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Liver Transplant Outcomes in Patients With Postcapillary Pulmonary Hypertension

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Background. Postcapillary pulmonary hypertension (PH) can be seen in cirrhosis. Research and treatment goals exist for patients with portopulmonary hypertension but not for postcapillary PH. The aim of this study was to investigate outcomes after liver transplant (LT) for patients with postcapillary PH. **Methods.** This was a retrospective cohort study of 1173 patients who underwent LT at our center between 2010 and 2020. Using a propensity score matched analysis followed by multivariable Cox modeling on matched patients, we compared post-LT survival between patients with and without postcapillary PH. We also compared several post-LT outcomes between patient with different types of PH. **Results.** Sixty-eight patients had PH, and 50 had postcapillary PH. The median age was 59 y and the sample was 54% male. There was no significant difference in mortality between patients with postcapillary PH and patients without PH (hazard ratio, 1.72; 95% confidence interval, 0.90-3.31; $P = 0.10$). There was no significant difference in survival between patients with any type of PH and those without PH. There was no significance difference in post-LT survival, acute kidney injury, or pulmonary edema between patients with different types of PH. Patients with postcapillary PH who survived had a higher cardiac output than those who died (11 L/min in patients who lived, as compared with 8 L/min in patients who died; $P = 0.03$). **Conclusions.** Postcapillary PH does not appear to convey a negative impact on post-LT survival. A higher cardiac output may be protective against mortality in patients with postcapillary PH.

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Pulmonary hypertension (PH) is a known complication of advanced cirrhosis. Up to 20% of patients undergoing liver transplantation (LT) may have elevated pulmonary artery pressures.[1] Portopulmonary hypertension (POPH), although not the most common, is the best described type of PH in patients with cirrhosis.[2] Patients with cirrhosis more commonly have postcapillary PH, a condition characterized by elevated pulmonary artery wedge pressure (>15 mm Hg) and normal pulmonary vascular resistance (PVR) (<3 Wood units).[3] This occurs in part due to volume overload in the context of secondary hyperaldosteronism and left ventricular diastolic dysfunction.[4]

POPH has a poor prognosis, and most of these patients die as a results of their liver disease.[5,6] Unfortunately, POPH patients present a challenge to LT committees given higher risks, and therefore this life-saving procedure is frequently denied, particularly in patients who do not achieve specific hemodynamic goals while receiving pulmonary arterial hypertension-specific treatment. Uncontrolled pulmonary arterial hypertension and the resultant right ventricular dysfunction increase the risk for

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complications such as acute right ventricular failure after LT because of the abrupt increase in preload and flow to the right side of the heart.[7] Guidelines exist for screening and treating POPH, in order to improve outcomes, ensure judicious allocation of organs, and to facilitate safe transplants. When POPH is adequately managed with pulmonary vasodilators, patients with POPH can undergo LT.[8]

Limited information is available regarding the management and outcomes of postcapillary PH in patients with cirrhosis that undergo LT. One small study showed no increase in mortality in patients with postcapillary PH undergoing LT when compared with patients with POPH or patients without PH.[9] A second study showed no increase in mortality in patients with mean pulmonary artery pressure (mPAP) >35 mm Hg at time of transplant, the majority of which had postcapillary PH.[10] The primary purpose of this study was to compare the outcomes after LT of patients with postcapillary PH with those without PH. Our secondary goals were to compare post-LT outcomes between patients with POPH and postcapillary PH, as well as patients with any type of PH to those without PH. This investigation is essential to determine the impact of postcapillary PH on post-LT outcomes.

MATERIALS AND METHODS

This is a single-center retrospective study of 1346 consecutive patients who underwent LT at Cleveland Clinic, between January 2010 and March 2020. Patients with multiorgan transplant or prior LT were excluded, leaving a sample size of 1173 patients. All LT candidates underwent screening echocardiogram as part of their pretransplant evaluation. Patients underwent right heart catheterization (RHC) within 1 y of LT if they had a right ventricular systolic pressure ≥40 mm Hg or any degree of RV dilation or dysfunction.

