



## 저작자표시 2.0 대한민국

이용자는 아래의 조건을 따르는 경우에 한하여 자유롭게

- 이 저작물을 복제, 배포, 전송, 전시, 공연 및 방송할 수 있습니다.
- 이차적 저작물을 작성할 수 있습니다.
- 이 저작물을 영리 목적으로 이용할 수 있습니다.

다음과 같은 조건을 따라야 합니다:



저작자표시. 귀하는 원저작자를 표시하여야 합니다.

- 귀하는, 이 저작물의 재이용이나 배포의 경우, 이 저작물에 적용된 이용허락조건을 명확하게 나타내어야 합니다.
- 저작권자로부터 별도의 허가를 받으면 이러한 조건들은 적용되지 않습니다.

저작권법에 따른 이용자의 권리는 위의 내용에 의하여 영향을 받지 않습니다.

이것은 [이용허락규약\(Legal Code\)](#)을 이해하기 쉽게 요약한 것입니다.

[Disclaimer](#) 

**Serum Complement Reactive Protein  
(CRP) Trends Following Free Flap in  
Lower Extremity Reconstruction**

by

**Young Moon Yoo**



**Major in Medicine**

**Department of Medical Sciences**

**The Graduate School, Aju University**

**Serum Complement Reactive Protein  
(CRP) Trends Following Free Flap in  
Lower Extremity Reconstruction**

by

**Young Moon Yoo**

**A Dissertation Submitted to The Graduate School of  
Ajou University in Partial Fulfillment of The  
Requirements for The Degree of Master of Medicine**

Supervised by

**Myong Chul Park, M.D., Ph.D.**

**Major in Medicine**

**Department of Medical Sciences**

**The Graduate School, Ajou University**

**August, 2012**

**This certifies that the dissertation  
Of Young Moon Yoo is approved.**



**SUPERVISORY COMMITTEE**

---

**Myong Chul Park**

---

**Shin Young Yim**

---

**Seung Hyun Yoon**

**The Graduate School, Aju University**

**June, 22<sup>nd</sup>, 2012**

- ABSTRACT-

## **Serum Complement Reactive Protein (CRP) Trends Following Free Flap in Lower Extremity Reconstruction**

Infectious complication remains a major cause of flap failure. Serum complement reactive protein (CRP) level is a customary measure for early recognition of infections. The aim of this study was to describe the time course of CRP in patients with free flap for trauma and chronic wound problems of the lower extremity. We further evaluated the effect of patient comorbidities influencing serum CRP level.

We retrospectively analyzed the data of all 21 patients who received free flap from June 2009 to March 2012 at the Department of Plastic and Reconstructive Surgery, Ajou University School of Medicine. CRP levels were measured routinely until postoperative 2 weeks. Patient CRP values were expressed as mg/dl and were averaged per day in each group.

