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Coronary computer tomographic angiography for preoperative risk stratification in patients undergoing liver transplantation

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ABSTRACT

The assessment of the cardiovascular risk profile in patients with end-stage liver disease is essential prior to liver transplantation (LT) as cardiovascular diseases are major causes of morbidity and mortality in the posttransplant course. The aim of this study was to evaluate the accuracy of a 64-slice coronary computed tomographic angiography (CTA) and coronary calcium scoring (CCS) to predict the postoperative cardiovascular risk of patients assessed for LT.

In this single center, observational study we included 54 consecutive patients who were assessed for LT and consequently transplanted. Twenty-four patients (44%) presented with a high CCS above 300 and/or a significant stenosis (>50% percent narrowing due to stenotic plaques) and were further referred to coronary angiography. Three of these patients had a more than 70% LAD stenosis with subsequent angioplasty ($n = 1$) or conservative therapy ($n = 2$). The other patients showed only diffuse CAD without significant stenosis. The remaining 30 patients with normal CTA findings were listed for LT without further tests. None of the 54 patients developed cardiovascular events peri- and postoperatively.

This study indicated that CTA combined with CCS is a useful non-invasive imaging technique for pre-LT assessment of coronary artery disease and safe tool in the risk assessment of peri- and postoperative cardiovascular events in patients undergoing LT.

1. Introduction

Orthotopic liver transplantation (LT) is the only curative therapy for patients with an acute or chronic liver failure with reported 5–10 years patient survival rates around 70% [1,2]. Several studies indicated that coronary artery disease (CAD) is an increasing clinically relevant problem in patients with end-stage liver disease [3–6]. There is emerging evidence that the incidence of CAD in patients with end-stage liver disease (5–30%) is equal or even higher compared to an age-matched general population [4–6]. CAD often remains asymptomatic. Therefore, identification and treatment of patients with subclinical CAD is mandatory in the pre-LT assessment. Moreover, the referral of older candidates for LT has increased in the last years as well as the prevalence of cardiac risk factors for CAD, such as arterial hypertension, hyperlipidemia, diabetes mellitus and smoking, in the end-stage liver disease population [5,7].

The optimal method to detect cardiac risk in the pre-LT assessment is still controversial. In a recent review Keeffe et al. suggested dobutamine stress echocardiography (DSE) as the method of choice to evaluate the presence of CAD and to assess myocardial and valvular function [5]. However, stress nuclear imaging is limited by a low sensitivity to detect CAD in LT candidates [5,8,9]. Furthermore, patients with severe liver disease are not suitable candidates for conventional stress testing [9–11]. Coagulation abnormalities in patients with chronic liver disease lead to an increased bleeding risk [5], thus limiting the use of invasive coronary angiography as a general preoperative CAD screening tool.

Coronary computed tomographic angiography (CTA) is a new non-invasive imaging technique for cardiac imaging with the advantages of vessel wall and plaque depiction in addition to its ability to assess the luminal diameter, course and anatomic relationship of the coronary arteries in relation to the adjacent myocardium [12,13]. Therefore, CTA seems to be an interesting non-invasive method to evaluate cardiac risk in patients assessed

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Table 1
Demographic data of patients undergoing liver transplantation ($n = 54$).

Age	56 ± 6.4 (range 39–70)
	n (%)
Gender	
Male	42/54 (78%)
Female	12/54 (22%)
Underlying liver disease	
Alcoholic liver disease	17/54 (31%)
NASH cirrhosis	6/54 (11%)
Viral heapatitis	
Hepatitis C	11/54 (20%)
Hepatitis B	2/54 (4%)
Primary biliary cirrhosis	4/54 (7%)
Cryptogenic liver disease	2/54 (4%)
Budd-chiari syndrom	3/70 (4%)
Alpha-1-antitrypsin deficiency	2/54 (4%)
Wilson disease	1/54 (2%)
Hemochromatosis	1/54 (2%)
Autoimmune hepatitis	1/54 (2%)
Concomittant hepatocellular carcinoma (HCC)	4/54 (7%)
Child-Pugh scores	
A	11/54 (20%)
B	32/54 (59%)
C	11/54 (20%)
MELD scores	
Mean score (range)	15.9 ± 6 (range: 6–29)
<10	10/54 (19%)
10–19	29/54 (53%)
20–29	15/54 (28%)

for LT. In a recent study a 16-slice CT was used to define the prevalence of coronary artery calcification in association with other established cardiovascular risk factors in order to determine non-invasively the prevalence of occult CAD in patients undergoing LT assessment [14]. There was a strong correlation between coronary artery calcification scores and a number of known cardiovascular risk factors, such as age, blood pressure and fasting glucose. However, no data about the correlation of these findings with cardiovascular events postoperatively were given.