PH was defined as an mPAP of ≥25 mm Hg on RHC.[11] The "no PH" group was defined as patients who had right ventricular systolic pressure <40 mm Hg on echocardiogram without signs of right ventricular strain and therefore did not undergo a screening RHC or patients who had an RHC but were found to have mPAP of <25 mm Hg. Patients who had PH were divided into categories based on the hemodynamic profile on their RHC in accordance with the 5th World Symposium on Pulmonary Hypertension.[3,11] Patients with pulmonary capillary wedge pressure (PCWP) >15 mm Hg and PVR <3 Woods units (WU) fell into the category of "postcapillary PH." Patients with PCWP <15 mm Hg and PVR >3 WU fell into the category of POPH. Patients with PVR >3 WU but with PCWP >15 mm Hg were defined as having "mixed PH." Patients with PCWP <3 WU and PCWP <15 mm Hg, with cardiac index >4 L/min were defined as having "PH due to high CO."

We collected baseline characteristics including Model for End-stage Liver Disease (MELD) score and age at transplant for the entire sample. For the patients with PH, data were also collected on various outcomes including mortality data, cause of death, intensive care unit (ICU) length of stay (LOS), hospital LOS, post-LT pulmonary edema, and post-LT acute kidney injury (AKI). The primary outcome of interest was to compare the survival of patients with postcapillary PH to patients without PH. Secondary outcomes included comparing the survival of patients with postcapillary PH with those with POPH and comparing survival of patients with any type of PH with patients without PH.

Statistical Methods

Data are described using mean and SD for normally distributed continuous variables, median and quartiles for non-normally distributed continuous variables, and frequency (percentage) for categorical variables. Shapiro-Wilk test was used to determine the distribution of continuous variables. ANOVA or the nonparametric Kruskal-Wallis tests were used to compare continuous variables. Chi-square test and Fisher exact test were used to compare categorical variables as appropriate. Kaplan-Meier cumulative incidence curves with 95% confidence intervals (CIs) were conducted. The median follow-up time was calculated by the reverse Kaplan-Meier Estimator.

To assess the survival difference between patients with postcapillary PH and without PH, propensity score (PS) matching was performed. The matching ratio was 1:5 (PH: non-PH). After matching, we created a multivariable Cox model on survival adjusted by 2 confounders (age and MELD score). This analysis was then performed in 2 subgroups according to mPAP (mPAP 25–35, and mPAP 35 and above). To assess the survival difference between patients with any type of PH and patients without PH, a similar PS matching and multivariable model was performed.

Log-rank test was used to assess the survival difference between the different groups of PH. The starting point of the survival analysis was the date of LT. Survival was assessed by chart review and documented "alive vs. dead" status at last follow-up. Linear regression analysis was used to assess the association between each PH group and ICU and hospital LOS. The logarithm of hospital LOS was modeled as the outcome variable and the square root of ICU LOS was modeled as the outcome variable in the univariate analysis. Analyses were performed using SAS software (version 9.4; Cary, NC) and R (version 3.6.2; Vienna, Austria) software. $P < 0.05$ was considered statistically significant.

Guidelines

The study was approved by the Institutional Review Board and was conducted according to their standards. Informed consent was waived for this retrospective chart review. Our study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for observational studies.[12]

RESULTS

Of the 1173 patients that underwent LT, 68 (6%) were found to have PH of any type. Fifty patients had postcapillary PH, 9 had POPH, and 8 fit into the category of "PH due to high cardiac output." One patient had a component of both pulmonary arterial and venous hypertension ("mixed" PH). This patient was receiving vasodilator therapy for POPH, so they were analyzed along with the POPH group. Baseline characteristics of these patients are described in Table 1. In addition, there were 5 patients who were found to have mPAPs between 20 and 25, which meets the criteria for PH according to the 6th World Symposium on Pulmonary Hypertension.[3] All of these patients had a normal PVR. Three had postcapillary PH and 2 had "PH due to high CO." However, these patients did not meet the mPAP threshold for the purpose of this study and thus were analyzed in the non-PH group.

There was no significant difference between the 3 groups in terms of age at LT, MELD score, sex, and presence of

TABLE 1.

