Peer review file

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Reviewer A

The authors describe rates, patient factors, institutional factors, specific reasons and outcome in a cohort of patients undergoing esophagectomy and requiring early or intermediate-term readmission over two years as captured in the National Readmissions Database. They identify separate patterns for the two intervals of readmission diagnosis and risk factors. They conclude that specific interventions may exist to lower readmission for each interval.

The manuscript is well written, provides clear descriptions of the issues relevant to the topic and is equally clear on the limitations pertaining to this specific database.

Comments:

Comment #1:
The authors describe the early and intermediate readmissions group as completely separate and without overlap. Do they confirm there were no patients who belonged to both groups?
Reply #1: Thank you for your question. We did confirm that there were no patients who belonged to both groups. The National Readmissions Data Base tracks each hospital admission independently using unique IDs for each patient. To calculate the days until readmission, we calculated the difference between the index admission and the next closest admission. We used this value to classify them into the three appropriate groups: no readmission, short-term readmission, and intermediate-term readmission.
Changes Made: No changes made.

Comment #2:
Line 190 Prevention ... prevented - check style.

Reply #2: We thank the reviewer for catching this typo. The appropriate change will be made.

Changes made: We have revised the sentence (see Page 10 line 219).

Comment #3:

Readmission may have been limited to 23 hour observation; this status is relevant because of the large group of patients with gastrointestinal obstruction some of whom may have undergone endoscopic dilatation. Does the NRD regard observation as distinct from readmission?

Reply #3: We appreciate the reviewer's question. The NRD does regard observation as distinct from readmission. We included patients in the readmission groups (short- and intermediate-term) if they had a separate hospital admission distinct from the initial admission. This is tracked using the patient's unique ID number.

Changes Made: No changes made.

Comment #4:

Table 2 To what comorbidity does pulmonary circulation refer?

Reply #4: Thank you for pointing this out. "Pulmonary circulation" refers to pulmonary circulation disorders. Unfortunately, the National Readmissions Database does not provide any further granularity.

Reviewer A Changes made: We added the word 'disorder' to Table 2 after 'pulmonary circulation' (see page 17 table 2).

Comment #5:

Supplemental Table 1:

1. What type of esophagectomy is referenced by "esophagoesophagostomy"? How certain are the authors that esophagectomy occurred in these patients?

Reply #5: We appreciate the reviewer's question. The "esophagoesophagostomy" refers to an anastomosis between two portions of the esophagus without the use of a conduit. The coding for esophagoesophagostomy was considered as an esophagectomy based off of previous work by Molena et al. (J Gastrointest Surg (2014) 18:310–317).

Changes made: no changes made.

Comment #6:

2. What does antesternal anastomosis of esophagus mean? An extrathoracic conduit?

Reply #6: Antesternal anastomosis refers to the anastomosis being made superior to the sternum. The use of an extrathoracic conduit is dependent on the approach as listed in Supplemental Table 1.

Changes made: no changes made.

Reviewer B

Comment #1:

Dear Author thank you very much for your manuscript. Indeed, this is very interesting and important topic. However, the data presented is not new. Unfortunately, the limitations of the data base as presented from your discussion are too wide and significant.

Reply #1: We thank the reviewer for their comment, and we acknowledge the limitations in the study. However, we believe that this study provides information into the post-operative complications associated with esophagectomy and may provide guidance to perioperative clinical decision making.

Reviewer C

Comment #1:

1) you chose to use ICD9, can you explain why? In the introduction, you suggest that modern studies are lacking, yet use an 8 year old database. What was it about ICD10 that makes using 2017 (for example) not palatable? (Side note: I prefer ICD9 as I think its easier, but appreciate that ICD10 includes useful granularity)

Replly #1: We appreciate the reviewer's point. The reason we chose to focus on data from 2013-2014, as the reviewer alluded to, is because of the use of ICD-9 codes. For the year 2015, a combination of ICD-9 and ICD-10 procedural codes are used in the National Readmissions Database. We decided not to include year 2015 due to

potential coding problems with the combination of ICD-9 and ICD-10 procedural codes. Starting in 2016, only ICD-10 codes were used. However, we decided to focus on ICD-9 procedural codes due to the familiarity of these codes when compared to the ICD-10 procedural codes.

Changes Made: no changes were made

Comment #2:

2) Your 30-day readmission rate is higher than the majority of the cited literature (as you point out). How do you justify the difference or what factors do you hypothesize underlie this difference? I think this is interesting and important to consider. 30% 90-day readmission is VERY high and problematic. I think some discussion about this should be central to your discussion rather than just a passing statement.

