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## Increased risk of in-hospital mortality and non-ICU death in patients with cirrhosis after cardiac arrest

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### Keywords

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Rohit Loomba: study concept and design, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript, obtained funding, study supervision, approved final submission

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## Introduction

Liver cirrhosis is a growing problem with a sharp increase in number of deaths due to this from 676,000 in 1980 to over one million in 2013. In the United States alone there were 53,252 deaths attributable to liver cirrhosis in 2013 compared to 37,419 in 1980 [1-4]. Patients with decompensated cirrhosis are routinely admitted to the hospital and impact in-hospital mortality[5, 6]. However, there are limited data on the etiology and outcomes of inpatient cardiac arrest in cirrhotics. This study aims to provide novel data on the causes, underlying rhythms and survival after in-hospital cardiac arrest in patients with cirrhosis compared to those without cirrhosis at a large tertiary care center.

## Methods

This is a retrospective-prospective longitudinal study of 954 patients with in-hospital cardiac arrest at a large tertiary care hospital system between July 2005 and April 2016. A multi-disciplinary team reviewed all cardiac arrests, classified the etiologies, confirmed presenting rhythm and adjudicated the outcomes. Patients with diagnoses of cirrhosis in the electronic medical record were then selected out of the general cardiac arrest population for subgroup analysis. Thorough chart review for medical history, clinical presentation, and confirmation of cirrhosis via ultrasound and/or biopsy and underlying disease was completed.

## Statistical Analysis

Cardiopulmonary arrest etiology, prevalence of rhythms (shockable v. non-shockable) and patient characteristics were compared using either chi square or Fisher's exact tests for comparisons between categorical variables and independent samples t-test for mean differences between continuous variables. Using logistic regression models, un-adjusted and multivariable-adjusted odds ratio of in-hospital mortality after cardiac arrest was examined. All statistical analyses were performed using SAS 9.4 (Cary, NC, USA).

## Results

There were 954 patients (63.7% men, mean age 59.3 years  $\pm$ 16.8) with in-hospital, primary cardiac arrest events that occurred during the 11-year study period including 88 (9.2%) in patients with cirrhosis and 866 (90.8%) in patients without cirrhosis.

### Baseline Characteristics

Of patients who experienced an in-hospital cardiac arrest, patients with cirrhosis were younger than patients without cirrhosis ( $53.9 \pm 11.7$  vs.  $59.9 \pm 17.1$ ,  $p < 0.0001$ ). Patients with cirrhosis were more likely to experience a cardiac arrest in a non-intensive care unit (ICU) setting than patients without cirrhosis (78.4% v. 61.2%,  $p$ -value 0.0015) (Figure 1A). The distribution of sex, rhythm (shockable v. non-shockable), day of week, time of day and location of cardiac arrest (non-ICU v. ICU) was similar between both groups.

### Increased In-Hospital Mortality in Cirrhosis

In-hospital mortality after cardiac arrest was higher in patients with cirrhosis than those without cirrhosis (86.4% v. 64.3%,  $p < 0.0001$ ) (Figure 1B). Compared to those without

cirrhosis, the odds of in-hospital death after cardiac arrest among those with cirrhosis was 3.51 (95% CI, 1.88-6.56,  $p < 0.0001$ ). These results remained significant even after multivariable adjustment by age, sex, location, time, day and rhythm with an OR of 3.90 (CI 2.06-7.36,  $p < 0.0001$ ).

### Causes of Cardiac Arrest in Cirrhosis

In patients with cirrhosis the most common cause of cardiac arrest was circulatory failure including bleeding (25.0%) and sepsis (18.2%). Respiratory failure led to cardiac arrest in 37.5% of patients, followed by dysrhythmias such as primary ventricular fibrillation or vagal events, which led to cardiac arrest in 12.5% of patients. The etiology of cardiac arrest was more likely to be due to circulatory causes in patients with cirrhosis compared to patients without cirrhosis (46.6% v. 34.6%,  $p = 0.0275$ ).

### Discussion

Utilizing a well-characterized, consecutive cohort of patients with primary in-hospital cardiac arrest, here we report that patients with cirrhosis have significantly higher risk of mortality after in-hospital cardiac arrest than patients without cirrhosis. The main causes of in-hospital cardiac arrest in patients with cirrhosis include bleeding, sepsis, and respiratory failure, all of which are potentially preventable[7]. Furthermore, patients with cirrhosis are more likely to experience a cardiac arrest in a non-ICU setting than non-cirrhotic patients. These data suggest that patients with cirrhosis should have a lower threshold for transfer to the ICU especially in the setting of suspected bleeding, SIRS/sepsis, or respiratory distress. These data are novel and provocative and if validated may help us develop specific care pathways that continue to promote early recognition of deterioration, prompt resuscitation for bleeding, early initiation of antibiotics for sepsis, and early intubation in patients with cirrhosis to reduce in-hospital mortality due to liver disease. To our knowledge, ours is the first systemic study investigating the etiology of arrest and outcomes of in-hospital cardiac arrest in cirrhosis patients[8]. Additional research is needed to further examine the causes of in-hospital cardiac arrest and mortality in patients with cirrhosis and to identify potential areas of intervention.

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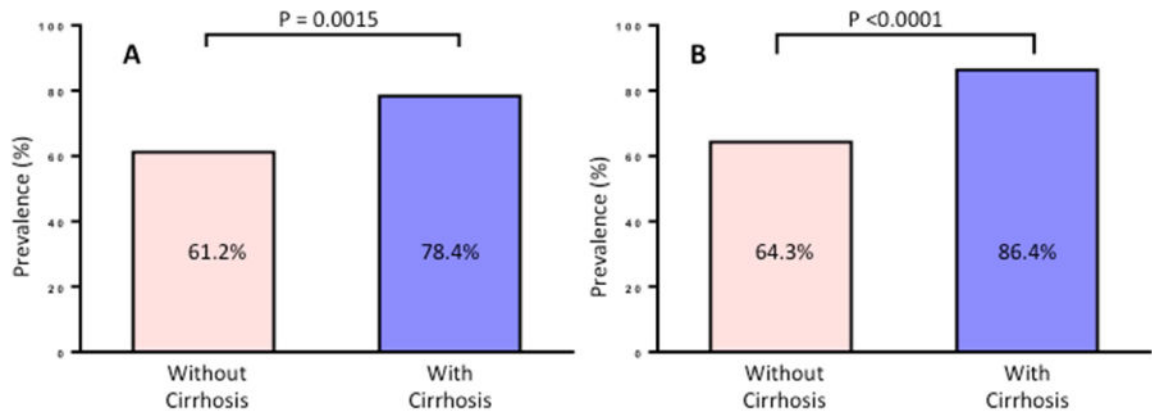
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## Abbreviations

ICU            intensive care unit



**Figure 1.**

(A) Prevalence of non-ICU cardiac arrest in patients with cirrhosis compared to patients without cirrhosis (B) Prevalence of in-hospital mortality after cardiac arrest in patients with cirrhosis compared to patients without cirrhosis.