

Is procalcitonin a more sensitive parameter than other acute phase reactants for early infection in arthroplasty?

[Artroplastide erken enfeksiyon için prokalsitonin diğer akut faz reaktanlarından daha hassas bir parametre mi?]

Ahmet Özmeriç^{1,3},
Halil Burç²,
Nevres Hürriyet Aydoğan³,
Yakup Barbaros Baykal²,
Tolga Atay²

¹ Dr. Nafiz Körez Hospital, Department of Orthopedics and Traumatology, Ankara, Turkey

² University Of Süleyman Demirel, Department of Orthopedics And Traumatology, 32040, Çünür, Isparta, Turkey

³ Ankara Hospital, Department of Orthopedics And Traumatology, Ankara, Turkey

Yazışma Adresi

[Correspondence Address]

Dr. Ahmet Özmeriç

Ankara Hospital, Department of Orthopedics And Traumatology, Ankara, Turkey
Şükriye Mh. Ulucanlar Cd. No:89 Altındağ 06340 ANKARA

Tel. 0.312 595 30 00

Fax. 0.312 363 33 96

E-mail. aozmeric77@yahoo.com

ABSTRACT

Objectives: The routine laboratory parameters for detection of early infection could be increased after surgical trauma in endoprosthesis surgery. The aim of this study was to compare the early infective complication marker Procalcitonin with routine markers.

Methods: Twenty patients with primary total hip prosthesis and 30 knee prosthesis were enrolled. The changes in procalcitonin, C-reactive protein levels, white blood cell count, and erythrocyte sedimentation rate were evaluated preoperatively, at postoperative first day, postoperative fifth day and on the day of discharge.

Results: Procalcitonin values of patients who developed superficial infection were statistically high in comparison with uncomplicated patients at post-op Day 1 and Day 5 ($p < 0.05$). The level of C-reactive protein, white blood cell count, and erythrocyte sedimentation rate peaked on postoperative Day 1. These levels decreased by postoperative Day 5 and on the day of discharge but did not reach preoperative mean values.

Conclusion: Procalcitonin is a more selective parameter to predict early infection status following total endoprosthetic surgery. When factors that cause an inflammatory response were eradicated, procalcitonin levels dropped more rapidly and followed a standard postoperative kinetic pathway.

Key Words: acute phase response, C-reactive protein, procalcitonin, total endoprosthesis

Conflict of Interest: No conflict of interest was declared by the authors.

ÖZET

Amaç: Total endoprotez cerrahisi sonrası enfeksiyonu değerlendirmek için rutin olarak kullanılan laboratuvar parametreleri, enfeksiyondan bağımsız olarak cerrahi travma sonrası da artış gösterebilmektedir. Bu çalışmada, enfektif komplikasyonları teşhis için, erken enfeksiyon belirteci olan Prokalsitonin ile rutin belirteçleri karşılaştırmak amaçlanmıştır.

Yöntem: Yirmi hastaya primer total kalça protezi, 30 hastaya diz protezi uygulanmıştır. Her iki grupta preoperatif, postoperatif 1. gün, postoperatif 5. gün ve taburcu olurken prokalsitonin, C-reaktif protein, beyaz küre sayısı ve eritrosit sedimentasyon hızı değerlerindeki değişimler incelenmiştir.

Bulgular: Diz ve kalça protezlerinde prokalsitonin düzeyleri postoperatif 1. günde artmıştır. Postoperatif 1. ve 5. günde erken enfeksiyon gelişen hastalarda, komplikasyon görülmeyenlere göre istatistiksel olarak anlamlı bir fark izlenmiştir ($p < 0.05$). C-reaktif protein, beyaz küre sayısı ve eritrosit sedimentasyon hızı değerlerine bakıldığında, bütün parametrelerde birinci günde artış gözlenmiştir. Bunların seviyeleri postoperatif 5. günde ve taburcu sırasında düşüş göstermiştir ancak postoperatif değerlere ulaşmamıştır.

Sonuç: Prokalsitoninin değerlendirilen diğer parametrelerle kıyaslandığında cerrahinin yaratmış olduğu enflamatuvar yanıtın az etkilendiği ve daha hızlı cevap verdiği, enflamatuvar yanıtın neden olan etken ortadan kalktıktan sonra çok daha hızlı düştüğü ve standart bir postoperatif kinetik izlediği gözlenmiştir.

Anahtar Kelimeler: akut faz reaksiyonu, C-reaktif protein, prokalsitonin, total endoprotez

Çıkar Çatışması: Yazarların hiçbir çıkar çatışması yoktur.

