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The natural trends of C-reactive protein after hip arthroplasty for femoral neck fracture without infection

Myung-Rae Cho, MD, Won-Kee Choi, MD, Chung-Mu Jun, MD, Suk-Kyoon Song, MD*

Abstract

The aim of this study was to estimate the degree of normalization of C-reactive protein (CRP) at 2-weeks and 4-weeks after hip arthroplasty after femoral neck fracture. We also wished to determine whether the degree of CRP normalization differs after total hip arthroplasty (THA) compared to bipolar hemiarthroplasty (BH). We also wanted to analyze the patient factors that may influence CRP normalization.

We conducted a retrospective study of 135 patients who had undergone THA (32 cases) or BH (103 cases) for femoral neck fracture by single surgeon from January 2015 to December 2019. We analyzed CRP levels during the preoperative period, the early postoperative period, the 2-week postoperative period, and the 4-week postoperative period.

In THA, CRP was normalized in 4 patients (12.5%) and in 15 patients (46.9%) within 2-weeks and 4-weeks after surgery, respectively. In BH, CRP was normalized in 16 patients (15.5%) and in 52 patients (50.5%) within 2-weeks and 4-weeks after surgery, respectively. There were no statistical differences between THA and BH. Compared to women, men were 3.78 (95% confidence interval, 1.05–13.63) times less likely to have normalized CRP at 2-weeks after surgery ($P = .042$). Compared to women, men were 3.01 (95% confidence interval, 1.44–6.27) times less likely to have normalized CRP at 4-weeks after surgery ($P = .003$).

Only 50% of patient's CRP level was normalized during 4-week postoperative period. In men, CRP levels were significantly higher than women in whole period. In the case of THA, the CRP level was higher only in early postoperative period compared to BH, and there was no difference since then.

Abbreviations: BH = bipolar hemiarthroplasty, BMI = body mass index, CI = confidence interval, CRP = C-reactive protein, EMR = electronic medical records, IL-6 = interleukin-6, PJI = periprosthetic joint infection, THA = total hip arthroplasty.

Keywords: arthroplasty, C-reactive protein, femoral neck fracture, hip

1. Introduction

Infection after hip arthroplasty is one of the most serious complications. The prevalence of infection after hip arthroplasty is reported to be about 2%.[1] Surgeon should do his best to prevent postoperative infections because infection increases the cost of treatment and mortality.[1,2] However, acute postoperative infections often show typical clinical progress, such as abscess drainage, severe pain, heat sensation, etc. in the surgical area, but if not, early diagnosis is extremely difficult.[3,4] Therefore, serum C-reactive protein (CRP) testing has been widely used as a method for assessing postoperative infection.[5] CRP is an acute phase protein produced by hepatocytes with a normal value of less than 5 mg/L.[6] It is reported that the CRP level after joint arthroplasty is generally at its highest level for 2 to 3 days after surgery and then gradually decreases, recovering to a level similar to that of preoperative in the 2 to 3 weeks after surgery.[7,8] Observing the trends of CRP level is useful in early detection of postoperative infection due to its rapid response by stimulus such as infection or tissue injury.[9,10] However, the CRP level is nonspecific and have a lot of variations, often causing surgeons to be confused in predicting infections.[3,11] In particular, it is more difficult to diagnose infection in patients with femoral neck fractures after surgery because the CRP can be elevated by the fracture itself.[12–14] Therefore, in this study, we compared the CRP trends in patients who underwent total hip arthroplasty (THA) and bipolar hemiarthroplasty (BH) after femoral neck fracture. According to Pulido et al,[15] 27% of infections after arthroplasty were diagnosed within 30 days from surgery. Because of this results, it is important to identify the early CRP trend after surgery. The purpose of this study was to estimate the degree of normalization of CRP at 2-weeks and 4-weeks after hip arthroplasty after femoral neck fracture. We also wished to determine whether CRP normalization differs after THA compared to BH. We also wanted to analyze the patient factors that may influence CRP normalization.

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All data generated or analyzed during this study are included in this published article [and its Supplementary information files].

