

Original Research Article

Pre-existing heart failure subtype and in-hospital mortality in liver transplantation: a nationwide analysis

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Received: 10 September 2026

Revised: 14 October 2026

Accepted: 19 October 2026

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ABSTRACT

Background: Heart failure (HF) is increasingly encountered in liver transplant candidates, yet the influence of HF phenotype on perioperative outcomes remains unclear. We evaluated the association between pre-existing HF subtype and in-hospital mortality among liver transplant hospitalizations.

Methods: We conducted a retrospective cohort study of the National Inpatient Sample, 2016-2022. Adult liver transplant hospitalizations were stratified into no HF, chronic diastolic HF, and chronic systolic HF (surrogates for HF with preserved and reduced ejection fraction, respectively). The primary outcome was in-hospital mortality; secondary outcomes included acute kidney injury, acute HF, cardiogenic shock, cardiac arrest, discharge disposition, length of stay, and hospital charges. Survey-weighted multivariable logistic regression was adjusted for demographics, comorbidities, and hospital characteristics.

Results: Among 53,910 weighted hospitalizations, 98.1% had no HF, 1.5% had chronic diastolic HF, and 0.4% had chronic systolic HF. Patients with chronic diastolic HF were older with a greater comorbidity burden, including hypertension, diabetes, arrhythmias, and renal failure (all $p < 0.01$). Unadjusted in-hospital mortality was higher in chronic diastolic HF (5.7%) and chronic systolic HF (7.0%) than in no HF (2.9%; $p = 0.03$), as were acute kidney injury, cardiac arrest, length of stay, and charges. After adjustment, neither chronic diastolic HF (adjusted odds ratio 1.6, 95% confidence interval 0.7-3.4) nor chronic systolic HF (2.1, 0.7-6.7) was independently associated with mortality.

Conclusions: Pre-existing HF is associated with worse unadjusted outcomes in liver transplant hospitalizations, but HF subtype is not independently associated with in-hospital mortality after adjustment. Comorbidity burden, rather than HF phenotype, appears to drive mortality risk in this highly selected population.

Keywords: Heart failure, HFpEF, Liver transplantation, Mortality

INTRODUCTION

Pre-existing heart failure (HF) is a recognized predictor of adverse perioperative outcomes in major noncardiac surgery.¹ According to the 2024 American Heart Association/American College of Cardiology (AHA/ACC) perioperative guidelines, patients with HF with preserved ejection fraction (HFpEF) have approximately a 1.5-fold increased risk of postoperative

mortality, whereas those with severely reduced left ventricular ejection fraction ($<30\%$) have a 2.35-fold increased risk compared with patients without HF.²

The relationship between HF and liver transplantation is particularly complex because patients with end-stage liver disease may independently develop cirrhotic cardiomyopathy, characterized by impaired systolic or diastolic reserve despite preserved resting cardiac function. Cirrhotic cardiomyopathy has been reported in

up to 23% of liver transplant candidates and is increasingly recognized as a contributor to perioperative morbidity and mortality.³⁻⁵ During liver transplantation, major hemodynamic fluctuations, reperfusion injury, vasoplegia, and rapid fluid shifts may further unmask occult cardiac dysfunction.³⁻⁵

Cardiovascular disease has become increasingly important in modern liver transplant populations because transplant candidates are older and have a greater burden of obesity, diabetes mellitus, hypertension, chronic kidney disease, and coronary artery disease.^{6,7} This shift is reinforced by a change in the underlying etiology of end-stage liver disease. Metabolic dysfunction-associated steatotic liver disease has displaced chronic hepatitis C as a leading indication for liver transplantation in the United States and, together with alcohol-associated liver disease, now accounts for the majority of transplants; it is also the fastest-growing indication among candidates with hepatocellular carcinoma.⁸ Consequently, the cardiometabolic traits that increasingly bring patients to transplantation obesity, insulin resistance, and hypertension are the same traits that drive HFpEF, so the two conditions are converging in the same patients rather than occurring independently.

