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Evaluation of Cardiac Allograft Vasculopathy by Multidetector Computed Tomography and Whole-Heart Magnetic Resonance Coronary Angiography

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Background: Cardiac allograft vasculopathy (CAV) is a major complication that limits the long-term survival of recipients of heart transplants. In the present study the feasibility of 2 noninvasive approaches for detecting CAV (multidetector computed tomography (MDCT) and whole-heart magnetic resonance coronary angiography (MRCA)) was compared with conventional coronary angiography (CCAG).

Methods and Results: Of 22 heart transplant recipients who underwent CCAG screening, 13 had only MDCT, 16 had only MRCA, and 7 had both noninvasive modalities. The coronary arterial tree was divided into 9 segments. Detection of vasculopathy by coronary segments was compared between 16-/64-detector computed tomography (CT) or MRCA and CCAG. The sensitivity of both 16- and 64-detector CT for diagnosing CAV was 69.6%, and specificity was 96.8%. The sensitivity and specificity by 64-detector CT alone were 90.0% and 97.5%, respectively; its positive and negative predictive values were 81.8% and 98.7% respectively. For MRCA, sensitivity was 60%, specificity, 100%, positive predictive value, 100% and negative predictive value, 92.2%. MRCA showed no false positives.

Conclusions: MDCT, especially 64-detector CT, is feasible for detecting CAV, whereas MRCA currently shows limited sensitivity. (*Circ J* 2010; **74:** 946–953)

Key Words: Cardiac allograft vasculopathy; Heart transplantation; Multidetector computed tomography; Whole-heart magnetic resonance coronary angiography

The outcome of solid-organ transplantation (eg, kidney or heart) has improved dramatically over the past 20 years, because of advancements in immunosuppressive therapy and improvements in surgical techniques. More than 3,000 heart transplants are performed annually worldwide,[1] with a 1-year survival in adults of nearly 90%. However, survival falls to 50–55% by 10 years.[1]

Cardiac allograft vasculopathy (CAV), a type of cardiovascular disease that occurs uniquely in heart transplant recipients, is a rapidly progressive form of atherosclerosis. The disease is characterized in its early stages by intimal proliferation, and in the later stages by luminal stenosis of epicardial branches, occlusion of smaller arteries and myocardial infarction.[2] CAV is a major factor limiting the long-term survival of heart transplant recipients.[1,3] Because the heart is partially denervated after heart transplantation, the patient most often fails to present ischemic symptoms until congestive heart failure or sudden death because of life-threatening arrhythmia occurs.[4,5] Therefore, most institutions screen heart transplant recipients annually using conventional coronary angiography (CCAG), which demonstrates the prevalence of CAV to be 40–50% within 5 years of transplantation.[6] CAV is often diffuse and concentric in nature, which is significantly different from the focal and eccentric pattern of atherosclerotic coronary artery disease (CAD).[5,7] Because CCAG only shows luminal changes and the arterial wall is not directly visualized,[5,7] it can be difficult to detect CAV by CCAG only. Additional intravascular ultrasound (IVUS) can provide great detail regarding mural changes, and has recently been recognized as the most sensitive tool for early detection of CAV.[5,7,8] IVUS detects CAV in 75% of patients at 3 years following transplantation;[7] however, it is not widely used because it is invasive, has a high risk of complications, and cannot be performed in small or distal vessels.[8]

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Studies have described multidetector computed tomography (MDCT) as a useful noninvasive alternative to both CCAG and IVUS for detecting CAV in heart transplant recipients, because this technique takes advantage of technological advances that enable it to have high spatial and temporal resolution with regard to both luminal and mural changes in coronary vessels.[5,8–11]

Over the past decade, magnetic resonance coronary angiography (MRCA) has also evolved as a potential alternative to CCAG among patients with suspected anomalous CAD and coronary artery aneurysms. MRCA has 2 main advantages: neither radiation exposure nor administration of nephrotoxic contrast medium is required.[12] The whole-heart, 3-dimensional (D), steady-state free precession (SSFP) technique, different from earlier methods of MRCA, is currently widely used, and has been well-validated for assessing patients with CAD.[13] The technique provides superior signal-to-noise and contrast-to-noise ratios, decreases dependence on the inflow of unsaturated protons, and facilitates multiplanar reconstructions. However, the feasibility of this whole-heart technique for detecting CAV has not been reported.

Our aim in this study was to assess the feasibility of MDCT and whole-heart MRCA for detecting and evaluating CAV in heart transplant recipients, using CCAG as the reference method.

Methods

Patients

Between December 2003 and July 2007, 22 consecutive heart transplant recipients (17 men, 5 women; 13–57 years old, mean, 34.9±15.7 years at the examination) underwent MDCT and/or whole-heart MRCA, in addition to CCAG, as screening examinations for detecting CAV. The underlying diseases were dilated cardiomyopathy in 14 patients, restrictive cardiomyopathy in 5, and dilated phase of hypertrophic cardiomyopathy in 3; 13 patients underwent MDCT; 16 had whole-heart MRCA, and the other 7 underwent both MDCT and whole-heart MRCA. Of those patients who underwent MDCT, 3 underwent 16-detector computed tomography (CT) and 10 underwent 64-detector CT. All gave written informed consent.

CCAG

Invasive CCAG was performed by experienced cardiologists using standard techniques, and the angiograms were visually interpreted by the same cardiologists, who were unaware of the findings of MDCT or whole-heart MRCA.

