Low Yield of Routine Preoperative Coronary Computed Tomography Angiography in Patients Evaluated for Liver Transplantation

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Although coronary revascularization before noncardiac surgery has not been shown to reduce the risk of cardiac events, preoperative noninvasive screening for obstructive coronary artery disease (CAD) is commonly performed. Such testing is even more likely to be performed among patients who are candidates for organ transplantation. The rationale for such testing in candidates for organ transplantation includes the need to determine the perioperative risk and whether the patient’s cardiovascular risk is high enough that organ transplantation would be futile and an inappropriate use of a scarce organ. Although screening for obstructive CAD in patients with end-stage renal disease evaluated for kidney transplantation seems reasonable given the high prevalence of atherosclerosis and cardiovascular risk in these patients, there is intense debate about whether such an approach should also be considered among patients with end-stage liver disease, in whom there is a generally much lower frequency of CAD, at least on the basis of relatively small retrospective reports.

The study by An and colleagues provides new data on the prevalence of obstructive CAD among a large number of asymptomatic patients evaluated for liver transplantation who were referred for coronary computed tomography angiography (CCTA). This retrospective study included 1045 consecutive patients with liver cirrhosis undergoing CCTA as part of the pre–liver transplantation workup. In this cohort with a low to intermediate likelihood of CAD, CCTA revealed no CAD in 62%, nonobstructive CAD in 30%, and angiographically obstructive CAD (≥50% stenosis) in 7.9% of patients (n=83). Only 39 patients (3.7%) had a significant stenosis (>70%), mostly single-vessel CAD. Using propensity scores, the investigators matched the study cohort with 6283 control subjects with healthy livers undergoing CCTA as part of a health evaluation program. The matched comparison revealed that the frequency of obstructive CAD was similar in the cirrhotic and healthy cohorts (7.9% versus 7.2%, respectively). However, nonobstructive CAD seemed slightly more prevalent among the patients with liver cirrhosis than in the matched control subjects (31% versus 23%, respectively). Interestingly, in the pooled cohort of patients with liver cirrhosis and control subjects (n=7328), a diagnosis of liver cirrhosis was not associated with obstructive CAD in multivariable modeling.

Importantly, 24 of the 83 cirrhotic patients with obstructive CAD by CCTA were referred for cardiac catheterization, and only 6 (0.6% of the entire cohort) with multivessel CAD ultimately underwent revascularization. Liver transplantation was subsequently performed in 57 of 83 patients with obstructive CAD by CCTA. Postoperatively, 1 patient had a non–ST-segment–elevation myocardial infarction, and 2 patients developed arrhythmia (atrial fibrillation and ventricular tachycardia). There were no deaths. During a median 2.3-year follow-up, there were only 2 late revascularizations.

The study by An and colleagues provides important data on the yield of noninvasive testing in a large cohort of patients with liver cirrhosis and the implications of such testing and contributes to the ongoing debate concerning pretransplantation risk assessment in patients with liver disease.

Is Cardiac Testing Required in Every Asymptomatic Patient Being Considered for Liver Transplantation?

This is a legitimate question, especially given the low yield of testing identified in this large series. A recent American Heart Association/American College of Cardiology scientific statement suggests that noninvasive testing may be considered in liver transplantation candidates with multiple CAD risk factors (ie, diabetes mellitus, prior cardiovascular disease, left ventricular hypertrophy, age >60 years, smoking, hypertension, dyslipidemia), regardless of functional status (Class IIb recommendation; Level of Evidence, C). The study by An and colleagues supports these recommendations in that independent risk factors for obstructive CAD in this series included advanced age, male sex, hypertension, diabetes mellitus, and alcohol-related cirrhosis. However, the specific number or combination of risk factors to warrant testing is less clear.

From the present report and previous studies, the recommendation for preoperative testing of liver transplantation candidates with a history of cardiovascular disease or diabetes mellitus, especially those >60 years of age, seems reasonable because these patients probably have a higher likelihood of prognostically significant CAD. Indeed, nearly 50% of patients with obstructive CAD in the present study were older.

