

## Peer Review File

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### Reviewer A

1. This is an article presenting the etiology of shock in Mainland China. Despite only enroll patients in tertiary hospitals, the case number is huge enough to help clinical physicians to comprehend the shock etiology.

#### **Response:**

Thank you very much for your comments. The aim of the article is to help clinical physicians to comprehend the shock etiology in China mainland.

**Changes in the text:** NA

2. The authors only use ICD-10 codes to analyze the cases. This cannot let the readers to see the detail data and true clinical condition of the patients. The category is too rough. For different clinical specialists, it provided limited information for the subsequent treatment. For example, the author analyzed the single shock and mixed shock. But that only reminds the readers that shock might be mixed. It did not provide any information about when mixed shock should be impressed or how to differentiate mix shock.

#### **Response:**

Thank you very much for your comments. Our data came from the homepage. Because different hospitals across the country have inconsistent uniform names for the same diagnosis, the use of ICD-10 codes plays an important role in unifying these diagnoses. However, more detailed information cannot be retained, and more standards may be needed to unify related diagnostic term fields. This is a large amount of work that requires specialized expertise and is not done through the capabilities of a team of doctors. Our analysis is done by the ICU doctors to answer actual questions from clinicians. We think the classification of ICD-10 diagnosis can solve our problems. We can see a basic situation of shock to guide our clinical work. For example, the proportion of mixed shock is large. The data shows that the mortality and risk of mixed shock are very high. This reminds us that when dealing with clinical shock, we should emphasize the diagnosis of the cause, be alert to mixed shock, and not miss the diagnosis. In this way, more etiological prompts through this study can help doctors think more about the related types of shock, better identify mixed shock and carry out appropriate and timely treatment. We acknowledged the limitations of our study and discussed with medical record experts. In this revised

manuscript, we expanded the ICD code to explain the specific disease as clearly as possible. In each part, we presented to you in the form of supplementary materials.

**Changes in the text:**

Please see the and the relevant information in the results section (line 253-280).

Supplemental Table 3.1 Types of mixed shock

Supplemental Table 3.2 Different shock types combined with other shock

Supplemental Table 5.1 The concomitant disease in patients with septic shock

Supplemental Table 5.2 The concomitant disease in patients with cardiogenic shock

Supplemental Table 5.3 The concomitant disease in patients with hypovolemic shock

Supplemental Table 5.4 The concomitant disease in patients with obstructive shock

3. After reviewing the Figures and Tables, I think this article is of limited value. As a clinical physician, I did not see any novel finding which is helpful in clinical decision making or in specific treatment for different shock etiology. I think this article only provides the big data from China. I suggest this article should be categorized and submitted to journals of public health related, instead of general medicine journals.

**Response:**

Thank you very much for your comments.

I have expanded the analysis of these data as Q2. We think the information is of tremendous significance for optimizing the allocation of medical resources and reducing the mortality of patients with shock in China. Of course, we admit that this study has considerable limitations due to the data itself. However, this does not affect the significance of the data in this study to the clinicians, especially ICU doctors. This is convenient for the first time to make a clear judgment on the cause of the patient, which is very important. It is the same purpose that we need to publish pathogenic bacteria and drug susceptibility monitoring every year. Therefore, it is very necessary to understand the basic situation of shock patients. In addition, we have also added the further analysis of further classification of four shock-related frequency complication and shock severity were shown in the Supplemental Table 5 and Table 6.

**Changes in the text:**

Please see the and the relevant information in the results section (line 253-280).

Supplemental Table 3.1 Types of mixed shock

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Supplemental Table 5.4 The concomitant disease in patients with obstructive shock

Supplemental Table 6 Intervention of single types of shock

4. Frankly speaking, I did not suggest publication in ATM.

**Response:** Thank you very much for your decision. We strongly believe that different majors may have different needs for relevant information. For ICU and emergency departments, or doctors who are responsible for treating more critically ill patients, this information is the basic knowledge to be possessed. In addition, we have added a lot of new information to help professionals related to the epidemiological characteristics of shock in this version, .

**Changes in the text:** NA

## **Reviewer B**

In this original manuscript entitled, “Shock in China 2018 (SIC-study): a cross-sectional survey”, Su et al. present a timely epidemiological survey study using the Hospital Quality Monitoring System from the China. In over 289,428 patients with shock, they demonstrate that shock is associated with high fatality rate and higher utilization of healthcare costs. I have a few comments for the authors’ consideration.

Major comments:

1. “A total of 79,668,156 medical records were included in HQMS in 2018, from which a total of 289,428 patients with shock were identified.”

As authors have mentioned this study has following limitation “Chinese medical policies are different from those in foreign countries; many patients may be admitted to multiple hospitals multiple times, and the home page of the medical record cannot reflect each previous visit. In addition, all data were anonymously encrypted, and we were unable to determine if multiple analyses were performed on the same patient.” – Should this reflect no. of hospitalizations with shock rather than actual patient number that was identified.

**Response:** Thank you very much for your question. It is correct. So, we have discussed this point in the limitations. However, based on the relatively large number of patients in China, relatively few patients can be transferred. Therefore, the overall result will not be affected.

**Changes in the text:** Limitation section (line 404-406) “However, we speculated that the proportion of such patients is relatively small due to the China's large population base. Therefore, we calculated the cases number in this study.”