Daegu Catholic University Medical Center, Daegu, Korea.

* Correspondence: Suk-Kyoon Song, [42472] 33, Duryugongwon-ro 17-gil, Nam-gu, Daegu, Korea (e-mail: ryansong10@naver.com).

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Table 1

Epidemiology of all patients.

Variable	Group 1 (N = 32)	Group 2 (N = 103)	Total (N = 135)	*P* value
Age (yr)	64.81 ± 9.72	81.03 ± 9.57	77.19 ± 11.81	.001
Body mass index (m/kg^2)	22.39 ± 3.13	22.28 ± 3.84	22.31 ± 3.68	.882
Preoperative CRP	28.61 ± 29.18	30.40 ± 41.39	29.98 ± 38.75	.820
Gender (F/M)	(15/17)	(71/32)	(86/49)	.033

Group 1: Total hip arthroplasty for femoral neck fracture.
Group 2: Bipolar hemiarthroplasty for femoral neck fracture.
CRP = C-reactive protein, F = female, M = male, N = number.

2. Methods

2.1. Patients

We conducted a retrospective study of patients who had undergone THA or BH for femoral neck fracture by single surgeon in our hospital from January 2015 to December 2019. We have retrospectively analyzed the electronic medical records (EMRs) of the patients. Among the 187 patients who had undergone primary hip arthroplasty for femoral neck fracture during this period, 135 patients were eligible for inclusion (Table 1). Patients were excluded if they showed signs of complications during the early postoperative period, had infection during the first year after surgery, or CRP values were unavailable in the EMR (Fig. 1). This trial was approved by the

