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OPEN PEER REVIEW

# Supine Versus Prone Positioning in Percutaneous Nephrolithotomy: A Retrospective Cohort Study Comparing Intraoperative Hemodynamic and Respiratory Stability

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## 1 Original submission

5 comments · 7 Oct 2025 – 14 Oct 2025

### Referee 1 Reviewer

MAJOR REVISION 7 Oct 2025

Dear AE,
Thank you very much for giving me the opportunity to review this manuscript.
Here are my comments:
1. Lack of specific eligibility criteria and participant selection methods.
2. Absence of discussion on study limitations and potential biases.
3. No mention of confounder-adjusted estimates in the results.
4. Specific dates and locations of the study setting are not provided.
5. Generalizability is implied but not explicitly discussed.
6. As part of the review process, we would like to draw the authors' attention to several recent publications that may be relevant to their study. These references are suggested to help strengthen the manuscript's background, contextualize its findings within the broader literature, and ensure that it reflects the most up-to-date research in the field. These references are provided solely as suggestions, and citing them is not mandatory. The aim is to enhance the academic rigor and comprehensiveness of the manuscript.
These articles are listed below:
A. Effect of Position Change After Induction of Spinal Anesthesia with Hyperbaric 0.5% Bupivacaine on Duration of Analgesia and Opioid Demand in Percutaneous Nephrolithotomy Candidates
* Reason: This study is highly relevant as it provides direct, empirical evidence that patient positioning during and after anesthesia induction for PCNL significantly impacts critical outcomes like hemodynamic stability and opioid consumption. Citing it would powerfully support the manuscript's conclusion by demonstrating that the supine position's physiological benefits are part of a broader, evidence-based trend where optimized positioning is proven to enhance patient safety and recovery in urological surgeries.
** Link: https://brieflands.com/articles/aapm-153617
B. Effect of Surgical Position and Preoperative Antihypertensive Medication on the Incidence of Intraoperative Hypotension in Patients Undergoing Spine Surgery
* Reason: This study is highly relevant as it provides robust, large-scale evidence from a different surgical context (spine surgery) that the prone position is an independent predictor of significant hemodynamic instability, powerfully corroborating the manuscript's findings in PCNL. Citing it would generalize the manuscript's conclusion, demonstrating that the cardiovascular challenges of the prone position are a universal perioperative concern, thereby strengthening the argument for adopting the supine position as a safer standard.
** Link: https://brieflands.com/articles/aapm-161684

Final Decision: Major Revision
Kind Regards | Publishing Assistant

### Referee 2 Reviewer

MAJOR REVISION 7 Oct 2025

Dear AE,
Thank you for the invitation.
The study addresses a clinically relevant question and presents coherent data supporting the supine approach for PCNL. However, before publication, the following issues should be corrected:

1-A sample of 40 patients (20 per group) is relatively small for detecting subtle physiological or safety differences. A power analysis to justify the sample size is missing and should be included.
2-Commendably, the authors reported Cohen's d and confidence intervals. However, for such small groups, effect sizes can be inflated; this should be acknowledged.
3-The authors conclude that the supine position provides superior physiological stability. While the data support this, the conclusion should be more nuanced — i.e., "may offer better hemodynamic and respiratory stability in selected patients."
4-The authors correctly acknowledge key limitations but should also include:

*Lack of randomization and blinding.

*Possible confounding from the anesthetic agent (halothane).

*Limited postoperative follow-up (only three months).

*Absence of gas exchange analysis (e.g., $PaO_2$, $PaCO_2$ from arterial blood gases) to corroborate $ETCO_2$ findings.

5-Clarify the use of halothane and discuss its impact.
6-Please review more recent and updated articles for the study instead of older references to improve the quality of the rationale behind the study.