2. What is the sensitivity and specificity for the ICD codes used to define shock in this population? Often these patients have more than one form of shock (<https://pubmed.ncbi.nlm.nih.gov/33257304/>). Therefore, it is important to evaluate these patients for type of shock and the overlap.

**Response:** Thank you very much for question. In the study you mentioned that “Shock was cardiogenic in 65%, septic in 10% and mixed cardiogenic-septic in 15%.” However, our population included is the occurrence of shock for the entire hospitalized patient based on the shock classification of hemodynamics. There is a fundamental difference in the criteria for shock classification. In order to clarify the situation of mixed shock, we have divided all mixed shocks and provided the following table.

**Changes in the text:** We have added this information in the Supplementary Materials. (line 254-256)

Supplemental Table 3.1 Types of mixed shock

Supplemental Table 3.2 Different shock types combined with other shock

3. The shock severity is not assessed or presented in this study. For example, mechanical ventilation, acute organ failure, CRRT, mechanical circulatory support, etc. Also, the etiologies of shock are not delineated – cardiogenic shock from AMI has a different prognosis from ADHF. Similarly, hypovolemic shock from motor vehicle collision is different from diarrheal dehydration. This is very crucial and important to clarify.

**Response:** Thank you very much for question. The shock severity and etiologies of shock of different types of shock were provided as the supplemental tables as the following.

**Changes in the text:**

Please see the and the relevant information in the results section (line 253-280).

Supplemental Table 3.1 Types of mixed shock

Supplemental Table 3.2 Different shock types combined with other shock

Supplemental Table 5.1 The concomitant disease in patients with septic shock

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Supplemental Table 5.4 The concomitant disease in patients with obstructive shock

Supplemental Table 6 Intervention of single types of shock

4. Cardiogenic shock had the highest mortality rate (31.6%), compared to other types of shock?

Did the authors assess for variabilities in the use of advanced therapies for CS across the various hospitals to better understand why this patient cohort had high mortality? In addition, were there any cardiac related diagnoses in these patient cohort like Acute Myocardial Infarction.

**Response:** Thank you very much for your question. In the revised MS, we analyzed the reasons for the high mortality rate of cardiogenic shock from multiple angles and

levels. We have further analyzed death composition and death risk associated with cardiogenic shock itself (Supplemental Table 10), cardiogenic shock with septic shock (Supplemental Table 11). Similar to the above analysis results, it also shows that tumors are the most important risk factor for death in patients with cardiogenic shock.

**Changes in the text:**

I have added relevant information (line 314-319). “Cardiogenic shock had the highest mortality rate (31.6%), compared to other types of shock. We have further analyzed death composition and death risk associated with cardiogenic shock itself (Supplemental Table 10), cardiogenic shock with septic shock (Supplemental Table 11). Similar to the above analysis results, it also shows that tumors are the most important risk factor for death in patients with cardiogenic shock.”

5. “The top three mortality rates for patients with complications were as follows: septic shock: neoplasms (31.77%)> SSACL (28.41%)> DNS (28.38%); cardiogenic shock: neoplasms (45.68%)> DBDIM (38.03%)> DGS (36.78%); hypovolemic shock: neoplasms (28.57%)> DNS (25.47%)> SSACL (25.34%); and obstructive shock: PCP (45.45%)> neoplasms (33.33%)> SSACL (30.72%).”

In this study, authors report neoplasms to be major contributor to be mortality in Cardiogenic shock. This is subject to bias, as neoplasms in this patient cohort can be co-morbidity and can authors comment on cardiac etiologies (like H/o coronary artery disease, history of percutaneous coronary interventions)

**Response:** Thank you very much for your question. From the Q4, we confirmed Tumor is the chief culprit and the leading cause of death in cardiac shock. It shows that many patients with tumors finally died of cardiogenic shock.

**Changes in the text:** NA

6. In this large epidemiological survey from China, authors concluded patients with malignant tumors have poor prognosis in most types of shock.

Neoplasm occurrence can vary from geographic region to geographic region, and certainly different in foreign countries. Can authors report the types of underlying malignancies?

**Response:** Thank you very much for question. Tumors do not cause cardiogenic shock. Patients with tumors are at higher risk of death. In other words, if a shock patient has malignant tumors, the probability of death is higher than that of patients without tumors. The patient is high, which has nothing to do with the occurrence of shock, or which kind of shock occurs, but may be related to the poor basic physical condition of the tumor patient itself, or the older age. We want to say that early identification and adequate treatment of patients with malignant tumor is important.

**Changes in the text:** NA

#### Minor comments

1. In this article, we used patient medical records from 31 provinces and cities in mainland China in 2018 to explain the epidemiology of shock, mortality of shock, and identify factors that related to hospital death

Since authors only included tertiary hospitals in the analysis, I would specify this in the above sentence. In addition, can authors provide more details about location of these tertiary hospitals (Urban vs Rural).

**Response:** Thank you very much for question. We have added this information.

**Changes in the text:** “A total of 79,668,156 patients medical records from 1,064 tertiary hospitals (Urban 79.21% vs Rural 20.79%) were included in this study.”

Please line 172-174.

2. For the shock patients with other diagnoses (as shown in Figure 3 and Supplemental Table 5), patients with malignant tumors had the highest mortality rate (...%). Mortality value (%) is missing

**Response:** Thank you very much for question. We have revised the relevant parts.

**Changes in the text:** “For the shock patients’ cases with other diagnoses (as shown in Figure 3 and Supplemental Table 85), patients’ case with malignant tumors had the highest mortality rate”. Please line 283.