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ORIGINAL ARTICLE

Detection of significant coronary artery stenosis with cardiac dual-source computed tomography angiography in heart transplant recipients

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Summary

Present study evaluates clinical feasibility of cardiac dual-source computed tomography angiography (DSCTA) to detect significant coronary stenosis because of chronic allograft vasculopathy (CAV) after heart transplantation (HTX). An overall of 51 consecutive heart transplant recipients (43 men, 8 women, mean age: 52.3 ± 13.6 years) underwent DSCTA 1 ± 2 days before annual routine invasive coronary angiography (ICA). Three patients were excluded from further analysis. Total 714/717 (99.6%) segments in remaining 48 patients were depicted in diagnostic image quality by DSCTA with three vessel segments in two patients being additionally excluded because of motion artefacts. On a segment-based analysis, sensitivity, specificity, and diagnostic accuracy (DA) for detection of significant stenosis were calculated as 100%, 98.9% and 98.9% respectively. On a patient-based evaluation, sensitivity, specificity and DA were 100%, 86.0% and 93.0% respectively for remaining 46 patients. Negative predictive value (NPV) was 100%. DSCTA enables diagnosis and especially the exclusion of significant coronary artery stenosis in patients after HTX with a high NPV. The low rate of excluded vessel segments compared with former studies indicates improvement in image acquisition and robustness of latest scanner technology and thus may make subsequent annual invasive coronary angiography unnecessary.

Introduction

Despite major improvements in immunosuppressive therapy over the last decade, cardiac allograft vasculopathy (CAV) still remains a leading cause of morbidity and mortality after heart transplantation (HTX). According to the registry of the International Society of Heart and Lung Transplantation (ISHLT), invasive coronary angiography (ICA) detects CAV in 8% of 1-year-survivors, in 30% within the first 5 years, and in >50% within the first 10 years after HTX [1]. A large majority of patients will not develop classical symptoms of angina, but rather present with silent myocardial ischaemia, heart failure, or death because of denervation of the graft. Generally non-invasive screening tests such as exercise ECG or thallium scintigraphy are insensitive to identify CAV [2–5], and therefore annual ICA examinations are frequently performed in many centres. As an invasive procedure ICA is associated with a small, but potential clinically important risk of complications leading investigators to consider and evaluate further noninvasive modalities [6].

Dual-source computed tomography angiography (DSCTA) with improved temporal and spatial resolution enables noninvasive visualization of the whole coronary

artery tree and thus might be a promising new modality for these particular patients to visualize CAV. Several studies already demonstrated good correlations between ICA and computed tomography angiography (CTA) for stenosis detection in case of coronary heart disease (CHD) [7,8]. Also initial feasibility studies utilizing mainly older equipment such as 16- and 64-slice scanner technology raise hope that CTA is able to exclude CAV [9–14]. One major problem in these particular patients was unsatisfying image quality because of rapid vessel movement on the basis of untreatable high heart rates or arrhythmia like atrial fibrillation leading to exclusion of a considerable amount of vessel segments from further analysis [14]. Thus, this study sought to evaluate the clinical feasibility of dual-source computed tomography (DSCT) scanner technology especially with regard to visualization of distal vessel segments to detect significant focal stenosis in HTX patients with ICA as the reference method.

Methods

Patients

We included 51 consecutive heart transplant recipients (43 men, 8 women, mean age: 52.3 ± 13.6 years) who underwent DSCTA 1 ± 2 days before annual routine ICA as part of the study protocol. Exclusion criteria were as follows: (i) former stent implantation procedure or bypass grafting, (ii) severe renal insufficiency (blood creatinine >1.5 mg/dl), (iii) severe cardiac insufficiency, (iv) previous allergic reaction to iodinated contrast media and (v) unstable clinical conditions. The study protocol was approved by the institutional review board and all patients gave written and informed consent. The mean post-transplant time was 6.9 ± 4.1 years (range: 2 weeks to 15 years). Blood creatinine levels were recorded before ICA (baseline value) and the day after DSCTA (mean time interval: 38.1 ± 2.4 h). Standard hospital care included adequate hydratation for at least 12 h before and after contrast agent application. In addition, every patient received orally N-acetylcystein (600 mg twice daily). Detailed patient characteristics are given in Table 1.

