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**Title:** The NACSELD-ACLF Score Accurately Predicts Survival: An External Validation Using a National Cohort

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**Footnote page**

**Abbreviations**: Acute-on-chronic liver failure (ACLF); Chronic Liver Failure Acute-on-Chronic Liver Failure in Cirrhosis (CANONIC); Chronic liver failure-sequential organ failure assessment (CLIF-SOFA); North American Consortium for the Study of End-Stage Liver Disease (NACSELD); Nationwide Inpatient Sample (NIS); Healthcare Cost and Utilization Project (HCUP); Agency for Healthcare Research and Quality (AHRQ); Model for End-Stage Liver Disease (MELD); Area under the receiver operated curve (AUROC); Odds Ratio (OR)

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**Abstract**

Acute-on-chronic liver failure (ACLF) carries high short-term mortality. The North American Consortium for the Study of End-Stage Liver Disease (NACSELD) ACLF score, positive if ≥2 organ failures are present, is a bedside tool that predicts short-term mortality in patients with cirrhosis. However, it was created using major liver referral centers, where a minority of patients with cirrhosis are hospitalized. Therefore, this study utilized the Nationwide Inpatient Sample, a nationally-representative database, from 2005-2014 to externally validate the NACSELD-ACLF score in a cohort of patients with decompensated cirrhosis, who were identified by a validated algorithm. Organ failures were identified using diagnosis codes. The primary objective was to evaluate the association between the NACSELD-ACLF score and inpatient mortality, while secondary objectives compared outcomes depending on presence of infection or hospitalization at a transplant center. Multivariable logistic regression was utilized to compare outcomes and area under the curve was calculated. 1,523,478 discharges were included with 106,634 (7.0%) having a positive NACSELD-ACLF score. Patients were a mean 58 years old and mostly white men. Infection was present in 33.7% of the sample. Inpatient survival decreased with each organ failure and if infection was present. Patients with the NACSELD-ACLF score had significantly lower inpatient survival on crude (94.2% vs. 47.8%, p<0.001) and multivariable analysis (OR 0.08, 95% CI 0.07-0.08), AUROC 0.77 (95% CI 0.77-0.78). Liver transplant centers had clinically similar but significantly better survival at each number of organ failure, in patients with the NACSELD-ACLF score, and on multivariable analysis (OR 1.17, 95% CI 1.13-1.22). *Conclusion*: Using a national cohort, our study validated the NACSELD-ACLF score as an excellent, simple bedside tool to predict short-term survival in patients with decompensated cirrhosis.

**Introduction**

Acute-on-chronic liver failure (ACLF) is a highly prevalent condition among hospitalized patients with decompensated cirrhosis and is associated with high morbidity and mortality. Definitions of ACLF vary across different societies, with European and North American consortiums generally requiring at least the presence of cirrhosis, while the Asian definition includes patients without cirrhosis but with chronic liver disease in addition to those with compensated cirrhosis.(1,2) Nonetheless, ACLF is widely considered to be present when a severe acute decompensation occurs in the setting of chronic liver disease, leading to multi-organ failure.(1,3) Based on this definition, studies estimate ACLF to be present in 30% of hospitalized patients with decompensated cirrhosis and is associated with 34% one-month mortality.(4) Because of the high prevalence and short-term mortality, accurately prognosticating patients with ACLF is imperative.

Prior literature has investigated the use of scoring systems derived from prospective cohorts to prognosticate ACLF patients. First, the Chronic Liver Failure Acute-on-Chronic Liver Failure in Cirrhosis (CANONIC) group in Europe evaluated 1,343 patients and established 3 prognostic stages of ACLF based on the presence of organ failures, defined by the chronic liver failure-sequential organ failure assessment (CLIF-SOFA) score.(4) The North American Consortium for the Study of End-Stage Liver Disease (NACSELD), a consortium of liver referral centers from the United States and Canada, also identified the presence and number of organ failures as the key driver of mortality in hospitalized patients with cirrhosis; and thus further refined the predictive model.(5) More recently, the NACSELD centers reported that the presence of at least 2 organ failures (such as shock, grade III/IV encephalopathy, renal failure requiring hemodialysis, respiratory failure requiring mechanical ventilation), defined as the NACSELD-ACLF score, accurately predicted 30-day survival.(6) This easily calculated bedside score theoretically enhances clinical decision-making, but the generalizability of using the score is unknown.