However, patients who ultimately undergo liver transplantation represent a highly selective population following extensive cardiovascular screening and multidisciplinary evaluation. Current liver transplant protocols routinely incorporate electrocardiography and transthoracic echocardiography to evaluate systolic function, diastolic dysfunction, valvular disease, pulmonary pressures, and right ventricular function.^{9,10} Patients with advanced or poorly compensated HF, severely reduced left ventricular systolic function, pulmonary hypertension, or impaired contractile reserve frequently undergo additional cardiology evaluation and may be considered poor transplant candidates because of concerns regarding perioperative cardiogenic shock, arrhythmias, and multiorgan failure.¹¹ Consequently, overt HF may be underrepresented among liver transplant recipients despite the substantial cardiovascular comorbidity burden in end-stage liver disease populations.

Recognition of HFpEF physiology has further expanded cardiovascular risk stratification in liver transplantation. Shin et al. demonstrated that approximately 6.6% of patients with end-stage liver disease undergoing liver transplantation had a high probability of HFpEF using the HFA-PEFF score.¹² Importantly, patients with higher HFA-PEFF scores demonstrated lower long-term survival probabilities and higher rates of major adverse cardiovascular events after transplantation.¹²

Despite increasingly stringent cardiovascular screening, it remains unclear whether carefully selected patients with pre-existing HF continue to experience unfavorable perioperative outcomes following liver transplantation. A better understanding of these risks may help refine current

screening strategies and determine whether existing transplant selection thresholds are appropriately balanced between perioperative safety and access to transplantation.

Accordingly, this study aimed to evaluate the association between pre-existing chronic diastolic and chronic systolic HF used as administrative surrogates for HFpEF and HF with reduced ejection fraction (HFrEF), respectively and in-hospital outcomes among adult patients undergoing liver transplantation, compared with patients without HF.

METHODS

Data source

We performed a retrospective cohort study using the Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS), maintained by the Agency for Healthcare Research and Quality. The study period extended from January 1, 2016, to December 31, 2022. The NIS is the largest publicly available all-payer inpatient database in the United States, containing a 20% stratified sample of discharges from community hospitals across participating states; the study population was therefore drawn from hospitals across the United States rather than from a single institution. Discharge weights provided by HCUP allow the generation of nationally representative estimates of hospitalizations.

Study population

We included all adult hospitalizations (≥ 18 years) involving liver transplantation during the index hospitalization between January 1, 2016, and December 31, 2022. Liver transplantation was identified using the International Classification of Diseases, Tenth Revision, Procedure Coding System (ICD-10-PCS) procedure code 0FY00Z0, which corresponds to allogeneic liver transplantation via an open approach. Hospitalizations were then categorized according to pre-existing HF status using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes into three groups: no HF, chronic diastolic HF, and chronic systolic HF. Given the limitations of administrative coding in the NIS, chronic diastolic and chronic systolic HF codes were used as surrogates for HFpEF and HFrEF, respectively. Specifically, chronic diastolic HF was identified using code I50.32 (chronic diastolic [congestive] heart failure), whereas chronic systolic HF was identified using code I50.22 (chronic systolic [congestive] heart failure).

Hospitalizations of patients younger than 18 years were excluded. In addition, to preserve phenotype specificity, hospitalizations in which HF was coded as combined systolic and diastolic HF (ICD-10-CM I50.40-I50.43), right-sided HF (I50.81), or unspecified HF (I50.9) were excluded, because these codes do not allow assignment to a preserved or reduced ejection fraction phenotype.

Variables and outcomes

Baseline variables included patient demographics (age, sex, race), primary payer, median household income quartile, and hospital characteristics (bed size, teaching status, and region). Comorbidities were defined using the Agency for Healthcare Research and Quality Elixhauser Comorbidity Software. Sex was recorded in the NIS as the binary administrative sex documented in the discharge record; the database does not distinguish sex assigned at birth from gender identity, and no data on gender are available. Sex was therefore modeled as a covariate, and the study was not designed or powered for sex-stratified analyses.

The primary outcome was in-hospital mortality. Secondary outcomes included acute heart failure, acute kidney injury (AKI), cardiogenic shock, cardiac arrest, discharge disposition, length of stay (LOS), and total hospital charges.

Statistical analysis

We applied survey weights, stratification, and clustering to all analyses to generate nationally representative estimates in accordance with HCUP guidelines. Descriptive statistics were used to summarize baseline characteristics across HF subtypes. Continuous variables were reported as means $\pm$ standard deviations (SD) or medians with interquartile ranges (IQR), as appropriate, whereas categorical variables were summarized as weighted percentages. Comparisons between groups were performed using survey-adjusted chi-square tests for categorical variables and survey-adjusted linear regression or quantile regression for continuous variables, as appropriate.

