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Research article

Common inflammatory markers after cardiac surgery in infants and their relation to blood stream sepsis

Shaad Abqari [a,*], Mahesh Kappanayil [a], Abish Sudhakar [a], Rakhi Balachandran [b], Suresh G. Nair [b], R. Krishna Kumar [a]

[a] Department of Pediatric Cardiology, Amrita Institute of Medical Sciences and Research Center, Cochin, Kerala, India
[b] Department of Cardiac Anesthesiology, Amrita Institute of Medical Sciences and Research Center, Cochin, Kerala, India

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ABSTRACT

Background: Limited information exists on trends of common inflammatory markers after infant heart surgery and their role in identifying post-operative sepsis.
Methods: 275 consecutive infants undergoing cardiac surgery (231 with and 44 without Cardiopulmonary Bypass) were studied prospectively. Daily trends (0–4 day post-operative) of leucocyte counts, platelet counts and C-reactive protein were recorded. Association of these trends with early post-operative bloodstream sepsis, Cardiopulmonary Bypass and surgical outcomes were studied.
Observations: Trends of these inflammatory markers were noted. While off-Cardiopulmonary Bypass Surgery, and sepsis were associated with a statisticaly insignificant rise in total leucocyte count peaking on first post-operative day, Cardiopulmonary Bypass exposure was associated with significant decline ($p = 0.002$), more pronounced with Cardiopulmonary Bypass-exposure exceeding 150 min. Percentage of neutrophils showed a rise (maximum on first post-operative day) but no significant association with sepsis or Cardiopulmonary Bypass.
Platelet counts significantly declined after surgery, with nadir on 2nd POD ($p < 0.001$), the drop being more marked in patients operated on Cardiopulmonary Bypass ($p < 0.005$). Counts were significantly lower in patients exposed to >150 min Cardiopulmonary Bypass compared to those with shorter Cardiopulmonary Bypass. Septic patients had significantly lower platelet counts than uninfected patients, decline >2 SD from mean pre-operative level strongly associated with sepsis ($p < 0.001$).
C-Reactive Protein levels rose markedly after surgery, peaking on 2nd POD; levels were significantly higher if operated on Cardiopulmonary Bypass. Cardiopulmonary Bypass >150 min was associated with lower mean C-Reactive Protein on first post-operative day, but significantly higher values on third and fourth post-operative days, as compared to Cardiopulmonary Bypass <150 min. Comparison of infected versus non-infected patients showed significantly higher mean C-Reactive Protein in the former group.
Conclusion: While leucocyte count, platelet count and C-Reactive Protein emerged as useful markers of post-operative inflammatory response and reaction to Cardiopulmonary Bypass, they proved unsatisfactory predictors of early post-operative sepsis.

1. Introduction

Cardiac surgery, especially under cardiopulmonary bypass, is known to be associated with an inflammatory response [1, 2, 3, 4, 5]. This inflammatory response often intensifies into a systemic inflammatory response syndrome (SIRS) which can potentially lead to considerable post-operative morbidity and mortality [4, 5]. Infants are believed to be particularly prone to inflammatory responses after cardiac surgery [5, 6].

Early post-operative blood stream sepsis is a major complication and independent determinant of mortality/morbidity after congenital heart surgery among infants, particularly relevant to resource-limited environments [7, 8] Prevention, early identification and proactive management is of utmost importance.

The gold standard for defining blood-stream infection remains blood culture. Because of the time delay in obtaining blood culture, alteration in levels of inflammatory markers like total leucocyte counts (TLC),

* Corresponding author.
E-mail address: drshaadabqari@gmail.com (S. Abqari).

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differential leucocyte counts (DLC), platelet counts and C-reactive protien (CRP) are often used as early markers of infection. Decisions on antibiotic coverage, ionotrope use, fluid management, and ventilation strategy are often influenced by trends of these markers. While the value of these markers for suspecting or identifying infection in the general clinical setting is undisputed, their value in the early post-operative period after cardiac surgery in infants is uncertain, surgery-related inflammation being a major confounder.

Several studies have discussed the possible reasons for the post cardiac surgery inflammatory response, its effects on post-operative mortality and morbidity, the mechanism and extent of derangement of several biomarkers, and possible interventions for curtailing an aggressive inflammatory reaction [9, 10, 11, 12, 13, 14]. A large number of inflammatory mediators including tumour necrosis factor-alpha (TNFα), interleukins and interferons have been studied and proposed as potential measures of the inflammatory response [14, 15, 16]. However, most of these studies have focussed on adult cardiac surgery, and infant heart surgery has received little attention. Moreover, there is paucity of data on accurate trends of simple laboratory markers - total and differential leucocyte counts, platelet counts and C-reactive protein, in infants early after cardiac surgery. The effect of cardiopulmonary bypass (CPB) on these trends has also not been systematically studied in infants. As a result, there is considerable empericism in their clinical interpretation, and the management decisions thereof.

We undertook this prospective study to systematically understand the trends in the levels of total leucocyte counts, percentage of neutrophils on the differential leucocyte counts, platelet counts and C-reactive protein, in the early post-operative period after cardiac surgery in 275 consecutive infants. We also attempted to determine the association of these markers with post operative sepsis.

2. Methods

2.1. Study setting

The study was conducted in a tertiary care pediatric cardiology center in Southern India.

