


# An elevated C-reactive protein level in an inpatient rehabilitation setting after joint replacement

## To act or not to act? – that is the question

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### Abstract

C-reactive protein (CRP) is part of a battery of “routine bloods” performed by residents on patients when they are admitted into a rehabilitation unit. Generally, an elevated CRP is considered to be an indicator of an acute infective process. Numerous studies have indicated that the CRP peaks on the 2nd or 3rd day post total hip arthroplasty (THR) and total knee arthroplasty (TKR) and returns to normal by day 7. When the CRP level remains elevated, it is generally felt that infection should be excluded.

We performed a prospective study on 45 consecutive patients admitted into a rehabilitation unit post hip and knee arthroplasty over a 6 months period, to evaluate the incidence of an elevated CRP on admission, to determine whether an isolated elevated CRP on admission to a rehabilitation setting should not be considered as an indicator of an infective process.

We found all patients (100%) had elevated CRP's on admission, ranging from 8.6mg/L to 139.2mg/L, between days 5–7 post-operatively. By day 14, CRP's reduced, but 91% of patients still had elevated CRP's, ranging from 2.1 mg/L to 47.3mg/L after THR and 4.8mg/L to 40mg/L after TKR at day 14.

These results suggest that even in uncomplicated elective joint arthroplasty, CRP's can remain elevated up to 14 days post-procedure, in the absence of an infective process.

An isolated elevated CRP on admission to a rehabilitation setting should not be considered as an indicator of an infective process, but rather part of the normal post-operative inflammatory response. The elevated CRP should be monitored and only an upward trend requires further investigation and management.

**Abbreviations:** CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, THR = total hip replacement, TKR = total knee replacement.

**Keywords:** C-reactive protein, joint replacement, rehabilitation

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## 1. Summary

This study showed that CRP levels can remain significantly elevated for up to 14 days post-operatively in uncomplicated THR and TKR and should not be used as an isolated biomarker of post-operative infection, as the elevated CRP level appears to be part of the normal post-operative inflammatory response. The result should be used as a baseline and only an upward trend requires further investigation.

## 2. Introduction

Total hip (THR) and knee arthroplasty (TKR) are common elective procedures that require inpatient rehabilitation. The devastating consequences of post-operative joint infection are of concern to both the surgeon and physician.<sup>[1]</sup> In the early acute and subacute phase of recovery serological inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are often used as indicators of infection, as they are inexpensive and widely available.<sup>[2]</sup>

CRP is a substance produced by the liver in response to inflammation and is considered to be a marker of inflammation in the body.<sup>[3]</sup> An elevation in CRP is part of the acute-phase response to inflammation.<sup>[3,4]</sup> It is considered to be more

responsive and specific for inflammation than ESR.<sup>[5]</sup> Measuring CRP is also more precise and reproducible.<sup>[5]</sup>

While CRP elevation is suggestive of inflammation or infection in the certain clinical situations, it can also be elevated in obesity<sup>[6]</sup> and renal dysfunction.<sup>[7]</sup> Conversely, a lack of CRP elevation in inflammation may be seen with hepatic failure, as well as during flares up of conditions such as systemic lupus erythematosus<sup>[8]</sup>

Any condition that results in sudden or severe inflammation may increase CRP levels. These include cancer, connective tissue disease, ischaemic heart disease, infection, inflammatory bowel disease, pneumococcal pneumonia, and rheumatoid arthritis.<sup>[9]</sup>

While an elevation in CRP is not specific for any condition, it is considered to be a fairly sensitive marker of inflammation (greater than 90%), and so provides a valuable adjunct to a careful clinical assessment.<sup>[3,4]</sup> There is often no clear correlation between CRP concentrations and disease severity. The bulk of CRP tests are requested for the detection of inflammatory responses associated with infection, autoimmune diseases and drug allergies (especially to antibiotics). CRP is measured in milligrams per litre of blood (mg/L).<sup>[10]</sup>

Previous studies have examined trends in CRP in post-operative, uncomplicated joint replacements and have shown that CRP peaks between the 2<sup>nd</sup> and 3<sup>rd</sup> post-operative day.<sup>[11-14]</sup> Their results indicated that CRP levels should decrease to normal by day 7, and if levels remain elevated, infection or haematoma should be excluded.

In our study, we examined the CRP on admission into 2 inpatients rehabilitation units and then repeated the CRP on day 14 to evaluate the merit of measuring CRP's on admission to a rehabilitation hospital (generally 5-7 days) to assess the utility of CRP's as a monitoring and diagnostic marker of post-operative joint infection.

### 3. Methods

A prospective cohort study was conducted on 45 consecutive patients, aged 18 to 90 years of age who underwent uncompli-

cated THR and TKR and were subsequently admitted to 2 different inpatient rehabilitation centres, over a 6 month period. Each of these hospitals were general subacute rehabilitation hospitals accepting patients after elective total hip replacements (THR) & total knee replacements (TKR) for post-operative inpatient rehabilitation around day 5-7, post-operatively. We had 18 patients who had THR and 27 patients who had TKR.

