Author's response to reviews

Title: Systematic Review of Surgical Treatment Techniques for Adult and Pediatric Patients with Pectus Excavatum

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Author's response to reviews: see over
Author’s Response to Reviewers

Title: A Systematic Review of Pediatric versus Adult Patients in Current Pectus Excavatum Treatments

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Author’s Response to Reviews: See over

Thank you for consideration of our manuscript for publication in Journal of Cardiothoracic Surgery. We have reviewed the above manuscript according to your reviewers comments.

Reviewer # 1 (A Protopapas)

MAJOR REVISIONS:

1. The follow up needs to be completed after the removal of bars, otherwise the patients with incomplete procedures (e.g. Nuss bars in situ) should be excluded from the data.
   a. We agree that it would be ideal if there was less variability in the length of follow-up among patient cohorts and, more specifically, if the bar removals had been completed before several of the included studies were published. Therefore, we added the following statement to the last paragraph of the discussion: “Additionally, the follow-up time was minimal in some included investigations, which may underrepresent the long-term complications, outcomes, and reoperations; however, these provided significant information for the majority of the outcome measures assessed (operation duration, analgesia duration, blood loss, and length of stay).” Nevertheless, we do not believe that data from the studies with short-term follow-up should be excluded because operation duration, analgesia duration, blood loss, and length of stay (the majority of our outcome measures) can all be adequately examined with short-term follow-up.

2. The comparison of outcomes needs to be by p-values.
   a. We appreciate and anticipated this suggestion, recognizing that p-values are the currency for scientific comparison. In our investigation, we determined that reporting p-values would overreach the data available to us because we only had access to the published data, rather than the raw data. Nevertheless, in keeping with the statistical basis of p-values, we adopted an approach utilizing the means and ranges of the reported data to allow readers to make reliable statistical conclusions without overreaching the boundaries of the reported data. The result is a carefully designed semi-qualitative statistical approach to facilitate a systematic quantitative discussion. The explanation behind the descriptions (e.g. similarity, tendency, slight difference, and clear difference) is
enumerated in the final paragraph of the methods section. We believe that this approach clearly communicates the differences and similarities among the cohorts, while accentuating the need for more information and investigation.

3. The timing of pectus repair is a complex decision that needs to be discussed at depth should the conclusions include guidance on optimum age for MIRPE etc.
   a. We agree. The esteemed reviewer clearly identifies one of the central goals of our investigation, helping to guide surgeons’ decisions about when to repair PEx. The complexity of the decision, especially with respect to age, is one of the factors that motivated this investigation. We make significant strides toward answering this question, but realize that there is insufficient information in the scientific information to completely answer the question. To that end, we hope that this investigation will allow investigators to identify the gaps in the literature and provide motivation to fill those holes. To that end, the investigation identifies “there is no clear difference in outcome rating between the Nuss and Ravitch populations across age groups....” Therefore, the biggest take away is that “...completely asymptomatic PEx patients do not need to undergo operative treatment at an earlier age in order to achieve a better outcome,” as stated in the opening sentence of the conclusion. As previously mentioned, we recognize that this does not completely clarify when to operate/repair PEx, but it does start to answer the question by identifying when not to operate/repair.

4. I have not done a Ravitch for a couple of years, yet I find difficult to understand the concept of bar displacement in Ravitch.
   a. This may be confusing. As a result, we added emphasis to the difference at first mention in the methods section stating, “Note that pectus bars are used in Nuss procedures and substernal struts are used in some Ravitch procedures.” In addition, we reviewed all uses of “bar” and “strut” to ensure that they were properly paired with Nuss and Ravitch procedures respectively. The Adkins strut is the commonly used piece of equipment in the Ravitch procedure. The reference below provides some description of one way that the strut is used in a modified Ravitch procedure.

