



Evaluation of the Normal Range of C-reactive Protein and Erythrocyte Sedimentation Rate Serum Level after Total Knee Arthroplasty and Total Hip Arthroplasty in Osteoarthritis Patients without Complications

Mohammad Amin Aslani¹, Fateme Mirzaee², Amin Karimi³, Amir Farahanchi Baradaran⁴, Zohreh Zafarani⁴ and Hamidreza Aslani^{4*}

¹Tehran University of Medical Sciences, Knee and Sport Medicine Research Center, Milad Hospital, Tehran, Iran.

²Department of Orthosis and Prosthesis, University of Social Welfare and Rehabilitation Sciences, Knee and Sport Medicine Research Center, Milad Hospital, Tehran, Iran.

³Faculty of Orthopedics, Shahid Beheshti University of Medical Science, Taleghani Hospital, Tehran, Iran.

⁴Shahid Beheshti University of Medical Sciences, Knee and Sport Medicine Research Center, Milad Hospital, Tehran, Iran.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2021/v33i1931077

Editor(s):

(1) Dr.Chan-Min Liu, Xuzhou Normal University, China.

Reviewers:

(1) Vishwas Sharad Phadke, SSPM Medical College, India.

(2) Shikhar Dalbir Singh, DY Patil School Of Medicine, India.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/72866>

Original Research Article

Received 19 June 2021
Accepted 29 August 2021
Published 06 September 2021

ABSTRACT

Aims: Infection is one of the most serious complications of joint replacement surgeries. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) serum levels are widely used for the evaluation of acute infections after joint replacement surgeries. The aim of our study is to determine normal changes in these inflammatory mediators after total hip arthroplasty (THA) and total knee arthroplasty (TKA).

Methodology: In our study, we enrolled 100 patients with mean age of 68 y/o (57–77) and the diagnosis of primary osteoarthritis who underwent joint replacement surgery. ESR and CRP serum levels were measured before surgery, as well as one, three, and five days after surgery and then again 14, 42, and 90 days after surgery. The results were compared in two groups of TKA and THA, and patients who had undergone THA were further divided into cemented and uncemented groups.

Results: The CRP serum level increased rapidly and reached its maximum level (130.47) on the third day after surgery and returned to its pre-surgery level at the end of three months in all patients. The ESR serum level reached its peak (142.65) on the fifth day after surgery and then decreased; however, it was still slightly higher than the pre-surgery levels at the end of three months. CRP showed faster and more remarkable level changes following surgery compared to ESR, and this elevation was unrelated to the pre-surgery levels. No significant difference was observed between the cemented and uncemented groups.

Conclusion: Changes in CRP and ESR levels after TKA and THA surgeries are reliable indicators for assessment of prosthetic infections. In cases with an elevated CRP serum level on the third day of surgery, a strong suspicion of infection seems completely rational.

Keywords: Total knee arthroplasty; total hip arthroplasty; erythrocyte sedimentation rate; C-reactive protein; surgical site infection.

1. INTRODUCTION

Infection is one of the most serious complications of joint replacement surgeries. Early and accurate diagnosis plays a key role in the treatment to provide early intervention. Diagnosis is especially important in the brief period of time after surgery, and appropriate treatment can eliminate infection and save the prosthesis [1–6].

Several diagnosis methods have been proposed and used in assessment of infection in artificial joints. Every method has its limitations in terms of sensitivity and specificity, making it difficult to make an appropriate decision about starting the treatment. Although the standard method of diagnosis for detecting periarticular infections in artificial joints is bacterial culture, sensitivity is affected by antibiotic administration prior to culture, bacterial adhesion, and the presence of slow-growing microorganisms and biofilms [7].

ESR and CRP are acute phase reactants that are widely used for assessment of the post-surgery stage in joint replacement surgeries. Their three dominant characteristics are as follows:

1. Notable increase in serum levels
2. Short delay in serum level increase
3. Noninvasive and low cost (compare to other modalities of investigations) [8].

However, with respect to nonspecificity for infections and different values before surgery, it is difficult to interpret. Although there are several

studies of CRP and ESR serum levels after TKA and THA surgeries, most of these had limitations such as not determining the highest acceptable level in a normal range, the effect of using cement on the normal range, and the effect of pre-surgery levels that influenced their effective application [1,9].