2.2. Study period

September 2008–January 2010.

2.3. Patients

All infants (≤1 year) who underwent corrective and palliative operations for congenital heart disease at our centre during the study period were included prospectively into the study, irrespective of basic cardiac diagnosis and type of surgery performed. Infants with blood-culture-proven sepsis in the immediate pre-operative period were excluded. All patients undergoing surgery under cardiopulmonary bypass were managed according to the standard institutional protocol for management of Cardiopulmonary Bypass. Cardiopulmonary bypass was managed using a membrane oxygenator (Dideco Lilliput, Sorin Group, Italy). Myocardial protection was achieved with intermittent doses of cold blood cardioplegia. All patients weighing less than 5 kg were also subjected to conventional ultrafiltration (CUF) and modified ultrafiltration using a hemoconcentrator, HPH40 (Hemocor, Minntech, Minneapolis, USA).

2.4. Study design

This was a prospective observational study, approved by the institutional ethics committee. A written and informed consent was obtained from all the patients (guardians) for the study. A comprehensive database was created to capture the following data: age, sex, weight, pre-operative infection status, cardiac diagnosis, procedure performed, cardiopulmonary bypass time (where applicable), aortic cross-clamp (wherever applicable), laboratory markers as detailed below and presence or absence of blood-culture proven early post-operative blood stream infection.

2.5. Measurements

In addition to routine pre-operative blood investigations that included complete hemogram, C-Reactive Protein level was assayed for all patients undergoing cardiac surgery, within 48 h prior to the surgical procedure. The tests were repeated every day starting immediately after surgery until the fourth post-operative day. Results were noted and the trends were plotted. Blood culture/sensitivity tests ordered by the treating Intensive Care Unit physicians during the early post-operative period (defined as first 7 days after surgery) were tracked and their results recorded.

Leucocyte and platelet counts were measured using Cell-Dyn® automated hematology analyzer, and C-Reactive Protein using immunoturbidometric assay on Olympus® biochemistry analyzer. Samples for blood culture were obtained through standard aseptic precautions and were processed and reported in the centralized microbiology laboratory using standard automated techniques (Bactec®).

2.6. Sepsis

All children with clinical suspicion of infection and blood culture positive for suspected organism.

2.7. Analysis

Pre-operative values of total leucocyte counts (TLC), percentage neutrophils, platelet counts and C-Reactive Protein were taken as the baseline for each individual patient. Analysis of post-operative trends were restricted to the values recorded as per protocol upto post-operative day four. Blood cultures ordered beyond first week following surgery were also similarly ignored.

The daily trends of the above markers were analyzed for the whole study group. Mean values of the each of the markers on each post-operative day was derived, and compared with baseline (preoperative) levels. We compared the trends of the markers in infants operated on Cardiopulmonary Bypass against those who were not exposed to Cardiopulmonary Bypass. Among those exposed to Cardiopulmonary Bypass, we compared the trends in patients exposed to ≤150 min of Cardiopulmonary Bypass against those exposed to more than 150 min. Infants with blood-culture proven bloodstream sepsis were identified, and their trends were compared to patients without bloodstream infection. Also, the effect of Cardiopulmonary Bypass duration on the trends was re-analyzed after excluding the patients with proven infection.

Statistical analysis was performed using SPSS version 11.5 statistical package for Windows (SPSS. Chicago, IL). Continuous variables were expressed as mean ± standard deviation (Gaussian distribution) and median (range) for skewed distribution. Significance of difference in the mean values in the post and preoperative (baseline) values were determined by using "paired t-test". All p values were two tailed and values of <0.05 were considered to indicate statistical significance. Pearson Linear correlation was used to study correlation between Cardiopulmonary Bypass duration and the biomarkers.

3. Results

A total of 275 consecutive infants (166 males) were studied. Median age was 3 months, with 92/275 (33%) being ≤30 days age at time of surgery. 231 patients underwent cardiac surgery on Cardiopulmonary Bypass and 44 without Cardiopulmonary Bypass.

The major surgical procedures performed in this cohort included - closure of ventricular septal defects (26%), arterial switch operation for transposition of great arteries (16%), total correction of tetralogy of Fallot (11.6%), aorto-pulmonary shunt (9.8%), repair of total anomalous pulmonary venous connection (11%), bidirectional Glenn shunt (4.7%), pulmonary artery banding (4.7%), coarctation repair (3.3%), repair of complete atrioventricular canal defects (3.6%) and others (9.6%).

Twenty eight infants (10.2%) had positive blood cultures within first seven post-operative days.

3.1. Trends of inflammatory markers (Figs. 1, 2, 3, and 4)

The trend of inflammatory markers were followed for 4 post operative days. Figures depicting the trends as A. Comparison with and without bypass, B. With prolonged bypass, C. Comparison after septic patients were excluded, D. Comparison between septic and non septic patients.

3.1.1. Total leucocyte counts (TLC)

Fig. 1 shows the trends of total leucocyte counts (TLC) in the patient cohort. While mean counts in patients operated without Cardiopulmonary Bypass showed a modest rise on the first post-operative day, those operated on Cardiopulmonary Bypass showed a modest fall instead ($p = 0.002$). There was no statistically significant difference in the trends for the remaining three post-operative days.