The NACSELD cohort was derived from patients with cirrhosis from large liver transplant (LT) referral centers, and, therefore, the applicability of the NACSELD-ACLF score to the general population remains unclear. The inclusion of only LT referral centers could lead to potential bias

by identifying only the sickest patients, or, conversely better LT candidates who are less frail with fewer comorbidities. When assessing the hospitalization patterns of patients with cirrhosis on a national scale, the majority are not hospitalized at a teaching or major metropolitan hospital,(7) and may not necessarily be represented within the NACSELD cohort. Therefore, this study aimed to evaluate performance and externally validate the NACSELD-ACLF score among hospitalized patients with decompensated cirrhosis throughout the United States using a large, nationally representative database.

**Methods**

*Data source and participant selection*

This study utilized the Nationwide Inpatient Sample (NIS) (called National Inpatient Sample from 2012-2014), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality (AHRQ), from 2005-2014.(8) The NIS is a large, nationally representative database of hospital discharges for all payers. The sampling methodology of the NIS changed in 2012 from a sample of 20% of hospitals participating in HCUP to a 20% sample of discharges from all participating hospitals. NIS data includes demographic information, discharge disposition, diagnoses, procedures, length of stay, hospital charges, and inpatient mortality. The discharges are weighted to provide nationally representative estimates.

All discharges of patients aged 18-99 years old with both a diagnosis of cirrhosis (defined by ICD-9-CM code 571.2, 571.5, 571.6) and the presence of a decompensating event (defined by ICD-9-CM code of bleeding esophageal varices [456.0, 456.21], spontaneous bacterial peritonitis [567.23 along with the code for paracentesis 54.91], ascites [789.5, 789.59], and hepatic encephalopathy [572.2]) were included in the study. This identification algorithm was modified from a previously validated algorithm.(9) Our selection of a cohort of patients with decompensated cirrhosis was specifically chosen to be similar to those who were eligible for the definition of ACLF under the NACSELD cohort.(2) Exclusion criteria were similar to that of the NACSELD studies – history of a prior LT, human immunodeficiency virus, actively pregnant, or extrahepatic malignancy (**Appendix**).(5) Additionally, patients were excluded if

they underwent LT within one day of admission, as their hospitalization would be primarily for LT and not for a complication of cirrhosis.

*Outcomes and Exposures*

Similar to the NACSELD study,(6) organ failure was defined by the presence of shock, grade III/IV encephalopathy, renal failure requiring hemodialysis, or respiratory failure requiring mechanical ventilation. Previously used algorithms were used to identify organ failures. Shock was identified by the presence of an ICD-9-CM code for septic shock (785.52), circulatory shock (785.59), or vasopressor use (00.17).(10) Hepatic encephalopathy was diagnosed by the ICD-9-CM code (572.2) – unlike in the NACSELD cohort, grade and severity could not be determined using this database. Renal failure requiring hemodialysis was diagnosed by the presence of both acute kidney injury (ICD-9-CM 584.5, 584.6, 584.7, 584.8, 584.9) and hemodialysis (ICD-9-CM 39.95, V45.11,V56.0, V56.1).(11) Respiratory failure requiring mechanical ventilation was defined as the ICD-9-CM code for invasive mechanical ventilation (ICD-9-CM 96.04, 96.70, 96.72) or tracheostomy placement (ICD-9-CM 31.1, 31.2, 31.21, 31.29). Patients with infection were, based on previous studies,(7,12) identified as having a diagnosis of either pneumonia, urinary tract infection, *Clostridium difficile* infection, spontaneous bacterial peritonitis, sepsis, bacteremia, or cholangitis (**Appendix**).

*Objectives*

The primary objective of the study was to evaluate the association of the NACSELD-ACLF score and inpatient survival. Secondary objectives included evaluating the impact of infection and the impact of hospital type, defined as LT or non-LT centers. LT centers were determined based on the whether a LT was performed at the hospital over the study period.

*Statistical analysis*

STATA 14.0 was used to analyze the data.(13) Continuous variables were expressed as means with interquartile ranges and analyzed by the adjusted Wald test. Categorical variables were expressed as percentages and analyzed by chi-squared. Multivariable logistic regression

was performed to analyze outcomes. As the NIS does not provide laboratory or vital sign information, the same model used by the NACSELD (including age, Model for End-Stage Liver Disease [MELD] score, white blood cell, albumin, and the presence of infection)(6) could not be utilized, and thus a unique multivariable logistic regression model was constructed. The model controlled for covariates that were selected *a priori* and were known to impact survival in patients with cirrhosis - including age, gender, the presence of infection, presence of ascites, gastrointestinal bleeding, and the Elixhauser comorbidity index.(14) Interaction terms were included if found to be significant. Standard errors were clustered by center to limit the impact of potential outliers. Area under the receiver operated curve (AUROC) was calculated for the models.

