

# C-reactive Protein Values and Erythrocyte Sedimentation Rates after Total Hip and Total Knee Arthroplasty

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We studied the changes in serum C-reactive protein levels (CRP) and erythrocyte sedimentation rates (ESR) in patients with primary osteoarthritis, who underwent uncomplicated arthroplasty. Of the 28 patients studied, 12 had cementless total hip replacement (THR), and 16 underwent cemented total knee replacement (TKR) with a tourniquet. In both groups serum CRP levels increased rapidly after surgery, peaking on day 2 (THR 23.17 mg/dl, TKR 26.02 mg/dl), and dropping gradually to pre-operative values

on day 21 in THR patients and at the end of the second month in TKR patients. ESR peaked on day 5 after operation (THR 100.5 mm/h, TKR 101.3 mm/h), dropping close to pre-operative values at the end of the third month in THR patients and at the end of the ninth month in TKR patients, although, even after a year, ESRs were slightly above their pre-operative values. Serum CRP levels changed more rapidly than ESRs and returned to normal more rapidly. CRP and ESR values tended to be higher in TKR than in THR patients.

**KEY WORDS:** C-REACTIVE PROTEIN; ERYTHROCYTE SEDIMENTATION RATE; ARTHROPLASTY

## Introduction

Establishing a diagnosis of deep infection after arthroplasty is difficult, and early diagnosis assists the choice of treatment and the likelihood of a successful outcome.<sup>1-4</sup> Investigations of plasma C-reactive protein (CRP) levels and erythrocyte sedimentation rates (ESR) in patients with infected arthroplasty have produced varied results.<sup>2,5-9</sup> In cases of infected arthroplasty, the sedimentation level may be between 16 mm/h and 62 mm/h (mean 35 mm/h) and the CRP

value between 89 mg/l and 135 mg/l (mean 115 mg/l).<sup>2</sup> There were, for example, statistically significant differences in plasma CRP levels but not in ESRs before revision in total hip prosthesis patients undergoing revisions because of mechanical loosening ( $n = 23$ ), compared with those whose revisions were needed because of septic loosening ( $n = 5$ ).<sup>2</sup> ESRs reached normal levels within 3 – 6 months in 75 uncomplicated total hip replacement (THR) patients but always failed to reach the normal levels in

18 patients with radiological and clinical findings of deep infection, and there was a statistically significant difference between the ESRs of the two groups.<sup>5</sup> In a study of 229 total knee replacement (TKR) patients and 301 THR patients, there were no statistically significant differences in ESRs or CRP levels when 82 patients with wound infections (six of which were deep infections) were compared with those without wound problems.<sup>4</sup> In another study about a quarter of CRP levels and ESRs were normal before revision in 23 THR patients in whom revisions were done because of deep infection.<sup>8</sup>

After uncomplicated arthroplasty, the time taken for CRP levels and ESRs to reach their peaks, and then to return to normal levels seems to vary.<sup>1,2,6,10-13</sup> In the present study, we investigated the timing of the changes in plasma CRP levels and ESRs in patients with uncomplicated arthroplasty.

## Patients and methods

We studied 28 uncomplicated cases of primary osteoarthritis, 12 of whom underwent THR (43%) and 16 (57%) of whom underwent TKR between January 1998 and May 1998. The THR group comprised eight women and four men with a mean age of 64 years and the TKR group, four men and 12 women with a mean age of 61 years. For infection prophylaxis a 1500-mg dose of cefuroxime was given intravenously before and two 750-mg doses were given after the operation. For prophylaxis of deep venous thrombosis low-molecular-weight heparin (Dalteparine) 5000 IU was injected subcutaneously pre-operatively and then once daily for 2 weeks. Regional anaesthesia was used in all cases. In the THR group non-cemented prostheses were inserted using a posterolateral approach but in TKR patients cemented prostheses were inserted using an anterior approach and a tourniquet.