However, patients exposed to over 150 min Cardiopulmonary Bypass showed significantly lower total leucocyte counts (TLC) on all four post-operative days (Fig. 1B). The difference between these trends remained significant even after excluding the septic (positive blood culture) patients from the above cohort (Fig. 1C).

Fig. 1D shows a comparison of the mean total leucocyte counts (TLC) trends between the infected and the uninfected patients, irrespective of Cardiopulmonary Bypass exposure. Patients with sepsis tend to have a higher total leucocyte counts (TLC) than the uninfected patients. However, this difference was not statistically significant.

3.1.2. Percentage neutrophils

Fig. 2 shows the trends of mean neutrophil percentage. Neutrophilic preponderence in the differential leucocyte count became more pronounced in the immediate post-operative period, attaining its peak on the first post-operative day (75% of the total leucocyte counts (TLC) ($p < 0.001$), and subsequently declining marginally to plateau off towards the fourth post operative day, not reaching the baseline though. The trend was similar in patients operated with or without Cardiopulmonary Bypass, but Cardiopulmonary Bypass was associated with higher neutrophil percentage on second ($p = 0.007$) and third ($p = 0.028$) post-operative days (Fig. 2A).

Comparison of long Cardiopulmonary Bypass exposure (>150 min) with shorter exposure showed similar trends, but higher neutrophil percentage on the third post-operative day (statistically insignificant). Mean values on all other days were identical (Fig. 2B). This observation remained unchanged after excluding septic patients from the analysis.

Fig. 2D compares trends in infected with uninfected patients and shows that patients who had early post-operative blood stream sepsis had higher neutrophil percentage at baseline and then on the first post-operative day. There was no statistically significant difference between the mean values for any of the other days.

3.1.3. Platelet counts

Cardiac surgery was associated with a marked, statistically significant fall in platelet count with the nadir being attained on the second post-operative day (mean 1,55,000) ($p < 0.001$). The trends in the first four post-operative days is shown in Fig. 3A. Though trends were similar, the mean values were significantly lower in patients operated on Cardiopulmonary Bypass through all four post-operative days ($p < 0.001$ for first three post-operative days, and $p = 0.005$ for the fourth post-operative day) (Fig. 3A). The counts remained well below the baseline on the fourth post-operative day (mean 1,60,000).

Longer Cardiopulmonary Bypass exposure (>150 min) was associated with significantly lower platelet counts on the second, third and fourth post-operative days, irrespective of the presence or absence of bloodstream infection (Figs. 2B, 2C).

Infected patients had a significantly lower mean value starting from the pre-operative stages right through to the fourth post-operative day (Fig. 3D).

3.1.4. C-Reactive Protein

C-Reactive Protein showed a sharp rise following cardiac surgery in all the infants in this study (Fig. 4A). The mean C-Reactive Protein level showed a > ten-fold rise to 56 mg/L ($p < 0.001$) on the first post operative day with the highest mean value on the second post-operative day (mean 147 mg/L) ($p < 0.001$). Maximum value of C-Reactive Protein recorded in any patient in the cohort on second post-operative day was 260 mg/L. Subsequent to the peak on second post-operative day, the levels showed a gradual decline but remained well above baseline values. Patients operated on Cardiopulmonary Bypass had significantly higher C-Reactive Protein than those operated without Cardiopulmonary Bypass ($p = 0.055$ for first, $p = 0.008$ for second, $p = 0.001$ for third and $p = 0.014$ for the fourth post-operative days).

While the mean C-Reactive Protein value on the first post-operative day was *lower* in the longer Cardiopulmonary Bypass exposure group (>150 min), and the peaks attained on second post-operative day were similar, the mean levels on the third and fourth post-operative days were significantly higher (Fig. 4B). In infants with 150 min or less of Cardiopulmonary Bypass exposure, the levels started declining after the second day. Those with >150 min Cardiopulmonary Bypass time had significantly higher levels on day 3 and 4(Fig. 4C). Exlusion of infected patients did not significantly alter these trends (Fig. 4D).

Comparison of infected with uninfected patients also showed a similar trend with septic patients having higher mean C-Reactive Protein values on third and forth post-operative days (Fig. 4D).

Association between the markers and bloodstream sepsis:

Figs. 1D, 2D, 3D, 4D show the graphic trends of the markers in infected versus uninfected patients. Table 1 depicts the statistical correlation between the mean levels of the markers and culture-proven bloodstream sepsis.

Low mean platelet count was most consistently associated with sepsis, starting from the pre-operative period through the fourth post-operative day. A decline in platelet count >2 standard deviations from the mean pre-operative levels, was significantly associated with bloodstream sepsis ($p < 0.001$).

A high C-Reactive Protein on the third and fourth post-operative days was significantly associated with sepsis.

ROC curves were plotted for the platelet counts and C-Reactive Protein levels for the four post-operative days. No cut-off values could be arrived at to predict bloodstream sepsis for an individual patient.

Total leucocyte counts (TLC) and percentage of neutrophils were found to have no utility in identifying or predicting sepsis.

