

# Survey the Level of C-Reactive Protein, Erythrocyte Sedimentation Rate and Complete Blood Count After Anterior Cruciate Ligament Reconstruction

Salman Ghaffari<sup>1</sup>, [MD]

Masoud Shayesteh Azar\*, [MD]

Mohammad Jafari<sup>1</sup>, [MD]

Bahman Ghaffari<sup>2</sup>, [MD]

1, Mazandaran University of Medical Science,  
Orthopedic Research Center, Sari, Iran.

2, Mazandran International University, Mazandaran,  
Iran.

\* Corresponding Author: Masoud Shayesteh  
Azar, Mazandaran University of Medical Science,  
Orthopedic Research Center,  
Mazandaran, Iran  
e-mail: Mshayestehazar@yahoo.com  
Phone: +981133377169

## ABSTRACT

**Objective:** Due to few lack of researches in the field of changes of inflammatory factors after post-operative knee surgery in our country in order to improve the health status of the patients, in this study, erythrocyte sedimentation rate, C-reactive protein and white blood cells changes after uncomplicated arthroscopic anterior cruciate ligament reconstruction of the knee were investigated.

**Material and Methods:** In this prospective experimental study, patients undergoing arthroscopic anterior cruciate ligament reconstruction of the knee with uncomplicated postoperative course in Imam Hospital were studied.

**Results:** We included 60 patients, 56 (93.3%) were male and mean age of patients was  $29.58 \pm 7.15$  years. C-reactive protein levels peaked on the 2<sup>nd</sup> post-operative day and then declined and returned to the pre-operative levels on 7<sup>th</sup> day. erythrocyte sedimentation rate in patients after surgery has been peaked on the 2<sup>nd</sup> post-operative day, and returned to the pre-operative levels 14 days after surgery. The age of the patients had a direct correlation with post-operative C-reactive protein on the seventh and twenty-eighth, respectively  $r = 0.39$ ,  $p = 0.04$  and  $r = 0.84$ ,  $p = 0.009$ . Patient age had a direct correlation with erythrocyte sedimentation rate day 7 and 14, respectively  $r = 0.49$ ,  $p = 0.012$ ;  $r = 0.44$ ,  $p = 0.046$ .

**Conclusion:** Post-operative C-reactive protein and erythrocyte sedimentation rate levels returned to pre-operative levels in days two and fourteen respectively. If C-reactive protein and erythrocyte sedimentation rate levels not reduced after the seventh and fourteenth day, respectively or increase again, definitive diagnosis of infection should be investigated.

**Key words:** ACL reconstruction, CRP, ESR, septic arthritis

Received: 11 March 2018, Accepted: 29 March 2018,  
Published online: 31 March 2018

## INTRODUCTION

Anterior cruciate ligament (ACL) is an intra-articular and extrasynovial element in the knee joint [1]. It prevents excessive deflection forward, tibial rotation too and varus, valgus angulation between two directions are also involved. ACL tear is a common injury related to exercise and one of the most common causes of knee surgery in youths and 200,000 people encounter with this injury in America annually [2]. Stability of the knee is reduced after ACL tearing and also cause difficulties in individual athletic performance, increase the risk of premature degeneration of the knee and meniscus lesions. The main goal of ACL reconstruction is stability in the knee. To achieve this goal, several methods have been introduced [3, 4]. Different methods of ACL reconstruction is being used in patients who suffer from knee instability and the results have been

good to excellent [5]. Several ways with different sources such as autograft, allograft, and synthetic grafts have been used for the reconstruction of ACL. Now autologous patellar tendon grafts, semitendinosus and gracilis tendons are the most common grafts that use for ACL reconstruction [6,7]. Every one of the above methods is associated with certain problems. Evaluation of the problems helps physicians to choose the best treatment [8]. The level of activity after surgery determines the overall outcome of treatment. Obviously, care before and after surgery to reduce complications is very important [8]. Inflammatory mediators such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and the number of white blood cells (WBC) is used to diagnosis and follow-up of all medical science including orthopedics and orthopedic surgeons have

tried to anticipating the normal pattern of these factors, to be informed in a timely manner of surgical complications especially infection and resolve the problems before crisis situation [9]. CRP is one of acute phase proteins that liver began to build it in 8 to 12 hours after infection or trauma and the natural amount in adults is less than 10 mg per liter. ESR in the first hour is normally less 20 mm per hour and also increases in the inflammatory process like an infection [10]. This study aimed to survey changing of ESR, CRP, and WBC after ACL reconstruction.