We excluded patients with known post-operative wound infection, post-operative upper/lower respiratory tract infections, urinary tract infections or other infections, complicated post-operative course, such as venous thrombus or haematoma. We also excluded patients if they were febrile on admission with a temperature of greater than 38 degrees Celsius, history of autoimmune, inflammatory disorders, hepatitis, liver disease or malignancy.

Full blood counts, white cell differentials, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were the biomarkers that were measured on admission, generally day 5-7 post-operative and again at day 14 post-operatively.

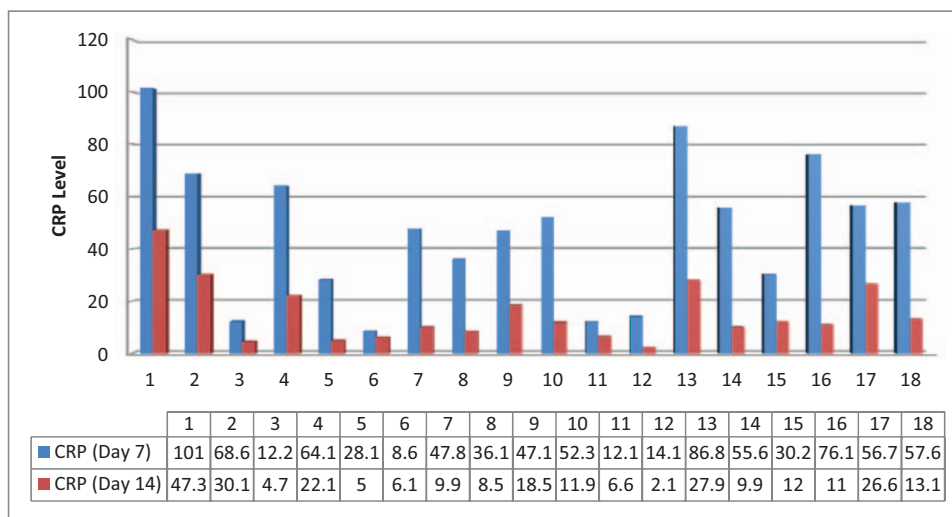
All patients also had urine analysis, chest auscultation, and wound inspection on admission. Patients were monitored for development of any signs of wound, urinary tract and respiratory infections. Any patient who developed wound infection, had a positive urinalysis or had an upper or lower respiratory tract infections were excluded.

The study was approved by the local Ethics Review Committees. All participants were provided with written informed consent to be included in the study.

### 4. Results

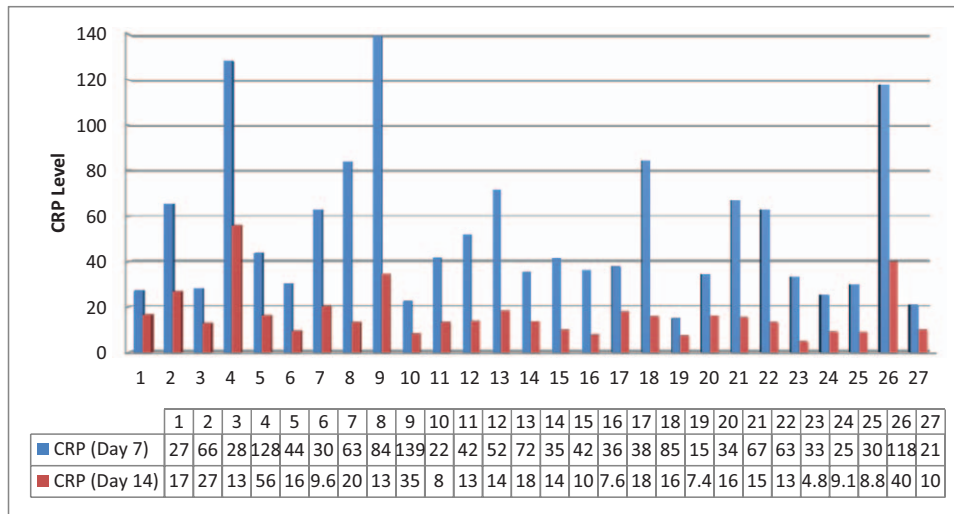
All patients (100%) showed elevated CRP's (>5mg/L) on admission, without any evidence of wound or any other infection. Results varied widely ranging from 8.6mg/L to 101.4mg/L after THR and 14.9mg/L to 139.2mg/L after TKR.

By day 14, CRP's had reduced but were still elevated in 91% of patients, ranging from 2.1mg/L to 47.3mg/L after THR (Fig. 1) and 4.8mg/L to 40.0mg/L after TKR (Fig. 2).



