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Outcomes After Listing for Liver Transplant in Patients With Acute-on-Chronic Liver Failure: The Multicenter North American Consortium for the Study of End-Stage Liver Disease Experience

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Abstract

Acute-on-chronic liver failure (ACLF) characterized with ≥2 extrahepatic organ failures in cirrhosis carries a high mortality. Outcomes of patients listed for liver transplantation (LT) after ACLF and after LT are largely unknown. The North American Consortium for the Study of End-Stage Liver Disease prospectively enrolled 2793 nonelectively hospitalized patients with

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cirrhosis; 768 were listed for LT. Within 3 months, 265 (35%) received a LT, 395 remained alive without LT, and 108 died/delisted. Compared with nonlisted patients, those listed were younger and more often had ACLF, acute kidney injury, and a higher admission Model for End-Stage Liver Disease (MELD) score. ACLF was most common in patients who died/delisted, followed by those alive with and without LT respectively, (30%, 22%, and 7%, respectively; $P < 0.001$). At LT, median MELD was 27.9% and 70% were inpatients; median time from hospitalization to LT was 26 days. Post-LT survival at 6 months was unchanged between those with and without ACLF (93% each at 6 months). There was no difference in 3- and 6-month mean post-LT creatinine in those with and without ACLF, despite those with ACLF having a higher mean pre-LT creatinine and a higher rate of perioperative dialysis (61%). In conclusion, patients with and without ACLF had similar survival after transplant with excellent renal recovery in both groups.

The prevalence of cirrhosis is expected to steadily increase over the next decade and is likely to be driven by the rising prevalence of nonalcoholic fatty liver disease (NAFLD) and the downstream consequences of progressive liver disease due to nonalcoholic steatohepatitis (NASH).[1] The complications of cirrhosis have and will lead to more hospitalizations and acute-on-chronic liver failure (ACLF), which will increase the demand for liver transplantation (LT).[2] In addition, we expect to transplant older people with more chronic kidney disease (CKD) secondary to the decline in hepatitis B virus– and hepatitis C virus (HCV)–related advanced liver disease and a continued increase in the prevalence of NAFLD.[3]

With an increased need for LT and the changes in the patient population listed for transplant, we expect more patients to need hospitalization before transplant.[2] In addition, we anticipate ACLF will also continue to increase in incidence[2] before LT. Current data have shown that transplant-free survival is markedly reduced in patients who develop ACLF, regardless of the definition of ACLF used.[4–7] This is also applicable to patients listed for LT who have a high mortality before LT once ACLF develops.[8,9]

If patients are transplanted after developing ACLF, most data show either a numerical increase or statistically significant increase in mortality after LT.[4,8,10–12] When the European Association for the Study of the Liver (EASL)–chronic liver failure (CLIF) grading for ACLF was used, a marked difference in outcome was observed in patients after LT depending on the severity of ACLF: ACLF grade 1 and 2 had acceptable post-LT outcomes, whereas ACLF grade 3 had unacceptable post-LT outcomes.[10] A more recent report showed similar outcomes between all 3 EASL-CLIF grades of ACLF. However, it is important to note that in this study, 53% of patients had alcohol-induced cirrhosis, 49% of patients had septic shock that resolved before LT, and the number of organ failures improved in many patients before LT.[12] In a similar observation, post-LT outcomes markedly improved if ACLF resolved prior to transplant compared with those patients who underwent transplantation while still experiencing organ failure(s) associated with ACLF.[4] Not only was post-LT mortality affected by ACLF, but intensive care unit (ICU) length of stay and total hospital length of stay were longer in patients with versus without ACLF and rose with worsening grades of ACLF.[10] It is important to highlight that the vast majority

of studies either eliminated simultaneous liver-kidney transplantation (SLKT) recipients or showed inferior outcomes among them when transplant occurred after ACLF.[10–12]

Currently, it is unclear how ACLF and its complications, often resulting in acute kidney injury (AKI) and other organ failure, will affect the selection of candidates for LT, their outcomes while awaiting LT, and then ultimately their post-LT outcomes, particularly of renal recovery. Thus, to address these questions, we analyzed the data from the cohort of nonelectively hospitalized patients with cirrhosis in the North American Consortium for the Study of End-Stage Liver Disease (NACSELD).

