Serum procalcitonin and C-reactive protein concentrations in dogs with degenerative mitral valve disease and infective endocarditis

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ABSTRACT

This study aimed to investigate the clinical significance of serum C-reactive protein (CRP) and procalcitonin (PCT) concentrations in dogs with degenerative mitral valve disease (DMVD) and infective endocarditis. It also aimed to evaluate whether there is a relationship between the degree of disease and serum PCT and CRP concentrations. A total of 100 dogs with MVD were prospectively recruited into the study. According to clinical/laboratory signs and echocardiography, the dogs were divided into infective and degenerative groups. The degenerative group was also classified into four stages based on the American College of Veterinary Internal Medicine (ACVIM) guidelines (Stages A-D). Serum PCT and CRP concentrations were determined with dog-specific commercial test kits. The serum CRP (P<0.05) and PCT (P<0.001) concentrations in the infective group were significantly higher than the degenerative group. In the degenerative group, the serum CRP concentration of stage D dogs was significantly higher than the other stages (P<0.001), and the degree of disease correlated significantly positively with serum CRP concentration (r=0.531 P=0.000). In conclusion, serum CRP and PCT concentrations may aid traditional diagnostic techniques to differentiate infective and degenerative mitral valve disease. This study also demonstrated that serum CRP concentrations were elevated in Stage D dogs, and that there is a positive correlation between the degree of disease and serum CRP concentration. This can be useful in determining the severity of the inflammatory state in dogs with DMVD.

Keywords: canine; C-reactive protein; heart disease; mitral valve disease; procalcitonin

Introduction

In small animal medicine, the importance of cardiopulmonary system diseases is increasing day by day. By effectively using technological developments and research results in daily life, the life span and the life quality of cats and dogs have been increased. In dogs, as in humans, the incidence of heart disease increases with increasing age (GUGLIELMINI, 2003, LUNG and VAHANIAN, 2014). Acquired heart diseases in dogs are generally degenerative and less commonly infective. Other pathological processes, such as neoplasia, rarely affect the heart valves (ABBOTT, 2008).

Mitral valve insufficiency due to valve degeneration may result in progressive heart enlargement and, in some cases, congestive heart failure (CHF). Mixomatous degeneration of the
mitral valve is the most common cardiological disorder in dogs, and is the third most common cause of death in these species (KEENE et al., 2019). Current data suggest that mitral regurgitation (MR) owing to myxomatous mitral valve diseases (MMVD) contributes significantly to cardiovascular morbidity and mortality in dogs (EGENVALL et al., 2006). Seventy-five to eighty per cent of heart diseases and 75% of congestive heart failure occur due to degenerative mitral valve diseases (DMVD) (KEENE et al., 2019). The clinical symptoms of DMVD occur primarily in elderly and small breed dogs (ABBOTT, 2008, ATKINS et al., 2009, KEENE et al., 2019). In dogs, another form of acquired valvular disease is infective endocarditis (IE) (ABBOTT, 2008). The disease symptoms are often nonspecific and associated with sepsis, thromboembolism and CHF. Infective endocarditis usually affects middle-aged, medium and large breed dogs (ABBOTT, 2008).

Inflammation plays a role in the pathogenesis and progression of many forms of heart failure. Therefore, cardiac patients’ inflammation biomarkers in human and veterinary medicine have been investigated intensively (BOSWOOD, 2009). C-reactive protein (CRP) is a major acute-phase protein in dogs, characterised by a marked increase in serum concentration, consistent with systemic inflammatory activity (GOMMEREN et al., 2018). The serum/plasma CRP concentration is reported to be increased in various pathological conditions in dogs, including congenital and acquired heart diseases (NAKAMURA et al., 2008, DOMANJKO PETRIĆ et al., 2018).

