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The Pre-Transplant Profile of Cardiovascular Risk Factors and Its Impact on Long-Term Mortality After Liver Transplantation

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Background: Cardiovascular disease (CVD) is an important aggravating factor for orthotopic liver transplantation (OLT) outcomes. CVD still seems to be one of the most common cause of death in the long-term post-transplant period. Nevertheless, there are some limited data regarding the optimal strategy of risk assessment during OLT candidate evaluation.

Material/Methods: Routine pre-transplant cardiac workup in 360 patients with end stage liver disease (ESLD) included electrocardiogram, echocardiography, and exercise stress testing. The aim of this retrospective study was an analysis of the impact of cardiovascular risk profile on overall mortality in the 2-year follow-up of 160 patients who underwent liver transplantation.

Results: Cardiovascular risk factors or a history of CVD were found in 23.1% of patients who received transplants. The cardiovascular risk factors most common in our group of transplant recipients with ESLD were: diabetes (26.3%), hypertension (25.6%), and hepatopulmonary syndrome (23.1%). Only 3.8% of patients had a positive exercise test. Coronary angiography revealed at least 50% stenosis in some epicardial arteries in 1.9% of patients. The risk of death in long-term follow-up of liver transplant recipients was most strongly associated with 3 cardiac variables: history of coronary artery disease (CAD), angiographically confirmed coronary stenosis, and reduced ejection fraction (EF).

Conclusions: Our study identified pre-transplant CAD with its consequences as a factor associated with increased risk of negative post-transplant outcomes.

MeSH Keywords: **Cardiovascular Diseases • End Stage Liver Disease • Liver Transplantation • Risk Factors**

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Background

The recent European Society of Cardiology (ESC) and European Society of Anesthesiology (ESA) guidelines on cardiovascular assessment and management before non-cardiac surgery list orthotopic liver transplantation (OLT) as a type of procedure with high risk of cardiovascular death and myocardial infarction within 30 days of surgery [1].

Cardiovascular disease (CVD) is an important aggravating factor for OLT outcomes. Patients with coronary artery disease (CAD) treated either medically or surgically before OLT were reported to have 3-year mortality of 50% and morbidity of 81% [2]. CVD was also found to be the third most common cause of death in the 5-year post-transplant period, accounting for 12–16% of deaths [3], and the calculated 10-year post-transplant CVD risk was estimated to be 7.9% in a Framingham study population [4]. The risk of CAD in OLT candidates has not been accurately defined. The routine screening tests for CAD should be further evaluated in this group of patients. Nevertheless, there are some limited data available regarding the optimal strategy of risk assessment during OLT candidate evaluation.

Material and Methods

This study was conducted in 360 consecutive patients with end stage liver disease (ESLD), who underwent consultations by a designated cardiologist at the First Department of Cardiology at the Medical University of Warsaw. All 360 patients were candidates for OLT and underwent a cardiac assessment between April 1, 2011 and April 30, 2013. All patients were hospitalized, and liver transplantations were performed in the Department of General Transplant and Liver Surgery of the Medical University of Warsaw. There were designated consulting cardiologists for all OLT candidates in our center. Routine pre-transplant cardiac workup included electrocardiogram, echocardiography, and exercise stress testing. In cases of abnormal findings, the consulting cardiologist would order further diagnostic assessment, consisting of coronary angiography (CAG) or right-heart catheterization (Figure 1). Out of the evaluated 360 patients, 160 underwent liver transplantation at our university hospital and were included in this analysis.

ESDL severity

The following data were retrospectively recorded: demographic characteristics, laboratory results, cardiovascular risk factors, ESLD etiology (alcoholic, viral, nonalcoholic steatohepatitis, cryptogenic, or other), severity of liver disease (the Child-Pugh classification and model for end stage liver disease (MELD score), ascites, gastroesophageal varices, and history of overt encephalopathy. The term "compensated disease" refers to Child-Pugh class A and "decompensated disease" includes Child-Pugh class B and C.

Cardiovascular risk factors

The cardiologist obtained medication history for CAD and heart failure, previous myocardial revascularization procedures, renal failure, and previous stroke. The cardiovascular risk factors recorded were advanced age (men ≥55 years old and women ≥65 years old), diabetes mellitus, hypertension, hyperlipidemia, smoking habit, and family history positive for premature CAD.