Patients and Methods

Fourteen centers in North America prospectively enrolled admitted patients with cirrhosis regardless of transplant listing. The protocol received a priori approved by the institutional review boards at each institution before enrollment began. Patients with and without acute infections were included in this cohort. Patients with human immunodeficiency virus infection, those with a history of prior transplant, or patients with nonhepatic malignancy were excluded from the study. Also, patients electively admitted were excluded (eg, planned procedures). Cirrhosis had to have been confirmed with either liver biopsy, clinical evidence of decompensation, or endoscopy/radiologic evidence of portal hypertension.

After informed consent, patient data were collected and entered into the Research Electronic Data Capture (REDCAP) database. Infections were defined according to our prior description.[13] Data were collected on the severity and complications of cirrhosis, number and type of organ failures, laboratory values, and medication usage. Mortality was assessed during hospitalization and after discharge for 6 months.

Analyses were performed on the entire cohort divided into 2 groups based on if patients were ever listed for transplant during the study period from index hospitalization through 6 months after discharge. Similar analyses were performed on LT-listed patients dependent on their outcome: death or delisting, alive with a transplant, or alive without a transplant. Brain failure was defined as West Haven grade 3 or 4 encephalopathy, and renal failure was based on the need for renal replacement therapy.[6,7] The definition of renal failure is different from AKI, which has been redefined by the International Ascites Club.[14] Respiratory failure was defined as the need for bilevel positive airway pressure (BIPAP) or mechanical ventilation, and shock was defined as the need for pressor support or a mean arterial pressure <60 mm Hg or a reduction of >40 mm Hg in systolic blood pressure from baseline despite adequate fluid resuscitation.[6,7] NACSELD-ACLF, as previously defined and validated, was the development of 2 or more organ failures.[6,7] Model for End-Stage Liver Disease (MELD) was always represented as calculated MELD, not MELD-sodium nor based on a MELD upgrade.

Continuous variables are presented as either means with standard deviations or medians with interquartile ranges and analyzed using either a 1-way analysis of variance or a Kruskal-Wallis H test. Categorical variables are presented as percentages and analyzed using

a chi-square test. Multivariate stepwise regression was used to find predictors of survival after ACLF.

Statistical significance was defined as a P value <0.05. Data were analyzed with SAS, version 9.2 (SAS Institute, Cary, NC).

Results

PATIENTS LISTED VERSUS NOT LISTED FOR LT

There were 2793 nonelectively admitted patients with cirrhosis who were prospectively enrolled at 14 tertiary care hepatology centers throughout North America. Of these inpatients, 768 were listed for LT at some point either prior to or during their index admission. There were significant differences between the patients listed versus not listed for transplant as shown in Table 1. Notably, listed patients were younger, more likely to have HCV–induced liver disease, had been admitted with an infection or developed a second infection, had ascites or refractory ascites, had been admitted within the previous 6 months, or had an episode of AKI. Medications were also different between the groups; listed patients were more likely to have been on a proton pump inhibitor (PPI), lactulose, rifaximin, and spontaneous bacterial peritonitis (SBP) prophylaxis. As expected, admission laboratory values were markedly different between the 2 groups. The serum bilirubin, international normalized ratio (INR), serum creatinine, calculated MELD score (exception points were not used), and Child-Turcotte-Pugh (CTP) score were all higher in listed versus nonlisted patients.

Outcomes were compared between patients listed versus not listed for LT (Fig. 1). There was a higher rate of organ failures among listed patients with West Haven grade 3/4 hepatic encephalopathy (18% versus 14%; $P = 0.01$), with respiratory failure (18% versus 11%; $P < 0.001$) being most common and renal failure having the greatest difference between the groups (14% versus 5%; $P < 0.001$). The number of organ failures was also different between the groups with listed patients having more organ failures than nonlisted patients ($P < 0.001$) resulting in more patients meeting NACSELD-ACLF criteria (15% versus 9%; $P < 0.001$). Admitted patients listed for LT also had an average length of stay 4 days longer than nonlisted patients (15.4 versus 11.4 days; $P < 0.001$), and they were more likely to require ICU admission (32% versus 20%; $P < 0.001$). Although in-hospital survival remained the same between groups, 3-month (84% versus 78%; $P = 0.002$) and 6-month survival (78% versus 68%; $P < 0.001$) was higher in listed than nonlisted patients despite all markers of illness severity being higher among listed patients.