Procalcitonin (PCT) is one of the parameters that have been added to infection markers in humans in recent years. PCT is a prehormone of calcitonin, secreted by thyroid C cells in response to hypercalcemia. Under normal conditions, serum PCT levels are low, and PCT production is stimulated by bacterial endotoxins, exotoxins and cytokines (TROIA et al., 2018). PCT appears as an earlier and better marker than inflammatory response parameters such as body temperature, CRP, and leukocyte count in sepsis and severe infections (SCHUETZ et al., 2016). It is widely used in humans to detect bacterial infection and evaluate antibiotic therapy effectiveness. Also, PCT value is important in patients with respiratory system infections and cardiovascular problems such as heart failure, endocarditis, cardiac arrest, and acute coronary syndrome (CANBAY et al., 2015). There is a limited number of studies on PCT in dogs in veterinary medicine compared to human medicine. In dogs, plasma/serum PCT concentration was evaluated after endotoxin administration, Babesia canis infection, experimental Pseudomonas aeruginosa infection, aseptic surgery, trauma, gastric dilatation-volvulus and sepsis (YILMAZ et al., 2008, GOGGS et al., 2018).

To our knowledge, there is no study on serum PCT concentrations in dogs with heart disease. This study aimed to investigate the clinical significance of serum CRP and PCT concentrations in dogs with MVD. It also aimed to evaluate whether there is a relationship between the degree of disease and serum PCT and CRP concentrations.

**Materials and methods**

The Animal Research Ethics Committee of Aydın Adnan Menders University reviewed and approved all study procedures under protocol number: 64583101/2016/199.

**Animal material.** This prospective study was conducted from March 2017 to March 2020 at the Department of Internal Medicine of Aydın Adnan Menders University Veterinary Faculty, Aydın, Turkey. One hundred client-owned dogs with MVD, of different breeds, ages and sex were enrolled in the study. The signalment, medical histories, anamnesis information and physical examination findings of all dogs were recorded. A routine cardiological examination protocol (Auscultation, X-ray, electrocardiography and echocardiography) was applied to the dogs. Radiographic evaluation of the thorax and heart was made using a digital radiography system (Comed Medical System, Korea and Konika Minolta R Sigma II) and routine radiographic techniques (lateral and ventrodorsal positions). ECG examination was performed in the right lateral recumbency, and with limb leads using a Cardiofax VET ECG-1950K device (Nihon Kohden Cor. Japan) under appropriate conditions (25 mm/sec, 5 mm/mV). Echocardiographic
examination was performed using standard imaging techniques (THOMAS et al., 1993). Short/long axis two-dimensional and single anatomical cross-section (M-mode) images of the heart were taken in the right parasternal position. Mitral blood flow abnormalities were determined by colour doppler using the right parasternal long-axis 4-chamber view. For M-mode, the right parasternal short-axis view was used at the level of the papillary muscles at the end of the diastole (CORNELL et al., 2004). For DMVD, dogs with congenital heart disease, other acquired cardiovascular disorders, concurrent non-cardiac disorders, including other illnesses and chronic inflammation (e.g., infection, cancer, chronic renal failure, and pancreatitis) were excluded (on the basis of the history, routine clinical examination, echocardiographic examination and laboratory analyses). Dogs with IE were selected for this study if they only had mitral valve lesions. Also, dogs were excluded if any antibacterial and anti-inflammatory drugs had been administered during the previous three months.

Study design. The dogs were classified into two main groups on the basis of clinical, laboratory and cardiological examination findings.

Group 1. Dogs with infective mitral valve problems (Infective group): The diagnosis of IE was made in six dogs on the basis of the modified Duke criteria (KITTLESON, 1998). One major (mitral valve lesions with typical characteristics of endocarditis) and two minor criteria (Pyrexia of unknown origin and medium to large breed dogs) were considered as a definitive diagnosis of IE. Also, the dogs in this group had arthritis in different extremities.

Group 2. Dogs with degenerative mitral valve problems (Degenerative group): Dogs with degenerative mitral valve disease were divided into four stages on the basis of the severity of their heart disease and heart failure, as proposed by the American College of Veterinary Internal Medicine (ACVIM) (ATKINS et al., 2009, KEENE et al., 2019).

Group 2a dogs. Stage A: Twenty healthy dogs with no identifiable structural impairment in the heart were still included this stage. These dogs were at high risk of developing heart disease due to their breed (e.g. Cavalier King Charles Spaniels), size (under 20 kg) and genetics.