Echocardiographic examination

Transthoracic echocardiographic examinations were performed in all patients at the echocardiography laboratory by experienced cardiologists using a Philips iE33 ultrasound system. The echocardiographic variables recorded were chamber sizes, valvular dysfunction, diastolic dysfunction, intracardiac and intrapulmonary shunting, contractility abnormalities, and ejection fraction (EF). Left ventricular EF was determined by Simpson's method, with reduced EF diagnosed below 50%. Additionally, echocardiography studies with agitated saline contrast ("bubble") were performed in 96 patients (53.3%).

Exercise testing

According to the algorithm used in our hospital at that time, we performed exercise testing in routine cardiac assessment for OLT. Every exercise test was performed on a treadmill using Bruce protocol or modified Bruce protocol. What made an exercise test positive was the presence of a typical horizontal or down-sloping ST-segment depression at least 0.1 mV in at least one lead.

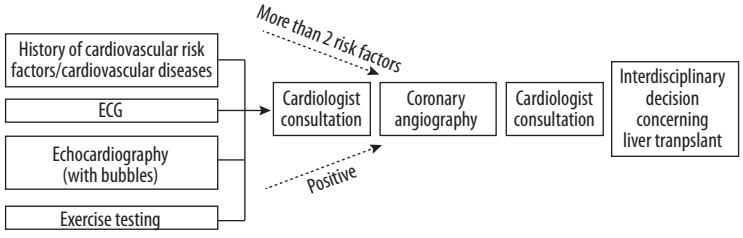

Figure 1. Protocol for cardiac evaluation before liver transplantation.

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CAG

The consulting cardiologist could order CAG based on a previous history of cardiovascular events, CVD, at least 2 cardiovascular factors, or abnormal exercise test results. Coronary angiographies were performed via a radial approach and at the time of qualification for liver transplantation.

Follow-up

This study was a single-center study, with a register-based follow-up design. We used the Polish Civil Personal Registration Numbers, which are unique to each Polish citizen, to link the information from the national registry of deaths at the Ministry of the Interior and Administration to the clinical data obtained in this study.

The single endpoint of the study was all-cause mortality. Observations were censored at the date of last available follow-up (July 18, 2014).

Statistical methods

The patients were categorized into 2 groups according to post-OLT survival. Continuous variables were summarized as means ± standard deviation, whereas frequencies and percentages were used for categorical variables. Unpaired *t*-tests were used for comparison of continuous normally distributed variables. Differences between dead and alive patients at the end of follow-up were analyzed by the independent-samples *t*-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data.

Multivariate analyses (by stepwise multivariate model building) were assessed with a Cox proportional hazards model. Hazard ratios were presented with 95% confidence intervals. The corresponding Kaplan-Meier curves for stroke occurrences were also plotted, and then compared using log-rank test. Statistical significance for all analyses was determined at $P<0.05$. All analyses were undertaken by using STATISTICA version 12 software.

Data integrity

The authors had full access to the data sets and vouch for data integrity. All authors have read and approved this form of the manuscript. The study was approved by the Ethics Committee at the Medical University of Warsaw.

Table 1. Baseline characteristics of patients.

Characteristic/Variable	Value
Demographics	
Age (years), mean ±SD	49±12.3
Gender (male), n (%)	99 (61.9%)
Etiology of end-stage liver disease	
Alcoholic, n (%)	29 (18.1%)
Viral hepatitis (Hepatitis B or C), n (%)	72 (45%)
Autoimmunogenic (AIH, PSC, PBC)	33 (20.6%)
Cryptogenic	8 (5%)
Other	18 (11.3%)
Severity of ESLD at the time of cardiac consultation	
Child-Pugh score (units), mean ± SD	7.8±2.1
Child-Pugh class A, n (%)	52 (32.5%)
Child-Pugh class B, n (%)	78 (48.8%)
Child-Pugh class C, n (%)	30 (18.8%)
MELD score (units), mean ± SD	11.8±4.6
Complications of end-stage liver disease	
Hepatocellular carcinoma (HCC), n (%)	32 (20%)
Ascites, n (%)	43 (26.9%)
Gastroesophageal varices grade III-IV, n (%)	50 (31.1%)
History of bleeding from gastroesophageal varices	29 (18.1%)
History of overt encephalopathy, n (%)	31 (19.6%)
Laboratory parameters	
INR, mean ±SD	1.3±0.3
Creatinine (mg/dL), mean ± SD	0.8±0.3
Bilirubin (mg/dL), mean ± SD	2.9±3.3

MELD – model for end-stage liver disease.

