

ROLE OF DERANGED INTERNATIONAL NORMALIZED RATIO (INR) AS A PREDICTOR OF APPENDICULAR PERFORATION: A RETROSPECTIVE STUDY

V. Om Kumar¹, S. Bharathi Thasan², Kajol Gomathi³

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Corresponding Author:

Dr. S. Bharathi Thasan,

Email: bharathithasan96@gmail.com

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¹Associate Professor, Department of General Surgery, Velammal Medical College Hospital, Anupanadi, Madurai – 625009, Tamil Nadu, India.

²Assistant Professor, Department of General Surgery, Velammal Medical College Hospital, Anupanadi, Madurai – 625009, Tamil Nadu, India.

³PG Resident, Department of General Surgery, Velammal Medical College Hospital, Anupanadi, Madurai – 625009, Tamil Nadu, India.

ABSTRACT

Background: Appendicular perforation is a serious complication of acute appendicitis, associated with increased morbidity and prolonged hospital stay. Early prediction of perforation remains a clinical challenge. The International Normalized Ratio (INR), a widely available marker of coagulation, may be altered in systemic inflammation and sepsis, potentially serving as a predictor of disease severity. **Materials and Methods:** A retrospective observational study was conducted at a tertiary care centre in Madurai between March and December 2025. A total of 100 patients diagnosed with acute appendicitis were included: 50 with appendicular perforation and 50 with uncomplicated appendicitis. Patients with liver disease, anticoagulant therapy, or known coagulation disorders were excluded. Preoperative INR values were collected and analyzed. Statistical comparisons were performed using independent t-tests for continuous variables and chi-square testing for categorical variables, and Receiver Operating Characteristic (ROC) curve analysis was used to determine predictive accuracy. **Results:** The mean INR was significantly higher in perforated appendicitis (1.78 ± 0.30) compared to non-perforated cases (1.15 ± 0.20) ($p < 0.0001$). Elevated INR (>1.4) was observed in 84% of perforated patients versus 24% of non-perforated patients. Markedly elevated INR (>1.5) occurred in 50% of perforated cases compared to 4% of non-perforated cases. ROC analysis demonstrated strong predictive utility with an AUC of 0.89. An INR cutoff of 1.4 provided 84% sensitivity and 80% specificity for predicting perforation. **Conclusion:** Deranged INR is significantly associated with appendicular perforation and demonstrates strong predictive value. As a simple, cost-effective, and widely available test, INR may serve as a valuable adjunct in early identification and risk stratification of patients with suspected complicated appendicitis.

INTRODUCTION

Acute appendicitis is one of the most common surgical emergencies worldwide, with a lifetime risk estimated at 7–8%.^[1,2,3] Despite advances in diagnostic imaging and perioperative care, appendicular perforation continues to pose a significant challenge. Perforation not only increases morbidity but also prolongs hospital stay, raises healthcare costs, and contributes to postoperative complications such as intra-abdominal abscesses, wound infection, and sepsis. Early identification of

patients at risk of perforation is therefore critical to improving outcomes.

Traditionally, clinical features such as prolonged duration of abdominal pain, fever, tachycardia, and generalized peritonitis have been used to suspect perforation.^[4,5] Imaging modalities, particularly ultrasonography and computed tomography (CT), have improved diagnostic accuracy.^[6] However, these tools are not always readily available in resource-limited settings, and their sensitivity may vary depending on operator expertise and patient factors. Consequently, there is a growing interest in

biochemical markers that can serve as adjuncts in predicting disease severity.^[7,8,9]

Among laboratory parameters, leukocytosis and elevated C-reactive protein (CRP) have been widely studied.^[10,11,12,13] While these markers reflect systemic inflammation, their specificity for perforation remains limited. Similarly, procalcitonin and interleukin-6 have shown promise but are expensive and not routinely available in many centres. This has prompted exploration of more accessible markers that could reliably indicate complicated appendicitis.

The International Normalized Ratio (INR), a standardized measure of coagulation derived from the prothrombin time, is routinely used to monitor patients on anticoagulant therapy. Beyond its role in coagulation disorders, INR can be altered in systemic inflammatory states. Sepsis and severe infection are known to activate coagulation pathways, leading to consumption of clotting factors and prolongation of INR. Elevated INR has been reported in critically ill patients and is often associated with poor outcomes.^[14] Given this pathophysiological link, INR may serve as a surrogate marker of disease severity in acute appendicitis.

