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# Comparison of Coronary Artery Calcium Scoring with Dobutamine Stress Echo for Detection of Coronary Artery Disease Before Liver Transplantation

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**Background:** Dobutamine stress echocardiography (DSE) is commonly used for cardiovascular assessment before orthotopic liver transplantation (OLT). The coronary artery calcium score (CACS) is a useful screening tool for coronary artery disease (CAD). We aimed to compare the sensitivity and specificity of DSE and CACS for CAD in OLT candidates.

**Material/Methods:** A total of 265 of the 1589 patients who underwent OLT at our center between 2008 and 2019 had preoperative coronary angiography (CAG). Of these, 173 had DSE and 133 had a CT scan suitable for CACS calculation within 1 year of OLT. Patients with a nondiagnostic DSE were excluded (n=100). Two reviewers evaluated CACS on CT scans. The sensitivity/specificity of DSE and CACS for detection of angiographically significant CAD were calculated for patients with both tests (n=36).

A separate analysis compared the sensitivity/specificity of a diagnostic DSE (n=73) and CACS (n=133) against CAG for all patients with either test.

**Results:** Sensitivity and specificity were 57.1% and 89.7%, respectively, for DSE, compared with 71.4% and 62.1% for CACS at ≥100 Agatston score. For the analysis of all patients with either test, the sensitivity/specificity of DSE for detection of CAD and CACS were 30.8% and 85.0% and 80.0% and 62.8%, respectively. On ROC analysis, CACS was a satisfactory predictor of obstructive CAD (AUC, 0.76±0.06, 95% CI, 0.66-0.87; $P$<0.001).

**Conclusions:** CACS may be an important tool for cardiovascular assessment in patients undergoing OLT. DSE was nondiagnostic in a large percentage of OLT candidates, limiting its use in this population.

**Keywords:** **Coronary Artery Disease • Coronary Vessels • Echocardiography, Stress • Liver Transplantation**





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**Abbreviations:** **CACS** – coronary artery calcium scoring; **DSE** – dobutamine stress echocardiography; **CAD** – coronary artery disease; **OLT** – orthotopic liver transplant; **CAG** – coronary angiography; **CT** – computerized tomography; **AS** – Agatson score; **ROC** – receiver operating characteristic; **CI** – confidence interval; **SD** – standard deviation

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## Background

Major adverse cardiovascular events have a significant impact on survival after orthotopic liver transplantation (OLT). While cardiovascular mortality after liver transplantation has declined, it remains a leading cause of early and late mortality after transplantation [1]. The presence of pre-existing coronary artery disease (CAD) is one such predictor of early cardiovascular mortality [1]. Therefore, it is essential to stratify the risk for ischemic CAD in patients listed for OLT. The current American Association for the Study of Liver Disease guidelines recommend that patients with traditional risk factors for CAD, including diabetes, smoking, and obesity [2], should undergo noninvasive testing with stress echocardiography, and subsequently with coronary angiography (CAG) if CAD cannot be definitively excluded (class IB recommendation) [3]. Dobutamine stress echocardiography (DSE) is a widely used screening test for preoperative risk assessment before OLT. Existing literature suggests that the sensitivity of DSE for CAD is low in liver transplant patients, ranging from 13% to 41% [4-6]. Furthermore, patients with cirrhosis have hyperdynamic ventricles with poor chronotropic response as well as vasodilated circulatory systems with a low systemic vascular resistance [7]. Hence, they may not meet the target heart rate or generate an appropriate heart rate response to dobutamine required for the pharmacologic stress test to be considered diagnostic. As a result, many patients with cirrhosis have a nondiagnostic DSE test and subsequently need invasive CAG for risk stratification, which has its own associated risks of bleeding and contrast-induced nephropathy [8].

In patients with end-stage liver disease, the coronary artery calcium score (CACS) has been shown to have a positive correlation with many cardiovascular risk factors, such as family history of cardiovascular disease, systolic/diastolic blood pressure, and metabolic syndrome [9]. Additionally, some studies, including a study by Agatston et al, which defined a "high" CACS as ≥400 AS, found that that a high CACS is associated with higher rates of early postoperative cardiac complications after liver transplantation, including nonfatal myocardial infarction, arrhythmia, heart block, and cardiac death [10]. Patients with higher CACSs are also more likely to have significant CAD (defined as > 50% occlusive disease) [11].

