A population-based cohort study of mortality of intensive care unit patients with liver cirrhosis

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Yu-Feng Huang
Mackay Memorial Hospital Taitung Branch Hospital

Chao-Shun Lin
Taipei Medical University Hospital

Yih-Giun Cherng
Taipei Medical University Shuang Ho Hospital Ministry of Health and Welfare

Chun-Chieh Yeh
China Medical University Hospital, Taiwan

Ray-Jade Chen
Taipei Medical University Hospital

Ta-Liang Chen
Taipei Municipal Wan-Fang Hospital

Chien-Chang Liao jacky48863027@yahoo.com.tw
Taipei Medical University Hospital

Corresponding Author
ORCiD: 0000-0001-6694-0730

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Abstract

Background: The impact of liver cirrhosis on the outcomes of admission to intensive care unit (ICU) is not completely understood. Our purpose is to identify risk factors for mortality in ICU patients with liver cirrhosis.

Methods: Using reimbursement claims from Taiwan’s National Health Insurance Research Database from in 2006-2012, 1,250,300 patients were identified as having ICU stays of more than one day, and 37,197 of these had liver cirrhosis. With propensity score-matching for socioeconomic status, pre-existing medical conditions, and cirrhosis-related morbidities, 37,197 ICU patients without liver cirrhosis were selected for comparison. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of cirrhosis associated with 30-day, ICU, and one-year mortality were calculated.

Results: Compared with control, cirrhotic patients had higher 30-day mortality (aOR 1.60, 95% CI 1.53 to 1.68), particularly those with jaundice (aOR 2.23, 95% CI 2.03 to 2.45), ascites (aOR 2.32, 95% CI 2.19 to 2.46) or hepatic coma (aOR 2.21, 95% CI 2.07 to 2.36). Among ICU patients, liver cirrhosis was also associated with ICU mortality (aOR 144, 95% CI 1.38 to 1.51) and one-year mortality (aOR 1.40, 95% CI 1.35 to 1.46). Associations between cirrhosis of liver and increased 30-day mortality were significant in both sexes and every age group.

Conclusions: Liver cirrhosis was associated with 30-day mortality in ICU patients. Jaundice, ascites, hepatic coma, more than 4 admissions due to cirrhosis, and more than 30 days of hospital stay due to cirrhosis were exacerbated factors in cirrhotic ICU patients.
Background

Cirrhosis of the liver results in various complications and mortality worldwide, but especially in developed regions [1]. It is the fourth most common cause of death in Europe and leads to more than a million deaths around the globe annually [2,3]. The main etiologies of liver cirrhosis in most areas are infection with hepatitis B or C virus and alcohol abuse [1]. A French screening program estimated prevalence at 0.3%, and European studies found annual incidences of 15.3-132.6 per 100,000 people [3].

In the United States, annual medical expenditures related to intensive care unit (ICU) admissions are US $3 billion, with mean charges of US $116,200 per admission [4]. Patients in late-stage liver cirrhosis are likely to be admitted to ICUs for critical conditions such as sepsis and renal or respiratory failure [4,5]. Though some studies reported improving outcomes in patients with cirrhosis admitted to ICUs [6], the prognosis remains poor, with mortality rates as high as 45% or even higher [7,8].

It is important to identify the risk factors of cirrhosis of the liver and associated adverse outcomes of patients admitted to ICU. Several prognostic scoring systems have been proposed for risk assessment [9-12], such as the Child-Pugh score [13], the Model for End-stage Liver Disease [14], the Acute Physiology and Chronic Health Evaluation [15], and the Sequential Organ Failure Assessment [16]. Most previous reports only analyzed risk factors that predict outcomes when stratifying cirrhotic patients admitted to ICU, but did not assess the influence of cirrhosis itself on mortality in ICU or one-year survival after discharge.

We conducted a nationwide population-based retrospective cohort study using Taiwan’s National Health Insurance Research Database to investigate ICU mortality
in patients with and without liver cirrhosis. We also evaluated the impacts of different comorbidities and cirrhosis-related clinical indicators on ICU mortality and on one-year survival in further stratified analyses.

Methods

Data sources
We conducted this study using reimbursement claims data from Taiwan’s National Health Insurance Program. This program merged former insurance systems in March 1995 and covers more than 99% of Taiwan’s 23 million residents. The National Health Research Institutes established a National Health Insurance Research Database (NHIRD) to record all beneficiaries’ inpatient and outpatient medical services. This information includes basic patient demographics, physician’s primary and secondary disease diagnoses, treatment procedures, prescribed medications and medical expenditures for all health care services. The validity of this database has been favorably evaluated, and research articles based on it have been accepted in prominent scientific journals worldwide [17-20].

