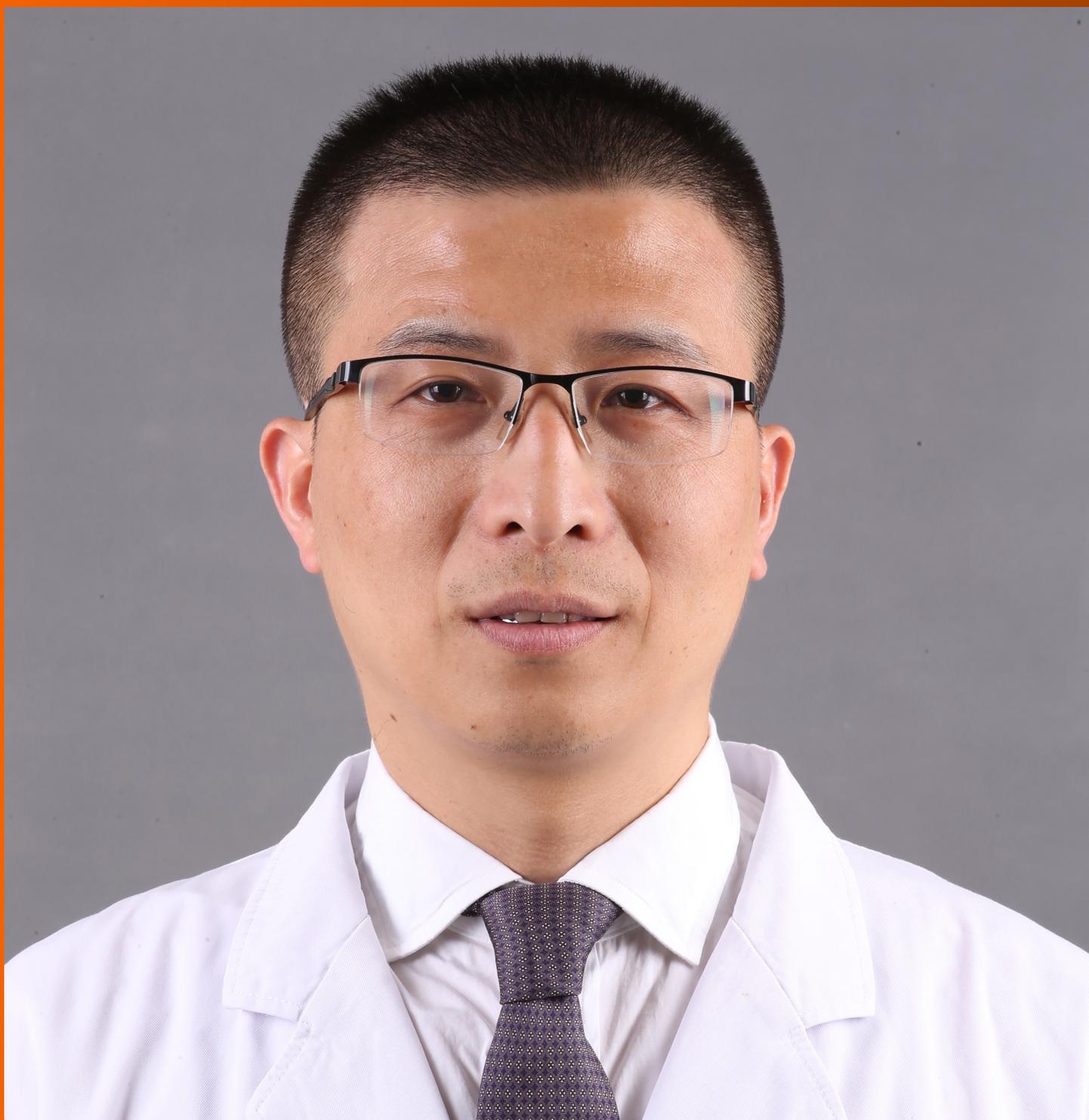


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ABOUT COVER

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The primary aim of *World Journal of Hepatology (WJH, World J Hepatol)* is to provide scholars and readers from various fields of hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJH mainly publishes articles reporting research results and findings obtained in the field of hepatology and covering a wide range of topics including chronic cholestatic liver diseases, cirrhosis and its complications, clinical alcoholic liver disease, drug induced liver disease autoimmune, fatty liver disease, genetic and pediatric liver diseases, hepatocellular carcinoma, hepatic stellate cells and fibrosis, liver immunology, liver regeneration, hepatic surgery, liver transplantation, biliary tract pathophysiology, non-invasive markers of liver fibrosis, viral hepatitis.