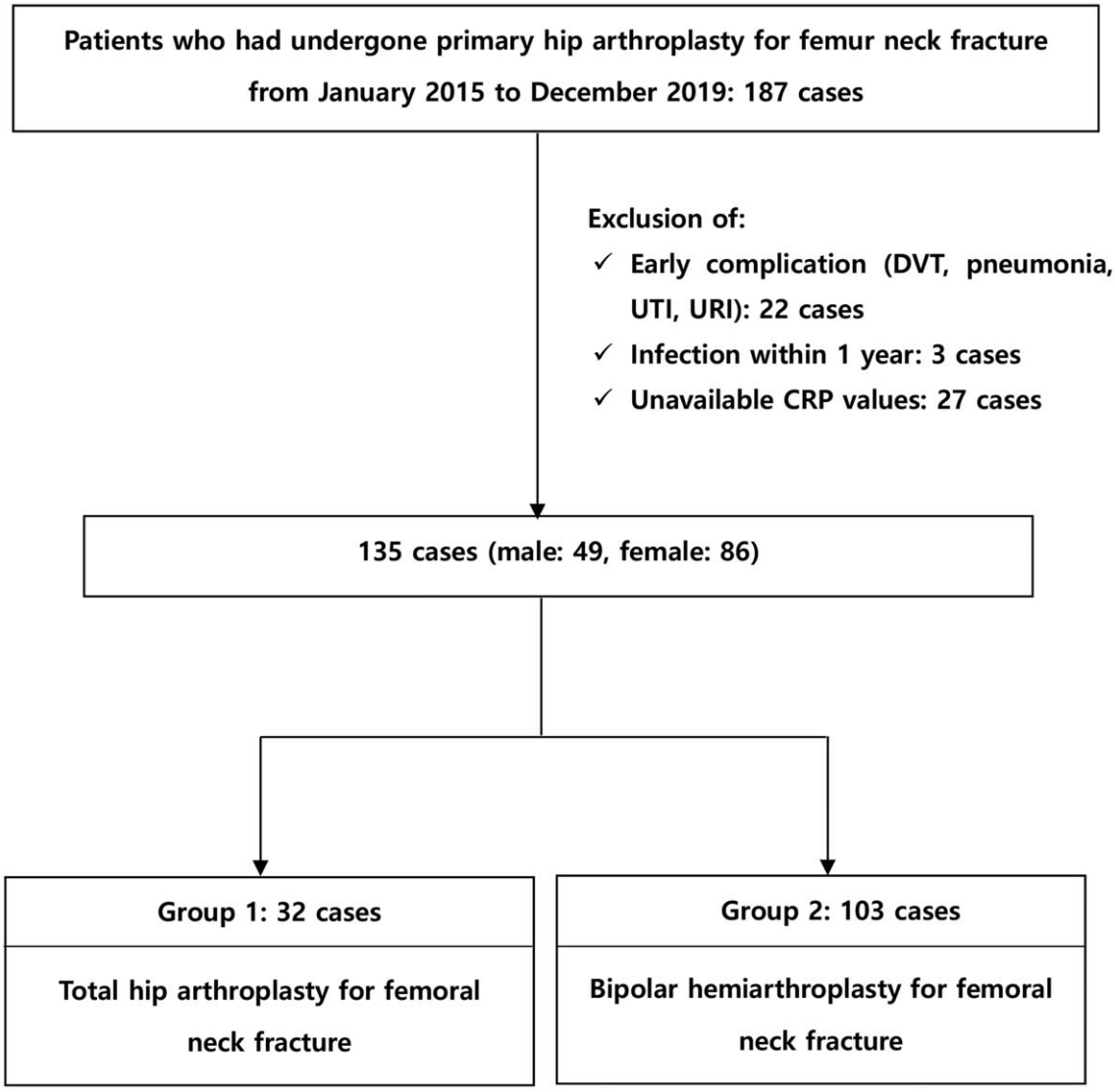

Figure 1. Flow chart of patients with femoral neck fracture.

institutional review board (approval number: CR-20-216) of our hospital and conducted in accordance with the Declaration of Helsinki.[16]

2.2. Surgical methods

All surgical procedures were performed by a senior surgeon of our hospital using a modified Hardinge approach with patient in a lateral position. Porous-coated cementless acetabular cups (Trilolgy; Zimmer Inc.) and highly crosslinked polyethylene acetabular liners (Longevity) were used for all THA cases. M/L taper femoral stem (Zimmer, Warsaw, Indiana) were inserted using standard press–fit techniques to ensure longitudinal and rotational stability. M/L taper femoral stem with bipolar head was used in all BH cases. The incision was closed over a drain catheter which was removed at second postoperative day. Wound closure for all cases was performed with absorbable sutures for deeper tissue (capsule, abductors, fascia, subcutaneous layer, and deep dermal) layer by layer. The skin layer was then closed with staples. Patients were allowed to sit on the first postoperative day and stand with support according to their ability after blood drainage removal. There was no range of motion limitation immediately after surgery. No abduction pillow was used in any patient.

2.3. Measurement of CRP

We retrospectively analyzed CRP values obtained in the preoperative period, the early postoperative period (5–7 days after surgery), the 2-week postoperative period (12–14 days after surgery), and in the 4-week postoperative period (25–30 days after surgery), using values that were available in the EMR. CRP was measured in the department of laboratory medicine at the hospital where operation had been performed. Analysis of CRP was done using a particle enhanced immunoturbidometric technique on a COBAS C 702 autoanalyzer (Roche, Rotkreuz, Switzerland) and the normal range of serum CRP was set as less than 5 mg/L.

2.4. Patient factors affecting CRP normalization

We have assumed age, gender, body mass index (BMI), preoperative CRP, immunosuppressive medication, and liver failure as the potential patient factors associated with CRP normalization. Normalized CRP values were defined as less than 5 mg/L.

2.5. Statistical analysis

All analyses were performed with IBM SPSS version 19.0 software (SPSS Inc., Chicago, IL) for Windows. The chi-square test was used to compare the rate of patients with CRP normalization after THA and BH. Regression analysis was used to assess the association between several patient factors and CRP normalization. A P value $\leq .05$ was considered to indicate statistical significance.

