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REVIEWER'S REPORT

Manuscript No.: IJAR-56749
Title: Predictors of Hemodynamic Complications in Pediatric Anesthesia: A Prospective Study with Multivariate

Recommendation:
Accept as it is .....
Accept after minor revision.....
Accept after major revision .....YES.....
Do not accept (*Reasons below*) .....

Rating	Excel.	Good	Fair	Poor
Originality		√		
Techn. Quality			√	
Clarity			√	
Significance		√		

Reviewer's ID: JPR-094

Detailed Reviewer's Report

Summary of the Study

This manuscript presents a **prospective observational study** of 470 pediatric patients evaluating the incidence and predictors of perioperative cardiovascular complications. The authors identify **ASA score and emergency surgery** as independent risk factors and propose a **risk stratification algorithm** for clinical use.

Major Strengths

1. Prospective Study Design

* The **prospective nature** enhances data reliability and reduces recall bias.
* Consecutive inclusion improves internal validity.

2. Adequate Sample Size

* Inclusion of **470 pediatric patients** provides good statistical power.

3. Clinically Relevant Topic

* Hemodynamic complications in pediatric anesthesia are highly important for **patient safety and perioperative management**.

4. Robust Statistical Analysis

* Use of:

  * Univariate + multivariate logistic regression
  * ROC curve (AUC = 0.936)
  * Model diagnostics (Hosmer-Lemeshow, collinearity)
* Indicates strong analytical rigor.

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5. Practical Risk Stratification Tool

* The proposed **simple scoring system (0–3 factors)** is:

  * Easy to apply clinically
  * Potentially useful in resource-limited settings

6. Identification of Independent Predictors

* Clear identification of:

  * **ASA score**
  * **Emergency surgery**
* These are clinically meaningful and actionable.

 # **Major Weaknesses**

1. Single-Center Study

* Limits **external validity and generalizability**.
* Results may not apply to other populations/settings.

2. Definition of Outcomes is Broad

* Inclusion of **all events requiring intervention** may:

  * Overestimate incidence (36.2%)
  * Limit comparison with studies reporting only severe events

3. Exclusion of Important Variable from Multivariate Model

* **Duration ≥2h excluded due to quasi-separation**

  * This is a key predictor but not fully modeled
  * Alternative statistical methods (e.g., penalized regression) should be considered

4. Lack of Temporal Relationship

* Cannot determine:

  * Whether complications caused prolonged surgery
  * Or prolonged surgery caused complications
    Raises **reverse causality bias**

5. Missing Important Confounders

* Not included:

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* Type of anesthesia agents
* Experience of anesthesiologist
* Intraoperative fluid management
  Limits model completeness

6. No Severity Stratification

* All complications treated equally
* No grading (mild/moderate/severe)

7. No External Validation of Risk Model

* The proposed algorithm is:

  * Not validated in an independent cohort
    Limits clinical adoption

 # **Minor Weaknesses**

* Formatting issues (line numbers, table structure)
* Duplicate reference (APRICOT study repeated)
* Grammar and language need minor editing
* No ethical approval statement mentioned
* No trial registration (if applicable)

 # **Key Points**

* High reported incidence (**36.2%**) due to broad definition
* Independent predictors:

  * ASA score (aOR = 2.54)
  * Emergency surgery (aOR = 2.22)
* Duration ≥2h shows extremely strong association but statistical limitation
* Proposed **risk algorithm (≥2 factors = very high risk)** is clinically useful
* Interesting but non-causal findings:

  * Female sex association (confounded)
  * Lower complications in anxious children

 # **Significance of the Study**

Clinical Significance

* Helps anesthesiologists:

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* Identify **high-risk pediatric patients**
* Optimize **perioperative monitoring**
* Improve **resource allocation**

Scientific Significance

* Adds data from **North African population**, which is underrepresented
* Supports existing evidence on **ASA and emergency surgery as key predictors**

Practical Impact

* The **risk stratification model** can be:

* Implemented at bedside
* Useful in **low-resource settings**

 # **Recommendations for Improvement**

Major Revisions Required

1. Include **severity grading of complications**
2. Address **duration variable issue** using:

* Penalized logistic regression (Firth method)
3. Add missing confounders if data available
4. Clarify **temporal relationship** of complications
5. Include **ethical approval statement**
6. Improve manuscript formatting

Suggested Additions

* External validation (if possible)
* Sensitivity analysis
* Subgroup analysis (age groups, surgery type)

 # **Final Recommendation**

Decision: MAJOR REVISION

The manuscript has **strong clinical relevance and good methodology**, but requires:

* Methodological clarification
* Statistical refinement
* Improved presentation

before it is suitable for publication.

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Optional Editorial Comment

The study is promising and clinically meaningful, particularly due to its practical risk stratification tool. However, methodological limitations and lack of external validation must be addressed to strengthen its impact and reliability.

 # **Reviewer Report – Major Revision Justification**

**Overall Decision: MAJOR REVISION**

The manuscript addresses an important clinical topic with a good dataset and promising findings. However, **significant methodological, analytical, and reporting issues** must be addressed before the manuscript can be considered for publication.

Line-by-Line Reviewer Comments

TITLE & ABSTRACT

Lines 1–5 (Title formatting)

* Issue: Title contains numbering artifacts ("2, 3, 4, 5").
* Justification: Indicates poor manuscript preparation.
* Recommendation: Remove formatting errors and standardize title.