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Retrospective Cohort Study

Cardiac risk factors limiting survival to liver transplantation in patients with nonalcoholic fatty liver disease

Michael Delicce, Joseph Mauch, Abel Joseph, Ruishen Lyu, Heather Kren, Rose Bartow, Donna Ferchill, Maan Fares, Jamile Wakim-Fleming

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Abstract**BACKGROUND**

Nonalcoholic fatty liver disease (NAFLD) describes the hepatic manifestations of metabolic syndrome, which is estimated to affect 25% of adults, and currently represents the second most common indication for liver transplant in the United States. Studies have shown that patients with NAFLD are at an increased risk for heart failure, arrhythmia, and coronary artery disease (CAD), which may impact outcomes of liver transplantation. However, it remains unclear whether the presence of cardiac disease affects survival prior to liver transplant. If so, this would represent an important opportunity to optimize cardiac status and improve outcomes before liver transplant.

AIM

To identify cardiac factors that impact survival to liver transplantation in patients with NAFLD and on the transplant waitlist.

METHODS

The aim of this study was to identify cardiac risk factors that limit survival to transplant in patients with NAFLD. We performed a retrospective analysis of patients with NAFLD listed for liver transplant at a tertiary academic medical center in the United States from January 2015 to January 2021, identified through United Network of Organ Sharing registry. Exclusion criteria included a concurrent etiology of liver disease and removal from the transplant list due to chemical dependency, lack of social support, improvement in liver disease, or being lost to follow-up. We manually reviewed patient charts including electrocardiogram, echocardiogram, and cardiac catheterization reports as well as physician notes to identify cardiac disease states (*i.e.*, heart failure, arrhythmia, valvular disease and CAD) and other related diagnoses. We performed a survival analysis by Cox proportional hazards regression model to analyze the association between cardiac factors at the time listed for transplant and death or clinical deterioration prior to transplant.

RESULTS

Between January 2015 and January 2021, 265 patients with nonalcoholic fatty liver disease were listed for liver transplant at our institution. Our patient sample had a median age of 63 and an even distribution between sexes. The median Model for End-Stage Liver Disease (MELD) score was 17 and the median body mass index was 31.6. Of these 265 patients, 197 (74.3%) survived to transplant and 68 (25.7%) died or clinically deteriorated prior to transplant. The presence of mild or moderate CAD represented a hazard ratio of 2.013 (95%CI 1.078-3.759, $P = 0.029$) for death or clinical deterioration when compared to patients without CAD, after adjustment for age, sex, and MELD. MELD represented an adjusted hazard ratio of 1.188.

CONCLUSION

Mild or moderate CAD represents a hazard for waitlist mortality prior to liver transplant in patients with NAFLD. Aggressive management of CAD may be needed to improve patient outcomes.

Key Words: Nonalcoholic fatty liver disease; Liver transplant; Cardiovascular disease; Pre-transplant outcomes; Coronary artery disease; Risk factors

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Core Tip: Nonalcoholic fatty liver disease (NAFLD) continues to rise in prevalence as a leading indication for liver transplantation. Due to its metabolic features, NAFLD is a risk factor for cardiovascular disease such as coronary artery disease (CAD), atrial fibrillation and heart failure. In our study, we examined the impact of cardiac factors on survival to liver transplant, once listed, in patients with NAFLD. We observed that even mild or moderate CAD represents an independent hazard for waitlist mortality before liver transplant after adjustment for confounding variables. This compels improved treatment of less severe forms of CAD in patients undergoing liver transplant.

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INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) describes the hepatic manifestations of metabolic syndrome. NAFLD encompasses a spectrum of disease that ranges from simple steatosis to nonalcoholic steatohepatitis and cirrhosis. The prevalence of nonalcoholic fatty liver disease is increasing in Europe and the United States, becoming one of the most frequent causes of end-stage liver disease and hepatocellular carcinoma. NAFLD is now the second most common etiology of liver disease among patients listed for liver transplant (LT) in the United States, with an increase in the prevalence of NAFLD as an indication for liver transplant by 170% between 2004 and 2013[1].