The coronary tree was divided into 9 segments for analysis: left main stem; proximal left anterior descending (LAD); middle LAD; distal LAD; proximal left circumflex (LCX); distal LCX; proximal right coronary artery (RCA); middle RCA; and distal RCA. Findings in the first diagonal branch were evaluated with those of the middle LAD, and in the second diagonal branch, with those of the distal LAD. The obtuse marginal branches were assessed together with the distal LCX. Only vessels >1.5 mm in diameter were evaluated in the present study.

Each coronary segment was visually assessed and graded on a 3-step severity scale: no disease, wall thickening, and stenosis. Wall thickening was defined as an irregularity in the arterial wall or luminal narrowing without significant stenosis (≤50% in diameter), and stenosis was defined as significant arterial stenosis (>50% in diameter) or occlusion. The presence of CAV was established if the segment was classified as either wall thickening or stenosis.

MDCT

Of the 13 patients who underwent CT coronary angiography with retrospective ECG-gated helical scan, 3 were on a 16-detector scanner (Lightspeed Ultra 16; GE Healthcare, Milwaukee, WI, USA) and 10 were on a 64-detector scanner (LightSpeed VCT; GE Healthcare). Scan parameters for 16-detector CT were as follows: individual detector width, 0.625 mm; gantry rotation time, 500 ms; tube voltage, 120 kV; tube current, 400 mA. For 64-detector CT, the respective parameters were: 0.625 mm, 350 ms, 120 kV, and 700 mA.

Unlike most patients undergoing CT coronary angiography at our institution, the transplant patients were not given β-blockers, because the denervated transplant heart shows regular R-R intervals on ECG. All patients were administered sublingual nitroglycerin (0.3 mg: Nitropen; Nippon Kayaku, Tokyo, Japan) before acquisition of noncontrast localization images. Thereafter, CT coronary angiography was performed after intravenous administration of nonionic iodine contrast medium, iopamidol (Iopamiron; Bayer HealthCare, Osaka, Japan), with an iodine concentration of 370 mgI/ml; a delay was calculated during the timing bolus scan. For 16-detector CT scanning, a bolus of 86–115 ml contrast medium was injected at a flow rate of 3.5–4.5 ml/s, followed by a 30–50-ml saline bolus at a flow rate of 4.5 ml/s. For 64-detector CT scanning, a bolus of 0.7 ml/kg body weight contrast medium was injected for 12 s, followed by a 30-ml saline bolus for 12 s. After scanning, axial images were reconstructed using retrospective ECG-gating in multiple phases, covering the cardiac cycle in increments of 10% of the R-R interval.

The reformatted images were then transferred to a workstation (Advantage Workstation version 4.3; GE Healthcare) for post-processing and analysis by 2 experienced radiologists who were unaware of the findings of CCAG and any findings of whole-heart MRCA. Analysis used the same classification of coronary segments as for CCAG. The visual assessment of each segment was graded on a similar severity scale to that for CCAG, and the presence of CAV was diagnosed by the same criteria as for CCAG.

Whole-Heart MRCA

Following sublingual administration of 0.3 mg of nitroglycerin (Nitropen), 16 patients underwent noncontrast whole-heart MRCA. Each patient was placed in the supine position with anteriorly placed ECG leads in a 1.5-Tesla magnetic resonance scanner (Avanto; Siemens Medical Systems, Erlangen, Germany). The phased-array body coil was placed anteriorly and the spine coil posteriorly. The transplant patients were not given β-blockers prior to this procedure. An ECG-gated, 3-D, segmented SSFP (True FISP) sequence was used in combination with free-breathing, prospective navigator gating without tracking of the imaged volume position, T_2 preparation to suppress myocardial signal, and a chemical shift-selective technique to suppress the signal from surrounding epicardial fat. The following scan parameters were used: field of view, 20×20 cm; matrix, 192×192; slice thickness, 1.5 mm (no gaps); voxel size, approximately 1.0×1.0×1.5 mm^3; repetition time, 3.0 ms; echo time, 1.5 ms; flip angle, 90 degrees. The scanned images were analyzed, using the same classification of coronary segments as for CCAG, by an experienced radiologist who was unaware of the findings of CCAG and any findings of MDCT. As stated in the MDCT section, each segment was visually assessed and graded on a severity scale similar to that used for CCAG, and the presence of CAV was diagnosed by the same criteria as for CCAG.

Table 1. Cardiac Allograft Vasculopathy Detection by Coronary Segments

	Proximal	Mid	Distal	Total
CCAG (n=198)	14	9	16	39 (19.7%)
MDCT (n=117)	12	4	3	19 (16.2%)
MRCA (n=144)	6	4	5	15 (10.4%)

CCAG, conventional coronary angiography; MDCT, multidetector computed tomography (CT); MRCA, magnetic resonance coronary angiography.

Data Analysis

For each patient, the severity grade of each of the 9 coronary segments assessed by MDCT and whole-heart MRCA was compared with those assessed by CCAG, which served as the reference. Furthermore, we compared the presence of CAV in each segment detected by MDCT and whole-heart MRCA with that detected by CCAG. From the data obtained, we calculated the sensitivity, specificity, and positive and negative predictive values of CAV detection per segment by MDCT and whole-heart MRCA.

Results

Of 22 patients who underwent CCAG, 7 underwent both MDCT and whole-heart MRCA, 6 had MDCT alone; and 9 had whole-heart MRCA alone.