Results

Baseline characteristics

Patient baseline characteristics and clinical aspects of ESLD are shown in Table 1. The most common indications for liver transplantation were viral cirrhosis (45%), alcoholic cirrhosis (18.1%), and autoimmune cirrhosis (20.6%). The average age was 49 years; 61.9% of the patients were male.

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Table 2. Cardiovascular risk factors.

Cardiovascular risk factors	All		Survivors		Non survivors		p
	n	%	n	%	n	%	
History of coronary artery disease	8	31.25	5	62.50	3	37.50	0.0171
Previous MI	0	0.00	0	0.00	0	0.00	NS
Previous PCI	3	18.75	1	33.33	2	66.67	0.0025
Previous CABG	1	6.25	1	100.00	0	0.00	NS
Previous stroke	1	6.25	1	100.00	0	0.00	NS
Family history of cardiovascular disorder	3	18.75	3	100.00	0	0.00	NS
History of hypertension	41	25.63	34	82.93	7	17.07	NS
History of hyperlipidemia	20	12.50	19	95.00	1	5.00	NS
History of diabetes mellitus	42	26.35	36	85.71	6	14.29	NS

Table 3. Multivariate analysis of variables associated death events after OLT.

Factor	HR	95% CI	p Value
History of coronary artery disease	4.70	1.36–16.30	0.015
Presence of coronary stenosis on coronary angiography	7.78	1.78–33.97	0.006
Reduced ejection fraction < 50% on echocardiography	10.71	1.41–81.20	0.02

History of cardiovascular disorders

The prevalence of pre-transplant cardiovascular risk factors in patients with ESLD in our study population are shown in Table 2.

History of cardiovascular disorders or cardiovascular risk factors were present in 37 patients (23.1%). The cardiovascular risk factors most common in our group of patients with ESLD were hypertension (41 patients; 25.6%), diabetes (42; 26.3%), and hepatopulmonary syndrome (37; 23.1%). Forty-one patients had a history of hypertension, but no patient had elevated blood pressure at the time of cardiac consultation. No patient had previous myocardial infarction, but 4 patients (2.5%) had had a revascularization procedure (3 percutaneous coronary angioplasties and 1 coronary artery bypass grafting). Eight patients (5%) had a known history of CAD.

Echocardiography

Systolic dysfunction with a reduced EF (below 50%) was found only in 1 patient in the whole population of transplantation patients with ESLD. In a subgroup of 96 patients (53.3%) whom had agitated saline contrast ("bubble") studies performed, intrapulmonary shunts were reported in 37 patients (38.5%) and intracardiac shunts in 2 patients.

Exercise test

Only 6 patients (3.8%) had positive exercise tests with electrocardiographic abnormalities. Those patients had a consult by a cardiologist and then referred for CAG.

CAG

CAG was done in 12 patients (7.5%), and 3 of whom it revealed at least 50% stenosis in some epicardial arteries. All CAG patients had single-vessel coronary disease, and none had indication for further coronary revascularization prior to liver transplantation.

Follow-up

Overall, there were 18 post-liver-transplantation deaths (11.3%) in the study population, with no observed cases of sudden cardiac death during the hospital stay. The mean follow-up period was over 2 years (736.5±260.6 days). The mean time spent

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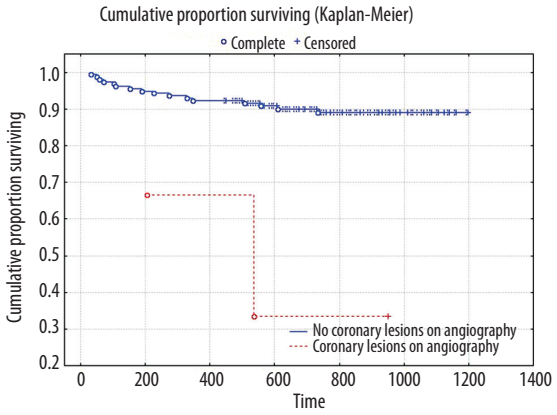

Figure 2. Kaplan-Meier curves of survival in patients with coronary artery lesions on coronary angiography *vs.* patients without coronary artery disease.