5. Similarly, the 8% pneumothorax incidence in Nuss is possibly underdiagnosis especially where endoscopic capnothoraces are utilised. The esteemed authors need to define the recording of pneumothorax is a robust fashion: clinical, radiological, etc.
   a. This is an excellent point. Unfortunately, our discussion of the data is only as strong as the previously reported data. The definition of pneumothorax is not clear, as it should be, in the collected data from the published literature. As a result, we cannot further define it.
6. Overall the esteemed authors need to rethink the manuscript and the message. The pigeon holing of three names masks a whole spectrum of operations that need to be discussed in detail. Any speculation has to be removed and only data supported by robust metanalytic stats should be included.
   a. Certainly such a topic as tackled here, comparing four major groups (pediatric Nuss, Adult Nuss, pediatric Ravitch, and adult Ravitch), may be addressed in a variety of ways. In fact, as the reviewer thoughtfully points out, each of these groups really represents a spectrum of both operations and patients, which may be suitable to four entirely separate investigations. However, in order to begin answering the questions about when and how to operate on patients with PEx, it is necessary to categorize for comparison sake. We carefully selected this categorization based on these questions and the available literature, so that we formulate a consolidated investigation to answer these complex questions and to identify the gaps in the publicized database.

Reviewer # 2 (Qi Zeng)

Discretionary Revisions:
1. Ravitch procedure has a long history, and this technology is much mature, Nuss surgery is relatively new technic, just about twenty years’ experience. Some of the indicators for compare, such as LOS, pending a long time follow-up and comparison of large sample. In our hospital, the average time to discharge was 4-5 days, less than 7.3 days.
   a. We agree. We comment on the variability of follow-up throughout the discussion and think that LOS is a reasonable marker for comparison given the lack of long-term follow-up. We suspect that with improving surgical technique, increased volume, and increased surgical expertise that the LOS following Nuss procedure will trend downward, as your hospital data suggests.

2. Some of the reference articles about Nuss surgery were not a large sample research. There will be some differences between the different research centers, such as surgical experiences, the data of length of stay, etc.
   a. We agree that the variation in the size of the studies is a limitation, as noted in final paragraph of the discussion section. Hopefully, we will continue to see more large-scale studies in the future.

3. Nuss procedure in the treatment of pectus excavatum has been a remarkable innovation. The statistical comparison in this article found that the difference between Nuss and Ravitch surgery was not significant, but from the perspective of the patient’s family or personal perspective on the aesthetic requirements, Nuss procedure has several advantages like smaller wound, more covert, less injury, etc., it should be better than Ravitch surgery.
   a. Good point. The patient satisfaction associated with smaller scars should favor the Nuss procedure. In discussion of limitations, we added statement, "We did not examine patient satisfaction, which theoretically may favor the Nuss procedures because of smaller
wounds/scars...” Interestingly, however, the meta-analysis by Nasr et al (2010) did not find difference in patient satisfaction.

4. **With the increase in the number of cases, and experience, Nuss procedure can be applied in complex, intractable, asymmetric cases, and also can achieve good postoperative results and long-term results.** In Beijing Children’s Hospital, we had completed 2431 cases of Nuss surgery with a good postoperative results. A paper about ten years of experience of Nuss surgery in our hospital is writing in process.
   a. This observation may also help to favor the Nuss procedure, but we did not find enough data to include a sub-analysis of these patients. We look forward to seeing your paper in the literature and using it to improve our practice.

**Reviewer # 3: Andre Hebra**

**Major Revisions:**

1. **The authors should consider changing the title from “A systematic Review of Pediatric versus Adult Patients in Current Pectus Excavatum Treatments” to Systematic review of surgical treatment techniques for adult and pediatric patients with pectus excavatum”**
   a. Done.

