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OPEN PEER REVIEW

Effect of Surgical Position and Preoperative Antihypertensive Medication on the Incidence of Intraoperative Hypotension in Patients Undergoing Spine Surgery

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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Contents

1 **Original submission** Referee 1, Referee 2, Fatemeh Moftakhar, Associate Editor, Editor-in-Chief 2

2 **Revision 1** Referee 2, Associate Editor, Editor-in-Chief 4

Authors' reply to reviewers 5

Reviewer and editor comments 12

1 Original submission

5 comments · 9 Apr 2025 – 21 Apr 2025

Referee 1 Reviewer

ACCEPT 9 Apr 2025

Hi, thanks for your invite. I read the manuscript multiple times. I'd prefer to accept it.
Best wishes

Referee 2 Reviewer

MAJOR REVISION 9 Apr 2025

Dear Associate Editor
I thank the authors and express my appreciation to the researchers.
Here I have some suggestions and comments that should be addressed:

1-Some sentences lack references.
FOR EXAMPLE: The first sentence of the background.
All sentences quoted from other articles must have references at the end.

2-While the study acknowledges that doses of remifentanil and propofol are not recorded, this remains a critical confounder.

3-Although the five main classes of antihypertensive medications are analyzed, there is no direct comparison between classes (e.g., beta-blockers vs. ARBs). Additionally, the study does not explore whether specific drug combinations have synergistic or antagonistic effects on IOH risk.

4-Without adjusting for surgical region in a multivariable model, causal interpretation of surgical position is limited.
5-Patients on multiple antihypertensives were grouped only by the number of drugs (1, 2, ≥3), rather than by specific combinations.
6-The lack of standardized anesthetic protocols across patients and surgeons further complicates interpretation.
7-Please review more recent articles for your study, as well as updated ones, instead of old references, in order to improve the quality of the rationale behind your study.

Fatemeh Moftakhar Reviewer

ACCEPT 15 Apr 2025

Dear Author,
Thank you for your study. Your study is accepted.
Best Regards,

Associate Editor

MINOR REVISION 21 Apr 2025

Dear EIC,
I thank the authors and express my appreciation to the researchers. The manuscript is a valuable piece of research. The reviewers have provided constructive feedback to help improve the clarity and presentation of the manuscript. I encourage the authors to carefully address each of the reviewers' comments and submit a

revised version of the manuscript. The authors should revise it based on the comments. Also, a minor change should be made in the abstract:
* A summary of the statistical analysis results should be mentioned in the result section.

Editor-in-Chief MINOR REVISION 21 Apr 2025

Dear Author,
I would like to extend my gratitude to the authors for their contribution and commend the researchers for their valuable work presented in the manuscript. However, I believe that certain revisions are necessary, and I kindly request that you consider incorporating these suggested changes based on the provided comments.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear editor and reviewers of Anesthesiology and Pain Medicine.
My name is Myungjin Ko, the corresponding author of the manuscript entitled “Effect of surgical position and preoperative antihypertensive medication on the incidence of intraoperative hypotension in patients undergoing spine surgery”
We sincerely appreciate your thoughtful and constructive reviews. Please find below our detailed responses to the reviewers’ comments.

Reviewers’ Comments

Reviewer 1:

Hi, thanks for your invite. I read the manuscript more times. I'd prefer to accept it. Best wishes

Answer) Thank you so much for your kind review. I sincerely hope that this article will be published in the journal “Anesthesiology and Pain Medicine” soon.

Reviewer 2:

Dear Associate Editor
Thanks to the authors and appreciation to the researchers.
Here I have some suggestions and comments that should be addressed:

1-Some sentences lack references.

FOR EXAMPLE: First sentence of background.
All sentences quoted from other articles must have references at the end of themselves.
Answer) Thank you for your comment. As you suggested, we also found that some sentences in the background and discussion lacked references. I supplemented the references and highlighted the revised and added parts in the text. I also modified the references to be placed at the end of the sentences. Thank you.

For Example)
Background
1) Spinal surgery is typically performed to address degenerative conditions such as spinal stenosis and herniated intervertebral discs, which are more prevalent among the elderly population (1).

1.Birkmeyer NJ, Weinstein JN, Tosteson AN, Tosteson TD, Skinner JS, Lurie JD, Deyo R, Wennberg JE. Design of the Spine Patient outcomes Research Trial (SPORT). Spine (Phila Pa 1976). 2002 Jun 15;27(12):1361-72. doi: 10.1097/00007632-200206150-00020. PMID: 12065987; PMCID: PMC2922028.

2) Patients undergoing these procedures often present with multiple chronic illnesses, with hypertension being particularly common (2, 3).
2.National Center for Health Statistics (US). Health, United States, 2020-2021: Annual Perspective [Internet]. Hyattsville (MD): National Center for Health Statistics (US); 2023. PMID: 36888733.