## MATERIALS and METHODS

In this prospective study, patients undergoing arthroscopic anterior cruciate ligament reconstruction at Imam Khomeini Hospital during 2015-2016 were examined. The study population included all patients with sports or non-sports injury that suffer from anterior cruciate ligament tearing. Inclusion criteria: all the patients with sports or non-sports injury to the anterior cruciate ligament that candidate to surgery. Exclusion criteria: included patients with postoperative joint infection and patients who discontinue cooperation were excluded. The participants were interviewed and after obtaining informed consent the plan approved in Orthopedic Research Center and also confirmed it into ethics committees (Code of IR.MAZUMS.REC.94-1659). All patients filled informed consent. Blood samples were sent laboratory before ACL reconstruction and also the second, seventh, fourteenth and twenty-eight-day post operation and the results with other data such as age, gender, mechanism of injury, underlying disease, smoking were recorded in a questionnaire form. The results of the laboratory tests, including the haemoglobin (HB), platelet (PLT), leucocyte (WBC), lymphocyte (LYM), neutrophil (PMN) counts, CRP, ESR, along with data obtained from

patients enter in statistical data sheet finally.

## Statistical Analysis

To determine the changes in ESR and CRP was used Generalized Estimating Equation and test repeated measures. The Pearson correlation test was used for quantitative data communications. p value less than 0.05 was considered statistically significant.

## RESULTS

A total of 68 ACL reconstruction were performed, and 60 patients included in this study and 8 patients were excluded. Fifty-six patients (93.3%) were male and 4 patients (6.7%) were female. The mechanism of injury in 54 patients (90%) was a sport and in 6 patients (10%) was due to traffic accidents. Two patients because of suspicious to infection after surgery, 6 patients according to incomplete follow-up, total 8 patients were excluded. Twenty-eight patients (45.9%) underwent ACL reconstruction with a right hamstring graft, 15 patients (25.8%) underwent ACL reconstruction with left hamstring autograft and 17 patients (28.3%) underwent ACL reconstruction with a patellar tendon graft.

They have no underlying disease including diabetes mellitus, hypertension, and dyslipidemia; 14 patients (23.3%) were smoker. The mean age of patients was  $29.58 \pm 7.15$  years. The average age of men was  $29.22 \pm 6.65$  years and for women was  $34.63 \pm 11.66$  years and there was significant difference ( $p = 0.039$ ). The average age was  $29.43 \pm 6.45$  years in sports events, and  $30.71 \pm 11.42$  years in traffic events, and there was no significant difference ( $p = 0.53$ ). The average age in non-smokers was  $29.77 \pm 7.55$ , in smokers  $28.96 \pm 5.75$  years and there was no significant difference ( $p = 0.60$ ). Haemoglobin, platelets, WBC, values of PMN, CRP and ESR before surgery and on 7th, 14th, and 28th

Table: Mean and standard deviation of hematological variables and CRP, ESR before and after treatment

Time	Pre-OP	2th day post OP	7th day post OP	14th day post OP	28th day post OP
Variable	SD±Mean	SD±Mean	SD±Mean	SD±Mean	SD±Mean
HB (mg/dl)	13.93±1.33	13.84±1.26	13.82±1.94	13.62±1.62	13.65±1.6
PLT (103)	296±84	286±71	284±74	280±84	267±76
WBC (103)	8.3±6.5	7.7±2.2	9.3±9.6	7.5±1.4	7±2.5
Lymp (%)	32.8±17.6	32.8±17.9	22.8±16.7	28±16.7	31.1±13.9
PMN (%)	62±8.3	66.8±10.1	597±13.3	63.8±12.3	586±4.5
CRP (mg/l)	9±8.3	19.46±12.8	8.9±3.6	5.8±2.1	4.5±3.8
Min-max	0.0-14	0.0-35	0.0±12	0.0±8	0.0±8
ESR (mm/h)	23.5±9.9	24.7±12.2	20.5±5.7	18.8±5.4	14.3±4.8
Min-Max	2-35	5-70	5-45	5-32	5-25

In the evaluation of white blood cells count, on the seventh day after surgery, the WBC had reached its maximum, while the total WBC changes were not significant after surgery ( $p = 0.79$ ).

