

## Comparison of post-operative C-reactive protein levels between elective general and orthopedic surgery in dogs

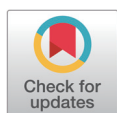
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### Abstract

C-reactive protein (CRP) is an acute-phase protein produced by hepatocytes. The plasma concentration of CRP peaks around 48 hours following stimulation. A rapid decrease in CRP levels is observed when the stimuli end. Considering these characteristics of CRP, it is used to evaluate acute inflammatory responses in clinics. In addition, as it reflects the degree of surgical trauma, measuring the CRP concentration is an effective method of evaluating tissue damage depending upon the surgical method. As CRP is also an acute-phase protein in dogs, the purpose of the present study was to compare the factors related to acute inflammatory responses between dogs undergoing elective general surgery (GS) and orthopedic surgery (OS). A total of 44 healthy dogs were included in this study. The sex ratio of dogs that underwent OS was similar. Both groups showed increased CRP levels and white blood cell (WBC) counts on post-operative day (POD) 1-2. The CRP level in the OS group on POD 1-2 was significantly higher than that of the GS group and it was increased about 16-fold compared to the pre-operative value. No significant difference in WBC counts was observed between the two groups. Although a slight increase in the WBC count was observed on POD 1-2 in both groups, it was near the reference range during follow-up. Thus, measuring CRP levels can be more effective in evaluating acute inflammatory responses than WBC counts. Although a high level of post-operative serum CRP concentrations was observed in the OS group, it rapidly decreased to a level similar to the pre-operative value if there were no post-operative complications.

**Keywords:** C-reactive protein; leukocytes; inflammation; trauma; dog

## INTRODUCTION

C-reactive protein (CRP) is a nonspecific acute-phase protein and is involved in most forms of inflammation, infection, and necrosis [1]. Plasma CRP is produced by the liver and the serum concentration peaks around 48 hours after stimulation [2]. As the plasma half-life of CRP is about 19 hours, circulating CRP concentrations decrease exponentially when the stimuli end [3, 4]. The

### Conflict of Interest

The authors declare no potential conflict of interest.

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### Ethics Approval

This study was approved by the Chungbuk National University Institutional Animal Care and Use Committees (CBNUA-1484-21-02).

plasma CRP concentration is affected by the degree of tissue damage and is, therefore, used to assess the severity of surgical trauma [5–7]. In an effort to reduce the trauma response, minimally invasive surgical techniques are widely applied in human medicine and CRP levels are used to evaluate tissue damage between surgical methods [5, 8, 9]. Although CRP is not a major acute-phase protein in all animals, such as cats, it is applicable to dogs [10]. Recent studies of CRP in dogs showed similar results compared to human medicine [11, 12]. A previous study that compared the factors participating in the acute-phase response in dogs undergoing elective general surgery (GS) revealed that CRP was a more reliable parameter than white blood cell (WBC) counts [13–15]. It also reflects the degree of surgical stress or the current status of dogs with acute or chronic diseases [16–19]. Changes in CRP levels varied depending upon the invasiveness of the surgical method, as in human medicine [16, 20]. In orthopedic surgery (OS), it is known that the effect on the CRP response varies according to the type of surgery [21]. Specifically, surgery that damages the bone marrow may have significant effect on the CRP response [6, 22]. Thus, under the hypothesis that the degree of surgical stress in GS and OS would be different, the purpose of this study was to evaluate the factors related to the acute-phase response in dogs that underwent elective GS or OS.

## MATERIALS AND METHODS

### Case selection criteria

The medical records of dogs who visited Chungbuk National University Veterinary Teaching Hospital, Naepo Animal Medical Center, Naeum Animal Medical Center, and Bupyeong SKY Animal Medical Center in 2021 were reviewed. All surgeons were trained for 2–5 years in the Chungbuk National University Veterinary Teaching Hospital. The inclusion criteria for this study were dogs weighing  $\leq 20$  kg that underwent elective GS or OS.

### Medical record review

The medical records included age, sex, and the results of blood tests. The elective GS group was composed of dogs that underwent ovariohysterectomy (OHE). The orthopedic diseases consisted of medial patella luxation (MPL) and cranial cruciate ligament rupture (CCLR). Orthopedic diseases such as fractures and trauma that might have accompanying elevated pre-operative CRP levels were excluded. The surgical methods for MPL were composed of medial release, lateral tightening, groove-plasty, and tibial tuberosity transposition. Medial release and lateral tightening were performed using 2-0 or 3-0 braided polyglycolic acid sutures (Surgifit; AILEE, Pusan, Korea). The surgical methods for CCLR were extracapsular fixation, tibial plateau leveling osteotomy (TPLO), and cranial tibial wedge osteotomy (CTWO). During extracapsular fixation, lateral fabella-tibial suture using 2 or 2-0 braided polyblend suture material (FiberWire; Arthrex, Naples, FL, USA) was applied. TPLO or CTWO was performed by the conventional method. WBC counts and serum CRP levels were evaluated on the pre-operative day, post-operative day (POD) 1-2, and POD 10.