Introduction

Arthroplasty is a procedure frequently used to remedy complaints such as pain and restricted movement caused by dysfunctions of the knee and hip joint surfaces when conservative treatment and other surgical procedures have failed. The number of patients treated with total knee and hip prostheses is increasing everyday in line with the increase in the elderly population, and extended life expectancy. Thus the rate of complications is also increasing. Infection remains a serious complication [1], with current rates of infection in the primary prosthesis reported as 1.5% - 2.5%, and 3.2% - 5.6% after revision arthroplasty [2,3].

Nowadays, acute phase reactants such as body temperature, white blood cells (WBC), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), which are used as systemic infection parameters, are not considered as specific markers. The inflammatory response that develops after orthopedic endoprosthesis surgery is not an infection, but causes an increase in those parameters. Therefore, studies and research are still underway to find an infection marker that identifies infective complications that develop during the early post-operative period, is not affected by surgical trauma, is specific to bacterial infections, and responds quickly after suitable antibiotic treatment at the same time. In recent years, procalcitonin (PCT) as a new parameter, has been added to the list of infection markers.

The purpose of this study was to investigate the kinetics demonstrated by PCT, a new marker for the detection of early infection, in patients that underwent total endoprosthesis surgery. PCT was also assessed in comparison to laboratory parameters such as CRP, WBC, and ESR in order to identify superiority.

Materials and Methods

Fifty patients who had undergone a primary total arthroplasty, and were being monitored between December 2007 and September 2008 were enrolled in the present study. Patients experiencing any form of bleeding disorders, with a history of bone infection, previous surgery on the same side, and all revision arthroplasty were excluded from the study.

Demographic data, such as age and gender, and clinical symptoms of the patients related to the need for total arthroplasty were recorded. The patients were monitored for clinical and laboratory infection and post-op complications during the period before surgery until postoperative discharge. Four blood samples were taken from all patients at the same time in the morning one day before surgery, post-op Day 1, 5, and on the day of discharge (Day 12).

5 – 7 ml blood samples, to be used for PCT monitoring, were placed in disposable, vacuumed, non-anticoagulant glass tubes, and left until the blood clotted. They were centrifuged for 10 minutes at 1500 g within half an hour,

and separated into serum. The separated serum tubes were kept at -70°C until the assay. Each serum sample was examined only once on study day. VIDAS B.R.A.H.M.S. PCT which is an automated test for use on the mini VIDAS instruments for the determination of human PCT in human serum was used (**bioMérieux Clinical Diagnostics**, F-69280 Marcy l'Etoile, France). VIDAS B.R.A.H.M.S. PCT ELFA (Enzyme-Linked Fluorescent Assay) technique was performed to evaluate serum PCT. The coefficient of variation (CV) of the test was 6% at a PCT plasma concentration of 0.01 ng/ml, and 15% at 8.9 ng/ml. The serum samples taken for CRP were tested using a nephelometric method (Dade Behring, Germany BN II device) on the same day. An LH 750 Analyzer (Beckman Coulter, England) device was used for WBC, and the Westergren method (Therma-Lineer, Spain) was conducted for ESR measurements.

Informed consent was obtained from all patients and the study was approved by the Local Ethics Committee (1604-TU 08).

Statistical analysis

Data analysis was performed using the SPSS for Windows 15 package program. Descriptive statistics for continuous variables are shown as mean standard deviation or median (5 - 95 CI%), and those for nominal variables are shown as the number of observations and as percentages. The Wilcoxon paired comparison test was used to investigate significant differences between the independent groups and the Mann-Whitney U test was used to investigate significant differences between the groups in terms of median values. Test of normality was performed with Shapiro-Wilk test. Nominal variables were evaluated by Fisher's exact chi-square test. Changes in the PCT, CRP, WBC and ESR levels were assessed by repeated measures variance analysis. To determine the follow-up period, in which a significant difference was noted, a Bonferroni correction multiple comparison test was performed. A p value of <0.05 was considered to be statistically significant. However, in all of the possible multiple comparisons, a Bonferroni adjustment was made.

Results

The study comprised 30 total knee prosthesis (TKP) patients, and 20 total hip prosthesis (THP) patients. Eight (26.67%) of the patients receiving total TKP were male, and 22 (73.33%) were female. Five (25%) of the patients receiving THP were male, and 15 (75%) were female. There was no significant difference between the groups based on gender ($p>0.05$).

The average age of TKP patients was 70.2 years, while the average age of THP patients was 66.05 years. The average age of all the patients was 68.56 years. There was no significant difference between the groups based on age ($p>0.05$). In all patients the diseases related to other systemic origin, hypertension was noted in 11

(22%) cases. This was followed by diabetes in 3 patients (6%). All of the patients were in good health and well controlled regarding their systemic diseases. Their clinical and biochemical parameters were in normal range.

