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# NONINVASIVE DIAGNOSIS CORONARY COMPUTED TOMOGRAPHIC ANGIOGRAPHY LESIONS OF CORONARY ARTERIES OF THE TRANSPLANTED HEART

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**Background.** Coronary artery disease (CAD) is one of the leading causes of graft loss after heart transplantation (HT). Owing to cardiac denervation, myocardial ischemia in transplanted hearts is typically clinically silent, necessitating regular screening of recipients to detect transplant vasculopathy. Routine annual invasive coronary angiography (iCAG), however, is associated with potentially life-threatening complications, prompting the search for safe and equally effective non-invasive diagnostic alternatives. Multislice computed tomography coronary angiography (MSCT-CAG) has been widely and successfully used for many years in CAD diagnosis, with a high class and level of evidence, and has long been an alternative to iCAG. This underscores the relevance of evaluating its applicability in heart transplant recipients. **Objective:** to assess the diagnostic effectiveness of MSCT-CAG in detecting cardiac allograft vasculopathy in comparison with iCAG. **Materials and methods.** The study included 46 heart transplant recipients (36 men, 78%) aged 29–68 years (mean age 51.1 ± 10.9 years) who underwent HT between 2012 and 2023. The interval from transplantation to CAG ranged from 201 to 4,285 days (mean 1,097 days). All patients underwent scheduled iCAG and MSCT-CAG. Coronary arteries were evaluated using a 16-segment model. Segments that could not be reliably assessed on MSCT-CAG images were excluded from the analysis. **Results.** Heart rate during MSCT-CAG ranged from 65 to 105 beats per minute (median 90 bpm) and was not adjusted with medication prior to scanning. Invasive CAG allowed assessment of 690 coronary segments, while 683 segments were of diagnostic quality on MSCT-CAG. According to iCAG, coronary lesions were identified in 25 segments. MSCT-CAG detected lesions in 15 segments, yielded false-positive findings in 14 segments, and failed to identify stenoses detected by invasive CAG in 10 segments. X-ray dose was significantly higher during MSCT-CAG (22.6 mSv) compared with iCAG (10 mSv; p = 0.001). MSCT-CAG also required a larger volume of contrast medium (90 mL *vs.* 60 mL; p = 0.001). Serum creatinine levels before and after MSCT-CAG were 91.35 ± 18.09 and 95.17 ± 18.53 μmol/L, respectively, while glomerular filtration rate (GFR) values were 86.28 ± 17.79 and 82.96 ± 17.72 mL/min/1.73 $m^2$. Despite the higher contrast load and compromised renal function due to the nephrotoxicity of immunosuppressive therapy, no cases of contrast-induced nephropathy were observed following MSCT-CAG. Comparative analysis demonstrated that MSCT-CAG had a sensitivity of 60%, specificity of 97%, positive predictive value of 52%, and negative predictive value of 98% relative to iCAG. **Conclusion.** In the diagnosis of cardiac allograft vasculopathy, MSCT-CAG can be used to rule out coronary artery stenosis, demonstrating high specificity (97%) and negative predictive value (98%). The use of MSCT-CAG for the detection of stenosis/restenosis of the coronary vasculature in transplanted hearts requires further study.

*Keywords: cardiac allograft vasculopathy, MSCT coronary angiography, heart transplant.*

## INTRODUCTION

Coronary artery disease is the leading cause of graft functional decline following heart transplantation (HT). Early detection and timely management of cardiac allograft vasculopathy (CAV) are therefore critical for improving long-term outcomes in transplant recipients [1].

According to the 2023 guidelines of the International Society for Heart and Lung Transplantation (ISHLT), invasive coronary angiography (iCAG) remains the reference standard for diagnosing CAV [2]. At the same time, current clinical guidelines strongly recommend (Class I, Level A) the use of multislice computed tomography coronary angiography (MSCT-CAG) for the detection of coronary artery disease in patients with ischemic heart disease [3]. This has led to increasing interest in the application of this noninvasive modality in heart transplant recipients.