**Results**

*Patient demographics*

Of the 1,612,930 discharges of patients with decompensated cirrhosis identified, 1,523,478 were included in the study with 106,634 (7.0%) meeting the threshold for the NACSLD-ACLF score (positive when there are 2 or more organ failures) (**Figure 1**). The prevalence of the NACSELD-ACLF score increased from 2005 to 2014 (5.7% to 8.6%) (**Supplemental table 1**). Men and patients with alcohol-related liver disease were significantly more likely to have the NACSELD-ACLF score (**Supplemental table 2**).

The mean age was 58 years, 36.4% of patients were women, and patients were mostly white (65.9%) (**Table 1**). Most patients were from the lowest socioeconomic quartile, measured by median household income in the patient's ZIP code (31.8%). Most patients were admitted in densely populated areas and 246,124 (16.2%) patients were hospitalized at a liver transplant center. Alcohol-related liver disease was the most common etiology of liver disease and was significantly more common in patients with NACSELD-ACLF score. Alcoholic hepatitis, although unreliably diagnosed using ICD-9-CM codes,(15) was present in 6.9% of the sample and had increased of prevalence of the NACSELD-ACLF score (9.9% vs. 6.7%). Ascites (92.5%) was the most common sign of decompensation. There were 516,089 (33.7%) of patients who were infected during their hospitalization. The most common infection was a urinary tract infection

190,792 (12.4%) followed by pneumonia (7.0%), spontaneous bacterial peritonitis (5.2%), cellulitis and soft tissue infection (5.2%), *Clostridium difficile* infection (2.3%), and cholangitis (0.7%). Of the patients with infection, 11.9% had sepsis or septicemia. Of patients with an infection, 38.4% had at least 2 infections.

*Crude Survival*

Overall, 1,386,365 (91.0%) patients survived their hospitalization during the study. Patients with the NACSELD-ACLF score had significantly lower survival (47.8% vs. 94.2%, p<0.001) (**Figure 2A**). Survival in patients with the NACSELD-ACLF score significantly improved from 2005 to 2014 (38.9% to 52.5%) (**Supplementary table 1**). Survival was also inversely correlated with the number of organ failures – starting at 96.8% survival for those without organ failure and decreasing to 26.4% for those with 4 organ failures (**Figure 2B**). At each level, of organ failure, infected patients had significantly worse inpatient survival. Patients with multiple infections had higher rates of multiple organ failures (31.5% vs. 4.7%, p<0.001) and worse overall survival (67.7% vs. 93.1%, p<0.001) than those with a single infection.

When evaluating survival rates of specific organ failures, patients with infection had higher prevalence and worse survival for each specific organ failure (**Figure 2C**). Overall, HE was the most common (26.6% prevalence) organ failure but also had the highest associated survival (86.0%). Shock and respiratory failure had the lowest inpatient survival (48.3% and 47.1%, respectively).

*Regression Analysis*

Univariable logistic regression demonstrated that increasing number of organ failures is associated with decreased odds of inpatient survival (**Table 2**). Once at least 2 organ failures, or the NACSELD-ACLF score, was present, the combination of organ failures did not substantially change survival (**Supplemental table 3**). Multivariable analysis controlling for age, gender, the interaction of gastrointestinal bleeding and presence of ascites, presence of infection, and the Elixhauser comorbidity index, the NACSELD-ACLF score was significantly associated with a marked reduction in inpatient survival (adjusted OR 0.08, 95% CI 0.07-0.08, p<0.001) (**Table 3**).

In this multivariable model, the presence of infection (adjusted OR 0.42, 95% CI 0.41-0.43, p<0.001) and the interaction of gastrointestinal bleeding and ascites (adjusted OR 0.79, 95% CI 0.74-0.84, p<0.001) were both significantly associated with reduced inpatient survival. The AUROC for the NACSELD was 0.77 (95% CI 0.77-0.78).

*Liver Transplant Center*

Of the 246,124 patients hospitalized at a LT center, 7,654 (3.1%) underwent LT during their hospitalization. Patients who were hospitalized at a LT center were more likely to have at least one organ failure (66.7% vs. 62.2%, p<0.001) but less likely to have the NACSELD-ACLF score (6.3% vs. 10.2%, p<0.001). Survival at each number of organ failure (**Figure 3A**) was significantly higher in LT centers compared to non-LT centers (p<0.001)**.** This remained true even when excluding any patient who underwent an LT. Survival in respiratory failure was significantly higher in LT centers (47.9% vs. 46.9%, p<0.001), while survival in shock and renal failure was higher in non-LT centers (49.5% vs. 43.5%, p<0.001 and 62.6% vs. 59.0%, p<0.001, respectively) (**Figure 3B**). On multivariable analysis, controlling for age, gender, the interaction of gastrointestinal bleeding and presence of ascites, presence of infection, the Elixhauser comorbidity index, and NACSELD-ACLF score, hospitalization at an LT center was associated with increased survival (adjusted OR 1.17, 95% CI 1.13-1.22, p<0.001) (**Table 4**).