Due to its metabolic features, NAFLD is a reported risk factor for cardiovascular disease such as coronary artery disease, atrial fibrillation, diastolic dysfunction, and heart failure[2-6]. Cardiovascular disease is the leading cause of early mortality after liver transplant, accounting for over 40% of early deaths related to both coronary and non-coronary events[7]. However, whether cardiovascular disease influences outcomes while on the waitlist for liver transplantation remains to be established. The purpose of this retrospective cohort study is to identify cardiac factors that impact patient survival to liver transplantation in patients with NAFLD and on the transplant waitlist.

MATERIALS AND METHODS

Study design

We performed a retrospective cohort study assessing the impact of cardiac risk factors on death or clinical deterioration prior to liver transplant among patients with nonalcoholic fatty liver disease.

Subject identification

Our study was approved by the institutional review board prior to subject identification. We identified all patients listed for LT at a tertiary academic referral center in the Midwest United States from January 1st 2015 to January 31st 2021 *via* review of United Network of Organ Sharing (UNOS) registry. Adult patients (> 18 years) with a clinical diagnosis of NAFLD, as listed by UNOS, were included in our study. Exclusion criteria included a concurrent etiology of liver disease and removal from the transplant list due to chemical dependency, medical non-adherence, or clinical improvement. Patients who remained active on the transplant list during the study period were also excluded due to a lack of outcome at the time of investigation. We reviewed all patient charts to confirm the etiology of liver disease and reasons for removal from the liver transplant list.

Data collection

We extracted demographics and clinical information from UNOS that included patient name, medical record number, date of birth, date listed for transplant, liver disease diagnosis, indication for transplant, Model for End-Stage Liver Disease (MELD) score, body mass index (BMI), date removed from the transplant list, and reasons for removal. We reviewed all patient charts to confirm the reason for removal from the transplant list. Patients were classified into two categories: transplanted *vs* death or clinical deterioration. Patients who successfully received LT were categorized into the transplanted group. Clinical deterioration was defined as acute illness, progression of hepatocellular carcinoma, and incidence of concurrent illness that prompted removal from the LT list. Patients removed from the LT list because of chemical dependency, medical non-adherence or improvement in liver disease were excluded from analysis.

Study data were collected and managed using REDCap electronic data capture system hosted at our home institution. All most recently available data were collected at the time of listing for LT. We utilized natural language processing and electronic medical record coding to extract numerical data from patient charts. The data extracted included high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride count, hemoglobin A1c, troponin, NT Pro BNP and left ventricular ejection fraction. We performed a random manual review of these data to confirm accuracy.

We also performed manual chart reviews including review of diagnostic reports and physician documentation to identify and assess cardiac risk factors. Electrocardiogram reports were reviewed to identify QTc and arrhythmia defined as atrial fibrillation or atrial flutter. Echocardiogram reports were reviewed to identify left ventricular ejection fraction, estimated right ventricular systolic pressure and valvular abnormality (*i.e.*, aortic stenosis, aortic insufficiency, mitral regurgitation and tricuspid regurgitation). Valvular abnormalities described as moderate or severe were included; trivial or mild valvular abnormalities were not included. Cardiac catheterization reports were reviewed to identify coronary artery disease (CAD). Severe CAD was defined as luminal stenosis of 70% or greater in a main coronary vessel (*i.e.*, left main, left circumflex, left anterior descending, right coronary artery or posterior descending artery), and/or history of myocardial infarction (MI), percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG)[8]. Moderate CAD was defined as luminal stenosis of 50-69% in a main coronary vessel[8]. Mild CAD was defined as luminal stenosis < 50% in a main coronary vessel. No significant CAD was defined as absence of luminal irregularity on cardiac catheterization or negative cardiac stress testing without a history of MI, PCI or CABG. We reviewed right heart catheterization reports to identify Fick's cardiac index, Fick's cardiac output, pulmonary capillary wedge pressure and right ventricular systolic pressure. We identified the presence of heart failure, hypertension, obstructive sleep apnea and need for renal replacement therapy by manual review of diagnosis codes and physician documentation.

Statistical analysis

The statistical methods of this study were reviewed by Ruishen Lyu, a biostatistician in the Department

of Quantitative Health Sciences at the author's institution. Patient characteristics were described using means and standard deviations for normally distributed continuous variables, medians and quartiles for non-normally distributed continuous variables, and frequency (percentage) for categorical variables. Analysis of variance or the non-parametric Kruskal-Wallis tests were used to assess differences in continuous variables. The chi-square test and Fisher's exact test were used to compare categorical variables as appropriate.

