novel imaging strategy employed primarily to diagnose CAD that, in the course of these studies, can also potentially identify other important but previously unrecognized cardiovascular abnormalities.

METHODS Consecutive 64-slice MDCT angiography studies were obtained in 4,543 patients with suspected atherosclerotic CAD at the Minneapolis Heart Institute, over a 29-month period (2005 to 2007).

RESULTS Nonatherosclerotic-related cardiovascular abnormalities judged to be of potential clinical relevance were identified in 201 patients (4.4%). In 50 of these patients (1.1% of 4,543) the abnormality was previously unrecognized despite other imaging studies performed in 40%. Most common among the 50 patients were: congenital coronary artery anomalies (38%; largely right coronary artery from the left aortic sinus); ascending aortic aneurysms ≥ 45 mm (22%); hypertrophic cardiomyopathy with apical left ventricular (LV) wall thickening (14%); valvular heart diseases (8%), congenital heart diseases, including ventricular septal defect (6%); pulmonary embolus (6%); as well as LV noncompaction, left atrial myxoma, and LV apical aneurysm (2% each). As a consequence of MDCT angiography findings, new management strategies were instituted in 15 of 50 patients (30%), including surgical correction of coronary artery anomalies of wrong sinus origin, ascending aneurysm graft repair, thrombolytic therapy for pulmonary embolism, and myxoma resection.

CONCLUSIONS Approximately 1% of patients undergoing MDCT angiography for suspicion of CAD proved to have otherwise unsuspected, but clinically relevant, cardiovascular abnormalities unrelated to coronary atherosclerosis. Almost one-third of these patients had cardiovascular diseases with major clinical implications for subsequent therapy. These findings underscore the value of MDCT angiography and the importance of careful assessment of scans for the recognition of a variety of cardiovascular abnormalities. (J Am Coll Cardiol Img 2009;2:1085–92) © 2009 by the American College of Cardiology Foundation

From the *Cardiovascular Services, Minneapolis Heart Institute, Minneapolis, Minnesota; †Hypertrophic Cardiomyopathy Center, Minneapolis Heart Institute Foundation, Minneapolis, Minnesota; and the ‡Children's Heart Clinic, Minneapolis, Minnesota. This work received support from The Hearst Foundations, New York, New York.

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Multidetector computed tomography (MDCT) angiography is a novel imaging strategy that is performed with increasing frequency as a means of diagnosing (or excluding) obstructive atherosclerotic coronary disease (CAD) (1–12). However, the potential role that MDCT angiography might play in general cardiology practice for the fortuitous identification of structural (nonatherosclerotic) cardiovascular disease has not been emphasized or defined. To this purpose, we have analyzed a large consecutive series of patients who underwent 64-slice MDCT angiography at our institution to determine the power of this new imaging modality in diagnosing unsuspected cardiac disease.

METHODS

Patient selection. The study group was comprised of 4,543 patients consecutively undergoing MDCT angiography scans at the Minneapolis Heart Institute and Abbott Northwestern Hospital between January 2005 and May 2007. In the vast majority of patients, MDCT angiography was performed for clinical indications either because of a history of chest pain or 12-lead electrocardiogram (ECG) or exercise testing abnormalities that suggested underlying CAD.

Ages were 60 ± 13 years; 2,435 (54%) were men. All patients provided written consent as research subjects, approved by the institutional review board. Exclusion criteria were: known allergy to contrast dye, renal failure (serum creatinine >1.8 mg/dl), pregnancy, arrhythmias, and inability to receive beta-blockade.

From January 2005 to February 2007, studies were performed with a Somatom Sensation 64 cardiac scanner (Siemens Medical Systems, Forchheim, Germany) (13,14), and from February to May 2007, studies were performed with a Dual Source Definition scanner (Siemens Medical Systems) (15–17). In preparation, all patients with an initial heart rate >60 beats/min received oral and/or intravenous metoprolol to reduce heart rate to <60 beats/min at the time of the scan.