**Discussion**

The purpose of this study was to utilize a nationally representative database to externally validate the performance of NACSELD-ACLF score in predicting inpatient survival. We identified 1.5 million hospitalized patients with decompensated cirrhosis over 10 years and confirmed that organ failures are indeed a major driver of mortality in this population across the United States, particularly when infected. Furthermore, by selecting a population where the majority were hospitalized at non-LT centers, this analysis also validates the use of NACSELD-ACLF score among patients who may not have the option for LT.

The use of a database with national sampling in order to validate the NACSELD-ACLF score is crucial because the majority of patients in the United States are seen at non-transplant

centers; despite only one-sixth of the hospitalized cirrhosis population being seen at academic LT centers, LT centers generate the vast majority of the literature advising inpatient cirrhosis management. Similar to this study, an analysis of the Veterans Administration database over a similar timeframe consisted of less than 10% of patients hospitalized at LT centers, but this population was predominantly comprised of male veterans, limiting its external validation.(16) The NACSELD-ACLF score demonstrates its broadest appeal among patients and providers at non-LT hospitals. Patients seen in these hospitals do not have access to prompt salvage LT, and the presence of the NACSELD-ACLF score can quickly stratify these patients into low (less than 50%) and high (greater than 90%) chance of survival. These stark differences warrant a consideration of changing the goals of care when the NACSELD-ACLF score is present. Given the underuse of palliative care services in patients with liver disease who are denied liver transplantation,(17) early identification of these patients would allow for a smoother transition to palliative care. For example, other diseases, most notably metastatic non-small cell lung cancer, have demonstrated not only improved quality of life and mood but also longer survival in patients who received early palliative care and avoided aggressive care.(18) At the same time, patients who are potential transplant candidates, meet the criteria of the NACSELD-ACLF score, and are at a non-transplant hospital require urgent transfer to a transplant-capable hospital. The presence of the NACSELD-ACLF can be used as an early indicator to initiate a timely transfer in a non-LT hospital, or similarly, warrant a rapid LT evaluation for a patient already in an LT hospital.

While there were minor differences between the results of our analysis and the initial NACSELD-ACLF paper(6) overall, the findings of both studies are quite similar. Survival for all organ failures was poor in both cohorts, but our cohort had notably reduced survival among patients with shock and especially with respiratory failure. Interestingly, we observed a significantly worse survival (10% higher mortality) among patients with NACSELD-ACLF compared to the NACSELD study group cohort.(6) While there are no clear explanations for this discrepancy, it is likely driven by patients who are not LT candidates or a lack of inpatient liver services that are typical at major liver referral centers. Unsurprisingly, despite utilization of a different multivariable regression model, our study also found that NACSELD-ACLF was

associated with a more potent effect on survival (OR 0.08 vs. OR 0.16). When comparing the impact of NACSELD-ACLF score in the original and validation study, the NACSELD-ACLF score shows itself to be simpler and more strongly linked with inpatient survival when compared to MELD (OR 0.95) in the original NACSELD-ACLF study. Notably, our analysis was also in agreement with O'Leary et al in that infection was associated with significantly worse outcomes. This finding is in contrast to the CANONIC study, in which there was similar mortality among patients with and without infection.(4) However, it is worth noting that infection was associated with ACLF, which, in the CANONIC study, was associated with poor outcomes.

