

## Peer Review File

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### Reviewer Comments:

#### Reviewer A:

##### Comment 1:

The authors presented a very interesting review article that provides a comprehensive look at the problem of pectus excavatum and pectus carinatum. They have done a great job collecting the existing knowledge about etiopathogenesis and the most important etiological factors of the most popular chest deformities.

However, a major revision is required for the article to be published.

The epidemiology part is well described. As the authors write, the exact epidemiology is unknown, and the data often vary. An interesting direction worth mentioning is an attempt to use Google Trends: DOI:10.21037/jtd-20-2924.

Reply 1: We thank you for your time and effort in reviewing our manuscript and the compliments and comments provided. We have added a statement to the epidemiology section that though the interest in pectus excavatum is still higher than in pectus carinatum, the global trend in internet searches related to the topic pectus excavatum is decreasing. We also added the suggested reference (line 136-139).

##### Comment 2:

As for the further structure of the article, I think it needs to be changed. The chapter on etiopathogenesis is too long. The theories described are very interesting, but it is difficult for the reader to read. I suggest significantly shortening the entire fragment describing the etiopathogenesis and each theory.

Reply 2: Thank you for your comment and we understand your concern about the length of the etiopathogenesis chapter. However, our aim has been to provide a comprehensive overview that aligns with the historical timeline of research in this field. We revised the fragment in terms of readability (lines 141-290).

##### Comment 3:

The following fragments are much better written, and the proportions are preserved regarding content. However, in this article, I would like a little more information about the treatment and clinical topics of both deformities. In the "Cardiopulmonary function" subsection, where information about Nuss or Ravitch operations suddenly begins to appear in a somewhat chaotic manner, a few sentences of the introduction would be helpful: describe that the Ravitch operation is one of the older methods of surgical correction, which, however, is losing its importance in due to the popularity of the Nuss procedure and the development of video-thoracoscopy. In addition, when writing about Ravitch's procedure, one should mention the unsightly scar that this procedure leaves and the extensiveness of this procedure. This can also be described in a separate

subsection regarding the treatment of this deformity.

Reply 3: The authors thank you for this comment. We have added information regarding the surgical procedures of both pectus excavatum and carinatum to the introduction (lines 86-98).

Comment 4:

When it comes to pectus carinatum, the whole composition is better here. Still, I would expand on the topic of surgical treatment a bit: the Ravitch method should be mentioned, which, although extensive and gives a poor cosmetic effect, is still often performed in many centers. In addition, the topic of the Abramson method should be expanded, which is beginning to appear more and more often in the literature, is being modified and brings better and better results - for example, as described in one of the JTD articles: DOI:10.21037/jtd-22-956

Reply 4: We thank you for your comment. Please see the reply to comment 3.

#### **Reviewer B:**

Comment 1: This is a well written and comprehensive review on some aspects of pectus excavatum and carinatum. My opinion is that the paper should be published. I would suggest some minor modifications and I have some comments to the Authors:

90% of pectus excavatum is probably not accurate. In my experience, pectus carinatum has an increasing incidence, and now in my activity it is almost as frequent as pectus excavatum. Maybe you could add a range and other references.

Reply 1: The authors thank the reviewer for his/her critical review of our manuscript and the comments and compliments provided. We acknowledge that pectus carinatum has an increasing incidence and incidence rates vary depending on the population being studied. One study in Brazil even reports that. We have added additional references (range of 65-95%) to the excavatum chapter, and mentioned a study conducted in Brazil reporting that pectus carinatum is even more prevalent than pectus excavatum (0.9% versus 0.04%) to the pectus carinatum chapter (lines 120-121, 443-445).

Comment 2: Regarding indexes, it can be useful for the reader to have a reference of a recent paper from our group, aiming at creating a semi-automatic way to calculate classical indexes (such as Haller and correction index) and proposing volumetric indexes, which could be more precise than the classical indexes. Please see Trò R et al: A new tool for assessing Pectus Excavatum by a semi-automatic image processing pipeline calculating the classical severity indexes and a new marker: the Volumetric Correction Index. BMC Med Imaging 2022 Feb 20;22(1):30. doi: 10.1186/s12880-022-00754-0

Reply 2: The authors thank you for your suggestion. We mentioned the tool and added the reference to the corresponding section in the manuscript (lines 398-399).

