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Usefulness of Measuring Serum Procalcitonin Levels in Patients with Inflammatory Bowel Disease

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See editorial on page 491.

Background/Aims: The relationships between serum procalcitonin, inflammatory bowel disease (IBD) and intestinal Behçet's disease (BD) have not been completely determined. We aimed to evaluate the usefulness of measuring serum procalcitonin levels to assess disease activity and infection stage in patients with IBD and intestinal BD. **Methods:** We retrospectively analyzed clinical data from 129 patients with IBD and intestinal BD for whom serum procalcitonin and C-reactive protein (CRP) levels were measured between January 2006 and February 2013. **Results:** The median serum procalcitonin levels in the IBD and intestinal BD with septic shock or sepsis (n=8), with localized infection (n=76), and without infection (n=45) were 3.46 ng/mL (range, 0.17 to 63.66 ng/mL), 0.22 ng/mL (range, 0.05 to 140.18 ng/mL), and 0.07 ng/mL (range, 0.00 to 31.50 ng/mL), respectively (p=0.001). The serum CRP levels in the IBD and intestinal BD patients did not differ according to the infection stage. Variations in serum procalcitonin levels were not observed in the IBD and intestinal BD patients with different disease activities. **Conclusions:** Serum procalcitonin levels may not be affected by IBD and intestinal BD activity itself, although they may be affected by concomitant infection. Serum procalcitonin measurements could be more useful than CRP in determining the infection stage that reflects the severity of infection in IBD and intestinal BD patients. **(Gut Liver 2016;10:574-580)**

Key Words: Procalcitonin; Inflammatory bowel disease; Intestinal Behçet's disease; Infection; Disease activity

INTRODUCTION

Inflammatory bowel disease (IBD) and intestinal Behçet's disease (BD) are chronic intestinal inflammatory disorders with repeated remissions and relapses and they have complex causes.[1-3] Deterioration in disease stage of IBD can occur due to disease aggravation itself, but it is often attributed to combined infection with a pathogenic organism.[4] Similar to IBD, intestinal BD is also a chronic intestinal inflammatory disease with repeated episodes of relapse and remission.[5] Early detection and treatment of infection can prevent infection-related disease exacerbation and serious complications such as septic shock in patients with IBD and intestinal BD. These infectious complications are facilitated by the use of immunomodulators or biologics. However, in patients with IBD, clinical manifestations associated with bacterial infections and disease exacerbation cannot be easily differentiated from time to time.[6] Reliable and rapid biomarkers for infection might help early detection and treatment, which might induce good prognosis of infection in IBD and intestinal BD patients. Procalcitonin, a precursor of calcitonin, is known to be an acute-phase protein and a good marker of bacterial infection and sepsis.[7-9] Procalcitonin is mainly produced by the thyroid C cells.[10] In infection, procalcitonin is produced by extra thyroidal organs including liver, intestines, monocytes, and some neuroendocrine cells.[10,11] In patients with bacterial sepsis, serum procalcitonin might be a more useful marker for assessing the bacterial infection stage with higher specificity and sensitivity than C-reactive protein (CRP).[12] However, the usefulness of serum procalcitonin measurement in identifying infection stage in IBD and intestinal BD patients remains unanswered. Also, the relationship between disease activity and serum procalcitonin level in IBD and intestinal BD

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patients is yet to be determined. Therefore, we aimed to evaluate the usefulness of measurement of serum procalcitonin and CRP levels in the infected and noninfected states of patients with IBD and intestinal BD. We also investigated the serum procalcitonin level as markers for disease activity of IBD and intestinal BD.

