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Association of Serum C-Reactive Protein with Intraoperative Findings in Acute Appendicitis: A Prospective Observational Study from a Tertiary Care Centre

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ABSTRACT

Background: Preoperative assessment of disease severity in acute appendicitis remains challenging. C-reactive protein (CRP) may provide additional information on the extent of appendiceal inflammation. This study evaluated the association of CRP with intraoperative disease severity and its relationship with the Alvarado score, total leukocyte count and sonographic appendiceal diameter.

Methods: This prospective observational study included 70 consecutive patients aged >10 years undergoing appendectomy at a tertiary care hospital in Jodhpur, India. Preoperative CRP, total leukocyte count, ultrasonography and Alvarado score were recorded. Intraoperative findings classified disease as mild, moderate or severe. The Kruskal–Wallis, Spearman's correlation and Fisher–Freeman–Halton exact tests were used as appropriate.

Results: The mean age was 41.80 ± 17.50 years, with 58 (82.86%) males. Mild, moderate and severe disease occurred in 22, 23 and 25 patients, respectively. Alvarado score, CRP, total leukocyte count and sonographic diameter increased significantly with severity (all $p < 0.0001$). Mean CRP was 21.45 ± 12.23, 70.43 ± 18.76 and 116.76 ± 20.44 in mild, moderate and severe disease, respectively. CRP differed significantly across intraoperative diagnoses ($H = 52.858$, $df = 7$, $p < 0.001$) and correlated with Alvarado score ($r = 0.593$), total leukocyte count ($r = 0.809$) and sonographic variables ($r = 0.800$; all $p < 0.0001$). Gender was significantly associated with severity ($p = 0.001$).

Conclusion: CRP increased with intraoperative severity and correlated with clinical, laboratory, and sonographic parameters. It may be a useful adjunct for preoperative severity assessment.

Keywords*: Acute appendicitis; Alvarado score; C-reactive protein; Disease severity; Leukocyte count; Ultrasonography.*

INTRODUCTION

Acute appendicitis is one of the most common surgical emergencies worldwide. Timely diagnosis and appropriate management are important because the risk of rupture increases with prolonged untreated symptoms. In one study, the risk of rupture was ≤2% among patients with less than 36 hours of untreated symptoms and increased to approximately 5% during each subsequent 12-hour period (Bickell et al., 2006). However, in patients with an equivocal diagnosis in whom advanced appendicitis is considered less likely, a correct diagnosis may be more important than simply achieving a rapid diagnosis (Andersson, 2007). Therefore, accurate identification of patients with advanced appendicitis remains clinically important.

Diagnosis is primarily based on clinical history and physical examination, although diagnostic uncertainty may persist even with the use of imaging and laboratory investigations. Imaging is frequently incorporated into the evaluation of suspected appendicitis. In a prospective comparison, ultrasonography and unenhanced multidetector computed tomography demonstrated comparable diagnostic performance, although ultrasonography resulted in more inconclusive examinations

(Keyzer et al., 2005). In another prospective study of 125 patients, an appendiceal diameter of ≥6 mm was the most accurate ultrasonographic finding, while leukocytosis and C-reactive protein (CRP) were also evaluated as laboratory markers (Kessler et al., 2004). Clinical history, physical findings, and inflammatory parameters have also been assessed for their diagnostic value, with no single variable demonstrating sufficient accuracy to serve as a definitive diagnostic test (Andersson et al., 1999). The Alvarado score has been evaluated both alone and in combination with biological markers such as CRP, procalcitonin, and neopterin, with the addition of these markers improving its diagnostic performance (Dal et al., 2019). Similarly, normal inflammatory marker values may help exclude acute appendicitis; in one prospective study, the combination of normal white cell count and CRP had a negative predictive value of 100% (Sengupta et al., 2009).

C-reactive protein (CRP) is an acute-phase inflammatory marker that is inexpensive and widely available. Its diagnostic usefulness in acute appendicitis has been investigated, although its performance as a standalone early diagnostic test may be limited (Jangjoo et al., 2011). The predictive value of CRP also varies with the duration of symptoms. In a retrospective study of 568 patients, different CRP cut-off values according to the first, second, and third days after symptom onset were identified for distinguishing acute appendicitis and perforated appendicitis from other acute abdominal conditions (Wu et al., 2005). Higher preoperative CRP levels have also been associated with more severe appendicitis, particularly gangrenous or necrotic disease, and with an increased risk of postoperative complications (Shelton et al., 2014; Yokoyama et al., 2009).