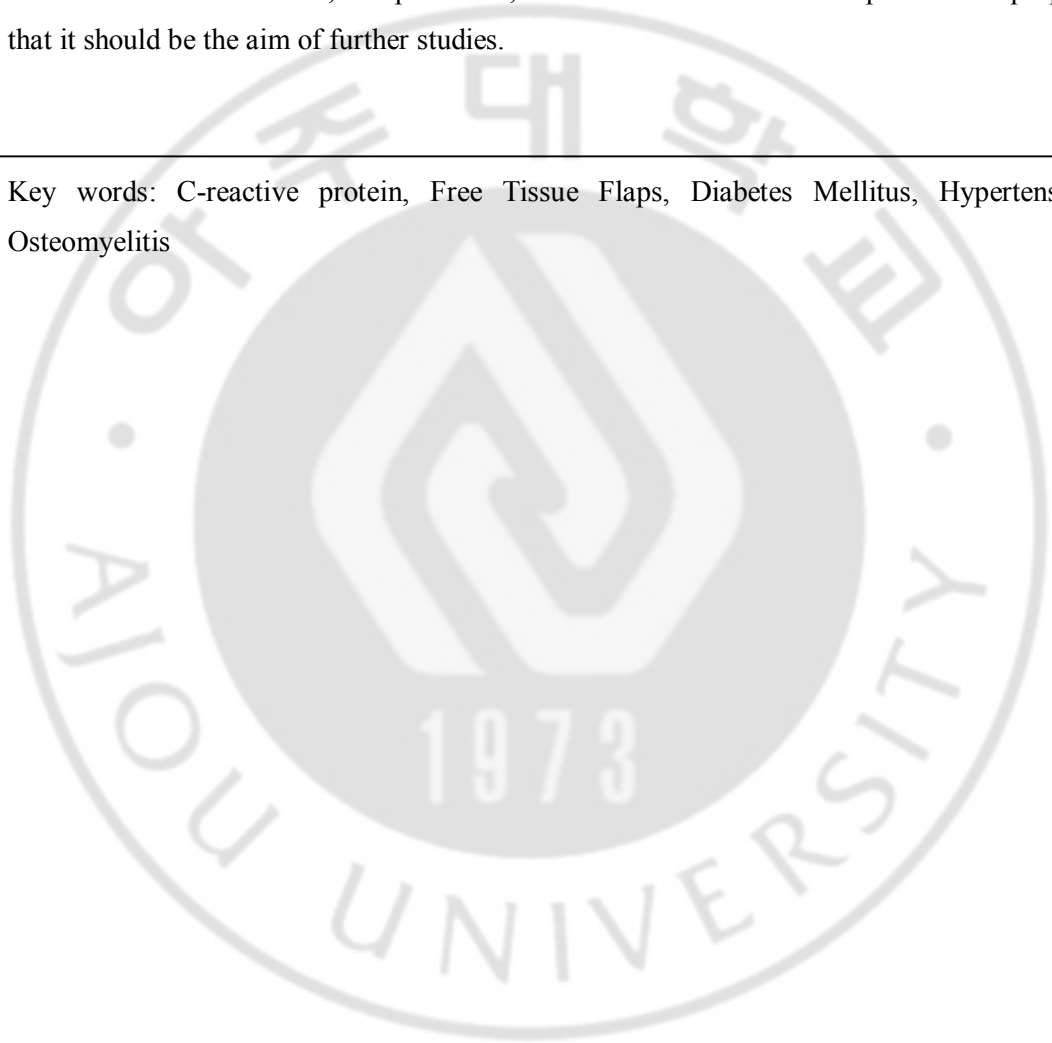
Fourteen (66.7%) of the patients reached peak CRP within 3 days. Of the seven patients peaking after day 3, two patients (28.57%) had infective complications (postoperative wound infection and remained wound abscess) and showed a high level and a second peak of CRP about 2 days before symptoms were evident. The other two patients (28.57%) had side effects of antibiotics (drug fever and pseudomembranous colitis) and also displayed a high level of CRP, which subsequently lowered slowly. In these four complication cases, a change in antibiotics guided by a consultant microbiologist was necessary. In all disease-free patients, mean CRP rose from postoperative day 1, peaked at day 2, and decreased significantly from day 4. On the contrary, in the diabetes and hypertension group, the mean CRP rose from postoperative day 2, peaked at day 3, and decreased significantly from day 5. Also, an unexpected and irregular pattern was shown in the diabetes and hypertension group. There was statistical relevance of diabetes and hypertension on CRP trends. However, the non-osteomyelitis group showed more irregular and higher CRP trends than did the osteomyelitis group. There was no statistical significance, perhaps because patients who had complications were all included in the non-osteomyelitis group. Also, all patients of

osteomyelitis were early phase and were well-controlled by antibiotics.

Our results confirm that CRP is a very efficient parameter for diagnosis and prognosis of infectious complications after free flap. We also noted the positive correlation between the diabetes, hypertension, and the CRP level in free flap. However, study limitations include the number of patients who met the inclusion criteria. We understand that correlation of serum CRP level to inflammation, complications, and comorbidities can be important and propose that it should be the aim of further studies.