In the analysis of repeated measures changes in WBC also did not differ between men and women ( $p = 0.63$ ). Changes in PMN before and after surgery was not statistically significant ( $p = 0.74$ ).

The average CRP on the second day after surgery has reached its maximum and then have decreased  $p = 0.063$ . CRP levels in 70% of patients on the seventh day after surgery returned to normal. On the fourteenth day 77% and within 28 days after surgery in 90% of patients, CRP levels had returned to normal. CRP changes in both males and females did not differ before and after surgery ( $p=0.81$ ). Changes in CRP levels before and after surgery were not significantly different in smokers and non-smokers ( $p = 0.95$ ).

Average ESR in patients after surgery has been reached its maximum on the second day, and ESR changes before and after surgery were significant ( $p = 0.025$ ). ESR levels returned to normal in 64% of patients on 7th day after surgery, on 14th day 71% and on 28th day 82% of patients. ESR changes before and after surgery had no significant difference between males and females ( $p = 0.53$ ). ESR changes before and after surgery were not significantly different in smokers and non-smokers ( $p = 0.75$ ).

The age of patients did not have a significant correlation with WBC changes before and after surgery ( $p > 0.05$ ). The age of patients with postoperative CRP had a direct correlation on the seventh and twenty-eighth day, respectively  $r = 0.39$ ,  $p = 0.04$ ;  $r = 0.84$ ,  $p = 0.009$ . ( $R =$  Pearson correlation coefficient). The age of patients with ESR had a direct correlation on 7th and 14th day after surgery, respectively  $r = 0.49$ ,  $p = 0.012$ ;  $r = 0.44$ ,  $p = 0.046$ . In the relationship between CRP and WBC on the second day after surgery were observed a significant negative correlation, ( $r = -0.319$ ,  $p = 0.042$ ) while there was no correlation between ESR and WBC ( $p > 0.05$ ).

## DISCUSSION

This study demonstrated that CRP levels in 40% of patients on the 2<sup>nd</sup> day after surgery, 70% on the 7<sup>th</sup> day, 77% on the 14<sup>th</sup> day and in 90% of patients on the 28<sup>th</sup> day returned to normal. ESR levels on the second day after surgery in 52% of patients, 64% on the 7<sup>th</sup> day, 71% on the 14<sup>th</sup> day and in 82% of patients on the 28<sup>th</sup> day after surgery returned to normal.

However, CRP and ESR changes in males and females

have no differences in smokers and non-smokers and also in sports or traffic events. It was also observed that there is a significant correlation between CRP and, ESR level and age so CRP and ESR increase more after surgery in an older patient.

CRP and ESR increase after surgery and then gradually decline. CRP has faster response and a more quickly return in comparison of ESR, so 28 days after surgery CRP in 90% and ESR in 82% of patients returns to normal level.

Larsson et al [10] in Sweden studied levels of CRP and ESR in four types of elective orthopedic surgery without complication and found that CRP usually returned to normal range within 21 days after surgery (less than 10 mg/l). So, back faster CRP compared to ESR indicated CRP is a more sensitive marker for complications after surgery [1,11]. In the present study, it was observed that CRP and ESR reached to maximum on the 2<sup>nd</sup> day after ACL reconstruction but CRP returns to a normal level more quickly than ESR.

Spangehl et al also showed that levels of CRP in 202 patients before and after total hip revision surgery as marker for diagnosis of infection has 96% sensitivity, 96% specificity, 74% positive predictive value and negative predictive value 96%, which is significantly higher than the values obtained for ESR[12]. The authors also showed that CRP and ESR normal values are reliable for forecasting the absence of infection. Of course, it is considered that definitive diagnosis needs to evaluation including physical examination, aspiration and sometimes bone scan. Researchers demonstrated if CRP remains high after two weeks or rising after decline, more evaluation need to rule out of infection. Individual response to rising CRP after surgery is different for every person and it is considered in the interpretation of CRP level. In this situation, consecutive CRP measurements can help [1]. Underlying disease, recent surgery, and the inflammatory process must also be ruled out. It should also be considered that high body mass index (BMI) can be increased normal levels of CRP.