We postulated that the CACS may be a useful tool for cardiovascular risk stratification prior to OLT and be a good alternative test in many patients when DSE is nondiagnostic or inconclusive. The CACS offers several advantages, including that it is noninvasive, does not require contrast administration, and does not require patients to reach a target heart rate [12]. While the sensitivity and specificity of CACS and DSE have been assessed independently in OLT candidates, they have not been directly compared against each other in the same sample of patients for their ability to detect CAD against the criterion standard test, CAG. The goal of this study was to compare the diagnostic accuracy of DSE with CACS for the detection of significant CAD in patients undergoing OLT.

## Material and Methods

This was a retrospective observational study which included all consecutive patients undergoing OLT at a high-volume tertiary care transplant center between 2008 and 2019 (n=1589). The patients who did not undergo CAG 1 year prior to OLT were excluded (n=1324). This study was approved by the institution's Institutional Review Board, and informed consent was not required. Data regarding demographics, baseline comorbidities, and results of the most recent CAG (just prior to OLT) were retrieved by a manual chart review of electronic medical records. Additionally, we gathered the results of DSE for patients who had it as their initial preoperative cardiac screening test prior to CAG (n=173). Patients with a nondiagnostic DSE were excluded (n=100). We also identified patients who had a non-contrast computed tomography (CT) scan of the chest suitable for calcium scoring (n=133) within 1 year prior to OLT. Patients who had a history of coronary stents or coronary artery bypass graft were excluded for CT calcium scoring, since the software used interpreted stents and grafts as calcium and therefore would have confounded the results.

For patients who had a suitable CT scan of the chest, the CACS was calculated using radiology software (syngo.via). The calcium score was first calculated for a small subset of patients (n=30) by 2 independent scorers to ensure consistent intra- and inter-rater reliability. The intra-class correlation of the CACS





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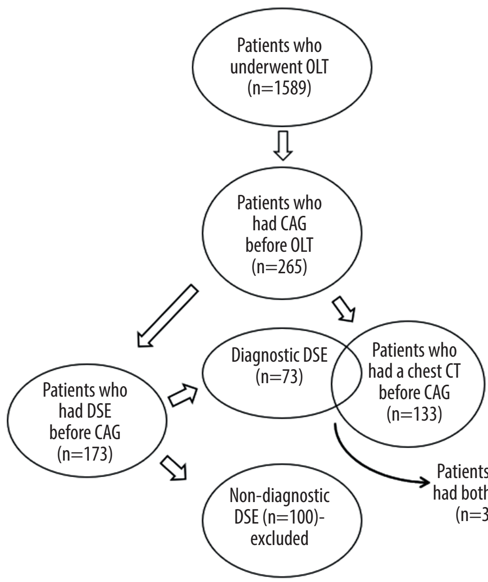


**Figure 1. Flow diagram of study population selection.** A total of 265 patients underwent coronary angiography prior to orthotopic liver transplantation. Of this sample, 173 patients had dobutamine stress echocardiography (DSE). Only patients with a diagnostic DSE were used for data analysis (n=73). A total of 133 patients had a chest computed tomography scan suitable for calcium scoring. A total of 36 patients had a diagnostic DSE and could be used for the head-to-head comparison of the 2 tests. *Figure was created using Microsoft Word version 2010.*

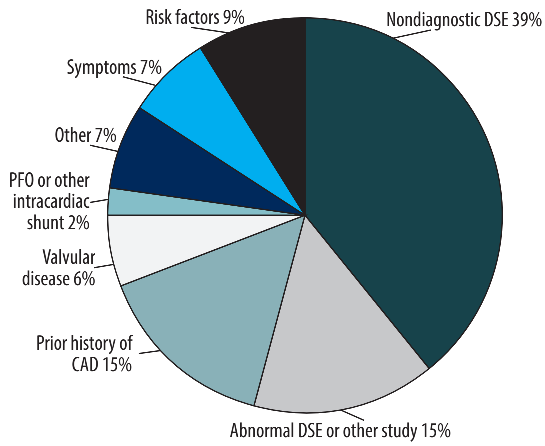


**Figure 2. Distribution of various indications for angiography.** Of the 265 patients who had coronary angiography (CAG), manual chart review was performed to determine why the patients were referred for CAG. The most common reason for referral for CAG was nondiagnostic dobutamine stress echocardiography (DSE) (39%), followed by an abnormal DSE (15%), and prior history of coronary artery disease (15%). *Figure was created using Microsoft Word version 2010.*