Comment 3: There is a lot of discrepancy between the space dedicated to pectus excavatum and carinatum. Maybe the Authors can comment on that or add more information about pectus carinatum

Reply 3: We appreciate your observation regarding the difference in the space dedicated to pectus excavatum and pectus carinatum within the manuscript. We acknowledge that the sections on these two chest wall deformities are unequal in length. The reason for this difference is that we extensively elaborate on the etiopathogenesis of pectus excavatum. Literature on the etiopathogenesis of pectus carinatum is extremely limited and available literature suggests that pectus carinatum has a similar origin to that of pectus excavatum, as briefly mentioned in our manuscript. We choose to only present the unique aspects of the deformity.

**Reviewer C:**

Comment 1: The authors described an overview of what is currently known about the clinical features, epidemiology, etiopathogenesis, and classification of the most common chest wall deformities (i.e., pectus excavatum and carinatum).

Clinical features, epidemiology, etiopathogenesis, and classification of pectus excavatum and carinatum are very helpful in diagnosis and treatment of patients.

I think it would have been better if you had reviewed more data on how the classification of the disease is related to the treatment method and how it affects the treatment outcome.

The authors provided an overview of the current knowledge on the most common chest wall deformities.

Reply 1: We thank the reviewer for his/her critical review of our manuscript and your suggestion to look deeper into the relationship between disease classification and treatment methods, as well as their impact on treatment outcomes. Understanding how classification influences treatment decisions and outcomes is indeed crucial in providing comprehensive care to patients with chest wall deformities. Besides the clinical experience that more severe, asymmetric or complex deformities like pectus concavo-convexus are more difficult to correct, there is a gap in knowledge on how classification affects the surgical outcome.

The choice of treatment often depends on various factors, including patient age, chest wall flexibility, and specific morphology, which is however not within the scope of our current review, and more studies are required to provide an answer for this interesting relation

We will certainly take your suggestion into consideration for future research and reviews, aiming to bridge the gap in knowledge between classification and treatment (outcomes)(line 437-438).

**Reviewer D:**

Comment 1: In considering the etiopathogenesis of disease, it is important to consider its genetic predisposition. Therefore, an exhaustive table of reported genetic predispositions of pectus excavatum is desired to be added.

Reply 1: The authors thank you for your time and effort in reviewing our manuscript. We discussed the possible genes associated with isolated pectus excavatum in the genetic predisposition paragraph since pectus is mostly non-syndromic. However, we agree that awareness of the existence of genetic conditions associated with pectus excavatum is important and therefore added information along with references to two reviews on underlying genetic conditions to the manuscript (lines 310-313).

Comment 2:

In Genetic predisposition section, it is desirable to include TGFBR1, TGFBR2, SMAD3, TGFB2, and TGFB3 related to TGF $\beta$  protein as affected genes of Marfan syndrome. Alternatively, the Lois-Dietz syndrome may be added as a syndrome similar to Marfan syndrome, and as its affected genes.

Reply 2: We thank you for this comment and added information on the Loeys-Ditz syndrome and its affected genes to the genetic predisposition paragraph (lines 277-287).

Comment 3:

In CLINICAL PRESENTATION section, the author is desired to be separately describe symptoms directly related to skeletal anomalies of pectus excavatum, symptoms associated with common comorbidities, and symptoms associated with reported incidentally complicated diseases. As the symptoms associated with common comorbidities, the authors should describe the symptoms of cardiovascular complications associated with common comorbidities such as Marfan syndrome and Ehlers-Danlos syndrome (and may Lois-Diets syndrome).

Reply 3: Thank you for this suggestion. We added information on symptoms associated with common comorbidities and incidentally complicated diseases, as well as symptoms associated with major cardiovascular complications to the clinical presentation paragraph (313-322).

Comment 4:

The authors should mention the prognostic impact of comorbid cardiovascular disease and therefore the symptoms associated with major cardiovascular complications in CLINICAL PRESENTATION section.

Reply: The authors thank the reviewer for this comment. Please see the reply to comment 3.

Comment 5:

Regarding the description of improvement in cardiac function in the Cardiopulmonary function section, the authors is desired to describe the more detailed improvement in size and function of the right and left heart systems by pectus excavatum repair.

Reply: The authors thank you for your suggestion. We added a more detailed description of cardiovascular improvement to the cardiopulmonary function paragraph (lines 352-356).