Baseline characteristics of patients with various types of PH

Factor	N	Overall	Postcapillary PH (N = 50)	POPH (N = 10)	PH because of high CO (N = 8)	*P*
Age at transplant, median (Q1–Q3)	68	59.0 (52.5–62.5)	59.0 (53.0–63.0)	57.0 (53.0–60.0)	58.5 (50.0–62.5)	0.55[a]
Gender, n (%)	68					0.93[b]
Female		31 (45.6)	22 (44.0)	5 (50.0)	4 (50.0)	
Male		37 (54.4)	28 (56.0)	5 (50.0)	4 (50.0)	
MELD score, median (Q1–Q3)	68	22.0 (17.0–31.5)	23.5 (17.0–32.0)	18.0 (17.0–20.0)	20.5 (13.5–33.0)	0.14[a]
mPAP, median (Q1–Q3)	68	32.0 (28.0–38.0)	32.0 (28.0–38.0)	35.5 (28.0–43.0)	28.0 (25.5–31.0)	0.06[a]
Renal failure, n (%)	68					0.10[b]
No		26 (38.2)	16 (32.0)	7 (70.0)	3 (37.5)	
Yes		42 (61.8)	34 (68.0)	3 (30.0)	5 (62.5)	
On dialysis, n (%)	68					0.56[b]
No		53 (77.9)	37 (74.0)	9 (90.0)	7 (87.5)	
Yes		15 (22.1)	13 (26.0)	1 (10.0)	1 (12.5)	

[a] Wilcoxon rank-sum test (*P* values).
[b]Fisher exact test (*P* values).
Statistics are presented as median (P25–P75) or N (column %).
CO, cardiac output; MELD, Model for End-stage Liver Disease; mPAP, mean pulmonary artery pressure; PH, pulmonary hypertension; POPH, portopulmonary hypertension.

TABLE 2.

Comparison of patients with and without PH after PS matching

Comparison: Postcapillary PH vs non-PH

Factor	Overall (N = 300)	Control (non-PH) (N = 250)	Case (postcapillary PH) (N = 50)	Standardized difference[a]
Age at transplant, median (Q1–Q3)	59.0 (53.0–63.0)	58.5 (53.0–63.0)	59.0 (53.0–63.0)	0.01
MELD score, median (Q1–Q3)	23.5 (16.8–31.9)	23.5 (16.8–31.8)	23.2 (16.7–32.1)	0.02

Comparison: PH vs non-PH

Factor	Overall (N = 408)	Control (non-PH) (N = 340)	Case (PH) (N = 68)	Standardized difference
Age at transplant, median (Q1–Q3)	58.0 (53.0–62.0)	58.0 (53.0–62.0)	59.0 (52.5–62.5)	<0.01
MELD score, median (Q1–Q3)	21.7 (16.6–31.1)	21.8 (16.4–31.0)	21.6 (16.7–31.6)	0.01

[a]Standardized difference = difference in rank-based means divided by SE; imbalance defined as absolute value >0.20 (small effect size).
Statistics are presented as median (P25–P75) or N (column %).
MELD, Model for End-stage Liver Disease; PH, pulmonary hypertension; PS, propensity score.

pretransplant renal failure. All patients with postcapillary PH had a normal ejection fraction on echocardiogram. Five patients had moderate-to-severe valvular heart disease (4 patients with moderate mitral regurgitation and 1 patient with severe aortic regurgitation).

Comparison of Patients With Postcapillary PH Versus No PH

We compared baseline characteristics (age at transplant and MELD) between patients with no PH and those with postcapillary PH. There was a significant difference in MELD score between the 2 groups (median MELD score of 23 in the postcapillary PH group as compared with 20 in the group of patients without PH [$P = 0.01$]). MELD scores ranged from 14 to 27 in the non-PH group and ranged from 17 to 32 in the postcapillary PH group. There was no significant difference in age at transplant between the 2 groups (59 y in the postcapillary PH group versus 58 y in the non-PH group; $P = 0.55$).

We also compared the survival of all patients with postcapillary PH (n = 50) matched in a 1:5 ratio with patients without PH (n = 250). Table 2 shows the summaries by patient status after PS matching. There was no significant difference in age or MELD score between the groups. There was a significant difference in raw mortality rate from date of transplant to last follow-up between the 2 groups (34% for the postcapillary PH group versus 18% for the non-PH group). After matching, the standardized mean difference in age and MELD score was <0.2, indicating good matching between the 2 groups. The median follow-up time for the postcapillary PH group was 75 and 53 mo for the non-PH group. The Kaplan-Meier curve is demonstrated in Figure 1. The 1-, 3-, and 5-y survival in the postcapillary PH group was 78%, 76%, and 71%, respectively.