THE IMPACT OF ACUTE INFECTION STATUS

We then compared listed patients admitted with an infection versus those listed without an infection during their index hospitalization (Table 2). Infected patients were younger (53.99 versus 56.47; $P = 0.004$), had higher admission serum bilirubin levels (8.73 versus 7.95 mg/dL; $P = 0.02$), had a higher probability of more organ failures ($P = 0.008$), specifically circulatory failure (15% versus 8%; $P = 0.002$) and respiratory failure (24% versus 16%; $P = 0.008$) resulting in a more frequent diagnosis of NACSELD-ACLF (21% versus 12%; $P =$

0.001). Admission medications were similar between the 2 groups except that nonselective beta-blockers (NSBB) were less commonly used in patients who presented with an infection (35% versus 44%; $P = 0.03$). Transplant-free survival was similar at 3 and 6 months between the 2 groups regardless of infection.

THE 3-MONTH POSTDISCHARGE OUTCOMES

We then evaluated 3-month postdischarge outcomes for listed patients; 395 remained alive without LT, 265 had received a LT, and 108 died or were delisted (Table 3). Transplanted patients were younger than either alive without transplant or dead patients (55.60 and 54.78 and 58.40 respectively; $P = 0.002$), and had an intermediate risk for developing a second infection during admission (11%, 7% versus 19% respectively; $P = 0.005$). When comparing organ failures, transplanted patients were less likely to have hepatic encephalopathy ($P = 0.002$), renal failure ($P < 0.001$), or circulatory failure ($P < 0.001$) than dead/delisted patients, but they were most likely to have respiratory failure than dead/delisted patients. Patients who remained alive without transplant were most likely to have no organ failures compared with transplanted or dead/delisted patients (78%, 50%, and 47% respectively; $P < 0.001$). Patients alive with a LT more commonly had 1 organ failure than the other 2 groups, and patients who were dead/delisted were more likely to have 2 or more organ failures and qualify for NACSELD-ACLF (7% alive without transplant, 22% alive with LT, and 30% dead/delisted; $P < 0.001$). Admission bilirubin, INR, and MELD score were highest among patients who were alive with a LT (all $P < 0.001$). However, admission serum creatinine was highest among dead/delisted patients (1.46 mg/dL alive without transplant, 2.00 mg/dL alive with LT, and 2.26 mg/dL dead/delisted; $P < 0.001$). Although admission MELD was highest among patients who were alive with a LT (19.51 alive without transplant, 26.50 alive with LT, and 25.36 dead/delisted; $P < 0.001$), discharge MELD (from the index admission) was markedly lower (18.40 alive without transplant, 20.99 alive with LT, and 28.15 dead/delisted; $P < 0.001$). As a result, the delta MELD (discharge-admission MELD) during admission was markedly different for the groups (−1.2 alive without transplant, −5.1 alive with LT, and 2.7 dead/delisted; $P < 0.001$). Medication usage was comparable between all groups except for SBP prophylaxis, which was equally used in patients who were alive with a LT and dead/delisted patients versus those who were alive without a LT, who were less likely to have received it (36%, 36%, and 25% respectively; $P = 0.005$).

Multivariate stepwise regression was performed to determine predictors of survival after ACLF. Only 3 variables had a statistically significant impact on transplant-free survival, and all negatively impacted it: fungal infection (odds ratio [OR], 0.42; 95% confidence interval [CI], 0.20–0.92), nosocomial infection (OR, 0.53; 95% CI, 0.29–0.97), and admission MELD score (OR, 0.97; 95% CI, 0.93–1.00).

When we evaluated patients at the time of LT, the median calculated MELD score was 27.9 (Table 4). The delta MELD from admission to the time of transplant was 1.4 points. Surprisingly, 70% of patients underwent transplantation while admitted to the hospital, 72% of whom were on the floor and 28% of whom were in the ICU. Although admitted to the hospital before transplant, the average time from index hospitalization to transplant was 39.8 days indicating the need for readmission in more than half of the patients (60%).

