PEER REVIEW HISTORY

BMJ Paediatrics Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Comparing postoperative analgesia of bilateral serratus anterior plane block and thoracic paravertebral block for children following the Nuss procedure: Protocol for a randomized, double-blind, non-inferiority clinical trial
AUTHORS	He, Yi Xu, Mingzhe Jiang, Xiaojuan Li, Zhi Du, Bin

VERSION 1 - REVIEW

REVIEWER	Prof. Mustafa Kemal Arslantas TC Demiroglu Bilim University, Department of Anesthesiology and Reanima
REVIEW RETURNED	27-Jun-2023

GENERAL COMMENTS	The proposed research presents an admirably robust and well-considered protocol for comparing two modalities of postoperative pain management in pediatric patients subjected to the Nuss procedure. Utilizing a randomized, double-blind design is commendable, and the ethical approvals in place contribute significantly to the study's credibility. Notwithstanding, I noticed some essential elements not clearly outlined in the study, which could potentially impact the study's outcomes. Specifically, it would be beneficial to explore and discuss the influence of the severity of deformity and certain surgical factors, such as the number of steel bars used during the surgery, on postoperative pain levels. The inclusion of indexes like the Haller Index (HI), Anthropometric Index (AI), and Lower Vertebral Index (LVI) could provide a more comprehensive understanding of the severity of pectus excavatum. This could potentially influence the complexity of the surgical procedure and subsequent postoperative pain, enriching the analysis. The abstract did not clarify whether these factors have been considered in the study design or analysis. Furthermore, assessing the potential impact of the number of steel bars used during surgery would be valuable, as this could influence the complexity of the intervention and the subsequent postoperative pain. In summary, while the study design is commendable, incorporating these additional factors in the analysis would enhance our understanding of the variables affecting postoperative pain and,

	thus, bolster the clinical relevance and generalizability of the study findings. I highly recommend that the authors deliberate on these suggestions and clarify these points in the final manuscript. Elaborating on these factors would substantially enhance the depth and clinical relevance of the study. I eagerly anticipate the revised manuscript and the final results of this promising trial.

REVIEWER	Dr. Peter Flom Peter Flom Consulting
REVIEW RETURNED	29-Jun-2023

GENERAL COMMENTS	I confine my remarks to statistical and methodological aspects of this paper. Bur I noted some English language problems, e.g the tense changes from past to future and back again; I am sure BMJ editors can fix these, they were not severe. I am glad to read protocol papers and I commend BMJ for publishing them. General comment Given that you are going to be collecting data at multiple time points, there are more powerful statistical methods available, such as multilevel models. The statistical analysis section needs more detail; it seems to only discuss the primary endpoint. But the other outcomes will require different analysis. E.g time of first rescue analgesia may need survival analysis (if it is censored), medication is categorical. Etc. Things need to be spelled out. Specific comments More details are needed on the numeric rating scale that will be the main outcome. There are different scales; the authors need to pick one. Similarly for all the other outcomes. There are two issues: First, the paper should be thorough enough that other researchers can duplicate it, if they wish. Second, the nature of the outcomes (and how they are scored) will affect the statistical methods. For example, if the pain scale is an integer (e.g. a Likert scale) then that would need different methods than if it is a continuous scale (e.g. a visual analog scale). p. 11 I am guessing that the (0.92) is a standard deviation, but this needs to be specified. p. 12 "missing data will not be superseded" is unclear. What does "superseded" mean here? Do you mean "imputed"? And, if so, why not do multiple imputation?

VERSION 1 – AUTHOR RESPONSE

Reviewer 1:

Comment 1. I noticed some essential elements not clearly outlined in the study, which could potentially impact the study's outcomes. Specifically, it would be beneficial to explore and discuss the influence of the severity of deformity and certain surgical factors, such as the number of steel bars used during the surgery, on postoperative pain levels. The inclusion of indexes like the Haller Index (HI), Anthropometric Index (AI), and Lower Vertebral Index (LVI) could provide a more comprehensive understanding of the severity of pectus excavatum. This could potentially influence the complexity of the surgical procedure and subsequent postoperative pain, enriching the analysis. The abstract did not clarify whether these factors have been considered in the study design or analysis.

Response: We deeply appreciate your warm work on our article and totally agree with your opinion. Several clinical characteristics, including diagnosis (e.g., deformity severity and Haller index), will be collected before surgery, and subgroup analyses will be conducted if necessary. Moreover, the surgical procedure will be performed by a single surgeon using the same surgical technique in order to prevent certain surgical influences. Whether the pectus severity will influence the postoperative pain after the Nuss procedure is controversial1 2. It would be beneficial to explore and analyze these factors in our final results to enrich the clinical relevance of our study. We have described these in our revised manuscript and made some changes to the "Abstract" and "Method" sections, which are highlighted in blue. Thank you very much for your kind suggestions.