It must be understood that septic arthritis is serious complications after surgery ACLR that its prevalence is between 0.1 to 2.25% (8). In a study Wang et al have shown that in patients without infection, increased levels of CRP on the 3<sup>rd</sup> to 5<sup>th</sup> day has fallen significantly (from 47.3 to 16.9) [7]. However, in patients with infection CRP levels reached above 100. Also in this study, the researchers noted that CRP is a more sensitive indicator of ESR in predicting and assessing response to treatment of infection. In another study by Ruiz-Ibán MA et al showed that after ACL surgery alteration of CRP have been significant in half of the patients and it had higher levels in

men, surgery by less experienced surgeons, and patients with cartilage lesions [13]. CRP level turned back to pre-operative level in 70% of patients at 7<sup>th</sup> day. ESR level turned back to pre-operative level in 71% of the patient at 14th day. CRP and ESR level remained above the normal range on day 28 in 10% and 18% of patients, respectively. According to CRP levels rise faster and return sooner than to the ESR, also CRP is a more sensitive indicator.

## STUDY LIMITATION

In this study, patients with uncomplicated infections were evaluated and changes in CRP and ESR were not assessed in patients with septic arthritis.

## REFERENCES

- [1] Wang C, Ao Y, Fan X, et al. C-reactive protein and erythrocyte sedimentation rate changes after arthroscopic anterior cruciate ligament reconstruction: guideline to diagnose and monitor postoperative infection. *Arthroscopy* 2014; 30(9): 1110-5.
- [2] Yazdi H, Moradi A, Herbort M. The effect of gentamicin in irrigating solutions on articular infection prophylaxis during arthroscopic ACL reconstruction. *Archives of orthopedic and trauma surgery* 2014; 134(2): 257-61.
- [3] Whelan DB, HE Rosenberg, Yardley NJ. Managing the Infected ACL Reconstruction. In:RG Marx (ed). *Revision ACL Reconstruction: Indications and Technique*. 2014, New York; Springer, 2014: 157-169.
- [4] Calvo R, Figueroa D, Anastasiadis Z, et al. Septic arthritis in ACL reconstruction surgery with hamstring autografts. Eleven years of experience. *The Knee* 2014; 21(3): 717-20.
- [5] Im YM, Joo YB. Clinical Presentation of Staphylococcus epidermidis Septic Arthritis Following Anterior Cruciate Ligament Reconstruction. *Knee surgery & related research* 2012; 24(1): 46-51.
- [6] Jabalameli M, Rahbar M, Hadi H, et al. Septic arthritis of the knee following anterior cruciate ligament reconstruction. *Shafa Orthopedic Journal* 2013; 1(2): 6-11.
- [7] Wang C, Ao Y, Wang J, et al. Septic arthritis after arthroscopic anterior cruciate ligament reconstruction: a retrospective analysis of incidence, presentation, treatment, and cause. *Arthroscopy* 2009; 25(3): 243-9.
- [8] Mouzopoulos G, Fotopoulos VC, Tzurbakis M. Septic knee arthritis following ACL reconstruction: a systematic review. *Knee Surgery, Sports Traumatology, Arthroscopy* 2009; 17(9): 1033-42.
- [9] Margheritini F, Camillieri G, Mancini L, et al. C-reactive protein and erythrocyte sedimentation rate changes following arthroscopically assisted anterior cruciate ligament reconstruction. *Knee Surgery, Sports Traumatology, Arthroscopy* 2001; 9(6): 343-5.
- [10] Larsson S, Thelander U, Friberg S. C-reactive protein (CRP) levels after elective orthopedic surgery. *Clinical orthopaedics and related research* 1992; 275: 237-42.
- [11] Schutz R, Boukebous B, Boutroux P, et al. C-reactive protein levels for early detection of early postoperative complications after proximal femoral fracture surgery. *Eur J Orthop Surg Traumatol* 2017. doi: 10.1007/s00590-017-2080-z. [Epub ahead of print]
- [12] Spangehl MJ, Masri BA, O'Connell JX, et al. Prospective analysis of preoperative and intraoperative investigations for the diagnosis of infection at the sites of two hundred and two revision total hip arthroplasties. *J Bone Joint Surg Am*. 1999 May;81(5): 672-83.
- [13] Ruiz-Ibán MA, Díaz Heredia J, Martínez Val IC, et al. Evolution of C-reactive protein values in the first month after anterior cruciate ligament reconstruction: reference values. *Knee Surg Sports Traumatol Arthrosc* 2015 Mar; 23(3): 763-9. doi: 10.1007/s00167-013-2702-x. Epub 2013 Oct 11.

