

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors presented a report on Identifying survival protective factors for chronic dialysis patients. The paper is well formulated, and is novel and provides insights into mesenteric ischemia associated with ESKD. However, there are minor changes identified, the author is requested to modify the script accordingly.

1) Authors with different affiliations should be properly identified.

Reply:

Thank you for the comment. We will add author contributions below to the manuscript.

"HH Hsu is the guarantor of the integrity of the entire study, designed the study, defined the intellectual content, participated in the literature search, and reviewed the manuscript; SK Liau performed the research, wrote the first draft, and analyzed the data; YJ Lin analyzed the data; and George Kuo, CY Chen, YA Lu, CC Lee, CC Hung, and YC Tian participated in the literature search and reviewed the manuscript. All authors read and approved the final manuscript."

2) There are repeated sentences, which are sounding awkward (We retrospectively evaluated 103 chronic dialysis patients who were surgically confirmed to have acute mesenteric ischemia in a tertiary medical center over a 14-year period.) this repeated a lot. It is better to use sample 1 and sample 2.

Reply:

Thank you for the comment. We will revise the sentences to the following:

"One hundred and three chronic dialysis patients with surgically confirmed acute mesenteric ischemia in a tertiary medical center over 14 years were retrospectively analyzed."

3) Second, since surgical risk is higher in chronic dialysis patients than in nondialysis patients, most physicians prefer aggressive medical treatment first, which may prolong the time of surgery delay. What do you mean by aggressive in this.

Reply:

Thank you for the comment. We will revise the sentences to the following:

“Second, since surgical risk is higher in chronic dialysis patients than in nondialysis patients, most physicians prefer to administer supportive treatment first, including gastrointestinal decompression, aggressive intravascular volume resuscitation, hemodynamic monitoring and support, correction of electrolyte abnormalities, pain control, and initiation of broad-spectrum antibiotics, which may prolong the time of surgery delay. “

4) Shock status, what does it mean by shock, what is its status.

Reply:

Thank you for the comment. We defined shock as using vasopressors or inotropes during hospitalization, such as norepinephrine, dopamine, or vasopressin. We will add this definition to the manuscript

5) Unclear explanation about the figures 1, 2, 3. The legend should be more informative.

Reply:

Thank you for the comments. We will add more information to the figure legend as below.

Figure 1. Kaplan–Meier plot for in-hospital survival with a surgery delay or less than or not less than 4.5 days

In patients with a surgery delay < 4.5 days, the 20-day discharge probability was 44.4%, whereas the discharge probability was 50% on day 22. For surgery delays \geq 4.5 days, the 20-day discharge probability was 14.9%, whereas the discharge probability was 50% on day 54.

Surgery delay was defined as the time from the onset of signs and symptoms of acute mesenteric ischemia to surgery.

Figure 2. Kaplan–Meier plot for in-hospital survival with bowel resection involving or not involving the colon

For resection not involving the colon, the 20-day discharge probability was 48.0%, whereas the discharge probability was 50% on day 21. For resection involving the colon, the 20-day discharge probability was 24.7%, whereas the discharge probability was 50% on day 36.

Figure 3. Kaplan–Meier plot for in-hospital survival with a total bowel resection length less than or not less than 110 cm

In patients with a total bowel resection length <110 cm, the 20-day discharge probability was 45.8%, whereas the discharge probability was 50% on day 21. In patients with a total bowel resection length ≥110 cm, the 20-day discharge probability was 20.1%, whereas the discharge probability was 50% on day 40.

6) The mortality rate in the patients with Heart failure, Atrial fibrillation, Hypertension, Chronic obstructive pulmonary disease is very high, what could be the reason? (In table 1)

Reply:

Thank you for the comment. The mortality rates of mesenteric ischemia in chronic dialysis patients with heart failure, atrial fibrillation, hypertension, or chronic obstructive pulmonary disease were 45.5%(5 of 11), 60.0%(3 of 5), 46.2%(30 of 65), 66.7%(2 of 3) respectively, which were comparable to the mortality rate of our whole study population, 46.6%(48 of 103). After both univariate and multivariate analysis, all of the above factors are not significantly associated with survival.

7) Why female patients' mortality rate is high? (In table 1)

Reply:

Thank you for the comment. The mortality rates of mesenteric ischemia in chronic dialysis patients among male or female were 41.0%(16 of 39) and 50.0%(32 of 64), respectively, which were comparable to the mortality rate of our whole study population, 46.6%. After both univariate and multivariate analysis, gender is not significantly associated with survival.

8) why peritoneal dialysis is killing more patients? (In table 1)

Reply:

Thank you for the comment. We discussed the issue about even higher mortality rate of mesenteric ischemia among PD than in HD patients in the 5th paragraph of the discussion.

Since the presentation of NOMI is similar to that of peritonitis, the presence of peritonitis may mask the condition, and the key to correct diagnosis is a high

index of suspicion in predisposed patients. The high mortality rate is a reflection of failure to recognize the syndrome at an earlier, treatable stage.

9) The table 2 needs more explanation about the governing factors.

Reply:

Thank you for the comments. We put the explanation about surgery delay in paragraph 2 of discussion, bowel resection site and resection length in paragraph 4 and 5 of discussion, CRP in paragraph 7 of discussion, WBC in paragraph 8 of discussion, shock in paragraph 9 of the discussion, potassium in paragraph 10 of discussion, and Ejection fraction in paragraph 11 of discussion.

10) Conclusions can be more elaborate.

Reply:

Thank you for the comment. We will revise or conclusions to below.