CAV was detected in 39 of 198 segments (19.7%) by CCAG, comprising 14 in proximal segments, 9 in middle and 16 in distal segments (Table 1). CAV was detected in 19 of 117 segments by MDCT (16.2%), comprising 12 in proximal segments, 4 in middle and 3 in distal segments (Table 1). CAV was detected in 15 of 144 segments by whole-heart MRCA (10.4%), comprising 6 in proximal segments, 4 in middle and 5 in distal segments (Table 1).

Correlation of the grading of CAV between CCAG and 16- and 64-detector CT is shown in Table 2. The sensitivity of 16- and 64-detector CT for detecting CAV was 69.6%; specificity, 96.8%; positive predictive value, 84.2%; and

Table 2. Comparison of Coronary Arterial Stenosis Severity Between CCAG and MDCT or 64-Detector CT

	CCAG		
	0	≤50%	>50%
MDCT[a]			
0	91	5	2
≤50%	3	9	3
>50%	0	0	4
64-CT[b]			
0	78	1	0
≤50%	2	4	3
>50%	0	0	2

[a]Sensitivity 69.6%, specificity 96.8%, positive predictive value 84.2%, negative predictive value 92.8%.
[b]Sensitivity 90.0%, specificity 97.5%, positive predictive value 81.8%, negative predictive value 98.7%.
Abbreviations see in Table 1.

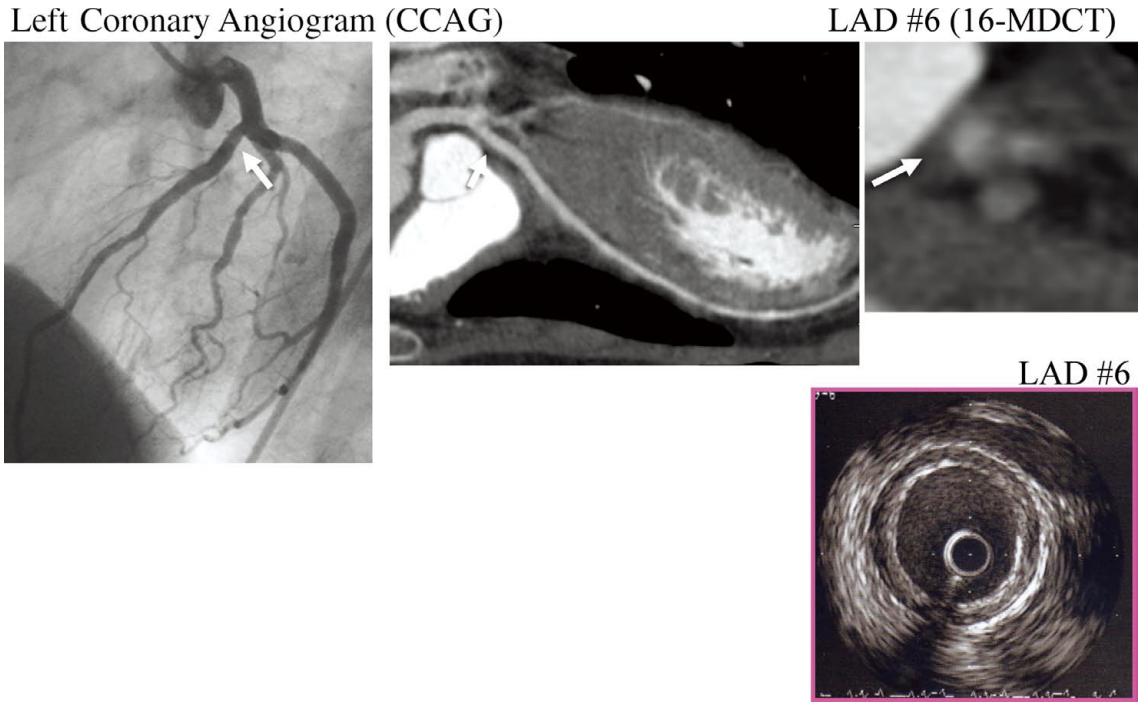

Figure 1. Representative heart transplant recipient whose cardiac allograft vasculopathy was detected by both CCAG and 16-MDCT. The left coronary angiogram and curved multiplanar and short-axis images obtained by 16-detector CT, taken in December 2006, show wall thickening in the proximal LAD (arrows) and middle LAD. IVUS performed at the same time confirmed the intimal hyperplasia in the proximal LAD. CCAG, conventional coronary angiography; CT, computed tomography; IVUS, intravascular ultrasound; LAD, left anterior descending artery; MDCT, multidetector computed tomography.