The scanner collimators were 0.6 mm, and reconstructed slices were 0.75 mm (for Sensation 64) and 0.6 mm (for Definition) with 50% slice overlap. The temporal resolution of the scanners was 164 ms (for Sensation 64) and 83 ms (for Definition). A bolus tracking technique was used in the ascending

aorta and set to trigger at a threshold of 100 to 150 Hounsfield units, depending upon the scan length and scanner type. All scans were timed to optimize the assessment of native or bypass graft coronary anatomy. Omnipaque 350 (GE Healthcare, Milwaukee, Wisconsin) contrast was delivered at a rate of 5 ml/s with a total dose of 80 to 100 ml. A retrospective ECG-gated scan was obtained with ECG pulsing (Kvp: 100 to 120 mV; mA 650 to 900; pitch 0.2 to 0.38). The portion of the cardiac cycle set to decrease to 20% of the programmed dose was dependent upon the presence of ectopy and the patient's heart rate. This dose reduction pulsing protocol allowed review of systolic phases for cine-analysis of left ventricular (LV) wall motion.

Four experienced computed tomography readers evaluated all images with an offline workstation (Vitrea, Vital Images, Minnetonka, Minnesota) as part of the initial clinical interpretation. Systematic review of study data was performed with thin maximum intensity projection images in the axial, coronal, and sagittal planes as well as oblique orientations. A dataset was reconstructed from an R-R interval optimized to minimize coronary motion. The field-of-view was initially small to optimize spatial resolution, and then a separate reconstruction expanded the field-of-view to fully include all the scanned structures within the chest.

Findings were reviewed from the MDCT angiography database to identify patients with non-atherosclerotic cardiovascular pathology (18–23). Two of the readers (T.K., J.L.) confirmed the initial interpretation of the scans and agreed with the diagnoses. Left ventricular cavity size and wall thickness were measured from a mid-diastolic interval. The maximal aortic diameter was measured with a modified centerline technique.

Hypertrophic cardiomyopathy (HCM) was diagnosed on the basis of the hypertrophied nondilated LV with maximum wall thickness ≥ 15 mm in the absence of another cardiac systemic disease capable of producing the magnitude of hypertrophy evident (22). LV noncompaction was defined as a ratio of noncompacted to compacted myocardium ≥ 2.3 to 1 in diastole (18). Coronary artery anomalies were characterized by origin and course (19). Our analysis included only vascular abnormalities with potential clinical implications and excluded incidental pathology: parenchymal pulmonary disease, nodules, patent foramen ovale, aortic root dimensions ≤ 44 mm, or pericardial effusion.

ABBREVIATIONS AND ACRONYMS

- CAD** = coronary artery disease
- CMR** = cardiovascular magnetic resonance
- ECG** = electrocardiogram
- HCM** = hypertrophic cardiomyopathy
- LV** = left ventricle/ventricular
- MDCT** = multidetector computed tomography

Table 1. Cardiovascular Abnormalities Identified by MDCT Angiography in 4,543 Patients

Abnormality	Prior Diagnosis*	New MDCT Angiography Diagnosis	Specific Treatment
Congenital coronary artery anomalies	23 (15)	19 (38)	Coronary bypass (n = 6) Coil embolization (n = 1)
Aortic aneurysm (ascending aorta \geq 45 mm)	59 (39)	11 (22)	Prophylactic root graft (n = 2)
Hypertrophic cardiomyopathy	18 (12)	7 (14)	None
Valvular heart disease	29 (19)	4 (8)†	Pacemaker (n = 1)
Congenital heart disease	7 (5)	3 (6)‡	Prophylactic ICD (n = 1)
Other	15 (10)	6 (12)§	Thrombolysis with heparin (n = 3) Surgical resection of myxoma (n = 1)
Total	151	50	

Values are n (%). *By non-multidetector computed tomography (MDCT) angiography diagnostic modalities, including contrast angiography, echocardiography, or cardiovascular magnetic resonance. †Includes 1 patient with mitral stenosis and 3 with bicuspid aortic valve. ‡Includes 2 patients with ventricular septal defect and 1 patient with left ventricular noncompaction. §Includes 3 patients with pulmonary embolus and 1 with left atrial myxoma.
 ICD = implantable cardioverter-defibrillator.

