

# Preoperative coronary calcium score is predictive of early postoperative cardiovascular complications in liver transplant recipients

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## **Editor's key points**

- Patients undergoing liver transplantation have a high incidence of coronary artery disease and cardiovascular complications are common.
- In this retrospective study, a high coronary calcium score determined by coronary CT was associated with cardiovascular complications after liver transplant.
- Prospective data in an external cohort are required to confirm these findings.

**Background.** Coronary computed tomographic angiography (coronary CT) is a non-invasive test for diagnosis of cardiac function. Coronary calcium scores determined by coronary CT are associated with cardiovascular risk factors. However, no studies have investigated the association between coronary calcium scores and cardiovascular complications after liver transplantation (LT). We therefore evaluated the utility of preoperative coronary calcium scores for predicting early postoperative cardiovascular complications in LT recipients.

**Methods.** Between 2010 and 2012, 443 LT recipients were analysed retrospectively. Preoperative cardiovascular assessments, including coronary CT, were performed. A coronary calcium score >400 was defined as a positive finding. Predictive factors of early postoperative cardiovascular complications were evaluated by univariate and multivariate analyses. Major cardiovascular complications occurring during a period of 1 month after LT were noted.

**Results.** Of the 443 patients, 38 (8.6%) experienced one or more cardiovascular complications. Positive coronary CT findings were seen in 11 (2.5%) patients. In the multivariate analysis, a coronary calcium score >400 {odds ratio (OR)=4.62 [95% confidence interval (CI): 1.14–18.72], P=0.032} and female sex [OR=2.76 (1.37–5.57), P=0.005] were predictive of cardiovascular complications.

**Conclusions.** A preoperative coronary calcium score of >400 predicted cardiovascular complications occurring 1 month after LT, suggesting that preoperative evaluation of coronary calcium scores could help predict early postoperative cardiovascular complications in LT recipients.

**Keywords:** coronary CT; early postoperative cardiovascular complications; liver transplantation Accepted for publication: 11 August 2014

Liver transplantation (LT) is the curative therapy for patients with advanced liver disease. <sup>1</sup> Cardiovascular complications are a leading cause of death after LT. The reported incidence of cardiovascular complications after LT ranges from 25 to 70%, and these complications are regarded as a major cause of postoperative morbidity and mortality in LT recipients. <sup>2-4</sup> Furthermore, LT recipients are at high risk of cardiac diseases such as coronary artery disease (CAD). <sup>5</sup> Therefore, accurate preoperative cardiac examinations should be performed to prevent postoperative cardiovascular complications. However, the optimal method to evaluate such cardiovascular risks in LT recipients remains controversial. <sup>67</sup>

A preoperative cardiac evaluation includes electrocardiography (ECG), echocardiography, and thallium single photon emission computed tomography (thallium SPECT).<sup>6 7</sup> Generally, when an abnormal finding is detected using these methods,

a further investigation using coronary angiography (CAG) can be performed. However, preoperative cardiac evaluations such as ECG, echocardiography, and thallium SPECT cannot be effective because of their relatively low sensitivity to detect CAD in LT recipients. <sup>8 9</sup> In contrast with these evaluating tools, CAG was identified as a good diagnostic and preventive modality with reduction of overall all-cause mortality and also the incidence of both fatal and non-fatal myocardial infarction in LT recipients. <sup>10</sup> Nevertheless, CAG may not be an appropriate screening test for patients with relatively advanced liver diseases, because coagulation abnormalities can increase the risk of bleeding during CAG. <sup>11</sup>

To address the aforementioned drawbacks, coronary computed tomographic angiography (coronary CT) has been suggested as a non-invasive imaging test for diagnosis of cardiac function, because it has the advantage of being able to identify

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coronary vessel wall characteristics and stenosis. <sup>12</sup> Coronary calcium scores, obtained from coronary CT, are a particularly useful determinant of the prevalence of CAD in LT candidates. <sup>13</sup> Several previous studies report a significant correlation between coronary calcium scores and known cardiovascular risk factors in LT recipients. <sup>14</sup> <sup>15</sup> In addition, a coronary calcium score of >400 is significantly associated with CAD on CAG in LT recipients. <sup>16-18</sup> However, no studies have investigated the association between coronary calcium scores and cardiovascular complications after LT.