Ethics
This study was conducted in accordance with the Helsinki Declaration. To protect personal privacy, the electronic database was decoded with patient identifications scrambled for further academic access for research. According to Taiwan National Health Research Institutes regulations, informed consent is not required because patient identifications were decoded and scrambled [18-20]. Ethical approval for this study (TMU-JIRB-201504008) was provided by the Institutional Review Board of Taipei Medical University.

Study design
Among 23 million beneficiaries, 1,250,300 patients were admitted to ICU between 2006 and 2012 (supplementary Figure S1). We identified 79,528 patients aged ≥ 20 years who had histories of liver cirrhosis from the National Health Insurance Research Database. Patients with liver cirrhosis were defined as having at least two visits for medical care with physician’s primary diagnosis of liver cirrhosis within the 24 months before ICU admission. To select appropriate comparison groups, we matched each ICU patient with cirrhosis with one randomly selected ICU patients without liver cirrhosis by the analysis with a propensity score-matched pair procedure (case-control ratio=1:1). These matched factors included age, sex, low income, stay in medical center or not, diabetes, hypertension, mental disorder, chronic obstructive pulmonary disease, fracture, pneumonia, stroke, asthma, traumatic brain injury, congestive heart failure, immune thrombocytopenia, renal dialysis, hyperlipidemia, epilepsy, atrial fibrillation, peripheral vascular disease and systemic lupus erythematosus, causes of admission to ICU according to physician’s primary diagnosis (digestive disease, cancer, respiratory disease, circulatory disease, infectious disease, injury and poisoning, symptom-defined conditions, genitourinary disease, endocrine disease, musculoskeletal disease, neurological disease, skin disease, mental disorder, tumors, blood diseases, congenital anomalies, disease of perinatal period, complications of pregnancy, ICU complications (such as septicemia, pneumonia, acute renal failure, urinary tract infection, stroke, acute myocardial infarction and pulmonary embolism). After matching selection, there were 37,197 patients with cirrhosis of liver in the exposure group and 37,197 people without liver cirrhosis in non-exposure group. We investigated the impact of liver cirrhosis on 30-day mortality, ICU mortality, and one-year mortality among ICU patients in this study.
Measures and definitions

Income status was identified by defining low-income patients as those who qualified for waived medical copayment, as this status is verified by the National Health Insurance Bureau. Whether patients stayed in medical center ICUs or those in other hospitals was also recorded. We used the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) to define coexisting medical conditions and ICU complications. Details codes of ICD-9-CM for these diseases were listed in supplementary Table S1. Cirrhosis of liver before ICU stay was defined as the major exposure. Coexisting medical conditions determined from medical claims within the 24-month period before ICU stay included diabetes, hypertension, mental disorders, chronic obstructive pulmonary disease, fracture, pneumonia, stroke, asthma, traumatic brain injury, congestive heart failure, immune thrombocytopenia, hyperlipidemia, epilepsy, atrial fibrillation, peripheral vascular disease, and systemic lupus erythematosus. Renal dialysis was defined by administration code (D8, D9). Seven major complications during the ICU stay were analyzed (and those having severe cases of these diseases before ICU were excluded) including septicemia, pneumonia, acute renal failure, urinary tract infection, stroke, acute myocardial infarction, and pulmonary embolism. Length of hospital stay and ICU medical expenditure were analyzed as secondary outcomes. Causes of admission to ICU (according to physician’s primary diagnosis at admission) were also identified and described with disease codes including digestive disease, cancer, respiratory disease, circulatory disease, infectious disease, injury and poisoning, symptom-defined conditions, genitourinary disease, endocrine disease, musculoskeletal disease, neurological disease, skin disease, mental disorder, tumor, blood disease, congenital anomalies, disease of perinatal
Statistical analysis