The number of organ failures was highly predictive of outcome in patients who were not transplanted, but it was not predictive of outcome in patients who underwent transplantation (Supporting Table 1). In patients without transplant, 3-month mortality was 16%, 30%, 53%, 73%, and 100% in those with 0, 1, 2, 3, and 4 organ failures, respectively ($P < 0.001$). In transplanted patients, 3-month mortality was 5%, 4%, 3%, 13%, and 0% in those with 0, 1, 2, 3, and 4 organ failures, respectively (P = not significant [NS]). Although no statistically significant differences were detected, this latter analysis was underpowered.

ACLF'S IMPACT ON TRANSPLANT OUTCOMES

Finally, we compared patients who underwent transplantation with versus without having experienced an episode of ACLF during their index admission (Table 5). Most patients received a cadaveric LT (94%) despite a median serum creatinine of 2.48 versus 1.62 mg/dL in ACLF versus non-ACLF patients ($P = 0.003$). ACLF patients also more commonly needed perioperative dialysis (61% versus 22%; $P < 0.001$), but there was no difference in need for SLKT (9% versus 6%; $P = 0.43$). Despite transplanting this sick patient population, 84% were able to be discharged home from their index transplant admission. No difference in 3-month survival (94% versus 96%; $P = 0.66$) and 6-month survival (93% versus 93%; $P = 0.87$) was found. Despite the difference in creatinine at LT, the median creatinine declined to 1.56 versus 1.28 mg/dL in the ACLF group versus the no ACLF group ($P = 0.08$) at 3-month follow-up, and 1.78 versus 1.34 mg/dL in the ACLF group versus the no ACLF group ($P = 0.06$) at 6-month follow-up.

Discussion

The NACSELD cohort is unique because of its multinational prospective nature that documented longer-term follow-up of patients, including through LT, after hospital admission in 2793 patients with cirrhosis. Approximately one-quarter (27%) of these patients were listed for LT. Indications for transplant were almost evenly split between alcohol, NASH, and HCV-induced liver disease. It is not surprising that listed patients were younger and sicker, as measured by the MELD and CTP scores. Despite this, in-hospital survival was similar between the groups, but 3- and 6-month survival rates were markedly higher among listed patients, likely secondary to more aggressive care and ultimately LT.

Listed patients had a longer length of stay and were more frequently admitted to the ICU than patients who were not listed for LT. Given that listed patients were sicker (higher MELD and CTP score), we assume that the increased resource utilization was needed secondary to their increased illness severity.

Listed patients also had a higher admission creatinine and more frequently were dialyzed during the index admission than nonlisted patients. Serum creatinine at admission also strongly correlated with outcome; dead/delisted patients had the highest mean serum creatinine, patients alive after transplant had an intermediate mean serum creatinine, and those alive without transplant had the lowest mean serum creatinine. This strong correlation between renal function before transplant and outcome is not surprising, and it supports the ongoing focus on smaller changes in serum creatinine in patients with cirrhosis, which we now know to have a significant impact on prognosis, even if resolution occurs.[14–17]

ACLF occurred in 15% of listed patients and 22% of transplanted patients. The syndrome of ACLF is usually precipitated by an acute event, such as bacterial infection, which leads to organ failure(s) and subsequently ACLF.[18] Outcomes of smaller cohorts or single-center retrospective analyses of patients with ACLF who received a LT have shown that there is a decrement in overall survival after transplant in patients with ACLF before transplant.[8–12] However, more in-depth analyses have previously shown that less severe disease (as defined by EASL-CLIF grade 1 and 2 ACLF) did not portend a worse prognosis after LT, but more severe disease (EASL-CLIF grade 3 ACLF) did.[10] Although not all data have shown differences in mortality after transplant for different grades of ACLF, the data consistently show longer lengths of stay and greater complications after transplant at higher grades of ACLF.[10,12] Also, ACLF at the time of transplant and infection in the month before transplant were independent predictors of death in a retrospective single-center cohort of 140 patients transplanted with ACLF[10]; conversely patients who had organ function recovery before transplant had the best outcome after LT.[4,8,10–12] Here we show, in a prospective multicenter cohort, that patients transplanted while they had ACLF had similar outcomes after LT to those without pretransplant ACLF. This was despite having a higher MELD at transplant, a higher pretransplant creatinine, and greater use of perioperative dialysis. Furthermore, 3- and 6-month posttransplant renal outcomes were similar between the 2 groups.