for scorer A was 0.88 (95% confidence interval [CI] 0.80-0.94) and for scorer B was 1.00 (95% CI 1.00-1.00). Inter-class correlation at patient level was 0.90 (0.83-0.94). The rest of the patients were evaluated by either scorer A or B. For the purpose of our study, significant CAD was defined as ≥50% occlusion of the left main coronary artery or ≥70% occlusion in any of the other coronary arteries (left anterior descending, ramus intermedius, right coronary artery, or left circumflex artery), or one of their branches (septal perforator, diagonal, obtuse marginal, posterolateral, or posterior descending artery).

### Statistical Analysis

Continuous data were reported as medians (interquartile range) and means (standard deviation) based on the distribution of the data. Categorical data were reported as a count (proportion). We used the Wilcoxon rank-sum test and *t* test to compare medians and means, respectively. Pearson's chi-squared test was used for comparing categorical data. Patients missing either DSE or CACS were excluded. The sensitivity and specificity of the CACS was calculated at various CACS cutoffs (≥100, 200, 300, and 400 Agatston score [AS]), and the cutoff with the highest area under the receiver operating characteristic (ROC) curve (AUC) was used. For the head-to-head comparison, the sensitivity and specificity of DSE and CACS were compared using CAG as the criterion standard test among patients who had both a diagnostic DSE and CT scan that could be used for the CACS. For the direct comparison between the 2 tests, the sensitivity and specificity of DSE and CACS were compared using a 2×2 contingency table stratified by the actual CAD outcome. The sensitivity and specificity of DSE and CACS were statistically significantly different if the confidence interval did not include 0. Additional secondary analyses were conducted to evaluate the diagnostic accuracy of DSE and CACS compared separately with CAG for all patients who had a diagnostic result for either test. All sensitivity/specificity analyses were done using STATA SE 13 (STATA Corp, College Station, TX, USA). ROC analysis was performed using CACSs for their ability to detect presence of obstructive CAD using SPSS version 25 (IBM Corp, Armonk, NY, USA). No adjustments were performed for multiplicity. A *P* value <0.05 was considered statistically significant.

## Results

Our cohort consisted of 265 patients who underwent invasive CAG prior to OLT. Fifty-one patients out of the 265 were excluded because they had neither a DSE nor a chest CT suitable for calcium scoring. Of the remaining cohort, 133 had chest CT scans suitable to calculate CACS, and 173 had a DSE prior





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**Table 1.** Baseline characteristics of patients.

| | All patients (n=265) | DSE (n=173) | CACS (n=133) |
|---|---|---|---|
| Average age at transplant (years) (±standard deviation) | 60.1±7.1 | 60.4±6.3 | 60.4±6.8 |
| Gender | Male: 61.5% | Male: 60.1% | Male: 59.7% |
| | Female: 27.5% | Female: 26.0% | Female: 26.9% |
| | Unknown: 10.9% | Unknown: 13.9% | Unknown: 13.4% |
| Race | White: 73.9% | White: 71.7% | White: 68.7% |
| | African American: 5.3% | African American: 5.2% | African American: 6.7% |
| | Hispanic: 3.4% | Hispanic: 3.5% | Hispanic: 3.0% |
| | Asian: 0.4% | Asian: 0.0% | Asian: 0.8% |
| | Other: 6% | Other: 5.8% | Other: 8.2% |
| | Unknown: 10.9% | Unknown: 13.9% | Unknown: 13.4% |
| Hypertension | Yes: 66.4% | Yes: 64.2% | Yes: 70.1% |
| | No: 22.6% | No: 22.0% | No: 16.4% |
| | Unknown: 11.0% | Unknown: 13.8% | Unknown: 13.5% |
| Hyperlipidemia | Yes: 37.0% | Yes: 36.4% | Yes: 37.3% |
| | No: 52.1% | No: 49.7% | No: 49.3% |
| | Unknown: 10.9% | Unknown: 13.9% | Unknown: 13.4% |
| Obesity | Yes: 23.0% | Yes: 23.1% | Yes: 28.9% |
| | No: 66.0% | No: 63.0% | No: 59.7% |
| | Unknown: 11.0% | Unknown: 13.9% | Unknown: 11.4% |
| Average MELD Score (±standard deviation) | 21.5±9.5 | 21±9.6 | 22.1±9.6 |
| Indication for OLT | ASH cirrhosis: 16.6%<br>NASH cirrhosis: 17.0%<br>HCV/HBV Cirrhosis: 10.2%<br>PSC/PBC: 7.9%<br>AH: 1.1%<br>HCC: 3.4%<br>Other: 29.1%<br>Unknown: 14.7% | ASH cirrhosis: 19.7%<br>NASH cirrhosis: 19.1%<br>HCV/HBV cirrhosis: 15.6%<br>PSC/PBC: 11.0%<br>AH: 0.6%<br>HCC: 3.5%<br>Other: 24.3%<br>Unknown: 6.2% | ASH cirrhosis: 21.6%<br>NASH cirrhosis: 18.7%<br>HCV/HBV cirrhosis: 14.9%<br>PSC/PBC: 7.5%<br>AH: 0.0%<br>HCC: 3.7%<br>Other: 30.0%<br>Unknown: 3.6% |