Multivariable logistic regression was performed to estimate adjusted odds ratios (aORs) for in-hospital mortality across HF subtypes compared with patients without HF. The model was adjusted for age, sex, race/ethnicity, primary payer, hypertension, diabetes mellitus, cardiac arrhythmias, valvular disease, pulmonary circulation disorders, renal failure, obesity, and hospital characteristics (bed size, location/teaching status, and region). Results were reported as aORs with corresponding

95% confidence intervals (CIs). A two-sided p -value <0.05 was considered statistically significant. Total hospital charges were adjusted for inflation to 2022 U.S. dollars using the U.S. Bureau of Labor Statistics Consumer Price Index. All analyses were performed using Stata version 18.0 (StataCorp LLC, College Station, TX).

Ethical considerations

This study was a secondary analysis of de-identified, publicly available administrative discharge data and did not involve direct contact with human participants. It was therefore exempt from institutional review board review and from the requirement for informed consent, and was conducted in accordance with the Declaration of Helsinki. The NIS contains no donor-level information, and the investigators had no role in organ procurement, allocation, or donor authorization. All transplants captured in the database were performed at United States centers operating under the Organ Procurement and Transplantation Network, which requires documented authorization for donation from the donor or their next of kin, free from coercion, and under which organs and tissues are not sourced from executed prisoners or prisoners of conscience.

Use of artificial intelligence

An artificial intelligence tool (Claude, Anthropic) was used to generate Figure 1 from the study results, and for language editing and formatting of the manuscript. It was not used for data acquisition, statistical analysis, or interpretation of the findings. All content was reviewed and verified by the authors, who take full responsibility for the manuscript.

RESULTS

Study cohort and baseline characteristics

From 2016 to 2022, a total of 53,910 weighted liver transplant hospitalizations were identified. Of these, 52,900 (98.1%) had no pre-existing HF, 795 (1.5%) had chronic diastolic HF, and 215 (0.4%) had chronic systolic HF. Baseline characteristics are summarized in Table 1.

Table 1: Baseline characteristics of liver transplant hospitalizations by pre-existing heart failure subtype.

Variables	No HF (n=52,900)	Chronic diastolic HF (n=795)	Chronic systolic HF (n=215)	P value
Age (years), mean$\pm$SD	54.9 $\pm$ 11.7	60.4 $\pm$ 7.7	55.2 $\pm$ 9.8	<0.01
Female, %	36.7	40.3	30.2	0.45
Race, %				
White	67.9	66.7	62.5	0.78
Black	7.6	9.8	12.5	
Hispanic	16.0	17.7	20.0	
Asian/Pacific Islander	3.8	2.0	5.0	
Native American	0.9	0.0	0.0	
Other	4.0	3.9	0.0	

Continued.

Variables	No HF (n=52,900)	Chronic diastolic HF (n=795)	Chronic systolic HF (n=215)	P value
Primary payer, %				
Medicare	29.6	45.9	30.2	0.02
Medicaid	15.3	14.5	25.6	
Private insurance	49.7	32.7	37.2	
Self-pay	0.8	1.3	2.3	
No charge	0.6	0.6	0.0	
Other	4.0	5.0	4.7	
ZIP income quartile, %				
1st quartile	23.3	21.9	14.3	0.07
2nd quartile	25.0	18.7	23.8	
3rd quartile	26.4	33.6	42.9	
4th quartile	25.4	25.8	19.1	
Hospital location/teaching status, %				
Rural	0.0	0.0	0.0	0.95
Urban non-teaching	1.2	1.3	0.0	
Urban teaching	98.8	98.7	100.0	
Hospital bed size, %				
Small	2.1	3.1	0.0	0.65
Medium	13.1	12.6	9.3	
Large	84.8	84.3	90.7	
Hospital region, %				
Northeast	17.1	17.0	18.6	0.27
Midwest	22.7	30.8	27.9	
South	39.3	32.7	32.6	
West	21.0	19.5	20.9	
Comorbidities, %				
Hypertension	49.1	69.2	60.5	<0.01
Diabetes mellitus	31.4	42.8	39.5	<0.01
Anemia	5.7	6.3	4.7	0.91
Cancer	24.7	20.1	23.3	0.39
Cardiac arrhythmias	20.0	33.3	41.9	<0.01
Valvular disease	3.4	7.6	7.0	<0.01
Pulmonary circulation disorders	5.3	18.2	9.3	<0.01
Chronic pulmonary disease	9.4	12.6	11.6	0.35
Renal failure	26.5	47.8	46.5	<0.01
Obesity	18.5	31.5	14.0	<0.01
Coagulopathy	71.3	76.7	81.4	0.10
Alcohol abuse	38.9	31.5	34.9	0.14