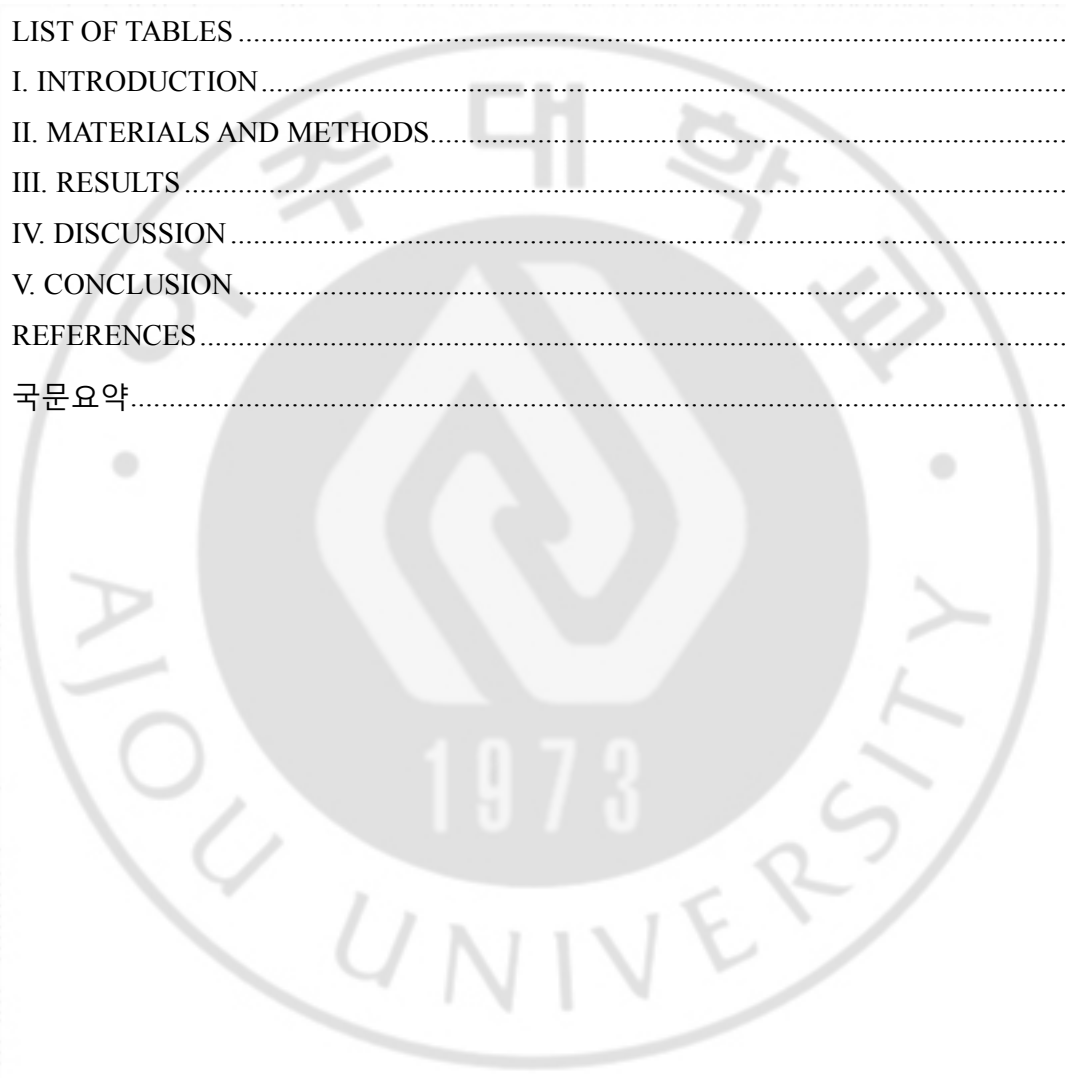
---

Key words: C-reactive protein, Free Tissue Flaps, Diabetes Mellitus, Hypertension, Osteomyelitis



## TABLE OF CONTENTS

ABSTRACT .....	i
TABLE OF CONTENTS .....	iii
LIST OF FIGURES .....	iv
LIST OF TABLES .....	v
I. INTRODUCTION .....	1
II. MATERIALS AND METHODS .....	2
III. RESULTS .....	4
IV. DISCUSSION .....	10
V. CONCLUSION .....	13
REFERENCES .....	14
국문요약 .....	16



## LIST OF FIGURES

Fig 1. Number of patients reaching peak serum CRP at each day .....	7
Fig 2. Serum CRP trends with or without complications .....	8
Fig 3. Serum CRP trends of each group .....	9





## LIST OF TABLES

Table 1. Basic characteristics of patients .....	5
Table 2. Definition of surgical site infection and criteria for defining superficial infection....	6



## I. INTRODUCTION

Open fractures of the lower extremity and chronic wound problems like decubitus ulcer and diabetic foot can cause a risk of nonunion, osteomyelitis, and subsequent amputation. Definite treatment is debridement of all non-viable tissues and coverage with well-vascularised tissue. Furthermore, meticulous postoperative monitoring can raise the success rate of free flap and early detection and treatment of infection (Wright et al., 2010). Infectious complication remains a major cause of flap failure. Early diagnosis and treatment of infection are critical and are associated with better outcome (Mitra et al., 2008).

Diagnostic clinical findings of infection include fever or localized heating sensation, tenderness, and erythematous change of the wound. Laboratory tests, primarily erythrocyte sedimentation rate (ESR), serum complement reactive protein (CRP), and leukocyte (WBC) count, are commonly used when there is a suspicion of postoperative infection (James et al., 2008). Especially, serum CRP level is a customary measure for early recognition of infections because of measurement of CRP has the several advantages of familiarity, simplicity, and good sensitivity of detecting an infection early. It increases even before clinical infection is apparent, which makes a precise and rapid assessment of the course of the infection possible (Nidal et al., 2008). Also, serum CRP has a narrow normal range and it is stable because the effect of drugs and most pathologies except liver failure is minimal (James et al., 2008).

Also, several studies suggest that serum CRP level is associated with patient's comorbidities include hypertension, diabetes, and osteomyelitis. According to previous studies, serum CRP is an independent risk factor for the development of hypertension (Leonelo et al., 2001) and is associated with insulin resistance (Weng et al., 2010).

The aim of this study was to describe the time course of CRP in patients with free flap for trauma and chronic wound problems of lower extremity to predict postoperative infection earlier. We further evaluated the effect of patient comorbidities influencing serum CRP level.

