

Reply to Editor in Chief:

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Column: Retrospective Cohort Study

Title: The effect of liver cirrhosis on long-term outcomes after acute respiratory failure: a population-based study

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Reviewer comments

The authors showed the mortality ratio of patients who required mechanical ventilation according to the presence or absence of liver cirrhosis (LC) by retrospective observational study. And they further stratified the mortality risk according to a cause of LC, and clarified it.

I have some comments about this article as follows.

Major

1. This article is consistent totally with phenomenology, and no causal relation has been shown at all. Although the authors described in Discussion that it is one of the limitation inherent in retrospective research, it is critical matter in this paper that what is the cause of each death and how the LC was related to them was utterly unknown. Further investigation about the cause of death were required.

Reply: This study is using the NHIRD database, which cannot provide the specific cause of death. Therefore, we can only investigate the all cause of death in this study. However, further investigation about the cause of death using other databank is required.

2. How about the mortality risk for patients with LCs due to major causes other than

viral infection like alcoholic or NASH?

Reply: We did agree with you. Alcoholic and NASH were the two major cause of LC. However, this study is using the NHIRD database, which cannot provide history of alcoholic using and the diagnosis of NASH. Therefore, we cannot make sure the diagnosis of alcoholic LC and analysis the effect of alcoholic LC.

3. Diagnostic criteria for liver cirrhosis is crucial issue, I think, in this paper, but it is ambiguous. The authors indicated that some of the diagnosis might be incorrect (page 13, line 10). This was a description that rocks the fundamental value of the article.

Reply: We mention this issue as possible limitations of claim data. However, the Taiwan NHI Bureau randomly reviews patient charts and interviews patients to verify the accuracy of the coding. Hospitals with outlier charges or practices might be audited and subsequently heavily penalized for malpractice or discrepancies. Therefore, the potential risk for bias based on coding practices can be minimized.

4. LC positive patients had more organ failures (page 9, line 3). Authors described there were no significant differences in mortality risk for patients with \geq two organ failures between LC positive patients and negative patients (page 9, line 11 and table 2). However, multiple organ failure itself is the definitive and direct risk of death. Authors' analysis about this area provokes a very uncomfortable feeling.

Reply: Although we found LC positive with MOF had higher risk of death than without MOF, the difference did not reach statistical significance. It may be due to the limited case number. Further larger scale study may be warranted to investigate this issue.

5. As for table 3, authors and we are not able to know whether the disease requiring a mechanical ventilator was affecting mortality of 5 or 10 years later. Then I think that it was meaningless to compare the survival rate with having LC or not.

Reply: We did agree with you and deleted table 3 accordingly. The differences regarding mortality between study groups were shown in first year and persistent in the following year (figure 2).

Minor

1. In figure 1, the item at the end described 'The risk of mortality was compared among groups' was unnecessary.

Reply: This sentence was deleted.

This is a study about liver failure and morbidities. I have some suggestions. 1- What is LHID2000 database?

Reply: Longitudinal Health Insurance Database 2000 (LHID2000) contains 1 million randomly selected NHI beneficiaries (about 4.34% of the total population) from the year 2000 Registry of Beneficiaries of the NHIRD that are representative of the demographic distribution of Taiwanese population. The LHID2000 provides data on outpatient and inpatient medical care, diagnoses, surgical procedures, and prescribed medications on a longitudinal cohort from 1996 to 2013.

2- "Several major complications, such as variceal bleeding, ascites, spontaneous bacterial peritonitis, hepatorenal syndrome....." 'major rectal-gastrointestinal bleeding and signs of lymphatic obstructions may also occur'

Reply: In this study, we focus on all cause of death. Therefore, we did not obtain the data regarding complications. However, further study should be warranted.

3- Why did you use SAS 9.4?

Reply: The reason we use the SAS 9.4 was our institution offer this powerful statistical software to clean and analyze data.