This study was carried out in Taleghani and Milad Hospital in Tehran, Iran, in 2019. The aim was to determine the normal changes in ESR and CRP after joint replacement surgeries. The result of this study can be used to assess changes in these inflammatory mediators after TKA and THA, as well as the effect of using bone cement on the normal range.

2. MATERIALS AND METHODS

In our study, we enrolled 100 patients who underwent TKA and THA surgeries in Tehran's Taleghani and Milad Hospital in 2019 due to knee and hip pain, and diagnosis of primary osteoarthritis. The mean age of the patients was 68 y/o (57–77). Sixty-eight patients were female and 32 were male. Out of these patients, 70 underwent TKA involving straight midline incision and a standard medial parapatellar capsular arthrotomy, and the prosthesis was fixed in tibia and femur bones with bone cement. Tourniquet was used in all patients. A total of 54 patients in the TKA group were female and 16 were male.

In 30 patients that underwent THA, posterior or anterolateral approach was used and the decision on using cemented or uncemented

stems was based on the patients' condition and bone quality. An acetabular uncemented component was used in all patients. Cemented stems were used in 21, while nine patients received uncemented stems. Sixteen patients were male (11 uncemented and five cemented) and 14 were female (10 uncemented and four cemented). Systemic inflammatory disorders were ruled out in all patients before surgery, and no patients had a history of previous surgery in three months prior to the surgery. Eight patients were excluded from the survey due to infection in the wound area (in three patients the infection was deep), femoral expanding hematoma (in one patient), and not referring for follow-ups at the defined intervals (four patients).

Patients' blood samples were collected before surgery and on the first, third, and fifth days after surgery, and then again on the 14th, 42nd, and 90th days after surgery. ESR and CRP levels were also measured. Immunoturbidometric tests were performed to determine CRP, the normal level of which was less than 10 mg/L. to determine the ESR serum level; the photometrical capillary stopped-flow kinetic analysis method or the Westergren method was used. The normal level in both the methods was less than 20 mm/hr. Prophylactic antibiotics were administrated one hour before surgery and for two days after surgery on all patients. All the patients were ambulated in two days after surgery and were discharged from hospital in five days.

During the first follow-up (two weeks after surgery) and subsequent follow-ups (six weeks after surgery and three months after surgery), besides the determination of ESR and CRP serum levels, patients were examined for clinical signs of infection, delayed wound healing, and continuous pain after surgery. All data was compared with the two variables of CRP and ESR in two groups of TKA and THA, as well as in the cemented and uncemented groups of THA patients. All data was collected using SPSS 16.0, and parametric and nonparametric variables were assessed. $P < 0.05$ was defined as significant.

3. RESULTS

From the 92 patients that remained in the study (63 females and 29 males), CRP and ESR serum levels were collected before and after surgery. Mean value plus standard deviation was determined on every defined date.

CRP serum level changes in the first 24 hours after surgery were notable and it peaked on Day 3. The exponential increase in CRP was greater than ESR values (Fig. 3). The ESR peak was observed on Day 5. In a number of patients, a small decrease was noted in the ESR level in the first 24 hours after surgery compared to the pre-surgery values. ESR increased with a lower speed than CRP, and its maximum level was also lower than CRP.

After hitting the peak following surgery, CRP started to fall, which was rapid in the first two weeks similar to its rapid increase. There was a slowdown in decrease in the CRP level until Day 42. CRP serum levels returned to pre-operative values at the end of the third month. ESR decreased after reaching its maximum level on the fifth day, but this varied among patients. However, at the end of the 90th day, it was still slightly higher than the pre-surgery levels.

The assessment of CRP and ESR serum levels before and after surgery revealed that CRP levels peaked on Day 3 day after surgery regardless of the pre-surgery values, and that the speed of decrease was not related to pre-surgery values.

In case of ESR serum levels, there was a direct relationship between the pre-surgery levels and the rate of increase after surgery. With respect to two groups of TKA and THA, CRP levels increased rapidly after surgery in both groups and peaked on the third day after surgery; however, the maximum level was higher in TKA patients than in THA patients (Table 1). After hitting the peak, CRP levels showed a decrease in both groups. CRP serum levels returned to pre-surgery levels quicker in the THA group (42 days) than in the TKA group (90 days).