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To date, several studies have demonstrated the high diagnostic accuracy of MSCT-CAG in detecting coronary pathology in this patient population [4–7]. A meta-analysis of 13 prospective studies evaluating MSCT-CAG in patients after HT, which included 615 patients (mean age 52 years, 83% male) and analyzed 9,481 coronary segments, demonstrated that, in HT recipients, MSCT-CAG achieves a sensitivity of 94%, specificity of 92%, negative predictive value (NPV) of 99%, and positive predictive value (PPV) of 67% for the detection of stenoses >50% compared with iCAG. The incorporation of quantitative plaque analysis may further enhance sensitivity for detecting CAV [8].

Overall, current evidence suggests that MSCT-CAG is a sufficiently informative noninvasive modality for visual assessment of the coronary vasculature in HT recipients, with sufficiently high sensitivity (86–89%) and specificity (89–99%). It is important to note that, although iCAG is the gold standard for diagnosing CAV, it requires hospitalization and is associated with procedural risks. The growing number of transplant recipients under long-term follow-up underscores the need for noninvasive screening approaches. In this context, MSCT-CAG may serve as a valuable tool for identifying patients with signs of CAV and assessing disease progression, thereby helping to define indications and prioritize hospitalization.

**Objective:** to evaluate the diagnostic effectiveness of MSCT-CAG in detecting CAV in comparison with iCAG.

## MATERIALS AND METHODS

The study included 46 heart transplant recipients (36 men, 78%) aged 29–68 years (mean age 51.1 ± 10.9 years) who underwent HT between 2012 and 2023. The interval from transplantation to CAG ranged from 201 to 4,285 days (mean, 1,097 days). The clinical characteristics of the study population are presented in Table 1.

All recipients underwent both elective iCAG and MSCT-CAG. Assessment of the coronary vasculature was performed using the 16-segment model proposed by the American Heart Association [9]. Segments that were not assessable on MSCT-CAG were excluded from the analysis.

Heart rate during the procedure and changes in serum creatinine levels were also recorded. Contrast-induced nephropathy was defined as an increase in serum creatinine of more than 25% from baseline.

Table 1

**Clinical characteristics of the patients**

| Quantitative indicators | M ± SD / Me | n | min | max |
|---|---|---|---|---|
| Age, years | 51.13 ± 10.95 | 46 | 29.00 | 68.00 |
| BMI, kg/m$^2$ | 27.58 ± 3.91 | 46 | 18.80 | 35.80 |
| Time from HT, Me (days) | 1097.50 | 46 | 201.00 | 4285.00 |
| Serum creatinine level before MSCT-CAG, μmol/L | 91.35 ± 18.09 | 46 | 58.00 | 140.00 |
| GFR before MSCT-CAG, ml/min/1.73 m$^2$ | 86.28 ± 17.79 | 46 | 53.00 | 119.40 |
| EF, Me (%) | 65.00 | 46 | 46.00 | 73.00 |
| EDV, Simpson–L, Me (mL) | 78.00 | 46 | 59.00 | 122.00 |
| ESV, Simpson–L, Me (ml) | 28.50 | 46 | 18.00 | 59.00 |

| Absolute indicators | Categories | n | % |
|---|---|---|---|
| Recipient's gender | male | 36 | 78.3 |
| | female | 10 | 21.7 |
| Reason for performing the HT procedure | DCM | 22 | 47.8 |
| | ICM | 21 | 45.7 |
| | Other reasons | 3 | 6.5 |
| Diabetes | Present | 9 | 19.6 |
| | Absent | 37 | 80.4 |
| High blood pressure | Present | 29 | 63.0 |
| | Absent | 17 | 37.0 |
| Dyslipidemia | Present | 23 | 50.0 |
| | Absent | 23 | 50.0 |
| Chronic kidney disease | Present | 18 | 39.1 |
| | Absent | 28 | 60.9 |

*Abbreviations:* BMI, body mass index; GFR, glomerular filtration rate; MSCT-CAG, multislice computed tomography coronary angiography; EF, ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume; DCM, dilated cardiomyopathy; ICM, ischemic cardiomyopathy.

All patients underwent a standard diagnostic workup, including 12-lead electrocardiography (ECG) and transthoracic echocardiography. ECG recordings were obtained using a Megacart system (Siemens, Germany), and echocardiography was performed with a VIVID 9 system (GE Healthcare, USA).