AH – autoimmune hepatitis; ASH – alcoholic steatohepatitis; HBV – hepatitis B virus; HCC – hepatocellular carcinoma; HCV – hepatitis C virus; NASH – non-alcoholic steatohepatitis; PBC – primary biliary cirrhosis; PSC – primary sclerosing cholangitis.

to CAG. After excluding patients with a nondiagnostic DSE (n=100), 36 patients who had both a diagnostic DSE and a CT scan suitable for calcium scoring were included in the head-to-head comparison (**Figure 1**).

Of all patients who underwent CAG, the most common reason for referral to CAG was a nondiagnostic DSE (39%), followed by an abnormal DSE/other cardiovascular screening test (15%), and a history of CAD (15%) (**Figure 2**). Of the 173 patients who had a DSE before CAG, 100 (57.8%) had a non-diagnostic DSE, usually due to failure to achieve the target maximal heart rate. The patients who were referred to CAG despite having a negative DSE were mostly referred because they had risk factors for cardiovascular disease or had symptoms that were suspected to be cardiac in origin.

Baseline characteristics for the patients are presented in **Table 1**. The mean age of the entire cohort was 60.1±7.1 years,



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**Table 2.** Sensitivity, specificity, and positive and negative predictive value of dobutamine stress echocardiography vs coronary artery calcium score (head-to-head-comparison).

| | Sensitivity | Specificity |
|---|---|---|
| DSE (n=36) | 0.571 (0.184 to 0.901) | 0.897 (0.727 to 0.978) |
| CACS with 100 as cutoff (n=36) | 0.714 (0.290 to 0.963) | 0.621 (0.423 to 0.793) |
| CACS with 400 as cutoff (n=36) | 0.571 (0.184 to 0.901) | 0.862 (0.683 to 0.961) |

**Table 3.** Sensitivity, specificity, and positive and negative predictive value of coronary artery calcium score compared with dobutamine stress echocardiography for detection of coronary artery disease prior to liver transplantation (all patients with valid result for either test).

| Outcome = obstructive CAD | Comparing equality of sensitivity | Comparing equality of specificity |
|---|---|---|
| DSE vs CACS with 100 as cutoff | 0.14 (-0.12 to 0.40) | **-0.28 (-0.51 to -0.04)** |
| DSE vs CACS with 400 as cutoff | 0.00 (-0.40 to 0.40) | -0.03 (-0.21 to 0.14) |

and 61.5% of the entire cohort were men. The CACSs ranged from 0 to 3440 AS, with an average CACS of 334.1±standard error (SE) of 51.5 AS. The mean CACS for a patient with no quantifiable CAD on CAG was 73.6 AS±SE of 21.7 AS (range: 0-870 AS). In comparison, the average CACS for a patient with obstructive CAD was 770.0 AS±SE of 194.6 AS (range: 0-3163 AS).

### DSE vs CACS: Head-to-Head Comparison

We compared the sensitivity, specificity, positive predictive value, and negative predictive values of DSE and CACS for CAD in patients who had both studies (n=36). A cutoff CACS of ≥100 was used for comparison. The CACS has a sensitivity of 71.4% for the detection of obstructive CAD, while DSE had a sensitivity of 57.1%. The specificity of DSE was significantly higher than that of the CACS when a cutoff of ≥100 AS in the CACS was used (89.7% and 62.1%, respectively). However, when the cutoff for the CACS was increased to ≥400 AS, the specificity increased to 86.2%, while the sensitivity decreased to 57.1% (**Table 2**).