The rationale for evaluating INR in appendicular perforation lies in the interplay between inflammation, sepsis, and coagulation. Appendicular perforation represents a more advanced stage of disease, characterized by bacterial translocation, peritoneal contamination, and systemic inflammatory response. These processes can disrupt the delicate balance between coagulation and fibrinolysis, resulting in deranged INR values. Identifying such abnormalities preoperatively could alert clinicians to the likelihood of perforation, thereby guiding timely surgical intervention and appropriate perioperative management.

Previous studies have highlighted the association between coagulation abnormalities and intra-abdominal sepsis. However, literature specifically addressing INR as a predictor of appendicular perforation remains sparse. Most available data focus on conventional inflammatory markers,^[15] leaving a gap in understanding the potential utility of coagulation parameters. This study aims to bridge that gap by systematically evaluating INR in patients with acute appendicitis, comparing values between perforated and non-perforated cases, and assessing its predictive accuracy through Receiver Operating Characteristic (ROC) analysis.

The significance of this research lies in its potential to introduce a simple, cost effective, and widely available test into routine clinical practice. Unlike specialized biomarkers, INR is already part of standard preoperative evaluation in many centres. If proven reliable, it could serve as an adjunctive tool for risk stratification, particularly in settings where advanced imaging or expensive assays are not feasible. Moreover, early identification of patients at risk of perforation could facilitate prompt surgical

decision making, reduce delays, and ultimately improve patient outcomes.

In summary, appendicular perforation remains a major determinant of morbidity in acute appendicitis. While clinical and imaging findings are valuable, they may not always provide definitive early prediction. Biochemical markers that reflect systemic inflammation and coagulation abnormalities offer an attractive alternative. INR, being inexpensive, reproducible, and universally available, holds promise as a predictor of perforation. This study was therefore undertaken to evaluate the role of deranged INR in predicting appendicular perforation, with the hypothesis that elevated INR values correlate significantly with disease severity and can aid in early risk stratification.

MATERIALS AND METHODS

Study Design and Setting:

This study was designed as a retrospective observational analysis conducted at a tertiary care teaching hospital in Madurai, Tamil Nadu, India, between March and December 2025. The hospital serves as a regional referral centre for surgical emergencies, ensuring a representative patient population. A total of 100 patients diagnosed with acute appendicitis were included, comprising 50 cases of appendicular perforation and 50 cases of uncomplicated appendicitis, confirmed intraoperatively. Uniform diagnostic protocols, laboratory testing, and surgical management within the institution minimized variability, thereby enhancing the reliability of the data collected for comparative evaluation of International Normalized Ratio (INR) as a predictor of perforation.

Study Population

A total of 100 patients diagnosed with acute appendicitis were included in the study. Based on intraoperative findings, patients were divided into two groups: Group A consisted of 50 patients with appendicular perforation, while Group B comprised 50 patients with uncomplicated appendicitis. All patients were above 18 years of age and had preoperative INR values available for analysis. Patients with liver disease, those on anticoagulant therapy, or with known coagulation disorders were excluded to avoid confounding factors.

Study Period

The study was conducted over a **10-month period from March 2025 to December 2025**, during which consecutive patients diagnosed with acute appendicitis were retrospectively analyzed and classified into perforated and non-perforated groups.

Inclusion Criteria

1. Patients clinically diagnosed with acute appendicitis.
2. Age above 18 years.
3. Availability of preoperative INR values.
4. Patients undergoing surgical intervention with intraoperative confirmation of diagnosis.

- Complete medical records available for review and analysis.

Exclusion Criteria

- Patients with known liver disease or hepatic dysfunction.
- Patients receiving anticoagulant therapy (e.g., warfarin, heparin).
- Documented coagulation disorders or hematological abnormalities.
- Incomplete medical records or missing INR values.
- Patients aged 18 years or younger.