Postoperative complications were observed in 10 of the total 50 patients; 7/30 that underwent TKP and 3/20 that underwent THP developed superficial infections during the postoperative period. PCT values on post-op day 1 and post-op day 5 of the patients who developed superficial infection in the TKP group were statistically high in comparison with uncomplicated TKP patients ($p < 0.05$). CRP and WBC values of these 7 patients were statistically high on the day of discharge ($p < 0.05$). PCT values on post-op day 1 of the 3 THP patients with complications were statistically high ($p < 0.05$). There was no statistically significant difference between the other parameters of these 3 patients.

The average Pre PCT for TKP patients was 0.05 ng/ml, in comparison to the average Pre PCT for THP patients, which was 0.03 ng/ml. The mean PCT value on post-op day 1, was 1.13 mg/ml for TKP patients, and 0.52 ng/ml for THP. On post-op day 5, the PCT values regressed to a level close to the norm interval. The average PCT on post-op Day 5 for TKP patients was 0.16 ng/ml, and 0.14 ng/ml for THP. The average PCT on the day of discharge was 0.05 ng/ml for TKP patients, and 0.04 ng/ml for THP. However, no significant differences were demonstrated in the PCT values between the TKP and THP groups throughout the whole examination period ($p > 0.05$) (Fig1).

There was a statistically significant difference between the PCT of TKP patients based on measurements taken pre-op, post-op Day 1, and post-op Day 5 ($p < 0.05$). There was no statistically significant difference between the PCT level at pre-op and the PCT level at discharge

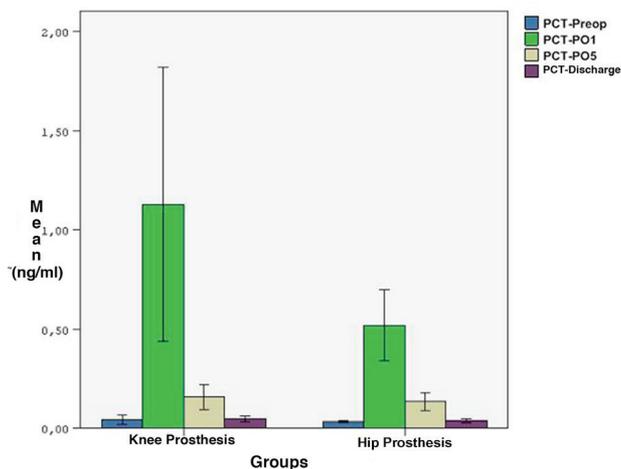


Figure 1. Day-based distribution of Procalcitonin values of total knee and total hip prosthesis patients.

($p > 0.05$). There was a statistically significant difference between the PCT at post-op Day 1, the PCT at post-op Day 5, and the PCT at discharge ($p < 0.05$). There was also a statistically significant difference between the PCT at post-op Day 5 and the PCT at discharge ($p < 0.05$). Similarly, there was no statistically significant difference between the pre-op PCT and discharge PCT of THP patients ($p > 0.05$). There was a statistically significant difference between the PCT levels between all other days ($p < 0.05$) (Table 1).

The pre-op CRP value of TKP patients participating in the study was 4.71 ± 2.19 mg/L (median 3.51 mg/L; min-max 3.02- 10 mg/L), and the pre-op CRP value of THP patients participating in the study was 3.34 ± 0.67 mg/L (median 3.02 mg/L; min-max 3.02-5.13 mg/L). These values were within normal limits (< 10 mg/L). There was a significant difference between the pre-op CRP values

Table 1. Comparison of Procalcitonin (ng/ml) values on the preoperative day, postoperative Day 1, postoperative Day 5 and the day of discharge between total knee prosthesis and total hip prosthesis groups.

| Total Knee Prosthesis | | Total Hip Prosthesis | |
|-----------------------|--------------------|----------------------|---------|
| | Median (Min-Max) | Median (Min-Max) | p-value |
| Preop | 0.032 (0.018-0.36) | 0.032 (0.019-0.06) | 0.744 |
| Post-op Day 1 | 0.3 (0.07-5.19) | 0.48 (0.15-8.93) | 0.812 |
| Post-op Day 5 | 0.09 (0.022-0.73) | 0.12 (0.023-0.4) | 0.559 |
| Discharge | 0.033 (0.018-0.21) | 0.039 (0.019-0.09) | 0.789 |

