

April 4, 2016

Ze-Mao Gong  
Science Editor, Editorial Office  
*Baishideng Publishing Group Inc*  
*World Journal of Gastroenterology*

RE: Manuscript Number 24990

Title: Post-Discharge Complications after Esophagectomy Account for High Readmission Rates

Authors: Sophia Y. Chen, Daniela Molena, Miloslawa Stem, Benedetto Mungo, Anne O. Lidor

Dear Dr. Gong,

Thank you very much for the opportunity to revise our manuscript and for your interest in publishing this work in *World Journal of Gastroenterology*. We have responded to your questions raised in the manuscript below. We have also responded directly to all points raised by the peer-reviewers (reviewers' comments in *italic*, followed by our response in **bold**). Please find attached a copy of the revised manuscript with changes highlighted.

Sincerely,

Daniela Molena, MD

### Editor Comments

*You need to provide the grant application form(s) or certificate of funding agency for every grant, or we will delete it.*

**Thank you for this comment. The support provided by Mr. Edwin Lewis is not a grant/funding agency but rather a generous patient's gift, so no documentation is available. We would like to acknowledge his support in the Acknowledgments section.**

*In order to attract readers to read your full-text article, we request that the author make an audio file describing your final core tip. It is necessary for final acceptance. Please refer to Instruction to authors on our website or attached Format for detailed information.*

**Thank you for this comment. We have created an Audio Core Tip and included it in this submission.**

*Don't forget to submit some files in your revised manuscript [Conflict-of-Interest Statement, Institutional review board statement, Biostatistics statement, Informed consent statement, Data sharing statement, Copyright (need signature of all authors in order) (.pdf)] and Audio core tip (.mp3).*

**Thank you for this reminder. We have submitted the files described above.**

*Abbreviations and acronyms are often defined the first time they are used within the main text and then used throughout the remainder of the manuscript. Please consider adhering to this convention.*

**Thank you for this comment. We have adhered to this convention.**

*Need to correct references.*

**Thank you for this comment. We have corrected the references.**

### Reviewer 03547495 Comments

Classification: Grade C – Good

Language Evaluation: Grade A – Priority publishing

Conclusion: Accept

*Huge sample, clear presentation and analysis, interesting discussion*

**Thank you very much. We appreciate your kind words.**

#### Reviewer 00503565 Comments

Classification: Grade B: Very good

Language Evaluation: Grade A – Priority publishing

Conclusion: High priority for publication

*The authors identify rates of post-discharge complications, associated risk factors, and their influence on early hospital outcomes after esophagectomy. This reviewer recognizes the interesting and priority in this paper.*

**Thank you very much. We appreciate your kind words.**

#### Reviewer 03509021 Comments

Classification: Grade C: Good

Language Evaluation: Grade B – Minor language polishing

Conclusion: Minor revision

*In the abstract and under the Study Population heading, the operative approaches are listed as “transhiatal, Ivor-Lewis, 3-field, and conduit”. Please define the specific types of esophagectomies in terms of their anatomic location especially as the term “transthoracic” is used later in the paper. Also please include your definition of “conduit”.*

**Thank you for your comment. We precisely defined the 3 groups in the methods session.**

*The authors note that PDC occurred less frequently in patients who had pre-discharge complications and prolonged length of stay (LOS). This seems self-evident as the NSQIP database only includes patient data up to 30 days post-operatively. Thus in those with pre-discharge complications or longer LOS, there was less time to develop a PDC within the time period these patients were followed. It is not apparent to this reviewer that there is any biological significance to shorter LOS resulting in increased PDC (may be more related to increased time at risk). Can the authors comment?*

**Yes, you are correct, and we have deleted all comments to this regard. Since the median LOS for patients who had a pre-discharge complication was 14 days, it is not fair to state that staying in the hospital longer decrease the rate of PDC; it is more likely that we do not have a long enough follow-up to comment on this. We have included this in the limitations, and we decided to keep this group to compare patients’ demographics.**

*Do the authors have data pertaining to readmission beyond the 30-day period?*

**No, unfortunately patients are followed only for 30 days in the NSQIP database. This is indicated in the limitations section.**

*How many patients were excluded from analysis?*

**First, we identified 4872 patients who underwent esophagectomy between 2005 and 2013. However, 389 (7.98%) patients were not discharged before the 30-day period and were excluded for this very reason. In addition, patients who experienced in-hospital mortality (n=104) were excluded from the univariate logistic regression analysis (Table 3), as these patients were never discharged and thus were not at risk of experiencing post-discharge complications. This was added to the manuscript.**

*Did the pattern of patients who experienced PDC differ from those who had pre-discharge complications?*

**Yes, it was interesting to note that the types of complications are different (more bleeding and sepsis in the pre-discharge group and more DVT and wound infection in the PDC group). The patient population is also different since pre-discharge complications were more common in black, ASA 2, emergency cases, and patients with smoking history and COPD. This is well highlighted in the manuscript.**