3. Results

3.1. Postoperative course of CRP

Average CRP in patients who underwent THA (32 cases) in the preoperative, early postoperative, 2-week postoperative, and 4-week postoperative period was 28.61 ± 29.18 mg/L, 86.73 ± 60.90 mg/L, 24.38 ± 24.16 mg/L, and 12.46 ± 16.97 mg/L, respectively. Average CRP in patients who underwent BH in the preoperative, early postoperative, 2-week postoperative, and 4-week postoperative period was 30.40 ± 41.39 mg/L, 46.04 ± 29.58 mg/L, 25.26 ± 24.36 mg/L, and 12.58 ± 14.17 mg/L, respectively (Fig. 2). Early postoperative CRP was significantly higher in

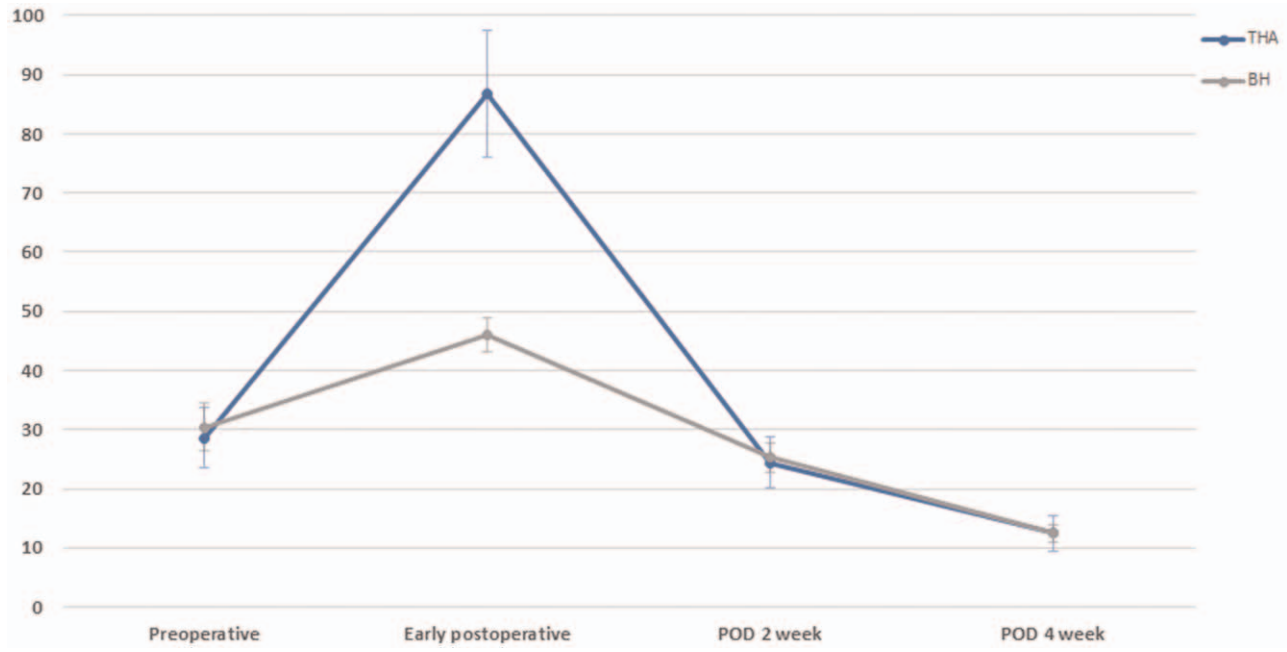

Figure 2. Mean C-reactive protein level over time in patients undergoing hip arthroplasty. BH = bipolar hemiarthroplasty, POD = postoperative day, THA = total hip arthroplasty.

Table 2

A chi-square test to identify the difference in C-reactive protein normalization at 2 weeks postoperation.

	CRP normal	CRP abnormal	Total	*P* value
THA	4 (3.0%)	28 (20.7%)	32 (23.7%)	.673
BH	16 (11.9%)	87 (64.4%)	103 (76.3%)	
Total	20 (14.8%)	115 (85.2%)	135 (100%)	

BH = bipolar hemiarthroplasty, CRP = C-reactive protein, THA = total hip arthroplasty.