Group 2b dogs. Stage B: A total of 32 dogs with structural heart disease (those with a typical murmur with mitral regurgitation) who had not developed clinical signs caused by heart failure were evaluated in this group. B1: 16 dogs without radiographic or echocardiographic cardiac remodelling findings in response to valve disease, B2: 16 dogs with hemodynamically significant valve insufficiency (with radiographic or echocardiographic findings of left heart enlargement).

Group 2c dogs. Stage C: 20 dogs with past or current clinical signs of HF, compensated with cardiac therapy were included in this stage. Also, this stage included dogs with echocardiographic and radiographic changes consistent with HF due to DMVD. These dogs presented mild to moderate clinical signs (those with a murmur caused by mitral regurgitation, clinical cough, dyspnea/tachypnea) and responded to diuretic therapy.

Group 2d dogs. Stage D: This stage included 22 dogs with the end-stage disease with clinical signs of heart failure caused by chronic DMVD (coughing, exercise intolerance, dyspnoea, syncope, pulmonary oedema, cyanosis, cardiac cachexia) that are refractory to standard therapy.

Laboratory analysis. Blood samples were taken from vena cephalica antebrachii into anticoagulant (K3-EDTA) and serum separator tubes. Complete blood counts were performed with an Abacus Junior Vet haematology device (Abacus Junior Vet, Diatron MI LTD, Hungary). Blood samples taken into serum separator tubes were centrifuged at 3000 g for 10 minutes, and the serum was separated. Serum samples were stored at –20 °C for PCT, CRP and serum biochemical analysis. Serum PCT and CRP concentrations were analysed at Adnan Menderes University, Faculty of Veterinary Medicine, Department of Biochemistry. Serum PCT concentrations were measured using the canine PCT ELISA kit (Canine Procalcitonine ELISA Kit, Cusabio, Chine) with a dog-specific quantitative sandwich enzyme immunoassay technique, according to the manufacturer’s instructions. According to the manufacturer’s instructions, serum CRP concentrations were determined with a
solid sandwich ELISA commercial test kit (Tridelta, Ireland) using a specific monoclonal antibody technology ELISA reader device (Optic Iyymen System, Spain). Routine serum biochemistry to determine the health status of dogs was measured on an auto-analyzer device (Sinnova D 280, China) with commercial test kits (Archem Diagnostic, Turkey).

Statistical analysis. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 19.0 (IBM Corporation, Armonk, USA). Arithmetic means (mean), standard deviations (SD), median, interquartile range (IQR), and minimum-maximum (min-max) values were computed using standard descriptive statistic procedures. The distribution of numerical data was evaluated using the Kolmogorov-Smirnov and Shapiro-Wilk tests. The Student t-test was used for comparing group averages of normally distributed parameters, and one-way analysis of variance (ANOVA) was used to compare the normally distributed parameters of more than two groups. The transformation was applied to the data without normal distribution. The non-parametric test, the Man-Whitney U test was used to compare the median values of the parameters that did not provide normal distribution after transformation. The non-parametric Kruskal Wallis test was used to compare the parameters of more than two groups. Pearson’s correlation test was used to assess the relationship between the variables. Differences at P<0.05 were considered statistically significant.

Results

In total, 100 dogs with MVD of both sexes (43 males and 57 females) and ages (between two and 15 years old) were enrolled in this study. The most commonly recruited breed was Terrier (n=24), followed by crossbreed (n=18) and Cavalier King Charles Spaniel (n=16). Most of the degenerative group consisted of small breed dogs, while the majority of the infective group consisted of large breed dogs (Table 1).

The characteristic echocardiographic lesion on the mitral valves was regarded as the major duke criteria in the infective group (Fig. 1). Also, dogs in this group were positive for systemic inflammatory response syndrome (SIRS), as reported by HAUPTMAN et al., (1997) and SILVERSTEIN (2015) on the basis of their body temperature (mean 40.00 ± 0.40 °C), heart rate (mean 147.33 ± 17.08/ min), respiratory rate (mean 37.83 ± 9.15/min) and WBC counts (mean 33.97 ± 9.10 x10³/µL).