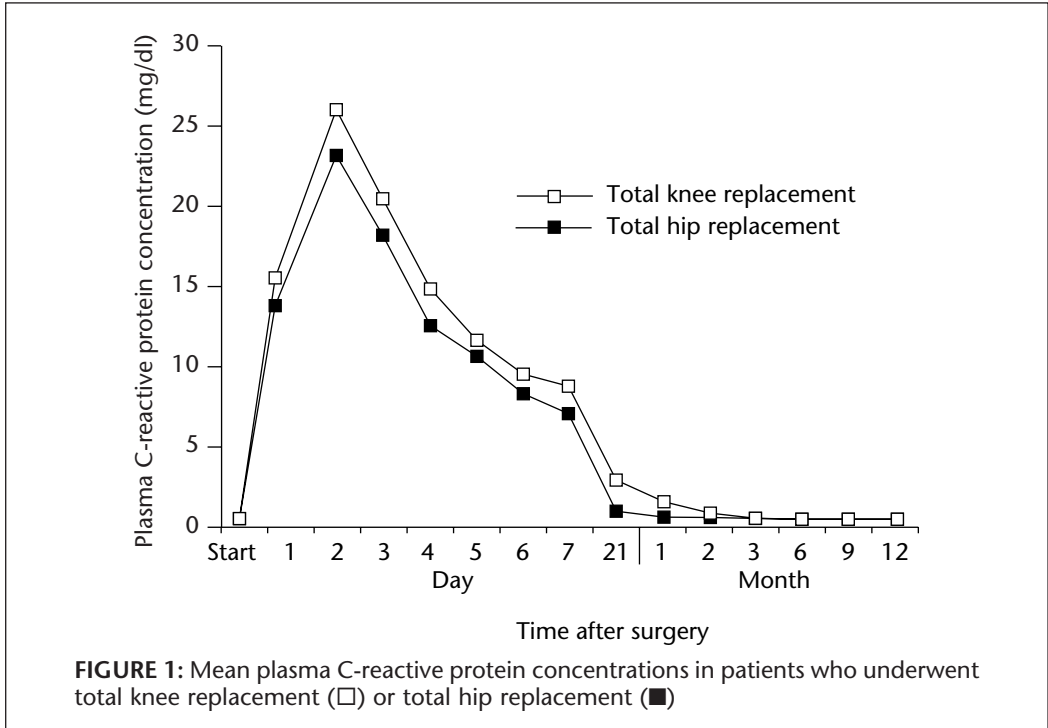
To determine CRP and ESR levels, blood samples were taken before breakfast pre-operatively, and post-operatively on days 1, 2, 3, 5, 6, 7 and 21, and at the end of the first second, third, sixth, ninth and twelfth months. Plasma CRP levels were measured quantitatively by Behring® nephelometer (Behring Marburg GmbH, Marburg, Germany) and ESR was determined by the Westergren method.

We calculated mean percentage changes from the initial values for plasma CRP concentrations and ESR. Statistical comparisons were done using the Wilcoxon test.

## Results

The mean pre-operative CRP values in the THR and TKR groups were equal at 0.54 mg/dl and the mean ESRs were 14.12 mm/h and 16.08 mm/h, respectively. The highest mean CRP values, 26.02 mg/dl in TKR patients and 23.17 mg/dl in THR patients, occurred on day 2 after operation (Fig. 1). Plasma CRP values decreased thereafter to means of 1.0 mg/dl in THR patients (by day 21) and 0.88 mg/dl in the TKR group (at the end of the second month); these values did not differ significantly from the pre-operative values ( $P > 0.05$ ). By the end of the third month the mean plasma CRP values in both groups were similar to the pre-operative values. There were statistically significant differences between the mean plasma CRP values in THR and TKR patients on day 21 and at the end of the first month ( $P < 0.05$ ). There were no other statistically significant differences but mean CRP values in TKR patients were also higher on days 1, 2, 3 and 7, and at the ends of the second and third months. These differences were slightly more marked when the changes were calculated as percentages of the pre-operative value (data not shown).

Mean ESRs were at their highest, 100.5 mm/h and 101.3 mm/h in THR and TKR patients, respectively, on post-operative day 5 (Fig. 2).