MATERIALS AND METHODS

1. Study subjects and measurement of procalcitonin

Between January 2006 and February 2013, our retrospective study included a total of 129 patients with IBD and intestinal BD at Severance Hospital in Korea whose serum procalcitonin and CRP levels were measured. According to the diagnostic criteria for IBD, the patients were diagnosed as ulcerative colitis (UC), Crohn's disease (CD), or intestinal BD.[13,14] We retrospectively analyzed their clinical data at the time when their serum procalcitonin levels were measured. The exclusion criteria were patients with previous other systemic inflammatory diseases, malignancies, pregnant women, adolescents and a history of abdominal operation. The serum procalcitonin level was measured in patients with IBD and intestinal BD using a commercially available enzyme-linked fluorescent assay (bioMerieux Co., Marcy L'Etoile, France). The normal range of serum procalcitonin level was 0 to 0.5 ng/mL. The serum CRP levels were measured by the particle enhanced immunoturbidimetric assay (Roche Diagnostics GmbH, Mannheim, Germany). The normal range of CRP level was 0 to 8 mg/L. The Institutional Review Board of Severance Hospital at Yonsei University College of Medicine approved the study protocol (approval number: 4-2014-1012).

2. Determination of disease activity

According to the American College of Gastroenterology, the severity of UC was categorized as remission, mild, moderate, and severe disease.[15] The severity of CD was categorized as remission, mild-moderate, moderate-severe, and severe-fulminant disease.[16] The disease activity of intestinal BD was assessed using the disease activity index for intestinal Behçet's disease (DAIBD).[17] The DAIBD consists of eight categories such as general well-being, fever, extraintestinal manifestations, abdominal pain, abdominal mass, abdominal tenderness, intestinal complication, and the number of liquid stools, and it ranges in value from 0 to 325.

3. Definition of infectious complications

Bacterial infection was diagnosed by identification of pathogenic bacteria from suspicious specimens[6] or if the clinical characteristics of patients were clearly associated with infection. Sepsis was defined as the presence of infection combined with signs of the systemic inflammatory response syndrome (SIRS). SIRS was diagnosed when two or more of the following conditions were present:[18] (1) temperature >38°C or <36°C; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or PaO_2 <32 mm Hg; and (4) white blood cell count >12,000/μL, <4,000/μL, or >10% immature (band) forms. Septic shock was defined as sepsis-induced hypotension in spite of adequate fluid supply combined with organ dysfunction or hypoperfusion abnormalities.[19]

4. Statistical analysis

Nonparametric continuous variables were compared using the Kruskal-Wallis and Mann Whitney U tests. Receiver operating characteristic (ROC) curve was reconstructed and area under the curves (AUC; with 95% confidence interval [CI]) of procalcitonin and CRP were compared. All statistical analyses were performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). In all cases, p-values <0.05 were considered statistically significant.

RESULTS

1. Types of IBD and infection

Among the 129 patients, the number of patients with UC,

Table 1. Clinical Characteristics of Patients according to the Disease Type

Characteristic	UC (n=20)	CD (n=38)	Intestinal BD (n=71)	p-value
Age, yr	41.9±18.2	28.8±10.4	43.18±13.00	<0.001
Male/female	14 (70.0)/6 (30.0)	21 (55.3)/17 (44.7)	25 (35.2)/46 (64.8)	0.010
Disease activity				0.079
Active state	5 (25.0)	4 (10.5)	21 (29.6)	
Inactive state	15 (75.0)	34 (89.5)	50 (70.4)	
Therapy				
5-ASA	10 (50.0)	17 (44.7)	19 (26.8)	0.061
Azathioprine	2 (10.0)	14 (36.8)	7 (23.9)	0.075
Steroid	8 (40.0)	13 (34.2)	39 (54.9)	0.097
TNF-α blocker	3 (15.0)	7 (18.4)	4 (5.6)	0.100

Data are presented as mean±SD or number (%).
UC, ulcerative colitis; CD, Crohn's disease; BD, Behçet's disease; 5-ASA, 5-aminosalicylic acid; TNF-α, tumor necrosis factor α.

CD, and intestinal BD was 20, 38, and 71, respectively (Table 1). The infection sites were respiratory tract in 18 patients (21.4%), gastrointestinal tract in 50 patients (59.5%), genitourinary tract in four patients (4.8%), skin in 10 patients (11.9%), heart in one patient (1.2%), and bone in one patient (1.2%).