Compared with the non-PH group, on multivariable Cox regression analysis adjusted for age and MELD score, patients with postcapillary PH had increased mortality with a hazard ratio (HR) of 1.72 (95% CI, 0.90-3.31), but the difference was not statistically significant ($P = 0.10$). After redoing the multivariable Cox regression analysis after PS matching with patients grouped according to various mPAP thresholds, patients with mPAP 25–35 had an HR of death of 1.12 ($P = 0.75$) compared with the non-PH group. However, patients with mPAP 35+ had an HR of death of 2.97 ($P = 0.06$).

Analysis of Hemodynamics of Patients With Postcapillary PH

We compared hemodynamic characteristics on preoperative RHC of patients with postcapillary PH who lived with those who died (Table 3). Patients who survived had a significantly higher cardiac output (CO). The median CO was

11 L/min in patients who lived as compared with 8 L/min in those who died (P = 0.04). There was no significant difference in any of the other hemodynamic parameters. Of the 17 patients with postcapillary PH who died, causes of death included cardiac arrest (n = 6), stroke/myocardial infarction (n = 2), respiratory failure (n = 3), sepsis (n = 2), and unknown causes (n = 1). Of those who died from cardiac arrest, 2 died intraoperatively from cardiac arrest and the other 4 had out-of-hospital cardiac arrest after the transplant hospitalization. One of the patients who died from intraoperative cardiac arrest had acute right ventricular failure and severe PH just before the reperfusion phase of the transplant, followed by a pulseless electrical activity arrest. The second patient died of an intraoperative pulseless electrical activity arrest in the setting of coagulopathy and hemorrhagic shock.

We also compared the initial intraoperative mPAP and CO at the time of LT between patients with postcapillary PH who lived and those who died (Table 3). This information was available from operative reports for 36 of the 50 patients. Intraoperative data on PVR and PCWP were not available.

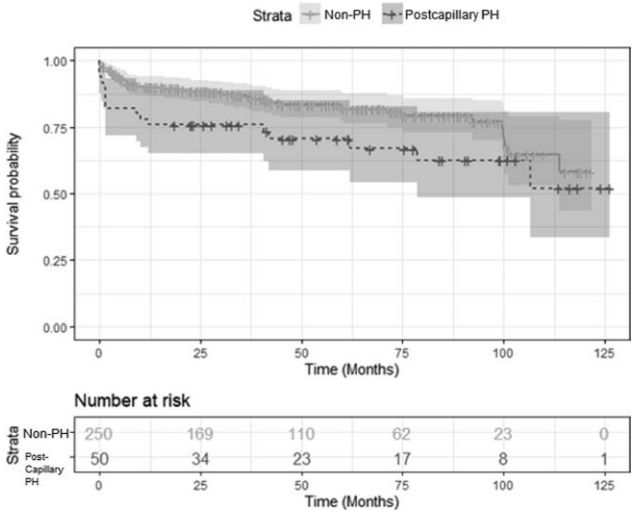

FIGURE 1. Kaplan-Meier survival: postcapillary PH vs no PH. Kaplan-Meier curve comparing survival of patients with postcapillary PH to matched patients with no PH. The 1-, 3-, and 5-y survival in the postcapillary PH group was 78.0%, 76.0%, and 70.7%, respectively. The 1-, 3-, and 5-y survival in the non-PH group was 89.4%, 84.7%, and 79.0%, respectively. PH, pulmonary hypertension.

The mean mPAP in patients who lived was 21.6, and the mean mPAP in patients who died was 24.5 (P = 0.33). There was a significant difference in mean CO at time of transplant as well (9.9 in patients who lived, as compared with 7.7 in patients who died; P = 0.03). We also compared the preoperative use of continuous renal replacement therapy in patients who lived as compared with those who died and found no significant difference in its use (15.2% of those who lived had preoperative continuous renal replacement therapy versus 17.6% of those who died; P = 0.99).

Comparison of Patients With and Without PH of Any Type

We compared the survival of patients with PH (n = 68) matched in a 1:5 ratio with patients without PH (n = 340) by age and MELD score. Table 2 shows the summaries by patient status after matching including patients with and without PH. There was no significant difference in age, MELD score, or raw mortality rate between the matched groups. After matching, the standardized mean difference of age and MELD score between the 2 groups was decreased to <0.2, indicating a good balance between 2 groups. The median follow-up time for PH group was 80 mo and the median follow-up in the non-PH group was 53 mo. The Kaplan-Meier curve is shown in Figure 2. Survival at 1, 3, and 5 y was 89%, 85%, and 79%, respectively, in the control group, and 84%, 82%, and 76% in the PH group, respectively. On multivariable Cox regression analysis adjusted for age and MELD score, we found no significant difference in survival between patients with and without PH (HR, 1.16; 95% CI, 0.68-1.95; P = 0.59).