RESULTS

Identification of nonatherosclerotic diseases. Of the 4,543 study patients, 201 (4.4%) were found to have cardiac abnormalities unrelated to coronary atherosclerosis and judged to be of potential clinical relevance. Of these 201 abnormalities, 151 (75%) had been known or suspected previously by clinical evaluation or other imaging modalities/tests (i.e., cardiovascular magnetic resonance [CMR], echocardiography, or contrast angiography) (Tables 1 and 2). The remaining 50 patients (1.1% of 4,543 patients) had morphologic findings of potential clinical significance, recognized for the first time (i.e., not suspected before MDCT angiography imaging), which represent the focus of this analysis (Tables 1 and 2, Fig. 1).

Unsuspected cardiac abnormalities. The 50 patients were 18 to 83 years of age (mean 57 ± 15 years); 31 (62%) were men. At the time of MDCT angiography, 44 of 50 patients (88%) had experienced symptoms judged to be cardiac in origin, including chest pain (n = 29), syncope (n = 5), exertional dyspnea (n = 8), fatigue (n = 1), and symptomatic atrial fibrillation (n = 1). Eight of 50 patients (16%) also had obstructive atherosclerotic narrowing of \geq 1 major epicardial coronary artery.

CORONARY ARTERY ANOMALIES. Congenital anomalies of coronary arterial origin comprised the largest subgroup identified by MDCT angiography (19 patients; 38%): most commonly right coronary artery from left aortic sinus, with interarterial course between aorta and pulmonary trunk (n = 10); also, left main coronary from right aortic sinus (n = 2, including 1 coursing between the great arteries), left circumflex from right sinus (n = 2), and left anterior descending

from right sinus (n = 2). Three other patients had a fistula connecting the arterial and venous systems (i.e., between left coronary artery and pulmonary trunk [n = 2] and left circumflex to coronary sinus [n = 1]) (Tables 1 to 3, Figs. 1 and 2).

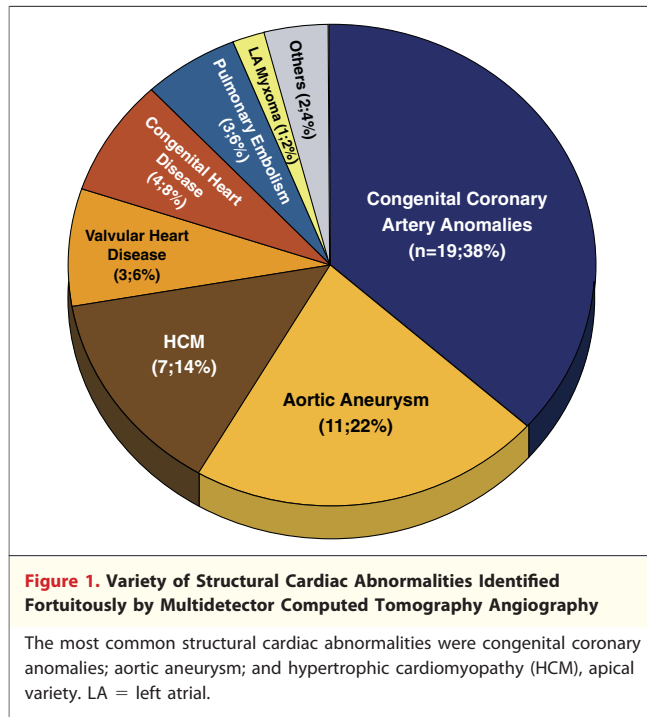
AORTIC ANEURYSM. Dilation of the ascending aorta \geq 45 mm was identified in 11 patients (22%). Maximal aortic dimension was: 45 or 46 mm (n = 8), 47 or 48 mm (n = 2); and 54 mm (n = 1). Two of these patients also had bicuspid aortic valve (Fig. 3).