There was a non-significant difference in Procalcitonin levels between Total Knee Prosthesis and Total Hip Prosthesis groups ($p > 0.05$).

of both groups ($p < 0.05$). There was an increase in the CRP values of all patients after knee and hip surgery. Even though CRP peaked on Day 2, the values were also high on post-op Day 1. The average post-op Day 1 values for TKP and THP patients were 132.45 ± 42.06 mg/L (median 138 mg/L; min-max 61.4-204 mg/L) and 135.07 ± 34.99 mg/L (median 139 mg/L; min-max 59.1-193 mg/L), respectively. There was no statistically significant difference between the post-op Day 1 CRP values for both groups ($p > 0.05$). Even though there was a decrease in CRP levels on post-op Day 5, they were still high. The average post-op Day 5 values for TKP and THP patients were 85.99 ± 44.04 mg/L (median 83.5 mg/L; min-max 26.7-162 mg/L) and 80.18 ± 31.01 mg/L (median 77.9 mg/L; min-max 40.2-149 mg/L), respectively. There was no significant difference between the post-op Day 5 CRP values for both groups ($p > 0.05$). Although the decreased kinetic in average CRP values was continued at discharge, they were still higher in comparison to the pre-op CRP values. The average discharge value for TKP patients was 18.77 ± 22.71 mg/L (median 13.2 mg/L; min-max 3.02-126 mg/L), and 23.43 ± 24.77 mg/L (median 13.7 mg/L; min-max 3.02-88.1 mg/L) for THP patients. There was no significant difference between the discharge CRP values for both groups ($p > 0.05$) (Fig2) (Table 2).

The average pre-op WBC count for TKP patients was 6.84 ± 1.57 cellx 10^9 /L (median 6.6 cellx 10^9 /L; min-max 4.1-10.9 cellx 10^9 /L), and it was 7.19 ± 1.65 cellx 10^9 /L (median 6.9 cellx 10^9 /L; min-max 5.2-10.6 cellx 10^9 /L) for THP patients. The pre-op WBC count was within normal limits for all patients (< 11 cellx 10^9 /L). There was an increase in WBC count of all patients on post-op Day 1. The average post-op Day 1 WBC count for TKP patients was 12.84 ± 3.58 cellx 10^9 /L (median 12.6 cellx 10^9 /L; min-max 7.9-25.2 cellx 10^9 /L), and 13.89 ± 3.64 cellx 10^9 /L

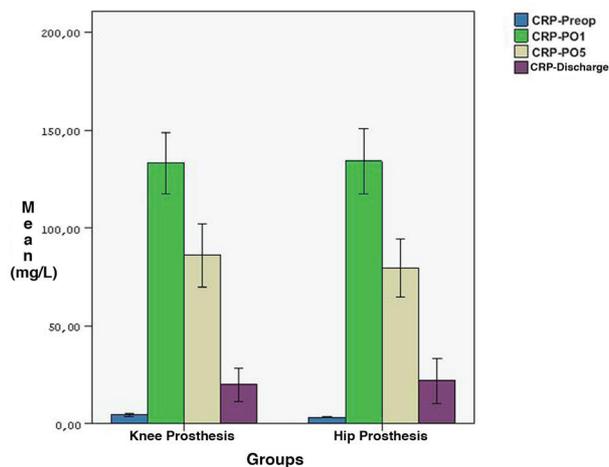


Figure 2. Day-based distribution of C-reactive protein values of total knee and total hip prosthesis patients.

(median 12.9 cellx 10^9 /L; min-max 9.2-24.3 cellx 10^9 /L) for THP patients. There was a sharp decrease in WBC counts on post-op Day 5. The average post-op Day 5 WBC count for TKP patients was 8.59 ± 3.55 cellx 10^9 /L (median 7.6 cellx 10^9 /L; min-max 5.1-24.9 cellx 10^9 /L), and 9.3 ± 2.61 cellx 10^9 /L (median 8.6 cellx 10^9 /L; min-max 6.3-15.5 cellx 10^9 /L) for THP patients. The WBC count reduced at discharge to a level close to normal. The average discharge WBC count for TKP patients was 7.52 ± 1.61 cellx 10^9 /L (median 7.4 cellx 10^9 /L; min-max 5.2-11.3 cellx 10^9 /L) and 8.21 ± 1.41 cellx 10^9 /L (median 8.2 cellx 10^9 /L; min-max 4-11 cellx 10^9 /L) for THP patients. There was no statistically significant difference between the values for both groups ($p > 0.05$) (Fig3) (Table 3).