Lines 10–13 (Methods in abstract)

* Issue: "complete diagnostics" is vague.
* Justification: Lacks clarity on what diagnostics were performed.
* Recommendation: Specify (e.g., ROC analysis, goodness-of-fit tests).

Lines 15–16 (Incidence 36.2%)

* Issue: Very high incidence compared to literature.
* Justification: Likely due to **broad definition of complications**.
* Recommendation: Clarify definition and consider stratification by severity.

Lines 16–18 (Univariate analysis – OR = 163.9)

* Issue: Extremely high OR suggests **statistical instability or separation bias**.
* Justification: Raises concerns about model validity.
* Recommendation: Apply penalized regression (e.g., Firth method).

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Lines 18–19 (Multivariate model)

* Issue: Important variable (duration ≥2h) excluded.
* Justification: Weakens model completeness.
* Recommendation: Use alternative modeling to include this predictor.

□ Line 20 (AUC = 0.936)

* Issue: Very high AUC without validation.
* Justification: Risk of **overfitting**.
* Recommendation: Add internal validation (bootstrapping/cross-validation).

Lines 21–23 (Sex-based findings)

* Issue: Interpretation may be misleading.
* Justification: Confounding not fully controlled.
* Recommendation: Clearly state non-causality and adjust analysis.

INTRODUCTION

Lines 34–36

* Issue: Limited literature review.
* Justification: Lacks recent/global evidence.
* Recommendation: Add updated references and expand rationale.

METHODS

Lines 40–42 (Study design)

* Issue: Single-center design.
* Justification: Limits generalizability.
* Recommendation: Acknowledge explicitly in methods and discussion.

Lines 44–47 (Definition of complications)

* Issue: Broad composite outcome.
* Justification:

  * Includes mild + severe events together
  * Inflates incidence
* Recommendation:

  * Add **severity grading (mild/moderate/severe)**

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* Report separately

Line 48 (Duration ≥2h)

* Issue: Arbitrary cutoff.
* Justification: No justification or citation provided.
* Recommendation: Provide rationale or sensitivity analysis.

Lines 49–51 (Statistical analysis)

* Issue:

  * No mention of **sample size calculation**
  * No handling of missing data
* Justification: Weak methodological transparency.
* Recommendation:

  * Add sample size justification
  * Describe missing data handling

Line 52 (Software)

* Issue: Excessive detail (Python version not necessary).
* Recommendation: Simplify (mention software only).

RESULTS

Line 59 (No cardiac arrest)

* Issue: Important but under-discussed.
* Recommendation: Highlight clinical relevance.

Table 1 (Lines 60–61)

* Issue: Poor formatting.
* Recommendation: Reformat as per journal guidelines.

Lines 62–63 (Univariate analysis)

* Issue: Extremely high OR (163.9).
* Justification:

  * Suggests quasi-complete separation

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* Recommendation:

  * Reanalyze using penalized regression

Lines 64–66 (Multivariate model)

* Issue: Exclusion of duration variable.
* Justification:

  * Major predictor omitted → biased model
* Recommendation:

  * Use Firth logistic regression or exact methods

Line 68 (AUC = 0.936)

* Issue: No validation performed.
* Justification: Overestimation of predictive ability.
* Recommendation:

  * Perform internal validation

DISCUSSION

Lines 86–89 (Comparison with literature)

* Issue: Comparison not fully balanced.
* Justification:

  * Different definitions used
* Recommendation:

  * Emphasize heterogeneity in definitions

Lines 91–94 (Risk factors)

* Issue: Overinterpretation of duration variable.
* Justification:

  * Not included in multivariate model
* Recommendation:

  * Interpret cautiously

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Lines 95–103 (Sex and anxiety findings)

* Issue:

  * Speculative explanations
* Justification:

  * No supporting analysis
* Recommendation:

  * Clearly label as hypothesis

Lines 104–107 (Risk algorithm)

* Issue: No validation of model.
* Justification:

  * Limits clinical applicability
* Recommendation:

  * Add validation or clearly state limitation

Lines 109–112 (Causality)

* Strength: Limitation acknowledged
* Issue: Not sufficiently addressed analytically
* Recommendation: Add time-based analysis if possible

Lines 113–115 (Limitations)

* Issue: Missing key limitations:

  * No ethical approval mention
  * No confounder adjustment
* Recommendation: Expand limitations section

CONCLUSION

Lines 117–121

* Issue: Overstated conclusions.
* Justification:

  * Model not validated
* Recommendation:

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* Tone down claims

REFERENCES

Lines 125–142

* Issues:

* Duplicate reference (APRICOT)
* Old references

* Recommendation:

* Update and correct references

Key Reasons for MAJOR REVISION

1. **Statistical concerns**

* Quasi-separation bias
* Exclusion of key variable
* No validation

2. **Outcome definition issues**

* Overestimation of incidence

3. **Model reliability concerns**

* High AUC without validation
* No external validation

4. **Methodological gaps**

* Missing confounders
* No sample size calculation

5. **Presentation issues**

* Formatting errors
* Reference issues

Final Recommendation

Decision: MAJOR REVISION REQUIRED
The manuscript has:

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* Strong clinical relevance
* Good dataset

BUT requires:

* **Substantial statistical correction**
* **Improved methodological transparency**
* **Better reporting and validation**

before it can be accepted.