HCM. Seven patients, 14% (4 women and 3 men; ages 42 to 82 years) had LV hypertrophy in the absence of cavity dilation. Maximal LV wall thickness was 15 to 32 mm (mean 21 mm). In 5 of 7 patients, hypertrophy was predominantly situated in the distal LV chamber (apical HCM), including 1 who also had

Table 2. Specific Congenital Coronary Artery Anomalies Identified by MDCT Angiography

Anomaly	With Prior Diagnosis*	With New MDCT Angiography Diagnosis
RCA from left aortic sinus of Valsalva	9	10†
LMCA from right sinus	6	2‡
Left circumflex from right sinus	2	2
LAD from RCA	3	2
Fistulas		
Left circumflex to coronary sinus	0	1
LAD and MPA connection	2	1
LMCA (and RCA) to MPA	1	1
Total patients	23	19

*By non-multidetector computed tomography (MDCT) angiography diagnostic modalities, including contrast angiography, echocardiography, or cardiovascular magnetic resonance. †Anomalous right coronary artery (RCA) with interarterial course between aorta and pulmonary trunk in each patient; also includes 4 patients with RCA orifice judged to be slit-like. ‡Includes 1 patient with interarterial course between aorta and pulmonary trunk.
 LAD = left anterior descending; LMCA = left main coronary artery; MPA = main pulmonary artery (trunk); RCA = right coronary artery.



a small apical aneurysm (Fig. 4). In each patient systolic anterior motion of the mitral valve (and outflow tract obstruction) was absent.

VALVULAR HEART DISEASE. One patient had previously unrecognized mitral stenosis with calcification of the leaflets and annular region (subsequent echocardiography showed mean gradient of 5 mm Hg). Three other patients had bicuspid aortic valves, including 1 with a mild degree of stenosis (mean gradient, 6 mm Hg) and 2 associated with a dilated aortic root (45 and 49 mm) (Fig. 3).

CONGENITAL HEART DISEASE. Three patients (6%) had newly recognized congenital heart malformations. One patient (a 52-year-old man), referred

with exertional dyspnea and nonsustained ventricular tachycardia, proved to have LV noncompaction on the basis of the characteristic trabecular patterns (noncompacted to compacted myocardium = 3.4) (19) (Fig. 4). Two other patients had small ventricular septal defects with evidence of left-to-right shunting; a membranous defect with aneurysm was present in 1 and 3 small muscular defects in the other.

OTHERS. Three other patients had pulmonary embolism (presenting with acute chest pain), 1 had left atrial myxoma, 1 had unsuspected apical aneurysm due to CAD, and another was identified with cardiomyopathy characterized by LV systolic dysfunction unrelated to CAD.

Comparison of MDCT angiography diagnosis with prior non-MDCT angiography imaging findings. Twenty of the 50 patients in whom MDCT angiography preferentially identified an unexpected (and clinically relevant) cardiovascular abnormality had echocardiographic studies performed (before MDCT angiography). In none of these 20 patients was the cardiovascular abnormality recognized by echocardiography (Table 3).

In 9 (6%) of 151 patients with cardiovascular abnormalities previously diagnosed by echocardiography, CMR, or contrast angiography, MDCT angiography subsequently enhanced the assessment of cardiac morphology in a clinically relevant fashion. Of these 9 patients, the relevant diagnostic information added by MDCT angiography was as follows: in 4 patients with congenital coronary anomalies, MDCT angiography identified interarterial course (i.e., between aorta and pulmonary trunk; $n = 2$) or intraseptal course ($n = 1$) and recognized coronary artery to pulmonary artery fistula ($n = 1$); in addition, MDCT angiography

Table 3. Comparative Echocardiographic Findings in Patients With MDCT Angiography-Identified Cardiovascular Abnormalities