“Outcomes of acute mesenteric ischemia in chronic dialysis patients were poor, and only 53.3% of these patients survived the index hospitalization. A surgery delay less than 4.5 days, no shock during admission, bowel resection not involving the colon, and a total bowel resection length <110 cm were associated with better in-hospital survival. This study emphasizes that early diagnosis and prompt surgical intervention in chronic dialysis patients with acute mesenteric ischemia are beneficial.”

Overall the paper excellent and the work is appreciable.

Reply:

It is our pleasure to have your compliment. Thank you.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: An interesting and well-done study showing that surgery delay, no shock, no resection of the colon, total bowel resection length <110 cm, and lower neutrophil levels after 1 week of treatment predicted better outcomes in chronic dialysis patients with mesenteric ischemia. I think the conclusions of the study are of a remarkable interest for the scientific community.

Reply:

Thank you for the comment.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: Liau, S.K. and the co-authors have in this retrospective study, investigated the factors associated with the survival of chronic dialysis patients treated surgically for acute mesenteric ischemia. It is an interesting and valuable study performed on a group of patients with critical systemic disease of well-known high mortality. The authors have identified chronic dialysis patients with acute mesenteric ischemia identified/ diagnosed with laparotomy. They have evaluated the patients' demographics and comorbidities as a whole study population as well as compared the study patients based on the survival or non-survival. They have employed uni- and multi-variate analysis in the Cox proportional hazards models to analyse the significance of different factors on the in-hospital survival of the patients. The result of this study shows 46.6% in-hospital mortality. They have found surgical delay <4.5 days as a cut-off associated with better survival in a univariate analysis. Besides no shock, higher potassium level on hospital admission, no colon resection, and total bowel resection length <110 cm favouring survival. After 1 week of hospitalization, lower WBCs, lower Neutrophils, higher lymphocytes and lower CRP was associated with survival. Multivariate analysis higher potassium at admission, lower neutrophils 1 week after admission, no colon resection, and total bowel resection <110 cm were significantly associated with survival. It is a well written manuscript and also well structured with appropriate headings. The methods are clear and with acceptable statistical analysis. Results are also in accordance with the aims of the study and the predefined methods.

Limitations of the study as the authors themselves mentioned in the discussion section is the retrospective design of the study as well as the small number of patients in the groups to show significant difference for certain variables of interest. One important limitation is the **lack of information about the treatment of acute mesenteric ischemia**, ie., revascularization procedures before or after the intestinal resection. This information is of immense importance to understand the survival or non-survival of the patients in the study. Point wise comments and suggestion to the abstract and the manuscript is as follows: Criteria Checklist for peer-review

Reply:

Thank you for the comment. We will add paragraph below to discuss the

issue about the treatment of acute mesenteric ischemia in our study population.

“Tran et al. analyzed 212 patients undergoing surgery for acute mesenteric ischemia with a predominant etiology of embolism or in situ thrombosis and found that the time to revascularization was associated with predicted 30-day and all-cause 2-year mortality, total bowel resection length and postoperative short-bowel syndrome.[16] They emphasized that early and routine vascular surgery consultation and definitive revascularization may mitigate outcomes of patients suspected to have acute mesenteric ischemia. However, in the present study, all of our study population received bowel resection without documented revascularization procedures before or after intestinal resection. The reason for the lack of revascularization procedures may be that NOMI, rather than vascular occlusion, was the leading cause of acute mesenteric ischemia among the chronic dialysis patients.”

1 Title. Does the title reflect the main subject/hypothesis of the manuscript?

Yes

Reply:

Thank you for the comment.

2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes

Reply:

Thank you for the comment.

3 Key words. Do the key words reflect the focus of the manuscript?

4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes

Reply:

Thank you for the comment.

5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? Yes. However, the information about the **how the cut of of 4.5 days delay for surgery** was determined has to be mentioned in the methods section.

Reply:

Thank you for the comment. We will add the explanation below in to the method.

"We used the predictive model of classification and regression tree (CART) to define a cutoff value of 4.5 days for surgery delay and 110 cm for total bowel resection length."

6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? Yes, this study increases our knowledge about the development of a extremely lethal diagnosis of acute mesenteric ischemia in patients with chronic dialysis. We do not have enough publications about acute mesenteric ischemia in this population.

Reply:

Thank you for the comment.

7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? Yes

Reply:

Thank you for the comment.

8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? Figures and the tables are appropriate and self-explanatory.

Reply:

Thank you for the comment.

9 Biostatistics. Does the manuscript meet the requirements of biostatistics? Yes

Reply:

Thank you for the comment.

10 Units. Does the manuscript meet the requirements of use of SI units? Yes

Reply:

Thank you for the comment.

11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? Mostly

Reply:

Thank you for the comment. By using RCA database, we added some recent publication concerning this topic to our article.

- Seong-2018- The Relationship between Intradialytic Hypotension and Hospitalized Mesenteric Ischemia A Case-Control Study
- Sumbal-2022- Predictors of Mortality in Acute Mesenteric Ischemia: A Systematic Review and Meta-Analysis
- Toda -2022- Prognostic factors for the successful conservative management of nonocclusive mesenteric ischemia
- Tran -2022-Hospital-based delays to revascularization increase risk of postoperative mortality and short bowel syndrome in acute mesenteric ischemia

12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? Well written manuscript with understandable language and grammar.

Reply:

Thank you for the comment.

13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? The authors have mentioned in the manuscript that it is a retrospective study.

Reply:

Thank you for the comment.

14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics

documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? Yes

Reply:

Thank you for the comment.