Invasive coronary angiography

The ICA was performed in Judkins technique using a 6-F catheter in a standardized procedure. All acquired images were digitally stored on a hard drive and transferred to an external workstation (HICOR; Siemens Medical Solutions, Erlangen, Germany). For Quantitative Coronary Analysis (QCA) the Quant-Cor QCA software package (Quantcor.QCA; CAAS II, V.5.0; Pie Medical Imaging, Maastricht, Netherlands) was used. At least two orthogonal views were obtained for each coronary angiogram and assessed by one experienced reader blinded to the DSCTA results. Percentage luminal stenosis was recorded and interpreted in a clinical useful scale depending on the QCA results. Thereby significant disease was defined as luminal diameter obstruction ≥50% or total vessel occlusion. Nonsignificant disease was defined as arterial lumen irregularity or loss of concentric vessel profile without significant stenosis (<50% in luminal diameter). As a luminographic modality, ICA is limited in detection of vessel wall changes is general, and thus vessels appearing nondiseased in ICA were also grouped under latter category (exemplified in Fig. 1). Finally the status for each coronary segment was documented according to the AHA 15-segment model [15].

Table 1. Patient characteristics.

Patients	*n* = 51 (43 male; 8 female)
Mean recipient age at DSCTA	52.3 ± 13.6 years
Mean recipient age at HTX	45.4 ± 13.6 years
Mean donor age at DSCTA	41.4 ± 12.4 years
Mean donor age at HTX	34.5 ± 11.9 years
Time after HTX	6.9 ± 4.1 years (range: 2 weeks – 15 years)
Cause of HTX	DCM: 39 / 51 cases (76.5%)
	ICM: 10 / 51 cases (19.6%)
	Other: 2 / 51 cases (3.9%)
Heart rate before / after betablocker treatment	94 ± 14 b.p.m. (range: 63–120 b.p.m.)
	88 ± 14 b.p.m. (range: 61–116 b.p.m.); NS ($P < 0.10$)
Blood creatinine before ICA / after DSCTA examination	1.2 ± 0.2 mg/dl
	1.2 ± 0.2 mg/dl; NS ($P = 0.421$)

DCM, dilatative cardiomyopathy; DSCTA, dual-source computed tomography angiography; HTX, heart transplantation; ICA, invasive coronary angiography; ICM, ischaemic cardiomyopathy; NS, nonsignificant.

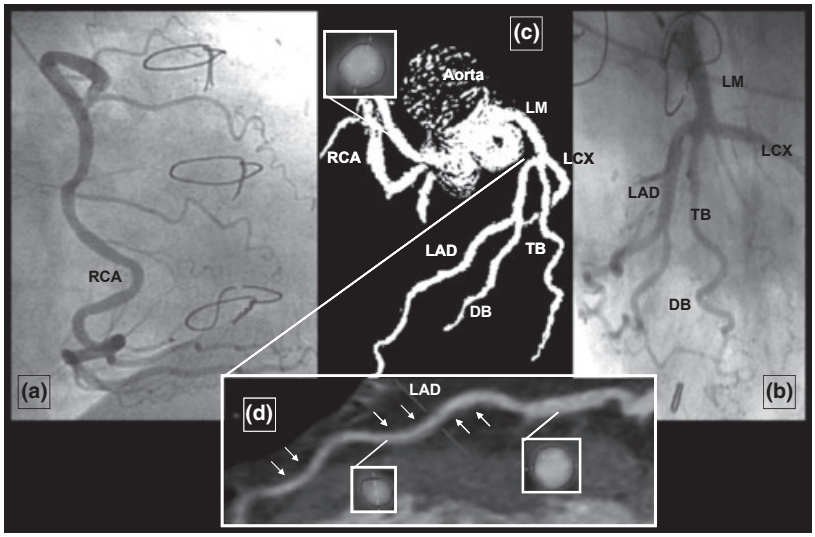

Figure 1 Nonsignificantly diseased patient. This 68-year-old patient 5 years after heart transplantation illustrates the case of a nonsignificantly diseased patient. Image a and b show the results of invasive coronary angiography with vessel wall irregularities in right (Image a) and left coronary artery (Image b). Image c is a volume rendering technique (VRT) image reconstruction of the whole coronary artery tree in CTA with additional magnified MPR cross-sectional image of RCA illustrating no plaque formation. To evaluate the whole coronary artery tree MPRs longitudinal (Image d; LAD) and orthogonal to the vessel course (cross-sectional MPRs) were utilized. Note the dark concentric tissue surrounding the contrast enhanced vessel lumen (white arrows) representing CAV without causing significant stenosis. Comparing ICA with CTA the diffuse nature of CAV seems to be underestimated by using the conventional angiography approach. DB: diagonal branch; LAD: left anterior descending coronary artery; LCX: left circumflex coronary artery; LM: left main coronary artery; RCA: right coronary artery; TB: trifurcational branch.