To reduce confounding bias, we used a propensity score-matched pair combined with frequency matching procedure to balance the covariates between ICU patients with and without liver cirrhosis. We developed a non-parsimonious multivariable logistic regression model to estimate a propensity score for pre-ICU cirrhosis of the liver. We matched cirrhotic patients to patients without liver cirrhosis, using a greedy matching algorithm (without replacement) with a caliper width of 0.2 SDs of the log odds of the estimated propensity score. Clinical significance guided initial choices of covariates in this multivariable logistic regression model: age, sex, low income, ICU stay in medical center or not, diabetes, hypertension, mental disorders, chronic obstructive pulmonary disease, fracture, pneumonia, stroke, asthma, traumatic brain injury, congestive heart failure, immune thrombocytopenia, renal dialysis, hyperlipidemia, epilepsy, atrial fibrillation, peripheral vascular disease, systemic lupus erythematosus, septicemia, pneumonia, acute renal failure, urinary tract infection, stroke, acute myocardial infarction, pulmonary embolism, digestive disease, cancer, respiratory disease, circulatory disease, infectious disease, injury and poisoning, symptom-defined conditions, genitourinary disease, endocrine disease, musculoskeletal disease, neurological disease, skin disease, mental disorder, tumor, blood disease, congenital anomalies, disease of perinatal period, and complications of pregnancy. A structured iterative approach was used to refine this model to achieve covariate balance within matched pairs. We used chi-square tests to measure covariate balance, and $p < 0.05$ was suggested to represent meaningful covariate imbalance. We matched patients with and without cirrhosis using a greedy-matching algorithm with a caliper width of 0.2 SD of the log
odds of the estimated propensity score. This method could remove 98% of bias from measured covariates.

Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) for 30-day mortality, ICU mortality, and one-year mortality for patients with and without cirrhosis were analyzed with multiple logistic regression models by controlling for age, sex, low income, stay in medical center or not, coexisting medical conditions, ICU complications and admission causes. To confirm associations between liver cirrhosis and ICU mortality, we also performed stratification analysis by age, sex, low income, stay in medical center or not, coexisting medical conditions, ICU complications and causes of ICU admission. The impacts of liver-related indicators and medical care on 30-day mortality in ICU patients with cirrhosis were also measured by calculating adjusted ORs and 95% CIs in the multivariate logistic regression models. SAS version 9.1 (SAS Institute Inc., Cary, NC, USA) statistical software was used for data analyses; two-sided \( p < 0.05 \) indicated significant differences.

Results

The supplementary Figure S1 shows the flow chart for selecting ICU patients with and without liver cirrhosis. Table 1 shows the distributions of age, sex, low income, stay in medical center or not, coexisting medical conditions (diabetes, hypertension, mental disorders, chronic obstructive pulmonary disease, fracture, pneumonia, stroke, asthma, traumatic brain injury, congestive heart failure, idiopathic thrombocytopenic purpura, renal dialysis, hyperlipidemia, epilepsy, atrial fibrillation, peripheral vascular disease, systemic lupus erythematosus), ICU complications (septicemia, pneumonia, acute renal failure, urinary tract infection,
stroke, acute myocardial infarction, pulmonary embolism), causes of admission to ICU (digestive disease, cancer, respiratory disease, circulatory disease, infectious disease, injury and poisoning, symptom-defined conditions, genitourinary disease, endocrine disease, musculoskeletal disease, neurological disease, skin disease, mental disorders, tumor, blood disease, congenital anomalies, disease of perinatal period, pregnancy complications) as well as surgery and endotracheal intubation balanced between surgical patients with and without cirrhosis of liver using the matching procedure by propensity score.

In Table 2, patients with cirrhosis showed higher ICU medical expenditure than patients without (12,008±9890 vs. 11,366±8742 USD, p<0.0001). Cirrhosis was associated with a significant increase in 30-day mortality (aOR 1.60, 95% CI 1.53 to 1.68), ICU mortality (aOR 1.44, 95% CI 1.38 to 1.51), and one-year mortality (aOR 1.40, 95% CI 1.35 to 1.46) in ICU patients.

Compared with ICU patients without cirrhosis (Table 3), cirrhotic ICU patients had increased 30-day mortality when they also had liver cancer (aOR 1.85, 95% CI 1.74 to 1.97), hepatitis B or C virus infection (aOR 1.75, 95% CI 1.50 to 2.03), alcohol dependence syndrome (aOR 1.82, 95% CI 1.62 to 2.04), jaundice (aOR 2.23, 95% CI 2.03 to 2.45), ascites (aOR 2.32, 95% CI 2.19 to 2.46), gastrointestinal hemorrhage (aOR 1.90, 95% CI 1.78 to 2.03), hepatic coma (aOR 2.21, 95% CI 2.07 to 2.36), more than 4 admissions due to LC (aOR 2.52, 95% CI 2.20 to 2.89), more than 30 days of hospital stay due to LC (aOR 2.97, 95% CI 2.66 to 3.31), and albumin supplement (aOR 1.93, 95% CI 1.83 to 2.04). The aORs of alcohol-related cirrhosis and previous hospitalization associated with 30-day mortality were 1.75 (95% CI 1.66 to 1.85) and 1.52 (95% CI 1.46 to 1.58), respectively.