Table 1. Breed distributions of dogs included in the study.

<table>
<thead>
<tr>
<th>Breed</th>
<th>Infective Group</th>
<th>Degenerative Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terrier</td>
<td>-</td>
<td>24</td>
</tr>
<tr>
<td>Crossbreed</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>Cavalier King</td>
<td>-</td>
<td>16</td>
</tr>
<tr>
<td>Charles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>French bulldog</td>
<td>-</td>
<td>12</td>
</tr>
<tr>
<td>Yorkshire terrier</td>
<td>-</td>
<td>12</td>
</tr>
<tr>
<td>Golden retriever</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Pekinese</td>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td>Pug</td>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td>Cocker spaniel</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pomeranian</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>German Shepherd</td>
<td>1</td>
<td>-</td>
</tr>
</tbody>
</table>

Fig. 1. The characteristic echocardiographic lesion from dogs in the infective group

Dogs in the infective group had significantly higher heart rates (P<0.01), respiratory rates (P<0.01) and body temperatures (P<0.001) compared with the degenerative group (Table 2). In the degenerative group, the mean heart
rates of Stage B and Stage D were significantly higher than Stage A and Stage C (P<0.001). There was no statistical difference in respiratory rate between stages (P>0.05). Although the mean body temperature in Stage C was significantly higher than Stage A (P<0.05), body temperatures in the 4 stages were also within the reference values reported for the dogs (REECE, 2015) (Table 3).

Table 3. Heart rate, respiratory rate and body temperature of dogs in the degenerative group classified according to ACVIM (x±SD, median, IQR ve Xmin-Xmax).

<table>
<thead>
<tr>
<th></th>
<th>Stage A</th>
<th>Stage B</th>
<th>Stage C</th>
<th>Stage D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (/min)</td>
<td>97.00±5.85 a</td>
<td>120.38±26.87 b</td>
<td>105.11±27.86 a</td>
<td>138.45±20.34 b</td>
</tr>
<tr>
<td>Median</td>
<td>98</td>
<td>127</td>
<td>96</td>
<td>140</td>
</tr>
<tr>
<td>IQR</td>
<td>12</td>
<td>44</td>
<td>39</td>
<td>32</td>
</tr>
<tr>
<td>X_{min}-X_{max}</td>
<td>88-102</td>
<td>81-174</td>
<td>75-161</td>
<td>94-163</td>
</tr>
<tr>
<td>Respiratory rate (/min)</td>
<td>30.05±3.97</td>
<td>29.12±5.35</td>
<td>30.35±4.70</td>
<td>32.70±4.53</td>
</tr>
<tr>
<td>Median</td>
<td>30</td>
<td>30</td>
<td>30.5</td>
<td>34</td>
</tr>
<tr>
<td>IQR</td>
<td>4.5</td>
<td>6.5</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>X_{min}-X_{max}</td>
<td>19-36</td>
<td>20-36</td>
<td>21-40</td>
<td>26-40</td>
</tr>
<tr>
<td>Body temperature (°C)</td>
<td>38.70±0.32a</td>
<td>38.62±0.27ab</td>
<td>38.95±0.22b</td>
<td>38.87±0.36ab</td>
</tr>
<tr>
<td>Median</td>
<td>38.60</td>
<td>38.62</td>
<td>38.90</td>
<td>38.90</td>
</tr>
<tr>
<td>IQR</td>
<td>0.58</td>
<td>0.40</td>
<td>0.33</td>
<td>0.50</td>
</tr>
<tr>
<td>X_{min}-X_{max}</td>
<td>38.30-39.40</td>
<td>38.20-39.2</td>
<td>38.60-39.4</td>
<td>38.10-39.60</td>
</tr>
<tr>
<td>n</td>
<td>20</td>
<td>32</td>
<td>20</td>
<td>22</td>
</tr>
</tbody>
</table>

Abbreviations: ACVIM: American College of Veterinary Internal Medicine; Min-Max: minimum-maximum; IQR: interquartile range; SD: standard deviations x: mean. a, b ACVIM group in which there is a statistically significant difference within each row (P<0.05).
Significantly higher WBC counts (p<0.001, median 31.02 x10^3/µL, IQR 8.75 x10^3/µL), serum CRP (P<0.05, median 119.65 mg/L, IQR 81.77 mg/L) and serum PCT concentrations (P<0.001, median 120.70 pg/mL, IQR 149.93 pg/mL) were found in the infective group compared with the degenerative group (Fig. 2).