3.Yoshihara H, Yoneoka D. Complications Associated With Spine Surgery in Patients Aged 80 Years or Older: An Analysis of 262 Cases. Global Spine J. 2017;7(7):636–641.
https://pmc.ncbi.nlm.nih.gov/articles/PMC5624380/

3)Spinal surgery may be conducted in various positions, including supine, lateral, and prone, depending on the specific surgical site and technique employed (8).
8.Cunha PD, Barbosa TP, Correia G, Silva R, Cruz Oliveira N, Varanda P, Direito-Santos B. The ideal patient positioning in spine surgery: a preventive strategy. EFORT Open Rev. 2023 Feb 21;8(2):63-72. doi: 10.1530/EOR-22-0135. PMID: 36805330; PMCID: PMC9968999.

Discussion

4)Hypertension is a prevalent chronic condition, and to enhance treatment efficacy, dual or combination therapy with antihypertensive drugs is increasingly utilized (21).
21.Smith DK, Lennon RP, Carlsgaard PB. Managing Hypertension Using Combination Therapy. Am Fam Physician. 2020 Mar 15;101(6):341-349. PMID: 32163253.

5) Additionally, the hypotensive effects of general anesthetic agents may exacerbate the severity of hypotension (26, 27).

26.Saugel B, Sessler DI. Perioperative Blood Pressure Management. Anesthesiology. 2021 Feb 1;134(2):250-261. doi: 10.1097/ALN.0000000000003610. PMID: 33206118.

27.Roshanov PS, Rochwerg B, Patel A, Salehian O, Duceppe E, Belley-Côté EP, Guyatt GH, Sessler DI, Le Manach Y, Borges FK, Tandon V, Worster A, Thompson A, Koshy M, Devereaux B, Spencer FA, Sanders RD, Sloan EN, Morley EE, Paul J, Raymer KE, Punthakee Z, Devereaux PJ. Withholding versus Continuing Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Blockers before Noncardiac Surgery: An Analysis of the Vascular events In noncardiac Surgery patIents cOhort evaluatioN Prospective Cohort. Anesthesiology. 2017 Jan;126(1):16-27. doi: 10.1097/ALN.0000000000001404. PMID: 27775997.

2-While the study acknowledges that doses of remifentanil and propofol are not recorded, this remains a critical confounder.

Answer) Thank for your thoughtful comment. I deeply agree with your opinion. The lack of exact dosage documentation for remifentanil and propofol limits precise evaluation of their effects on intraoperative hypotension. We regret that we were unable to conduct an analysis of the exact doses of remifentanil and propofol. Although insufficient, we have mentioned in the text the range of dosages of drugs actually used in anesthesia at the institution to overcome this limitation.

We also added the following to the limitations of the discussion: Notably, the doses of remifentanil and propofol are known to influence blood pressure however, this retrospective design limited our ability to quantify remifentanil and propofol dosages, which are known to influence hemodynamics and may act as unmeasured confounders.

3-Although the five main classes of antihypertensive medications are analyzed, there is no direct comparison between classes (e.g., beta-blockers vs ARBs). Additionally, the study does not explore whether specific drug combinations have synergistic or antagonistic effects on IOH risk.

Answer) Thank you for your comment. In our study, we investigated the incidence of intraoperative hypotension in each class of antihypertensive drugs, but did not conduct a direct comparison between the drugs. In particular, we deeply agree with the point that each combination of drugs may have different effects on blood pressure depending on the synergistic or antagonistic effects between them. Since there are so many different combinations of drugs, it may be a limitation of this study

that we could not investigate and compare them all for each patient or each combination of drugs. We expect that it would be good to plan follow-up studies focusing on this perspective in the future.
We added following sentence in the result of Table 3: Although individual drug classes showed varying associations with hypotension, direct comparisons between classes (e.g., ARBs vs. BBs) were not statistically tested in this study.
We added following sentence in the discussion section: Future studies should directly compare specific drug classes and investigate potential synergistic or antagonistic interactions in combination therapies.

4-Without adjusting for surgical region in a multivariable model, causal interpretation of surgical position is limited.

Answer) Thank you for your valuable comment regarding the need to adjust for surgical region in the multivariable model. In response, we have conducted an additional multivariable logistic regression analysis that includes surgical region as a covariate to more accurately assess the relationship between surgical position and intraoperative hypotension.

Our results demonstrated that, when adjusting for potential confounders including surgical region, lumbar spine surgery was significantly associated with a lower risk of intraoperative hypotension compared to cervical spine surgery (OR 0.564, 95% CI 0.467–0.681, $P < 0.001$). Similarly, for severe hypotension, both lumbar and thoracic spine surgeries were associated with significantly reduced risk relative to cervical spine surgery (lumbar: OR 0.339, 95% CI 0.239–0.480, $P < 0.001$; thoracic: OR 0.538, 95% CI 0.322–0.900, $P = 0.018$).