The association between liver cirrhosis and ICU mortality was significant in relation
to the following causes of ICU admission: digestive disease (aOR 3.23, 95% CI 2.91 to 3.58), cancer (aOR 1.15, 95% CI 1.05 to 1.27), respiratory disease (aOR 1.24, 95% CI 1.12 to 1.38), circulatory disease (aOR 1.47, 95% CI 1.28 to 1.70), infectious disease (aOR 1.32, 95% CI 1.19 to 1.48), injury and poisoning (aOR 1.95, 95% CI 1.61 to 2.35), symptom-defined conditions (aOR 1.86, 95% CI 1.43 to 2.42), genitourinary disease (aOR 1.74, 95% CI 1.10 to 2.75), musculoskeletal disease (aOR 3.49, 95% CI 1.79 to 6.82), and neurological disease (aOR 2.94, 95% CI 1.30 to 6.65). The 30-day mortality was also associated with LC in ICU patients with 2 scores (aOR 1.49, 95% CI 1.31 to 1.70), 3 scores (aOR 1.45, 95% CI 1.25 to 1.69), and 4 scores (aOR 1.40, 95% CI 1.17 to 1.67) of Charlson Comorbidity Index. Stratified analysis and effects of cirrhosis-related clinical indicators on ICU mortality and one-year mortality of ICU patients were showed in supplementary Table S3 and supplementary Table S4.

Discussion

In this large-scale, nationwide, population-based propensity score-matched study, patients with cirrhosis of the liver admitted to ICU showed significantly higher ICU mortality as well as increased medical expenditure compared with non-cirrhotic controls. The stratified analyses showed higher ICU mortality among patients with increasing numbers of co-morbidities. Associated with even higher ICU mortality were cirrhosis-related clinical conditions, liver cancer, alcohol dependence syndrome, jaundice, ascites, gastrointestinal hemorrhage and hepatic coma. Regarding long-term outcomes after ICU discharge, higher one-year mortality was noted in liver cirrhosis patients with older age, male gender, ICU in medical center, anemia, renal dialysis, congestive heart failure, and complications in ICU such as
septicemia and pneumonia.

To the best of our knowledge, this is the first report investigating the influence of liver cirrhosis on 30-day mortality, ICU mortality, and one-year mortality in ICU patients using a nationwide database. Previous studies were mostly conducted from a single center [10,12,21-24], which may represent a certain type of patient group and medical practice. Although these studies evaluated risk factors among patients with liver cirrhosis admitted to ICU, they did not note various cirrhosis-related clinical characteristics nor assess the impact of cirrhosis per se, adjusting all covariates with the control group to the ICU mortality [7,10-12,25,26]. In our subgroup analyses, the odds ratios of ICU mortality in cirrhotic patients’ ICU admissions with primary diagnoses such as cancer, respiratory disease and infectious disease were lower than other causes of ICU admission. This might be attributed to cancer, pneumonia, COPD and sepsis having more impact on ICU mortality than cirrhosis after adjustment [27-29].

Regarding the effects of cirrhosis-related clinical indicators on ICU mortality, cirrhotic patients with liver cancer, alcohol dependence syndrome, jaundice, ascites, gastrointestinal hemorrhage and hepatic coma had higher ICU mortality than those without cirrhosis. Of these cirrhosis-related clinical indicators, jaundice, ascites and hepatic coma were consistent with the Child-Pugh score risk factors of the most commonly used prognosis predicting model in cirrhotic patients [13]. The development of ascites, gastrointestinal hemorrhage, encephalopathy and jaundice mark the decompensated stage of liver cirrhosis that results in poorer prognoses [30,31]. These complications might contribute to the increased ICU mortality found in patients of liver cirrhosis with more hospitalization. Liver cancer, especially hepatocellular carcinoma, is one of the leading causes of death in Taiwan [34], so it
is reasonable that cirrhotic patients with liver cancer would have higher ICU mortality than those without it.