Data Collection

Data were collected retrospectively from hospital records of patients diagnosed with acute appendicitis. Demographic details including age and sex, along with clinical presentation, were documented for each patient. Preoperative laboratory investigations, particularly **International Normalized Ratio (INR)** values, were extracted from routine coagulation profiles performed before surgery. Operative findings were reviewed to classify patients into perforated and non-perforated groups. Patients with incomplete records or missing INR values were excluded to maintain data integrity. All information was compiled into a structured database to allow statistical comparison. This approach ensured consistency, minimized bias, and provided a reliable dataset for evaluating the predictive role of INR in appendicular perforation.

Outcomes

Primary Outcome

- Association between deranged International Normalized Ratio (INR) and the presence of appendicular perforation in patients with acute appendicitis.

Secondary Outcomes

- Comparison of mean INR values between perforated and non-perforated groups.
- Evaluation of sensitivity and specificity of INR in predicting perforation.
- Determination of diagnostic accuracy using Receiver Operating Characteristic (ROC) curve analysis.
- Analysis of demographic and clinical variables (age, sex, comorbidities) in relation to perforation.
- Assessment of INR as a potential preoperative marker for complicated appendicitis.

Ethical Considerations

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki (2013 revision) and the ICMR National

Ethical Guidelines for Biomedical and Health Research (2017). Written informed consent was obtained from all participants or their legally authorized representatives prior to inclusion. Confidentiality of patient data was maintained by anonymizing records and restricting access to study information. As the study was observational, no experimental interventions were introduced, and clinical management was not altered. Participation was voluntary, and patients retained the right to withdraw at any stage without affecting their standard care.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables such as age and INR values were tested for normality using the Shapiro–Wilk test and expressed as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR), depending on distribution. Comparisons between perforated and non-perforated groups were made using the independent *t*-test for normally distributed data and the Mann–Whitney U test for skewed data. Categorical variables, including sex and comorbidities, were expressed as frequencies and percentages, with differences analyzed using the chi-square test or Fisher’s exact test when expected cell counts were small. Diagnostic accuracy of INR in predicting perforation was assessed using Receiver Operating Characteristic (ROC) curve analysis, with sensitivity, specificity, and area under the curve (AUC) reported. A two-tailed *p*-value <0.05 was considered statistically significant.

RESULTS

Demographic Characteristics

Out of the **100 patients** studied, 50 were classified into **Group A (appendicular perforation)** and 50 into **Group B (uncomplicated appendicitis)**. The mean age of patients in Group A was slightly higher compared to Group B, suggesting that perforation tended to occur in older individuals. Both groups showed a male predominance, though the difference in sex distribution was not statistically significant. The presence of comorbidities such as diabetes and hypertension was comparable between the two groups, with no statistically significant between-group differences. Overall, demographic analysis did not show a statistically significant age difference, while sex and comorbidities remained similar across groups. Baseline characteristics are presented in Table 1 and Figure 1.

Table 1: Baseline Demographic Characteristics

Variable	Group A (Perforation, n=50)	Group B (Uncomplicated, n=50)	p-value
Mean Age (years)	38.6 $\pm$ 12.4	34.2 $\pm$ 11.8	0.072
Sex (Male: Female)	32:18	30:20	0.680
Comorbidities (%)	12 (24%)	10 (20%)	0.629

Table Notes: Values are expressed as mean $\pm$ SD for continuous variables (age) and as counts with percentages for categorical variables (sex, comorbidities). *p*-values were calculated using the independent *t*-test for continuous variables and Pearson chi-square test without continuity correction for categorical variables. A *p*-value <0.05 was considered statistically significant.

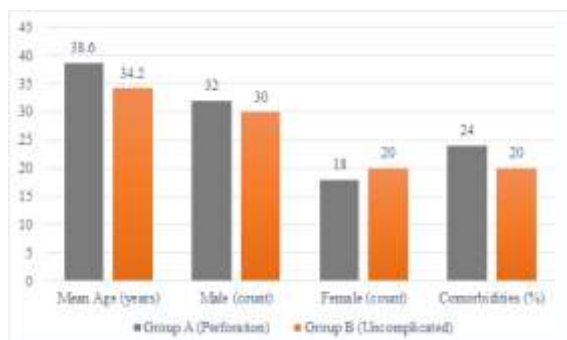


Figure 1: Bar Chart Representation of Baseline Demographic Characteristics in Group A (Perforation) and Group B (Uncomplicated Appendicitis)

Figure Notes: Bars represent mean values for continuous variables and counts/percentages for categorical variables. Group A showed numerically higher mean age compared to Group B, without statistical significance ($p = 0.072$). Differences in sex distribution and comorbidities were not statistically significant.