### DSE and CACS Subsets (All Patients with Valid Result for Either Test)

The sensitivity and specificity of DSE and the CACS were calculated separately for all patients in the sample with a valid result for either test. In the DSE subset (n=73), the sensitivity and specificity for detecting obstructive CAD were 30.8% and 85%, respectively. In the CACS subset (n=133), the sensitivity was 80.0% at a cutoff of ≥100 AS and 55.0% at a cutoff of ≥400 AS. The specificity of the CACS was 62.8% at ≥100 AS, which improved to 79.6% at the higher cutoff of ≥400 AS (**Table 3**). Because the sensitivity and specificity were not calculated on the same patients for each test in a head-to-head

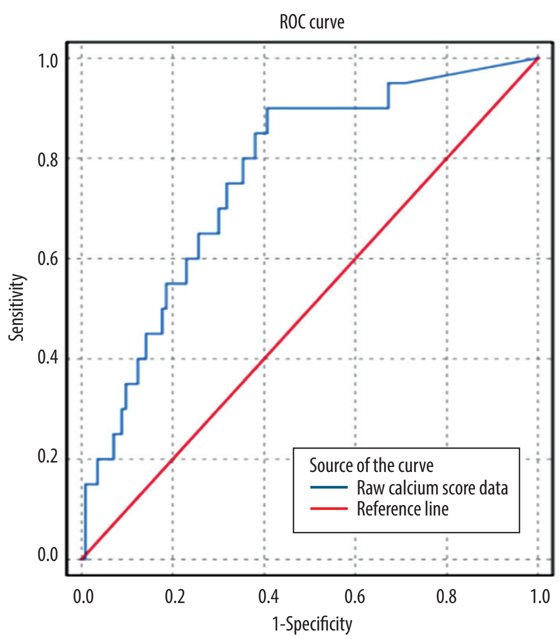


**Figure 3. Receiver operating characteristic (ROC) curve for coronary artery calcium score (CACS) to predict obstructive coronary artery disease (CAD).** Using the raw calcium score values, ROC analysis was performed to pictorially represent how the sensitivity and specificity of the CACS varied at different Agatston score (AS) values. CACS was a satisfactory predictor of the presence of obstructive CAD at a cutoff of ≥100 AS (AUC 0.76±0.06; 95% CI 0.66-0.87, *P*<0.001). *Figure was created using SPSS v25.*





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**Table 4.** Prior studies that have evaluated the sensitivity and specificity of dobutamine stress echocardiography for coronary artery disease in liver transplant candidates.

| | Sensitivity | Specificity |
|---|---|---|
| DSE (n=73) | 0.308 (0.091 to 0.614) | 0.850 (0.734 to 0.929) |
| CACS with 100 as cutoff (n=133) | 0.800 (0.563 to 0.943) | 0.628 (0.532 to 0.717) |
| CACS with 400 as cutoff (n=133) | 0.550 (0.315 to 0.769) | 0.796 (0.71 to 0.866) |

**Table 5.** Literature review: sensitivity/specificity of the coronary artery calcium score for coronary artery disease.

| Title | Number in references | Number of patients in study | Type of study | Findings |
|---|---|---|---|---|
| *Predictive value of dobutamine stress echocardiography for coronary artery disease detection in liver transplant candidates* | (4) | 64 | Retrospective chart review | DSE had a 13% sensitivity and 85% specificity for obstructive CAD |
| *Utility of dobutamine stress echocardiography as part of the pre-liver transplant evaluation: An evaluation of its efficacy* | (5) | 63 | Retrospective chart review | DSE had a 41% sensitivity and 47% specificity for moderate to severe CAD (defined as > 50% stenosis) |
| *Dobutamine stress echocardiography in patients undergoing orthotopic liver transplantation: A pooled analysis of accuracy, perioperative and long term cardiovascular prognosis* | (6) | 110 | Quantitative systematic review | DSE had a 32% sensitivity and a 78% specificity for CAD |

fashion, it was not possible to determine whether this difference was statistically significant.