However, evidence directly examining the relationship between preoperative CRP and specific intraoperative findings, particularly when considered alongside routinely available clinical, laboratory and sonographic parameters, remains limited. Therefore, the present study was undertaken to assess the association of serum CRP with intraoperative findings and complications of acute appendicitis, including appendicular perforation, abscess and gangrenous changes, and to examine its relationship with the Alvarado score, total leukocyte count and sonographic appendiceal diameter.

MATERIALS AND METHODS

Study design and setting

This prospective observational study was conducted in the Department of General Surgery, Mathura Das Mathur Hospital, affiliated with Dr. S. N. Medical College, Jodhpur, India, over a period of approximately 3 months, from May 2025 to the first week of August 2025.

Participants

Consecutive patients aged >10 years with a clinical diagnosis of acute appendicitis who underwent emergency or elective laparoscopic or open appendectomy were eligible for inclusion. Patients aged <10 years, pregnant women, and those with comorbidities that could affect CRP levels, including inflammatory bowel disease, rheumatoid arthritis, and osteomyelitis, were excluded.

Sample Size

The sample size was calculated to compare two independent means, assuming a 5% alpha error and 80% power. A pooled standard deviation of CRP of 32 and a minimum difference of 27 in CRP between mild and severe appendicitis were derived from a previously published study (Xharra et al., 2012), resulting in a minimum sample size of 22 patients per severity group (66 patients in total). A total of 70 patients were enrolled.

Data Collection

After admission, a detailed history and physical examination were performed. Before surgery, blood samples were collected for quantitative serum C-reactive protein (CRP) and complete hemogram, including total and differential leukocyte counts. Abdominal ultrasonography was performed to measure appendiceal diameter, and the Alvarado score was calculated for each patient. Computed tomography was performed only in selected patients. Intraoperative findings were recorded and evaluated in relation to the preoperative CRP level.

Disease severity was classified intraoperatively as follows: *mild*, a swollen and inflamed appendix without complications; *moderate*, a swollen and inflamed appendix adherent to surrounding structures, including the caecal wall, omentum, or peritoneum; and *severe*, perforated or gangrenous appendicitis or appendicular abscess.

Outcome Measures

The primary outcome was the association between preoperative serum C-reactive protein (CRP) level and intraoperative severity of acute appendicitis, including mild, moderate and severe disease and specific intraoperative findings such as appendicular perforation, abscess and gangrenous appendicitis. The secondary outcomes were the correlations of preoperative CRP with the Alvarado score, total leukocyte count and sonographic appendiceal diameter. The association between gender and intraoperative disease severity was also assessed.

Statistical Analysis

Data were entered into a spreadsheet and analysed using SPSS version 21 (IBM Corp., Armonk, NY, USA). Categorical variables are presented as number (percentage), while continuous variables are presented as mean ± standard deviation (SD) and median. The Kruskal–Wallis test was used to compare continuous variables across three or more groups, and Spearman's rank correlation was used to assess relationships between CRP and other variables. The Fisher–Freeman–Halton exact test was used to assess the association between gender and disease severity because several expected cell counts were <5. A p value <0.05 was considered statistically significant.

Ethical Considerations

The study was conducted after obtaining approval from the Institutional Ethics Committee of Dr. S. N. Medical College, Jodhpur, India. Written informed consent was obtained from all participants before enrolment. Patient confidentiality was maintained throughout the study, and the collected information was used solely for research purposes. Participation was voluntary, and participants were informed of their right to withdraw from the study at any stage without affecting their treatment.

RESULTS

Patient Characteristics

A total of 70 patients were included, with a mean age of 41.80 ± 17.50 years and a median age of 43.50 years. Most patients were male (58; 82.86%). Disease severity was classified as severe in 25 patients (35.71%), moderate in 23 (32.86%), and mild in 22 (31.43%). The mean Alvarado score was 6.32 ± 1.86, mean CRP level was 71.58 ± 42.94, mean total leukocyte count was 14,087.55 ± 7,706.90, and mean sonographic appendiceal diameter was 8.50 ± 2.98 mm.