The limitations of this study are inherent to the use of large databases in general, which is prone to administrative coding error. Despite this limitation, the power of using 1.5 million hospitalizations is profound and is a tradeoff of administrative databases. The NIS specifically lacks laboratory data, which is crucial in determining liver disease severity, such as calculation of MELD-Na or Child-Pugh Turcotte score. Furthermore, a key element within the NACSELD-ACLF multivariable model is white blood cell count, which was appreciated as an important marker of both inflammation and prognosis.(6) Nonetheless, the model utilized in this study, although lacking laboratory covariates, included factors known to increase mortality in patients with cirrhosis. Due to only one ICD-9-CM code being used to diagnose HE, we were unable to differentiate between stages of HE severity. The inclusion of HE at all stages in our study likely explains why survival in our study is higher for patients with HE compared to the study by O'Leary et al.(6) Unfortunately, due to poor coding algorithms, acute insults such as alcoholic hepatitis and acute viral hepatitis are challenging to diagnose and study individually when using a large database.(15) Additionally, as this study is retrospective, it merely can confirm the findings demonstrated by the NACSELD-ACLF through association and is not, by itself, predictive of inpatient survival. While the weaknesses of large databases are well documented, the external validity of this study is substantial given its broad representation of LT and non-LT hospitals in various locations in the country as compared to well-recognized liver referral hospitals included the NACSELD study group. It is also worth noting that ACLF is a clinical syndrome that results in organ failures, in which laboratory values would be helpful but not fully necessary to diagnose.

Still, this analysis brings to light an increasingly important question – whether the NACSELD-ACLF score prior to LT impacts post-LT survival. Unfortunately, while our database is limited in its ability to analyze the relationship between the timing of organ failures and LT, a recent analysis of the United Network for Organ Sharing database noted that despite the number of organ failures being associated with a worse post-transplant mortality, the absolute difference between those with no organ failures (90% 1-year survival) and those with 5-6 organ failures (81% 1-year survival) prior to liver transplant, was only 9%.(19) Similar to the MELD-Na score, the NACSELD-ACLF is excellent in predicting short-term mortality, but organ failures themselves do not necessarily indicate a poor post-transplant prognosis. In fact, patients meeting criteria for ACLF on the LT waiting list had higher mortality than those with acute liver failure, thought previously to confer highest short-term mortality for patients with liver disease.(20) In contrast to non-LT centers, LT centers should be incentivized to continue to consider patients with multiple organ failures for LT, especially when patients derive significant short and long-term survival benefit from LT.(21) Prospective data from the NACSELD cohort demonstrate higher rates of pre-LT mortality in those with ACLF but no difference in post-LT survival among listed patients.(22) However, retrospective studies have demonstrated mixed results – a study of patients with ACLF grade 3 from France had outcomes after LT similar to that of lower grade ACLF while other studies from France(23) and Germany(24) show ACLF to be a potent risk factor for post-LT mortality. Currently, there is difficulty predicting post-LT mortality confidently in patients who are entering LT in ACLF. Persistent renal failure post-LT, which is a known adverse post-LT outcome connected to mortality, may be a potential explanation for poor outcomes after LT in the setting of ACLF.(25) Frailty, which is a major driver of waiting list mortality,(26) is likely to be related to post-LT mortality as well. Future investigation is warranted as our study was limited by difficulties in interpreting timing of diagnoses and organ failures in relation to LT.

Given the rapid deterioration of patients with ACLF, prediction of poor prognosis early in the time course is crucial. Our study now further supports the broad application of the NACSELD-ACLF score to identify patients hospitalized with ACLF, regardless of hospital type, and offers an easy bedside tool that patients, caregivers, and their providers can use to better

recognize poor outcomes and enhance either early recognition of LT candidacy or, conversely, futile care in those without LT. In patients without access to LT who are very likely to die before discharge, presence of the NACSELD-ACLF score predicted dismal survival; while on the contrary, lack of two or more organ failures was associated with a more than 94% inpatient survival. These findings represent a call to action for non-LT hospitals, who can use this simple bedside test to determine disposition in patients, depending on their transplant candidacy, to provide better quality care and outcomes.



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**Figure 1 – Inclusion and Exclusion of the Study Cohort**

Inclusion and exclusion of the study cohort.

**Figure 2 – Inpatient Survival Stratified by NACSELD-ACLF Score, Number of Organ Failures, and Type of Organ Failure**

A. Inpatient survival by the presence of the NACSELD-ACLF score, stratified by presence of infection

B. Inpatient survival by the number of organ failures, stratified by presence of infection

C. Inpatient survival by the type of organ failure, stratified by presence of infection

**Figure 3 – Inpatient Survival Stratified by Hospitalization at a Liver Transplant Center**

A. Inpatient survival by the number of organ failures depending on hospitalization in liver transplant center

B. Inpatient survival by the type of organ failure depending on hospitalization in liver transplant center

**Table 1 – Demographic Characteristics of the Sample Comparing Patients Who Meet the NACSELD-ACLF Score with Those Who Do Not Meet Criteria**