The DSE and CACS subsets were also used to calculate the positive and negative predictive values for each of the tests. Using a threshold of ≥100 AS, the positive predictive value of the CACS was low at 28.2%, but the specificity was high at 93.4%. The positive predictive value of DSE was low at 28.2%, but the negative predictive value was high at 83.9%. However, the assessment of the predictive value of DSE did not include all of the patients owing to the high number of nondiagnostic studies.

ROC analysis showed that a CACS ≥100 AS was a robust predictor of the presence of obstructive CAD (AUC 0.76±0.06; 95% CI 0.66-0.87, $P$<0.001) (**Figure 3**).

## Discussion

There have been multiple studies in the past that have shown that DSE has a low sensitivity for detecting CAD in liver transplant candidates (**Table 4**). The calculated sensitivity has ranged from 13% to 41%, and the specificity has ranged from 47% to 90% [4-6,13,14]. A systematic review and meta-analysis published in 2021 found that DSE had a sensitivity of just 25% and a specificity of 68%. Despite this body of research demonstrating its suboptimal test characteristics, DSE is still used as a common preoperative cardiac risk stratifying test prior to liver transplantation at many transplant centers, including our own. In our head-to-head comparison, we found a higher sensitivity of DSE for CAD than prior studies at 57.1%, but in our larger sample of all patients with DSE, the calculated sensitivity was similar to prior studies at 30.8%.

Prior research on the CACS has demonstrated its utility as a screening test, with sensitivity ranging from 60% to 97%, depending on the AS cutoff that is used. Literature on the role of the CACS as part of OLT evaluation is more limited (**Table 5**) [15-17]. Our study found that the CACS has a similar sensitivity to DSE for detection of angiographically significant CAD at all AS cutoffs. A CACS of > 100 AS had a sensitivity of 71.4% compared with 57.1% for DSE for detection of obstructive CAD, but the difference was not statistically significant, which was likely owing to fewer number of patients in the head-to head analysis. The specificity of DSE, however was higher than that of the CACS only at the lowest CACS cutoff of ≥100 AS (89.7% vs 62.1%, 95% CI -0.51 to -0.04), but not for the higher cutoff. When we expanded our sample size to include all patients who had a valid result for either test, we found that the difference in sensitivity between the 2 tests was clinically significant (80.0% for CACS, compared with 30.8% for DSE). For this part of our analysis, the sensitivity and specificity were similar to prior studies of the CACS in the general population [15-17]. It is likely that the results of our head-to-head analysis were limited by type II error, since the number of patients in our study with obstructive CAD was relatively low. The difference in sensitivity between DSE and the CACS may reach statistical significance at larger sample sizes.

However, DSE was nondiagnostic in as many as 57.8% of patients in our study and was a frequent reason for referral to CAG for cardiovascular risk stratification prior to OLT. Of the patients who had a nondiagnostic DSE, 12.2% had obstructive CAD. Again, this highlights the need for additional complementary risk stratification testing for cirrhotic patients who have a chronic vasodilatory state or blunted chronotropic response [7]. Such a high percentage of nondiagnostic results makes DSE less desirable since more patients would be subjected to invasive CAG and its risks of bleeding and contrast-induced nephropathy in an already vulnerable population with coagulopathy and renal issues [18]. Furthermore, a recent study investigating the diagnostic accuracy of DSE in patients undergoing workup for OLT found that the use of atropine to increase the number of patients able to achieve the target heart rate still did not improve the sensitivity of the test [13].

In the literature, a CACS ≥400 AS is the value that has been shown to be associated with a much higher likelihood of coronary events. One large-scale study, the St. Francis Heart Study, showed that patients with a CACS ≥400 had a relative risk of coronary disease of events of 26.2 when compared with patients with calcium scores of 0 [19]. Conversely, a CACS of 0 is associated with an exceedingly low likelihood of cardiac events and all-cause mortality [20]. We investigated the sensitivity and specificity of CACS for CAD at various cutoffs. As expected, a CACS ≥100 AS had higher sensitivity for obstructive CAD than of ≥400 AS, but lower specificity. This pattern of change in sensitivity and specificity is similar to that of prior studies that have looked into the test characteristics of the CACS at various cutoffs [15,17]. A recent small retrospective study of the role of the CACS in OLT candidates determined that at the calculated "optimal" AS of ≥251, CACS had a sensitivity of 78% and a specificity of 87% [21].