4. Discussion

Standard complete blood counts (hemograms) are often routinely done for all patients in the early post-operative period in the surgical ICU following cardiac surgery. In most situations (including our own center), hemograms are repeated at least daily for the first few days after the cardiac surgery. It is inexpensive and simple and universally regarded as a basic guide to clinical status. While the hemoglobin levels and hematocrit indicate extent of blood loss and guide decisions for red-cell transfusion, leucocyte counts and platelet counts are valued as basic biomarkers of infection and inflammation. C-Reactive Protein is also a commonly used biomarker, though typically used more selectively. Despite such extensive use of these tests, the true significance of these markers for identifying sepsis or extent of inflammation has not been systematically studied, and their interpretation has been subject to considerable empiricism. Observation of platelet counts falling below

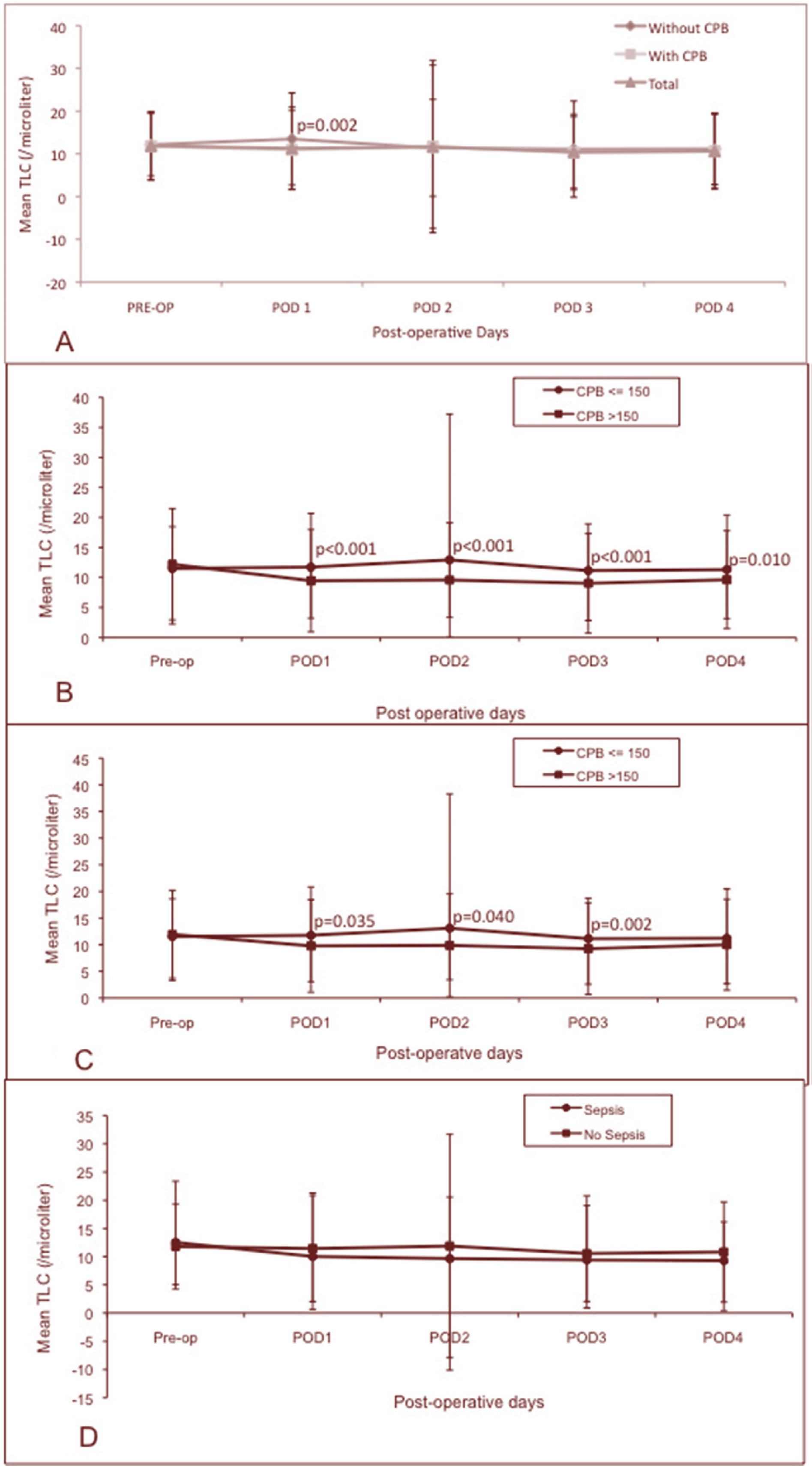

Fig. 1. TLC: (A). Overall trends. (B). Comparing CPB >150 min with </ = 150 min). (C). Comparing CPB >150 min with CPB </ = 150 min after excluding septic patients. (D). Comparing septic vs non-septic.