On intraoperative assessment, acute appendicitis with a mildly inflamed appendix was the most frequent finding (21; 30.0%), followed by phlegmonous appendicitis (17; 24.3%) and appendicular perforation (15; 21.4%). The remaining intraoperative findings included appendicular abscess, gangrenous appendicitis, and inflamed appendix adherent to the caecum, omentum, or terminal ileum (Table 1).

Table 1. Sociodemographic, clinical and descriptive characteristics of the study participants (N = 70)

Parameter	Category	No. of patients	Percentage (%)
Age (years)	11–20	9	12.86
	21–30	15	21.43
	31–40	7	10
	41–50	16	22.86
	51–60	13	18.57
	≥61	10	14.29
Gender	Male	58	82.86
	Female	12	17.14
Severity of disease	Mild	22	31.43
	Moderate	23	32.86
	Severe	25	35.71
Intraoperative diagnosis	Acute appendicitis with mild inflamed appendix	21	30
	Appendicular abscess	6	8.6
	Appendicular perforation	15	21.4
	Gangrenous appendicitis	3	4.3
	Inflamed appendix adhered to caecum	4	5.7
	Inflamed appendix adhered to omentum	3	4.3
	Inflamed appendix adhered to terminal ileum	1	1.4
	Phlegmonous appendicitis	17	24.3
Continuous variable	**Mean ± SD**	**Median**	
Age (years)	41.80 ± 17.50	43.5	
Alvarado score	6.32 ± 1.86	6	
CRP	71.58 ± 42.94	70	
Total count	14087.55 ± 7706.90	14678	
Sonographic diameter	8.50 ± 2.98	8.5	

Association of Study Parameters with Disease Severity

Age did not differ significantly across the severity groups, with mean ages of 42.40 ± 20.54 years in the mild group, 41.91 ± 19.38 years in the moderate group, and 41.16 ± 12.89 years in the severe group (p = 0.955). In contrast, the Alvarado score increased progressively with disease severity (p < 0.0001). Mean CRP levels also increased markedly from 21.45 ± 12.23 in mild disease to 70.43 ± 18.76 in moderate and 116.76 ± 20.44 in severe disease (p < 0.0001). Similarly, the mean

total leukocyte count increased from 9,437.22 ± 11,595 in mild disease to 13,950.21 ± 2,446.60 in moderate and 18,306.20 ± 3,042.30 in severe disease ($p < 0.0001$). Mean sonographic appendiceal diameter increased from 5.40 ± 1.65 mm in mild disease to 8.36 ± 1.54 mm in moderate and 11.36 ± 1.91 mm in severe disease ($p < 0.0001$) (Table 2). Overall, Alvarado score, CRP, total leukocyte count, and sonographic appendiceal diameter were significantly associated with increasing disease severity, whereas age was not.

Table 2. Association of age, Alvarado score, CRP, total count and sonographic diameter with severity of disease

Parameter	Severity of disease	Mean ± SD	Median	P value
Age (years)	Mild	42.40 ± 20.54	39	0.955 (NS)
	Moderate	41.91 ± 19.38	50	
	Severe	41.16 ± 12.89	45	
Alvarado score	Mild	5.18 ± 1.25	5	<0.0001 (S)
	Moderate	5.78 ± 1.73	6	
	Severe	7.84 ± 1.40	8	
CRP	Mild	21.45 ± 12.23	18	<0.0001 (S)
	Moderate	70.43 ± 18.76	66	
	Severe	116.76 ± 20.44	122	
Total count	Mild	9437.22 ± 11595	6124	<0.0001 (S)
	Moderate	13950.21 ± 2446.60	14523	
	Severe	18306.20 ± 3042.30	19000	
Sonographic diameter	Mild	5.40 ± 1.65	5	<0.0001 (S)
	Moderate	8.36 ± 1.54	8	
	Severe	11.36 ± 1.91	11	

Values are presented as mean ± SD and median. P values were obtained using the Kruskal–Wallis test. S, statistically significant; NS, not significant; CRP, C-reactive protein.