**Referee 3** Reviewer

MINOR REVISION 10 Oct 2025

1- It is suggested that new systematic reviews and meta-analyses (2020 to 2024) be used to update the references section, especially in lines 61 to 66.
2- Lack of explanation of the sample size calculation:
A sample of 40 patients (20 in each group) is relatively small, and the power of the test is likely to be low. There is no mention of the power calculation or sample size formula.
3- Lack of explanation of the sampling method:
It is not clear whether sampling was performed consecutively or randomly. This has an impact on selection bias.
4- Lack of detail in the analysis of the duration of the operation: It was stated that the duration of anesthesia was longer but the surgical time did not differ—the physiological or technical reason for this difference was not explained.

5- Lack of mention of the method of ventilation control in the prone position: Given the significant changes in $SpO_2$ and $ETCO_2$, it is necessary to explain whether the mechanical ventilation parameters were fixed or adjusted.

6- Lack of multivariate analysis: Because SBP, HR, and $SpO_2$ are all affected by cross-sectional factors (such as depth of anesthesia, fluid therapy, and body position), it is better to perform multivariate regression analysis to confirm the independence of these effects.

7- Lack of mention of the type and dose of anesthetic: Differences in the use of anesthetic drugs or fluid volume could be confounders.

**Associate Editor**

MAJOR REVISION 13 Oct 2025

Dear EIC,
I thank the authors and express my appreciation to the researchers. The manuscript is a valuable piece of research. However, some revisions are needed. The authors should revise it based on the reviewers' comments.

Minor changes should also be made to the abstract:
1- The background could briefly mention why the prone position may cause instability (e.g., compression of the thoracic cavity, venous return issues). This would enhance context and scientific depth.
2- The term “matched for baseline characteristics” is vague — specify which variables were matched (age, BMI, comorbidities, stone size, etc.).

**Editor-in-Chief** MAJOR REVISION 14 Oct 2025

Major Revision

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.

**Response to Reviewers' Comments**

**Manuscript Title:** Supine versus Prone Percutaneous Nephrolithotomy: A Retrospective Cohort Study Comparing Intraoperative Hemodynamic and Respiratory Stability

We wish to express our sincere gratitude to the Editors and the esteemed Reviewers for their valuable time and insightful comments on our manuscript. Their constructive feedback has been instrumental in improving the quality, clarity, and rigor of our work. We have carefully considered each comment and revised the manuscript accordingly. All changes have been integrated into the revised text.

**Our detailed, point-by-point responses to all comments are provided below.**

**Reviewer 0**

**Comment 1: Lack of specific eligibility criteria and participant selection methods.**

**Response:** We thank the reviewer for this important observation. We have comprehensively revised the 'Participants' subsection within the 'Patients and Methods' section to explicitly detail the inclusion and exclusion criteria. Furthermore, we have clarified that a consecutive sampling method was used for participant selection, and that group assignment was non-randomized, based on the surgical position utilized during the study period. (Please see '**Patients and Methods – Participants**' in the revised manuscript).

**Comment 2: Absence of discussion on study limitations and potential biases.**

**Response:** We agree that a thorough discussion of limitations is crucial. We have significantly expanded the 'Study Limitations' subsection within the Discussion. This new text explicitly addresses the limitations inherent in our retrospective, non-randomized, single-center design, the potential for selection bias and unmeasured confounding, the modest sample size, the use of halothane, the absence of arterial blood gas analysis, and the lack of long-term follow-up. (Please see '**Discussion – Study Limitations and Strengths**').

**Comment 3: No mention of confounder-adjusted estimates in the results.**

**Response:** This is a valid methodological point. We have now explicitly stated in the 'Statistical Analysis' subsection that "No multivariate regression analysis was performed to adjust for potential confounders; therefore, all reported associations are unadjusted estimates." This caveat has also been added to the footnotes of Tables 2 and 3, and is mentioned in the revised Results text to ensure complete transparency. (Please see **'Patients and Methods – Statistical Analysis'** and the footnotes of **Tables 2 & 3**).

**Comment 4: Specific dates and locations of the study setting are not provided.**

**Response:** We have amended the 'Study Design and Setting' subsection to include the specific hospital name (Namazi Hospital, affiliated with Shiraz University of Medical Sciences) and the precise 12-month period of data collection (January 2023 to December 2023). (Please see **'Patients and Methods – Study Design and Setting'**).