These findings have now been incorporated into the revised manuscript, and the relevant results are summarized in the updated Table 6 along with appropriate discussion in the results and discussion sections.

5-Patients on multiple antihypertensives were grouped only by the number of drugs (1, 2, ≥3), rather than analyzing specific combinations.

Answer) Thank you for raising this important point. We agree that evaluating specific drug combinations could provide further insight. However, in this retrospective dataset, the diversity of antihypertensive regimens made combination-level analysis complex and potentially less meaningful from a statistical standpoint. As such, we opted to group patients based on the number of antihypertensives used. This decision, as well as its limitations, is now described in the updated limitation section: Second, patients on multiple antihypertensives were grouped only by the number of drugs (0, 1, 2 or more), rather than analyzing specific combinations. Comprehensive analysis of all combinations of antihypertensive drugs was not feasible due to the extensive number of two or more combination therapies, making individual analysis impractical. Future studies should directly compare specific drug classes and investigate potential synergistic or antagonistic interactions in combination therapies.

6-The lack of standardized anesthetic protocols across patients and surgeons further complicates interpretation.

Answer) We appreciate your observation regarding this critical aspect of study design. We recognize this limitation and have explicitly addressed it in the revised manuscript. Although our institution maintains general clinical guidelines for anesthetic management, including remifentanil titration strategies, individual variations in adherence were not documented and could not be verified. This factor may have introduced inter-case variability in hemodynamic responses, and we have reflected this uncertainty in the limitation paragraph

: Third, as this study was retrospective in nature, there was limited control over various surgical conditions, including anesthesia methods and surgical procedures. Notably, the doses of remifentanil and propofol are known to influence blood pressure however, this retrospective design limited our ability to quantify remifentanil and propofol dosages, which are known to influence hemodynamics and may act as unmeasured confounders (6, 26). According to our hospital’s policy, remifentanil is administered at a low dose of 0.03–0.1 mcg/kg/min to maintain anesthesia. If blood pressure drops, the dose of remifentanil is first reduced to maintain appropriate blood pressure.

7-Please, investigate more recently articles for your study as well as updated ones instead of old references, in order to improve the quality of purpose behind your study.

Answer) Thank you for raising this important point. We have added seven new references, all of which are recently published (reference number 1, 2, 3, 8, 21, 26, 27). We have also updated one old reference to a more recent one (Reference number 13). We are very grateful for your help in improving the quality of our research.

Reviewer 3:
Dear Author,
Thank you for your study. Your study is accepted.
Best Regards,

Answer) Thank you so much for your kind review. I sincerely hope that this article will be published in the journal “Anesthesiology and Pain Medicine” soon.

Associate Editor's Comments:

Associate Editor 1:
Dear EIC,
Thanks to the authors and appreciation to the researchers. The manuscript is a valuable research. The reviewers have provided constructive feedback to help improve the clarity and presentation of your manuscript. I encourage authors to carefully address each of the reviewers’ comments and submit a revised version of the manuscript. Authors should revise it based on comments. Also minor change should be done in abstract:
***Summary of Statistical analysis results should be mention in result section.**

Answer) Thank you very much for your kind comment. We added summary of statistical analysis results at the end of Results section of abstract as follows: Older age, longer anesthesia duration, cervical surgical site, and the use of multiple antihypertensive agents were associated with an increased risk of intraoperative hypotension. In particular, taking two or more antihypertensive drugs (OR = 1.601) and undergoing surgery in the prone position (OR = 1.505) were independent predictors of hypotension and severe hypotension during spine surgery.

To editor.

We would like to request a minor modification in the Acknowledgement section. In addition to the existing content, we would appreciate it if we could include the following sentence:

"Statistical analysis was supported by Haeundae Paik Hospital."

This statement reflects institutional support for part of the study and we believe it is important to acknowledge this contribution. Thank you.

2 Revision 1

3 comments · 13 May 2025 – 13 May 2025

Referee 2 Reviewer

ACCEPT 13 May 2025

Dear AE.
Previous errors have been corrected, and there are no further recommendations.

Associate Editor

ACCEPT 13 May 2025

Dear EIC.
Previous errors have been corrected, and there are no further recommendations. The article could be accepted at this stage.

Editor-in-Chief

ACCEPT 13 May 2025

Dear AUTHORS,
Thank you for paying attention and responding to the reviewer's comments.
Your revisions have significantly improved the article, and it is now deemed acceptable for publication.
Congratulations on your hard work and dedication to enhancing the quality of your work.