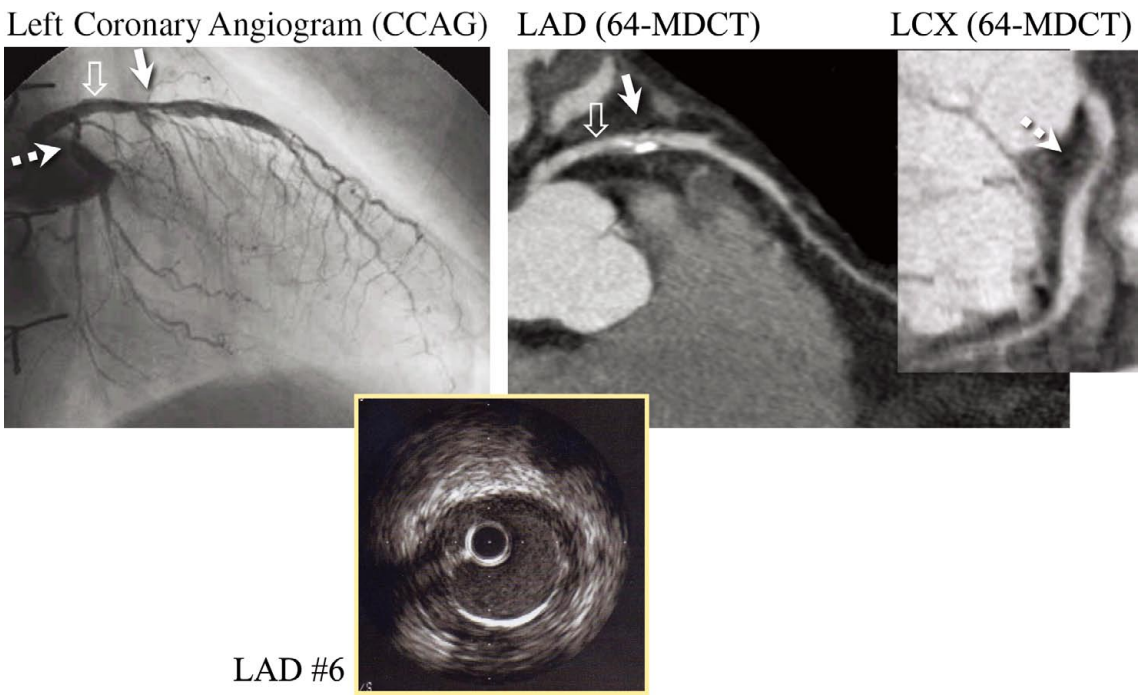

Figure 2. Coronary stenosis in the proximal–middle LAD and proximal LCX revealed by both CCAG and 64-detector CT. This patient underwent heart transplantation when he was 47 years old, and both CCAG and 64-MDCT were performed nine years after transplantation. The left coronary angiogram and curved multiplanar images obtained by 64-detector CT show significant stenosis in the proximal–middle LAD (solid arrows) and proximal LCX (dotted arrows). IVUS performed simultaneously confirmed the intimal hyperplasia in the proximal LAD (open arrows). CCAG, conventional coronary angiography; CT, computed tomography; IVUS, intravascular ultrasound; LAD, left anterior descending artery; LCX, left circumflex artery; MDCT, multidetector computed tomography.

negative predictive value, 92.8% (Table 2). Of the 3 false-positive segments compared with those on CCAG as the reference (Table 2), 1 was detected by 16-detector CT and the other 2 were detected by 64-detector CT (Table 2). Of 7 false-negative segments, 6 were revealed by 16-detector CT (Table 2), because of insufficient spatial resolution for distal lesions in 5 segments and because of motion artifacts in 1 segment; 64-detector CT resulted in only 1 false-negative segment (Table 2).

Figure 1 shows a representative heart transplant recipient whose CAV was detected by CCAG and by 16-detector CT. In May 2003, aged 13, the patient underwent heart transplantation performed with cytomegalovirus (CMV) mismatch, but 2 months later he showed severe humoral rejection, requiring steroid-pulse therapy and plasmapheresis. He also had post-transplant diabetes mellitus. The coronary angiogram and 16-detector CT images taken in December 2006 (Figure 1) showed wall thickening in the proximal and middle LAD. IVUS performed simultaneously showed intimal hyperplasia in the proximal LAD.

The sensitivity of 64-detector CT alone for detecting CAV was 90.0%; specificity, 97.5%; positive predictive value, 81.8%; and negative predictive value, 98.7% (Table 2). Greater than 50% stenosis was detected in 5 segments by CCAG, and in 2 by 64-detector CT (Table 2). Figure 2 shows coronary stenosis in the proximal–middle LAD and proximal LCX revealed by both modalities (CCAG and 64-MDCT) performed 9 years after transplantation. IVUS performed at the same time showed intimal hyperplasia in the proximal LAD. The patient received a heart transplant when he was 47 years old.

Table 3. Comparison of Coronary Arterial Stenosis Severity Between CCAG and Whole-Heart MRCA

	CCAG		
	0	≤50%	>50%
MRCA			
0	119	9	1
≤50%	0	3	4
>50%	0	0	8

Sensitivity 60.0%, specificity 100.0%, positive predictive value 100.0%, negative predictive value 92.2%.
Abbreviations see in Table 1.

Whole-heart MRCA was successfully performed in 16 transplant recipients without complications. Of 119 segments that were assessed by both CCAG and whole-heart MRCA, CAV was detected in 25 segments by CCAG and in 15 by whole-heart MRCA (Table 3). The sensitivity of MRCA for detecting CAV was 60.0%; specificity, 100%; positive predictive value, 100%; and negative predictive value, 92.2% (Table 3). Whereas no false-positive segments were detected, there were 10 false-negative segments by whole-heart MRCA, presumably because of insufficient spatial resolution and contrast-to-noise ratio for distal lesions (Table 3). Figure 3 shows wall thickening (irregularity) in distal LAD, and stenosis in LCX by CCAG, but whole-heart MRCA