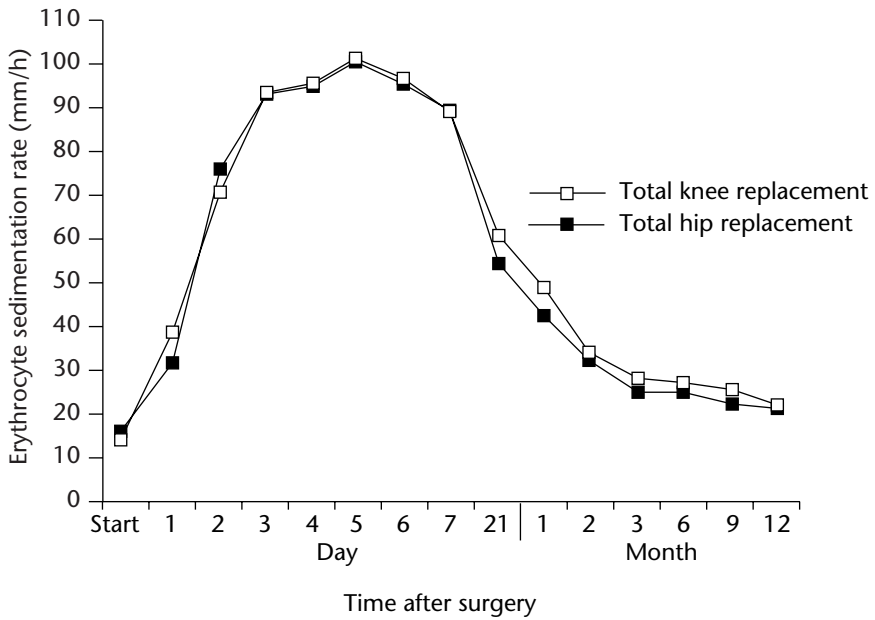
The ESRs decreased thereafter to means of 25 mm/h at the end of the third month in THR patients and 25.6 mm/h in the ninth month in TKR patients, values that did not differ significantly from the pre-operative values ( $P > 0.05$ ). The only significant difference between the ESRs of the THR and TKR groups was on day 1 ( $P < 0.05$ ). At the end of the twelfth month the ESRs in THR and TKR patients were 21.3 and 22.1 mm/h, respectively, higher than the pre-operative values. When the changes in ESRs were calculated as percentages of the pre-operative value, higher percentage variations were found in the TKR group than in the THR group (Fig. 3).

## Discussion

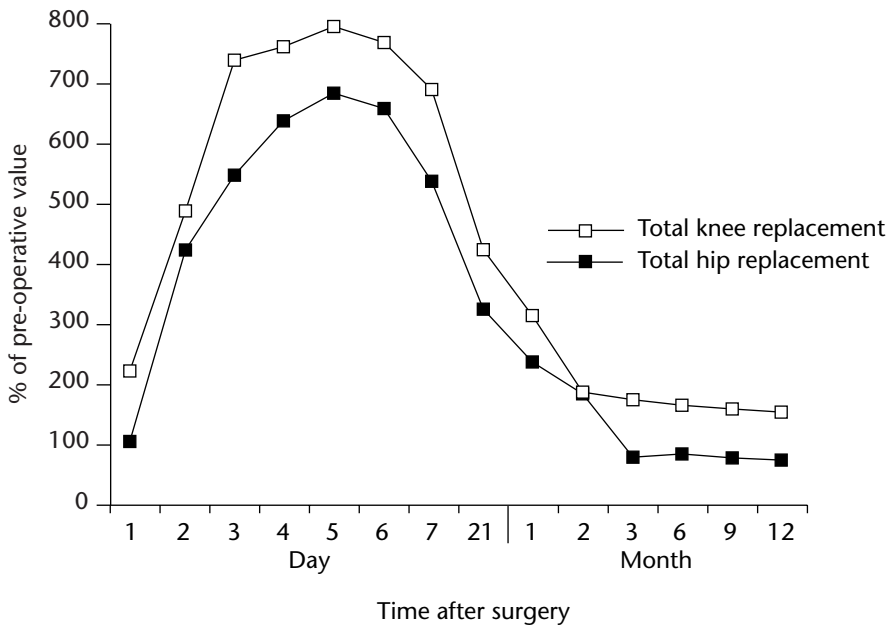
Plasma levels of acute-phase proteins, such as CRP, synthesized by hepatocytes, and of fibrinogen, which has an effect on the acceleration of erythrocyte aggregation, increase in response to tissue trauma in infection, inflammation and malignancy.<sup>14,15</sup>

Diagnosis of infection after arthroplasty is quite difficult. Besides clinical, radiological and scintillographic findings, laboratory determinations of plasma CRP levels and ESRs are valuable in the diagnosis of infection and in the selection of appropriate treatment.<sup>3,16 - 18</sup> The CRP level reacts more rapidly and is more sensitive than is the ESR.<sup>2,5,7,9,11,19,20</sup> Further, the use of cement and tourniquets in operations does not appear to affect CRP levels or ESRs.<sup>6,10,11,20,22</sup>