Dual-source computed tomography

Every patient received betablockers (metoprolol tartrat 50–100 mg) orally at least 1 h prior to the scan to lower and stabilize the heart rate. Heart rates before betablocker treatment and during scan procedure were recorded. All examinations were performed with a DSCT-scanner (Definition, Siemens Medical Solutions) according to a standardized acquisition protocol including bodyweight-adapted contrast agent administration. In case of heart motion artefacts, different datasets depending on the best achievable image quality for each major coronary artery were used for further analysis.

Every single CT dataset was independently evaluated by an experienced reader unaware of the ICA results at a dedicated external workstation (LEONARDO, Siemens Medical Solutions). All 15 coronary segments according to the AHA coronary segment model were considered for DSCTA evaluation. Maximum intensity projections (MIP) were used interactively to display the vessel path. Magnified multiplanar reformats (MPR) longitudinal and orthogonal to the vessel course were utilized for visual assessment of percentage lumen area stenosis (exemplified in Fig. 1). For comparison of DSCTA and ICA either segment- and patient-based, the same above mentioned two-step severity scale was applied. Those vessel segments with artefacts leading to invisibility of coronary vessel lumen were excluded from further analysis. The meaning of this sentence is not clear; please rewrite or confirm that the sentence is correct.

Statistical analysis

All statistical calculations were performed using MedCalc 7.0 (MedCalc Software, Mariakerke, Belgium) installed on a desktop computer. Variables are presented in mean ± SD. For comparison of blood creatinine levels at baseline and after MDCTA as well as heart rates before and after betablocker administration, paired *t*-test was employed. Calculations were considered to be significant at a *P*-value of <0.05. For evaluation of diagnostic performance of DSCTA detecting significant disease sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy compared with ICA were calculated.

Results

No patient needed to be excluded from DSCTA and no patient developed contrast-induced nephropathy (CIN). Blood creatinine levels at baseline (1.2 ± 0.2 mg/dl) showed no significant change after contrast agent application (1.2 ± 0.2 mg/dl; $P = 0.42$). Maximum increase was 0.4 mg/dl. DSCTA scan duration was 10 ± 3 s. Heart rates after oral betablocker treatment were still high

(mean: 88 ± 14 b.p.m.; range 61–116 b.p.m.). Compared with baseline heart rates (mean: 94 ± 14 b.p.m.; range: 63–120 b.p.m.) no statistically significant reduction was achieved ($P < 0.10$). Three patients had to be excluded from further analysis after CT scan. In two cases the patients did not follow breath-holding commands sufficiently during scan procedure and in the third case technical failure led to broken DSCTA datasets. In remaining 48 patients, an overall of 717 were evaluated by ICA and DSCTA was able to depict 714 (99.6%) segments in diagnostic image quality. Motion artefacts lead to three uninterpretable vessel segments (Segment 12 of LCX: $n = 1$; Segment 2 of RCA: $n = 2$) in an overall of two male patients (heart rate 68 and 87 b.p.m.) being excluded from patient-based analysis. Thus in remaining 46 patients (95.8%) with all coronary vessel segments being sufficiently visualized by DSCTA patient-based analysis was performed. Notably calcifications were present in 11/48 patients (22.9%): three with heavy calcified plaques not impairing visual coronary lumen assessment and eight showing only small calcified nodules.