2. Serum procalcitonin and CRP levels according to the stage of infection and disease activity

The serum procalcitonin levels were increased as the infection became severe in patients with IBD and intestinal BD. The median (minimum–maximum) serum procalcitonin levels in IBD and intestinal BD patients with septic shock or sepsis, localized infection, and no infection were 3.46 (0.17 to 63.66) ng/mL, 0.22 (0.05 to 140.18) ng/mL, and 0.07 (0.00 to 31.50) ng/mL, respectively (p=0.001) (Table 2). However, the serum CRP levels in IBD and intestinal BD patients were not different according to the stage of infection (Table 3). The median (minimum–maximum) serum procalcitonin and CRP levels in patients with IBD and intestinal BD were not different according to the stage of disease activity as shown in Table 4.

3. Serum procalcitonin and CRP levels according to the stage of infection at the same disease activity level

To determine the exact relationship between stage of infection and serum procalcitonin, the serum procalcitonin levels were compared in IBD and intestinal BD patients with the same level of disease activity. The median serum procalcitonin (Table 5) and CRP levels (Table 6) were not significantly different in patients with IBD according to the stage of infection at the same disease activity level. However, the median serum procalcitonin levels in active intestinal BD patients were increased significantly according to the stage of infection (Table 5). The median (minimum–maximum) serum procalcitonin levels in active intestinal BD patients with septic shock or sepsis, localized infection, and no infection were 13.57 (0.17 to 63.6) ng/mL, 0.25 (0.05 to 48.8) ng/mL, and 0.21 (0.0 to 31.50), respectively (p=0.020).

4. ROC curve, sensitivity, specificity, positive and negative predictive values of procalcitonin and CRP

ROC curves were plotted to evaluate the diagnostic power of the procalcitonin and CRP for infection status. In Fig. 1, ROC curve of (A) procalcitonin and (B) CRP were reconstructed. The AUC (95% CI) of procalcitonin and CRP were 0.636 (0.539 to 0.732) and 0.542 (0.437 to 0.646), respectively. In Table 7, the sensitivity, specificity, positive and negative predictive values of procalcitonin were 40.5%, 84.4%, 82.9%, and 84.4%, respectively. The sensitivity, specificity, positive and negative

Table 2. Categories of Infectious Complications in Patients with Inflammatory Bowel Disease and Intestinal Behçet's Disease

	No. of patients (n=129)		
	UC (n=20)	CD (n=38)	Intestinal BD (n=71)
Septic shock or sepsis	0	1 (2.6)	7 (9.8)
Infection	9 (45)	25 (65.8)	42 (59.2)
No infection	11 (55)	12 (31.6)	22 (31)

Data are presented as number (%).
UC, ulcerative colitis; CD, Crohn's disease; BD, Behçet's disease.

Table 3. Serum Procalcitonin Levels according to the Stage of Infection

	Septic shock or sepsis (n=8)	Infection (n=76)	No infection (n=45)	p-value
Procalcitonin, ng/mL	3.46 (0.17–63.66)	0.22 (0.05–140.18)	0.07 (0.00–31.50)	0.001
CRP, mg/L	64.73 (11–447)	47.97 (0–343)	40.78 (0–323)	0.284

Data are presented as the median (minimum–maximum).
CRP, C-reactive protein.

Table 4. Relationship between the Procalcitonin Level and Disease Activity in Patients with Inflammatory Bowel Disease and Intestinal Behçet's Disease

	UC (n=20)			CD (n=38)			Intestinal BD (n=71)		
	Remission (n=5)	Active (n=15)	p-value	Remission (n=4)	Active (n=34)	p-value	Quiescent (n=21)	Active (n=50)	p-value
Procalcitonin, ng/mL	0.05 (0–3.84)	0.15 (0–10.79)	0.553	0.07 (0.04–0.08)	0.11 (0–140.18)	0.521	0.20 (0–11.85)	0.32 (0–63.66)	0.452
CRP, mg/L	47.74 (0–116)	22 (1–191)	0.735	26.35 (0–268)	51.5 (1–197)	0.536	59.04 (0–287)	49.51 (0–447)	0.504

Data are presented as the median (minimum–maximum).
UC, ulcerative colitis; CD, Crohn's disease; BD, Behçet's disease; CRP, C-reactive protein.