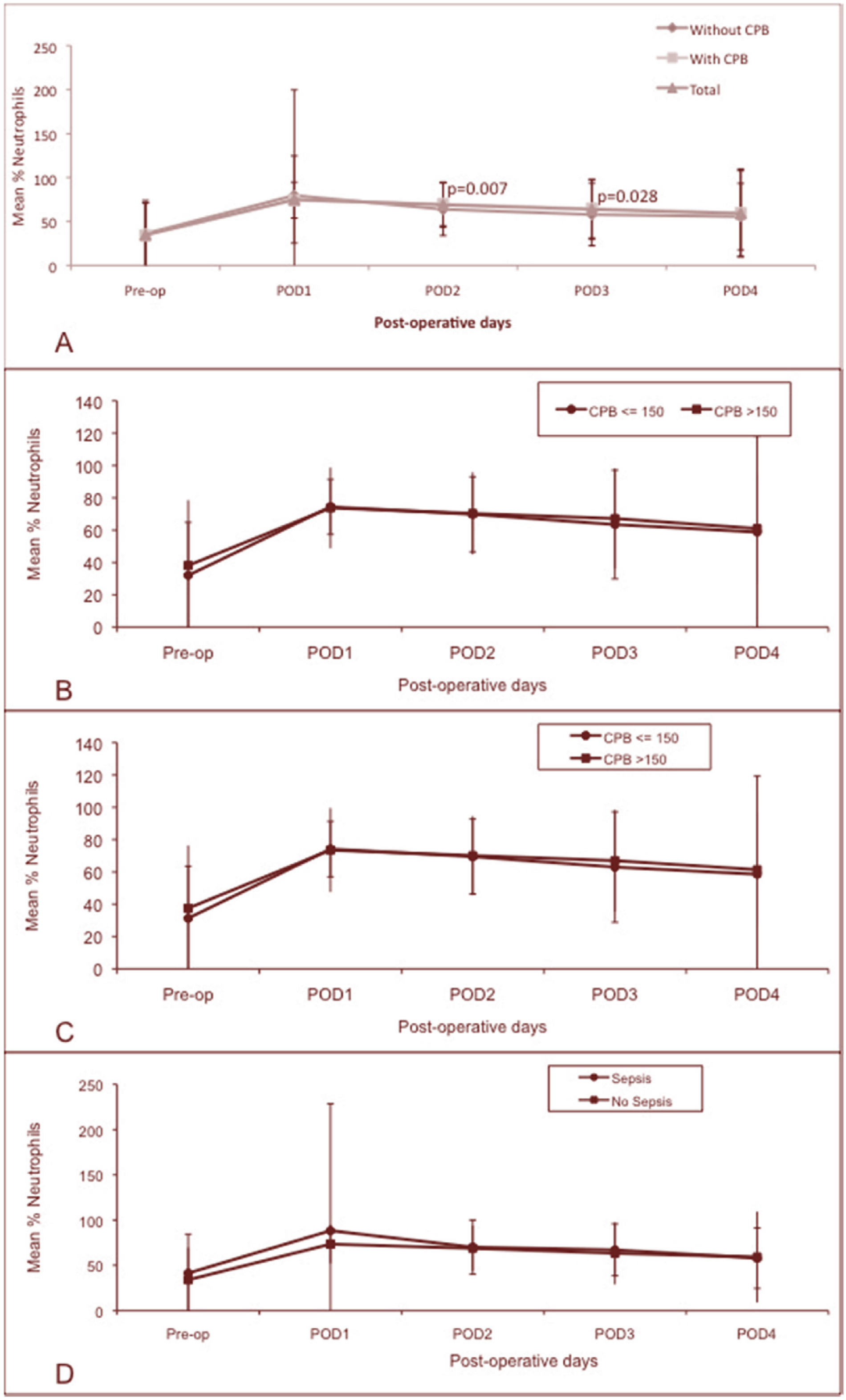

Fig. 2. % Neutrophils: (A). Overall trends. (B). Comparing CPB >150 min with </ = 150 min). (C). Comparing CPB >150 min with CPB </ = 150 min after excluding septic patients. (D). Comparing septic vs non-septic.

100,000/mm3, rise of total leucocyte counts to >20,000/mm3 or a fall to<4000/mm3, an exaggerated polymorphonuclear response, and/or a dramatic rise in C-Reactive Protein in the early post-operative period in infants, often trigger apprehension of impending sepsis, leading to detailed sepsis screens and empirical change of antibiotics to include a broader spectrum. This often leads to escalation of treatment costs, irrational antibiotic use and promotes development of antibiotic resistance.

Systemic inflammatory response to cardiac surgery is generated a result of multiple factors which include – direct surgical trauma,