Previous studies have reported that plasma CRP levels in THR and TKR patients increase rapidly after operation reaching maximum values within 2 - 3 days, after which they decrease rapidly.<sup>1,6,10 - 12</sup> In 186 patients undergoing uncomplicated cemented THR and TKR, plasma CRP reached a peak on day 2 after the operation whereas, in 87 patients undergoing uncemented THR and TKR, it reached its peak on day 3.<sup>6</sup> Plasma CRP levels peaked on day 3 in 109 THR patients, 97 of whom were



**FIGURE 2:** Mean erythrocyte sedimentation rates in patients who underwent total knee replacement (□) or total hip replacement (■)



**FIGURE 3:** Mean percentage variations in erythrocyte sedimentation rates in patients who underwent total knee replacement (□) or total hip replacement (■)

given cemented and 12 uncemented THR, whereas in 39 patients undergoing unicondylar knee replacement (UKR), plasma CRP level peaked on day 2 after operation.<sup>10</sup> In our group of patients plasma CRP levels reached their peak on day 2 after operation. Cemented or uncemented application of prosthesis to a knee or hip joint does not seem to influence the changes in plasma CRP levels after operation (Fig. 1).

In arthroplasty patients, the time taken for plasma CRP levels to return to normal after surgery has been reported as 2,<sup>13</sup> 3,<sup>2,10,11</sup> or 6 – 8<sup>1</sup> weeks, whereas White *et al.*<sup>12</sup> reported that, at the first follow-up visit after discharge from hospital, the CRP levels had returned to normal, although the exact time-period was not reported. White *et al.*<sup>12</sup> also reported that the post-operative CRP level in TKR patients was 50% more compared with that in THR patients until day 7 after operation; thereafter the difference became statistically insignificant and plasma CRP returned to normal levels at the same time in both groups. Niskanen *et al.*<sup>6</sup> also reported that the timing of the return to normal plasma CRP levels was the same in TKR and THR patients, and found higher plasma CRP levels in TKR patients than in THR patients. In our THR and TKR patients, the 3 months that the plasma CRP level took to reach its normal level was longer than the times previously reported but, as previously reported, the timing did not vary with technique.<sup>6,12</sup> In hip and knee arthroplasty, macrophages, which are found in greater numbers in bone and bone marrow than in muscle tissue, provide an effective means of determining plasma CRP levels. The severity of bone and bone marrow trauma was also an influencing factor. Since TKR is more traumatic, the plasma CRP level is expected to be higher.<sup>10</sup>

In our present study the only statistically significant differences between the mean

plasma CRP levels in the TKR and THR groups occurred on day 21 and at the end of the first month, but plasma CRP values were generally higher in TKR patients for the first 3 months after surgery; CRP levels had returned to pre-operative levels by day 21 in THR patients and by the end of the second month in TKR patients. These results suggest that in TKR patients, compared with THR patients, bone and bone marrow tissues were subjected to more trauma, and that in TKR patients the degree of inflammation was higher and the duration longer.

In many studies, in THR and TKR patients, post-operative ESR has been reported to peak on days 5 – 7 and to decline after day 7.<sup>2,5,10,11</sup> The present findings that the ESR reached its peak on day 5 after operation and began to decrease from day 6 are consistent with earlier findings.<sup>5</sup> The plasma CRP level reached its peak more rapidly than did the ESR, indicating that CRP levels are more responsive, a finding consistent with the literature.<sup>2,5,7,9,11,19,21</sup> Statistically significant differences between ESRs on day 1 after surgery in our THR and TKR patients may be attributable to haemodynamic changes resulting from plasma and blood transfusions during THR operations, as mentioned in earlier reports.<sup>2,11</sup>

In our study, ESRs at the end of the third month in THR patients and at the end of the ninth month in TKR patients did not differ significantly from pre-operative values. This shows that ESR tends to decrease slowly compared with CRP, as reported in arthroplasty<sup>10</sup> and in THR patients.<sup>22</sup> The later decrease in ESR in TKR patients compared with THR patients is likely to be for the reasons mentioned above in connection with the later decrease of CRP levels in TKR patients. The post-operative normalization of ESR in THR patients may take 3 – 6 months,<sup>5</sup> or 4 months in THR and TKR patients.<sup>13</sup> The slight elevation of ESR

in our patients at the end of a year is consistent with previous findings that ESR was high even a year after surgery in some THR and UKR patients.<sup>2,10,11</sup>