Nonsignificant disease

Detailed results are given in Table 2. An overall of 706/714 (98.8%) segments in 43 patients were classified as nonsignificantly diseased by ICA. In 698 (98.9%) segments in 37 (86.0%) patients DSCTA agreed (exemplified in Fig. 1). DSCTA overestimated eight segments in eight patients with two patients showing significant disease in one further vessel segment each and thus 6/46 (13.0%) false-positive patients were counted in patient-based analysis. Out of eight overestimated vessels, one vessel segment appeared without luminal irregularities in ICA and was located in distal LAD. Remaining seven segments showed luminal irregularities, but without significant obstruction (Segments 2, 3, 6, 9, and 11).

Table 2. Diagnostic performance of DSCTA for detection of significant stenosis on a patient- and segment-based analysis.

	Segment-based (n = 714 in 48 patients)	Patient-based (n = 46 patients)
True-positive	8	3
True-negative	698	37
False-positive	8	6
False-negative	0	0
Sensitivity	100%	100%
Specificity	98.9%	86.0%
Positive predictive value	50.0%	33.3%
Negative predictive value	98.9%	100%
Diagnostic accuracy	98.9%	87.0%
Disease prevalence	1.1%	6.5%

Stenosis detection

The ICA confirmed an overall of 8/714 (1.1%) significantly diseased segments (exemplified in Fig. 2) in three patients (6.5%) with a totally occluded proximal RCA (Segment 1). All of them were detected by DSCTA.

Diagnostic performance of DSCTA is summarized in Table 2. For detection of significant disease or total vessel occlusion by DSCTA on a segment-based analysis, sensitivity, specificity and diagnostic accuracy was calculated as 100%, 98.9% and 98.9% respectively. Negative predictive value (NPV) was 100% and positive predictive value (PPV) 50.0%. Patient-based analysis of 46 patients with evaluable coronary arteries by DSCTA revealed an overall sensitivity, specificity and diagnostic accuracy of 100%, 86.0% and 87.0% respectively. NPV was calculated 100% with a PPV of 33.3%.

Discussion

With this study, we demonstrated the ability of dual-source computed tomography angiography to noninvasively detect significant coronary artery stenosis because of chronic allograft vasculopathy in patients after heart transplantation. Diagnostic performance of DSCTA in comparison with the currently recommended reference method ICA is comparable to previously published results. Schepis *et al.* report a sensitivity and specificity of 85%, and 84%, respectively, in 30 patients examined with DSCTA after HTX compared with ICA and 1-vessel IVUS [16]. In case of CHD detection DSCTA offers the possibility to detect significant coronary artery stenosis with a pooled sensitivity and pooled specificity of 99% and 89% in a patient-based meta-analysis of 2303 patients reported by Salavati *et al.* [17] With regard to vessel segments our results are even better than in CHD detection. One major problem in evaluating patients with conventional atherosclerotic disease of their coronaries is severe calcification impairing correct vessel delineation because of blurring artefacts. In patients after HTX coronary calcifications are infrequently detectable [18]. In our patient population calcifications were present in 12/49 cases (24.5%) with only three heavily calcified plaques not impairing visual vessel lumen assessment partly explaining the better diagnostic accuracy in these particular patients. A second problem evaluators are confronted with as far as CTA is concerned are motion artefacts mainly in coronary vessel parts perpendicular to the plane of the image, such as mid parts of the right coronary artery (Segment 2) or mid and distal parts of left circumflex coronary artery (Segments 12–15). This was also the case in our patient population. Motion artefacts appeared in two patients in Segment 2 each and additionally in Segment 12 in one