Values are presented as weighted percentages unless otherwise specified; Chronic diastolic HF and chronic systolic HF were used as surrogate definitions for HFpEF and HFrEF, respectively; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; SD, standard deviation

Compared with patients without HF, patients with chronic diastolic HF were older (60.4 ± 7.7 vs 54.9 ± 11.7 years, $p < 0.01$), whereas patients with chronic systolic HF had a similar mean age (55.2 ± 9.8 years). Female sex distribution was numerically higher in chronic diastolic HF and lower in chronic systolic HF compared with patients without HF, although this did not reach statistical significance. Most liver transplant hospitalizations across all groups occurred in urban teaching hospitals ($>98\%$). Medicare was the primary payer in 45.9% of patients with chronic diastolic HF, compared with 30.2% of patients with chronic systolic HF and 29.6% of patients without HF. In contrast, Medicaid coverage was most common among patients

with chronic systolic HF (25.6% vs 15.3% in no HF and 14.5% in chronic diastolic HF, $p = 0.02$). ZIP income quartile distribution, hospital bed size, and hospital region were generally similar between groups.

Patients with both chronic diastolic and chronic systolic HF demonstrated a substantially greater cardiometabolic comorbidity burden compared with patients without HF. Compared with the no-HF group, patients with chronic diastolic HF had higher rates of hypertension (69.2% vs 49.1%), diabetes mellitus (42.8% vs 31.4%), pulmonary circulation disorders (18.2% vs 5.3%), renal failure (47.8% vs 26.5%), obesity (31.5% vs 18.5%), cardiac

arrhythmias (33.3% vs 20.0%), and valvular heart disease (7.6% vs 3.4%) (all $p < 0.01$). Similarly, patients with chronic systolic HF had higher rates of hypertension (60.5% vs 49.1%), diabetes mellitus (39.5% vs 31.4%), cardiac arrhythmias (41.9% vs 20.0%), valvular disease (7.0% vs 3.4%), pulmonary circulation disorders (9.3% vs

5.3%), and renal failure (46.5% vs 26.5%) compared with patients without HF. Cardiac arrhythmias were most prevalent among patients with chronic systolic HF. Rates of anemia, cancer, chronic pulmonary disease, coagulopathy, and alcohol abuse were generally similar across groups.

Table 2: In-hospital outcomes of liver transplant hospitalizations by pre-existing heart failure subtype.

Variables	No HF (n=52,900)	Chronic diastolic HF (n=795)	Chronic systolic HF (n=215)	P value
In-hospital mortality, %	2.9	5.7	7.0	0.03
Acute heart failure, %	1.9	0.6	0.0	0.32
Acute kidney injury, %	62.6	75.5	72.1	<0.01
Cardiogenic shock, %	1.4	1.3	2.3	0.86
Cardiac arrest, %	0.2	0.6	2.3	<0.01
Discharge disposition, %				<0.01
Routine/home	43.5	22.6	23.3	
Short-term hospital	0.7	0.6	4.7	
Other facility	20.2	31.5	20.9	
Home health care	32.7	39.6	44.2	
Against medical advice	0.0	0.0	0.0	
Died in hospital	2.9	5.7	7.0	
Length of stay, median (IQR), days	12 (8-24)	19 (11-37)	33 (14-51)	<0.01
Total hospital charges, median (IQR), US\$	494,123 (347,633-790,957)	668,704 (450,985-1,234,883)	939,071 (547,885-1,562,965)	<0.01

Values are presented as weighted percentages unless otherwise specified; Length of stay and total hospital charges are presented as median with IQR; Total hospital charges were adjusted for inflation to 2022 U.S. Dollars using the Consumer Price Index; HF, heart failure; IQR, interquartile range

Table 3: Multivariable logistic regression for in-hospital mortality in liver transplant hospitalizations.