Regarding increased ICU mortality and medical expenditures, there are some possible explanations why patients with liver cirrhosis had worse outcomes. First, patients with liver cirrhosis are presumed to have impaired immune function and are thus more susceptible to severe infection, leading to higher mortality [35,36]. A previous study demonstrated that infection increased mortality in patients with cirrhosis of liver fourfold, with 30% of patients dying within a month of infection and another 30% dying within a year [37]. This was consistent with our finding that septicemia and pneumonia in patients with cirrhosis were associated with higher ICU mortality. Second, portal hypertension and subsequent esophageal variceal bleeding and ascites play major roles as complications of cirrhosis and are associated with 1-year mortality of nearly 20% [1,5,38]. Third, as cirrhosis progresses, the development of renal vasoconstriction leads to hepatorenal syndrome. Renal failure is an indicator of end-stage liver disease and increases mortality risk by seven times, with half of patients dying within a month [39]. In our study, acute renal failure was also significantly associated with ICU mortality. To reduce ICU mortality in patients with liver cirrhosis, health care teams should optimize management of these specific issues according to updated guidelines.

Concerning long-term outcomes, variables such as serum albumin or bilirubin levels, ascites, encephalopathy, and prothrombin time for the Child-Pugh score are the most common independent predictors of mortality in patients with liver cirrhosis [5]. In our national cohort, ICU mortality among patients with liver cirrhosis increased with numbers of cirrhosis-related clinical conditions. These findings were compatible with previous studies demonstrating high mortality in cirrhotic patients with renal
failure and gastrointestinal hemorrhage [39,40]. However, our study focused on impacts on long-term mortality after ICU discharge, which was not investigated before. Considering specific management of these factors for ICU patients with cirrhosis of the liver is warranted to reduce mortality.

The present study has strengths of large sample sizes and adjustment for potential confounding factors by propensity score-matching method in a nationwide population-based retrospective cohort. It also has some limitations encountered in research based on secondary data. First, detailed information on laboratory data, physical examinations, and hemodynamic parameters was not available from reimbursement claim data. For example, the international normalized ratio of prothrombin time, bilirubin and creatinine level in blood would help to predict outcomes among cirrhosis patients [13,14]. Second, severity of liver cirrhosis noted by Child-Pugh score, Model For End-Stage Liver Disease score or other criteria was not found in reimbursement data for risk stratification of ICU mortality. Third, though the accuracy of major diagnosis codes from the Taiwan National Health Insurance Research Database has been accepted by scientific journals [17-20], the validity of liver cirrhosis, comorbidity and complication codes employed in this study might still be questioned. To reduce the possibility of misdiagnosis or miscoding, we applied inclusive criteria of at least two visits for medical services with physician’s primary diagnosis of liver cirrhosis. In addition, an important factor influencing ICU outcome is Do Not Resuscitate orders. However, we have no data regarding the Do Not Resuscitate order in this study because of the limitations of Taiwan’s National Health Insurance Research Database. Finally, we could not exclude the possibility that some patients with hepatitis without cirrhosis were included in cirrhotic group in this study because the diagnosis error by physicians
may occur in the clinical settings.

Conclusions

In conclusion, this nationwide population-based study showed that patients with liver cirrhosis admitted to ICU have higher ICU and one-year mortality after discharge in patterns that closely correlate with medical conditions and specific scenarios. These findings can help health care providers develop specific protocols to improve prognosis and long-term survival rates for ICU patients with liver cirrhosis.

Abbreviations

CI = confidence interval; ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification; ICU = intensive care unit; OR = odds ratio.

Declarations

Ethics approval and consent to participate: Ethical approval for this study (TMU-JIRB-201504008) was provided by the Institutional Review Board of Taipei Medical University.

Consent for publication: Not applicable.

Availability of data and materials: The data underlying this study is from the National Health Insurance Research Database (NHIRD), which has been transferred to the Health and Welfare Data Science Center (HWDC). Interested researchers can obtain the data through formal application to the HWDC, Department of Statistics, Ministry of Health and Welfare, Taiwan (http://dep.mohw.gov.tw/DOS/np-2497-113.html).
Competing interests: The authors declare that they have no competing interests.

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Authors’ contributions: Conception and design: YFH, CSL, YGC, CCY, RJC, TLC, CCL; Acquisition of data: TLC; Analysis of data: CCL; Interpretation of data: YFH, CSL, YGC, CCY, RJC, TLC, CCL; 2. Drafting the article: YFH, CCL; Revising it critically for important intellectual content: YFH, CSL, YGC, CCY, RJC, TLC, CCL; Final approval of the version to be published: YFH, CSL, YGC, CCY, RJC, TLC, CCL; Agreement to be accountable for all aspects of the work: YFH, CSL, YGC, CCY, RJC, TLC, CCL; RJC contributed equally with the first author; TLC contributed equally with the corresponding author.