## II. MATERIALS AND METHODS

### Patient population

We retrospectively analyzed the data of all 92 patients who received free flap from June 2009 to March 2012 at the Department of Plastic and Reconstructive Surgery of Ajou University School of Medicine. Fifty five patients with sepsis, pneumonia, collagen disease, and malignancy were excluded because of their possible confounding effect. Only thirty seven patients with free flap for trauma and chronic wound problems of the lower extremity were studied. Sixteen Patients were excluded from final analysis because of insufficient laboratory data. Thirteen men and eight women patients were included. Their mean age was 47.1 years (range, 16 to 71) (Table 1).

A chart review was performed to get information about patient demographics, medical history, hospital course, laboratory parameters, need for revision of the microanastomosis, flap survival or necrosis, and minor surgical complications like wound breakdown. Medical preconditions analyzed were hypertension, diabetes, and osteomyelitis.

### Methods

The serum CRP value was measured by Toshiba 200FR<sup>®</sup> using immunoturbidity assay. Absolute CRP values were expressed as mg/dl and upper limit of the normal value is 0.8 mg/dl. Serum CRP levels were measured routinely from immediate postoperative day 0 to postoperative day 14, then were averaged per day in each group.

Wound infection was diagnosed by Nosocomial Infection National Surveillance Scheme (NINSS) of Center for Disease Control (Seo et al., 2011) (Table 2). Antibiotic therapy was guided by a consultant microbiologist.

Hypertension was defined as a repeatedly elevated blood pressure exceeding 140 over 90 mmHg - a systolic pressure above 140 with a diastolic pressure above 90. Diabetes mellitus was defined as (1) symptoms of diabetes plus casual plasma glucose concentration  $\geq 200$  mg/dl (11.1 mmol/l) or (2) FPG  $\geq 126$  mg/dl (7.0 mmol/l) or (3) 2-h postload glucose  $\geq 200$  mg/dl (11.1 mmol/l) during an oral glucose tolerance test. Osteomyelitis was diagnosed by three phase bone scan and official reading was confirmed by radiologist.

### **Statistical analysis**

Raw data were transposed by log<sub>2</sub> ratio for comparing the trends of each phenotype. The unpaired t-test was used for continuous variables. A  $p < 0.05$  was taken as statistically significant.



### III. RESULTS

A total of 21 patients who had free flap for trauma and chronic wound problems were identified. Thirteen men and eight women patients were included. Their average age was 47.1 years (range, 16-71). In all cases, a defect requiring soft tissue coverage was located at the lower extremity. Anterolateral thigh fasciocutaneous free flap was most commonly used in fifteen cases, gracilis muscle free flap in two cases, vastus lateralis muscle free flap in one case, deep femoral artery perforator flap in one case, latissimus dorsi myocutaneous flap in one case, and thoracodorsal artery perforator flap was used in one case.

Fourteen (66.7%) patients attained peak CRP within 3 days. Of the seven patients peaking after day 3, two patients (28.57%) had infective complications (postoperative wound infection and remained wound abscess) and they showed a high level, irregular pattern, and second peak of CRP about 2 days before symptoms were evident. The other two patients (28.57%) displayed side effects of antibiotics (drug fever and pseudomembranous colitis) and displayed a high CRP level, which subsequently lowered slowly (Figure 1 and 2). In these four complication cases, the antibiotics needed to be changed, guided by a consultant microbiologist

In all disease-free patients, mean CRP rose from postoperative day 1, peaked at day 2, and decreased significantly from day 4. On the contrary, in diabetes and hypertension group, mean CRP rose from postoperative day 2, peaked at day 3, and decreased significantly from day 5. Also, an unexpected and irregular pattern was shown in the diabetes and hypertension group. There was statistical relevance of diabetes and hypertension on CRP trends. However, the non-osteomyelitis group showed more irregular and higher CRP trends than osteomyelitis group. There was no statistical significance (Figure 3).

**TABLE 1. Basic characteristics of patients**

Patient No.	Sex	Age	Diabetes mellitus	Hypertension	Osteomyelitis	Flap type
1	F	20	-	-	-	Gracilis
2	M	55	-	+	-	ALT
3	F	57	-	-	-	TDAP
4	M	19	-	-	-	ALT
5	F	50	+	+	-	DFAP
6	M	71	-	+	-	ALT
7	M	47	-	+	-	ALT
8	M	69	-	-	-	ALT
9	M	48	-	-	+	Gracilis
10	M	53	-	-	-	ALT
11	M	53	+	+	-	ALT
12	F	40	-	+	-	Vastus
13	M	54	-	-	+	ALT
14	M	39	-	-	-	ALT
15	F	16	-	-	-	ALT
16	M	25	-	-	+	ALT
17	F	66	+	+	-	ALT
18	F	56	+	+	+	LD
19	M	61	+	+	-	ALT
20	F	67	-	-	-	ALT
21	M	23	-	-	+	ALT