Conventional multiprojection CAG was carried out using the Judkins technique via femoral or radial access on an ALLURA XPER system (Philips, Netherlands). The standard imaging protocol included five projections for the left coronary artery and two for the right coronary artery.

Statistical analysis was performed using standard methods with Microsoft Excel and IBM SPSS Statistics software (version 22).

## RESULTS

At the first stage, all patients underwent iCAG. Radial access was used in 63% of cases (n = 29), while femoral access was employed in the remaining 37% (n = 17). The procedure was technically successful in all cases, with no intra-procedural complications or instances of contrast-induced nephropathy observed.

Based on angiographic findings, a total of 690 coronary segments were evaluated. Of these, 665 segments showed no evidence of lesions, while stenoses were identified in 25 segments. Chronic total occlusions were detected in 2 cases. Previously implanted stents were patent, with no signs of stenosis.

Lesions were localized as follows: in proximal segments – left anterior descending (LAD) artery (n = 5), left circumflex (LCx) artery (n = 1), and right coronary artery (RCA) (n = 2); in middle segments – LAD (n = 8), LCx (n = 1), and RCA (n = 2); and in distal segments – LAD (n = 5) and the diagonal branch (n = 1). No stenoses were identified in the left coronary artery (LCA), the distal segments of LCx and RCA, or in the second diagonal branch (D2), obtuse marginal artery (OMA), posterolateral artery (PLA) and posterior descending artery (PDA) of the RCA. No cases of coronary circulation involving an intermediate artery were observed.

At the second stage, occurring 1–3 days later, all recipients underwent MSCT-CAG. The procedure was technically successful in 100% of cases. Heart rate during MSCT-CAG ranged from 65 to 105 beats per minute (mean, 90 bpm) and was not pre-adjusted with medication.

According to MSCT-CAG data, 683 coronary segments were of diagnostic quality. Seven segments were excluded from analysis due to inability to reliably assess them: three because of poor image quality, two due to imaging artifacts, and two due to the inability to perform quantitative assessment, with these interpreted as diffuse lesions.

654 segments were free of lesions, while stenoses were identified in 29 segments. Lesions were localized as follows: proximal segments – LAD artery (n = 7), LCx artery (n = 1), and RCA (n = 4); middle segments – LAD artery (n = 7) and LCx artery (n = 1); distal segments – LAD artery(n = 3) and the diagonal branch (n = 2).

No stenoses were detected in the LCA trunk, distal LCx and RCA segments, or in the D2, OMA, PLA, or PDA of the RCA.

The results of iCAG and MSCT-CAG are illustrated in Fig. 1 using the 16-segment coronary artery model proposed by the American Heart Association.

A comparative analysis of MSCT-CAG and iCAG findings showed that, according to iCAG, lesions were identified in 25 segments. MSCT-CAG correctly detected 15 of these lesions, while 14 segments were classified as false-positive. In addition, 10 stenotic segments identified by iCAG were not detected by MSCT-CAG.

Based on these results, the diagnostic performance of MSCT-CAG for detecting CAV was as follows: sensitivity – 60%, specificity – 97%, PPV – 52%, and NPV – 98%.

A comparison of radiation exposure and contrast agent volume between the two methods was also performed (Table 2).

It should be noted that the radiation dose associated with MSCT-CAG was higher than that of conventional CAG (22.6 mSv *vs.* 10 mSv; p = 0.001). In addition, MSCT-CAG required a larger volume of contrast medium (90 mL *vs.* 60 mL; p = 0.001).

