Our study has determined the response of C-reactive protein (CRP) after total knee replacement (TKR). The peak level occurs on the second postoperative day and is significantly greater than that after total hip replacement (THR). The level returns to normal at similar times after both procedures. The physiological response to TKR as measured by the area under the CRP/time curve is significantly greater than that after THR. Rising CRP levels after the third postoperative day may indicate a complication of surgery such as infection.

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Measurement of the level of C-reactive protein (CRP) is of value in monitoring bacterial infection. There have been several studies on the response of CRP to operations such as total hip replacement (THR). Larsson et al. studied 39 patients having unicondylar knee replacements and showed the mean peak CRP level to be greater than that after THR. Only one study has examined the CRP response to total knee replacement (TKR) in isolation. It was found to be greater than that to THR. There was also a difference in the peak level of CRP after both operations but the authors did not comment on its significance. Both levels returned to normal at similar times after operation.

We have measured the levels of CRP in uncomplicated TKR and compared the peak level and the time taken for return to normal with those after THR.

Patients and Methods

We included in the study all patients with a diagnosis of osteoarthritis admitted to Crosshouse Hospital, Kilmarnock for THR or TKR from June 1996 to August 1996. Those with rheumatoid arthritis or any signs of postoperative complications were excluded. Informed consent was obtained from all the patients and data were collected prospectively. We performed analysis of CRP by the method of Choudhry et al. using an immunoturbidometric technique on a Hitachi 911 autoanlyser. Blood specimens were obtained before operation and on the 1st, 2nd, 3rd and 7th postoperative days. Further samples were taken on the 14th postoperative day and at the first follow-up after discharge. Patients were reviewed after one year to determine if any complications had developed.

In the THR group there were seven men and six women with a mean age of 67 years (43 to 82) and in the TKR group four men and nine women with a mean age of 72 years (61 to 79). There was no significant difference in the ages of the two groups (ANOVA, p = 0.151).

We performed all the TKRs through a standard medial parapatellar incision and the THRs through either a posterior or anterolateral incision. Routine pre- and postoperative antibiotic prophylaxis was given to both groups. Tourniquets were used for the TKR patients. The use of a tourniquet has been shown not to alter significantly the level of CRP after operation.

We noted the peak level of CRP and the changes in level with time and analysed the difference in the level in THR and TKR at each stage of sampling. The area under the CRP/time curve for each patient was calculated and the values for the THR and TKR responses were compared.

Table I. Mean values (mg/l, s.d.) for C-reactive protein after THR and TKR

<table>
<thead>
<tr>
<th></th>
<th>THR (n = 13)</th>
<th>TKR (n = 13)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop</td>
<td>4.8 (4.4)</td>
<td>4.7 (3.5)</td>
<td>0.911</td>
</tr>
<tr>
<td>Day 1</td>
<td>59.2 (18.2)</td>
<td>85.2 (39.1)</td>
<td>0.041</td>
</tr>
<tr>
<td>2</td>
<td>98.9 (34.5)</td>
<td>154.9 (47.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>3</td>
<td>100.4 (40.4)</td>
<td>154.2 (55.0)</td>
<td>0.014</td>
</tr>
<tr>
<td>7</td>
<td>31.7 (20.5)</td>
<td>56.8 (36.9)</td>
<td>0.051</td>
</tr>
<tr>
<td>14</td>
<td>25.4 (30.8)</td>
<td>40.2 (34.7)</td>
<td>0.445</td>
</tr>
<tr>
<td>Follow-up</td>
<td>5.9 (3.0)</td>
<td>7.75 (7.4)</td>
<td>0.420</td>
</tr>
</tbody>
</table>
21.5 mg/l for THR and 23.0 mg/l for TKR. Sample sizes were calculated to detect a difference of at least 24 mg/l. Similar differences in peak CRP levels had been noted by Niskanen et al. For a study of \( \alpha = 0.05 \) and \( 1-\beta = 0.80 \), 13 patients were required for each group.

We performed statistical analysis using ANOVA (analysis of variance).

**Results**

Before operation there was no significant difference in the CRP level between the two groups. After 24 hours the difference in response became obvious (Table I, Fig. 1). The peak level of the CRP was reached on the second and third postoperative days for both groups. Although it was achieved at the same time, the level after TKR was on average 50% greater than that after THR (ANOVA, \( p = 0.002 \)).

The increased CRP response to TKR was apparent up to the seventh postoperative day (ANOVA, \( p = 0.051 \)) when no statistically significant difference could be found. The CRP level then decreased during the remainder of the inpatient stay and no statistically significant difference was detected after this. When seen at the first follow-up after discharge again no statistically significant difference was seen. In both groups the level appeared to return to normal after discharge from hospital.

The area under the CRP/time curve was calculated for each patient in both groups. For TKR, the mean value was 741.7 ± 272.7 mg/day/l and for THR 469.2 ± 157.8 mg/day/l. Analysis of variance in the two groups showed a larger response in the TKR group (ANOVA, \( p = 0.005 \)), indicating a greater CRP response in patients with TKR.

There were no postoperative complications in either group during the inpatient stay or in the first year after operation.

**Discussion**

Macrophages which are important in the development of the acute phase response, are common in bone and bone marrow, but occur less often in skeletal muscle. The degree of bone and marrow injury produced during THR and TKR may be important in determining the level of the CRP response. It has been suggested that TKR is a more traumatic procedure and therefore induces a higher level of CRP.

It has also been proposed that measurement of the level of the CRP is a valuable addition to determination of the ESR in monitoring short- and long-term infection after THR. The same application could be made for TKR.

We have shown that the CRP response after TKR is significantly greater than that after THR. The peak level is reached at the same time after operation but that after TKR is significantly greater. The time taken for this elevated response to return to normal is similar for both THR and TKR. Our findings suggest that there is a difference in the CRP level up to the time of discharge but because of the small numbers in each group this difference could not be proven statistically (Fig. 1).

We used the area under the curve for the first seven postoperative days to estimate the total CRP response in both procedures. This time scale allowed analysis of data from all subjects since several patients with TKR were discharged before sampling on day 14. The CRP response to TKR was again significantly higher (ANOVA, \( p = 0.005 \)). We examined the area under the curve since it has been shown that with serial measurements the curve joining the means may not be a good descriptor of a typical curve for an individual.

Our findings agree with those of Niskanen et al. We have shown that the peak level of CRP is reached in the
first 48 hours after operation, but that it may be delayed until 72 hours, and that the differences noted between the two procedures are statistically significant. Thereafter, the level falls quickly in the remainder of the first week after operation and then decreases slowly until the first follow-up. Similar results have been found for patients with rheumatoid arthritis.¹

Our results reinforce previously published data regarding the level of CRP after TKR and suggest that it is as reliable an indicator of early postoperative infection after TKR as after THR. The peak level of CRP is greater after TKR than after THR but both peak at the same time after operation. For any individual patient the peak concentration of CRP may vary after either of these operations, but the level then decreases at a similar rate. Therefore, any upward trend in the CRP level after the third postoperative day may suggest infection. It is not the absolute level but the trend after the peak concentration has been reached which may indicate a complication.

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References