The mean ESR level peaked on Day 5 in both TKA and THA groups. We observed a descending pattern in ESR levels afterward. ESR maximum levels were not significantly different between TKA and THA groups (slightly higher in the TKA group). In the last follow-up (Day 90), the ESR mean level was slightly higher than the pre-surgery levels (a bit higher in the TKA group).

No significant differences in post-surgery ESR and CRP mean levels were observed between cemented and uncemented groups in the THA patients.

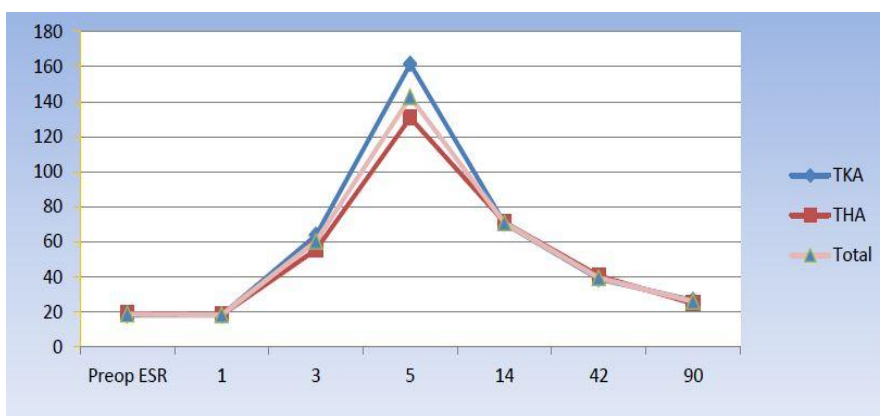


Fig. 1. ESR post operation serum levels

ESR: erythrocyte sedimentation rate, TKA: total knee Arthroplasty, THA: total hip Arthroplasty, Preop: pre-operation

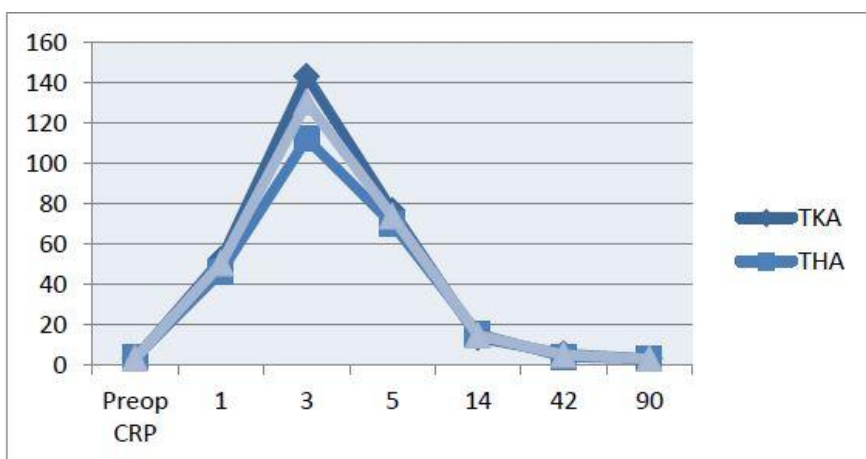


Fig. 2. CRP post operation serum levels

CRP: C-reactive protein, TKA: total knee Arthroplasty, THA: total hip Arthroplasty, Preop: pre-operation