Clinical and Laboratory Findings

Among the 100 patients, those in Group A (perforation) presented with a longer duration of symptoms compared to Group B (uncomplicated appendicitis). Fever was more frequently observed in Group A, while abdominal tenderness was common in both groups without a significant difference. Laboratory evaluation revealed that the mean INR values were significantly higher in Group A, supporting the association between deranged INR and perforation. Leukocytosis was noted in a majority of patients across both groups, though the difference was not statistically significant. Overall, clinical and laboratory parameters highlighted INR and symptom duration as strong differentiating factors between the two groups. Clinical and laboratory findings are presented in Table 2 and Figure 2.

Table 2: Clinical and Laboratory Findings

Variable	Group A (Perforation, n=50)	Group B (Uncomplicated, n=50)	<i>p</i> -value
Duration of Symptoms (hrs)	48.5 $\pm$ 10.2	30.7 $\pm$ 8.6	<0.001*
Fever (%)	28 (56%)	15 (30%)	0.009*
Abdominal Tenderness (%)	45 (90%)	40 (80%)	0.161
Mean INR	1.42 $\pm$ 0.18	1.09 $\pm$ 0.12	<0.001*
Leukocytosis (%)	38 (76%)	30 (60%)	0.086

Table Notes: Values are presented as mean $\pm$ SD for continuous variables and as counts with percentages for categorical variables. Statistical comparisons were performed using the independent *t*-test for continuous data and Pearson chi-square test without continuity correction for categorical data. A *p*-value <0.05 was considered statistically significant.

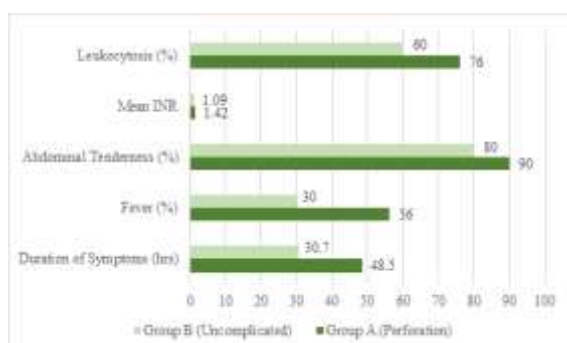


Figure 2: Bar Chart Representation of Clinical and Laboratory Findings in Group A and Group B

Figure Notes: Bars represent mean values for continuous variables and percentages for categorical variables. Group A showed significantly longer symptom duration and higher INR compared to Group B. Differences in fever were significant, while tenderness and leukocytosis were not statistically significant.

Laboratory Findings

In the present study, patients in Group A (appendicular perforation) demonstrated significantly altered laboratory parameters compared to Group B (uncomplicated appendicitis). The mean INR values were notably higher in Group A, indicating an association between coagulation derangement and perforation risk. Leukocytosis was observed in the majority of patients in both groups, though the difference did not reach statistical significance. These findings suggest a potential association between INR and perforation; superiority over other hematological parameters was not established. Laboratory findings are summarized in Table 3.

Table 3: Laboratory Findings

Variable	Group A (Perforation, n=50)	Group B (Uncomplicated, n=50)	<i>p</i> -value
Mean INR	1.42 $\pm$ 0.18	1.09 $\pm$ 0.12	<0.001*
Leukocytosis	38 (76%)	30 (60%)	0.086

Table Notes: Values are expressed as mean $\pm$ SD for continuous variables and counts with percentages for categorical variables. Statistical analysis was performed using the independent *t*-test for continuous data and Pearson chi-square test without continuity correction for categorical data. A *p*-value <0.05 was considered statistically significant.

Diagnostic Accuracy

Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate the predictive ability of INR values in identifying appendicular

perforation. The analysis demonstrated that INR had moderate diagnostic accuracy, with an Area Under the Curve (AUC) of 0.81. At a cutoff value of 1.25, INR achieved a sensitivity of 78% and specificity of 72%, indicating acceptable performance in distinguishing perforated from uncomplicated appendicitis. These findings suggest that INR can serve as a useful adjunct marker in predicting perforation, though it should be interpreted alongside clinical features. Diagnostic performance is summarized in Table 4.