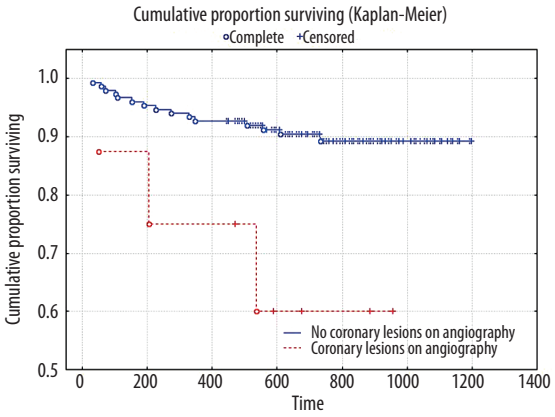

Figure 3. Kaplan-Meier curves of survival in patients with history of coronary artery disease *vs.* patients without history of coronary artery disease.

on the transplant waiting list was approximately 3 months (110.2±101.3 days). This contributed to the 21-month follow-up in patients with a successful liver transplantation (626.4±250.7 days). In a multivariate analysis of patient characteristics, the risk of death in long-term post-liver-transplantation follow-up was most strongly associated with 3 variables: history of CAD, angiographically confirmed coronary stenosis, and left ventricular EF below 50% (Table 3).

Figure 2 shows the cumulative incidence of death during an over 2-year follow-up period in patients with coronary artery lesions on CAG versus patients without CAD.

Kaplan-Meier curves of survival in patients with history of CAD versus patients without history of CAD are presented in Figure 3.

Discussion

In a frequently cited article by Plotkin et al., 1-year mortality of patients with CAD undergoing OLT was estimated at the level of 50% [2]. The optimal strategy for cardiovascular risk assessment in candidates for OLT remains, however, to be defined.

A scientific statement from the American Heart Association (AHA) and the American College of Cardiology (ACC) recommend screening for CAD in individuals with more than 3 CVD risk factors such as male sex, age >60 years, smoking, hypercholesterolemia, diabetes mellitus, and prior CVD, as those patients are more likely to have concomitant significant CAD. In such patients, stress testing is recommended as an initial screening tool, and it is to be followed by cardiac catheterization when the findings are positive [5].

Because non-invasive imaging test results tend to be inconsistent, some authors do not recommend their routine use in OLT candidates, recommending instead CAG in high-risk patients (individuals with known CAD, diabetes, or 2 or more CVD risk factors), as CAG has a recognized safety profile in patients with ESLD [6].

Unfortunately, preoperative noninvasive cardiac studies may have poor predictive value for detecting CAD in liver transplantation candidates. The usefulness of dobutamine stress echocardiography (DSE), which is one of the most widely used preoperative tests, has been put into question in different studies [7,8]. DSE was shown to be a poor tool for detecting pre-existing CAD as a significant factor associated with post-transplant cardiac mortality. Single-photon emission computed tomography has poor sensitivity in candidates for OLT [8–10].

Until April 30, 2013, we performed exercise testing as part of CAD screening at our center. Since then, we have decided to perform cardiopulmonary exercise testing instead, as a more comprehensive diagnostic tool, which is nowadays suggested as a method of choice for patients with ESLD [11].

AHA/ACC guidelines recommend that each program attempt to designate a primary cardiology consultant for questions related to potential (liver) transplantation candidates. In our center, there is a cardiology consultant designated for the OLT program.

In a retrospective review by Lee et al. [12], moderate stenosis was present in 23.5% of patients and 5.3% had severe stenosis. A study by Tiukinhoy-Laing et al. [13] showed the prevalence of moderate-to-severe CAD to be 24%. As in the previous study, CVD risk factors were common, with 55% of patients having 2 or more. Patients' risk of developing CAD was significantly

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higher if 2 or more risk factors were present. The patients with moderate-to-severe CAD (>50% stenosis) tended to be older males with history of hypertension and diabetes. Our study demonstrated a lower prevalence of pre-transplant hypertension and pre-transplant diabetes. Poor exercise capacity and chronotropic incompetence that are frequently experienced in ESLD could, indeed, mask some CVD symptoms.

The high rates of CAD found on CAG in ESLD patients evaluated for OLT may be due to many reasons. The mean age of OLT recipients has increased over time. Age is an established risk factor for CAD in both males and females [14] and it is associated with higher prevalence of other CVD risk factors such as BMI [15], hypertension [16], metabolic syndrome [17], and diabetes [16]. Studies of patients with ESLD showed high rates of CVD risk factors and a linear association between the number of CVD factors and the risk of CAD [14], with the presence of 2 or more risk factors significantly increasing the risk of CAD [15]. Nevertheless, some recent studies reported the prevalence of CAD at lower levels (4% to 8%) [7,18,19].