\* ALT : anterolateral thigh fasciocutaneous flap

LD : latissimus dorsi myocutaneous flap

DFAP : deep femoral artery perforator flap

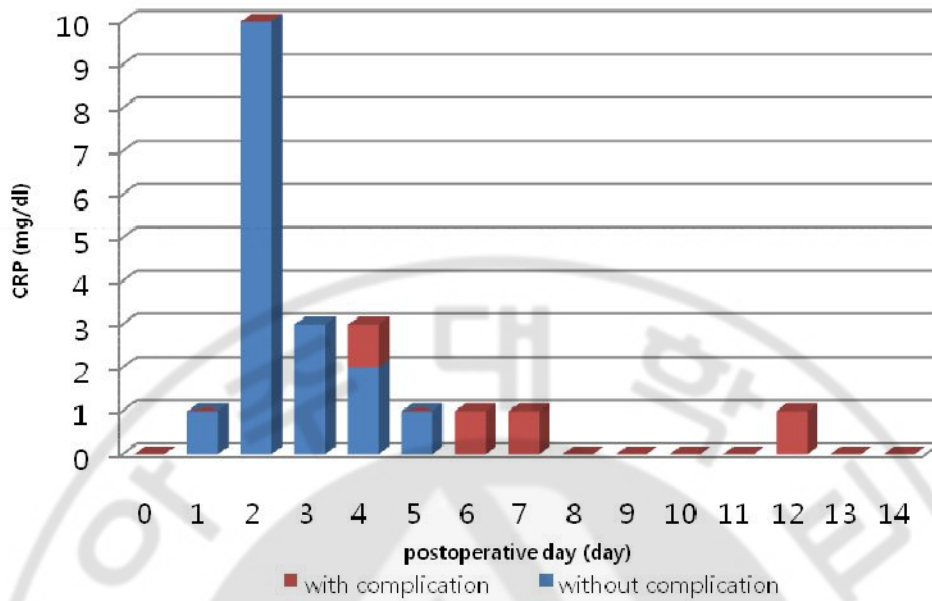
TDAP : Thoracodorsal artery perforator flap

Gracilis : gracilis muscle flap

Vastus : vastus lateralis muscle flap

**TABLE 2. Definition of surgical site infection and criterial for defining superficial infection**

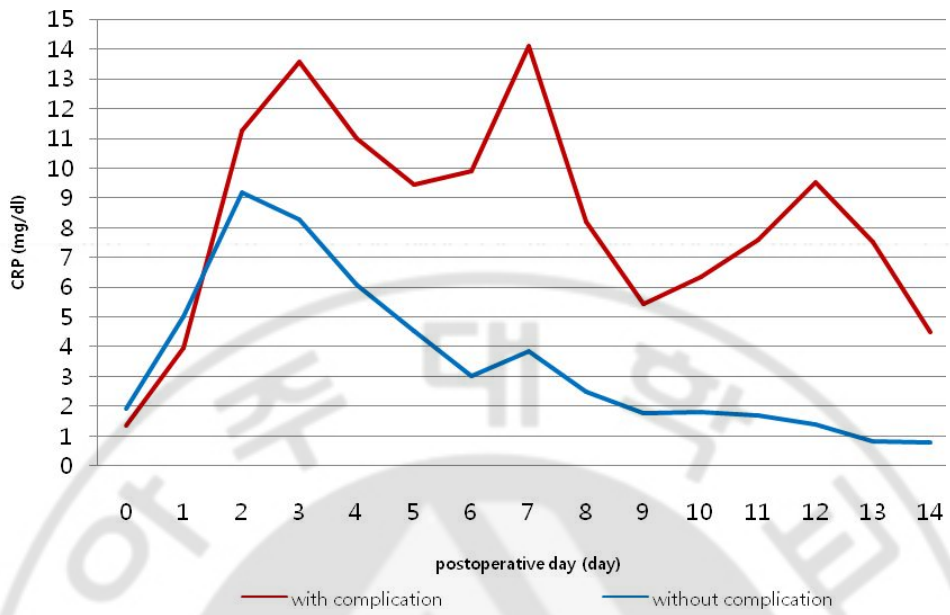
<b>Type of incisional infection</b>	
Superficial	Skin and subcutaneous tissue
Deep	Deep soft tissue
<b>Criteria for superficial infection</b>	
1. Purulent drainage from the superficial infection	
2. The superficial infection yields organisms from the culture of aseptically-aspirated fluid or tissue, or from a swab and pus cells are present	
3. At least two of the following symptoms and signs of inflammation:	
Pain or tenderness	
Localized swelling	
Redness	
Heat	
And a) The superficial infection is deliberately opened by a surgeon to manage the infection, unless the incision is culturenegative	
or	
b) A clinician's diagnosis of superficial incisional infection	