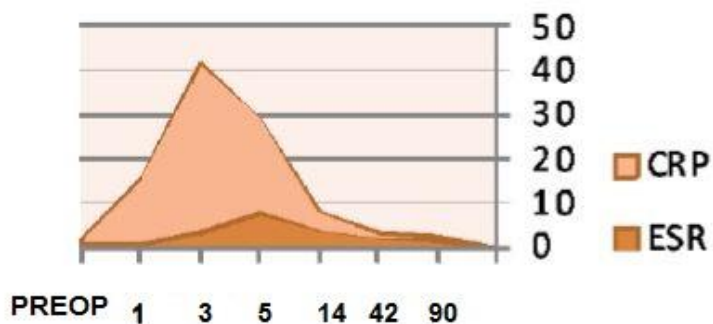


Fig. 3. Comparison between CRP and ESR exponential increase

CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, Preop: pre-operation

Table 1. CRP and ESR serum levels

Times	TKA				THA				Total	
	CRP		ESR		CRP		ESR		CRP	ESR
	Mean (mg/L)	SD	Mean (mm/hr)	SD	Mean (mg/L)	SD	Mean (mm/hr)	SD		
Preoperative	3.22	2.23	18.23	12.42	3.67	2.22	19.22	11.18	3.39	18.68
PO first day	52.45	35.42	18.10	14.23	46.49	31.07	18.34	14.09	50.48	18.21
PO third day	143.16	43.67	63.72	34.78	112.33	39.81	55.49	37.32	130.47	60.20
PO fifth day	76.54	31.65	161.49	64.43	70.12	32.40	130.81	58.30	73.88	142.65
PO fourteenth day	13.67	12.78	70.43	51.87	15.61	16.61	71.15	41.02	14.68	70.76
PO forty-second day	5.66	7.61	38.76	40.34	4.19	5.02	40.63	46.39	5.14	39.37
PO ninetieth day	3.11	3.69	26.59	31.33	3.21	4.15	24.83	33.03	3.14	25.91

PO: Post Operation, SD: standard deviation, TKA: total knee Arthroplasty, THA: total hip Arthroplasty, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein

4. DISCUSSION AND CONCLUSION

Infection is a serious complication that patients develop after joint replacement surgeries. Early and accurate diagnosis may help to treat the infection through washout and debridement, and save the prosthesis [10,11]. There is a variety of methods to make early diagnosis. CRP and ESR acute-phase inflammatory mediators are commonly used [5,7,11], but it is critical to determine the extent of prosthesis infection in the post-operative period. In the first place, it requires defining the normal range of changes in post-operational patients without complications.

ESR and CRP serum levels are affected by systemic disorders [5,12]. We tried to eliminate these effects by excluding patients with systemic inflammatory disorders; however, other diseases such as diabetes mellitus, cardiac diseases, chronic lung diseases, chronic renal diseases, malignancies, and many other disorders influence the levels of these mediators, which seem very difficult to eliminate.

Previous studies have attempted to find a tool for early diagnosis of surgical complications such as infection. Many studies evaluated ESR and CRP serum levels and reported different amounts for the normal range on different days. Reportedly, CRP level reached its peak mostly on Days 2 and 3, but more differences were reported for the ESR peak day, which varied from Days 5 to 9 [13]. In our study, CRP and ESR peaks were observed on the third and fifth days, respectively.

Moreover, many studies have been carried out on the descending patterns of ESR and CRP as well as the time taken to return to the normal range. In some studies, ESR normalized in six months, while others reported it to be higher than the normal range after one year [2,14]. It was higher than normal after 90 days in our study as well. The descending pattern and normalization of the CRP serum level varied from 21 days in some studies to six months after surgery in other studies [6,15]. In our study, CRP serum levels returned to their pre-operational levels at the end of three months.

In previous surveys, differences between ESR and CRP serum levels after TKA and THA were reported to be associated with differences in trauma to bone and bone marrow tissues, whereas trauma to soft tissue and muscles were reported to be unrelated to ESR and CRP changes. Since trauma to bone and bone marrow tissue is heavier in TKA than in THA,

ESR and CRP increase is 50% greater in TKA than in THA, as reported in previous studies. Also, it requires longer time for these mediators to return to the normal range in TKA [3,9,15,16]. We observed the same changes and differences in our study as well.

Although the change in the level of inflammatory factors is significant because of complications, their main limitation is nonspecific. Hence, they may increase in many other conditions such as hematoma, hemarthrosis, phlebitis, and infection in other areas of body [7,17]. As reported in a survey, these mediators increase to 28 times the normal range in skeletal infections and to 11 times the normal range in other infections. It is stated that a CRP level of 12 times the normal range at any time after surgery is symptomatic of prosthesis infection and requires surgical intervention [4,16,17].