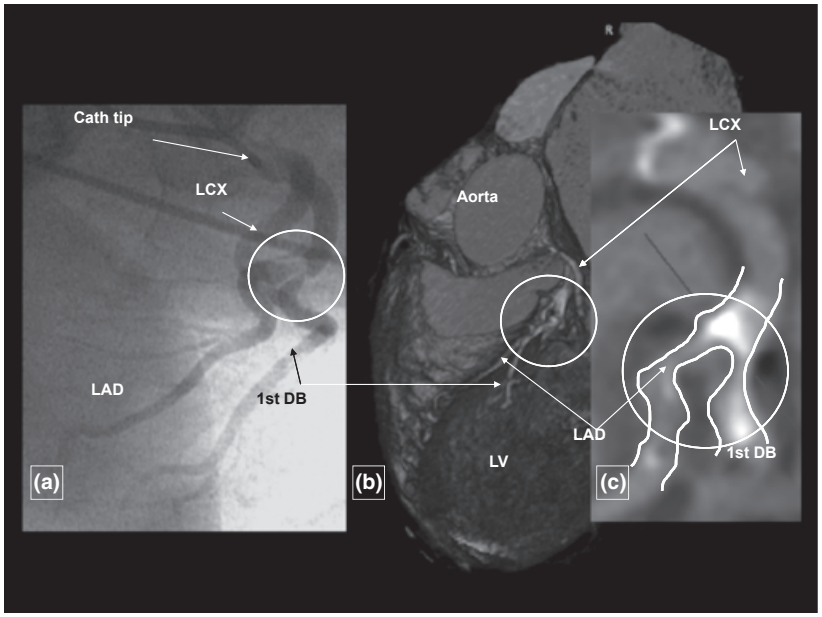

Figure 2 Significantly diseased vessel segment. In this case significant diseased mid LAD at the passing region of the diagonal branch, which itself appears significantly diseased in his proximal portion is clearly depicted by ICA (Image a) and CTA VRT image reconstruction (Image b) with additional longitudinal MPR and vessel contouring (Image c). This 66-year-old male patient 11 years after heart transplantation underwent stent implantation procedure. Note that in this case calcified tissue which is not impairing evaluation of vessel lumen causes the stenosis. Calcified plaques were rarely found in our study population. DB: diagonal branch; LAD: left anterior descending coronary artery; LCX: left circumflex coronary artery.

patient irrespectively of heart rates. Nonetheless, DSCTA was able to depict 99.6% of all segments in diagnostic image quality representing clear improvement in image acquisition compared with older scanner technology, such as 64-slice CT. In our previous study utilizing a 64-slice scanner, only 81.4% of all segments were evaluable [14]. Proving feasibility of DSCTA in a clinical setting was the first aim of our study. A high negative predictive value suggests this noninvasive modality being a useful tool for ruling out significant stenosis in HTX patients making subsequental annual ICA unnecessary in case of unremarkable findings. This assumption is supported by findings of Rohnean *et al.* who followed-up 65 heart transplant recipients over 5 years by CTA and reported safety of this modality for CAV detection [19]. Furthermore, they found that time to stenosis development was consistently greater than 3 years and thus a 2 year follow-up interval in case of normal baseline CTA might be possible. However, our results have to be appreciated under consideration of a small sample size with a limited number of significant stenosis. Disease prevalence was 6.5% in our patient population 6.9 ± 4.1 years after heart transplantation procedure, and thus explaining low values for positive predictive value. Furthermore, this low prevalence of disease raises suspicion of selection bias of a single centre experience with exclusion of patients after interventional procedures (stenting, bypasses) because of CAV. Therefore, calculated high NPV must also be appreciated with respect to that low number of significantly diseased vessel segments. Thus, a multicentre trial with higher disease prevalence would be desirable to validate DSCTA for the evaluation of CAV after heart transplantation before definitive conclusions can be drawn. A further limitation of our study is the utilization of ICA as the reference standard with its known limitations in case of CAV detection. Nonetheless our study design follows generally established recommendations for HTX patients in a clinical context according to current published guidelines of the ISHLT Working Group on classification of CAV [20]. Thereby usage of intravascular ultrasound (IVUS) is not advocated as a routine procedure, as at this time its value as a surrogate marker remains investigational. Furthermore, it is unlikely that IVUS will detect flow-limiting epicardial disease not demonstrated by ICA, although ICA is not perfect. Coronary lesions because of CAV appear often concentric, mimicking normal coronary arteries during early stages of disease in ICA, which has been proven to underestimate severity of disease [21,22]. Accepting this imprecision of ICA and thus mimicking every day clinical practice angiographic lesion had to be totally absent to exclude CAV in our study setting to account for this known limitation. Main concerns have