**Fig. 1. Number of patients reaching peak serum CRP at each day.**

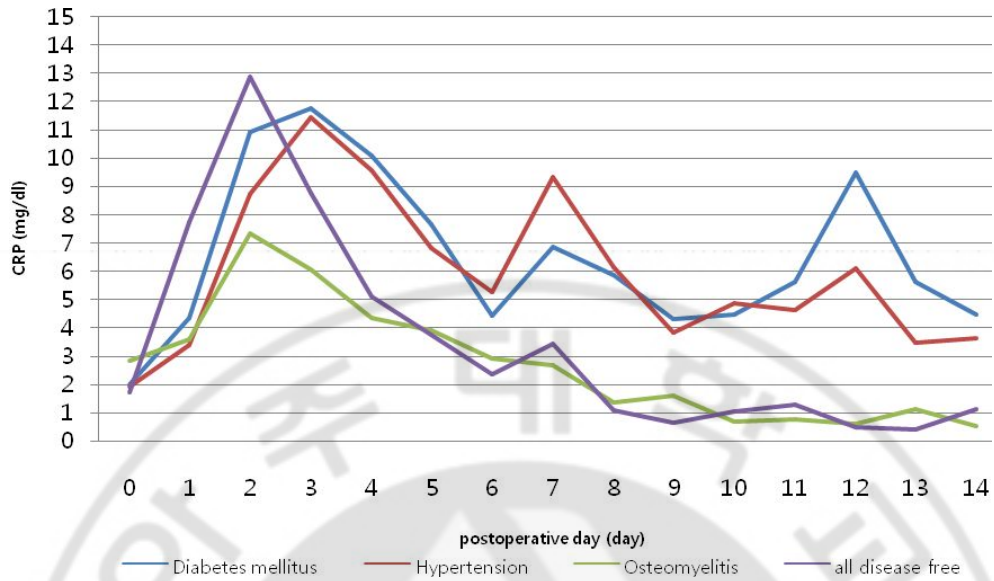
Fourteen (66.7%) patients reached their peak CRP within 3 days. Of the seven patients peaking after day 3, two patients (28.6%) had infective complications and two patients (28.6%) displayed side effects of antibiotics.





**Fig. 2. Serum CRP trends with or without complications.**

Patients with complications show higher level, irregular pattern, and second peak of CRP about 2 days before symptoms were evident.



**Fig. 3. Serum CRP trends of each group.**

In all disease-free patients, mean CRP rose from postoperative day 1, peaked at day 2, and decreased significantly from day 4. On the contrary, in diabetes and hypertension group, mean CRP rose from postoperative day 2, peaked at day 3, and decreased significantly from day 5. Also, an unexpected and irregular pattern was evident in the diabetes and hypertension group. There was statistical relevance of diabetes and hypertension on CRP trends. However, the non-osteomyelitis group showed more irregular and higher CRP trends than osteomyelitis group. There was no statistical significance.

## IV. DISCUSSION

CRP was first described in 1930 by Tillett and Francis, who isolated a previously unknown protein in the blood of a patient with a pneumococcal pneumonia infection (Nidal et al., 2008). In 1981, CRP was introduced for the early diagnosis of bacterial infections, including septic arthritis and osteomyelitis (Pentti et al., 1990).

According to Tillett and Francis, CRP is one of the normal constituents of serum and it is one of the acute phase proteins synthesized by hepatocytes (Pentti et al., 1990). CRP is produced by the liver in response to inflammation, infection, malignancy, and tissue damage with relatively high sensitivity, response speed, and range compared to other acute-phase reactants (James et al., 2008). The primary signal for this protein synthesis is interleukin-1 (IL-1), produced by macrophages at sites of tissue injury (Pentti et al., 1990) and CRP is synthesized following stimulus by various cytokines including tumor necrosis factor-alpha and IL-6 (Mitra et al., 2008). CRP activates the complement system, induces phagocytosis, and inhibits aggregation of thrombocytes. In addition, CRP can have a protective effect on the formation of arteriosclerotic vessels (Nidal et al., 2008).

Besides CRP, inflammatory markers, primarily erythrocyte sedimentation rate (ESR), leukocyte (WBC) count, and procalcitonin (PCT) are also commonly used when there is a suspicion of postoperative infection (James et al., 2008).

However, one of these markers (leukocytosis) in the diagnosis of infection is very poor, because it is influenced by many non-infectious factors such as myocardial infarction, catecholamines, corticosteroids, and acute bleeding (Mitra et al., 2008).