CRP and Intraoperative Diagnosis

CRP levels differed significantly across the intraoperative diagnosis groups (Kruskal–Wallis $H = 52.858$, $df = 7$, $p < 0.001$; Table 3). The highest mean ranks were observed in gangrenous appendicitis (60.17), appendicular perforation (56.57), and appendicular abscess (52.08). Lower mean ranks were observed in acute appendicitis with a mildly inflamed appendix (12.71), inflamed appendix adhered to the terminal ileum (30.50), and inflamed appendix adhered to the caecum (32.38). The mean ranks for inflamed appendix adhered to the omentum and phlegmonous appendicitis were 45.67 and 34.09, respectively.

Table 3. Association of CRP level with intraoperative diagnosis

Intraoperative diagnosis	Mean rank	Kruskal–Wallis H	df	P value
Acute appendicitis with mild inflamed appendix	12.71	52.858	7	<0.001 (S)
Appendicular abscess	52.08			
Appendicular perforation	56.57			
Gangrenous appendicitis	60.17			
Inflamed appendix adhered to caecum	32.38			
Inflamed appendix adhered to omentum	45.67			
Inflamed appendix adhered to terminal ileum	30.5			
Phlegmonous appendicitis	34.09			

Values are presented as mean rank. The Kruskal–Wallis test was used to compare CRP levels across intraoperative diagnosis groups. df, degrees of freedom; S, statistically significant; CRP, C-reactive protein.

Correlation of CRP with Alvarado Score, Total Count and Sonographic Variables

CRP showed a moderate positive correlation with the Alvarado score (Spearman's $r = 0.593$, $p < 0.0001$) and strong positive correlations with total leukocyte count ($r = 0.809$, $p < 0.0001$) and sonographic variables ($r = 0.800$, $p < 0.0001$) (Table 4; Figures 1–3). Thus, higher CRP levels were significantly associated with higher Alvarado scores, total leukocyte counts, and sonographic measurements.

Table 4. Correlation between CRP level and Alvarado score, total count and sonographic variables

Variable	Spearman's r	P value
Alvarado score	0.593	<0.0001 (S)
Total count	0.809	<0.0001 (S)
Sonographic variables	0.800	<0.0001 (S)

Spearman's rank correlation coefficient was used. S, statistically significant; CRP, C-reactive protein.