In the degenerative group, the mean WBC counts were significantly higher in Stage B (P<0.001, mean 14.33 ± 5.33 x10^3/µL) and Stage D (P<0.001, mean 14.91 ± 5.00 x10^3/µL) than Stage A (mean 9.15 ± 1.08 x10^3/µL). There were no statistically significant differences between Stage C (mean 12.49 ± 6.04 x10^3/µL) and the other three stages. Serum CRP concentration was significantly higher in Stage D (median 116.50 mg/L, IQR 59.97 mg/L) than Stage A (mean 9.15 ± 1.08 x10^3/µL). There were no statistically significant differences between Stage C (mean 12.49 ± 6.04 x10^3/µL) and the other three stages. Serum CRP concentration was significantly higher in Stage D (median 116.50 mg/L, IQR 59.97 mg/L) than Stage A (mean 9.15 ± 1.08 x10^3/µL). There were no statistically significant differences between Stage C (mean 12.49 ± 6.04 x10^3/µL) and the other three stages.

CRP and PCT values, and no statistically significant difference was found between the groups.

Serum CRP concentration significantly positively correlated with WBC (r=0.302, P=0.003) in the degenerative group, while no significant correlations were found in the infective group. There were no significant correlations between the serum CRP and PCT concentrations in the infective (r=0.086 P=0.872) and degenerative groups (r=0.118, P=0.257). The degree of disease significantly positively correlated with WBC (r=0.327 P=0.001) and CRP concentration (r=0.531 P=0.000) in the degenerative group.

**Discussion**

Cardiovascular disease is a significant cause of morbidity in dogs, estimated to affect at least 11% of the canine population (CUNNINGHAM et al., 2018). Among canine cardiac diseases, myxomatous mitral valve disease is by far the most common. This degenerative valvular disease evolves progressively, and ultimately leads to congestive heart failure, secondary to myocardial...
remodelling. Also, one of the diseases affecting the mitral valve is infective endocarditis. Although infective endocarditis is rare in dogs, diagnosis is quite tricky and fatal.

Acute-phase proteins, which are not specific for the disease but whose concentrations increase rapidly in tissue destruction and inflammation, have been used in the diagnosis, differential diagnosis and prognosis of many diseases and inflammatory conditions in veterinary and human medicine (KJELGAARD-HANSEN et al., 2011, DOMANJKO PETRIČ et al., 2018). Most human studies assessing CRP in IE settings have demonstrated its value in diagnosing the disease (NUNES et al., 2018). An elevated level of this marker supports diagnosis of IE, whereas normal levels indicate a low probability of this condition. Indeed, some investigators have suggested CRP inclusion as a minor Duke criterion for IE diagnosis (NUNES et al., 2018). Similar to the previous studies mentioned above, serum CRP concentration was higher in the infective group in this study (Fig. 2). Dogs in the infective group were also positive for SIRS criteria (Fig. 2, Table 2). This increase in serum CRP concentration in the infective group is thought to be associated with an inflammatory response in SIRS positive dogs, as GOMMEREN et al., (2018) reported.