*Please include your definition of hospital re-admission: were they related to the primary surgery? Were all patients re-admitted to the hospital in which surgery was performed? Is it known if patients were re-admitted to other hospitals?*

**We used the NSQIP definition of readmission that was introduced in 2011 and defined as “readmission to the same or another hospital, for any reason, within 30 days of the principal surgical procedure.” The readmission has to be classified as an “inpatient” stay by the readmitting hospital, or reported by the patient/family as such. In our study, the readmission rate for patients operated between 2011 and 2013 (excluding patients with in-hospital mortality) was 12.80% (334/2610). One year later in 2012, NSQIP started collecting data on whether the readmission was likely related to the principle surgical procedure. There were 253 readmission (253/1989, 12.72%) between 2012 and 2013 and 83.79% (212/253) of these readmissions were related to the surgical procedure. This was added to the manuscript.**

#### Reviewer 02493497 Comments

Classification: Grade C: Good

Language Evaluation: Grade A – Priority publishing

Conclusion: Major revision

*This is a review of the ACS-NSQIP esophagectomy database, meant to identify post-discharge complications. This is without doubt an important topic deserving of evaluation. That said, I have some concerns about the methodology and about the authors’ conclusions. I have the following questions and comments.*

**We thank the reviewer for their thoughtful consideration. We will be happy to address these questions and comments.**

*Is this even the correct database to use to answer the question? It includes followup only to 30 days after operation (not discharge). As such, it may miss a substantial number of post discharge complications (PDC), particularly in those patients with prolonged hospital stays. This may lead to underrepresentation of PDC in patients with pre-discharge complications whose median LOS was 15 days. This is particularly true given that the average time to PDC was 14 days. Should we therefore even try to meaningfully compare groups here? I think it would be better to just focus on incidence and predictors of early PDC and spent less time splitting and comparing groups 1-3.*

**We agree that this database is probably not the best to look at the entire group of patients, and the PDC rate in patients who had a pre-discharge complication is probably underestimated. We deleted all comments in regards to PDC in the pre-discharge complications group, but we decided to keep the 3 groups to look at differences in demographics and types of complications.**

*For procedures, I don't like the descriptors of "3-field" or "conduit". 3-field refers to the pattern of lymphadenectomy rather than the number of incisions. I assume the authors mean 3-hole esophagectomy and do not have data on lymph node fields dissected. Conduit is vague and should be defined. Presumably this refers to colon or jejunal interpositions. It would be helpful to clarify these and put totals in table 1, as it is highly relevant to surgeons.*

**Yes, we agree and better defined the groups in the Method section.**

*It seems odd to set the study up by defining three groups dependent upon PDC and then go on to say that PDC is the primary outcome (Methods). Again, it is fine to have PDC as primary outcome, but by setting up those groups a priori based upon that variable, you inherently bias the results.*

**We actually divided the entire population in 3 groups to have more homogeneous patients to compare. Combining patients with pre-discharge and post-discharge complications would bias our results even more since we were interested at looking at patients who had an uneventful postoperative course and then had a complication after discharge. We believed (and our study confirms this) that patients who had complications while in the hospital have longer hospital stays and are often not discharged to home.**

*Regarding "CORE TIP", I disagree that "evidence" is provided to implement strategies to decrease PDC. Rather I would emphasize the high rate of PDC and their nature.*

**Thank you for the suggestion, we have changed it.**

*Mortality rates are overestimated (ref 5-6) compared to several national databases which put rates at 3-6% (see review of STS/NSQIP/NIS in J Thorac Cardiovasc Surg. 2012 Nov; 144(5): 1152-7). For Table 1, it would be more intuitive and helpful to put PDC rates in aggregate after specific demographic and clinical characteristics, rather than splitting it by group. You could include pre-discharge complications on the y-axis and list rates of PDC in these settings.*

**The overall mortality rate was 3.12%. The 7.05% mortality rate presented in Table 2 is only for patients who experienced complications. The explanation was provided in the footnote of this table.**

*The observation that pre- and post discharge complications differ by type (Figure 2) is critical and should be the central message of this manuscript. This is the most helpful information along with time to PDC which can be used by treating physicians to predict and identify problems in these patients.*

*The statistical analysis is weak. Looking only at the univariate analysis, should we infer that we should keep our patients longer and encourage pre-discharge complications in order to prevent PDC? That would seem to be the message, but it obviously convoluted by inherent differences in these patients not brought forth in a univariate analysis. A multivariable analysis should be performed to look for independent associations with PDC. Effort should be made to account for collinear variables such as complications and length of stay, and distinct MVA models used.*

**Thank you for the suggestion. We have changed the central message of the manuscript.**

*I disagree that “reducing hospital stay should be approached warily as it may contribute to adverse health outcomes”. The data does not support this. It should be remembered that the limitation of 30 day data strongly biases the study to find post discharge problems in patients discharged earlier. I doubt this relationship would hold up with more granular data.*

**Yes, we agree and have changed the message of the study.**