Notably, 70% of patients underwent transplantation after having been admitted to the hospital for a reason other than transplantation. Although a few underwent transplantation during their index admission, most (60%) had to be readmitted before they underwent transplantation. This is a disturbing trend that shows the marked resource utilization needed for patients to survive to transplant. Novel therapeutics and nonpharmacologic interventions to prevent liver disease progression and infection-related complications are desperately needed to prevent these high-cost admissions.[19]

Because infections are one of the most common complications leading to ACLF and delisting,[6,7,13] it is imperative that clinicians reduce the risk for infectious complications for patients with cirrhosis.[9] Therefore, it is surprising that more than half of all admitted patients were taking a PPI. Notably, there was no difference in the percentage of listed versus not listed patients admitted with an infection and taking a PPI. With the documented increased risk of infection in patients with cirrhosis and frequent lack of indication for use, it is concerning that so many admitted patients were given a PPI.[20] Therefore, in the future, all clinicians need to attempt to discontinue PPI use whenever a clear indication is lacking.

Although we have the largest prospective multinational cohort of listed patients followed longer-term through transplant, limitations exist. The date of listing was not available for our patients, so we could not determine who was listed before and during versus after the index hospitalization. The date of death was not available for patients, which precluded Kaplan-Meier analysis and Cox proportional hazards modeling. As with all transplant studies, the patients who were listed, and even more so for those who underwent transplantation, were highly selected. Also, we did not determine who had ACLF versus resolved ACLF at the time of transplantation. In addition, the risk for rejection and infection peritransplant should be evaluated in future studies to determine if the inflammatory response related to

ACLF predisposes to rejection, or potentially the compensatory anti-inflammatory response syndrome that facilitates ACLF resolution predisposes patients to an increased risk for post-LT infections.[21] Furthermore, it would have been ideal to determine the precise reason for AKI and CKD in our patient population in order to evaluate the effect of AKI hepatorenal syndrome (HRS) versus non–AKI-HRS on renal outcomes and survival after LT. However, the marked improvement in renal function after LT suggests that most patients likely had AKI-HRS. Also, although it is desirable to evaluate outcomes in the AKI-HRS versus non–AKI-HRS cohorts following LT, it would be challenging without data, such as renal biopsy, and reliability of the pre-LT diagnosis of AKI-HRS. Finally, although we collected detailed data on the index hospitalization and post-LT data, we cannot exclude that some patients may have developed ACLF during a subsequent hospitalization prior to transplant in the non-ACLF group.

Our large prospective multinational study documents that ACLF is a significant problem (22% of listed patients) before LT and results in marked mortality. Patients selected for transplant after ACLF, despite higher serum creatinine at transplant and triple the use of perioperative dialysis, had similar 6-month serum creatinine levels after LT compared with patients transplanted without ACLF, indicating that renal recovery occurs following LT. This major observation is reassuring in that although an acute rise in creatinine translates to a higher MELD and greater probability of death, renal recovery is seen in those who are fortunate enough to undergo LT. Lastly, post-LT survival also remained similar, at 6 months after LT between those with and without ACLF before LT. Further studies are needed to determine a uniform listing and delisting policy for LT in the context of ACLF and to determine limits of ACLF severity that would determine continued eligibility of these patients for LT.

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Abbreviations:

ACLF	acute-on-chronic liver failure
AKI	acute kidney injury
BIPAP	bilevel positive airway pressure
CKD	chronic kidney disease
CI	confidence interval
CLIF	chronic liver failure
CTP	Child-Turcotte-Pugh