Variables	aOR	95% CI	P value
HF subtype (vs no HF)			
Chronic diastolic HF	1.6	0.7-3.4	0.24
Chronic systolic HF	2.1	0.7-6.7	0.21
Age (per year)	1.0	1.0-1.0	0.33
Female sex	1.1	0.8-1.4	0.68
Race (vs White)			
Black	1.9	1.2-2.8	<0.01
Hispanic	1.3	0.9-1.8	0.12
Asian/Pacific Islander	1.0	0.5-1.9	0.90
Native American	2.7	1.1-6.4	0.02
Other	1.0	0.5-1.9	0.96
Primary payer (vs Medicare)			
Medicaid	0.6	0.4-0.9	0.02
Private insurance	0.8	0.6-1.0	0.09
Self-pay	1.9	0.8-4.5	0.12
No charge	1.6	0.6-4.7	0.36
Other	0.6	0.3-1.3	0.19
Comorbidities			
Hypertension	0.5	0.4-0.7	<0.01
Diabetes mellitus	0.6	0.4-0.8	<0.01
Cardiac arrhythmias	2.4	1.9-3.1	<0.01
Valvular disease	0.5	0.3-1.1	0.11
Pulmonary circulation disorders	1.9	1.3-2.8	<0.01

Continued.

Variables	aOR	95% CI	P value
Renal failure	1.8	1.4-2.4	<0.01
Obesity	0.7	0.5-1.0	0.06

Multivariable logistic regression analysis was performed to evaluate predictors of in-hospital mortality among liver transplant hospitalizations; aORs are reported with corresponding 95% CIs; The multivariable model adjusted for demographic characteristics, primary payer status, major cardiovascular and metabolic comorbidities, and hospital characteristics (bed size, location/teaching status, and region); estimates for hospital characteristics are not shown; aOR, adjusted odds ratio; CI, confidence interval; HF, heart failure

In-hospital outcomes

In-hospital outcomes are summarized in Table 2 and Figure 1. Compared with patients without HF, unadjusted in-hospital mortality was significantly higher among patients with chronic diastolic HF (5.7% vs 2.9%) and chronic systolic HF (7.0% vs 2.9%, $p=0.03$). AKI occurred more frequently among patients with chronic diastolic HF (75.5% vs 62.6%) and chronic systolic HF (72.1% vs 62.6%, $p<0.01$). Cardiac arrest was also more common among patients with chronic systolic HF (2.3% vs 0.2%, $p<0.01$) and chronic diastolic HF (0.6% vs 0.2%, $p<0.01$). Rates of cardiogenic shock (1.3% and 2.3% vs 1.4%, $p=0.86$) and coded acute HF (0.6% and 0.0% vs 1.9%, $p=0.32$) did not differ significantly between groups.

Healthcare resource utilization

Patients with HF also demonstrated substantially greater healthcare resource utilization compared with patients without HF. Median LOS increased from 12 days (IQR 8-24) in patients without HF to 19 days (IQR 11-37) in chronic diastolic HF and 33 days (IQR 14-51) in chronic systolic HF. Similarly, median total hospital charges were higher among patients with chronic diastolic HF (\$668,704) and chronic systolic HF (\$939,071) compared with patients without HF (\$494,123). Routine discharge home was less common among patients with chronic diastolic HF (22.6%) and chronic systolic HF (23.3%) than among patients without HF (43.5%), whereas discharge to home health services or other facilities was more frequent in the HF groups.

Predictors of in-hospital mortality

Following multivariable adjustment (Table 3 and Figure 1D), neither chronic diastolic HF (aOR 1.6, 95% CI 0.7-3.4, $p=0.24$) nor chronic systolic HF (aOR 2.1, 95% CI 0.7-6.7, $p=0.21$) remained independently associated with in-hospital mortality compared with patients without HF. However, several comorbidities remained independently associated with mortality, including cardiac arrhythmias (aOR 2.4, 95% CI 1.9-3.1, $p<0.01$), pulmonary circulation disorders (aOR 1.9, 95% CI 1.3-2.8, $p<0.01$), and renal failure (aOR 1.8, 95% CI 1.4-2.4, $p<0.01$). Black and Native American race categories were also independently associated with increased in-hospital mortality, whereas hypertension and diabetes mellitus were inversely associated with mortality in the adjusted model.