Comparison of Patients With Various Types of PH

The median follow-ups for the postcapillary PH, POPH, and PH because of high CO groups were 75.27, 54.60, and 88.61 mo, respectively. The median follow-up for patients with PH was 80.20 mo.

Figure 3 shows the Kaplan-Meier curve between the 3 hemodynamic groups. There was a trend toward decreased survival in patients with postcapillary PH, but the difference in survival was not statistically significant (P = 0.11). The 1-, 3-, and 5-y survival was 78%, 76%, and 70.7%, respectively, in the postcapillary PH group. Survival at 1, 3, and 5 y was 100% in both the POPH and PH because of high CO groups. On binary logistic regression analysis, there was

TABLE 3.

Hemodynamic characteristics of patients with postcapillary PH by alive/dead status

Preoperative				
Factor	**(ALL), N = 50**	**Alive**	**Dead**	***P***
mPAP	32.0 (28.0–37.8)	32.0 (28.0–34.0)	33.0 (30.0–38.0)	0.37
PCWP	24.0 (20.0–27.8)	22.0 (20.0–26.0)	25.0 (20.0–28.0)	0.35
CO	10.0 (7.00–12.7)	11.0 (7.40–13.0)	8.00 (7.00–11.0)	**0.04**
PVR	1.00 (0.50–1.00)	1.00 (0.50–1.00)	1.00 (1.00–1.50)	0.15
Intraoperative[a]				
Factor	**N**	**(ALL)**	**Alive**	**Dead**	*P*
mPAP	37	22.5 ± 6.9	21.6 ± 5.5	24.5 ± 9.1	0.33
CO	36	9.2 ± 2.8	9.9 ± 2.8	7.7 ± 2.2	**0.03**

Statistics are presented as mean ± SD or median (P25–P75).
Bolded text indicates statistically significant findings.
[a]Intraoperative mPAP pressure and CO were not available for all patients, and intraoperative PCWP and PVR were not available for any patients.
ALL, all patients with postcapillary PH; CO, cardiac output; mPAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance.

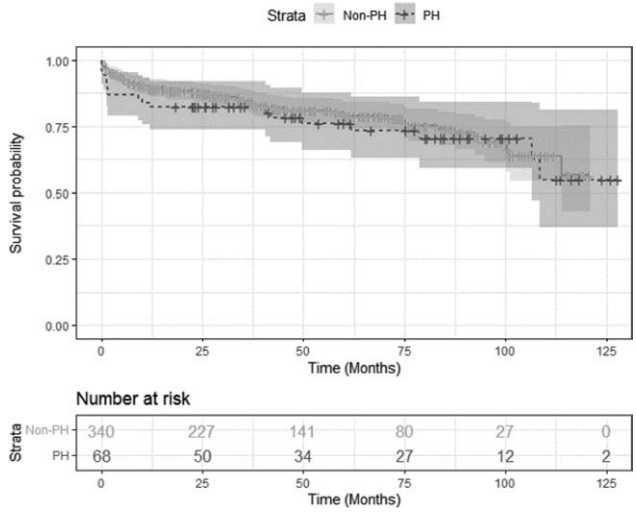

FIGURE 2. Kaplan-Meier survival: PH vs no PH. Kaplan-Meier curve comparing survival of patients with any type of PH to matched patients without PH. Survival at 1, 3, and 5 y was 89.4%, 84.7%, and 79.0%, respectively, in the group of patients without PH, and 83.8%, 82.3%, and 76.1%, respectively, in the group of patients with PH. PH, pulmonary hypertension.