In our study, due to more significant changes in CRP serum levels, unrelated increases in pre-surgery levels, and quicker changes in response to inflammatory process, variables such as age, sex, duration of surgery, amount of blood loss during surgery, use of tourniquet, use of bone cement, anesthetic drugs, and type of anesthesia are not associated with CRP changes [2,15] in cases with elevated CRP serum levels three days after surgery. Hence, a strong suspicion of infection is not unwarranted, and thorough investigation seems completely rational.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Paul HY, Cross MB, Moric M, Sporer SM, Berger RA, Della valle CJ. The 2013 frank stinchfield award: diagnosis of infection in the early postoperative period after total hip arthroplasty. *Clinical Orthopaedics and Related Research*. 2014;472(2): 424–9.
2. Park KK, Kim TK, Chang CB, Yoon SW, Park KU. Normative temporal values of crp and esr in unilateral and staged bilateral tka. *Clinical Orthopaedics and related Research*. 2008;466(1):179–88.
3. Azboy I, Çatal B, Başarir K, Mutlu M, Bilgen ÖF, Parvizi J. The natural course of serum d-dimer, c-reactive protein, and erythrocyte sedimentation rate levels after uneventful primary total joint arthroplasty. *The Journal of Arthroplasty*. 2021;
4. Triantafyllopoulos GK, Memtsoudis SG, Zhang W, Ma Y, Sculco TP, Poultsides LA. Periprosthetic infection recurrence after 2-stage exchange arthroplasty: failure or fate? *the Journal of Arthroplasty*. 2017;32(2):526–31.
5. Parvizi j, Fassihi SC, Enayatollahi MA. Diagnosis of periprosthetic joint infection following hip and knee arthroplasty. *Orthopedic Clinics*. 2016;47(3):505–15.
6. Berbari E, Mabry T, Tsaras G, Spangehl M, Erwin PJ, Murad MH, et al. inflammatory blood laboratory levels as markers of prosthetic joint infection: a systematic review and meta-analysis. *JBJS*. 2010;92(11):2102–9.
7. Larsson S, Thelander U, Friberg S. c-Reactive protein (crp) levels after elective orthopedic surgery. *Clinical Orthopaedics and Related Research*. 1992;(275):237–42.
8. Simon L, Gauvin F, Amre DK, Saint-louis P, Lacroix J. Erratum: serum procalcitonin and c-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis (clinical infectious diseases (july 15, 2004) 39 (206-217)). *Clinical Infectious Diseases*. 2005;40(9):1386–8.
9. White J, Kelly M, Dunsmuir R. C-reactive protein level after total hip and total knee replacement. *The Journal of Bone and Joint Surgery British Volume*. 1998;80(5):909–11.
10. Neumaier M, Metak G, Scherer MA. C-reactive protein as a parameter of surgical trauma: crp response after different types of surgery in 349 hip fractures. *Acta Orthopaedica*. 2006;77(5):788–90.
11. Herrero FA, Lozano RL, Muñoz AS. Descriptive analysis of c-reactive values after uncomplicated total hip and knee arthroplasty. *Acta Ortopedica Mexicana*. 2008;22(2):80–4.
12. Kuiper JWP, Willink RT, Moojen DJF, Van den bekerom MPJ, Colen S. Treatment of acute periprosthetic infections with prosthesis retention: review of current concepts. *World Journal of Orthopedics*. 2014;5(5):667.
13. Berbari E, Baddour FLM. Prevention of prosthetic joint and other types of orthopedic hardware infection.
14. Forster IW, Crawford R. Sedimentation rate in infected and uninfected total hip arthroplasty. *Clinical Orthopaedics and Related Research*. 1982;168:48–52.
15. Gaitonde S, Samols D, Kushner I. C-reactive protein and systemic lupus erythematosus. *Arthritis Care & Research*. 2008;59(12):1814–20.
16. Alijanipour P, Bakhshi H, Parvizi J. Diagnosis of periprosthetic joint infection: the threshold for serological markers. *Clinical Orthopaedics and Related Research*. 2013;471(10):3186–95.
17. Codine P, Barbotte E, Denis-laroque F, lansac H, dupetit T, Pradies F, et al. Surveillance biologique après chirurgie orthopédique. quel apport au diagnostic des complications infectieuses et thromboemboliques?: première partie: évolution de la crp et des leucocytes. place dans la stratégie diagnostique des infections postopératoire. in: *Annales de réadaptation et de médecine physique*. Elsevier; 2005;590–7.

© 2021 Aslani et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:

<https://www.sdiarticle4.com/review-history/72866>