Time to event was defined by the number of months from the date of listing to the date of transplant or the date of removal due to death or clinical deterioration. Unadjusted Cox proportional hazards regression models were used to assess the association between each risk factor and time to development of the competing event (death or clinical deterioration). Multivariable Cox proportional hazards regression model was performed to build a model to assess the association between the outcome, time to event, and risk factors collected at baseline, including confounding variables of age, sex, and MELD score. In the multivariable model development, the multivariate imputation by chained equation was performed to impute missing values to conduct a complete dataset for variable selection. The stepwise variable selection method based on Akaike information criterion was used to choose the final model. The variables that had a large portion of missing values, were unbalanced between levels with small number of events, or were highly correlated to others were excluded from the model. Analyses were performed using R software (version 3.6.2; Vienna, Austria) and P value < 0.05 was considered statistically significant.

RESULTS

Between January 2015 and January 2021, 265 patients with NAFLD were listed for LT at our institution. **Table 1** shows baseline patient characteristics at the time of listing for LT. Our patient sample had a median age of 63.1 [57.4, 67.2], median MELD score of 17 and median BMI of 31.6; 48.3% ($n = 128$) of patients were male and 51.7% ($n = 137$) female.

Of these 265 patients, 197 (74.3%) survived to transplant and 68 (25.7%) died or clinically deteriorated prior to transplant. **Table 1** shows that patient characteristics were similar between groups except for the presence of obstructive sleep apnea (32.4% *vs* 20.3%, P value = 0.043) and median elevation in estimated right ventricular systolic pressure (34.0 *vs* 30.0, P value = 0.012) in the group not transplanted because of death or clinical deterioration.

Table 2 describes the univariate analysis of factors' impact on death or clinical deterioration prior to transplant, and expressed in hazard ratios with 95% confidence intervals. MELD and renal replacement therapy had increased hazard ratios of 1.18 (95%CI 1.14-1.23, $P < 0.001$) and 3.20 (95%CI 1.49-6.88, $P = 0.003$), respectively. Tricuspid regurgitation had a hazard ratio of 3.50 (95%CI 1.26-9.72, $P = 0.016$) whereas hazard ratios were insignificant for aortic stenosis, aortic insufficiency and mitral regurgitation. Compared to no CAD, mild or moderate CAD represented a hazard ratio of 2.06 (95%CI 1.14-3.74, $P = 0.017$) and severe CAD represented a hazard ratio of 2.43 (95%CI 1.17-5.05, $P = 0.017$).

Table 3 describes results of the multivariable Cox proportional hazards regression model on survival failure to transplant after adjustment for possible confounders and statistically significant variables that were included in the regression model. Variables included in the model were age, sex, MELD score and coronary artery disease. When adjusted for other variables in the multivariable model, the presence of mild or moderate CAD independently represented a hazard ratio of 2.013 (95%CI 1.078-3.759, $P = 0.029$) for death or clinical deterioration. Severe CAD lost statistical significance after adjustment for other variables with 95%CI 0.968-4.538. MELD score represented a hazard ratio of 1.188 (95%CI 1.139-1.239, $P < 0.001$).

DISCUSSION

This retrospective cohort analysis aimed to identify cardiovascular disease that limit survival to liver transplant in patients with nonalcoholic fatty liver disease while on the LT waitlist. In our study, we found that the presence of mild or moderate coronary artery disease at the time listed for LT significantly increased the risk for patient death or clinical deterioration prior to receiving a transplanted organ when adjusted for potential confounders.

Contrary to our expectations, severe coronary artery disease did not represent a significant hazard for death prior to LT in our study. Patients with severe CAD met one of the following criteria: coronary artery occlusion of 70% or greater, history of myocardial infarction, history of PCI or history of CABG. Patients with severe CAD were, therefore, more likely to have received procedural or surgical intervention for CAD, and this may explain the lack of increased hazard on waitlist mortality.

It is established in numerous studies that patients with NAFLD are at an increased risk for cardiovascular disease including coronary artery disease, heart failure, and arrhythmia[2-6]. Despite this, few data exist that analyze the impact of cardiovascular disease on survival outcomes prior to LT in patients with NAFLD.