EASL	European Association for the Study of the Liver
HCV	hepatitis C virus
HRS	hepatorenal syndrome
ICU	intensive care unit
INR	international normalized ratio
LT	liver transplantation
MELD	Model for End-Stage Liver Disease
NACSELD	North American Consortium for the Study of End-Stage Liver Disease
NAFLD	nonalcoholic fatty liver disease
NASH	nonalcoholic steatohepatitis
NS	not significant
NSBB	nonselective beta-blockers
OR	odds ratio
PPI	proton pump inhibitor
REDCAP	Research Electronic Data Capture
SBP	spontaneous bacterial peritonitis
SIRS	systemic inflammatory response syndrome
SLKT	simultaneous liver-kidney transplantation
UTI	urinary tract infection
WBC	white blood cell

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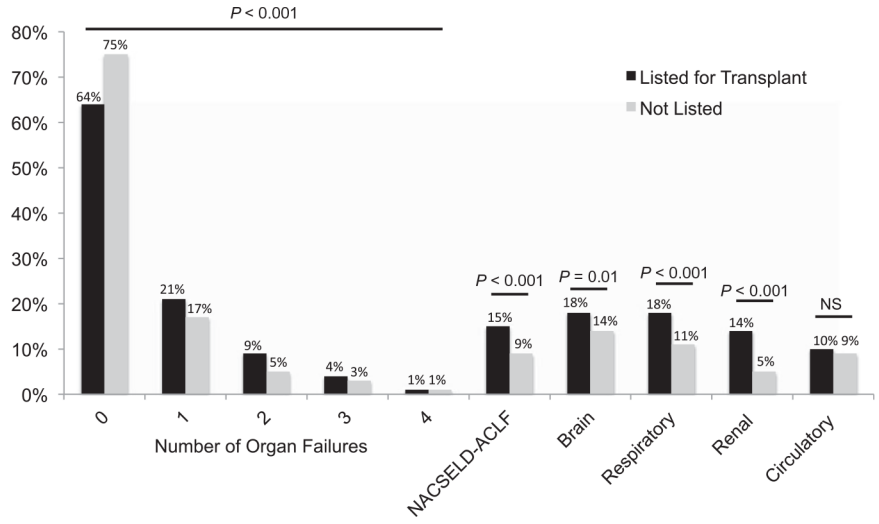

FIG. 1.

The number and types of organ failures found in patients listed for LT versus those not listed for LT.

TABLE 1.

Demographic and Laboratory Values Compared Between Patients Listed Versus Not Listed for LT

	Not Listed for Transplant (n = 2025)	Listed for Transplant (n = 768)	*P* Value
Age, years	57.77 (11.11)	55.71 (9.83)	<0.001
Sex, male	62 (1259/2022)	62 (477/767)	0.97
Etiology			<0.001
Alcoholic cirrhosis	34 (688/2015)	22 (170/762)	
HCV	18 (366/2015)	27 (203/762)	
HCV + alcoholic cirrhosis	16 (313/2015)	11 (82/762)	
NASH	21 (429/2015)	20 (154/762)	
Other	11 (219/2015)	20 (153/762)	
Diabetes	34 (685/1995)	34 (254/758)	0.68
Admitted with infection	25 (507/2009)	31 (235/766)	0.004
SBP on/during admission	7 (145/2025)	11 (88/768)	<0.001
UTI on/during admission	10 (202/2025)	12 (95/768)	0.07
Second infection	7 (140/2025)	10 (77/768)	0.006
Nosocomial infection	12 (247/2025)	14 (105/768)	0.29
Fungal infection	4 (86/1960)	6 (46/750)	0.06
Ascites	65 (1318/2022)	83 (636/766)	<0.001
Refractory ascites	29 (584/2022)	44 (335/766)	<0.001
Hospitalized in the last 6 months	64 (1194/1853)	76 (522/683)	<0.001
Medication used			
PPI	54 (974/1820)	58 (399/685)	0.04
NSBB	40 (787/1971)	41 (310/758)	0.64
SBP prophylaxis	13 (259/1953)	30 (225/746)	<0.001
Rifaximin	28 (565/1983)	55 (420/761)	<0.001
Lactulose	50 (990/1987)	69 (527/761)	<0.001
AKI during hospitalization	38 (678/1790)	53 (351/657)	<0.001
Serum bilirubin, mg/dL *	5.21 (8.26)	8.19 (9.30)	<0.001
Serum albumin, g/dL *	2.83 (0.66)	2.85 (0.71)	0.71
WBC *, 10^9/L	7.94 (5.23)	7.16 (5.82)	<0.001
INR *	1.61 (0.57)	1.88 (0.75)	<0.001
Serum sodium, mEq/L *	134.7 (7.17)	132.9 (6.31)	<0.001
Serum creatinine, mg/dL *	1.47 (1.29)	1.76 (1.47)	<0.001
Admission CTP score	9.6 (2.20)	10.3 (2.00)	<0.001
MELD score *	18.2 (7.30)	22.8 (7.90)	<0.001
SIRS	27 (530/1991)	27 (204/759)	0.89

NOTE: Data are given as median (standard deviation) or percentage (frequency).