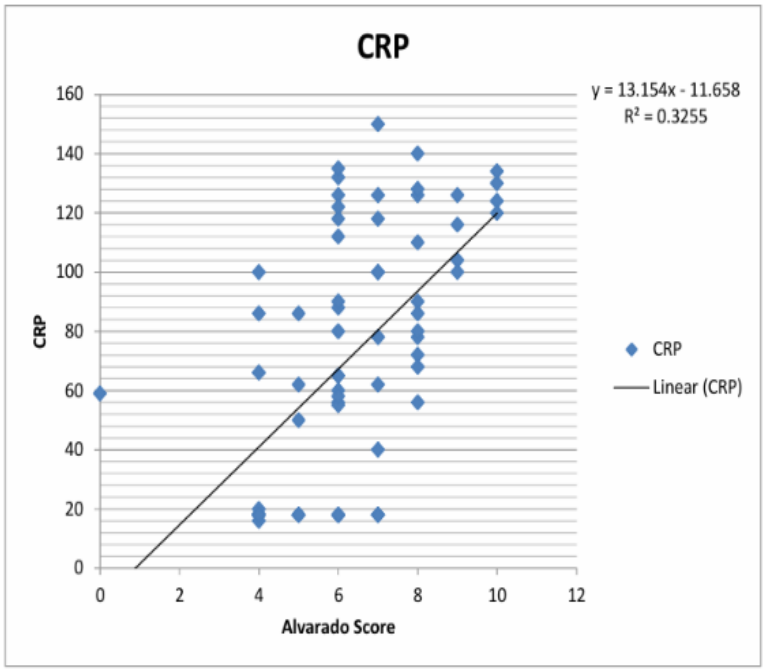


Figure 1. Correlation between C-reactive protein (CRP) and Alvarado score

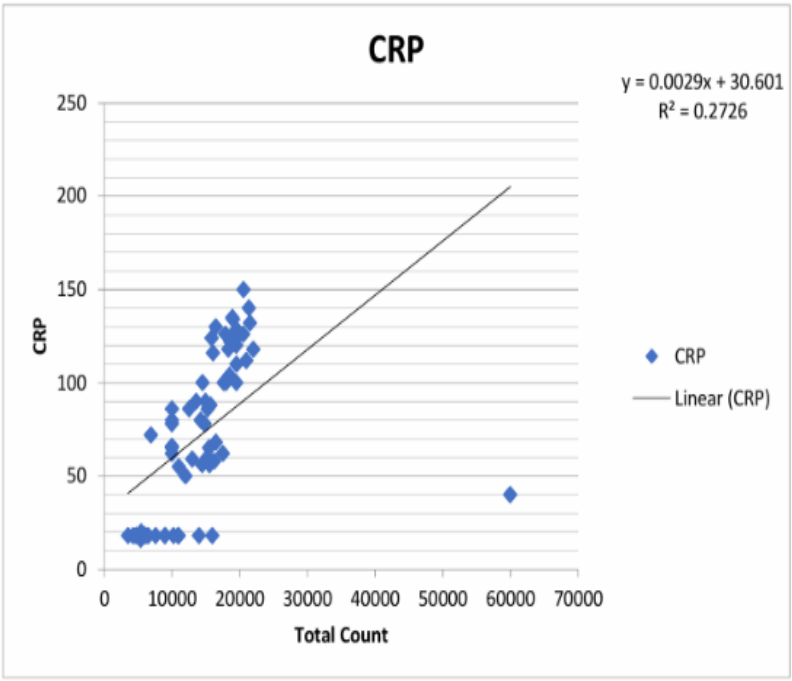


Figure 2. Correlation between C-reactive protein (CRP) and total leukocyte count

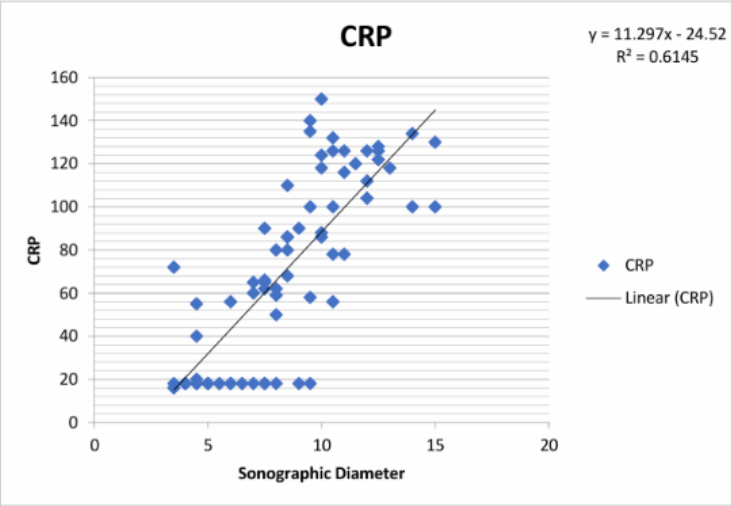


Figure 3. Correlation between C-reactive protein (CRP) and sonographic appendiceal diameter

Association of gender with disease severity

Disease severity differed significantly according to gender (Fisher–Freeman–Halton exact test, p = 0.001). Severe disease was observed in 25 of 58 male patients (43.1%), whereas none of the 12 female patients had severe disease. Mild disease was more frequent among female patients (8/12, 66.7%) than male patients (14/58, 24.1%). Moderate disease was observed in 4 female patients (33.3%) and 19 male patients (32.8%). Thus, in this study, severe appendicitis was significantly more frequent among male patients than female patients (Table 5).

Table 5. Association of gender with severity of disease

Gender	Mild, n (%)	Moderate, n (%)	Severe, n (%)	P value
Female	8 (66.7)	4 (33.3)	0 (0.0)	0.001 (S)
Male	14 (24.1)	19 (32.8)	25 (43.1)	
Total	**22 (100.0)**	**23 (100.0)**	**25 (100.0)**	

Values are presented as frequency and percentage. Because expected cell counts were below 5 in 3 cells (50.0%), the Fisher–Freeman–Halton exact test was used. S, statistically significant.