| Variable | Total (1,523,478) | NACSELD-ACLF (106,634, 7.0%) | No NACSELD-ACLF (1,416,844, 93.0%) |
|---|---|---|---|
| **Age (years)** | 58 (0.02) | 56 (0.08) | 58 (0.02) |
| **Female (%)** | 554,546 (36.4) | 43,826 (41.1) | 510,720 (33.8) |
| **Race (%)** | | | |
| **White** | 1,002,449 (65.8) | 68,566 (64.3) | 933,833 (65.9) |
| **Black** | 152,348 (10.0) | 10,237 (9.6) | 142,111 (10.1) |
| **Hispanic** | 269,656 (17.7) | 19,727 (18.5) | 249,929 (17.6) |
| **Asian** | 31,993 (2.1) | 2,666 (2.5) | 29,327 (2.1) |
| **Other** | 67,032 (4.3) | 8,138 (4.5) | 58,894 (4.2) |
| **Median household income by ZIP code quartile (%)** | | | |
| **1st** | 485,989 (31.9) | 31,990 (30.0) | 453,999 (32.0) |
| **2nd** | 400,675 (26.3) | 26,872 (25.2) | 373,803 (26.4) |
| **3rd** | 358,017 (23.5) | 25,486 (23.9) | 332,531 (23.4) |
| **4th** | 278,797 (18.4) | 22,180 (20.8) | 256,617 (18.2) |
| **Hospital location (%)†** | | | |
| **Metropolitan city center > 1mill** | 527,123 (34.6) | 39,988 (37.5) | 487,135 (34.4) |

| | | | |
|---|---|---|---|
| **Metropolitan county (not center > 1 mill** | 344,306 (22.6) | 24,632 (23.1) | 319,674 (22.6) |
| **County population 250,000-999,999** | 292,508 (19.2) | 19,514 (18.3) | 272,994 (19.2) |
| **County population 50,000-249,999** | 129,496 (8.5) | 8,317 (7.8) | 121,179 (8.6) |
| **Micropolitan county** | 143,207 (9.4) | 8,851 (8.3) | 134,356 (9.4) |
| **Other** | 86,838 (5.8) | 5,438 (5.1) | 81,400 (5.8) |
| **Liver transplantation hospital (%)** | 246,124 (16.2) | 25,379 (23.8) | 220,745 (15.6) |
| **Infection (%)** | 516,089 (33.7) | 75,710 (71.0) | 440,379 (30.9) |
| **Upper GI bleed (%)** | 278,796 (18.3) | 37,109 (34.8) | 241,687 (17.1) |
| **Esophageal variceal bleed (%)** | 132,543 (8.7) | 18,448 (17.3) | 114,095 (8.1) |
| **Ascites (%)** | 1,409,217 (92.5) | 89,999 (84.4) | 1,319,218 (93.1) |
| **Type of cirrhosis (%)** | | | |
| **Hepatitis C** | 457,043 (30.0) | 20,900 (19.6) | 436,143 (30.8) |
| **Alcohol-related** | 856,195 (56.2) | 70,805 (66.4) | 785,390 (55.5) |
| **Length of stay (days)** | 7.0 (0.01) | 14.5 (0.10) | 6.5 (0.01) |
| **Total charge ($)** | 54,920 (172) | 176,070 (1525) | 45,933 (130) |
| **Inpatient survival (%)** | 1,386,365 (91.0) | 50,971 (47.8) | 1,335,394 (94.2) |

[†] Only variable that was not significant ($p < 0.05$).

Continuous variables expressed as means with standard deviation in parentheses. Categorical variables expressed as number with percent in parentheses.

**Table 2 – Univariable Logistic Regression Survival Probability for Number of Organ Failures in the Entire Cohort**

| **Number of organ failures** | **Infection** | **No Infection** |
|---|---|---|
| | **Unadjusted Odds Ratio (95% CI)** | **Unadjusted Odds Ratio (95% CI)** |
| **No organ failure** | REF | REF |

| | | |
|---|---|---|
| **One organ failure** | 0.26 (0.25-0.27) | 0.26 (0.25-0.27) |
| **Two organ failures** | 0.05 (0.05-0.05) | 0.04 (0.04-0.05) |
| **Three organ failures** | 0.02 (0.02-0.03) | 0.02 (0.02-0.03) |
| **Four organ failures** | 0.02 (0.01-0.02) | 0.02 (0.02-0.03) |