The etiology of liver disease also plays a role in CVD risk factor profile. Non-alcoholic steatohepatitis is an independent risk factor for CAD [20], and hepatitis C virus is associated with an elevated risk of diabetes [21], which was the only independent risk factor of CAD found in CAG studies [15]. The lack of a significant association of other CVD risk factors with CAD in this group of patients might be due to the small number of participants in these studies. In our study, the most common etiology of ESLD was viral hepatitis C or B.

A recent study by Albeldawi et al. demonstrated metabolic syndrome in post-transplantation follow-up to be more prevalent in patients with cardiovascular events than in patients with no cardiovascular events [22]. The study found a few independent predictors of a post-OLT cardiovascular event, such as older age, male sex, post-transplantation diabetes, post-transplantation hypertension, and treatment with mycophenolate. Patients with post-transplantation diabetes and post-transplantation hypertension had a 2-fold higher risk of cardiovascular events within the 5-year follow-up period. In our study, we did not diagnose metabolic syndrome because, in our opinion, it is difficult to determine whether the waist circumference criterion is due to ascites.

Contrary to previous studies, Wray C et al. found that patients with angiographically proven obstructive and non-obstructive CAD had similar survival rates. The study concluded that current CAD treatment strategies for patients with obstructive CAD reduced the post-transplantation CVD risk so that it became comparable to that in patients without obstructive CAD. In our study, we identified pre-existing (i.e., pre-transplant) CAD as a factor associated with increased risk of a negative post-transplantation outcome [23].

Recent data suggested that early diagnostic protocols in patients with at least one CVD risk factor (including CAG in patients with at least 2 risk factors) reduce overall mortality after OLT [24].

Earlier reports of a high mortality in OLT recipients with CAD, including the commonly cited paper by Plotkin JS et al., were most likely a result of different management protocols, particularly including cardiac surgery (CABG) in OLT candidates with CAD [2].

No patients from our study group had indications for percutaneous coronary intervention. In our center, every patient diagnosed with CAD received medical treatment. Nevertheless, there are limited data on optimal management for CAD in patients with ESLD before OLT.

Study limitations

There were several limitations of our study. First, it was a the single-center study conducted in a retrospective manner. We did not correlate long-term mortality with the potential occurrence of perioperative cardiovascular events. We could not identify the cause of death because the exact information on the death and the time of death was not available. Based on this data we have planned other prospective studies including biomarker analysis, cardiopulmonary exercise testing, and follow-up.

Conclusions

According to our knowledge, this is the first European study concerning a prognostic impact of the pre-transplant CVD risk factor profile on long-term mortality after OLT, which indicates that the risk of death in long-term follow-up of liver transplant recipients was most strongly associated with 3 cardiac variables: history of CAD, angiographically confirmed coronary stenosis, and reduced left ventricular EF. However, the number of death was quite low but still had the prognostic impact. There is one point-based prediction model (risk score) for major 1-year CVD complications after OLT recently published, but the Cardiovascular Risk in Orthotopic Liver Transplantation risk score was not yet validated in European population [25] at the time of our study.

Acknowledgments

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Conflict of interest

None.

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References:

1. Kristensen SD, Knuuti J, Saraste A et al: 2014 ESC/ESA Guidelines on non-cardiac surgery: Cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: Cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). Eur Heart J, 2014; 35(35): 2383–431
2. Plotkin JS, Scott VL, Pinna A et al: Morbidity and mortality in patients with coronary artery disease undergoing orthotopic liver transplantation. Liver Transpl Surg, 1996; 2(6): 426–30
3. Watt KDS, Pedersen RA, Kremers WK et al: Evolution of causes and risk factors for mortality post liver transplant: Results of the NIDDK long term follow-up study. Am J Transplant, 2010; 10(6): 1420–27
4. Johnston SD: Cardiovascular morbidity and mortality after orthotopic liver transplantation. Transplantation, 2002; 73(6): 901–6
5. Lentine KL, Costa SP, Weir, MR et al: Cardiac disease evaluation and management among kidney and liver transplantation candidates. A scientific statement drom the American Heart Association and the American College of Cardiology Foundation. J Am Coll Cardiol, 2012; 60(5): 434–80
6. Raval Z, Harinstein ME, Skaro AI et al: Cardiovascular risk assessment of the liver transplant candidate. J Am Coll Cardiol, 2011; 58: 223–31
7. Nicolau-Raducu R, Gitman M, Ganier D et al: Adverse cardiac events after orthotopic liver transplantation: A cross-sectional study in 389 consecutive patients. Liver Transpl, 2015; 21(1): 13–21
8. Davidson CJ, Gheorghiade M, Flaherty JD et al: Predictive value of stress myocardial perfusion imaging in liver transplant candidates. Am J Cardiol, 2002; 89(3): 359–60
9. Gupta NC, Esterbrooks DJ, Hilleman DE, Mohiuddin SM: Comparison of adenosine and exercise thallium 201 single-photon emission computed tomography (SPECT) myocardial perfusion imaging. J Am Coll Cardiol, 1992; 19(2): 248–57
10. Chae WY, Hwang S, Yoon YI et al: Clinical value of preoperative coronary risk assessment by computed tomographic arteriography prior to adult living donor liver transplantation. Transplant Proc, 2012; 44(2): 415–17
11. Zardi EM, Zardi DM, Chin D et al: Cirrhotic cardiomyopathy in the pre- and post-liver transplantation phase. J Cardiol, 2016; 67(2): 125–30
12. Lee BC, Li F, Hanje AJ et al: Effectively screening for coronary artery disease in patients undergoing orthotopic liver transplant evaluation. J Transplant, 2016; 2016: 7187206
13. Tiukinhoy-Laing SD, Rossi JS, Bayram M et al: Cardiac hemodynamic and coronary angiographic characteristics of patients being evaluated for liver transplantation. Am J Cardioll, 2006; 98(2): 178–81
14. Benjamin EJ, Blaha MJ, Chiuve SE et al: Heart disease and stroke statistics – 2017 update: a report from the American Heart Association. Circulation, 2017; 135(10): e146–e603
15. Lyall DM, Celis-Morales C, Ward J et al: Association of body mass index with cardiometabolic disease in the UK Biobank: A mendelian randomization study. JAMA Cardiol, 2017; 2(8): 882–89
16. Vasan RS, Larson MG, Leip EP et al: Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart Study: A cohort study. Lancet, 2001; 358: 1682–86
17. Ervin RB, Ogden CL: Prevalence of metabolic syndrome among adults 20 years of age and over, by sex, age, race and ethnicity, and body mass index: United States, 2003–2006. Natl Health Stat Report, 2009; (13): 1–7
18. Weick A, Chacra W, Kuchipudi A et al: Incidence of cardiovascular and cerebrovascular events associated with sirolimus use after liver transplantation. Transplant Proc, 2015; 47(2): 460–64
19. Josefsson A, Fu M, Bjornsson E, Kalaitzakis E: Prevalence of pre-transplant electrocardiographic abnormalities and post-transplant cardiac events in patients with liver cirrhosis. BMC Gastroenterol, 2014; 14: 65
20. VanWagner LB, Bhave M, Te HS et al: Patients transplanted for nonalcoholic steatohepatitis are at increased risk for postoperative cardiovascular events. Hepatology, 2012; 56(5): 1741–50
21. Zein CO, Levy C, Basu A, Zein NN: Chronic hepatitis C and type II diabetes mellitus: A prospective cross-sectional study. Am J Gastroenterol, 2005; 100: 48–55
22. Albeldawi M, Aggarwal A, Madhwal S et al: Cumulative risk of cardiovascular events after orthotopic liver transplantation. Liver Transpl, 2012; 18: 370–75
23. Wray C, Scovotti JC, Tobis J et al: Liver transplantation outcome in patients with angiographically proven coronary artery disease: A multi-institutional study. Am J Transplant, 2013; 13(1): 184–91
24. Maddur H, Bourdillon PD, Liangpunsakul S et al: Role of cardiac catheterization and percutaneous coronary intervention in the preoperative assessment and management of patients before orthotopic liver transplantation. Liver Transpl, 2014; 20: 664–72
25. VanWagner LB, Ning H, Whitsett M et al: A point-based prediction model for cardiovascular risk in orthotopic liver transplantation: The CAR-OLT Score. Hepatology, 2017; 66: 1968–79

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