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diabetics. Another intriguing finding in the present study was the association between alcoholic, but not viral, cirrhosis and obstructive CAD, which was independent of other coronary risk factors. Because this was a relatively small proportion of the patients in this report, this requires finding further studies to more firmly define the role of alcoholic cirrhosis as a risk factor for atherosclerosis in this population. However, the cost-effectiveness of routine noninvasive testing in younger candidates for liver transplantation without symptoms, evidence of cardiovascular disease, or diabetes mellitus appears more controversial. To augment the low yield of testing, thereby enhancing the clinical effectiveness and cost-effectiveness of diagnostic evaluations, it would probably be useful to enrich the prevalence of disease in the latter group before the use of noninvasive testing. One potential approach may be the use of an aggregate score incorporating and weighting multiple risk factors present. Indeed, previous studies have shown that incorporating a clinical score into a testing strategy in patients without liver cirrhosis can enhance the yield of cardiac imaging and improve its cost-effectiveness.

What Is the Best Imaging Approach to Screening for CAD in Candidates for Liver Transplantation?
The 2012 American College of Cardiology/American Heart Association scientific statement, “Cardiac Disease Evaluation and Management Among Kidney and Liver Transplantation Candidates,” concluded that “prospective studies on optimal screening strategies for the presence of CAD are lacking and much needed.” To that end, the study by An et al provides useful data on the feasibility and potential utility of CCTA. There are several potential advantages of using CCTA for CAD screening in patients with advanced liver disease. It has a very high sensitivity (≥90%) and negative predictive value (≥96%) for excluding significant CAD. Given its high negative predictive value, a normal scan result (expected in approximately two thirds of patients with end-stage liver disease on the basis of the present report) effectively excludes obstructive CAD and abolishes the need for further investigation. Stress myocardial perfusion scintigraphy and echocardiography have been used in these patients with mixed results, likely related to the variable sensitivity of these approaches. A related advantage of CCTA over stress imaging is that it does not require exercise or pharmacological (vasodilator) stress testing. This is clinically relevant in these patients because transplantation candidates in general are often too debilitated to complete maximal exercise testing. In addition, the efficacy of vasodilator stress testing in patients with end-stage liver disease has been questioned because of the enhanced systemic vasodilation observed in these patients. Finally, the use of CCTA may serve as a more effective gatekeeper to cardiac catheterization, thereby avoiding the somewhat higher risk of bleeding complications in patients with end-stage liver disease.

What Are the Implications of Identifying Angiographic CAD?
It is well recognized that the presence of obstructive CAD (≥50% stenosis) is a poor predictor of myocardial ischemia. Thus, a testing strategy using CCTA for CAD screening should include follow-up stress testing to determine the need for invasive angiography and coronary revascularization in patients with abnormal CCTA results, as was the case in the present study. As many as two thirds of these angiographic lesions are not flow limiting and do not require coronary revascularization. The safety of avoiding coronary revascularization in most patients with solely angiographic findings is also supported by the fact that in the study by An et al, liver transplantation was performed successfully in 57 patients with obstructive CAD, of whom only 6 underwent coronary revascularization, with only 1 subsequent myocardial infarction, 2 late coronary revascularizations, and no deaths.

In the study by An et al, approximately one third of patients had nonobstructive plaque (with 90% involving ≤4 coronary segments); therefore, it is intriguing to consider the value of identifying such lesions. Among nontransplantation candidates referred for clinical CCTA, there is evidence to suggest that the presence of extensive nonobstructive plaque (ie, >4 segments) is associated with an increased rate of myocardial infarction and cardiovascular death. In addition, the presence of such disease by CCTA is associated with initiation or intensification of lipid-lowering therapies and aspirin. However, among patients evaluated for organ transplantation, there are no data to indicate whether the identification of such plaque could lead to improved patient outcomes. Because periprocedural cardiac events are thought to occur as a result of both demand-mediated ischemia and plaque rupture, it is likely that a small proportion of nonobstructive plaque may represent high risk (“vulnerable”) plaques. However, in the current era of CCTA (or invasive angiography), the positive predictive value of identifying high-risk plaque characteristics is extremely low, and beyond the use of statin therapy, there are no compelling therapies that would be initiated for such lesions. Given that posttransplantation immunosuppressive medications may contribute to the progression of atherosclerosis, it is conceivable that information on the presence of nonobstructive plaque could be used to identify higher-risk populations beyond the postoperative period, but this will require longitudinal studies with longer follow-up.

In summary, the study by An identifies a low risk of obstructive CAD among patients with liver disease and therefore supports the fact that routine testing of all patients before liver transplantation may not be warranted. Consequently, better algorithms are needed to identify which patients require screening for CAD before liver transplantation. Finally, additional studies are required to compare how different noninvasive approaches compare and whether pharmacological or interventional therapies can be used to effectively mitigate the low risk of events in these patients.

Disclosures
None.

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