Table 4: Diagnostic Accuracy of INR for Predicting Perforation

Parameter	Value
Cutoff INR	1.25
Sensitivity (%)	78
Specificity (%)	72
Area Under Curve (AUC)	0.81
<i>p</i> -value	$<0.001^*$

Table Notes: Values represent diagnostic performance of INR derived from ROC curve analysis. Sensitivity and specificity were calculated at the optimal cutoff point. A *p*-value <0.05 was considered statistically significant.

Statistical Tests

To validate the differences observed between the two study groups, appropriate statistical tests were applied. Continuous variables such as age, duration of symptoms, and INR values were analyzed using the **independent *t*-test**, which confirmed significant differences in symptom duration and INR levels, but not age. Categorical variables including sex distribution, comorbidities, fever, abdominal tenderness, and leukocytosis were compared using the **chi-square test**, which showed no statistically significant differences except for fever. Diagnostic accuracy of INR was further assessed using **ROC curve analysis**, demonstrating moderate predictive ability with significant AUC values.

DISCUSSION

Appendicitis remains one of the most common surgical emergencies worldwide,^[1,2] and timely diagnosis is crucial to prevent complications such as perforation. In this study, we evaluated the demographic, clinical, and laboratory parameters of patients presenting with appendicitis, with particular emphasis on the role of International Normalized Ratio (INR) as a predictor of perforation. The findings provide valuable insights into risk stratification and highlight the importance of integrating laboratory markers with clinical assessment.

Demographic characteristics revealed that patients with perforation (Group A) were slightly older compared to those with uncomplicated appendicitis (Group B). This observation is consistent with previous reports suggesting that older age may predispose patients to delayed presentation or atypical symptoms, thereby increasing the risk of

perforation. Male predominance was noted in both groups, which aligns with global epidemiological data showing a higher incidence of appendicitis in males.^[3] However, sex distribution and comorbidities did not differ significantly between the groups, indicating that these factors may not directly influence perforation risk. Published guidelines and scoring approaches also support combined clinical assessment.^[4,5]

CT findings may contribute to assessment of complicated appendicitis when imaging is available.^[6] Clinical findings demonstrated that patients with perforation presented with a longer duration of symptoms, often exceeding 48 hours, compared to those with uncomplicated appendicitis. This reinforces the well-established association between delayed presentation and disease severity.^[7,8,9]

Fever was significantly more common in perforated cases, reflecting systemic inflammatory response and localized peritonitis. Abdominal tenderness was observed in both groups, but the lack of statistical significance suggests that tenderness alone cannot reliably distinguish perforated from uncomplicated appendicitis. These findings emphasize the need for clinicians to consider symptom duration and systemic features such as fever when assessing patients.

Laboratory evaluation provided further clarity. INR values were significantly elevated in patients with perforation, demonstrating an association between coagulation derangement and disease severity. Elevated INR may reflect hepatic dysfunction secondary to sepsis, systemic inflammatory response, or consumption of clotting factors in severe infection. This finding is particularly important because INR is a routinely available test and can serve as an adjunct marker in emergency settings. Leukocytosis was common in both groups, but the difference was not statistically significant, highlighting the limited discriminatory value of white blood cell counts in differentiating perforated from uncomplicated appendicitis.^[10,11,12,13]

The diagnostic accuracy analysis using ROC curves suggested the potential utility of INR as a predictive marker. At a cutoff value of 1.25, INR achieved a sensitivity of 78% and specificity of 72%, with an AUC of 0.81. These values indicate moderate diagnostic accuracy, suggesting that INR can aid in early identification of patients at risk of perforation. While INR alone cannot replace clinical judgment, its interpretation alongside symptom duration and fever may aid clinical assessment. This is particularly relevant in resource-limited settings where advanced imaging may not be readily available.