Table 5. Procalcitonin Level according to the Status of Infection in Patients with the Same Activity Level of Inflammatory Bowel Disease and Intestinal Behçet's Disease

	UC (n=20)								CD (n=38)								Intestinal BD (n=71)							
	Remission (n=5)				Active disease (mild, moderate, severe) (n=15)				Quiescent (n=4)				Active disease (mild, moderate, severe) (n=34)				Quiescent (n=21)				Active disease (mild, moderate, severe) (n=50)			
	Septic shock or sepsis (n=0)	Infection (n=1)	No infection (n=4)	p-value	Septic shock or sepsis (n=0)	Infection (n=8)	No infection (n=7)	p-value	Septic shock or sepsis (n=0)	Infection (n=0)	No infection (n=4)	p-value	Septic shock or sepsis (n=1)	Infection (n=25)	No infection (n=8)	p-value	Septic shock or sepsis (n=1)	Infection (n=11)	No infection (n=9)	p-value	Septic shock or sepsis (n=6)	Infection (n=31)	No infection (n=13)	p-value
Procalcitonin, mg/L	-	32.97	0.025 (0-0.18)	0.147	-	0.18 (0-10.79)	0.07 (0-0.21)	0.350	-	-	0.06 (0.04-0.08)	-	0.77	0.12 (0-140.18)	0.07 (0-4.14)	0.616	1.11	0.23 (0-11.85)	0.19 (0-7.67)	0.539	13.57 (0.17-63.60)	0.25 (0.05-48.80)	0.21 (0-31.50)	0.020

Data are presented as the median (minimum–maximum).
UC, ulcerative colitis; CD, Crohn's disease; BD, Behçet's disease.

Table 6. C-reactive Protein Level according to the Status of Infection in Patients with the Same Level of Activity of Inflammatory Bowel Disease and Intestinal Behçet's Disease

	UC (n=20)								CD (n=38)								Intestinal BD (n=71)							
	Remission (n=5)				Active disease (mild, moderate, severe) (n=15)				Quiescent (n=4)				Active disease (mild, moderate, severe) (n=34)				Quiescent (n=21)				Active disease (mild, moderate, severe) (n=50)			
	Septic shock or sepsis (n=0)	Infection (n=1)	No infection (n=4)	p-value	Septic shock or sepsis (n=0)	Infection (n=8)	No infection (n=7)	p-value	Septic shock or sepsis (n=0)	Infection (n=0)	No infection (n=4)	p-value	Septic shock or sepsis (n=1)	Infection (n=25)	No infection (n=8)	p-value	Septic shock or sepsis (n=1)	Infection (n=11)	No infection (n=9)	p-value	Septic shock or sepsis (n=6)	Infection (n=31)	No infection (n=13)	p-value
CRP, mg/L	-	24.90	48.92 (0-116)	0.480	-	14.66 (1-191)	49.06 (1-100)	0.355	-	-	26.35 (0-268)	-	10.66	54.26 (1-192)	44.53 (12-197)	0.276	59	71.60 (0-287)	53.07 (0-259)	0.879	138.68 (34-447)	51.83 (0-343)	33.93 (2-323)	0.134

Data are presented as the median (minimum–maximum).
UC, ulcerative colitis; CD, Crohn's disease; BD, Behçet's disease; CRP, C-reactive protein.