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Tables

Table 1 Characteristics of ICU patients with and without liver cirrhosis

| Pre-hospital and in-hospital characteristics | No liver cirrhosis (N=37197) | Liver cirrhosis (N=37197) |
|---------------------------------------------|-----------------------------|---------------------------|
| Age, years                                  | n (%)                       | n (%)                     |
| 20-29                                       | 304 (0.8)                   | 304 (0.8)                 |
| 30-39                                       | 2261 (6.1)                  | 2261 (6.1)                |
| 40-49                                       | 6022 (16.2)                 | 6022 (16.2)               |
| 50-59                                       | 8939 (24.0)                 | 8939 (24.0)               |
| 60-69                                       | 7832 (21.1)                 | 7832 (21.1)               |
| 70-79                                       | 7841 (21.1)                 | 7841 (21.1)               |
| ≥80                                         | 3998 (10.8)                 | 3998 (10.8)               |
| Sex                                         |                             |                           |
| Female                                      | 10274 (27.6)                | 10274 (27.6)              |
| Male                                        | 26923 (72.4)                | 26923 (72.4)              |
| Low income                                  | 1192 (3.2)                  | 1192 (3.2)                |
| ICU in medical center                       | 11331 (30.5)                | 11331 (30.5)              |
| Coexisting medical conditions               |                             |                           |
| Hypertension                                | 8949 (24.1)                 | 8949 (24.1)               |
| Diabetes                                    | 8360 (22.5)                 | 8360 (22.5)               |
| Mental disorder                             | 6725 (18.1)                 | 6725 (18.1)               |
| Peptic ulcer disease                        | 6206 (16.7)                 | 6206 (16.7)               |
| Anemia                                      | 4507 (12.1)                 | 4507 (12.1)               |
| COPD                                        | 3561 (9.6)                  | 3561 (9.6)                |
| Fracture                                    | 2495 (6.7)                  | 2495 (6.7)                |
| Asthma                                      | 1250 (3.4)                  | 1250 (3.4)                |
| Atherosclerosis                             | 1197 (3.2)                  | 1197 (3.2)                |
| Traumatic brain                             | 1063 (2.9)                  | 1063 (2.9)                |
| Injury                                      | 832 (2.2)                   | 832 (2.2)                 |
| Congestive heart failure                    | 806 (2.2)                   | 806 (2.2)                 |
| Renal dialysis                              | 719 (1.9)                   | 719 (1.9)                 |
| Thrombocytopenia                            |                             |                           |
| Reasons for ICU admission                   |                             |                           |
| Digestive disease                           | 10198 (27.4)                | 10198 (27.4)              |
| Cancer                                      | 6726 (18.1)                 | 6726 (18.1)               |
| Respiratory disease                         | 4524 (12.2)                 | 4524 (12.2)               |
| e Circulatory disease                        | 4385 (11.8)                 | 4385 (11.8)               |
| e Infectious disease                        | 3518 (9.5)                  | 3518 (9.5)                |
| e Injury and poisoning                      | 2918 (7.8)                  | 2918 (7.8)                |
| Symptom-defined conditions                  |                             |                           |
| Genitourinary disease                       | 762 (2.0)                   | 762 (2.0)                 |
| Endocrine disease                           | 605 (1.6)                   | 605 (1.6)                 |
| Musculoskeletal disease                     | 598 (1.6)                   | 598 (1.6)                 |
| Mental disorder                             | 278 (0.8)                   | 278 (0.8)                 |
Neurological disease 304 (0.8) 304 (0.8)
Skin diseases 291 (0.8) 291 (0.8)
Tumor 254 (0.7) 254 (0.7)
Blood disease 76 (0.2) 76 (0.2)
Congenital anomalies 40 (0.1) 40 (0.1)
Disease of perinatal period 33 (0.1) 33 (0.1)
Pregnancy complications
Receiving surgery 15297 (41.1) 15297 (41.1)
Endotracheal intubation Complications in ICU
Septicemia 7338 (19.7) 7338 (19.7)
Pneumonia 2970 (8.0) 2970 (8.0)
Acute renal failure 1708 (4.6) 1708 (4.6)
Urinary tract infection 1681 (4.5) 1681 (4.5)
Stroke 1438 (3.9) 1438 (3.9)
Acute myocardial infarction 403 (1.1) 403 (1.1)
Pulmonary embolism 22 (0.1) 22 (0.1)