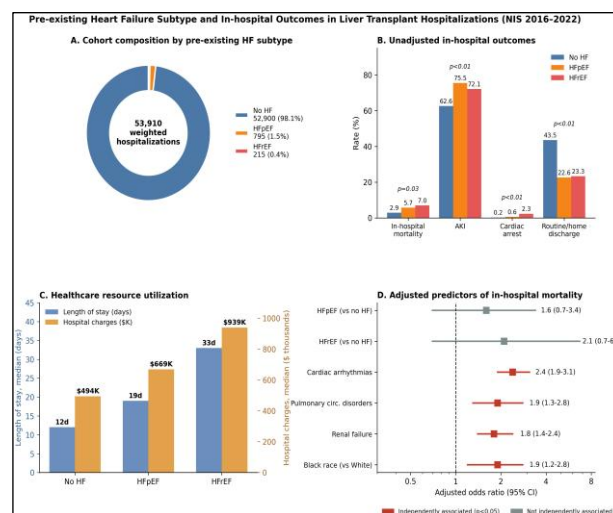


Figure 1: Pre-existing heart failure (HF) subtype and in-hospital outcomes among adult liver transplant hospitalizations, National Inpatient Sample 2016-2022. (A) Composition of the weighted study cohort ($n = 53,910$) by pre-existing HF status. (B) Unadjusted rates of in-hospital mortality, acute kidney injury (AKI), cardiac arrest, and routine discharge home by HF subtype; p -values are from survey-adjusted chi-square tests. (C) Median length of stay (days, left axis) and median inflation-adjusted total hospital charges (thousands of US dollars, right axis) by HF subtype. (D) Adjusted odds ratios with 95% confidence intervals (CIs) for in-hospital mortality for selected covariates from the multivariable logistic regression model; no HF is the reference group for the HF subtypes and White race is the reference for Black race.

Red markers denote covariates independently associated with mortality ($p<0.05$); gray markers denote associations that were not statistically significant. In the figure, HFpEF and HFrEF denote chronic diastolic HF (ICD-10-CM I50.32) and chronic systolic HF (I50.22), respectively, which were used as administrative surrogates for HF with preserved and reduced ejection fraction.

DISCUSSION

Principal findings and prevalence of pre-existing heart failure

This is the first nationally representative study evaluating the association between pre-existing HF subtypes and in-

hospital outcomes among patients undergoing liver transplantation. In our cohort, chronic diastolic HF and chronic systolic HF accounted for only 1.5% and 0.4% of liver transplant hospitalizations, respectively, substantially lower than rates reported in other solid organ transplant populations. Prior kidney transplant studies have reported pre-existing HF prevalence as high as 57.4% among transplant candidates and recipients, reflecting the significant cardiovascular burden in end-stage renal disease populations.^{13,14} The relatively low HF prevalence observed in our study likely reflects the highly selective nature of liver transplant candidacy and extensive cardiovascular screening prior to transplantation.⁹⁻¹¹ Cardiovascular disease has been reported to account for approximately 8% of liver transplant rejections during evaluation.¹⁵ Similar observations have been reported in kidney transplantation, where 10–20% of candidates may be removed from the waitlist because of cardiovascular burden.¹⁶

Female representation was relatively low across the overall liver transplant cohort, although women appeared more prevalent in the chronic diastolic HF subgroup than in the chronic systolic HF subgroup. This finding likely reflects the epidemiologic distribution of HF phenotypes, as HFpEF and diastolic dysfunction are more common among older women and patients with obesity, hypertension, and metabolic comorbidities.^{17,18}