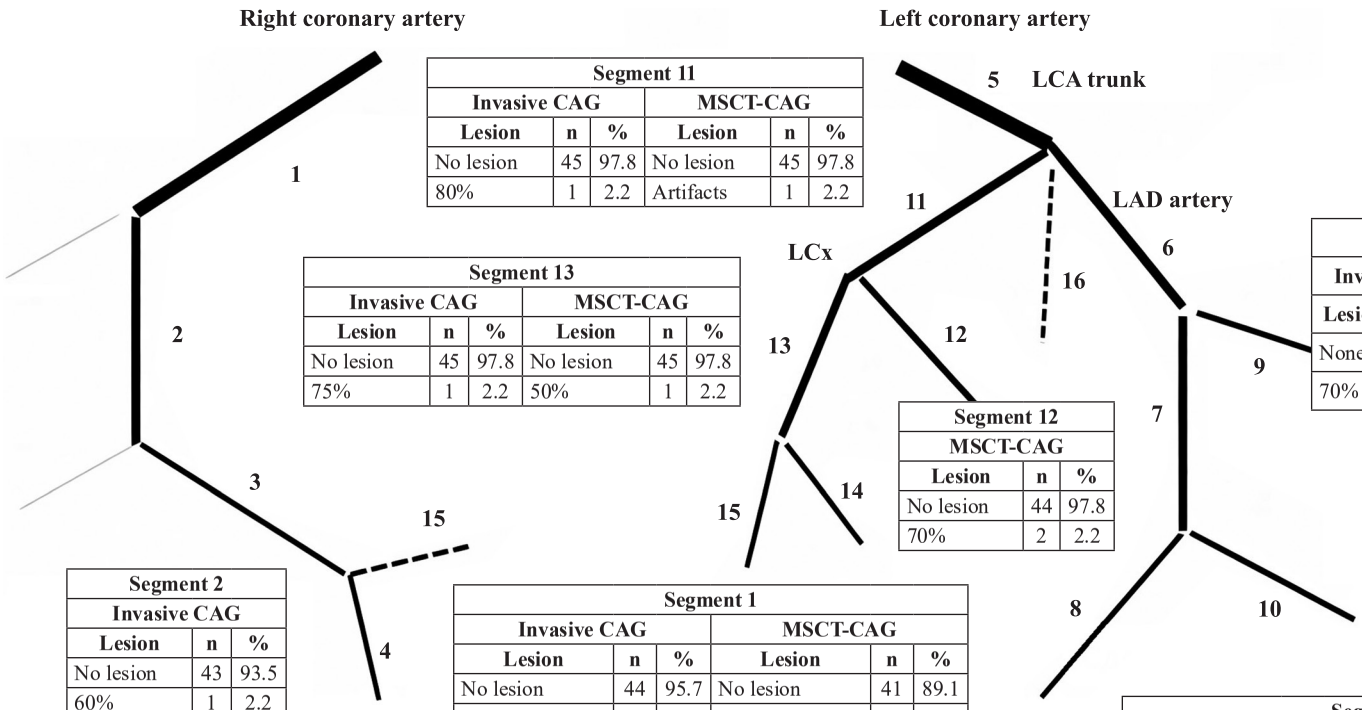
An analysis of renal function parameters before and after MSCT-CAG demonstrated minimal changes. Mean serum creatinine increased slightly from 91.35 ± 18.09 to 95.17 ± 18.53 μmol/L, while estimated glomerular filtration rate (eGFR) decreased from 86.28 ± 17.79 to 82.96 ± 17.72 mL/min/1.73 $m^2$. Further analysis evaluated the dynamics of serum creatinine and eGFR depending on the presence or absence of chronic kidney disease (CKD) (Fig. 2).

In recipients without CKD, serum creatinine levels did not differ significantly before and after MSCT-CAG (p = 0.896), measuring 74.36 ± 7.8 and 74.62 ± 8.48 μmol/L, respectively. In contrast, patients with CKD showed a statistically significant increase in serum creatinine following MSCT-CAG (p = 0.005), from 95.49 ± 17.5 μmol/L before the procedure to 100.17 ± 16.79 μmol/L afterward.

Table 2

**Comparison of radiation dose and volume of contrast agent used**

| Parameters | Groups | | p |
|---|---|---|---|
| | Invasive CAG | MSCT-CAG | |
| Dose, Me [IQR] | 10.00 [6.65; 11.30] | 22.60 [21.02; 25.00] | 0.001 |
| Contrast agent, Me [IQR] | 60.00 [50.00; 60.00] | 90.00 [90.00; 95.00] | 0.001 |




| Segment 11 | | | | | |
|---|---|---|---|---|---|
| Invasive CAG | | | MSCT-CAG | | |
| Lesion | n | % | Lesion | n | % |
| No lesion | 45 | 97.8 | No lesion | 45 | 97.8 |
| 80% | 1 | 2.2 | Artifacts | 1 | 2.2 |