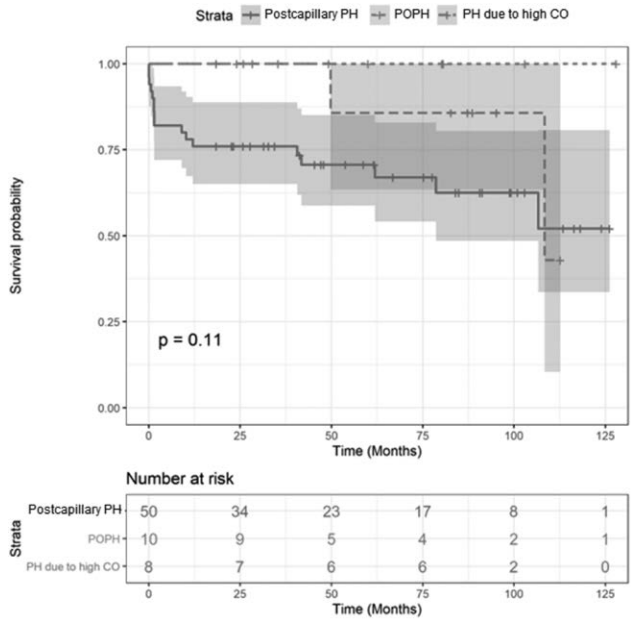

FIGURE 3. Kaplan-Meier curve: postcapillary PH vs POPH vs PH because of high CO. Kaplan-Meier curve comparing survival of patients with different types of PH. The 1-, 3-, and 5-y survival was 78.0%, 76.0%, and 70.7%, respectively, in the postcapillary PH group. Survival at 1, 3, and 5 y was 100% in the POPH group. CO, cardiac output; PH, pulmonary hypertension; POPH, portopulmonary hypertension.

also no significant difference between hospital LOS, ICU LOS, incidence of post-LT pulmonary edema, and post-LT AKI between the 3 groups (Table 4). The incidence of post-LT pulmonary edema could not be compared between the PH because of high CO group and the others because of insufficient number of events in that group. MELD score had a significant positive association with ICU and hospital LOS but no significant association with post-LT AKI or pulmonary edema.

TABLE 4.

Univariate analysis of various secondary outcomes in different PH groups

Hospital length of stay[a]		
Factors	**Estimate (95% CI)**	***P***
Age at transplant	0.00 (–0.02 to 0.03)	0.77
MELD score	0.03 (0.01-0.05)	**0.02**
POPH vs postcapillary PH	–0.16 (–0.74 to 0.42)	0.59
PH because of high CO vs postcapillary PH	–0.22 (–0.86 to 0.42)	0.50
ICU length of stay[b]		
Factors	**Estimate (95% CI)**	***P***
Age at transplant	–0.00 (–0.05 to 0.04)	0.91
MELD score	0.05 (0.02-0.08)	**0.00**
POPH vs postcapillary PH	–0.41 (–1.37 to 0.54)	0.40
PH because of high CO vs postcapillary PH	–0.44 (–1.49 to 0.62)	0.42
Post-LT acute kidney injury		
Factors	**Odds ratio (95% CI)**	***P***
Age at transplant	1.03 (0.96-1.11)	0.37
MELD score	0.99 (0.94-1.04)	0.64
POPH vs postcapillary PH	1.56 (0.38-6.32)	0.54
PH because of high CO vs postcapillary PH	1.4 (0.3-6.62)	0.67
Post-LT pulmonary edema		
Factors	**Odds ratio (95% CI)**	***P***
Age at transplant	1.07 (0.92-1.24)	0.37
MELD score	0.96 (0.86-1.06)	0.39
POPH vs postcapillary PH	1.28 (0.13-12.8)	0.84
PH because of high CO vs postcapillary PH	NA	NA

Bold text indicates statistically significant findings.
[a] The logarithm of hospital length of stay was modeled as the outcome variable.
[b] The square root of ICU length of stay was modeled as the outcome variable.
CI, confidence interval; CO, cardiac output; ICU, intensive care unit; LT, liver transplantation; MELD, Model for End-stage Liver Disease; PH, pulmonary hypertension; POPH, portopulmonary hypertension.

DISCUSSION

In this study, we found that after matching for important confounders (age and MELD score), patients with postcapillary PH had no statistically significant difference in mortality as compared with patients without PH. Although mortality was nearly 3 times higher in patients with mPAP >35, the difference was still not statistically significant. We also compared post-LT survival between patients with different hemodynamic types of PH in our cohort and found no significant difference between 3 groups of PH.

Previous research on this subject is sparse. One single-center study of 50 patients did not find a difference in mortality between patients with POPH, postcapillary PH, or lack of PH.[9] A second study found that when measuring pulmonary hemodynamics intraoperatively, a high pulmonary artery pressure >35 mm Hg because of any type of PH was not associated with increased mortality.[10] Both of these studies may also have been limited by small sample size and low event rate. Our study supplements these previous investigations and supports that the presence of postcapillary PH on preoperative RHC does not appear to significantly affect outcomes post-LT.