Heart failure subtype and in-hospital mortality

In the unadjusted analysis, patients with chronic diastolic and chronic systolic HF demonstrated substantially higher in-hospital mortality (5.7% and 7.0%, respectively) compared with patients without HF (2.9%). These findings are biologically plausible given the greater burden of cardiovascular and metabolic comorbidities among HF subgroups. Prior studies in kidney transplantation have similarly demonstrated worse perioperative outcomes among patients with pre-existing HF, including increased mortality, delayed graft function, prolonged hospitalization, and cardiovascular complications.¹⁹ Likewise, cardiovascular disease has consistently been identified as a major contributor to early morbidity and mortality following liver transplantation.⁶ VanWagner et al. reported a similar short-term mortality rate of 2.9% within 30 days after liver transplantation, comparable to the mortality observed in our non-HF cohort; however, cardiovascular complications accounted for 40.2% of early post-transplant deaths in their study.⁶ Furthermore, Shin et al demonstrated that patients with a high probability of HFpEF based on the HFA-PEFF score had substantially worse long-term outcomes, with a 12-year survival rate of 72.1% compared with 82.4% and 82.5% in the intermediate- and low-risk HFpEF groups, respectively.¹²

After multivariable adjustment, pre-existing chronic diastolic and chronic systolic HF remained positively associated with in-hospital mortality; however, these associations did not reach statistical significance. Patients

with chronic diastolic HF demonstrated 1.6-fold higher adjusted odds of in-hospital mortality, whereas patients with chronic systolic HF demonstrated 2.1-fold higher adjusted odds of mortality compared with patients without HF. Several explanations may account for these findings. First, the relatively small number of patients with pre-existing HF, particularly chronic systolic HF, may limit the statistical power to detect significant differences after adjustment. Second, these findings may reflect the effectiveness of current cardiovascular screening and transplant selection protocols, whereby only highly selected and medically optimized patients with HF ultimately proceed to liver transplantation. Consequently, although patients with HF demonstrated higher crude mortality and complication rates, rigorous pre-transplant cardiovascular evaluation may partially mitigate the independent mortality risk associated with pre-existing HF in carefully selected transplant candidates.

A counterintuitive observation was that hypertension and diabetes mellitus were inversely associated with in-hospital mortality in the adjusted model. The most plausible explanation is confounding by liver disease severity rather than a protective effect: advanced cirrhosis produces a hyperdynamic circulation with splanchnic vasodilation and low systemic vascular resistance, so patients with the most decompensated disease frequently become normotensive or hypotensive and no longer carry an active hypertension diagnosis, whereas a retained hypertension code may mark relatively preserved hemodynamics.³ Similar reasoning applies to diabetes, which is difficult to distinguish from hepatogenous diabetes in claims data and may be documented more consistently among patients well enough to sustain longitudinal outpatient care. Ascertainment may compound this, because chronic comorbidities are captured less completely in short, acutely fatal admissions. Finally, in a cohort that has already survived transplant selection, treated risk factors may act partly as markers of engagement with care. These estimates should be regarded as hypothesis-generating, and individual Elixhauser comorbidity flags should not be interpreted causally.

Perioperative complications and resource utilization

Pre-existing HF was also associated with increased risk of AKI and in-hospital cardiac arrest following liver transplantation, whereas rates of acute HF and cardiogenic shock did not significantly differ between groups. The higher AKI risk likely reflects impaired cardiac reserve, reduced effective arterial perfusion, and worsening cardiorenal physiology during the substantial hemodynamic stress of transplantation.^{20,21}

In addition to clinical outcomes, patients with HF demonstrated significantly greater healthcare utilization. Median LOS increased from 12 days in patients without HF to 19 days in chronic diastolic HF and 33 days in chronic systolic HF, with corresponding rises in median hospital charges from \$494,123 to \$668,704 and \$939,071,

respectively. Discharge to home was markedly less frequent in HF patients (22.6% in chronic diastolic HF and 23.3% in chronic systolic HF vs 43.5%), while greater proportions required home health services (39.6% and 44.2% vs 32.7%) or transfer to other facilities (31.5% and 20.9% vs 20.2%). These findings highlight significantly increased resource utilization and post-discharge care needs in this population and are consistent with prior literature on post-transplant resource utilization in cardiovascular-comorbid recipients.^{22,23}

Racial disparities

Racial disparities in outcomes were also evident. After multivariable adjustment, Black patients demonstrated 1.9-fold higher odds of in-hospital mortality compared with White patients. These disparities persisted even after adjustment for clinical and hospital-level factors, suggesting that non-clinical determinants, including access to care, timing of transplantation, and structural inequities, may substantially contribute to differences in outcomes. Similar findings were reported by Ross-Driscoll et al., who demonstrated a 21% significantly increased mortality risk among Black liver transplant recipients despite adjustment for Model for End-Stage Liver Disease (MELD) score, underlying liver disease etiology, and donor-related risk factors, further supporting the persistence of racial disparities in liver transplant outcomes.²⁴