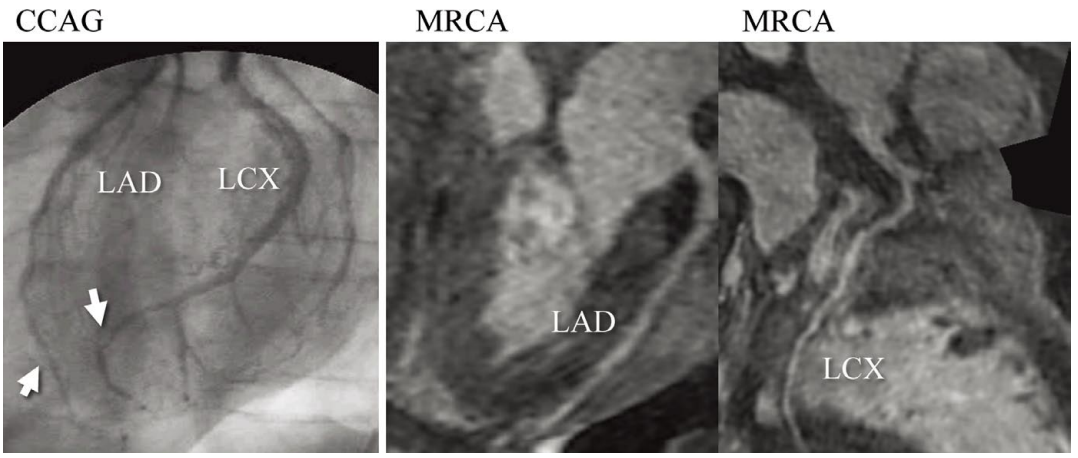

Figure 3. Wall thickening (irregularity) in the distal LAD and stenosis in the LCX revealed by CCAG (arrows), but no lesions in these segments are revealed by whole-heart MRCA (false-negative). This patient received a heart transplant when he was 44 years old and imaging examinations were performed 9 years after transplantation. CCAG, conventional coronary angiography; LAD, left anterior descending artery; LCX, left circumflex artery; MRCA, magnetic resonance coronary angiography.

Table 4. Incidence of False-Negative Segments With 16- and 64-Detector CT and MRCA

Modality	Incidence of false-negative segments	%
16-CT	6/13	46
64-CT	1/10	10
MRCA	10/24	42

Abbreviations see in Table 1.

revealed no lesion in these segments (false-negative). This patient received a heart transplant when he was 44 years old, and the imaging examinations were performed 9 years after transplantation.

Among the modalities used in this study, false-negative segments were identified in 6 of 13 segments (46%) by 16-detector CT, in 1 of 10 segments (10%) by 64-detector CT, and in 10 of 24 segments (42%) by whole-heart MRCA. These false negatives were the result of distal lesions or motion artifacts (Table 4).

Discussion

CAV and Invasive Screening Tests

Cardiac transplantation has been established as a therapeutic option for end-stage heart disease.[14,15] Because of improved immunosuppressive therapy, refined surgical techniques and awareness of post-transplant infections, cardiac transplant recipients may now expect a 1-year survival rate of nearly 90%. However, survival is reduced to nearly 75% by 5 years, and 50–55% by 10 years.[1] At 5 years post-transplant, CAV accounts for 33% of deaths, followed in prevalence by malignancies (23%).[1]

CAV is a rapidly progressive type of CAD that occurs after heart transplantation and is typically characterized by a diffuse concentric intimal hyperplasia that involves both epicardial and intramyocardial arteries.[2,7] Because transplant recipients with CAV lack early clinical symptoms as a result of the insufficiently re-innervated heart, they typically present late, with congestive heart failure, cardiac arrhythmia or sudden death that results from silent myocardial ischemia or allograft dysfunction.[4,5,16] CCAG is widely performed as a screening test for detecting CAV; the measurement of luminal diameter by CCAG and its comparison of the narrowing by vasculopathies to normal reference diameter aid in the understanding of the severity and disease progression.[17] However, because of vascular remodeling, CAV shows no initial decrease in luminal diameter.[17] In addition, because CAV involves the entire coronary artery tree concentrically, CCAG may give the impression of lower-than-actual vessel narrowing at the lesions, and even indicate normal thickness of the coronary arteries.[7] Thus, although CCAG is a good screening tool for CAD, it often underestimates CAV, especially during in its early stages.[7]

IVUS is the most sensitive procedure for detecting CAV. It can detect CAV in 50% of patients at 1 year after transplantation, whereas CCAG detects this disease in only 10–20% of patients.[18,19] IVUS, however, is physically restricted to the larger epicardial arteries and cannot be used throughout the entire coronary artery tree.[7] IVUS is also an invasive procedure, as with CCAG, and because of serious risks associated with intravascular catheter manipulation, it is not frequently performed.[8]

Noninvasive Screening of CAV by MDCT

Noninvasive modalities, including stress echocardiography, stress nuclear scintigraphy, and coronary calcium scanning, detect CAV poorly.[20,21] In contrast, owing to recent rapid technological advances, MDCT and whole-heart MRCA have been established as screening tests for CAD, and they may also be feasible for detecting CAV.

The 16-detector CT has a sensitivity of 75–82% and specificity of 88–92% in the detection of coronary atherosclerotic plaque, when IVUS is used as the reference method.[22,23] Similar results were observed in a study using 64-detector CT (sensitivity 84%, specificity 97%).[24] For more challenging detection of CAV compared with CCAG, sensitivity of 83% and specificity of 95% have been reported for 16-detector CT, and a sensitivity of 70% and specificity of 92% for 64-detector CT.[5,9]

In the present study, the sensitivity and specificity of MDCT for detecting CAV were 69.6% and 96.8%, respectively, which is insufficient as a screening method for CAV, despite the small sample size. Of 7 false-negative segments for detecting CAV by MDCT, 6 were identified on 16-detector CT, presumably because of insufficient spatial resolution for distal lesions or because of motion artifacts. Improvement of the temporal and spatial resolution of 64-detector CT, as compared with 16-detector CT, may contribute to improved sensitivity.