The average pre-op ESR levels were 15.79 ± 9.65 mm/hr (median 16 mm/hr; min-max 1-34 mm/hr) and 15.42 ± 8.09 mm/hr (median 14 mm/hr; min-max 1-33

Table 2. Comparison of CRP (mg/L) values on the preoperative day, postoperative Day 1, postoperative Day 5 and the day of discharge between total knee prosthesis and total hip prosthesis groups.

| Total Knee Prosthesis | | Total Hip Prosthesis | | p-value |
|-----------------------|---------------------|----------------------|--|---------|
| | Median (Min-Max) | Median (Min-Max) | | |
| Preop | 3.51 (3.02-10) | 3.02 (3.02-5.13) | | *0.009 |
| Post-op Day 1 | 138 (61.4-204) | 139 (59.1-193) | | 0.953 |
| Post-op Day 5 | 83.5 (26.7-162) | 77.9 (40.2-149) | | 0.736 |
| Discharge | 13.2 (3.02-126) | 13.7 (3.02-88.1) | | 0.898 |

*There was a significant difference in CRP levels between Total Knee Prosthesis and Total Hip Prosthesis groups ($p < 0.05$).

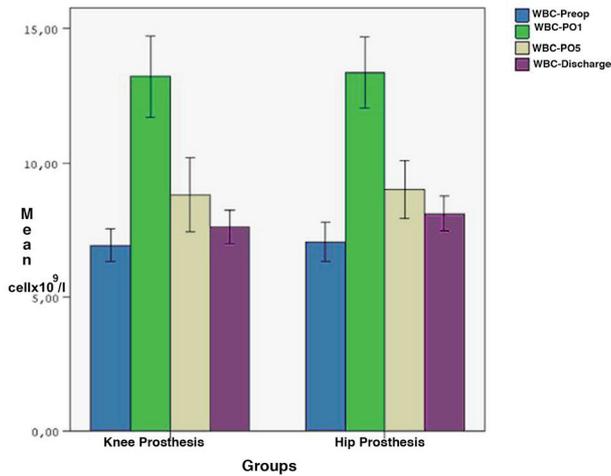


Figure 3. Day-based distribution of White Blood Cell counts of total knee and total hip prosthesis patients.

Table 3. Comparison of WBC (cellx10⁹/L) values on the preoperative day, postoperative Day 1, postoperative Day 5 and the day of discharge between total knee prosthesis and total knee prosthesis groups.

| Total Knee Prosthesis | | Total Hip Prosthesis | |
|-----------------------|------------------|----------------------|---------|
| | Median (Min-Max) | Median (Min-Max) | p-value |
| Preop | 6.6 (4.1-10.9) | 6.9 (5.2-10.6) | 0.766 |
| Post-op Day 1 | 12.6 (7.9-25.2) | 12.9 (9.2-24.3) | 0.566 |
| Post-op Day 5 | 7.6 (5.1-24.9) | 8.6 (6.3-15.5) | 0.272 |
| Discharge | 7.4 (5.2-11.3) | 8.2 (4-11) | 0.920 |

There was a non significant difference in WBC levels between Total Knee Prosthesis and Total Hip Prosthesis groups ($p > 0.05$).

mm/hr) for TKP and THP patients, respectively. Preop ESR values of all patients were within normal limits (< 20 mm/hr). There was an increase in ESR values on post-op Day 1, even though it was not as great as in other parameters. The average post-op Day 1 ESR of TKP patients was 51.65 ± 27.07 mm/hr (median 50 mm/hr; min-max 13-113 mm/hr), and it was 42.61 ± 19.71 mm/hr (median 40 mm/hr; min-max 18-97 mm/hr) for THP patients. ESR values peaked on post-op Day 5. The average post-op Day 5 ESR of TKP patients was 104.17 ± 22.74 mm/hr (median 102 mm/hr; min-max 57-157 mm/hr) and 98.28 ± 22.28 mm/hr (median 100 mm/hr; min-max 38-141 mm/hr) for THP patients. There was a decrease in the ESR of patients at discharge, which was a slower kinetic in comparison to other parameters. The average ESR of TKP patients at discharge was 75.27 ± 27.69 mm/hr (median 73 mm/hr; min-max 22-125

mm/hr) and it was 72.81 ± 28.17 mm/hr (median 77 mm/hr; min-max 6-128 mm/hr) for THP patients. There was no statistically significant difference between the ESR of both groups ($p > 0.05$) (Fig4) (Table 4).