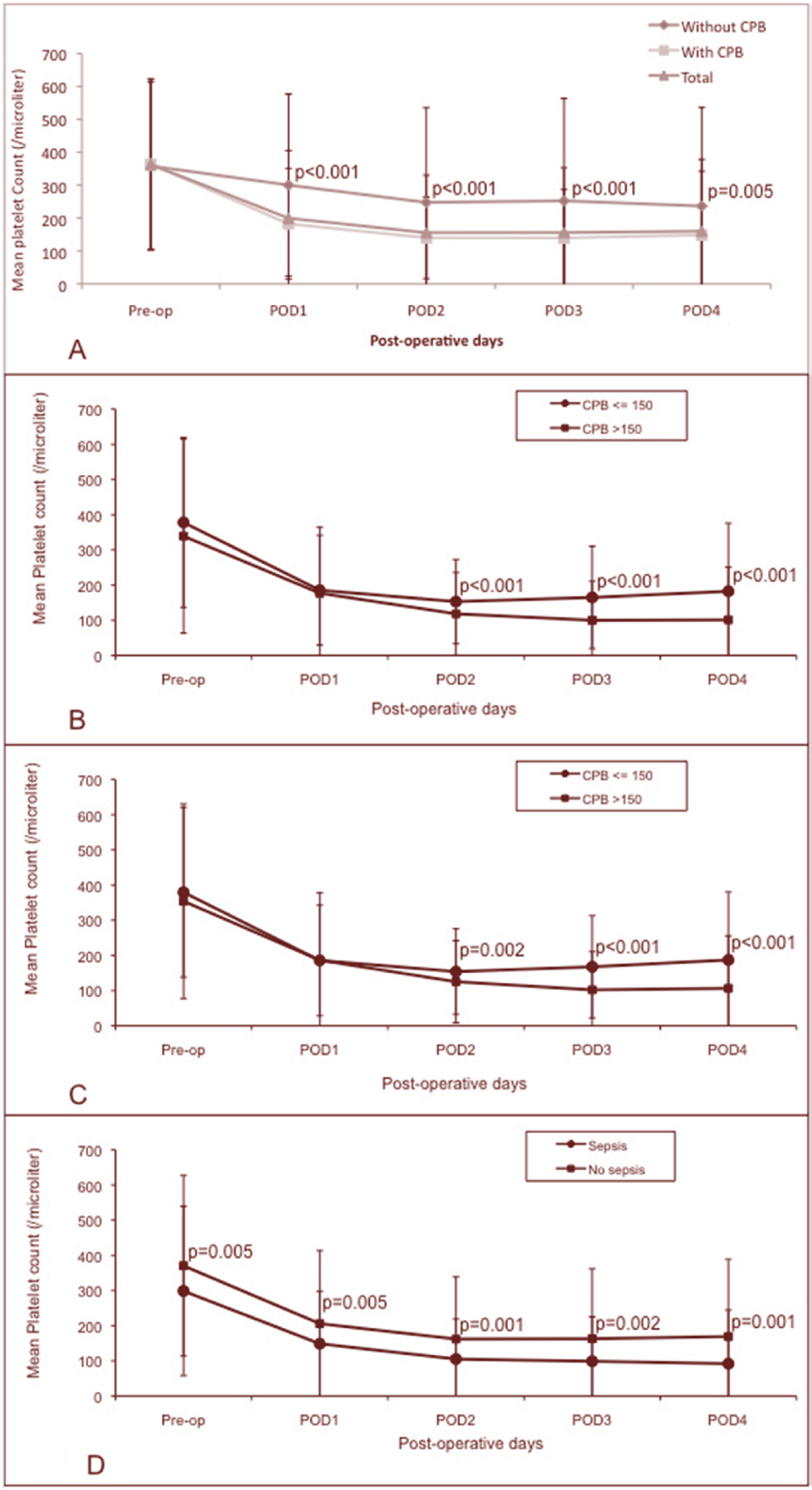

Fig. 3. Platelet Counts: (A). Overall trends. (B). Comparing CPB >150 min with </ = 150 min). (C). Comparing CPB >150 min with CPB </ = 150 min after excluding septic patients. (D). Comparing septic vs non-septic.