Cardiovascular Abnormality	Patients With MDCT Angiography Diagnosis	Patients With Prior Echocardiogram	Reason Abnormality Not Identified by Echocardiography
Coronary artery anomalies	19	10	No or imprecise description of coronary artery origins ($n = 10$)
Aortic aneurysm	11	4	Underestimated aortic root dimension ($n = 3$) Aortic root inadequately imaged ($n = 1$)
Hypertrophic cardiomyopathy	7	2	Failure to image most distal portion of LV ($n = 2$)
Valvular heart disease	4	1	Failure to image sclerotic, bicuspid valve in the presence of aortic dilation ($n = 1$)
Pulmonary embolism	3	2	Not expected to image the abnormality ($n = 2$)
Left atrial myxoma	1	1	Mass not clearly imaged because it was located largely out of the cross-sectional planes ($n = 1$)

LV = left ventricle; MDCT = multidetector computed tomography.

confirmed prior suspicion of LV noncompaction ($n = 1$), identified patent ductus arteriosus associated with dilated aorta ($n = 1$) and pseudoaneurysms of the ascending aorta ($n = 2$), and confirmed suspicion of HCM by defining increased wall thickness predominantly in the apical LV ($n = 1$).

Clinical correlates. Of the 50 patients with newly identified cardiovascular lesions, 15 (30%) had major medical or surgical interventions emanating directly from the MDCT angiography findings (Table 1). Six symptomatic patients with anomalous coronary artery (5 with anomalous right coronary and 1 with anomalous left coronary) had corrective surgical procedures: ligation of right coronary at its origin with reimplantation ($n = 3$), internal mammary graft to right coronary artery with ligation ($n = 1$), radial artery graft to right coronary artery ($n = 1$), and supra-arterial myotomy procedure ($n = 1$). All 6 operated patients previously had chest pain, and 4 had evidence of myocardial ischemia with stress testing.

One symptomatic patient with left anterior descending coronary artery to pulmonary artery fistula underwent therapeutic coiling of the fistula with resolution of symptoms. In addition, 2 patients with ascending aortic aneurysm (1 asymptomatic and 1 symptomatic) had prophylactic aortic root grafting; the other 9 patients are undergoing surveillance with serial CMR imaging. Each of the 9 operated patients has survived over 120 ± 107 days.

The patient with LV noncompaction subsequently had exercise-induced ventricular tachycardia, was judged to be at unacceptably high sudden death risk and received a prophylactic cardioverter-defibrillator. The patient with the left atrial myxoma underwent surgical resection. Three patients received pharmacologic intervention (i.e., thrombolytic agents or heparin in 2 patients with pulmonary embolus and anticoagulation [warfarin] in another with previously unsuspected LV apical aneurysm).

The 7 patients with HCM have not experienced disease complications, but are undergoing targeted surveillance and genetic counseling. None of the patients with aortic valve abnormalities or small ventricular septal defects required surgery. One patient with mitral stenosis and dense annular calcification received a pacemaker for bradyarrhythmias.

Of the 50 patients with MDCT angiography-identified abnormalities, 44 (88%) had cardiovascular symptoms (e.g., chest pain in 29 patients). Of these 44

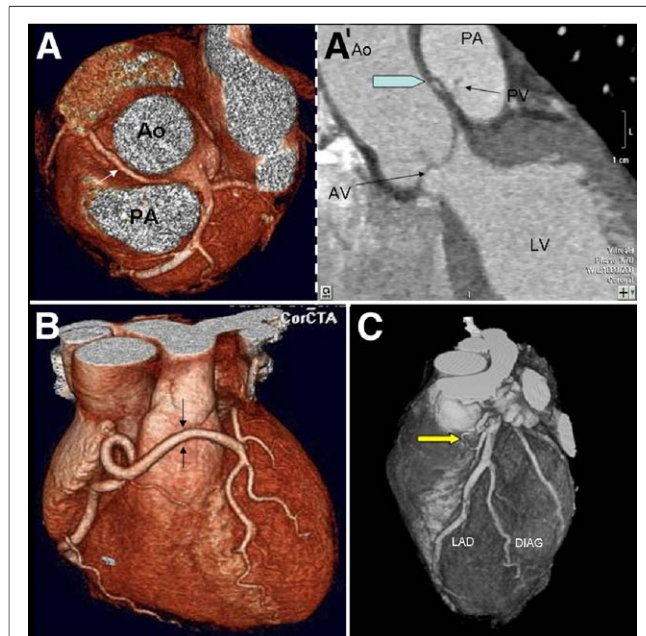


Figure 2. Congenital Coronary Anomalies Identified by Multidetector Computed Tomography Angiography