Discussion

Arthritis is a disabling condition that leads to long-term deterioration in quality of life. There has been a tremendous increase in arthroplasty throughout the world. Kurtz et al used a national database with 300,000 discharge records per year, to quantify trends in THA and TKA use in the United States between 1990 and 2002 [4]. They also assumed increases in primary and revision TKAs of approximately 600% to 670% over the next 25 years, and increases in primary and revision THAs of approximately 140% to 170% [5].

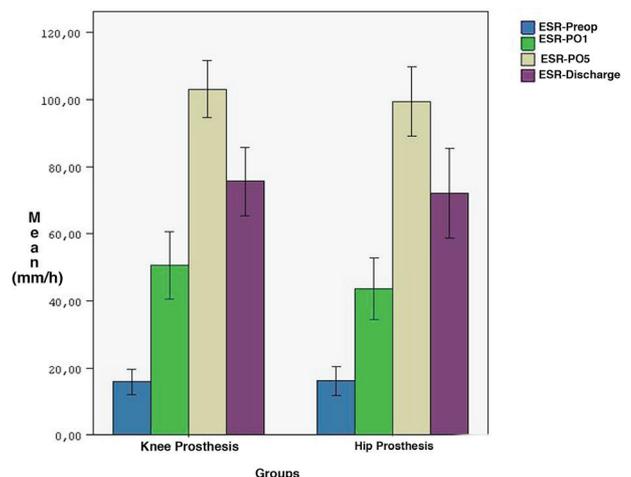


Figure 4. Day-based distribution of Erythrocyte Sedimentation Rate values of total knee and total hip prosthesis patients.

Table 4. Comparison of ESR (mm/h) values on the preoperative day, postoperative Day 1, postoperative Day 5 and the day of discharge between total knee prosthesis and total hip prosthesis groups.

| Total Knee Prosthesis | | Total Hip Prosthesis | |
|-----------------------|---------------------|----------------------|---------|
| | Median (Min-Max) | Median (Min-Max) | p-value |
| Preop | 16 (1-34) | 14 (1-33) | 0.692 |
| Post-op Day 1 | 50 (13-113) | 40 (18-97) | 0.446 |
| Post-op Day 5 | 102 (57-157) | 100 (38-141) | 0.827 |
| Discharge | 73 (22-125) | 77 (6-128) | 0.789 |

*There was non significant difference in ESR levels between Total Knee Prosthesis and Total Hip Prosthesis groups ($p>0.05$).

Taking into consideration of the importance of orthopedic surgical infection, it is extremely important that any infections that develop should be diagnosed early, and treated as soon as possible in order to avoid unnecessary economic burdens on the patient and healthcare institutions.

Nowadays, numerous laboratory parameters are used for the early diagnosis of infection. Recent studies are still underway to find an infection marker which identifies infective complications that develop during the early post-operative period, is not affected by surgical trauma, is specific to bacterial infections, and responds quickly after suitable antibiotic treatment at the same time. Based on this objective, the purpose of our study was to investigate PCT, which displays high selectivity, especially in bacterial infections, and has come into widespread use in recent years. PCT has been suggested as a more accurate and specific biomarker than other traditional molecules such as CRP with which to differentiate bacteria from other infectious agents such as viruses [6].

There are a limited number of studies conducted on the kinetic of PCT following surgical trauma. One such study conducted by Meissner et al. on 130 patients investigated the change in post-op plasma PCT and CRP levels for various surgery types [3]. It was concluded that the plasma PCT level increased in 95% of patients, after major abdominal surgery and surgery of the mediastinum. In the current study, pre-op values of PCT were measured below 0.5 ng/ml. Kim et al. demonstrated that a cut-off PCT concentration of 0.4 ng/ml was able to rule out bacteremia in patients with acute fever [7]. In the present study, the average post-op PCT levels for both groups of patients were higher than the normal

interval. The increase in PCT levels was considered to be connected to the type of surgery performed, and the duration of the operation.

Siassi et al. investigated the change in Mannan-binding lectin (MBL) and PCT levels in pre-op and post-op serum samples, in terms of postoperative infection, in 162 patients awaiting surgery due to GIS-based tumors. The study concluded that low preoperative MBL levels were related with postoperative infection development, while preoperative PCT serum levels did not display an important relationship in identifying the risk of postoperative infection development [8]. In the current study, the preoperative PCT levels of all patients were below normal limits. This study also concluded that there was no relationship between these low levels and the risk of postoperative complications. The other parameters investigated in this study were also border line, the main reason being that preoperative infection was examined and avoided in patients awaiting total endoprosthesis at our clinic.