We therefore evaluated the usefulness of preoperative coronary calcium scores assessed by coronary CT for predicting early postoperative cardiovascular complications in LT recipients. To this end, we evaluated the ability of a coronary calcium score of >400 to predict major cardiovascular complications occurring within 1 month of LT.

#### **Methods**

#### **Patients**

This was a single-centre, retrospective observational study of 443 patients who underwent LT at Asan Medical Center, Seoul, Korea, between 2010 and 2012. The following groups of patients were excluded from the study: (i) patients under 20 years of age, (ii) patients who did not undergo coronary CT before LT, (iii) patients who suffered significant cardiovascular events such as a myocardial infarction, or had a history of coronary angioplasty before LT, and (iv) patients who did not check troponin I assay in the postoperative period (Fig. 1). Medical records were reviewed and cardiovascular complications that occurred within 1 month of the LT were noted. The study protocol was approved by the Institutional Review Board of Asan Medical Center.

#### Routine cardiac evaluation

In our institution, routine preoperative cardiac assessments consist of an ECG, echocardiography, and thallium SPECT. On echocardiography, the presence of decreased left ventricle function (decreased ejection fraction), regional wall motion abnormality, significant valvular disease, or pulmonary hypertension

were categorized as abnormal findings. On thallium SPECT, the presence of a medium or large wall perfusion defect was regarded as an abnormal finding. Preoperative ECG and corrected QT (QTc) interval were also evaluated.

#### **Coronary CT**

Coronary CT scans using dual-source CTs (Somatom® Definition Flash or Somatom® Definition, Siemens Medical Solutions, Forchheim, Germany) were performed as part of the routine cardiac evaluations (Fig. 2). Coronary calcium scores were calculated with an automated, computerized software program using an Agatston scoring method. 19

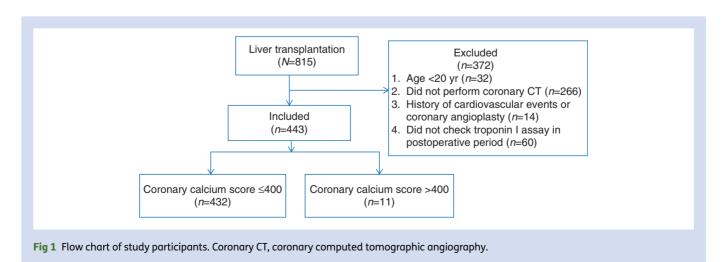
Total coronary artery calcification was classified as none (0), minimal (1–10), mild (11–100), moderate (101–400), or severe (>400) according to the total coronary calcium score.  $^{20}$  In the present study, patients with a coronary calcium score >400 were assigned to a positive coronary CT group, while patients with a coronary calcium score  $\leq\!400$  were assigned to the negative coronary CT group.  $^{16-18}$ 

#### Coronary angiography

Invasive CAG was performed to identify significant CAD in the positive coronary CT group before LT. The presence of significant stenosis in at least one coronary artery was regarded as a positive finding. However, based on the physician's assessment, some patients with severe coagulopathy did not undergo invasive CAG because of the risk of bleeding.

#### Posttransplant follow-up

In our institution, the combination of two or three different maintenance immunosuppressive drugs is used for the prevention of rejection after operation. The i.v. calcineurin inhibitors (tacrolimus and cyclosporine) are mainly used during hospital stay. Steroid such as methylprednisolone is almost universally used. Most recipients are also discharged with the oral tacrolimus as a primary immunosuppressant, with steroids which are gradually tapered and weaned in the following months. In addition, mycophenolate mofetil such as azathioprine is also commonly used to reduce tacrolimus dose and



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