## Data analysis

The data were analyzed by the Mann-Whitney U test to compare the differences in CRP levels and WBC counts between the GS and OS groups. Analyses were performed using SPSS for Windows version 12.0 and a  $p$ -value of  $<0.05$  was considered significant. All data are expressed as the mean  $\pm$  S.D.

## RESULTS

### Demographics

Forty-four dogs were included in this study. A total of 25 dogs underwent elective GS (OHE) and 19 dogs underwent OS for MPL and/or CCLR. The mean age was 49.5 months (range, 6 to 132 months) in the GS group and 59.1 months (range, 9 to 142 months) in the OS group. In the OS group, 10 were males and nine were females.

### Comparison of post-operative C-reactive protein (CRP) levels between the general surgery (GS) and orthopedic surgery (OS) groups

Serum CRP levels increased on POD 1-2 in both groups. It was significantly higher in the OS group ( $177.61 \pm 65.58$  mg/L) than in the GS group ( $39.51 \pm 41.57$  mg/L). However, the serum CRP levels in both groups decreased similarly to the pre-operative levels on POD 10. At that time, no significant difference was observed between the two groups (Table 1).

### Comparison of post-operative white blood cell (WBC) counts between the general and orthopedic surgery groups

WBC counts slightly increased on POD 1-2 and decreased on POD 10 in both groups. No significant difference was found between the two groups. Although the WBC counts increased, they were within the reference interval ( $5.05 - 16.76 \times 10^3/\mu\text{L}$ ) during the follow-up period (Table 2).

**Table 1.** Comparison of pre- and post-operative C-reactive protein levels (mg/L) between the elective general surgery (GS) and orthopedic surgery (OS) groups

	Pre-OP	POD 1-2	POD 10
GS	12.15 $\pm$ 3.57	39.51 $\pm$ 41.57	16.29 $\pm$ 4.45
OS	11.38 $\pm$ 7.85	177.61 $\pm$ 65.58*	16.14 $\pm$ 8.45

Mean  $\pm$  S.D.

\*  $p < 0.05$  comparing GS and OS.

Pre-OP, pre-operation; POD, post-operative day.

**Table 2.** Comparison of pre- and post-operative white blood cell counts ( $\times 10^3/\mu\text{L}$ ) between the elective general surgery (GS) and orthopedic surgery (OS) groups

	Pre-OP	POD 1-2	POD 10
GS	11.16 $\pm$ 3.15	12.80 $\pm$ 3.84	12.71 $\pm$ 5.01
OS	10.07 $\pm$ 3.01	14.40 $\pm$ 4.47	11.09 $\pm$ 4.36

Mean  $\pm$  S.D.

Pre-OP, pre-operation; POD, post-operative day.

## DISCUSSION

The present study was conducted on dogs considered healthy by clinical and laboratory tests, including complete blood counts and serum biochemistry profiles. Among the orthopedic diseases, MPL and CCLR were included in the orthopedic group because most of these diseases were chronic and generally not accompanied by elevated pre-operative CRP levels [14]. The ratio of male to female dogs in the OS group was similar (10 males and 9 females). No significant age- or sex-related differences in CRP levels were observed in previous studies [23, 24]. Like the commonly known characteristics of CRP, the serum CRP levels of both groups dramatically increased on POD 1-2 [3, 25]. The CRP levels in the GS group increased about 3-fold, similar to a previous study [16]. However, the CRP levels in the OS group significantly increased about 16-fold compared to the pre-operative values. Although OS that damages the bone marrow is known to affect the CRP response more [6, 22], highly elevated serum CRP concentrations were observed in relatively less invasive surgeries such as groove-plasty and extracapsular fixation in this study. The differences in serum CRP concentrations between the types of OS were not evaluated due to the small number of samples. When monitoring post-operative complications, a second rise or the persistence of elevated CRP levels occurred if there were infectious complications. Otherwise, a rapid decline in CRP levels was observed [11, 22]. The dogs that underwent OS in the present study showed rapid decreases in serum CRP concentrations on POD 3-4 (data not shown) and the return to levels similar to the pre-operative values on POD 10. In addition to measuring the serum CRP concentrations for monitoring acute inflammatory reactions, the degree of leukocytosis was also evaluated through WBC counts. Although a slight increase was observed in both groups on POD 1-2, it was generally near the reference range during the follow-up period. Due to similar post-operative leukocytosis results, the previous study also found that the WBC counts did not reflect the acute inflammatory response better than CRP levels [13]. Therefore, measuring serum CRP concentrations may be more effective when evaluating post-operative inflammation in GS or OS in dogs. Although the CRP levels of dogs in the OS group significantly increased on POD 1-2 compared to those in the GS group, these levels would rapidly return to normal if there were no complications such as infection.

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