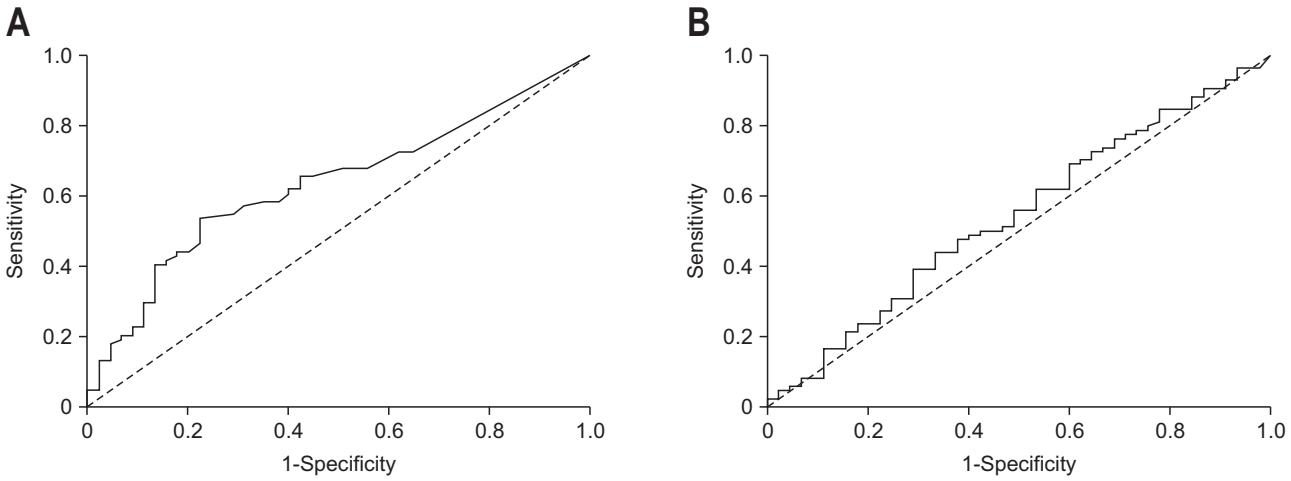

Fig. 1. Receiver operating characteristic curves for (A) procalcitonin and (B) C-reactive protein (CRP) were reconstructed. The areas under the curve (95% confidence interval) of procalcitonin and CRP were 0.636 (0.539 to 0.732) and 0.542 (0.437 to 0.646), respectively.

Table 7. Sensitivity, Specificity and Positive and Negative Predictive Values of Procalcitonin and C-reactive Protein

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Procalcitonin, %	40.5	84.4	82.9	84.4
CRP, %	84.5	17.8	65.7	38.1

CRP, C-reactive protein.

predictive values of CRP were 84.5%, 17.8%, 65.7%, and 38.1%, respectively.

DISCUSSION

In patients with IBD, symptoms and laboratory data in bacterial infections and disease flare up are similar and it is often difficult to differentiate between them.[6] It is important to differentiate bacterial infections from disease flare up because treatments according to the disease stage are totally opposite. Especially, in case of infection, early detection and treatment of infection can lead to good prognosis in patients with IBD. However, disease flare up necessitates the use of more powerful immunomodulatory drugs which can potentially exacerbate the infection. If the treatment is not performed accordingly, it could lead to rapid deterioration of general condition of the patients. Therefore, a reliable marker for discriminating bacterial infections and disease flares is needed. Procalcitonin is an acute phase protein whose level is increased in response to inflammatory stimuli, including infections.[20,21] The serum procalcitonin level above 0.5 ng/mL is used to discriminate infections from noninfection.[22] Serum procalcitonin is known to be a good marker for detecting bacterial infections and sepsis.[7-9] The serum procalcitonin level can be measured quickly and it helps to make an early diagnosis in an emergent situation such as systemic inflammation or septic shock.[10] In a meta-analysis, the sensitivity of procalcitonin ranged from 42% to 100% and the specificity of procalcitonin ranged from 48% to 100%, as a diagnostic test for sepsis.[10] There are several reports suggesting that procalcitonin is a good biomarker for infection.[7-9,23-25] Traditional inflammatory biomarkers such as CRP, leukocytes, and erythrocyte sedimentation rate could not help to decide treatment for discriminating bacterial infection and flare up of IBD.[6,26-28] Serum procalcitonin had better sensitivity and specificity than CRP for the exact diagnosis of bacterial infections.[6,12,29] In our report also, only serum procalcitonin levels were increased in infection stage of patients with IBD and intestinal BD. In this study, to determine the exact relationship between stage of infection and serum procalcitonin, the serum procalcitonin levels were compared in IBD and intestinal BD patients with the same level of disease activity. The median serum procalcitonin levels were increased significantly in only active intestinal BD patients according to the stage of infection. However, the serum procalcitonin levels were not changed significantly in IBD and inactive intestinal BD patients according to the stage of infection. Moreover, CRP levels were not increased significantly in patients with IBD and intestinal BD according to the stage of infection. One previous report showed that serum procalcitonin was a good diagnostic marker for differentiating IBD and self-limited colitis.[30] However, in this previous report, the authors did not investigate the relationship between the stage of infection and serum procalcitonin in IBD. Therefore, our report is unique because we evaluated the relationship between the stage of infection and serum procalcitonin level in patients with IBD and intestinal BD. In