Our study showed that the sensitivity of the CACS for the detection of CAD was numerically, but not statistically, greater than that of DSE in patients with end-stage liver disease. While DSE was more specific for this purpose compared with a lower CACS cutoff of ≥100, the specificity was comparable at higher cutoffs. It may be argued that for a screening test in this scenario, a higher sensitivity is more desirable to not miss patients with significant obstructive CAD. Furthermore, in the present study, ROC analysis demonstrated that the CACS was a satisfactory predictor for the presence of obstructive CAD (**Figure 3**).

While, in our study, we were not able to complete CACS scoring for all the patients as they did not have dedicated cardiac imaging for this purpose, we anticipate that for all patients (barring a few exceptions, such as patients with prior percutaneous coronary intervention or coronary artery bypass graft), the CACS could be useful in CAD risk stratification. Patients with prior percutaneous coronary intervention or coronary artery bypass graft are likely to have a greater risk of obstructive CAD, and therefore would benefit from DSE or CAG as their initial screening methods.

The CACS may be a useful alternative to DSE as the initial screening test for patients undergoing evaluation for OLT, particularly in patients with average without known CAD. Further research is needed in the liver transplant population to determine the optimal CACS to screen for the presence of obstructive CAD and therefore determine which patients should undergo CAG. A lower CACS threshold can increase its sensitivity to detect the presence of obstructive CAD, though with some loss of specificity.

### Limitations

A major limitation of our study is the potential bias introduced when considering that patients referred for CAG may have been at a high risk for CAD. It is important to note that the inclusion criteria for the study was all patients undergoing OLT evaluation who had a CAG prior to the transplant. This included patients who either had a nondiagnostic DSE or other indications for CAG as listed above. These patients could have had a higher risk of obstructive CAD than a general cohort of patients undergoing preoperative cardiac evaluation for OLT. The physicians who referred these patients to either CAG or DSE likely had a reasonable clinical suspicion that these patients had CAD, which may have confounded our results. This is a possible explanation for why in the head-to-head comparison, we found a higher sensitivity of DSE for obstructive CAD (57.1%) than other previous studies (**Table 4**). The disparity between the sensitivity of DSE of our study in the head-to-head comparison and that described in previous literature may have also been due to random error related to the small sample size, since our subset analysis of all patients who had either study found a sensitivity of 30.8%. Furthermore, our comparison of DSE and CACS subsets (all patients with a valid result for either test) compared test results in different patients. This analysis may have been affected by unknown confounders since the test subjects were different patients with different baseline demographics and comorbidities.





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Another limitation of this study is that the CT scans used for the calcium scoring were not originally intended for calcium scoring. Hence, the calcium scores may have been overestimated due to motion artifact. Additionally, the Agatston method was originally developed using electrocardiography-gated CT scans [12]. Our CT scans were non-gated. However, more recent research has shown that the CACS on non-gated CT scans correlated well with the Agatson score on gated CT scans [22].

Furthermore, there were still many patients with obstructive CAD who had calcium scores less than the various thresholds for what would be considered a "positive" result. Although the average CACS for patients without CAD (69.4 AS) and with obstructive CAD (769.8) were mostly divergent, there were still outliers in each category. For example, even some patients with obstructive CAD had calcium scores of 0. These patients with clinically significant CAD would be missed if calcium scoring alone was used to risk stratify patients and determine which patients should go on to invasive CAG. Because of this, it is important to consider the presence of clinical risk factors such as age, diabetes, hypertension, obesity, and family history of CAD when interpreting the CACS and using it to guide clinical decision making. For instance, patients with high risk based on clinical risk stratification may be preferentially evaluated using CAG, while patients with low to moderate risk could be further screened with the CACS (with DSE/CAG as the next step).

## Conclusions

In conclusion, the CACS has comparable sensitivity for the detection of obstructive CAD compared with DSE at all AS thresholds investigated in this study. ROC analysis showed that the CACS was a satisfactory test for detecting the presence of underlying obstructive CAD. DSE was nondiagnostic in an unacceptably high number of patients, restricting its utility as a screening test for CAD. Therefore, we conclude that calcium scoring may be a suitable alternative method for preoperative cardiac risk stratification prior to liver transplantation, at least in patients with low to moderate risk or when DSE is nondiagnostic. Until more prospective research is available, this retrospective study provides some insight into the role of the CACS as an alternative to DSE for preoperative cardiac risk assessment prior to liver transplantation.

### Declaration of Figures' Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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