We also compared post-LT outcomes in patients with postcapillary PH with those with POPH and PH because of high CO. Although there was trend toward decreased survival in patients with postcapillary PH compared with the other

2 groups, the difference was not statistically significant. There is currently no standard practice for risk stratifying or optimizing patients with postcapillary PH for LT like there is with POPH. Patients with POPH are treated with pulmonary vasodilators and have set hemodynamic targets that need to be reached before being listed for LT.[7] This is done because it has been demonstrated that patients with POPH who undergo LT with elevated mPAP or PVR have increased posttransplant cardiopulmonary complications and mortality rates.[13] There has been a large body of research on the treatment of postcapillary PH outside of the LT population. The mainstay of treatment for patients with isolated postcapillary PH without an elevation in PVR is diuretics and possibly vasodilators. Pulmonary selective vasodilators are not effective.[14]

Our data show that patients with postcapillary PH on preoperative RHC may have similar survival when compared with the remainder of the LT cohort even without PH-specific therapy. However, patients with postcapillary PH likely still need to be optimized as much as possible for surgery. It is important to note that the mean mPAP at the time of transplant for most patients had been reduced to <25 mm Hg, suggesting that they were optimized for the surgery with either diuresis or dialysis for patients with renal impairment. The fact that the patients were well-managed before the transplant likely explains the lack of significant difference in mortality or select postoperative complications.

Although our sample size was small, among the 17 patients with postcapillary PH who died, most of them died of cardiopulmonary complications, suggesting that there may be an association between the presence of postcapillary PH and post-LT cardiopulmonary death. Furthermore, we found that patients with postcapillary PH who survived had significantly higher CO, not only on the preoperative screening RHC, but also at the time of LT. Patients with postcapillary PH and a higher CO may have a more robust cardiovascular reserve and may be at lower risk of posttransplant mortality as a result. This may be an important factor to consider when risk stratifying patients with postcapillary PH before LT. Furthermore, patients with a high mPAP of 35 and above had an HR for death of nearly 3 times that of patients without PH, although the difference was not statistically significant. The impact of varied mPAP thresholds on survival in patients with postcapillary PH is an interesting clinical question that merits further study.

During LT, there are significant fluctuations in both preload and afterload, as well as metabolic derangements. Prior studies have found that in the reperfusion phase of LT, CO has a positive correlation with hepatic artery and portal venous flow.[15] The clamping in the inferior vena cava can result in a decrease in CO in the anhepatic phase.[16] Furthermore, it has been demonstrated that during LT cirrhotic patients are relatively hypovolemic in the intravascular compartment.[17] Patients with cirrhosis are also at risk of developing high output heart failure and cirrhotic cardiomyopathy.[18,19] Cirrhotic cardiomyopathy is characterized in part by a blunted cardiovascular response to stress and exercise and is associated with reduced sympathetic response and stiffened ventricles.[20] All of these factors may explain why in our sample, patients with postcapillary PH who survived had a significantly higher median CO than those who died. However, further prospective data are needed.

There were several limitations to our study. We had a relatively small sample size; however, PH is an overall rare condition in cirrhotic patients undergoing LT. Our sample size limited our ability to analyze or detect statistical significance in smaller subgroups of patients. We attempted to account for potential confounders as much as possible with the PS matching design, but because of the small sample size we were limited in how many factors we could include in the PS.

An important future direction for this topic is to conduct similar research involving multiple institutions and larger sample sizes. This will help determine if pre-LT postcapillary PH is related to post-LT cardiopulmonary complications and will gather further evidence to guide practices regarding appropriate screening and treatment goals for these patients. A larger sample size will also allow for adjustment for important comorbidities and further investigation into if the severity of PH according to mPAP affects survival in these patients. The impact of a high CO on survival in patients with postcapillary PH also merits further study.

In conclusion, patients with postcapillary PH can likely undergo LT without an increased risk of mortality when compared with the general LT population. However, like other comorbidities, postcapillary PH should be optimized before the time of LT. mPAP >35 mm Hg may portend a worse prognosis; however, further research with larger sample sizes is needed. A higher CO on preoperative transplant and intraoperatively may be a good prognostic indicator for patients with postcapillary PH selected for LT, and this may be something to consider when making transplant listing decisions for these patients. Further research with a larger sample size including multiple centers is needed to confirm our findings and investigate further.

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