Once it was understood that PCT followed a better kinetic after surgical trauma, its use became more widespread for various types of surgery. In a study by Aouifi et al. about the effect of cardiopulmonary bypass on PCT levels, the procalcitonin levels were observed preoperatively and five days postoperatively. The study concluded that the level of PCT increased in all patients; the values did not exceed 5 ng/ml, peaked on post-op Day 1, and regressed to normal levels on post-op Day 5 [9]. In the current study PCT similarly showed a maximum level on the post-op first day (5.19 ng/ml for TKP and 8.93 ng/ml for THP patients) and decreased to pre-op values at discharge (0.21 ng/ml for TKP and 0.09 ng/ml for THP patients). Oczeni et al. obtained similar

results from their study, which they conducted to define bacterial infections during the perioperative period. They reported that an increase in PCT levels was not expected after post-op Day 3 in patients with no post-op complications and normal wound healing, and it would reach normal values at most by post-op Day 5 due to its half-life of 25-30 hours. They emphasized that attention should be paid to a gradual decrease or an increase in PCT levels during the 5 days after surgery in terms of systemic inflammation or septic complications [10]. The results of the current study show similarities to previous studies as our results concluded that post-op Day 5 PCT levels regressed to a level close to the normal interval. These results prove that PCT levels rapidly regress back to normal if no other stimulus develops once the factor causing the inflammatory response is eliminated.

In contrast, even though CRP levels followed a decreasing kinetic on post-op Day 5, the post-op Day 5 CRP level was 18.5 times higher than preoperative values in TKP patients and 24 times higher in THP patients. There was no statistically significant difference between TKP patients and THP patients during this decreasing kinetic ($p=0.736$). Ellitsgaard et al. obtained similar results from their study conducted on 140 patients with hip fractures. The study concluded that early postoperative bronchopneumonia and deep tissue infections caused an increase in the CRP level; however, small infections had no effect on the CRP level [11]. The results of the current study conform with results in the relevant literature regarding data for post-op Day 5 and it was concluded that CRP is affected by the inflammatory response caused by surgery, and CRP follows a slower decreasing kinetic after peaking in comparison to PCT.

WBC displayed a better correlation with PCT in terms of average post-op Day 5 values (average for TKP patients was 8.59 ± 3.55 cell $\times 10^9/L$ (median 7.6 cell $\times 10^9/L$; min-max 5.1-24.9 cell $\times 10^9/L$), and 9.3 ± 2.61 cell $\times 10^9/L$ (median 8.6 cell $\times 10^9/L$; min-max 6.3-15.5 cell $\times 10^9/L$) for THP patients), and regressed close to preoperative level.

Serum ESR levels increased more slowly after surgical trauma in comparison to serum CRP concentration, as stated in literature, and reduced gradually [12,13]. The post-op Day 5 ESR level was significantly higher ($p=0.001$) in comparison to the preoperative ESR level for both TKP patients and THP patients. Park et al. conducted a study on the kinetic CRP and ESR followed in 320 TKP patients with no primary complications. Their results also support the results of the current study. Blood samples were taken from patients at pre-op, post-op Days 1, 2, 5, 7, 14, 42, and 90. CRP levels increased rapidly, peaked at post-op Day 2, and regressed to normal values at post-op Day 42. ESR peaked at post-op Day 5, and regressed to preoperative levels three months later [14].

In the literature, it has been stated that the number of infection cases after TKP is higher in comparison to the

number of infection cases experienced after THP. This is due to the fact that tissue around the knee is more prone to soft tissue trauma. Although a tourniquet is only used temporarily for TKP it creates an ischemic period, and a broad surface of the knee joint surface is covered with a foreign material, making it a factor that prepares a base for infection [15,16].

Quenzer et al. reported that the most feared complication after total endoprosthesis surgery was infection; they stated that the rate of developing infection after THP was lower in comparison to knee and shoulder prosthesis surgery. The reason for this was said to be due to the fact that the implants used in knee and shoulder surgery were closer to the skin surface [17]. A striking result of the current study was that the PCT level for all periods, in particular post-op Day 1, were higher in TKP patients in comparison to THP patients.

In recent years, PCT kinetic has become more common in orthopaedics, after being understood better. It is now used in the early diagnosis of postoperative complications where the levels are less affected by surgical trauma. Yasmin et al. conducted a study on 21 patients with a pertrochanteric hip fracture. The patients were enrolled into two groups; those that developed complications, and those that did not develop complications. They concluded that PCT followed a similar kinetic in both groups. While the average PCT values of the group that did not develop complications were within normal limits (PCT <0.5 ng/ml), the PCT values of the group that did develop complications was above normal [18]. In the current study, both TKP (0.58-5.19 ng/ml) and THP (0.54-8.93 ng/ml) patients with postoperative complications showed a tremendous increase in PCT values on the post-op first day. Bottner et al. conducted a study similar to ours, although they examined infection deeply located in the implants of 78 patients that had undergone revision of total joint prosthesis surgery [19] whereas our study was conducted with primary total joint prosthesis.