Table 3

A chi-square test to identify the difference in C-reactive protein normalization at 4 weeks postoperation.

	CRP normal	CRP abnormal	Total	*P* value
THA	15 (11.1%)	17 (12.6%)	32 (23.7%)	.721
BH	52 (38.5%)	51 (37.8%)	103 (76.3%)	
Total	67 (49.6%)	68 (50.4%)	135 (100%)	

BH = bipolar hemiarthroplasty, CRP = C-reactive protein, THA = total hip arthroplasty.

patients who underwent THA (86.73 ± 60.90 mg/L) than in those who underwent BH (46.04 ± 29.58 mg/L) ($P = .001$), while there were no statistically significant differences during the preoperative, 2-week postoperative, and 4-week postoperative period.

3.2. Differences in CRP normalization after THA and BH

Among the 135 patients, CRP was normalized in 20 patients (14.8%) within 2 weeks after surgery and in 67 patients (49.6%) within 4 weeks after surgery. In 68 patients (50.4%), CRP was still elevated 4 weeks after surgery. After THA, CRP was normalized in 4 patients (12.5%) and in 15 patients (46.9%) within 2 weeks and 4 weeks after surgery, respectively. After BH, CRP was normalized in 16 patients (15.5%) and in 52 patients (50.5%) within 2 weeks and 4 weeks after surgery, respectively. There were no statistical differences between patients who underwent THA or BH during the 2-week postoperative (Table 2) and the 4-week postoperative period (Table 3).

3.3. Patient factors affecting CRP normalization during the 2-week postoperative period

Gender was the only variable among the candidate patient factors which was significantly associated in univariate analysis with CRP normalization within 2 weeks after surgery. Compared to women, men were 3.78 (95% confidence interval [CI], 1.05–13.63) times less likely to have normalized CRP at 2 weeks after surgery ($P = .042$). In multivariate analysis of age, gender, BMI, preoperative CRP, immunosuppressive medication, and liver failure, men were 3.85 (95% CI, 0.97–15.29) times less likely to have normalized CRP at 2 weeks after surgery compared to women ($P = .049$) (Table 4).

3.4. Patient factors affecting CRP normalization during the 4-week postoperative period

Gender was the only variable among the candidate patient factors which was significantly associated in univariate analysis with CRP normalization within 4 weeks after surgery. Compared to women, men were 3.01 (95% CI, 1.44–6.27) times less likely to have normalized CRP at 4 weeks after surgery ($P = .003$). In multivariate analysis of age, gender, BMI, preoperative CRP, immunosuppressive medication, and liver failure, men were 2.91 (95% CI, 1.28–6.65) times less likely to have normalized CRP at 4 weeks after surgery compared to women ($P = .009$) (Table 4).

4. Discussion

Early diagnosis of infection after hip arthroplasty can have an important effect on the outcome of infection treatment and can have a serious impact on patient outcomes.[17] However, infection after hip arthroplasty is often difficult to be diagnosed early in itself, and many effective diagnostic methods have been reported.[7,18,19] Among blood tests, white blood cell count, erythrocyte sedimentation rate, CRP, interleukin-6 (IL-6) are widely used. The diagnostic accuracy for periprosthetic joint infection (PJI) was best for IL-6, followed by CRP, erythrocyte sedimentation rate, and white blood cell count. However, because of the small size of research on IL-6 and the convenience and low cost of the CRP in the clinical field, observing the trends of CRP level is most common method.[7,20] However, since the CRP always increases after hip surgery, it is necessary to interpret it with reference to the postoperative natural course in diagnosing infection. There have been studies of the natural course after hip arthroplasty,[21–23] but no comparison of the CRP course in patients who had THA or BH after the femoral neck fracture.