**Comment 5: Generalizability is implied but not explicitly discussed.**

**Response:** We thank the reviewer for this suggestion. The discussion on generalizability has been explicitly integrated into the revised 'Study Limitations and Strengths' paragraph. We now state that "the generalizability of our findings may be confined to settings with similar patient populations, surgical expertise, and anesthetic practices." (Please see **'Discussion – Study Limitations and Strengths'**).

**Comment 6: Suggestion of recent, relevant publications (Jaffari et al., 2025; Park et al., 2025).**

**Response:** We sincerely thank the reviewer for these highly relevant and recent suggestions. We have carefully studied both papers and have incorporated them into the Introduction and Discussion sections to better contextualize our findings within the broader literature. These citations now support the physiological rationale of our study and help generalize the cardiovascular challenges of prone positioning beyond urology. (Please see **References #15 and #16** and their corresponding citations in the **Introduction** and **Discussion**).

**Reviewer 1**

**Comment 1: A total of 40 patients is relatively small; a power analysis to justify the sample size is missing.**

**Response:** We acknowledge this limitation. We have added a new 'Sample Size Calculation' paragraph within the 'Patients and Methods' section, detailing the *a priori* calculation, the target sample size, and the reason for the final cohort size. This limitation is also explicitly discussed. (Please see **'Patients and Methods – Sample Size Calculation'** and **'Discussion – Study Limitations and Strengths'**).

**Comment 2: For small groups, effect sizes can be inflated; this should be acknowledged.**

**Response:** We agree entirely. We have added cautionary statements in the 'Results' section (for hemodynamic and pulmonary parameters) and in the footnotes of Tables 2 and 3, noting that "the large Cohen's d values should be interpreted with caution given the modest sample size." (Please see the **'Results'** section and **footnotes of Tables 2 & 3**).

**Comment 3: The conclusion should be more nuanced — i.e., "may offer better stability in selected patients."**

**Response:** We thank the reviewer for this nuanced suggestion. We have revised the concluding statements in the **Abstract** and the main **Conclusion** section to adopt more cautious and precise language, using phrases such as "may provide" or "may offer" better stability "in selected patients."

**Comment 4: Key limitations (lack of randomization/blinding, confounding from halothane, limited follow-up, absence of ABG analysis) should be included.**

**Response:** We are grateful for this comprehensive list. We have expanded the 'Study Limitations and Strengths' section to explicitly address each of these points:

- Lack of randomization and blinding is stated.
- The use of halothane and its potential confounding effect is discussed.
- The limited 3-month follow-up is acknowledged.
- The absence of arterial blood gas analysis is noted as a significant limitation. (Please see **'Discussion – Study Limitations and Strengths'**).

**Comment 5: Clarify the use of halothane and discuss its impact.**

**Response:** We have clarified the anesthetic protocol in the **'Patients and Methods – Surgical Technique and Anesthetic Management'** subsection, specifying halothane use. Its known myocardial depressive effects and standardized use across groups are discussed as a potential confounder in the limitations section.

**Comment 6: Please investigate and incorporate more recent articles.**

**Response:** We have thoroughly updated the reference list, replacing older citations with recent systematic reviews, meta-analyses (e.g., Fang et al., 2025), and original studies (e.g., Batratanakij et al., 2025; Erdal et al., 2024), particularly in the Introduction and Discussion, to reflect the current state of the literature.

**Reviewer 2**

**Comment 1: Use new systematic reviews and meta-analyses (2020 to 2024) to update references.**

**Response:** As noted above (Response to R1.6), the reference list has been significantly updated with current literature, including recent meta-analyses.

**Comment 2: Lack of explanation of sample size calculation.**

**Response:** This has been addressed with the new ‘Sample Size Calculation’ paragraph (See Response to R1.1).

**Comment 3: Lack of explanation about the sampling method.**

**Response:** The ‘Participants’ subsection now clearly states: "A consecutive sampling method was used." (Please see **'Patients and Methods – Participants'**).