Clinical implications

Cardiovascular disease is well recognized to contribute to both short- and long-term mortality following liver transplantation. However, optimal risk stratification in patients with pre-existing HF, particularly across HF subtypes, remains poorly defined. Current evidence suggests that reliance on left ventricular ejection fraction alone may underestimate subclinical myocardial dysfunction, especially in cirrhotic cardiomyopathy, where impaired cardiac reserve and diastolic dysfunction may only become clinically apparent during perioperative stress.^{9,21,25,26} Modern approaches increasingly incorporate multimodal assessment, including strain imaging, coronary artery calcium scoring, coronary computed tomography angiography, and liver transplant-specific cardiovascular risk scores such as CAD-LT and CAR-OLT.^{10,27-29}

In our study, the very low prevalence of pre-existing HF among liver transplant recipients likely reflects rigorous cardiovascular screening and highly selective transplant candidacy. Although pre-existing chronic diastolic and chronic systolic HF were associated with higher crude mortality and perioperative complications, neither remained independently associated with in-hospital mortality after adjustment. These findings suggest that current screening strategies may successfully identify medically optimized HF patients suitable for transplantation; however, patients with HF continued to demonstrate substantially greater perioperative burden,

including higher rates of AKI, cardiac arrest, prolonged hospitalization, and increased healthcare utilization. Further prospective studies are warranted to improve HF-specific risk classification and optimize cardiovascular screening strategies in liver transplant candidates.

This study has several important limitations. First, its retrospective design, based on the NIS, introduces inherent risks of selection bias and residual confounding despite multivariable adjustment. Administrative databases rely on ICD-10-CM coding, which may result in misclassification of both HF subtypes and clinical outcomes; in particular, HFpEF and HFrEF were assigned from diastolic versus systolic HF codes without echocardiographic verification of ejection fraction, and exclusion of unspecified HF (I50.9) and combined systolic/diastolic HF (I50.40-I50.43) may have removed a substantial proportion of patients who were clinically heart-failure affected but not phenotyped in claims data. A sensitivity analysis including these codes should be considered in future work. Second, the NIS records hospitalizations rather than unique patients, so a patient retransplanted within the study period would contribute more than one observation. Third, the NIS does not capture several variables central to transplant risk, including MELD or MELD-Na score, etiology of liver disease, donor characteristics, cold ischemia time, and induction immunosuppression each a potentially strong confounder. Fourth, transplant allocation policy changed during the study window, with acuity-circle allocation implemented in February 2020, and era effects were not modeled. In addition, the analysis is restricted to in-hospital outcomes and does not capture post-discharge complications or long-term mortality, which are particularly relevant in liver transplant populations where cardiovascular events frequently occur beyond the index hospitalization. The relatively low prevalence of HF may also have limited statistical power to detect independent associations with mortality after adjustment; with approximately 47 deaths among chronic diastolic HF patients and 15 among chronic systolic HF patients, events-per-variable in the adjusted model approached the conventional minimum threshold, and the wide confidence intervals should be interpreted accordingly. There is also potential for unmeasured confounding from factors such as frailty, socioeconomic status, and access to care, which are not fully captured in the dataset and may partially explain observed disparities.

CONCLUSION

In this nationally representative liver transplant cohort, pre-existing chronic diastolic and chronic systolic HF were not independently associated with adjusted in-hospital mortality. The prevalence of pre-existing HF was relatively low, with chronic diastolic HF and chronic systolic HF accounting for only 1.5% and 0.4% of liver transplant hospitalizations, respectively, likely reflecting highly selective transplant candidacy and rigorous cardiovascular screening prior to transplantation. Further prospective studies are needed to improve HF-specific risk

stratification and optimize cardiovascular screening among liver transplant candidates.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Sivakumar N, Puchongmart C, Padovese C, Abujulaydah M, Thiravetyan B, Maharaj V. Pre-existing heart failure subtype and in-hospital mortality in liver transplantation: a nationwide analysis. *Int J Res Med Sci* 2026;14:5047-56.