Serum CRP concentration in dogs with mitral valve disease has been evaluated in a limited number of studies (RUSH et al., 2006, TARNOW et al., 2007, LJUNGVALL et al., 2010, CUNNINGHAM et al., 2012, POLIZOPOULOU et al., 2015, REIMANN et al., 2016, DOMANJKO PETRIČ et al., 2018, NUNES et al., 2018). In a study on dogs classified according to ISACHC (the International Small Animal Cardiac Health Council), it was reported that the median serum CRP concentrations in dogs in ISACHC III group were higher than ISACHC groups I-II (DOMANJKO PETRIČ et al., 2018). Also, regardless of the analysis method used, two separate studies were carried out in dogs classified according to the degree of heart failure caused by DMVD/MMVD (POLIZOPOULOU et al., 2015, REIMANN et al., 2016). In these studies, groups with CHF had a significantly higher serum CRP concentration, and there was no statistically significant difference between other groups. Similar to these studies, the median serum CRP concentrations of dogs in Stage D were significantly higher (p<0.001) compared to different stages in this study (Fig. 3). There was no statistically significant difference between the other three stages. CRP concentrations are elevated by overexpression of myocardial cytokine in the atria and ventricles in dogs with heart failure induced by various cardiac diseases, including MVD (REIMANN et al., 2016). The inflammatory process can cause myocardial damage, and inflammatory agents also contribute to the worsening and progression of HF (OIKONOMOU et al., 2011). The increased CRP concentration in this study might be related to these factors. In contrast to our results, RUSH et al., (2006) reported that the CRP concentration was not significantly different between MMVD dogs with CHF or without CHF. This difference between studies could be explained by the differences in the study population and analysis method used. In addition, the results of this study were similar to studies in dogs that found a significant association between CRP and MMVD severity (CUNNINGHAM et al., 2012, REIMANN et al., 2016) but differed from LJUNGVALL et al., (2010), who reported that circulating CRP concentration was not associated with MMVD severity. However, unlike the study reported here, that study population was predominantly of CKCS, and CRP levels were higher in non-CKCS dogs.

Studies in humans have shown that procalcitonin is rapidly secreted in response to endotoxins and other mediators (IL-1B, TNF-a, and IL-6) during bacterial infections. The PCT level is directly related to the degree and severity of bacterial infections (SCHUETZ et al., 2016). In addition to bacterial infections, it is stated that PCT value is also important in patients with cardiovascular problems, such as possible heart failure, endocarditis suspicion, cardiac arrest and acute coronary syndrome (SCHUETZ et al., 2012, CANBAY et al., 2015, SCHUETZ et al., 2016). Many studies report that an increase in PCT value is related to bacteremia, the main diagnostic criteria for IE (LAUKEMANN et al., 2015, RAST et al., 2015). In this study, serum PCT concentrations of
dogs in the infective group were significantly higher (p<0.05) compared to the degenerative group (Fig. 2). Dogs in the infective group were evaluated as having infective endocarditis, considering the modified Duke criteria. It was thought that this increase in serum PCT concentration in this group might be related to possible bacteremia, as stated by the researchers above. In different studies in humans and various animals, increased plasma PCT concentration under SIRS or sepsis conditions is based on an increase in PCT-associated mRNA transcription (and increased synthesis in the acute phase response context (ASSICOT et al., 1993, KUZI et al., 2008, LEE et al., 2013, BONELLI et al., 2015a,b, BONELLI et al., 2017, BONELLI et al., 2018, GOGGS et al., 2018, TROIA et al., 2018b). Also, the high serum PCT concentration in the infective group may be associated with these mechanisms.

Degenerative mitral valve diseases in dogs are important causes of heart failure. Recently, studies have been conducted on the use of PCT as a prognostic marker in cardiovascular diseases and as a marker for antibiotic treatment in people with heart failure (SCHUETZ et al., 2016). Some studies in human medicine (WANG et al., 2014, CANBAY et al., 2015) have shown that serum PCT concentration is higher in HF patients without an infective clinical picture than in healthy control groups. There is a positive correlation between the degree of heart failure (NYHA class/decompensation) and the PCT value in these studies. Also, the increase in plasma PCT concentration in humans, other than with bacterial infection-related SIRS or sepsis conditions, is explained by pro-inflammatory mediators that also occur in the absence of bacteria. This explanation is attributed to the rapid decrease in plasma PCT concentration with inflammation control (MEISNER, 2002). In contrast to these studies, in our study no statistically significant differences were found in serum PCT concentrations between stages (Fig. 3), and there were no significant correlations between the serum PCT concentration and the degree of disease. This situation can be explained by studies showing that the PCT level is directly related to the degree and severity of bacterial infections and that non-infective inflammation does not affect PCT concentrations (MCCANN et al., 2012, SCHUETZ et al., 2016, GURBUZ and ULUTAS, 2017).