CRP: C-reactive protein

Figure 1. Changes in C-reactive protein levels day 7 and day 14 after total hip replacement in individual cases.



CRP: C-reactive protein

Figure 2. Changes in C-reactive protein levels day 7 and day 14 after total knee replacement in individual cases.

THR patients had comparatively lower CRPs (mean 58.8 mg/L) than TKR patients (mean 71.68 mg/L) at day 7. These differences were still present at day 14 (mean THR 16.57 mg/L vs mean TKR 27.5 mg/L).

However, the median THR CRP at day 7 (50.5 mg/L) was higher than the median TKR CRP at day 7 (41.6 mg/L). The day 14 median were comparatively lower with THR patients showing a much greater reduction (11.45 mg/L) as compared to TKR patients (13.5 mg/L) (Fig. 3).

5. Discussion

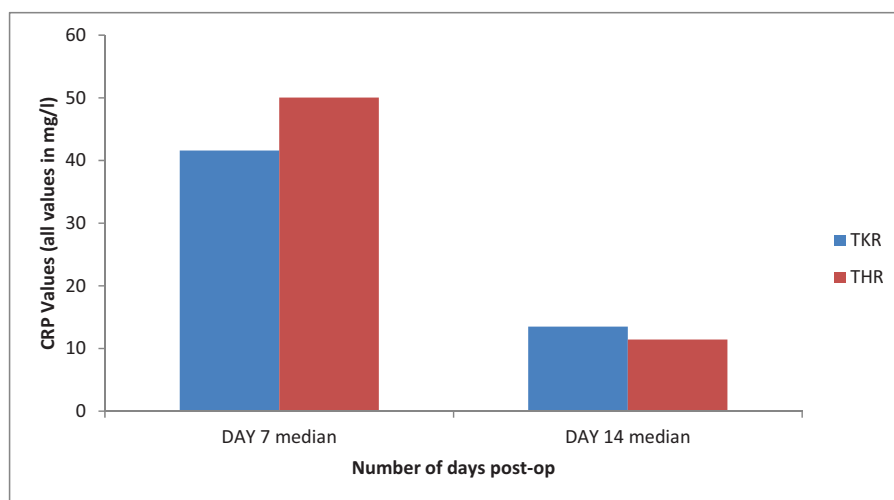
The devastating consequences of post-operative joint infection are concerning to the surgeon and the rehabilitation physician. In

the early phase of recovery serological inflammatory biomarkers such as C-reactive protein is often used as an initial inexpensive marker to exclude the joint infection.

We found that C-reactive protein at day 7 (the day of admission to a rehabilitation hospital) was elevated, even without any signs of infection. CRP continued to fall but was still above the normal range at day 14, in the absence of any signs of post-operative joint infection.

This observation was significant ( $P < .001$ ) and contrary to the previous studies which suggested that CRP levels in post-operative uncomplicated joint replacements peaks between the 2nd and 3rd post-operative day and decrease to normal pre-operative values by day 7.<sup>[11-14]</sup>

In our study, CRP was elevated beyond the 7th post-operative day with a gradual reduction over the next 7 days but still not



CRP: C-reactive protein

TKR: Total knee replacement

THR: Total hip replacement

Figure 3. Comparison of C-reactive protein levels post-operative at day 7 and day 14 after total hip replacement and total knee replacement.

returning to normal levels. This occurred in the absence of any signs of post-operative joint infection or haematoma. CRP levels were still elevated in 91% of patients, up to 47.3 mg/L after THR and 40 mg/L after TKR at day 14.

These results indicate the low sensitivity of CRP as a marker of post-operative joint infection and haematoma.<sup>[11]</sup> Also, spontaneous, fluctuations of CRP's have been seen even in healthy volunteers, with intra-individual variabilities of 42% to 63%.<sup>[15]</sup> The variability is not related to clinically apparent inflammation or infection.

Markers such as interleukin 6, have been suggested as being more sensitive markers for post-operative joint infection due to its much faster peak and return to normal and further studies into the utility of this as an indicator of post-operative joint infection could be considered.<sup>[16]</sup>

## 6. Conclusion

CRP remains significantly elevated at post-operative day 7 even in uncomplicated THR and TKR and should not be used in isolation as a marker of post-operative infection. Assessment for post-operative infection should remain in the domain of clinical judgement and an isolated elevated CRP should not be considered as an indicator of infection and does not require further investigations. The result should be used as a baseline and only an upward trend requires further investigation.

## Author contributions

**Conceptualization:** Arun Aggarwal.

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**Supervision:** Arun Aggarwal, Anuka Parapuram.

**Validation:** Arun Aggarwal.

**Writing – original draft:** Vikram Sinha, Arun Aggarwal.

**Writing – review & editing:** Arun Aggarwal, Eric Chan, Anuka Parapuram.

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