Replly #2: We thank the reviewer for the question. The database used in this study utilizes data captured by the Healthcare Cost and Utilization Project while other studies utilize data represented by organizations such as the American College of Surgeons. This may cause variability between the hospitals represented. Although we are unable to definitively determine the cause for this discrepancy, we suspect the difference may be attributed to factors such as hospital volume and surgeon experience. In a recent study published by Gregory et al. (*J Gastrointest Surg (2014) 18:310–317*), surgical experience was demonstrated to have a positive correlation with surgical outcomes. We have expanded on this possibility in our discussion section.

Changes made: we have expanded on the discussion section to include suspected reasons for the discrepancy (see page 9 line 205).

Comment #3:

3)You mention longer hospitalization and discharge to a non-home location as being predictors of readmission. Did you examine whether readmission was related to complications which occurred during the "index" admission?

Replly #3: Thank you for your question. Unfortunately, this is a limitation of the NRD. There is no way of determining what complications might have developed during the “index” admission. We will add this to our limitations.

Changes made: we have added to our limitations section in the discussion (see page

11 line 245).

Comment #4:

4) You point to post-operative infection as the most common cause of readmission. my "guess" is that many of these patients have organ space SSI, ie leak. Were there other factors associated with this, such as anastomosis location, etc? If leak really is driving the readmissions, can you offer any suggestions about meds to determine if leak is "ruled out" prior to discharge?

Replly #4: We appreciate the reviewer's comment. We used the ICD-9 diagnosis codes to determine the cause of readmission. The ICD-9 codes do not include any description or detail regarding factors such as anastomosis location. Additionally, the NRD does not provide any information regarding whether or not a leak was ruled out prior to discharge.

Changes made: No changes were made

Comment #5:

5) In your limitations section, your first and third points are the same (ie was the resection for benign vs malignant disease). Its an interesting point, but do you have any data that suggests these cohorts are different?

Replly #5: We thank the reviewer for your comment. The redundancy in the limitations section and the third point was changed to highlight a different limitation. We do not have any data to suggest that these cohorts are different. However, it is possible that patients with malignant disease may have higher rates of complication if they undergo neoadjuvant chemoradiation therapy when compared to patients with benign disease.

Changes made: the redundancy in the limitations section was changed to reflect a new limitation (see page 11 line 245).

Comment #6:

6) you report "Transfer or same day stay, No. (%)" in table 3, but I have no idea what this means. The data seems very granular and not meaningful. Can you explain what this means and why it is included?

Replly #6: We greatly appreciate the reviewer's opinion. With the reviewers input and

further discussion with our group, we decided to remove this portion of the data ("Transfer or same day stay"). This variable was meant to help capture if there were any transfers or multiple discharges from the hospital but we believe that this might confuse readers and does not offer great clinical insight.
Changes made: we have removed this portion of the data from Table 3.

Comment #7:
7) you have included a small number of patients with retrosternal conduit and colon interposition. This is (presumably) a higher risk group. Can you justify including them in this study? Certainly that would effect generalizability?
Replly #7: We thank the reviewer for their question. We agree that this group of patients who received an Antesternal conduit with colon interposition is a higher risk group. However, we based the patients included for esophagectomy on previous studies (Molena et al.).
Changes made: no changes were made

Comment #8:
8) you show that some specific diagnoses (for example COPD) are associated with readmission, but don't include those in your MV model. Why is that?
Replly #8: We greatly appreciate the reviewers question. We agree that it would be beneficial to include the comorbidities into the study. However, due to the small patient size (more specifically, the patients with comorbidities), when we tried running the model with the comorbidities it provided inaccurate MV modelling.
Changes made: no changes were made

Comment #9:
9) You suggest "the use of earlier follow-ups as a means to detect post-operative complications sooner". among the "early" readmission group, what was the mean/median time to readmission? What does that say about the ability to intervene? If follow-up is the answer, why so many "late" readmissions? what is to be done about this group?
Replly #9: Thank you for the question. The mean days to readmission for the short-term group was 10.8 days while the median was 9 days. These dates are similar to

those of previous studies (Bhagat et al. Ann Thorac Surg. 2018;105(5):1476-82.). The complications mentioned in that study are similar to complications mentioned in this study (e.g., infection, pulmonary, gastrointestinal). Follow-ups shortly after discharge could help reduce emergent complications such as post-operative infection. With regards to late-readmission, gastrointestinal stricture/dysphagia is one of the common causes of readmission. This may be due to anastomotic strictures forming and creating longer-term morbidity for the patient. In a study by Tanaka et al. (Surg Today. 2018 Apr;48(4):449-454), patients develop anastomotic strictures approximately 108 days after surgery.

Changes made: no changes were made

Comment #10:

10) With 30% readmission rates nationally, I'd expect that there are difference in rates of readmission between centers. Could you use your model to generate an observed: expected model to demonstrate differences in readmission? (this is a big ask, I realize that the statistics will be difficult and this is not meant to preclude my recommendation for acceptance if other revisions are done) I think these differences might be meaningful when discussing surgical quality.