| Segment 13 | | | | | |
|---|---|---|---|---|---|
| Invasive CAG | | | MSCT-CAG | | |
| Lesion | n | % | Lesion | n | % |
| No lesion | 45 | 97.8 | No lesion | 45 | 97.8 |
| 75% | 1 | 2.2 | 50% | 1 | 2.2 |

| Segment 12 | | |
|---|---|---|
| MSCT-CAG | | |
| Lesion | n | % |
| No lesion | 44 | 97.8 |
| 70% | 2 | 2.2 |

| Segment 6 | | | | | |
|---|---|---|---|---|---|
| Invasive CAG | | | MSCT-CAG | | |
| Lesion | n | % | Lesion | n | % |
| No lesion | 41 | 89.1 | No lesion | 38 | 80.4 |
| 50% | 3 | 6.5 | Occlusion | 1 | 2.2 |
| 60% | 1 | 2.2 | 20% | 1 | 2.2 |
| Occlusion | 1 | 2.2 | 30% | 1 | 2.2 |
| | | | 35% | 1 | 2.2 |
| | | | 50% | 2 | 4.3 |
| | | | 75% | 1 | 2.2 |
| | | | Diffuse changes | 1 | 2.2 |
| | | | Reliable assessment not possible | 1 | 2.2 |

| Segment 9 | | | | | |
|---|---|---|---|---|---|
| Invasive CAG | | | MSCT-CAG | | |
| Lesion | n | % | Lesion | n | % |
| None | 45 | 97.8 | None | 44 | 96 |
| 70% | 1 | 2.2 | 30% | 1 | 2.2 |
| | | | 50% | 1 | 2.2 |

| Segment 7 | | | | | |
|---|---|---|---|---|---|
| Invasive CAG | | | MSCT-CAG | | |
| Lesion | n | % | Lesion | n | % |
| No lesion | 37 | 80.4 | No lesion | 35 | 77.8 |
| Occlusion | 1 | 2.2 | Occlusion | 2 | 4.4 |
| 50% | 2 | 4.3 | 40% | 1 | 2.2 |
| 60% | 2 | 4.3 | 50% | 3 | 6.7 |
| | | | 60% | 1 | 2.2 |
| | | | 80% | 2 | 4.4 |
| | | | Artifact | 1 | 2.2 |
| | | | Reliable assessment not possible | 1 | 2.2 |

| Segment 2 | | |
|---|---|---|
| Invasive CAG | | |
| Lesion | n | % |
| No lesion | 43 | 93.5 |
| 60% | 1 | 2.2 |
| 70% | 1 | 2.2 |
| Patent stent, no restenosis | 1 | 2.2 |

| Segment 1 | | | | | |
|---|---|---|---|---|---|
| Invasive CAG | | | MSCT-CAG | | |
| Lesion | n | % | Lesion | n | % |
| No lesion | 44 | 95.7 | No lesion | 41 | 89.1 |
| 50% | 1 | 2.2 | 25% | 1 | 2.2 |
| 70% | 1 | 2.2 | 35% | 1 | 2.2 |
| | | | 50% | 1 | 2.2 |
| | | | 60% | 1 | 2.2 |
| | | | Diffuse changes | 1 | 2.2 |

| Segment 8 | | | | | |
|---|---|---|---|---|---|
| Invasive CAG | | | MSCT-CAG | | |
| Lesion | n | % | Lesion | n | % |
| No lesion | 41 | 89.1 | No lesion | 42 | 93.3 |
| 70% | 1 | 2.2 | 10% | 1 | 2.2 |
| 75% | 3 | 6.5 | 80% | 1 | 2.2 |
| Occlusion | 1 | 2.2 | Occlusion | 1 | 2.2 |
| | | | Reliable assessment not possible | 1 | 2.2 |

| Coronary segments without lesions | |
|---|---|
| Invasive CAG | MSCT-CAG |
| 3, 4, 5, 10, 12, 14, 15 | 2, 3, 4, 5, 10, 14, 15 |