Table 1 Patient characteristics with nonalcoholic fatty liver disease listed for liver transplant

Variable	Total (n = 265)	Transplanted (n = 197)	Not transplanted due to death or clinical deterioration (n = 68)	P value		
Demographics						
Age (yr)	63.1 [57.4, 67.2]	197	62.8 [56.6, 66.7]	68	64.1 [59.6, 68.5]	0.060 ^a
Sex		197		68		0.42 ^b
Female	137 (51.7)		99 (50.3)		38 (55.9)	
Male	128 (48.3)		98 (49.7)		30 (44.1)	
Model for End-Stage Liver Disease	17.0 [13.0, 24.0]	197	17.0 [13.0, 24.0]	68	18 [12.0, 24.5]	0.44 ^a
Body mass index (kg/m ²)	31.6 [28.3, 37.2]	197	32.2 [28.3, 36.8]	68	31.3 [28.2, 38.6]	0.79 ^a
Comorbid Conditions						
Renal replacement therapy	32 (12.1)	197	24 (12.2)	68	8 (11.8)	0.93 ^b
Hypertension	152 (57.4)	197	113 (57.4)	68	39 (57.4)	0.99 ^b
Obstructive sleep apnea	62 (23.4)	197	40 (20.3)	68	22 (32.4)	0.043 ^b
Cardiac disease						
Atrial fibrillation/ Atrial flutter	8 (3.0)	197	5 (2.5)	67	3 (4.5)	0.42 ^c
Heart failure	18 (6.9)	194	10 (5.2)	68	8 (11.8)	0.091 ^c
Left ventricular ejection fraction	65.0 [61.0, 70.0]	196	66.0 [61.5, 70.5]	67	65.0 [61.0, 70.0]	0.80 ^a
Estimated right ventricular systolic pressure	31.0 [25.0, 36.0]	142	30.0 [25.0, 35.0]	48	34.0 [26.5, 38.5]	0.012 ^a
Aortic stenosis	8 (3.0)	197	7 (3.6)	68	1 (1.5)	0.68 ^c
Aortic insufficiency	2 (0.75)	197	1 (0.51)	68	1 (1.5)	0.45 ^c
Mitral regurgitation	4 (1.5)	197	3 (1.5)	68	1 (1.5)	0.99 ^c
Tricuspid regurgitation	8 (3.0)	197	4 (2.0)	68	4 (5.9)	0.21 ^b
CAD		197		68		0.12 ^b
No significant CAD	196 (74.0)		152 (77.2)		44 (64.7)	
Mild or Moderate CAD	45 (17.0)		30 (15.2)		15 (22.1)	
Severe CAD	24 (9.1)		15 (7.6)		9 (13.2)	
History of myocardial infarction	12 (4.5)	197	7 (3.6)	68	5 (7.4)	0.19 ^c
History of coronary artery stenting	13 (4.9)	197	8 (4.1)	68	5 (7.4)	0.33 ^c
History of coronary artery bypass grafting	11 (4.2)	197	7 (3.6)	68	4 (5.9)	0.48 ^c
Lab values						
Hemoglobin A1c		125		46		0.37 ^b
< 5.6	59 (34.5)		47 (37.6)		12 (26.1)	
5.6-6.5	62 (36.3)		43 (34.4)		19 (41.3)	
> 6.5	50 (29.2)		35 (28.0)		15 (32.6)	
High-density lipoprotein		188		63		0.31 ^b
≥ 50	75 (29.9)		53 (28.2)		22 (34.9)	
< 50	176 (70.1)		135 (71.8)		41 (65.1)	
Triglycerides		190		65		0.37 ^c
≤ 150	240 (94.1)		177 (93.2)		63 (96.9)	

> 150	15 (5.9)	13 (6.8)	2 (3.1)
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^aWilcoxon Rank Sum test.

^bPearson's chi-square test.

^cFisher's Exact test. Statistics presented as Median [P25, P75] and *n* (column %). CAD: Coronary artery disease.