We found out that CRP level was higher in patients in THA than BH during the early postoperative period (5–7 days after surgery), but no statistically significant difference afterwards. We have also found out that there were no significant differences in 2-week postoperative and 4-week postoperative CRP normalization after THA compared to BH. Postoperative CRP rise is influenced by the degree of surgical trauma.[24] The THA patients were assumed to have a higher CRP after surgery because the degree of invasiveness and tissue damage of the THA procedure is larger than the BH procedure, but it was only statistically significantly higher in early postoperative period and there was no difference afterward.

Table 4

Multiple-variable logistic regression analysis of the difference in C-reactive protein normalization.

		Crude			Adjusted*		
Variable	POD	OR	95% CI	*P* value	OR	95% CI	*P* value
Gender	2 wk	3.78	1.05/13.63	.042	3.85	0.97/15.29	.049
	4 wk	3.01	1.44/6.27	.003	2.91	1.28/6.65	.009

CI = confidence interval, CRP = C-reactive protein, OR = odds ratio, POD = postoperative day.

* Adjusted by age, gender, body mass index, preoperative C-reactive protein, immunosuppressive medication, and liver failure.

In this study, we have found out that in men, CRP levels were significantly higher in whole period and were significantly less likely to normalize within 2-weeks and 4-weeks after hip arthroplasty. The authors stated in previous studies that men's CRP after total knee arthroplasty was higher than women,[25] and similar results were also obtained from this study of hip arthroplasty. It is well known that men have wider bone-cutting area which may contribute to higher increase of CRP after surgery than women.[26]

In general, the CRP level after joint arthroplasty is reported to be at its highest level for 2 to 3 days after the surgery and then gradually decreases, making it similar to preoperative level in 2 to 3 weeks after the procedure.[7,8] However, in our study of hip arthroplasty patients after femoral neck fracture, only 50% of patient's CRP level was normalized after 4 weeks from surgery. In patients with femoral neck fracture, the inflammatory factors released from damaged tissue may cause CRP to rise,[13,14] which should be interpreted differently from elective hip arthroplasty.

The present study has several limitations. First, because of the retrospective study design, patients for whom CRP values were not available in the EMR (14.4% of all cases) were excluded from the study sample and this may have caused selection bias. Second, in our study, normalization of CRP takes longer, so measurement of CRP for a longer period may have more clinical implications. Third, liver failure and Immunosuppressant which may have an effect on CRP, had a statistically insignificant effect on CRP normalization at 2 and 4 weeks postoperative. However, further studies will be needed to explore these factors because there were few patients with liver failure or immunosuppressant in this study. Fourth, the epidemiology between THA and BH patients is not the same. This is due to the influence of age and activity in determining surgery for femoral neck fracture patients. Fifth, energy impacted on the patient at the time of injury and the time to operation are also thought to be factors that can affect CRP normalization, but it is not considered in our study. Sixth, we have not compared the CRP levels to imaging modality like magnetic resonance imaging scan or nuclear scans. Since the development of advanced metal artifact reducing techniques, magnetic resonance imaging scans provided an optimal sensitivity and specificity for the diagnosis of PJI after hip arthroplasty with improved diagnostic value.[27] Also, nuclear scan such as leukocyte–bone marrow scintigraphy or fluorodeoxyglucose PET have been shown to be sensitive for diagnosis of PJI.[28] However, imaging modality is currently not part of the musculoskeletal infection society criteria for diagnosing PJI.[29]

5. Conclusion

Only 50% of patient's CRP level was normalized after hip arthroplasty for femoral neck fracture during 4-week postoperative period. In men, CRP levels were significantly higher than women in whole period. In the case of THA, the CRP level was higher only in early postoperative period compared to BH, and there was no difference since then.

Author contributions

Conceptualization: Myung-Rae Cho, Suk-Kyoon Song.
Data curation: Won-Kee Choi, Chung-Mu Jun, Suk-Kyoon Song.
Formal analysis: Won-Kee Choi, Suk-Kyoon Song.
Supervision: Suk-Kyoon Song.
Writing – original draft: Myung-Rae Cho, Suk-Kyoon Song.
Writing – review & editing: Myung-Rae Cho, Won-Kee Choi, Chung-Mu Jun, Suk-Kyoon Song.

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