A high heart rate reduces the image quality of MDCT, so most studies using 16-detector CT have recommended that the heart rate be reduced by administration of β-blockers before the scan is performed. Cardiac re-innervation is highly variable and reported as only 10–30% in heart transplant recipients, so the efficacy of β-blockers is also considered to be variable and limited.[5,7] Thus, β-blockers were not administered to the patients in the present study because of the insufficient benefit by this medication over the estimated risk.

The alternative use of dual-source CT scanners, which consist of 2 independent X-ray tubes with their corresponding detectors mounted onto a rotating gantry with an angular offset of 90 degrees, improve the constant temporal resolution to 83 ms and allow high-quality coronary artery imaging without β-blocker administration in a wide range of heart rates.[25] Dual-source CT actually allows very frequent, diagnostic-image-quality coronary angiograms (92.1% of the coronary segments) in heart transplant recipients with high heart rates and no β-blocker administration, and may have been highly useful also for our cohort.[26]

Of 3 false-positive segments that were all graded as wall thickening by MDCT, 2 were detected by 64-detector CT, although IVUS was not performed and the details of the disagreement are unknown in these cases. One segment was detected by 16-detector CT and confirmed by IVUS.

MDCT may detect mural lesions induced by CAV that are difficult to diagnose by CCAG alone. Some studies also report that 16- and 64-detector CT may be more sensitive than CCAG for detection of thickened coronary segments in heart transplant recipients.[5,8,9] Moreover, the diameter measurements of coronary vessel show excellent correlation between MDCT and quantitative CAG for heart transplant recipients, and MDCT may be helpful for revealing late lumen loss, which is a typical feature of CAV.[9,27] Thus, MDCT may be a promising noninvasive procedure for detecting CAV.

MDCT has some limitations, including the requirement for nephrotoxic contrast medium and radiation exposure.[9] A substantial number of heart transplant recipients have impaired renal function, mainly because of post-transplant administration of calcineurin-inhibitors, and are therefore at risk for contrast-induced nephropathy.[9] In addition, because of the smaller helical pitch and higher tube power, effective doses with 64-detector CT using retrospective ECG-gated helical technique (9.5–21.4 mSv) are higher than with 16-detector CT (3.1–9.4 mSv), as well as that required for recent routine diagnostic CCAG (≈2–10 mSv).[28,29] The use of ECG-controlled tube current modulation reduces the effective dose by approximately 40%, as well as the lifetime attributable cancer risk, compared with the standard retrospective ECG-gated helical technique, especially for women and younger patients, maintains diagnostic image quality, and is recommended to use whenever possible.[30–32] The recently introduced use of prospective ECG-gated axial technique allows further dose reduction by 77–83% to a level of lower than that with CCAG.[28,33–35] The latter 2 scan techniques, however, have limited indications for patients with high heart rate and/or high heart rate variability as those without β-blocker administration in the present study. The indications of these dose-reduction techniques are expected to be widened with further technological advancements.

Noninvasive Screening of CAV by Whole-Heart MRCA

We anticipate that whole-heart MRCA will become the ideal screening modality for heart transplant recipients, because it is noninvasive and does not require the use of nephrotoxic contrast medium or radiation exposure, which are essential for both CCAG and MDCT. This aspect of MRCA will be advantageous for transplant ecipients with renal dysfunction. To our knowledge, only a few previous studies have compared whole-heart MRCA with CCAG for the feasibility of detecting significant coronary arterial stenosis in heart transplant recipients.[12,36]

The feasibility of this current whole-heart technique has not been established for detecting CAV, which has a more challenging etiology than CAD. In this study, the sensitivity of CAV detection was 60.0%, and the specificity of whole-heart MRCA was 100%. Metallic clips and sternal sutures did not hamper these image assessments, although they might cause surrounding signal loss, create difficulties in shimming for fat-signal suppression, and preclude evaluation of coronary arteries.[36] Whereas no false-positive segments were detected, MRCA revealed 10 false-negative segments, 9 of which were graded as wall thickening by CCAG, presumably because of insufficient spatial resolution and contrast-to-noise ratio for distal lesions. In addition, 8 true-positive segments, which were graded as stenosis, were identified. Thus, the sensitivity was relatively lower for detecting CAV, as compared with MDCT. However, the use of cardiac-specific coils that were not available at our institution may enhance the signal-to-noise ratio, and the administration of β-blockers may improve temporal resolution.

It will be necessary to improve the temporal and spatial resolution of MRCA by further advances in both hardware and software in order to improve the detection of CAV. Specifically, 3.0-Tesla MR scanners can improve spatial resolution and/or reduce imaging time by the theoretical doubling of the signal-to-noise ratio from 1.5- to 3.0-Tesla.[37] The current SSFP imaging technique at 1.5-Tesla, which has gained wide acceptance, is prone to imaging artifacts at 3.0-Tesla because of the increased magnetic field inhomogeneity and RF distortion at higher field strengths; energy deposition is increased by a factor of 4 from 1.5- to 3.0-Tesla.[37] Instead of the SSFP technique at 1.5-Tesla, the spoiled gradient-echo imaging technique at 3.0-Tesla using gadolinium contrast medium is expected to reduce imaging time, improve the signal-to-noise and contrast-to noise ratios, and provide more accurate assessment of CAD, including CAV,[37] although the use of gadolinium contrast medium is contraindicated in patients with advanced renal dysfunction because of its association with nephrogenic systemic fibrosis. Combined with dedicated 32- or even 128-channel phased-array coils, 2-D parallel imaging with higher acceleration factors may allow further improvement in imaging speed and/or spatial resolution.