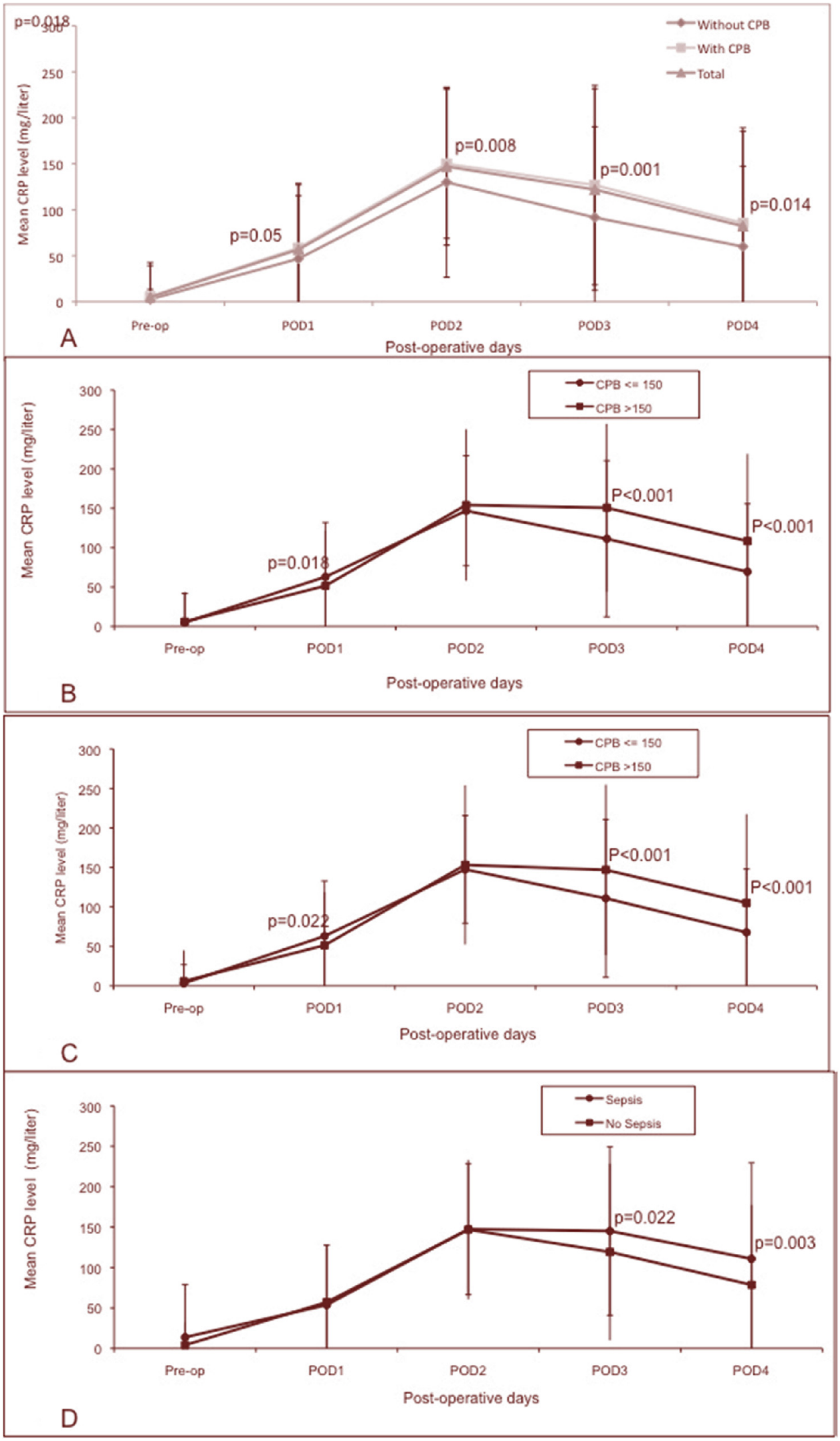

Fig. 4. CRP: (A). Overall trends. (B). Comparing CPB >150 min with </ = 150 min). (C). Comparing CPB >150 min with CPB </ = 150 min after excluding septic patients. (D). Comparing septic vs non-septic.

Table 1
Comparison of mean values of various markers in septic and non septic patients on various post operative days.

DAY	MARKER	SEPSIS	NO SEPSIS	p value
		M +/- SD	M +/- SD	
Pre-op	TLC	12.52 ± 5.42	11.74 ± 3.75	0.351
	% Neutrophils	41.29 ± 21.41	33.89 ± 17.79	***0.042***
	Platelets	298.70 ± 120.38	370.39 ± 128.35	***0.005***
	CRP	13.72 ± 32.55	4.01 ± 14.04	0.130
POD 1	TLC	10.03 ± 5.63	11.44 ± 4.70	0.144
	% Neutrophils	88.30 ± 70.09	73.41 ± 10.70	0.271
	Platelets	148.74 ± 74.73	205.96 ± 103.89	***0.005***
	CRP	53.74 ± 37.05	57.15 ± 34.95	0.628
POD 2	TLC	9.66 ± 5.46	11.88 ± 9.91	0.245
	% Neutrophils	70.05 ± 14.97	68.79 ± 12.52	0.623
	Platelets	105.20 ± 57.02	162.09 ± 88.34	***0.001***
	CRP	147.20 ± 40.54	146.95 ± 43.12	0.947
POD 3	TLC	9.42 ± 5.70	10.55 ± 4.25	0.226
	% Neutrophils	67.06 ± 14.30	63.26 ± 17.23	0.291
	Platelets	99.00 ± 63.16	162.91 ± 99.67	***0.002***
	CRP	145.20 ± 52.12	119.24 ± 54.60	***0.022***
POD 4	TLC	9.31 ± 3.43	10.82 ± 4.44	0.109
	% Neutrophils	57.86 ± 16.71	59.12 ± 25.10	0.81
	Platelets	92.21 ± 76.18	169.29 ± 109.78	***0.001***
	CRP	110.86 ± 59.33	78.57 ± 49.40	***0.003***

$p<0.05$ is considered significant.

ischemia-reperfusion injury, gut ischemia, contact activation of cells by extracorporeal circuit, hypothermia etc. [1, 2, 3]. Cardiopulmonary Bypass is believed to be a major contributor to this process. Even though it is recognized that the inflammatory response may vary considerably between infants and adults, systematic attempts at studying infants' response to cardiac surgery are lacking. With both sepsis and systemic inflammatory response syndrome (SIRS) posing significant post-operative survival and morbidity risks, there is surprisingly scant data on early identification and discrimination of these entities that can have overlapping manifestations. Even though Cardiopulmonary Bypass is recognized as a major cause of exaggerated inflammatory response, differences between the responses to cardiac surgery with and without Cardiopulmonary Bypass have not been extensively studied in infants.

This study attempted to understand the basic trends of simple, relatively inexpensive and easily available biomarkers – total leucocyte counts (TLC), neutrophil count, platelet count and C-Reactive Protein, with particular relevance to resource-limited environments in infants undergoing cardiac surgery. Trends were studied both in open and closed heart surgery, and in the presence or absence of culture-proven blood steam infection. We also attempted to discern the predictive value of these markers for sepsis.

Total leukocyte counts appeared to have no predictable trends. A wide range of responses was observed, with values as high as 30,000/mm^3 to as low as 2000/mm^3. The zeniths or nadirs were usually attained on first post-operative day. There was no statistical association with bloodstream sepsis, nor with any of the major outcome variables. However, total leucocyte counts (TLC) proved to have a consistent association with duration of Cardiopulmonary Bypass exposure, with a longer duration (>150 min) producing a drop in the counts that was statistically significant throughout the first four post-operative days. This association persisted even when septic patients were excluded (Fig. 1B and C). A significant early post-operative drop in the total leucocyte counts (TLC) is most likely to indicate Cardiopulmonary Bypass-related inflammatory responses.