2. **In page 3, Introduction, the authors stated: “While PEx is often considered a purely cosmetic disorder, Kelly and colleagues reviewed autopsies and concluded that patients with PEx have a shorter life expectancy.” There have been several articles published that describe the cardiopulmonary impairment caused by pectus excavatum, particularly in pediatric patients. The authors should add a statement about such observations as they are already describing factors related to the indications for surgical treatment.**
   a. Added “Furthermore, severity of pectus excavatum is associated with reduced pulmonary function.” Referencing:

3. **Under Discussion: Authors should comment about the occurrence/reports of life-threatening complications and mortality of pectus surgery. Given the fact that there are few reports in the literature and that most are “case reports”, it is difficult to extrapolate any information related to such rare adverse outcomes.**
   a. In last line of paragraph 8 of discussion, on page 13, added “Nonetheless, there have been few reports of life-threatening complications in the literature.” Reference:


4. **Under Discussion:** (page 11) Authors make comments related to cost comparison. They mention that the “the need for greater length of stay and pain management suggest that the Nuss procedure is more expensive”. Should add a comment that the “greater operative time of the Ravitch approach may offset the added cost of the Nuss procedure” (However specific data is not provided) In the middle of paragraph 4 of the discussion, on page 11, added “However, we postulate that the longer operative time of the Ravitch procedure may offset some of the costs.”

5. **Under Conclusion (page 15):** “…In addition, as new procedures are developed, such as the vacuum bell and mini-magnetic mover, they need to be compared with the Ravitch and Nuss procedure, which have become the standard for PEx treatment.” Change to “…have become the accepted standard for PEx treatment.”
   a. Done.

   a. Hebra et al excluded because age of patient population was not described.
   b. Moss et al excluded because there was no treatment specific cohort, rather a small series of case reports. This was, however, added as a reference for discussion of complications.

**Minor Revisions:**
1. **In the abstract, the authors must clarify** “Excluding displacements, pediatric and adult Nuss Patients (38% and 21% respectively) tended to have higher complication rates compared to pediatric and adult Ravitch patients (12.5% and 8% respectively)”. What do the 38%, 21%, 12.5%, and 21% refer to? Consider re-writing the sentence to clarify.
   a. Revised to “Excluding pectus bar and strut displacements, pediatric and adult Nuss patients tended to have higher complication rates (pediatric - 38%; adult - 21%) compared to pediatric and adult Ravitch patients (12.5%; 8%).

2. **Page 4:** must correct the statement “…force required to elevated…” (change “elevated” to “elevate”)  
   a. Done.
3. Page 5: must correct the statement "...publications that described surgical techniques that different significantly from current techniques..." (change “different” to “differ”)  
   a. Done.

4. Page 5: The authors should clarify the meaning of “non-displacement” and “self-resolving” complications. What is included in each category?  
   a. Upon first mention of non-displacement and self-resolving (3rd paragraph of methods) added clarification: “…percentage of non-displacement complications (i.e. complications that did not involve bar or strut displacement), self-resolving complications (e.g. mild atelectasis)…”

5. Page 7: change “atelectases” to “atelectasis”  
   a. Done.

6. Page 8: authors stated “The good-excellent outcomes, however were similar across all three procedures (Nuss 95%, Ravitch 96%, Robicsek 89%).” Authors should make a comment related to the subjective nature and limitations of such assessments like “good-excellent, excellent”.  
   a. Added specific comment on qualitative rating to limitations paragraph (final paragraph of discussion). Stating “The reports of outcomes were largely based on subjective, though previously published, qualitative ratings (e.g. good-excellent, excellent), which may limit the reproducibility and consistency across patients and providers.”
   Reference:  

7. Page 10: change “demonstrated showed” to “demonstrated”  
   a. Done.

8. Page 14, Discussion: “…In doing so, this study answers the question about the age appropriateness of differnet PEx treatments—namely the Nuss procedure and highly modified Ravitch procedure.” Revise to: “In doing so, this study attempts to address the qurestion about the age appropriateness of different PEx treatments…”  
   a. Done.

9. Under Conclucions (page 14): “…While many surgeons suggest that operating on children and adolescents results in better outcomes, the literature fails to corroborate this.” Should add a statement: “However many studies support the observation that the Nuss procedure is easier to perform in younger patients.”  
   a. Similar correction: Third sentence of conclusion (page 15) added, “Many studies do, however, support the observation that the Nuss procedure is easier to perform in younger patients.”