(A) From a 56-year-old man with chest pain. Volume-rendered image (in superior to inferior orientation) showing anomalous right coronary artery origin from the left aortic sinus with an interarterial course (between aorta [Ao] and pulmonary artery [PA]) (arrow). (A') Same patient shown in panel A. Coronal-axis plane demonstrates a slit-like right coronary artery ostia situated cephalad to the level of pulmonary valve (blue arrow). (B) Volume-rendered image from a 50-year-old woman with chest pain and exertional dyspnea shows left anterior descending coronary artery (arrows) origin from right aortic sinus, coursing anterior to the pulmonary artery. (C) Volume-rendered image from a 36-year-old man with exertional chest pain while biking, shows long tortuous fistula between left anterior descending coronary artery (LAD) and PA (arrow). AV = aortic valve; CorCTA = coronary computed tomography angiography; DIAG = diagonal coronary artery branch; LV = left ventricle.

patients, 8 also had obstructive CAD judged largely responsible for these symptoms. In the remaining 36 patients, cardiac symptoms were likely attributable to the cardiopulmonary abnormalities incidentally identified by MDCT angiography.

DISCUSSION

MDCT angiography is an important advance in the noninvasive diagnosis of atherosclerotic CAD that, in many cases, obviates the need for invasive contrast coronary arteriography (1–12). However, MDCT angiography is also a potentially powerful diagnostic modality with respect to overall LV anatomy, affording high-resolution tomographic images of myocardium, great vessels, and coronary arterial distribution. Indeed, in our MDCT angiography experience for detection of CAD, we

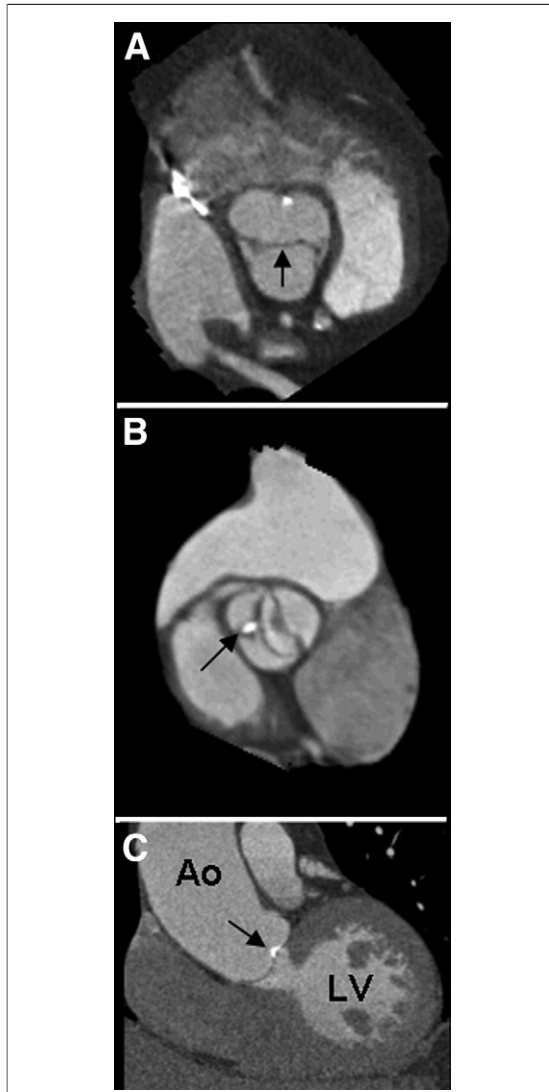


Figure 3. Bicuspid AV

(A) Short-axis view in diastole at the level of the aortic sinuses from a 64-year-old woman showing both aortic leaflets in the closed position (arrow). (B) Short-axis view from a 52-year-old man during systole with the valve open. A fused and calcified raphe is also evident (arrow). (C) Coronal long-axis in diastole from a 64-year-old man presenting with chest pain. Calcified bicuspid aortic valve is associated with dilation of ascending Ao (arrow). Abbreviations as in Figure 2.