Study Limitations

The main limitation of the present study was the small sample size, primarily because heart transplant recipients are rare in Japan. However, familiarity with CAV is mandatory, because of the increasing number of these recipients with this vas-

culopathy. Early diagnosis of CAV will therefore lead to earlier treatment and better outcomes. Furthermore, severe calcified plaque of coronary vessels may degrade image quality and preclude accurate diagnosis of CAV, especially on MDCT, even when using 64-detector CT. Generally, this severe calcified plaque is rare in patients with CAV, except in advanced cases, which is different from patients with CAD, as in the present study, and thus we think using MDCT is feasible for detecting CAV. A large-scale prospective study comparing these techniques with CCAG or IVUS is warranted in order to correctly assess the feasibility of MDCT, as well as MRCA, based on these preliminary results.

Conclusion

This preliminary study demonstrated the feasibility of using MDCT, especially 64-detector CT, for noninvasively detecting CAV in heart transplant recipients. Further improvements in image quality in whole-heart MRCA may be required. Both noninvasive modalities may replace invasive CCAG and additional IVUS as screening tools for CAV in the near future.

References

1. Taylor DO, Edwards LB, Aurora P, Christie JD, Dobbels F, Kirk R, et al. Registry of the International Society for Heart and Lung Transplantation: Twenty-fifth Official Adult Heart Transplant Report-2008. *J Heart Lung Transplant* 2008; **27:** 943–956.
2. Billingham ME. Histopathology of graft coronary disease. *J Heart Lung Transplant* 1992; **11**(Suppl)**:** S38–S44.
3. Valantine H. Cardiac allograft vasculopathy after heart transplantation: Risk factors and management. *J Heart Lung Transplant* 2004; **23:** S187–S193.
4. Silverman JF, Lipton MJ, Graham A, Harris S, Wexler L. Coronary arteriography in long-term human cardiac transplantation survivors. *Circulation* 1974; **50:** 838–843.
5. Romeo G, Houyel L, Angel CY, Brenot P, Riou JY, Paul JF. Coronary stenosis detection by 16-slice computed tomography in heart transplant patients: Comparison with conventional angiography and impact on clinical management. *J Am Coll Cardiol* 2005; **45:** 1826–1831.
6. Ramzy D, Rao V, Brahm J, Miriuka S, Delgado D, Ross HJ. Cardiac allograft vasculopathy: A review. *Can J Surg* 2005; **48:** 319–327.
7. Gao SZ, Alderman EL, Schroeder JS, Silverman JF, Hunt SA. Accelerated coronary vascular disease in the heart transplant patient: Coronary arteriographic findings. *J Am Coll Cardiol* 1988; **12:** 334–340.
8. Iyengar S, Feldman DS, Cooke GE, Leier CV, Raman SV. Detection of coronary artery disease in orthotopic heart transplant recipients with 64-detector row computed tomography angiography. *J Heart Lung Transplant* 2006; **25:** 1363–1366.
9. Gregory SA, Ferencik M, Achenbach S, Yeh RW, Hoffmann U, Inglessis I, et al. Comparison of sixty-four-slice multidetector computed tomographic coronary angiography to coronary angiography with intravascular ultrasound for the detection of transplant vasculopathy. *Am J Cardiol* 2006; **98:** 877–884.
10. Bae KT, Hong C, Takahashi N, Gutierrez F, Sharkey AM, Hirsch R, et al. Multi-detector row computed tomographic angiography in pediatric heart transplant recipients: Initial observations. *Transplantation* 2004; **77:** 599–602.
11. Tanaka A, Shimada K, Yoshida K, Jissyo S, Tanaka H, Sakamoto M, et al. Non-invasive assessment of plaque rupture by 64-slice multidetector computed tomography-comparison with intravascular ultrasound. *Circ J* 2008; **72:** 1276–1281.
12. Davis SF, Kannam JP, Wielopolski P, Edelman RR, Anderson TJ, Manning WJ. Magnetic resonance coronary angiography in heart transplant recipients. *J Heart Lung Transplant* 1996; **15:** 580–586.
13. Ishida M, Kato S, Sakuma H. Cardiac MRI in ischemic heart disease. *Circ J* 2009; **73:** 1577–1588.
14. Nunoda S, Shaddy RE, Bullock EA, Renlund DG, Hammond EH, Yowell RL, et al. The first pediatric Japanese case to undergo heart transplantation in the UTAH Cardiac Transplant Program in the United States. *Jpn Circ J* 1993; **57:** 873–882.
15. Saito S, Matsumiya G, Fukushima N, Sakaguchi T, Fujita T, Ueno T, et al. Successful treatment of cardiogenic shock caused by humoral cardiac allograft rejection. *Circ J* 2009; **73:** 970–973.
16. Aranda JM, Hill J. Cardiac transplant vasculopathy. *Chest* 2000; **118:** 1792–1800.
17. Nissen S. Coronary angiography and intravascular ultrasound. *Am J Cardiol* 2001; **87:** 15A–20A.
18. Schoenhagen P, Nissen S. Understanding coronary artery disease: Tomographic imaging with intravascular ultrasound. *Heart* 2002; **88:** 91–96.
19. Tuzcu EM, Kapadia SR, Tutar E, Ziada KM, Hobbs RE, McCarthy PM, et al. High prevalence of coronary atherosclerosis in asymptomatic teenagers and young adults: Evidence from intravascular ultrasound. *Circulation* 2001; **103:** 2705–2710.