One of the most widely used indicators of the acute-phase reactant proteins is the ESR. ESR has a reasonably high sensitivity and specificity with respect to inflammatory diseases and malignancies (Mitra et al., 2008). However, ESR is an indirect test of the albumin-globulin ratio in the serum (James et al., 2008). It depends largely on the serum concentration of fibrinogen and can be greatly influenced by size, shape, and number of erythrocytes, as well as by other serum constituents such as immunoglobulin, fluid status, age, nutrition, and time of day (Mitra et al., 2008). Consequently, the results are imprecise and sometimes misleading (Mitra et al., 2008).

The most promising indicator to date is the serum procalcitonin (PCT) level, which, in one study, had a sensitivity of 64.4% and a specificity of 86% for differentiating patients with SIRS from those with sepsis (Mitra et al., 2008). PCT is detectable 3–4 hours after an inflammatory stimulus and peaks at 14 hours, remaining elevated for 24 hours, with a half-life in serum of 22–35 hours. However, in our study there is no case of severe infection such as sepsis and PCT takes a long time and more expensive than other markers.

CRP is better than other inflammatory markers because an elevated blood CRP concentration is thought to be highly suggestive of acute infection or trauma (Mitra et al., 2008), the degree of the increase being proportional to the mass of inflamed or traumatized tissue (Nidal et al., 2008). In addition to infection and trauma, there are several other conditions that commonly lead to substantial changes in CRP concentrations. These include surgery, burn, tissue necrosis, immunologically mediated inflammatory diseases, crystal-induced inflammatory diseases, and advanced cancer (Mitra et al., 2008). CRP normally rises over 2–3 days, peaking at approximately 48 hours and can be thousands of times greater than the standard figure (Nidal and Mitra et al., 2008). Understanding the timing and pattern of peak value is important because values substantially higher, later, and irregular than expected may indicate an abnormal inflammatory reaction due to complications. As mentioned above, in our study patients with complications show higher level, irregular pattern, and second peak of CRP about 2 days before symptoms were evident. The antibiotics needed to be changed, guided by a consultant microbiologist. After the cause is managed successfully, value of CPR rapidly dropped.

In agreement with the literature, there was presently an association between comorbidities and the serum CRP level. Baseline levels of CRP ( $p < 0.001$ ) were significantly higher among diabetes cases than among controls, and the relative risks of future diabetes for women in the highest versus lowest quartile of CRP were 15.7. These results support a possible role for inflammation in diabetogenesis (Aruna et al., 2001). The observed effect of CRP on hypertension may be mediated through endothelial dysfunction. This means that a chronic inflammatory or chronic infectious status may induce endothelial dysfunction, which is followed by hypertension and cardiovascular disease (Leonelo et al., 2001). Osteomyelitis also significantly affects the serum CRP level (Markus et al., 2010). However, according to our results, the non-osteomyelitis group showed more irregular and higher CRP trends than

the osteomyelitis group. This may have been because patients who had complications were all included in the non-osteomyelitis group. Also, all osteomyelitis patients were in the early phase and were well-controlled by antibiotics.



## V. CONCLUSION

Our results show that CRP is a highly efficient parameter involving a simple and rapid test for diagnosis and prognosis of infectious complications after free flap. We also noted the positive correlation between the comorbidities (diabetes mellitus and hypertension) and the CRP level in free flap.

However, limitations of our study include the number of patients who met inclusion criteria. Daily blood sampling from a larger number of patients would strengthen the analysis. Also, absolute serum CRP level could be quite different depends on each patients and there could be limit to diagnose infection only based on serum CRP level. Additionally, in acute phase after operation, other inflammatory reactions or factors to increase serum CRP level could not be ruled out completely.

We understand that correlation of serum CRP level to inflammation, complications, and comorbidities can be important for the better outcome and propose that it should be the aim of further studies.

## REFERENCES

1. 서유성, 최형석, 노재휘, 원성훈, 최종원, 이재철, 박종석: 인공관절 치환술 후 CRP 수치를 이용한 급성 감염의 예측. *대한정형외과학회지* 47: 133-139, 2012
2. 이수찬, 윤지열, 정광암, 남창현, 정승현: 편측 및 양측 슬관절 전치환술후 C-반응성 단백 수치의 변화 양상. *대한정형외과학회지* 44: 442-448, 2009
3. Aruna DP, JoAnn EM, Nader R, Julie EB: C-Reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA* 286: 327-334, 2001
4. Christian H, Andreas G, Max MM, Andreas S, Andreas J, Bernhard V, Peter MV: Is there an association between comorbidities and the outcome of microvascular free tissue transfer? *J Reconstr Microsurg* 27: 127-132, 2011
5. James MM, Murat P, Samantha LP, Erin B, Sigurd HB, Shane B, Vedat D, Bobby T, Serena SH: Use of C-reactive protein after spinal surgery. *Spine* 33: 415-421, 2008
6. Leonelo EB, Patricio LJ, Lina MV, Juan PC, Ana PO, Ana IG: Is C-reactive protein an independent risk factor for essential hypertension? *J Hypertens* 19: 857-861, 2001
7. Markus P, Markku J, Pentti EK, Pentti EK, Heikki P: Sensitivity of erythrocyte sedimentation rate and C-reactive protein in childhood bone and joint infections. *Clin Orthop Relat Res* 468: 861-866, 2010
8. Michael M, Heide A, Joachim S: Correlation of procalcitonin and C-reactive protein to inflammation, complications, and outcome during the intensive care unit course of multiple-trauma patients. *Critical care* 10: 1-10, 2006
9. Mitra B, Faranak A, Mohammad AB, Mahbobe ST, Ahmad RS, Nosrat-lage B, Hamid K: Comparison of WBC, ESR, CRP and PCT serum levels in septic and non-septic burn cases. *Burns* 34: 770-774, 2008
10. Nidal T, Alexandra B, Thomas M: Specific C-reactive protein measurements in plastic surgery. *Scand J Plast Reconstr Surg Hand Surg* 42: 138-144, 2008