COPD = chronic obstructive pulmonary disease; ICU = intensive care unit

Table 2 Intensive care unit mortality in patients with and without liver cirrhosis

| Outcomes of ICU | No LC, % | LC, % | OR (95% CI)a |
|----------------|---------|-------|--------------|
| 30-day mortality | 10.9 | 15.9 | 1.60 (1.53 to 1.68) |
| ICU mortality | 12.9 | 17.2 | 1.44 (1.38 to 1.51) |
| One-year mortality | 17.3 | 22.1 | 1.40 (1.35 to 1.46) |
| Medical expenditure, USDb | 11366±8742 | 12008±9890 | p<0.0001 |
| Length of hospital stay, daysb | 8.6±29.6 | 8.3±29.2 | p=0.2174 |

CI = confidence interval; ICU = intensive care unit; OR = odds ratio.

aAdjusted all.covariates listed in Table 1

Table 3 Stratified analysis and effects of cirrhosis-related clinical indicators on 30-day mortality of ICU patients

| Pre-ICU characteristics within 2 years | 30-day mortality | n | Deaths | Mortality, % | OR (95%) |
|----------------------------------------|------------------|---|--------|-------------|---------|
| No LC | 1.00 (ref) | 37197 | 4046 | 10.9 | 1.48 (1.41) |
| LC without liver cancer | | 25758 | 3705 | 14.4 | |
| LC with liver cancer | | 11439 | 2190 | 19.2 | 1.85 (1.74) |
| LC with no HBV and HCV | | 22258 | 3366 | 15.1 | 1.55 (1.47) |
| LC with HBV or HCV | | 13573 | 2288 | 16.9 | 1.67 (1.55) |
| LC with HBV and HCV | | 1366 | 241 | 17.6 | 1.75 (1.55) |
| LC without ADS | | 34496 | 5450 | 15.8 | 1.59 (1.52) |
| LC with ADS | | 2701 | 445 | 16.5 | 1.82 (1.62) |
| LC without jaundice | | 33978 | 5171 | 15.2 | 1.54 (1.47) |
| LC with jaundice | | 3219 | 724 | 22.5 | 2.23 (2.03) |
| LC without ascites | | 26352 | 3332 | 12.6 | 1.30 (1.23) |
| LC with ascites | | 10845 | 2563 | 23.6 | 2.32 (2.15) |
| LC without GI | | 27652 | 4114 | 14.9 | 1.50 (1.43) |
| LC with GI hemorrhage | | 9545 | 1781 | 18.7 | 1.90 (1.76) |
| LC without hepatic coma | | 29252 | 4102 | 14.0 | 1.43 (1.37) |
| LC with hepatic coma | | 7945 | 1793 | 22.6 | 2.21 (2.07) |
| Admission | LC with 0 admission | LC with 1 admission | LC with 2 admissions | LC with 3 admissions | LC with ≥4 admissions |
|-----------|---------------------|---------------------|----------------------|----------------------|----------------------|
| hospital stay | 25677 | 3378 | 13.2 | 1.33 (1.26) | 2.16 (2.01) |
| | 6600 | 1411 | 21.4 | 2.14 (1.92) | 2.37 (2.03) |
| | 2449 | 521 | 21.3 | 2.30 (2.00) | 2.52 (2.22) |
| | 1059 | 248 | 23.4 | 2.97 (2.68) | 3.26 (2.98) |

| Days of hospital stay | LC with 0 days of hospital stay | LC with 1-9 days of hospital stay | LC with 10-19 days of hospital stay | LC with 20-29 days of hospital stay | LC with ≥30 days of hospital stay |
|-----------------------|---------------------------------|----------------------------------|-----------------------------------|----------------------------------|----------------------------------|
| Days of hospital stay | 25677 | 3378 | 13.2 | 1.33 (1.26) | 2.16 (2.01) |
| | 6600 | 1411 | 21.4 | 2.14 (1.92) | 2.37 (2.03) |
| | 2449 | 521 | 21.3 | 2.30 (2.00) | 2.52 (2.22) |
| | 1059 | 248 | 23.4 | 2.97 (2.68) | 3.26 (2.98) |

| Admission | LC with albumin supplement | LC without albumin supplement |
|-----------|-----------------------------|-------------------------------|
| admission | 13918 | 23279 |
| | 2755 | 3140 |
| | 19.8 | 13.5 |
| | 1.93 (1.83) | 1.40 (1.33) |

| Hospitalizations | LC with hospitalizations | LC without hospitalizations |
|------------------|--------------------------|-----------------------------|
| | 29983 | 7214 |
| | 5139 | 756 |
| | 17.1 | 10.5 |
| | 1.52 (1.46) | 0.91 (0.84) |

| Reasons for ICU admission | Digestive disease, no LC | Digestive disease, LC |
|---------------------------|--------------------------|-----------------------|
| | 10198 | 10198 |
| | 550 | 550 |
| | 5.4 | 1.00 (reference) |