been raised over the perceived increase in radiation dosage associated with implementation of CTA into clinical arena as well as technical improvements leading to more detector rows. According to a recently published study, mean effective patient dose of cardiac 16-slice MDCTA was found to be 14.7 ± 2.2 mSv vs. 5.6 ± 3.6 mSv in ICA [23]. Latest 2nd generation DSCT-scanner technology with systolic prospectively ECG-triggered image acquisition protocols reduces radiation dose down to 4.5 ± 1.2 mSv which is in the range of diagnostic conventional coronary angiography [24]. Nonetheless a careful patient selection is essential to prevent nonutilizable examinations as patients with cardiac arrhythmia (atrial fibrillation, bigeminy, etc.) are not feasible for radiation dose reduction modalities. Furthermore, a substantial number of heart transplant patients chronically show impaired kidney function being at risk for CIN. In clinical practice DSCTA compared with diagnostic ICA might be of limited value because of its noticeable higher amount of contrast agent needed, although intravenously administered contrast material seems to be less problematic [25]. We did not find a significant increase in blood creatinine levels after the scan procedure or contrast media related adverse event. Blood creatinine measurements were taken in average one day after CT angiography. This follow-up observation period might be not long enough as creatinine is known to peak up to 72 h after contrast media application with a rise in blood creatinine levels detectable in 80% of the patients within 24 h [26,27]. However, our study population consisted of patients with normal or only mild renal insufficiency representing low risk for developing CIN and thus not reflecting the common patient after HTX. Although DSCTA offers the possibility to detect significant stenosis in large epicardial vessels leading to intervention, this may not improve outcome of these particular patients. The assumption that palliative treatments like coronary angioplasty with or without stent placement will increase survival of the graft is increasingly disputed [28]. Nonetheless this limitation accounts for both DSCTA and ICA as clinical utility of routine invasive evaluation for detection of CAV has been questioned [29].

Conclusion

In conclusion DSCTA enables diagnosis and especially the exclusion of significant coronary artery stenosis in patients after HTX with a high NPV. The low rate of excluded vessel segments compared with former studies indicates an improvement in image acquisition and robustness of latest scanner technology and thus may make subsequent annual invasive coronary angiography unnecessary. In a clinical setting, ambiguous findings in DSCTA should prompt ICA with the possibility of stent implantation procedure. Follow-up of latter cases would only be with ICA.

Authorship

FZ: study design, paper preparation. JR: DSCTA evaluation. IK: statistical evaluation, editorial work. MG: ICA evaluation. JS: patient acquisition. SH: data collection. CB: DSCTA supervisor. BM: editorial work. AB: study design, ICA supervisor, editorial work.

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References

1. Stehlik J, Edwards LB, Kucheryavaya AY, *et al.* The Registry of the International Society for Heart and Lung Transplantation: twenty-seventh official adult heart transplant report – 2010. *J Heart Lung Transplant* 2010; **29**: 1089.
2. Ciliberto GR, Mangiavacchi M, Banfi F, *et al.* Coronary artery disease after heart transplantation: non-invasive evaluation with exercise thallium scintigraphy. *Eur Heart J* 1993; **14**: 226.
3. Pinney SP, Mancini D. Cardiac allograft vasculopathy: advances in understanding its pathophysiology, prevention, and treatment. *Curr Opin Cardiol* 2004; **19**: 170.
4. Smart FW, Ballantyne CM, Cocanougher B, *et al.* Insensitivity of noninvasive tests to detect coronary artery vasculopathy after heart transplant. *Am J Cardiol* 1991; **67**: 243.
5. Spes CH, Klauss V, Mudra H, *et al.* Diagnostic and prognostic value of serial dobutamine stress echocardiography for noninvasive assessment of cardiac allograft vasculopathy: a comparison with coronary angiography and intravascular ultrasound. *Circulation* 1999; **100**: 509.
6. Noto Jr TJ, Johnson LW, Krone R, *et al.* Cardiac catheterization 1990: a report of the Registry of the Society for Cardiac Angiography and Interventions (SCA&I). *Cathet Cardiovasc Diagn* 1991; **24**: 75.
7. Schuetz GM, Zacharopoulou NM, Schlattmann P, Dewey M. Meta-analysis: noninvasive coronary angiography using computed tomography versus magnetic resonance imaging. *Ann Intern Med* 2010; **152**: 167.
8. Taylor AJ, Cerqueira M, Hodgson JM, *et al.* ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 appropriate use criteria for cardiac computed tomography. A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the Society of Cardiovascular Computed Tomography, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the American Society of