Fig. 1. Results of invasive CAG and MSCT-CAG assessed using the 16-segment coronary artery model according to the American Heart Association classification. Right coronary artery (RCA): segment 1 – proximal RCA; 2 – mid RCA; 3 – distal RCA; 4 – posterior descending artery. Left coronary artery (LCA): segment 5 – left main coronary artery; 6 – proximal left anterior descending artery (LAD); 7 – mid LAD; 8 – distal LAD; 9 – first diagonal branch; 10 – second diagonal branch; 11 – proximal circumflex artery (LCx); 12 – first obtuse marginal branch; 13 – distal LCx; 14 – posterolateral branch; 15 – LCA; 16 – intermediate (ramus intermedius) branch

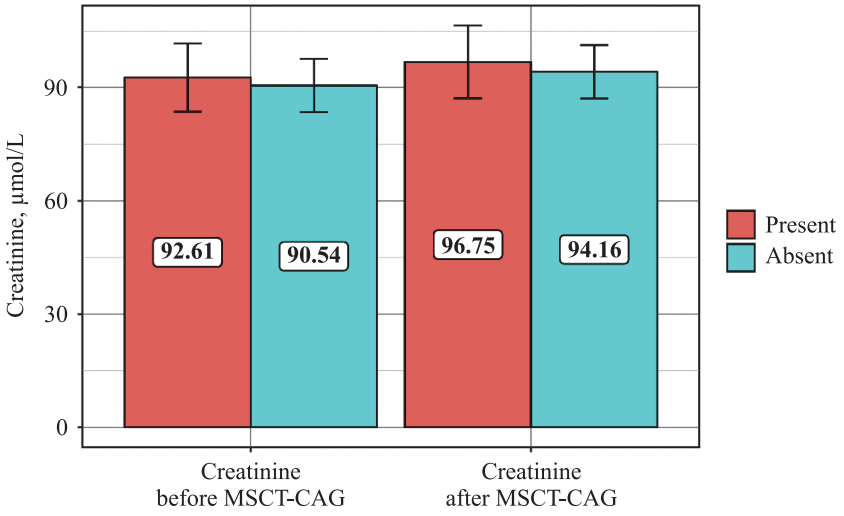



Fig. 2. Analysis of serum creatinine dynamics depending on the presence or absence of CKD

Notably, despite a significant increase in serum creatinine levels in recipients with CKD following MSCT-CAG, this increase did not exceed 5% of the baseline value.

## DISCUSSION

Over the past 15 years, the number of HT performed in Russia has increased substantially, reaching 450 procedures in 2024, of which 294 were carried out at Shumakov National Medical Research Center of Transplantology and Artificial Organs in Moscow. As a result, more than 3,000 recipients are currently under follow-up [10].

CAV remains the leading cause of graft loss. According to data from the ISHLT registry, it is detected in nearly 50% of recipients 10 years after transplantation [1, 11]. This underscores the need for continuous surveillance of the coronary vasculature.

Invasive CAG remains the gold standard for diagnosing CAV (Class I, Level of Evidence A, according to the 2023 ISHLT guidelines). However, the procedure is associated with a risk of life-threatening complications (arrhythmias, contrast-induced acute kidney injury, acute cerebrovascular events, coronary artery dissection, and bleeding at arterial access sites). Although the overall incidence of such complications is relatively low (approximately 1.8%), they may be life-threatening, with reported mortality rates of up to 0.1% [12].

In this context, there is a growing need to identify effective, noninvasive alternatives for diagnosing coronary artery disease in transplanted hearts. Recent studies indicate that the diagnostic results from such methods in HT recipients are becoming comparable to those obtained in patients with ischemic heart disease.

In a 2020 study by Foldyna et al., using a second-generation 128-slice MSCT scanner with quantitative coronary segment analysis, 50 HT recipients (84% men) with a mean age of 53.6 ± 11.9 years and a mean post-transplant follow-up of 6.7 ± 4.7 years were evaluated, including patients both with and without previously confirmed vasculopathy. The interval between iCAG and MSCT-CAG was one day.