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## References

- 1 Choudhry RR, Rice RP, Triffitt PD, Harper WM, Greg PJ: Plasma viscosity and C-reactive protein after total hip and knee arthroplasty. *J Bone Joint Surg Br* 1992; **74**: 523 – 524.
- 2 Shih LY, Wu JJ, Yang DY: Erythrocyte sedimentation rate and C-reactive protein values in patients with total hip arthroplasty. *Clin Orthop* 1987; **225**: 238 – 246.
- 3 Peltola H, Vahvanen V, Aalto K: Fever, C-reactive protein and erythrocyte sedimentation rate in monitoring recovery from septic arthritis. *J Pediatr Orthop* 1984; **4**: 170 – 174.
- 4 Gaine WJ, Ramamohan NA, Hullin MG, McCreath SW: Wound infection in hip and knee arthroplasty. *J Bone Joint Surg Br* 2000; **82**: 561 – 565.
- 5 Carlsson AS: Erythrocyte sedimentation rate in infected and non-infected total hip arthroplasties. *Acta Orthop Scand* 1978; **49**: 287 – 290.
- 6 Niskanen RO, Korkala O, Pammo H: Serum C-reactive protein levels after total hip and knee arthroplasty. *J Bone Joint Surg Br* 1996; **78**: 431 – 433.
- 7 Foster IW, Crawford R: Sedimentation rate in infected and uninfected total hip arthroplasty. *Clin Orthop* 1982; **168**: 48 – 52.
- 8 Sanzen L, Sundberg M: Periprosthetic low-grade hip infections erythrocyte sedimentation rate and C-reactive protein in 23 cases. *Acta Orthop Scand* 1997; **68**: 461 – 465.
- 9 Okafor B, MacLellan G: Postoperative changes of erythrocyte sedimentation rate, plasma viscosity and C-reactive protein levels after hip surgery. *Acta Orthop Belg* 1998; **64**: 52 – 56.
- 10 Larsson S, Thelander U, Friberg S: C-reactive protein (CRP) levels after elective orthopedic surgery. *Clin Orthop* 1992; **275**: 237 – 242.
- 11 Aalto K, Österman K, Peltola H, Rasanen J: Changes in erythrocyte sedimentation rate and C-reactive protein after total hip arthroplasty. *Clin Orthop* 1984; **184**: 118 – 120.
- 12 White J, Kelly M, Dunsmuir R: C-reactive protein level after total hip and total knee replacement. *J Bone Joint Surg Br* 1998; **80**: 909 – 911.
- 13 Kolstad K, Levander H: Inflammatory laboratory tests after joint replacement surgery. *Ups J Med Sci* 1995; **100**: 243 – 248.
- 14 Covey C, Albright AJ: Clinical significance of the erythrocyte sedimentation rate in orthopaedic surgery. *J Bone Joint Surg Am* 1987; **69**: 148 – 151.
- 15 Fischer CL, Gill C, Forrester MG, Nakamura R: Quantitation of 'acute-phase proteins' postoperatively. Value in detection and monitoring of complications. *Am J Clin Pathol* 1976; **66**: 840 – 843.
- 16 Gelman MI, Coleman RE, Stevens PM, Davey BW: Radiography, radionuclide imaging and arthrography in the evaluation of total hip and knee replacement. *Radiology* 1978; **128**: 677 – 682.
- 17 Tehranzadeh T, Schneider R, Freiberg RH: Radiological evaluation of painful total hip replacement. *Radiology* 1981; **141**: 355 – 362.
- 18 Lyons CW, Berquist TH, Lyons JC, Rand JA, Brown ML: Evaluation of radiographic findings in painful hip arthroplasties. *Clin Orthop* 1985; **195**: 239 – 251.
- 19 Kaperonis AA, Michelsen CB, Askanazi J, Kinney JM, Chien S: Effects of total hip replacement and bed rest on blood rheology and red cell metabolism. *J Trauma* 1998; **28**: 453 – 457.
- 20 Maury CPJ, Teppo AM, Raunio P: Control of the acute phase serum amyloid A and c-reactive protein response: comparison of total replacement of the hip and knee. *Eur J Clin Invest* 1984; **14**: 323 – 328.
- 21 Rosas MH, Leclercq S, Pegoix M, Darlas Y, Aubriot JH, Rousselot P, *et al*: Contribution of laboratory test, scintigraphy, and histology to the diagnosis of lower limb joint replacement infection. *Rev Rhum Engl Ed* 1998; **65**: 477 – 482.
- 22 Wroblewski BM: ESR and polymethylmethacrylate. *J R Coll Surg Edinb* 1974; **19**: 182 – 185.

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