* Admission laboratory values.

TABLE 2.

Listed Patients With Versus Without an Infection During Their Index Hospitalization

	Transplant List		
	Uninfected (n = 531)	**Infected (n = 235)**	***P* Value**
Age, years	56.47 (9.26)	53.99 (10.88)	0.004
Sex, male	340 (64)	136 (58)	0.12
Hepatic encephalopathy *	88 (17)	43 (19)	0.54
Respiratory failure	84 (16)	56 (24)	0.008
Renal failure	66 (13)	41 (17)	0.07
Circulatory failure	38 (8)	33 (15)	0.002
Number of organ failures			0.008
0	345 (65)	142 (60)	
1	120 (23)	43 (18)	
2	43 (8)	27 (11)	
3	18 (3)	16 (7)	
4	4 (1)	7 (3)	
NACSELD-ACLF	65 (12)	50 (21)	0.001
Second infection	35 (7)	42 (18)	<0.001
Admission bilirubin, mg/dL	7.95 (9.32)	8.73 (9.28)	0.02
Admission INR	1.87 (0.74)	1.93 (0.77)	0.36
Admission sodium, mEq/L	132.82 (6.50)	132.98 (5.88)	0.55
Admission albumin, g/dL	2.88 (0.68)	2.80 (0.76)	0.06
Admission creatinine, mg/dL	1.75 (1.47)	1.78 (1.45)	0.86
Admission MELD	22.43 (7.82)	23.48 (8.13)	0.10
Discharge MELD	20.78 (8.29)	20.28 (8.79)	0.57
Delta MELD (discharge-admission)	−1.59 (7.20)	−2.83 (8.11)	0.08
Medication used			
PPI	263 (57)	135 (61)	0.35
NSBB	229 (44)	81 (35)	0.03
SBP prophylaxis	150 (29)	74 (33)	0.25
Rifaximin	292 (55)	128 (55)	0.95
Lactulose	371 (70)	154 (66)	0.27
Outcome			0.67
Alive without transplant	275 (52)	120 (51)	
Transplanted	185 (35)	78 (33)	
Death/delisting	71 (13)	37 (16)	
Outcome			
90-day transplant-free survival	275 (79)	120 (76)	0.44
6-month transplant-free survival	217 (70)	96 (68)	0.61

NOTE: Data are given as median (standard deviation) or frequency (percentage).

* West Haven grade 3 or 4.

TABLE 3.

Demographics and Admission Events and Laboratory Values for Patients on the Basis of the 3-Month Outcomes That Occurred After Hospitalization for Patients Listed for LT