Mean radiation dose was 5.8 mSv. Among the study population (42 men and 8 women), the prevalence of CAV was 38% (19/50). At a mean heart rate of 74.1 ± 8.5 bpm, MSCT-CAG provided diagnostic-quality images for 692 coronary segments, of which 632 (91.4%) were comparable with CAG findings, while 56 segments were excluded due to poor image quality. Of the 632 evaluable segments, 190 (30.1%) were proximal and 442 (69.9%) were distal, with distal segments affected more frequently. Quantitative analysis of the coronary wall revealed that fibrous tissue accounted for 44.7%, fibro-fatty tissue for 18.6%, non-calcified (soft) plaques for 8.5%, and calcified plaques for 1.0%. Distal segments were affected more frequently than proximal ones.

This study demonstrated that MSCT-CAG is highly effective in detecting clinically significant stenoses (≥50%) and shows good agreement with iCAG in HT recipients, with an NPV of 98–100%, sensitivity of 78%, and specificity of 75%. Importantly, MSCT-CAG also enables early detection of CAV through quantitative assessment of plaque volume and composition, thereby facilitating timely adjustment of medical therapy [13].

In a subsequent 2022 study by Ojha et al., the diagnostic accuracy of dual-source MSCT (192-detector, 384-slice) for the CAV detection was evaluated in comparison with iCAG. The study included 38 patients, of whom 27 were men. The mean age of the patients was 33.66 ± 11.45 years, and the time since HT ranged from 10 to 226 months (median: 23.5 months). The prevalence of CAV (stenosis grades 1–5) was 44.7% (n = 17) according to MSCT-CAG and 39.5% (n = 15) based on iCAG. Clinically significant lesions (CAV grades 3–5)

were identified in 21.1% of patients (n = 8) by MSCT-CAG and in 15.8% (n = 6) by iCAG.

Diagnostic image quality was considered acceptable in 557 of 576 coronary segments (96.7%). Mean radiation dose was 4.24 ± 2.15 mSv for MSCT-CAG and 4.8 ± 1.8 mSv for iCAG, while the average volume of contrast agent used was 42 mL At the patient level, the detection of signs of vasculopathy of any severity showed a sensitivity of 100%, specificity of 91.3%, PPV of 88.2%, NPV of 100%, and an overall diagnostic accuracy of 94.73%. For the identification of clinically significant stenotic lesions, sensitivity remained 100%, while specificity was 94%, PPV 75%, NPV 100%, and diagnostic accuracy 95%.

Similar results were obtained in the segment-based analysis, with sensitivity, specificity, PPV, and NPV of 96%, 97.6%, 80%, and 99.6%, respectively. Notably, these outcomes were achieved at a relatively low radiation dose (4.24 ± 2.16 mSv), demonstrating high diagnostic accuracy of MSCT-CAG for detecting both early and significant manifestations of CAV when compared with iCAG [9].

When considered alongside the findings of the present study, which demonstrated a high specificity of 97% and an NPV of 98%, these data support the use of MSCT-CAG (including on an outpatient basis) for ruling out coronary lesions in transplanted hearts. This will optimize patient selection for hospitalization.

Another important consideration is the ability of MSCT-CAG to detect clinically significant coronary lesions. Based on both published data and the findings of the present study, the sensitivity of MSCT-CAG in assessing CAV remains insufficient to unequivocally support its use for precise grading of disease severity or for determining indications for revascularization.

It should also be emphasized that the diagnostic performance of MSCT-CAG in detecting coronary lesions is influenced by multiple factors, including the spatial resolution of the CT scanner, the presence of artifacts (e.g., sternal clamps, ECG leads and electrodes), heart rate during image acquisition, and the diameter of the evaluated coronary segments. These limitations highlight the need for further investigation.

## CONCLUSION

MSCT-CAG may be considered a useful noninvasive modality for the evaluation of CAV, particularly for ruling out significant stenotic lesions, given its high specificity (97%) and NPV (98%).

Despite the requirement for a higher volume of contrast agent and the presence of baseline renal impairment in many heart transplant recipients due to the nephrotoxic effects of immunosuppressive therapy, no cases of contrast-induced nephropathy were observed following MSCT-CAG in this study.

However, the role of MSCT-CAG in reliably detecting stenoses or restenoses in the coronary vasculature of transplanted hearts requires further study.

*The authors declare no conflict of interest.*

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