| Disease | Respiratory disease, no LC | Respiratory disease, LC |
|---------|---------------------------|------------------------|
| | 4524 | 4524 |
| | 968 | 968 |
| | 21.8 | 1.24 (1.12) |

| Disease | Circulatory disease, no LC | Circulatory disease, LC |
|---------|---------------------------|------------------------|
| | 4385 | 4385 |
| | 384 | 384 |
| | 8.8 | 1.00 (reference) |

| Disease | Infectious disease, no LC | Infectious disease, LC |
|---------|---------------------------|------------------------|
| | 3518 | 3518 |
| | 983 | 983 |
| | 27.9 | 1.32 (1.15) |

| Disease | Endocrine disease, no LC | Endocrine disease, LC |
|---------|---------------------------|-----------------------|
| | 605 | 605 |
| | 17 | 17 |
| | 2.8 | 1.00 (reference) |

| Disease | Musculoskeletal disease, no LC | Musculoskeletal disease, LC |
|---------|-------------------------------|-----------------------------|
| | 598 | 598 |
| | 42 | 42 |
| | 7.0 | 3.49 (1.75) |

| Disease | Mental disorder, no LC | Mental disorder, LC |
|---------|------------------------|---------------------|
| | 278 | 278 |
| | 0 | 0 |
| | 0.0 | 1.00 (reference) |

| Disease | Neurlogical disease, no LC | Neurological disease, LC |
|---------|---------------------------|------------------------|
| | 304 | 304 |
| | 11 | 11 |
| | 3.6 | 1.00 (reference) |

| Disease | Skin disease, no LC | Skin disease, LC |
|---------|-------------------|-----------------|
| | 291 | 291 |
| | 7 | 7 |
| | 2.4 | 1.00 (reference) |
| Condition                        | LC   | No LC | OR   | CI  |
|---------------------------------|------|-------|------|-----|
| Skin disease, LC                | 291  | 8     | 2.8  | 1.23 (0.35-4.39) |
| Tumor, no LC                    | 254  | 2     | 0.8  | 1.00 (reference) |
| Tumor, LC                       | 254  | 5     | 2.0  | 3.33 (0.51-21.8) |
| Blood disease, no LC            | 76   | 5     | 6.6  | 1.00 (reference) |
| Blood disease, LC               | 76   | 3     | 4.0  | 0.38 (0.05-2.84) |
| Congenital anomalies, no LC     | 40   | 1     | 3.0  | 1.00 (reference) |
| Congenital anomalies, LC        | 40   | 0     | 0.0  | - |
| Disease of perinatal period, no LC | 33 | 1     | 3.0  | 1.00 (reference) |
| Disease of perinatal period, LC | 33   | 0     | 0.0  | - |
| Complications of pregnancy, no LC | 7   | 0     | 0.0  | 1.00 (reference) |
| Complications of pregnancy, LC  | 7    | 1     | 14.3 | - |
| 0 CCI score, no LC              | 10476| 1066  | 10.2 | 1.00 (reference) |
| 1 CCI score, no LC              | 1165 | 101   | 8.7  | 0.97 (0.77-1.21) |
| 2 CCI score, no LC              | 8899 | 731   | 8.2  | 1.00 (reference) |
| 3 CCI score, no LC              | 6656 | 818   | 12.3 | 1.38 (1.21-1.58) |
| 4 CCI score, no LC              | 6573 | 592   | 9.0  | 1.00 (reference) |
| 5 CCI score, no LC              | 5116 | 592   | 11.6 | 1.49 (1.31-1.69) |
| 6 CCI score, no LC              | 3897 | 355   | 9.1  | 1.00 (reference) |
| 7 CCI score, no LC              | 5478 | 760   | 13.9 | 1.45 (1.25-1.67) |
| 8 CCI score, no LC              | 1823 | 209   | 11.5 | 1.00 (reference) |
| 9 CCI score, no LC              | 7085 | 1325  | 18.7 | 1.40 (1.17-1.67) |
| ≥5 CCI score, no LC             | 5529 | 1093  | 19.8 | 1.00 (reference) |
| ≥5 CCI score, LC                | 11697| 2299  | 19.7 | 1.08 (0.99-1.18) |

ADS = alcohol dependence syndrome; CI = confidence interval; GI = gastrointestinal; HBV = hepatitis B virus; HCV = hepatitis C virus; ICU = intensive care unit; LC = liver cirrhosis; OR = odds ratio.

*aAdjusted all covariates listed in Table 1.

Supplementary Files

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