Table 2 Univariate analysis on time to development of death/clinical deterioration prior to liver transplant

Variable	<i>n</i>	Events	Cox univariate hazard ratio (95%CI)	<i>P</i> value
Age	265	68 (26%)	1.018 (0.985, 1.053)	0.28
Sex				
Female	137	38 (28%)	-	
Male	128	30 (23%)	0.84 (0.52, 1.37)	0.49
Model for End-Stage Liver Disease	265	68 (26%)	1.18 (1.14, 1.23)	< 0.001
Body mass index	265	68 (26%)	0.975 (0.941, 1.011)	0.17
Renal replacement therapy				
No	233	60 (26%)	-	
Yes	32	8 (25%)	3.20 (1.49, 6.88)	0.003
Hypertension				
No	113	29 (26%)	-	
Yes	152	39 (26%)	1.15 (0.71, 1.88)	0.57
Obstructive sleep apnea				
No	203	46 (23%)	-	
Yes	62	22 (35%)	1.10 (0.66, 1.85)	0.72
Atrial fibrillation/ Atrial flutter				
No	256	64 (25%)	-	
Yes	8	3 (38%)	2.97 (0.92, 9.61)	0.069
Heart failure				
No	244	60 (25%)	-	
Yes	18	8 (44%)	1.81 (0.86, 3.82)	0.12
Left ventricular ejection fraction	263	67 (25%)	0.99 (0.96, 1.03)	0.69
Estimated right ventricular systolic pressure	190	48 (25%)	1.026 (0.997, 1.055)	0.075
Aortic stenosis				
No	257	67 (26%)	-	
Yes	8	1 (13%)	0.95 (0.13, 6.86)	0.96
Aortic insufficiency				
No	263	67 (25%)	-	
Yes	2	1 (50%)	1.38 (0.19, 10.04)	0.75
Mitral regurgitation				
No	261	67 (26%)	-	
Yes	4	1 (25%)	2.92 (0.40, 21.48)	0.29
Tricuspid regurgitation				
No	257	64 (25%)	-	
Yes	8	4 (50%)	3.50 (1.26, 9.72)	0.016

CAD				
No significant CAD	196	44 (22%)	-	
Mild or Moderate CAD	45	15 (33%)	2.06 (1.14, 3.74)	0.017
Severe CAD	24	9 (38%)	2.43 (1.17, 5.05)	0.017
History of myocardial infarction				
No	253	63 (25%)	-	
Yes	12	5 (42%)	2.29 (0.92, 5.74)	0.076
History of coronary artery stenting				
No	252	63 (25%)	-	
Yes	13	5 (38%)	1.86 (0.74, 4.66)	0.19
History of coronary artery bypass grafting				
No	254	64 (25%)	-	
Yes	11	4 (36%)	2.03 (0.73, 5.65)	0.17
Hemoglobin A1c				
< 5.6	59	12 (20%)	-	-
5.6-6.5	62	19 (31%)	1.11 (0.53, 2.32)	0.79
> 6.5	50	15 (30%)	0.80 (0.37, 1.76)	0.58
High-density lipoprotein				
≥ 50	75	22 (29%)	-	
< 50	176	41 (23%)	1.18 (0.69, 2.01)	0.54
Triglycerides				
≤ 150	240	63 (26%)	-	
> 150	15	2 (13%)	0.49 (0.12, 2.00)	0.32

CAD: Coronary artery disease.

Our study expands previous knowledge of the associations of NAFLD and cardiac disease[2-6], as well as the impact of cardiac disease on LT outcomes[7], by specifically evaluating the impact of these known cardiovascular associations of NAFLD on waitlist mortality. Our study identifies the negative impact of even mild or moderate coronary artery disease on patient outcomes prior to LT independent of severity of liver disease. This finding compels a better identification of CAD and treatment of less severe forms in patients who are undergoing liver transplant, especially in patients who otherwise are not candidates for coronary reperfusion therapy.

There is a large body of evidence showing that a comprehensive cardiovascular risk management strategy reduces risk of a variety of outcomes including cardiac events and death. These include weight loss in obesity[9,10], glycemic control in diabetes mellitus[11], intensive lipid-lowering therapy[12,13], management of hypertension[14], and smoking cessation[15]. In an effort to improve patient survival to LT, it may be beneficial to follow practice guidelines published by the American Heart Association and American College of Cardiology Foundation on secondary prevention and risk reduction therapy for patients with NAFLD and non-obstructive coronary disease who are listed for LT. Current guidelines recommend smoking cessation, use of beta-blockers and/or ACE inhibitors for blood pressure control, statin therapy to achieve an LDL-C of < 100 mg/dL or non-HDL-C of < 130 mg/dL in patients with triglycerides > 200 mg/dL, and weight management to maintain a BMI between 18.5 and 24.9 kg/m² [16].