DISCUSSION

In this study, CRP levels increased progressively with the severity of acute appendicitis. The mean CRP was 21.45 in mild disease, 70.43 in moderate disease and 116.76 in severe disease, with a statistically significant difference between the groups ($p < 0.0001$). CRP also varied across the different intraoperative diagnoses, with the highest mean ranks seen in gangrenous appendicitis, appendicular perforation and appendicular abscess. Ghimire et al. reported a similar increase in CRP with increasing appendiceal inflammation (Ghimire et al., 2016). Ahmed et al. also observed higher CRP levels in perforated appendicitis (Ahmed, 2017). The findings of these studies are comparable with the present results and indicate that increasing CRP levels are associated with more advanced appendiceal disease.

The mean CRP in patients with severe disease was 116.76 mg/L. Wu et al. reported that the CRP values associated with perforated appendicitis differed according to the duration of symptoms, with cut-off values of 33, 85 and 120 mg/L during the first, second and third days after symptom onset, respectively (Wu et al., 2005). The value observed in our severe group was close to the higher value reported in that study. However, direct comparison should be made with caution because symptom duration was not assessed in the present study and disease severity was determined from intraoperative findings. The Alvarado score increased with disease severity and showed a moderate positive correlation with CRP ($r = 0.593$, $p < 0.0001$). Dal et al. reported that CRP and other biological markers could add value to the Alvarado score, particularly in differentiating complicated from uncomplicated appendicitis (Dal et al., 2019). Our findings are in agreement with this observation and suggest that CRP may provide additional information when used with the clinical score.

Total leukocyte count showed a strong positive correlation with CRP ($r = 0.809$, $p < 0.0001$) and also increased across the severity groups. Coleman et al., however, reported that WBC count was not a reliable indicator of the severity of appendicitis in their large patient series (Coleman et al., 1998). This difference may be related to variations in the study populations and methods used to classify disease severity. In the present study, therefore, the leukocyte count appears more useful when considered together with other clinical and inflammatory parameters.

Sonographic appendiceal diameter increased from 5.40 mm in mild disease to 8.36 mm in moderate and 11.36 mm in severe disease ($p < 0.0001$). A strong positive correlation was also observed between CRP and the sonographic variables ($r = 0.800$, $p < 0.0001$). Kessler et al. identified an appendiceal diameter of ≥6 mm as the most accurate ultrasonographic

criterion for diagnosing acute appendicitis (Kessler et al., 2004). The progressive increase in diameter observed in our study suggests that this measurement may also provide an indication of the extent of appendiceal inflammation.

Keyzer et al. found that ultrasonography and unenhanced CT had comparable diagnostic performance, although ultrasonography resulted in more inconclusive examinations (Keyzer et al., 2005). In our study, sonographic measurements were significantly related to both CRP and disease severity. This supports the use of ultrasonographic findings as part of the overall preoperative assessment rather than as an isolated measure.

Age was not significantly related to disease severity in the present study ($p = 0.955$). Gender showed a significant association with severity ($p = 0.001$), with severe disease occurring in 25 (43.1%) male patients and in none of the female patients. This finding should be interpreted cautiously because only 12 participants were female and the study population was predominantly male. The observed difference may therefore reflect the composition of the study sample and cannot be taken as evidence of a causal relationship between gender and disease severity.

Overall, the present study demonstrates a consistent relationship between preoperative CRP and intraoperative severity of acute appendicitis. CRP was also related to the Alvarado score, total leukocyte count and sonographic findings, indicating that it may provide useful additional information during preoperative assessment. However, the study did not assess diagnostic accuracy, postoperative complications or conversion to open surgery. Its single-centre design, relatively small sample, marked male predominance and lack of information on symptom duration also limit the extent to which the findings can be generalised. Further studies involving larger and more diverse patient populations are needed to determine clinically useful CRP thresholds.

CONCLUSION

Preoperative serum CRP increased progressively with the intraoperative severity of acute appendicitis, differed significantly across intraoperative diagnoses, and showed positive correlations with the Alvarado score, total leukocyte count and sonographic findings. These findings suggest that CRP may serve as a useful and readily available adjunct for preoperative assessment of disease severity in acute appendicitis. Larger multicentre studies are warranted to validate these findings and establish clinically useful CRP cut-off values for preoperative severity assessment.

DECLARATIONS

Ethics approval and consent: Approved by the Institutional Ethics Committee; written informed consent was obtained from all participants.

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Conflicts of interest: The authors declare that they have no competing interests

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