Percentage of neutrophils in the differential leucocyte count, which is reflective of the polymophonuclear response to inflammation or infection, proved to be of very little value in predicting sepsis. It showed a uniform rising trend immediately after cardiac surgery, and peaked on the first post-operative day. This trend was identical in both Cardiopulmonary Bypass and non-Cardiopulmonary Bypass groups, and also very similar between the infected and uninfected patients. Notwithstanding a trend towards higher levels on third post-operative day in those with exposure (>150 min) to Cardiopulmonary Bypass, neutrophil count is not a useful marker of either infection or inflammation.

C-Reactive Protein demonstrated a remarkably consistent trend with a marked rise, peaking on second post-operative day followed by a gradual decline thereafter. The extent of rise had strong association with exposure To Cardiopulmonary Bypass as well as duration of Cardiopulmonary Bypass. Levels on third and fourth post-operative days were significantly higher for those with long duration (>150 min) of Cardiopulmonary Bypass. A strong linear correlation with Cardiopulmonary Bypass duration with C-Reactive Protein suggests that it should interpreted as a marker of the post-cardiac surgery inflammatory response in infants. Even though C-Reactive Protein levels on third and fourth post-operative days also had statistical association with bloodstream sepsis, it cannot be used to identify sepsis in an individual patient because of significant overlap of values between septic and non-septic patients.

This study highlights the remarkably consistent trends of platelet counts in infants following cardiac surgery. A major decrease in platelet count of approximately 40%–50% is reported to occur universally during the first 72 h after cardiac surgery [17]. As many as 25%–70% of patients are reported to develop anti-platelet factor 4 (PF4)–heparin antibodies detectable by immunoassays, and 4%–20% test positive by platelet activation assay, during the first 10 days post-cardiac surgery [18, 19, 20]. In addition to drug-induced thrombocytopenia, the mechanical destruction of platelets and hemodilution in the bypass circuit play important roles in the occurrence of postoperative thrombocytopenia. Sepsis, intraaortic balloon pump, and post transfusion purpura are also identified as causes of thrombocytopenia in post operative period. The nadir platelet count is on the second or third day after surgery, but >10% of patients continue to have a platelet count of <50% of baseline on the fourth postoperative day [17].

Our study demonstrated the post-operative declining trend in platelet count in the early post-operative period throughout the patient cohort, with the nadir being attained on the second post-operative day. Exposure to Cardiopulmonary Bypass was associated with a more drastic fall and lower mean levels throughout the first four post-operative days as compared to patients operated without Cardiopulmonary Bypass. Cardiopulmonary Bypass duration of >150 min produced significantly lower platelet counts on all four post-operative days. Also, despite excluding septic patients, patients with Cardiopulmonary Bypass >150 min had significanly lower platelet counts on all four days.

Subset of patients who proved to be septic, irrespective of Cardiopulmonary Bypass durations, had lower mean platelet counts on all four days, than those without sepsis. However, in the absence of statistically significant cut-off levels, platelet counts failed to be an accurate predictive marker of sepsis.

Thus, while C-Reactive Protein and platelet counts were found to have the best statistical association with sepsis among the markers studied, their utility as predictors of early post-operative sepsis was seriously limited. Rather, they emerged as stronger and more consistent markers of the post-operative inflammatory process. The findings were similar to study by Nasser et al who demonstrated that these inflammatory markers can not differentiate between inflammation and infection. [21], though role of procalcitonin in identifying infections after cardiac surgery is increasingly being recognised [22].

While discounting the utility of hemogram and C-Reactive Protein in identifying early post-operative sepsis, this study emphasizes their utility in identifying and understanding the inflammatory responses to infant cardiac surgery. Addressing it through strategies to minimize the inflammatory response, as well as to manage it effectively in the post-operative period may be vital to improvement in surgical outcomes.

These biomarkers may prove to be useful tools to assess the response to such interventions.

5. Study limitations

Blood culture, the 'gold standard' for identifying infection, was not done for all patients (in view of cost constraints); it was only done when infection was clinically suspected by ICU physicians. Some instances of sepsis may have been thus missed. We followed the trends of the biomarkers only until the fourth post-operative day, and did not track them to identify the duration until normalization to baseline values. No other biomarkers of inflammation or infection were tested, due to cost constraints.

6. Conclusions

This study provides a comprehensive documentation of the trends of common inflammatory markers after cardiac surgery in infants. While the utility of these markers in identifying sepsis in the early post-operative period is limited, they may be useful markers of inflammatory processes that influence outcomes. Until more specific biomarkers are available the diagnosis of sepsis early after cardiac surgery would remain a challenge and continue to depend on careful integration of a number of clinical and laboratory variables. Whenever clinical condition permits, antibiotic usage should be guided by blood cultures. There should be renewed emphasis on addressing the causes and management of the systemic inflammatory reactions resulting from cardiac surgery.

Declarations

Author contribution statement

Shaad Abqari: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Mahesh Kappanayil: Conceived and designed the experiments; Performed the experiments; Wrote the paper.

Abish Sudhakar, Rakhi Balachandran: Analyzed and interpreted the data.

Suresh G Nair: Conceived and designed the experiments.

Raman Krishna Kumar: Conceived and designed the experiments; Wrote the paper.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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