There are some limitations to our study. First, the etiological agents could not be revealed by blood culture in the diagnosis of dogs with IE. However, the dogs in this group were positive for one major and two minor criteria in relation to the modified Duke criteria. Second, as infective endocarditis is a rare disease in dogs, the number of dogs in the infective group is small. Third, we determined concurrent diseases and inflammatory conditions in the degenerative group by clinical examination, CBC, serum biochemistry, urinalysis and imaging methods. These dogs were excluded from the study. However, there is still the possibility that we could not identify some subclinical conditions. Also, in this study, blood samples were taken from dogs once they were brought to the clinic. The half-life of procalcitonin in the circulation is reported as 25-30 hours (MARUNA et al., 2000, NAKAMURA et al., 2013). Variability in the duration and severity of symptoms may affect plasma PCT concentrations.

In conclusion, Serum CRP and PCT concentrations were higher in dogs with IE than dogs with DMVD. Thus, serum CRP and PCT concentrations may adjunct traditional diagnostic techniques used to differentiate IE and DMVD in dogs. This study also demonstrated that serum CRP concentrations were elevated in Stage D dogs. There is a positive correlation between the degree of degenerative mitral valve disease and serum CRP concentration. Elevated CRP does not necessarily indicate the severity of heart disease. However, these results can be used to determine the inflammatory state in dogs with CHF. This study is the first to provide information on serum PCT concentrations in dogs with MVD, and supports the limited data available on serum CRP concentrations in these dogs. However, more comprehensive studies are needed to use serum CRP and PCT concentrations as a useful biomarker for diagnosis and prognosis in dogs with mitral valve disease.

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Cilj rada bio je istražiti kliničku važnost serumskih koncentracija C-reaktivnog proteina (CRP) i prokalcitonina (PCT) u pasa s degenerativnom bolešću mitralnog zaliska (DMVD) i infektivnim endokarditisom. Također, cilj je bio i procijeniti postoji li povezanost između stupnja bolesti i serumskih koncentracija PCT-a i CRP-a. U prospektivno istraživanje uključeno je 100 pasa s MVD-om. Prema kliničko laboratorijskim znakovima i ehokardiografiji psi su podijeljeni u skupinu s infektivnom i skupinu s degenerativnom bolešću. Psi s degenerativnom bolešću razvrstani su u četiri stadija (A-D) prema smjernicama American College of Veterinary Internal Medicine (ACVIM). Koncentracije serumskog PCT-a i CRP-a određene su komercijalnim testnim setovima specifičnima za pse. Koncentracije serumskog CRP-a i PCT-a u skupini pasa s infektivnom bolešću bile su znakovito više (P<0,05 i P<0,001) nego one u skupini pasa s degenerativnom bolešću. U skupini s degenerativnom bolešću serumne koncentracije CRP-a u pasa sa stadijem D bile su znakovito više nego u pasa s ostalim stadijima (P<0,001). Stupanj bolesti bio je u znakovitoj pozitivnoj korelaciji sa serumskim koncentracijama CRP-a (r = 0,531, P=0,000). Zaključno, serumskе koncentracije CRP-a i PCT-a mogu pomoći tradicionalnim dijagnostičkim metodama u razlikovanju infektivne i degenerativne bolesti mitralnog zaliska. Istraživanje je pokazalo i povišene serumne koncentracije CRP-a u pasa sa stadijem D te pozitivnu korelaciju između stupnja bolesti i koncentracije CRP-a. Navedeno može biti korisno pri procjeni težine upalnog stanja u pasa s DMVD-om.

Ključne riječi: pas; C-reaktivni protein; srčana bolešć; boleš mitralnog zaliska; prokalcitonin