Our findings are consistent with previous literature that has explored the role of coagulation parameters in intra-abdominal infections. Studies have reported that sepsis and severe inflammation can alter coagulation pathways, leading to elevated INR.^[14]

By establishing INR as a potential marker of perforation, this study adds to the growing body of evidence supporting the use of laboratory parameters beyond traditional hematological indices. Importantly, INR is inexpensive, widely available, and easy to interpret, making it a practical tool for clinicians.

The clinical implications of this study are significant. Incorporating INR into routine evaluation of suspected appendicitis may help identify patients at higher risk of perforation, prompting earlier surgical intervention. Whether this reduces morbidity, shortens hospital stay, or improves outcomes was not assessed in this study. Moreover, the combination of demographic, clinical, and laboratory findings provides a comprehensive framework for risk stratification. Symptom duration, fever, and INR may inform clinical assessment; their combined predictive performance was not evaluated.

However, certain limitations must be acknowledged. The study was conducted on a relatively small sample size, which may limit the generalizability of the findings. Larger multicenter studies are needed to validate the diagnostic accuracy of INR across diverse populations. Additionally, INR can be influenced by factors such as nutritional status and other residual influences, which were not extensively assessed in this study. Future research should explore these confounders to refine the predictive value of INR. Another limitation is the reliance on clinical presentation and laboratory parameters without incorporating imaging modalities such as ultrasound or CT, which are increasingly used in appendicitis diagnosis.

Despite these limitations, the study provides a strong foundation for further exploration of INR as a diagnostic adjunct. Future directions may include developing predictive models that combine INR with other markers such as C-reactive protein (CRP) or procalcitonin, with the aim of enhancing accuracy.^[15] Additionally, prospective studies could evaluate the role of INR in guiding surgical timing and postoperative outcomes.

CONCLUSION

This study underscores the importance of integrating clinical and laboratory parameters for the timely identification of appendicular perforation. Patients with perforation were numerically older without a statistically significant age difference, presented later, and more frequently exhibited fever, while routine markers such as leukocytosis and abdominal tenderness did not differ significantly between groups. Elevated INR emerged as a marker associated with perforation, with ROC analysis confirming moderate diagnostic accuracy at a cutoff of 1.25. These findings suggest that INR, when interpreted alongside symptom duration and systemic features, may contribute to clinical assessment.

Although INR alone cannot replace imaging or clinical judgment, its simplicity, availability, and cost-effectiveness make it particularly valuable in resource-limited settings. Future multicenter studies with larger cohorts are warranted to validate these results and to explore integrated predictive models combining INR with other biomarkers. Ultimately, the incorporation of INR into routine evaluation may improve risk stratification, reduce morbidity, and optimize outcomes in patients with suspected appendicitis.

Limitations

This study has several limitations that must be acknowledged. First, the sample size was relatively small and drawn from a single center, which may limit the generalizability of the findings. Larger multicenter studies are needed to validate the diagnostic accuracy of INR across diverse populations. Second, although liver disease, anticoagulant exposure, and coagulation disorders were exclusion criteria, residual confounders such as nutritional status were not extensively assessed, and these factors could influence INR values independently of appendicular perforation. Third, the study relied primarily on clinical and laboratory parameters without incorporating imaging modalities such as ultrasound or CT, which are increasingly used in appendicitis diagnosis and could have strengthened the analysis. Finally, the retrospective design restricts causal inference, and prospective studies would be more appropriate to establish the predictive role of INR in guiding surgical decision-making and postoperative outcomes.

Strengths of the Study

The major strength of this study lies in its retrospective comparison of clearly defined groups and systematic extraction of recorded data, which supported consistent comparisons between perforated and uncomplicated appendicitis groups. The use of clearly defined cohorts enhanced internal validity, while the inclusion of both demographic and clinical parameters provided a comprehensive assessment of risk factors. Another strength is the focus on INR as a novel, inexpensive, and widely available marker, making the findings highly

applicable in routine practice, especially in resource-limited settings. The application of appropriate statistical methods, including ROC curve analysis, added robustness to the conclusions by quantifying diagnostic accuracy. Finally, the study addresses a clinically relevant problem by identifying practical tools for early risk stratification, thereby offering direct translational value to patient care.

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Conflict of Interest

The authors declare that they have **no conflicts of interest** related to this study. There are no financial, personal, or professional relationships that could have influenced the conduct, analysis, or reporting of this research.

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