	Alive Without LT (n = 395)	Alive With LT (n = 265)	Dead/Delisted (n = 108)	*P* Value
Age, years	55.60 (10.44)	54.78 (9.03)	58.40 (8.99)	0.002
Sex, male	61 (241/395)	64 (168/264)	63 (68/108)	0.78
Hepatic encephalopathy *	15 (57/388)	17 (43/255)	30 (31/104)	0.002
Respiratory failure	7 (29/395)	32 (85/264)	24 (26/107)	<0.001
Renal failure	5 (18/393)	22 (58/265)	29 (31/107)	<0.001
Circulatory failure	5 (21/383)	11 (28/244)	22 (22/99)	<0.001
Number of organ failures				<0.001
0	78 (307/395)	50 (132/265)	47 (50/107)	
1	16 (62/395)	29 (76/265)	23 (25/107)	
2	4 (16/395)	14 (37/265)	16 (17/107)	
3	2 (9/395)	6 (16/265)	8 (9/107)	
4	<1 (1/395)	2 (4/265)	6 (6/107)	
NACSELD-ACLF	7 (26/395)	22 (57/265)	30 (32/107)	<0.001
Second infection	7 (27/395)	11 (29/265)	19 (21/108)	0.005
Bilirubin, mg/dL †	5.55 (6.06)	11.40 (11.34)	9.99 (10.64)	<0.001
INR †	1.70 (0.63)	2.11 (0.84)	1.99 (0.72)	<0.001
Sodium, mEq/L †	134.02 (5.88)	131.39 (6.34)	132.32 (6.94)	<0.001
Albumin, g/dL †	2.87 (0.63)	2.87 (0.82)	2.74 (0.68)	0.25
Creatinine, mg/dL †	1.46 (1.21)	2.00 (1.46)	2.26 (2.01)	<0.001
Admission MELD	19.51 (6.76)	26.50 (7.36)	25.36 (8.19)	<0.001
Discharge MELD	18.40 (6.74)	20.99 (7.92)	28.15 (10.70)	<0.001
Delta MELD (discharge-admission)	−1.2 (5.0)	−5.1 (8.7)	2.7 (8.8)	<0.001
Medication used				
PPI	59 (203/345)	60 (147/247)	53 (49/93)	0.50
NSBB	41 (160/394)	44 (114/260)	35 (36/104)	0.27
SBP prophylaxis	25 (96/386)	36 (93/259)	36 (36/101)	0.005
Rifaximin	58 (229/394)	52 (137/261)	51 (54/106)	0.23
Lactulose	70 (274/393)	70 (183/262)	66 (70/106)	0.74

NOTE: Data are given as median (standard deviation) or percentage (frequency).

* West Haven grade 3 or 4.

† Admission laboratory values.

TABLE 4.

Transplant-Specific Outcomes for the 265 Patients Alive at 3 Months After Discharge With a LT

	Alive with LT (n = 265)
Serum bilirubin at LT, mg/dL	15.9 (32.38)
INR at LT	2.1 (0.70)
Serum sodium at LT, mEq/L	134.8 (10.95)
MELD at LT	27.9 (7.19)
Delta MELD LT-admission	1.4 (7.30)
Time to LT, days	39.8 (89.15)
Type of donor	
Cadaveric	94 (173/184)
Living	6 (11/184)
Transplant type	
LT alone	94 (187/199)
SLKT	6 (12/199)
Creatinine at LT, mg/dL	2.48 (8.65)
Creatinine day 7, mg/dL	2.29 (6.82)
Creatinine at 3 months, mg/dL	2.27 (8.83)
Creatinine at 6 months, mg/dL	1.99 (5.23)
Hepatocellular carcinoma	17 (33/190)
Peri-LT dialysis	29 (57/194)
In hospital at LT	70 (132/188)
Location in hospital at LT	
Floor	72 (93/129)
ICU	28 (36/129)
LT outcome	
Died without relisting during hospitalization	1 (1/187)
Discharged home	84 (157/187)
Relisted and retransplanted	1 (1/187)
Transferred to another hospital	15 (28/187)

NOTE: Data are given as median (standard deviation) or percentage (frequency).

TABLE 5.

Transplanted Patients After a Hospital Admission With Versus Without Experiencing ACLF

LT Recipient	ACLF (n = 57)	No ACLF (n = 208)	*P* Value
Death at 3 months after LT	6%	4%	0.66
Death at 6 months after LT	7%	7%	0.87
Delta MELD LT-admission	−10.4 (11.7)	−3.6 (7.9)	<0.001
MELD at LT	31.1 (8.5)	27.3 (6.7)	0.008
Time to LT, days	27.0 (59.8)	43.5 (94.0)	<0.001
Inpatient at LT	86%	67%	0.02
Peri-LT dialysis	61%	22%	<0.001
SLKT	9%	6%	0.43
Creatinine at LT, mg/dL	2.48 (1.81)	1.62 (1.02)	0.003
Creatinine at 3 months after LT, mg/dL	1.56 (1.20)	1.28 (0.67)	0.08
Creatinine at 6 months after LT, mg/dL	1.78 (1.22)	1.34 (0.59)	0.06

NOTE: Data are given as median (standard deviation) unless otherwise indicated.