were impressed by anecdotal cases in which other cardiovascular abnormalities (unrelated to coronary artery atherosclerosis) were identified clinically for the first time in the course of routine screening examinations. For this reason we have systematically assembled our substantial experience with an MDCT angiography cohort of >4,000 patients studied over 29 months to assess the frequency with which routine MDCT an-

giography identified cardiovascular abnormalities (unrelated to CAD).

MDCT angiography identified a wide variety of such cardiovascular abnormalities in 201 patients, including congenital coronary artery anomalies, aortic root aneurysms, HCM, LV noncompaction, left atrial myxoma, and mitral or aortic valve disease. Although approximately 75% of these abnormalities had been known to referring physicians, abnormalities in the other 25% (1% of the overall study group of 4,543 patients) were previously unsuspected and fortuitously diagnosed for the first time solely due to the clinical decision to perform MDCT angiography (usually on the basis of the history of chest pain). Of note, 40% of those patients with MDCT angiography-identified non-CAD diseases had prior echocardiographic studies that failed to identify the cardiovascular abnormalities ultimately diagnosed by MDCT angiography. However, we wish to underscore that the fundamental message of these data is not necessarily that MDCT angiography is a generally more effective diagnostic imaging modality than echocardiography (or other imaging tests), nor that it should supplant these strategies, but rather that MDCT angiography has the capability of identifying incidental but clinically relevant nonatherosclerotic cardiovascular abnormalities.

The most common of the MDCT angiography-identified lesions were congenital coronary artery anomalies, largely those of wrong sinus origin. Most of these patients (i.e., 53%) had anomalous right coronary artery origin from the left sinus of Valsalva (coursing between aorta and pulmonary trunk) (19). The observation that such anomalies of right coronary artery origin were 5-fold more common than anomalous left main coronary (from the right aortic sinus) deviates from the conventional perception regarding the relative frequency with which these congenital malformations occur, either innocently or as a cause of sudden death in the young, including competitive athletes (20,21). It is also possible that the lower prevalence of anomalous left coronary artery in our adult cohort suggests that it may be more lethal than anomalous right coronary artery early in life.

Of note, 7 patients were identified for the first time with LV hypertrophy, consistent with HCM (22). In 5 of these patients, wall thickening was confined to the distal portion of the LV chamber, and in 2 of those patients an echocardiogram performed before MDCT angiography failed to detect the apical area of hypertrophy and aneurysm (23).