Nuclear Cardiology, the North American Society for Cardiovascular Imaging, the Society for Cardiovascular Angiography and Interventions, and the Society for Cardiovascular Magnetic Resonance. *Circulation* 2010; **122**: e525.
9. Gregory SA, Ferencik M, Achenbach S, *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.
10. 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.
11. Mastrobuoni S, Bastarrika G, Ubilla M, *et al.* Dual-source CT coronary angiogram in heart transplant recipients in comparison with dobutamine stress echocardiography for detection of cardiac allograft vasculopathy. *Transplantation* 2009; **87**: 587.
12. 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.
13. Sigurdsson G, Carrascosa P, Yamani MH, *et al.* Detection of transplant coronary artery disease using multidetector computed tomography with adaptative multisegment reconstruction. *J Am Coll Cardiol* 2006; **48**: 772.
14. von Ziegler F, Leber AW, Becker A, *et al.* Detection of significant coronary artery stenosis with 64-slice computed tomography in heart transplant recipients: a comparative study with conventional coronary angiography. *Int J Cardiovasc Imaging* 2009; **25**: 91.
15. Kuettner A, Kopp AF, Schroeder S, *et al.* Diagnostic accuracy of multidetector computed tomography coronary angiography in patients with angiographically proven coronary artery disease. *J Am Coll Cardiol* 2004; **43**: 831.
16. Schepis T, Achenbach S, Weyand M, *et al.* Comparison of dual source computed tomography versus intravascular ultrasound for evaluation of coronary arteries at least one year after cardiac transplantation. *Am J Cardiol* 2009; **104**: 1351.
17. Salavati A, Radmanesh F, Heidari K, Dwamena BA, Kelly AM, Cronin P. Dual-source computed tomography angiography for diagnosis and assessment of coronary artery disease: systematic review and meta-analysis. *J Cardiovasc Comput Tomogr* 2012; **6(2)**: 78.
18. Rickenbacher PR, Pinto FJ, Chenzbraun A, *et al.* Incidence and severity of transplant coronary artery disease early and up to 15 years after transplantation as detected by intravascular ultrasound. *J Am Coll Cardiol* 1995; **25**: 171.
19. Rohnean A, Houyel L, Sigal-Cinqualbre A, To NT, Elfassy E, Paul JF. Heart transplant patient outcomes: 5-year mean follow-up by coronary computed tomography angiography. *Transplantation* 2011; **91**: 583.
20. Mehra MR, Crespo-Leiro MG, Dipchand A, *et al.* International Society for Heart and Lung Transplantation working formulation of a standardized nomenclature for cardiac allograft vasculopathy-2010. *J Heart Lung Transplant* 2010; **29**: 717.
21. Dressler FA, Miller LW. Necropsy versus angiography: how accurate is angiography? *J Heart Lung Transplant* 1992; **11**: S56.
22. St Goar FG, Pinto FJ, Alderman EL, *et al.* Intracoronary ultrasound in cardiac transplant recipients. In vivo evidence of ''angiographically silent'' intimal thickening. *Circulation* 1992; **85**: 979.
23. Coles DR, Smail MA, Negus IS, *et al.* Comparison of radiation doses from multislice computed tomography coronary angiography and conventional diagnostic angiography. *J Am Coll Cardiol* 2006; **47**: 1840.
24. Bastarrika G, Broncano J, Arraiza M, *et al.* Systolic prospectively ECG-triggered dual-source CT angiography for evaluation of the coronary arteries in heart transplant recipients. *Eur Radiol* 2011; **21**: 1887.
25. Davidson C, Stacul F, McCullough PA, *et al.* Contrast medium use. *Am J Cardiol* 2006; **98**: 42K.
26. Friedewald VE, Goldfarb S, Laskey WK, McCullough PA, Roberts WC. The editor's roundtable: contrast-induced nephropathy. *Am J Cardiol* 2007; **100**: 544.
27. McCullough PA, Adam A, Becker CR, *et al.* Epidemiology and prognostic implications of contrast-induced nephropathy. *Am J Cardiol* 2006; **98**: 5K.
28. Benza RL, Zoghbi GJ, Tallaj J, *et al.* Palliation of allograft vasculopathy with transluminal angioplasty: a decade of experience. *J Am Coll Cardiol* 2004; **43**: 1973.
29. Stork S, Behr TM, Birk M, *et al.* Assessment of cardiac allograft vasculopathy late after heart transplantation: when is coronary angiography necessary? *J Heart Lung Transplant* 2006; **25**: 1103.