In this pilot study we included a consecutive cohort of patients who were assessed for LT at our center. In our observational study we included a consecutive cohort of patients who were assessed for LT at our center. The coronary artery calcification scores as well as coronary angiography results were analyzed in order to evaluate the accuracy of a 64-slice CT scan to predict the postoperative cardiovascular risk of these patients.

2. Methods

2.1. Study design and patients

This was a single center, retrospective observational study of 54 consecutive patients who were assessed for LT and consequently transplanted at our center between May 2005 and December 2006. In this study we retrospectively analyzed prospectively collected data. After obtaining informed consent, CTA was performed in all patients comprising the study group.

The main patients' demographic data are listed in Table 1. The severity of liver disease was calculated with the Model of End-stage Liver Disease (MELD) scoring system [15] as well as the Child-Pugh Classification.

Pre-LT cardiovascular evaluation included assessment of cardiovascular risk factors (pre-existing diabetes, arterial hypertension, cigarette smoking, lipid status, family history, calculation of the Framingham Risk Profile and body mass index), recording of symptoms (angina was classified according to the Canadian Cardiovascular Society functional classification of angina pectoris – CCSC, [16]), physical examination, electrocardiography and transthoracic rest echocardiography. Patients with a CCSC above 0 underwent treadmill ECG-stress testing, which was performed and interpreted according to the AHA guidelines.

Prior to this pilot study pre-LT cardiovascular assessment in our center consisted of transthoracic echocardiography, treadmill ECG stress testing (if possible) and dobutamine stress echocardiography. Coronary angiography (CA) was performed if one of the tests was positive or the patients' age was above 60 years and presented with at least one cardiovascular risk factor.

2.2. Coronary computed tomographic angiography (CTA)

CT data were acquired using a multidetector CT scanner (*Sensation* 64™, *Siemens Medical Systems*, *Forchheim*, *Germany*) with a 32-row detector collimation acquiring 64 × 0.6 mm slices by applying z-axis flying-focus technique, a table translation speed of 3.8 mm/rotation and a gantry rotation time of 0.33 s. Tube voltage was 120 kV and current 600–900 eff mAs. Scan direction was craniocaudally during a single mid-inspiratory breath-hold. A bolus of 90–120 ml iodine contrast agent, either iodixanol *(Visipaque320* ™, Amersham) or iomeprol (*Iomeron400*™, Bracco), was injected intravenously into an antecubital vein at a flow rate of 4.5–6 ml/s using a power injector. The scan was started automatically by applying bolus tracking technique (ascending aorta, threshold 100 HU). A beta-blocker was given intravenously before the CT scan if the heart rate was greater than 75 beats/min (5–15 ml metoprolol).

First, an unenhanced coronary calcium score (CCS) scan was performed, and the Agatston Score was calculated. Second, contrast enhanced ECG-gated coronary CT angiography was performed. The coronary arteries were evaluated by one experienced cardiac radiologist (G.M.F.) and double-checked by one experienced cardiologist (G.F.) for the presence of coronary stenosis of more than 50%. Image quality was graded as grade 1: good image quality (no artefacts); as grade 2: acceptable image quality (with minor limitations e.g. mild artefacts); or as grade 3: insufficient image quality due to artefacts.

Patients with a high CCS of more than >300 [17] and/or a significant stenosis (>50% luminal narrowing) were included in the "CTA positive group" and a coronary angiography was performed to exclude a significant CAD in these patients prior to LT listing. Patients with negative CTA result, as defined by low CCS of <300 and no significant stenosis (>50%), were assigned to the "CTA-negative" group and were listed for LT.

2.3. Coronary angiography (CA)

As mentioned above invasive CA was limited to patients who had a high CCS (>300) and/or significant stenosis (>50%) on CTA imaging (CTA-positive group).

CA was performed from a transfemoral percutaneous approach using the Judkins technique. Puncture sites were closed using the AngioSeal® (St. Jude) device.

2.4. Perioperative and post-transplant follow-up

The mean waiting time for all 54 patients, included in this study, to receive a suitable liver allograft was 9 months, ranging from one to 24 months.

All cardiovascular complications during LT were noted and any cardiovascular events (myocardial infarction, onset of angina symptoms, arrhythmia and heart failure) were recorded within the early (in-patient setting) and late post-operative period (hospital discharge and last follow-up visit). The mean follow-up period ranged from 9–15 months.