Reference

1. Papic JC, Finnell SM, Howenstein AM, et al. Postoperative opioid analgesic use after Nuss versus Ravitch pectus excavatum repair. J Pediatr Surg 2014;49(6):919-23; discussion 23.

2. Grosen K, Pfeiffer-Jensen M, Pilegaard HK. Postoperative consumption of opioid analgesics following correction of pectus excavatum is influenced by pectus severity: a single-centre study of 236 patients undergoing minimally invasive correction of pectus excavatum. Eur J Cardiothorac Surg 2010;37(4):833-9.

Comment 2. Furthermore, assessing the potential impact of the number of steel bars used during surgery would be valuable, as this could influence the complexity of the intervention and the subsequent postoperative pain.

Response: Thank you very much for your comment. We agree that the number of steel bars used may affect the complexity of the intervention and postoperative pain. We will record the related information as part of “intraoperative data” in our case report forms and perform subgroup analysis if necessary. We have revised the “data collection” section, and the modified parts are highlighted in blue in the revised manuscript.

Comment 3. In summary, while the study design is commendable, incorporating these additional factors in the analysis would enhance our understanding of the variables affecting postoperative pain and, thus, bolster the clinical relevance and generalizability of the study findings. I highly recommend that the authors deliberate on these suggestions and clarify these points in the final manuscript. Elaborating on these factors would substantially enhance the depth and clinical relevance of the study.

Response: Thank you very much for your detailed suggestions. We have revised these contents in our resubmitted manuscript, and the modified parts are highlighted in blue. We would greatly benefit from it as we proceed with our research.

Reviewer 2:

Comment 1. I noted some English language problems, e.g the tense changes from past to future and back again; I am sure BMJ editors can fix these, they were not severe.

Response: We are deeply appreciative of your warm work on our article. According to your nice suggestions, we polished the language by the Editage Language Editing Services to improve readability of the revised manuscript. We did not list the changes here but marked in blue in the revised manuscript (marked copy).

Comment 2. General comment: Given that you are going to be collecting data at multiple time points, there are more powerful statistical methods available, such as multilevel models. The statistical analysis section needs more detail; it seems to only discuss the primary endpoint. But the other outcomes will require different analysis. E.g time of first rescue analgesia may need survival analysis (if it is censored), medication is categorical. Etc. Things need to be spelled out.

Response: Thank you very much for your detailed suggestion. We have revised the “statistical analysis” section to make it more detailed as suggested (shown below). The modified parts are highlighted in blue in the revised manuscript (marked copy).

Comment 3. Specific comments: More details are needed on the numeric rating scale that will be the main outcome. There are different scales; the authors need to pick one. Similarly for all the other outcomes. There are two issues: First, the paper should be thorough enough that other researchers can duplicate it, if they wish. Second, the nature of the outcomes (and how they are scored) will affect the statistical methods. For example, if the pain scale is an integer (e.g., a Likert scale) then that would need different methods than if it is a continuous scale (e.g., a visual analog scale).

Response: Thank you for your comment. The intensity of pain will be assessed using the Numeric Rating Scale (NRS). The Numeric Rating Scale (shown below) is a segmented numerical version of the visual analog scale in which patients choose an integer from 0 to 10 that appropriately reflects their pain severity. Pain intensity assessment is as follows: no pain = 0, mild pain = 1–3, moderate pain = 4–6, and severe pain ≥7. We have described it in the "main outcome” section of the revised manuscript (marked copy).

Comment 4. p. 11 I am guessing that the (0.92) is a standard deviation, but this needs to be specified.

Response: Thank you very much for your careful checks. The (0.92) is the standard deviation of the pain score at 24 h following TVPB after the Nuss procedure in our preliminary experiment. We have revised our manuscript to make it clearer and the modified parts are highlighted in blue in the resubmitted manuscript (marked copy)

Comment 5. p. 12 "missing data will not be superseded" is unclear. What does "superseded" mean here? Do you mean "imputed"? And, if so, why not do multiple imputation?

Response: Thank you very much for the detailed comment. The missing data in our study will not be imputed. As we think the possibility of missing values of the primary outcome in our study will be very low. This is because data will be collected by specific researchers and the sample size of this study is small. Therefore, multiple imputations will not be used in this study. We have changed "superseded" to "imputed" in the manuscript and highlighted it in blue.