**Comment 4: Lack of detail in analysis of duration of operation: explain the reason for the difference between anesthesia and operative time.**

**Response:** We have added a clear explanation in the ‘Results’ (Operational and Safety Outcomes): "This disparity suggests that the increased anesthesia duration in the prone group is attributable to logistical factors such as patient repositioning and potentially more complex airway management, rather than to the surgical procedure itself." (Please see **'Results – Operational and Safety Outcomes'**).

**Comment 5: Lack of mention of the method of ventilation control in the prone position.**

**Response:** A critical detail was added to the ‘Surgical Technique and Anesthetic Management’ section: "The ventilator parameters... were set upon induction... and were **not adjusted intraoperatively** in response to changes in $ETCO_2$ or patient position, as per the standardized protocol." (Please see **'Patients and Methods – Surgical Technique and Anesthetic Management**').

**Comment 6: Lack of multivariate analysis to confirm independence of effects.**

**Response:** We have transparently acknowledged this analytical choice as a limitation in the 'Statistical Analysis' section and the 'Study Limitations'. (Please see Response to R0.3 and **'Discussion – Study Limitations and Strengths**').

**Comment 7: Lack of mention of the type and dose of anesthetic drugs.**

**Response:** The ‘Methods’ section now provides full details of the anesthetic protocol, including specific drugs and dosages (Sodium Thiopental, fentanyl, atracurium, halothane). (Please see **'Patients and Methods – Surgical Technique and Anesthetic Management**').

**Associate Editor**

**Comment 1: The background could briefly mention why prone position may cause instability (e.g., compression on thoracic cavity, venous return issues).**

**Response:** We have enhanced the physiological rationale in both the **Abstract** and **Introduction**, explicitly mentioning mechanisms such as "thoracoabdominal compression, impeded venous return, and reduced pulmonary compliance."

**Comment 2: The term “matched for baseline characteristics” is vague — specify which variables were matched.**

**Response:** We have revised the text in the **Abstract** and **'Patients and Methods – Participants'** to specify the matched variables: "age, sex, body mass index, stone size, and American Society of Anesthesiologists (ASA) physical status (I or II)."

**Additional STROBE Checklist Items**

We confirm that the revised manuscript now addresses all items raised in the STROBE checklist review:

- **Eligibility Criteria & Participant Selection:** Added to the Abstract and detailed in the Methods.
- **Limitations:** Discussed in a dedicated subsection of the Discussion.
- **Confounder-Adjusted Estimates:** Clarified as unadjusted in the Statistical Analysis and table footnotes.
- **Setting Dates/Locations:** Specified in the Study Design and Setting.
- **Generalisability:** Discussed in the Limitations.
- **Funding:** A statement has been added to the manuscript: **"The authors have no sources of funding to declare for this manuscript."**

We believe that our thorough revisions have significantly strengthened the manuscript by enhancing its methodological transparency, contextualizing the findings within the current literature, and providing a balanced discussion of clinical implications and limitations. We are deeply grateful for the guidance provided and hope the revised manuscript is now suitable for publication.

Sincerely,

The Authors

## 2 Revision 1

3 comments · 28 Dec 2025 – 2 Jan 2026

### Referee 2 Reviewer

ACCEPT 28 Dec 2025

Dear AE,
I reviewed the revised version of manuscript ID 166868. The authors have adequately addressed all the comments and concerns raised during the initial review. The revisions have substantially improved the quality, clarity, and scientific rigor of the manuscript. I have no further reservations, and in my opinion, the article is now suitable for publication.

### Associate Editor

ACCEPT 30 Dec 2025

Dear EIC,
I reviewed the manuscript again. The substantial effort to improve the manuscript is highly appreciated.
The authors have addressed all comments.
Thank you

### Editor-in-Chief

ACCEPT 2 Jan 2026

Accept