CI – confidence interval

**Table 3 – Multivariable Logistic Regression Survival Probability for NACSELD-ACLF Score in the Entire Cohort**

| Variable | Adjusted Odds Ratio (95% CI) | P-value |
|---|---|---|
| **NACSELD-ACLF Score** | 0.08 (0.07-0.08) | <0.001 |
| **Age** | 0.98 (0.98-0.99) | <0.001 |
| **Female** | 1.20 (1.16-1.23) | <0.001 |
| **Interaction of Gastrointestinal bleeding and Ascites** | 0.78 (0.73-0.84) | <0.001 |
| **Infection** | 0.42 (0.41-0.43) | <0.001 |
| **Elixhauser comorbidity index** | 0.990 (0.979-0.996) | 0.004 |

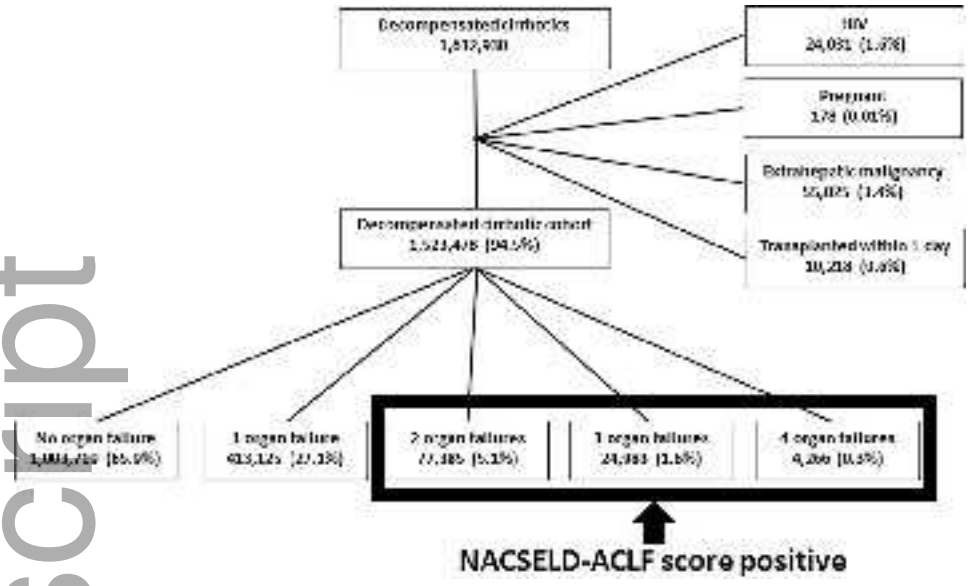
CI – confidence interval

**Table 4 – Multivariable Logistic Regression Survival Probability for NACSELD-ACLF Score in the Entire Cohort with Inclusion of Hospitalization at a Liver Transplant Center**

| Variable | Adjusted Odds Ratio (95% CI) | P-value |
|---|---|---|
| **Hospitalization at a Liver Transplant Center** | 1.17 (1.13-1.22) | <0.001 |
| **NACSELD-ACLF Score** | 0.08 (0.07-0.08) | <0.001 |
| **Age** | 0.98 (0.98-0.99) | <0.001 |
| **Female** | 1.20 (1.16-1.23) | <0.001 |
| **Interaction of Gastrointestinal bleeding and Ascites** | 0.79 (0.73-0.84) | <0.001 |
| **Infection** | 0.42 (0.41-0.43) | <0.001 |

| | | |
|---|---|---|
| **Elixhauser comorbidity index** | 0.990 (0.981-0.998) | 0.02 |