This study has several strengths. The identification of patients, NAFLD diagnosis and MELD score were collected from the United Network of Organ Sharing national database. We manually reviewed patient charts to ensure accuracy of diagnoses, lab values and reason not transplanted. We utilized rigorous methods in our statistical analysis to account for potential confounding variables.

A number of questions remain unanswered, such as the impact of mild CAD and moderate CAD independently on survival to LT. Our ability to analyze these variables independently was limited by a small number of events with patients with moderate CAD. Further prospective study with a larger sample of patients will help address this question. An important, but unanswered, question is how medical and lifestyle interventions for coronary artery disease will impact survival to transplant in

Table 3 Multivariable model on failure to survive to liver transplant

Variable	Hazard ratio	95%CI	P value
Age	1.008	0.973-1.044	0.655
Sex: Male <i>vs</i> Female	1.026	0.592-1.777	0.927
Model for End-Stage Liver Disease	1.188	1.139-1.239	< 0.001
Mild or Moderate CAD <i>vs</i> No significant CAD	2.013	1.078-3.759	0.029
Severe CAD <i>vs</i> No significant CAD	2.096	0.968-4.538	0.060
Observations	265		

CAD: Coronary artery disease.

patients with NAFLD. In our study, we did not identify the use of medications for risk reduction in CAD. We, therefore, did not analyze the influence of lifestyle intervention and risk-lowering medications on patient outcomes during the study period, and were not able to assess the duration of such intervention being a tertiary referral center. This represents a meaningful opportunity for future studies to evaluate the impact of lifestyle intervention and medical therapy on waitlist mortality.

One inherent limitation of our study is the observational methodology utilized. While we performed a multivariable analysis to minimize confounding variables, observational studies are prone to bias and confounding, and cannot be used to demonstrate causality. Additionally, inclusion of patients listed for transplant at a single tertiary academic medical center in the Midwest United States limited the generalizability of our findings to the broader population of patients with NAFLD.

CONCLUSION

Mild or moderate coronary artery disease in patients with NAFLD who are listed for liver transplant is associated with a significant risk of death or clinical deterioration leading to removal from the transplant list. Our findings suggest that management of mild or moderate CAD may be needed to improve patient outcomes in the pre-transplant period.

ARTICLE HIGHLIGHTS

Research background

Nonalcoholic fatty liver disease (NAFLD) is rising in prevalence and is a leading cause of liver transplant. Patients with NAFLD are at increased risk for cardiac disease, which is a known contributor to post-transplant mortality. We aimed to identify cardiac disease that limits survival while on the transplant waitlist.

Research motivation

To identify cardiac disease that limits survival while on the transplant waitlist. This would lead to further insights into how we may need to improve testing and optimization of cardiac disease for patients being considered to liver transplant.

Research objectives

To identify cardiac disease that limits survival while on the transplant waitlist. We found that non-obstructive coronary artery disease (CAD) is associated with failure to survive to liver transplant in patients with NAFLD. Further study is needed to assess impact on pre-transplant outcomes after improvement in medical management of patients with non-obstructive CAD.

Research methods

We performed a retrospective cohort study of patients with NAFLD listed for liver transplant. We analyzed the presence of various cardiac disease states and their association with failure to survive to transplant.

Research results

Mild or moderate coronary artery disease represented a hazard for death or clinical deterioration prior

to liver transplant in patients with NAFLD.

Research conclusions

Mild or moderate coronary artery disease represented a hazard for death or clinical deterioration prior to liver transplant. Improvement in identification and management of non-obstructive coronary artery disease may be needed to improved patient outcomes in the pre-transplant period.

Research perspectives

Further study is needed to assess impact on pre-transplant outcomes after improvement in medical management of patients with NAFLD and non-obstructive coronary artery disease who are listed for liver transplant.

FOOTNOTES

Author contributions: Delicce M, Wakim-Fleming J, Lyu R and Fares M designed the research study; Delicce M, Mauch J, Joseph A, Lyu R, Bartow R, Ferchill D and Kren H performed the research; Lyu R performed statistical analysis; Delicce M, Mauch J and Lyu R analyzed the data and wrote the manuscript; all authors have read and approve the final manuscript.

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