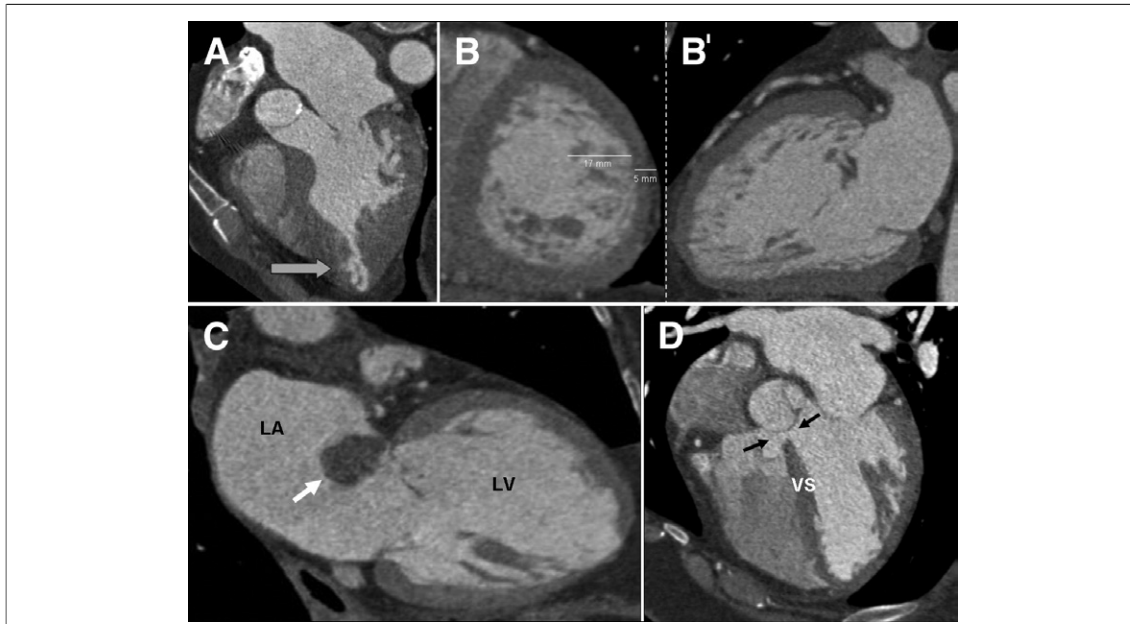


Figure 4. Spectrum of Structural Abnormalities of the LV, Unexpectedly Identified by Multidetector Computed Tomography Angiography

(A) Diastolic coronal view from a 69-year-old woman with HCM and exertional dyspnea shows LV wall thickening located predominantly in the distal (apical) portion of the chamber, associated with a thin-walled apical aneurysm (arrow). (B) Distal short-axis from a 52-year-old man shows "spongy" LV noncompaction with deep sinusoids and a diagnostic ratio of noncompacted (17 mm) to compacted myocardium (5 mm) of 3.4 who subsequently received a prophylactic implantable defibrillator. (B') Long-axis image from same patient with LV noncompaction shown in B. (C) Long-axis from 49-year-old woman with chest pain; left atrial myxoma (arrow) is attached by a short, atypically positioned stalk to the mitral annulus at the base of ventricular septum. The mass was resected surgically. (D) Four-chamber view from a 49-year-old woman with chest pain and small membranous ventricular septal aneurysm with defect (arrows). LV contrast is evident within the aneurysm. VS = ventricular septum; other abbreviations as in Figures 1 and 2.

Importantly, a substantial subset of patients experienced significant alteration in management strategy (and possibly clinical course) due to fortuitous MDCT angiography recognition of cardiovascular disease. For example, prophylactic surgical procedures were performed in 9 patients with congenital coronary artery anomalies, aneurysmal enlargement of the ascending aorta, and left atrial myxoma. In addition, 3 patients had timely and/or emergent medical treatment triggered solely by the results of MDCT angiography imaging, including 2 with pulmonary embolism. One patient with LV noncompaction, regarded at high-risk due to exercise-related ventricular tachyarrhythmias, had a cardioverter-defibrillator implanted for primary prevention of sudden death.

Contemporary CTA instruments with prospective gating (or retrospective gating with Mindose algorithm) are now in vogue, offering the advantage of substantial reduction in radiation exposure compared with the retrospective gating with pulse radiation used in the present study. Although this radiation benefit comes at the cost of lost functional information and systolic imag-

ing, we should underscore that such evolving technology would not alter the significance of the reported findings in which cardiovascular diagnoses were made on a morphologic (rather than functional) basis.

CONCLUSIONS

The present findings underscore the importance of broad-based interpretations of routine MDCT angiography imaging studies in clinical practice. MDCT angiography affords the capability of detecting a variety of cardiopulmonary abnormalities in a relatively small but clinically important subset of those patients referred for cardiac imaging in which the primary objective is the diagnosis or exclusion of CAD.

Reprint requests and correspondence: Dr. Barry J. Maron, Minneapolis Heart Institute Foundation, 920 East 28th Street, Suite 620, Minneapolis, Minnesota 55407. E-mail: bcm.maron@mhif.org.

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Key Words: computed tomography angiography ■ coronary artery disease ■ hypertrophic cardiomyopathy.