CI – confidence interval

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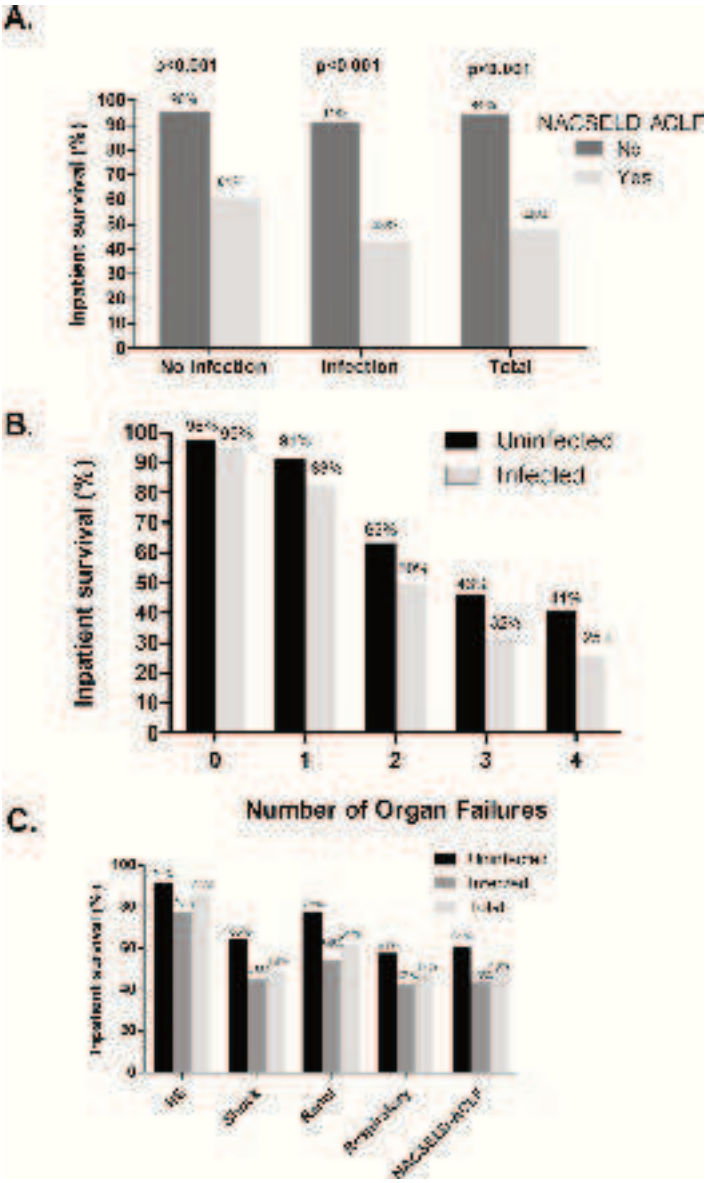


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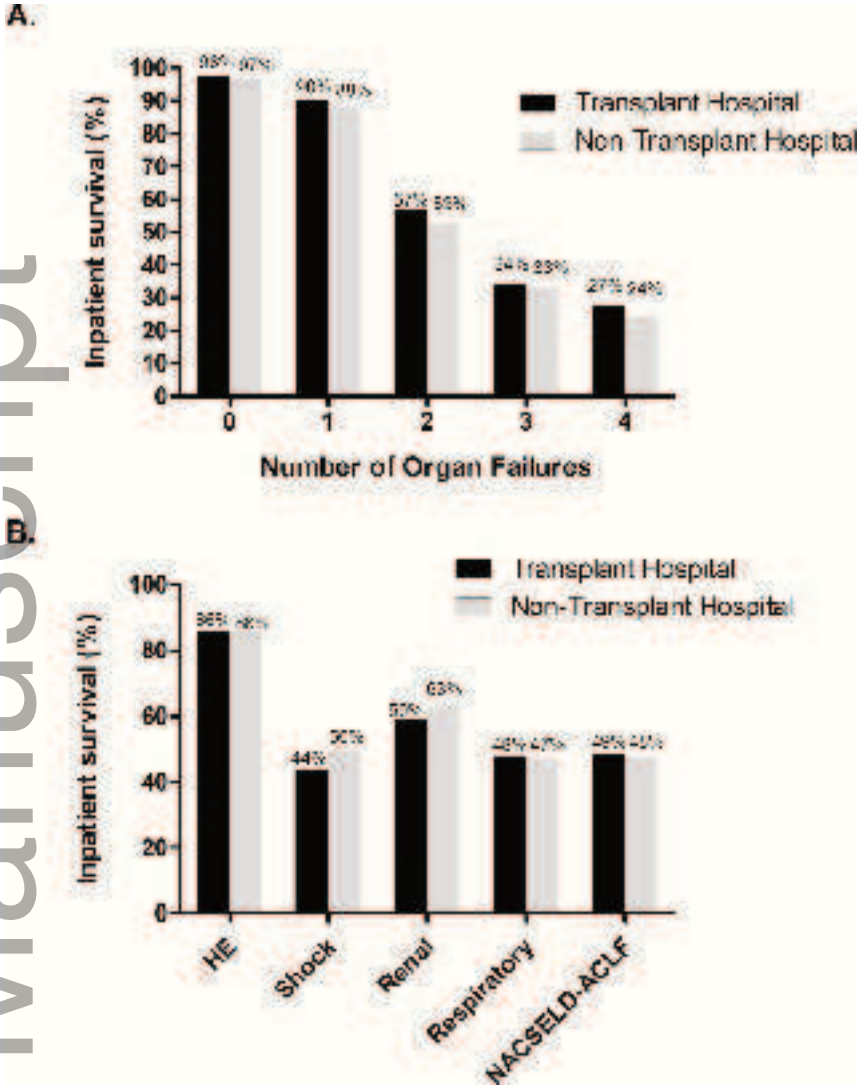


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