20. Ratliff NB, Jorgensen CR, Gobel FL, Hodges M, Knickelbine T, Pritzker MR. Lack of usefulness of electron beam computed tomography for detecting coronary allograft vasculopathy. *Am J Cardiol* 2004; **94:** 202–206.
21. Smart FW, Balllantyne CM, Cocanougher B, Farmer JA, Sekela ME, Noon GP, et al. Insensitivity of noninvasive tests to detect coronary artery vasculopathy after heart transplant. *Am J Cardiol* 1991; **67:** 243–247.
22. Achenbach S, Moselewski F, Ropers D, Ferencik M, Hoffmann U, MacNeill B, et al. Detection of calcified and noncalcified coronary atherosclerotic plaque by contrast-enhanced, submillimeter multidetector spiral computed tomography: A segment-based comparison to intravascular ultrasound. *Circulation* 2004; **109:** 14–17.
23. Leber AW, Knez A, Becker A, Becker C, von Ziegler F, Nickolaou K, et al. Accuracy of multidetector spiral computed tomography in identifying and differentiating the composition of coronary atherosclerotic plaques: A comparative study with intracoronary ultrasound. *J Am Coll Cardiol* 2004; **43:** 1241–1247.
24. Leber AW, Knez A, von Ziegler F, Becker A, Nickolaou K, Paul S, et al. Quantification of obstructive and nonobstructive coronary lesions by 64-slice computed tomography: A comparative study with quantitative coronary angiography and intravascular ultrasound. *J Am Coll Cardiol* 2005; **46:** 147–154.
25. Flohr TG, McCollough CH, Bruder H, Petersilka M, Gruber K, Suss C, et al. First performance evaluation of a dual-source CT (DSCT) system. *Eur Radiol* 2006; **16:** 256–268.
26. Bastarrika G, De Cesso CN, Arraiza M, Mastrobuoni S, Pueyo JC, Ubilla M, et al. Dual-source CT for visualization of the coronary arteries in heart transplant patients with high heart rates. *Am J Roentgenol* 2008; **191:** 448–454.
27. Tsutsui H, Ziada KM, Schoenhagen P, Iyisoy A, Magyar WA, Crowe TD, et al. Lumen loss in transplant coronary artery disease is a biphasic process involving early intimal thickening and late constrictive remodeling: Results from a 5-year serial intravascular ultrasound study. *Circulation* 2001; **104:** 653–657.
28. Earls JP, Berman EL, Urban BA, Curry CA, Lane JL, Jennings RS, et al. Prospectively gated transverse coronary CT angiography versus retrospectively gated helical technique: Improved image quality and reduced radiation dose. *Radiology* 2008; **246:** 742–753.
29. Einstein AJ, Moser KW, Thompson RC, Cerqueira MD, Henzlova MJ. Radiation dose to patients from cardiac diagnostic imaging. *Circulation* 2007; **116:** 1290–1305.
30. Budoff MJ, Achenbach S, Blumenthal RS, Carr JJ, Goldin JG, Greenland P, et al. American Heart Association Committee on Cardiovascular Imaging and Intervention; American Heart Association Council on Cardiovascular Radiology and Intervention; American Heart Association Committee on Cardiac Imaging, Council on Clinical Cardiology: Assessment of coronary artery disease by cardiac computed tomography; a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee Cardiac Imaging, Council on Clinical Cardiology. *Circulation* 2006; **114:** 1761–1791.
31. Einstein AJ, Henzlova MJ, Rajagopalan S. Estimating risk of cancer associated with radiation exposure from 64-slice computed tomography coronary angiography. *JAMA* 2007; **298:** 317–323.
32. Hausleiter J, Meyer T, Hadamitzky M, Huber E, Zankl M, Martinoff S, et al. Radiation dose estimates from cardiac multislice computed tomography in daily practice: Impact of different scanning protocols on effective dose estimates. *Circulation* 2006; **113:** 1305–1310.
33. Herzog BA, Husmann L, Burkhard N, Gaemperli O, Valenta I, Tatsugami F, et al. Accuracy of low-dose computed tomography coronary angiography using prospective electrocardiogram-triggering: First clinical experience. *Eur Heart J* 2008; **29:** 3037–3042.
34. Shuman WP, Branch KR, May JM, Mitsumori LM, Lockhart DW,

Dubinsky TJ, et al. Prospective versus retrospective ECG gating for 64-detector CT of the coronary arteries: Comparison of image quality and patient radiation dose. *Radiology* 2008; **248:** 431–437.
35. Hirai N, Horiguchi J, Fujioka C, Kiguchi M, Yamamoto H, Matsuura N, et al. Prospective versus retrospective ECG-gated 64-detector coronary CT angiography: Assessment of image quality, stenosis, and radiation dose. *Radiology* 2008; **248:** 424–430.
36. Mohiaddin RH, Bogren HG, Lazim F, Keegan J, Gatehouse PD, Barbir M, et al. Magnetic resonance coronary angiography in heart transplant recipients. *Coronary Artery Dis* 1996; **7:** 591–597.
37. Yang Q, Li K, Liu X, Bi X, Liu Z, An J, et al. Contrast-enhanced whole-heart coronary magntic resonance angiography at 3.0-T: A comparative study with X-ray angiography in a single center. *J Am Coll Cardiol* 2009; **54:** 69–76.