11. Pentti K, Jarl EM, Martti L, Tuomo H: C-reactive protein in tibial fractures. *J Bone Joint Surg* 72: 615-617, 1990
12. Wright EH, Khan U: Serum complement-reactive protein (CRP) trends following local and free-tissue reconstructions for traumatic injuries or chronic wounds of the lower limb. *J Plast Reconstr Aesthetic Surg* 63: 1519-1522, 2010
13. Weng CM, Chou CH, Huang YY, Lin CC, Liu YW, Tsai WC: Increased C-reactive protein is associated with future development of diabetes mellitus in essential hypertensive patients. *Heart vessels* 25: 386-391, 2010





- 국문요약 -

## Serum Complement Reactive Protein (CRP) Trends Following Free Flap in Lower Extremity Reconstruction

아주대학교 대학원의학과

유영문

(지도교수 : 박명철)

혈청 CRP 는 감염의 임상적 소견이 나타나기 전에 그 수치가 빠르게 상승하고 적절한 치료시에 빠르게 감소하는 등 민감도가 좋아 감염을 진단하는데 효용성이 입증된 지표이다. 하지의 연부 조직 결손에 대하여 유리 피관술을 시행함에 있어 감염을 비롯한 여러 합병증은 매우 위험한 실패 요인이 될 수 있다. 따라서 CRP 를 이용하여 합병증을 미리 진단하고 적합한 치료를 시행하는 일은 매우 중요하고 의미있겠다.

이번 논문은 2009년 6월부터 2012년 3월까지 외상 및 만성 창상으로 인해 발생한 하지 연부 조직 결손에 대하여 유리피관 재건술을 받은 21명의 환자들을 대상으로 1. 유리 피관술 후 CRP 의 변화 양상 및 2. 환자의 동반 질환(당뇨, 고혈압, 골수염)과 CRP 의 변화 양상의 연관성을 분석하였다.

연구 결과 1. 14 명 (66.7%)의 환자가 수술 후 3일 이내에 CRP 의 최고치를 보였다. 나머지 7명은 수술 후 3일 이후에 CRP 의 최고치를 나타냈으며, 그 중 4명 (57.14%) 에서 수술 부위 감염과 항생제에 대한 부작용 등의 합병증이 동반되었다. 합병증이 동반된 환자군은 동반되지 않은 환자군보다 높고 불규칙적인 CRP 경향을 보였고, 합병증의 증상이 발현되기 약 2일 전에 CRP 의 이차 상승이 있었다. 이들에 대해서는 즉시 항생제를 변경하였고 이후 상처는 호전되었으며 CRP 는 감소하였다. 2. 당뇨 및 고혈압 환자군에서 동반 질환이 없는 환자군보다 CRP 상승 및 감소가 1일씩 늦게 나타났으며 그 변화 양상이 불규칙하고 예측이

어려웠다. 하지만 골수염 환자군은 오히려 골수염이 동반되지 않은 환자군보다 CRP 가 더 낮고 빠르게 감소하였다. 이는 합병증이 보고된 환자가 모두 골수염이 동반되지 않은 환자군에 포함되었고, 골수염이 비교적 초기이며 항생제 치료에 잘 반응 했기 때문으로 분석된다.

결론적으로 CRP 는 유리 피관술을 받은 환자에서 합병증을 진단하고 이에 대해 빠르게 치료를 시작하는데 매우 유용한 지표이며, 당뇨, 고혈압 등의 동반 질환이 CRP 의 변화 양상에 유의하게 영향을 줄 수 있다는 것 또한 알 수 있었다. 따라서 유리 피관술 후 CRP를 면밀히 관찰하는 것이 수술의 성공 가능성을 높이는데 기여할 수 있을 것으로 판단된다.

---

Key words : C-reactive protein, Free Tissue Flaps, Diabetes Mellitus, Hypertension, Osteomyelitis