Replly #10: We greatly appreciate the reviewer's insight and also believe that would be a very interesting model. However, we do not currently have the statistical abilities to perform this analysis.

Changes made: no changes made

Comment #11:

11) did you adjust the regression using the weighting variable in the supplied by the the NRD?

Replly #11: We appreciate the reviewer's question. We did not adjust the regression using the weighting variable. With the recommendation of the other reviewers, we decided to change the premise of the study from a national study to a population-based study.

Changes made: we reframed the study to be a population-based study throughout the manuscript

Reviewer D

Comment #1:

1) Title: I feel the word national is misleading. The NRD database covers less than 60% of US population. Therefore, the database is not similar to many real national databases such as those from Nordic countries. The NRD covers 27 states. If the coverage is high in those states, you might call this a population-based…

Reply #1: We thank the reviewer for their opinion. After careful consideration, we have reframed the study (and the title) to be a population-based study instead of a national study.

Changes made: we have reframed the study to be considered a population-based study throughout the manuscript.

Comment #2:

2) The definition for short-term vs intermediate term readmissions: What is the clinical significance to differentiate readmissions within 30 days and 31 to 90 days? Nowadays, postoperative mortality in major surgery should state 90-d mortality rates and, similarly, this period, in my mind, is short-term or early postoperative period. A real intermediate period would be 3 to 6 months or even up to 1 year.

Reply #2: We thank the reviewer for your question. The reason we split up the grouping into 1-30 days and 31-90 days is because of the Healthcare Readmissions Reduction Program that penalizes hospitals for readmissions within 30 days. We wanted to provide granular data regarding readmissions between 1-30 days to hopefully provide clinicians information about methods to reduce the readmissions in the short-term to ultimately reduce the penalties levied by the Affordable Care Act.

Changes made: We have included further detail about the significance of identifying short-term readmissions (see page 4 line 90).

Comment #3:

3) Conclusions in Abstact and in Discussion: “Gastrointestinal stricture and dysphagia were ….. in the context of morbidity associated with pyloric procedures…” I don’t quite understand this. Do the authors suggest that pyloric procedures cause strictures

and dysphagia?? Where is the data to support this suggestion? The major cause for postoperative dysphagia is an anastomotic stricture. The rate of strictures at the population-level is well-stated in a recent study (BJS Open. 2019;3:634-640). According to this study, “Most strictures occurred during the first 6 months of surgery.”

Reply #3: We thank the reviewer for their comment. Pyloric procedures, such as pyloromyotomy, are sometimes performed with esophagectomy to help increase drainage. Patients should be considered for additional procedures such as pyloric procedures to help with drainage.

Changes made: we have changed the discussion in the abstract to include pyloric procedures performed with esophagectomy (see page 3 line 80).

Comment #4:

4) Study design: Why have you excluded patients with a previous history of cancer in this study of early outcomes after esophagectomy? “Due to the frailty of cancer survivors” as a cause for an exclusion after esophagectomy sounds a little odd. These patients have just tolerated major surgery!?

Reply #4: Thank you for your question. To clarify, we excluded patients with a history of cancer prior to the esophagectomy. Unfortunately, due to limitations of the NRD, we are unable to discern what kind of cancer and treatment they received. We believed that with certain treatments, such as chemoradiation, patients are at an increased likelihood of being readmitted and therefore would confound the data.

Changes made: no changes were made

Comment #5:

5) A missing variable:

a. open vs minimally invasive esophagectomy -this data would be highly interesting.

b. Indication for esophagectomy? Cancer is the most common indication but there are benign cases, as well. I would recommend to concentrate on cancer cases only.

Reply #5: We thank the reviewer for their comment. Unfortunately, the NRD does not provide specific information about whether an open vs minimally invasive approach was used. We agree this would be interesting. Additionally, the NRD does not provide any information about why surgery was indicated as discussed in our limitations

section.

Changes made: no changes were made

Comment #6:

6) Anastomotic technique/supplemental Table 1: This table does not describe the anastomotic technique (hand-sewn/stapled -linear or circular). It describes partly the level of anastomosis and the conduit. For the anastomotic stricture formation, the level of anastomosis (neck or chest) and the actual technique would be important to known.

Reply #6: We greatly appreciate the reviewer's recommendation. However, because the NRD uses ICD-9 procedural codes, instead of CPT codes, there is no information about the actual technique used.

Changes made: no changes were made

Comment #7:

7) Have you any data of actual center volumes?

Reply #7: Thank you for this question. Unfortunately, the NRD does not include data specifically on actual center volumes.

Changes made: no changes were made