In conclusion, PCT measurement can be used as a valuable tool for the prediction of early infections especially after TKP because of less soft tissue coverage. It can be concluded that PCT is more selective and sensitive than other acute phase reactants, thus alerting the surgeon to early infections. However, the current study results incorporate a short postoperative period. Future studies, conducted in the light of this study and on a larger number of participants, should include PCT as a parameter examined in addition to other laboratory parameters during routine check-ups conducted over a longer monitoring period, especially when septic complications develop.

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References

- [1] Senthil S, Munro JT, Ritto RP. Infection in total hip replacement; Metaanalysis. *Int Orthop* 2011; 35(2):253-60.
- [2] Leblebicioğlu H, Saniç A, Günaydın M, Sencan I, Dabak N, Nas Y. In-vitro release of vancomycin and netilmisin from bone cement. *Clin Microb Infect* 1996; 1(3):211-2.
- [3] Meisner M, Tschaikowsky K, Hutzler A, Schick C, Schuttler J. Postoperative plasma concentrations of procalcitonin after different types of surgery. *Intens Care Med* 1998; 24(7):680-4.
- [4] Kurtz S, Mowat F, Ong K, Chan N, Lau E, Halpern M. Prevalence of primary and revision total hip and knee arthroplasty in the United States from 1990 through 2002. *J Bone Joint Surg Am* 2005; 87(7):1487-1497.
- [5] Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007; 89(4):780-785.
- [6] Matwyloff GN, Prahl JD, Miller RJ, Carmichael JJ, Amundson DE, Seda G, Daheshia M. Immune regulation of procalcitonin: a biomarker and mediator of infection. *Inflamm Res* 2012; 61(5):401-9.
- [7] Kim MH, Lim G, Kang SY, Lee WI, Suh JT, Lee HJ. Utility of procalcitonin as an early diagnostic marker of bacteremia in patients with acute fever. *Yonsei Med J* 2011; 52(2): 276–81.
- [8] Siassi M, Reise J, Steffensen R, Meisner M, Thiel S, Hohenberger W, Schmidt J. Mannan-binding lectin and procalcitonin measurement for prediction of postoperative infection. *Crit Care* 2005; 9(5): 483–9.
- [9] Aouifi A, Piriou V. Effect of cardiopulmonary bypass on serum procalcitonin and C-reactive protein concentrations. *Br J Anaesthesia* 1999; 83(4):602-7.
- [10] Oczenski W, Fitzgerald RD, Schwarz S. Procalcitonin: a new parameter for the diagnosis of bacterial infection in the peri-operative period. *Eur J Anaesthesiol* 1998; 15(2):202-9.
- [11] Ellitsgaard N, Andersson AP, Jensen KV, Jorgensen M. Changes in C-reactive protein and erythrocyte sedimentation rate after hip fractures. *Int Orthop* 1991; 15(4):311-4.
- [12] Young B, Gleeson M, Cripps AW. C-reactive protein: A critical review. *Pathology* 1991; 23(2):118-24.
- [13] Rosalki SB. C-reactive protein. *Int J Clin Pract* 2001; 5(4): 269-70.
- [14] Park KK, Kim TK, Chang CB, Yoon SW. Normative temporal values of CRP and ESR in unilateral and staged bilateral TKA. *Clin Orthop Relat Res* 2008; 466(1):179–88.
- [15] Macdonald DA. The infected joint replacement: prevention, diagnosis and treatment. *Current Orthop* 1995; 9(1):21-7.
- [16] Taylor GJ, Bannister GC, Calder S. Perioperative wound infection in elective orthopaedic surgery. *J Hosp Infect* 1990; 16(3):241-7.
- [17] Quenzer RW, Brillaman JC. Osteoarticular infections. *Infectious Disease in Emergency Medicine*. Boston: Little Brown and Co. 1992: 841.
- [18] Yasmin D, Bulut G, Yıldız M. Can procalcitonin be used for the diagnosis and follow-up of postoperative complications after fracture surgery? *Acta Orthop Traumatol Turc* 2006; 40(1):15-21.
- [19] Bottner F, Wegner A, Winkelmann W, Becker K, Eren M, Götze G. Interleukin-6, procalcitonin and TNF-[alpha]: Markers of peri-prosthetic infection following total joint replacement. *J Bone Joint Surg Br* 2007; 89(1):94-9.