our study, the serum procalcitonin level was increased after infection in patients with IBD and intestinal BD. Especially, in cases with severe infection like septic shock or sepsis, the serum procalcitonin levels were 49 times higher compared to those in cases without infection 3.46 (0.17 to 63.66) ng/mL vs 0.07 (0.00 to 31.5) ng/mL. However, in cases of infection without sepsis, the serum procalcitonin levels were only three times higher compared to those in cases without infection (0.22 ng/mL [range, 0.05 to 140.18 ng/mL] vs 0.07 ng/mL [range, 0.00 to 31.5 ng/mL]). Based on our results, we drew a conclusion that elevation of serum procalcitonin level might be induced in proportion to the severity of infection in IBD patients. According to our results, serum procalcitonin could be a useful marker for detecting severe infection like septic shock or sepsis than merely minor localized infection.

With respect to the disease activity in IBD, there are inconsistent results about serum procalcitonin as a marker for disease activity of IBD. In one study, although the serum procalcitonin level was in the normal range, it was positively related with disease activity in patients with IBD.[30-32] In another study, serum procalcitonin was shown to be correlated with UC activity.[31,32] However in a separate study, the serum procalcitonin level was not related with disease activity in patients with UC,[11] CD,[33] and intestinal BD.[34] These inconsistent results about serum procalcitonin as a marker for disease activity of IBD might be due to different disease activity indices used in different studies and different combined infections. CRP has been known to be a reliable marker for assessing disease activity in patients with IBD[11] and intestinal BD.[34] In our report, CRP level could not differentiate between inactive and active disease activity when the disease was combined with infection in patients with active IBD and intestinal BD. Based on our results, elevated serum procalcitonin might have an important role of a useful marker for detecting infection in patients with IBD and intestinal BD.

Our study has some key strengths. First, serum procalcitonin levels were compared according to the severity of infection categorized as no infection, localized infection, and sepsis or septic shock. We also sought to determine the exact relationship between stage of infection and serum procalcitonin by evaluating serum procalcitonin levels in patients with the same level of disease activity of IBD and intestinal BD. Second, this is the first study to compare the serum procalcitonin levels in intestinal BD patients. Third, based on our study, it could be suggested that a higher procalcitonin level might reflect the severity of infection. However, there were a few limitations to our study. First, the number of patients included in our study was relatively small. In particular, the number of patients in inactive state of IBD and intestinal BD was very small, which might have hampered from drawing the concrete conclusion on the role of procalcitonin level in inactive disease stage. Second, patients with IBD were enrolled retrospectively from a single tertiary center, which might have caused an inevitable selection bias. Third, we measured the procalcitonin level only before antibiotic treatment. We could not compare the procalcitonin level before and after antibiotic treatments to know the relationship between the change in procalcitonin and infection. Fourth, although the median procalcitonin level in patients with infection was higher than that in patients without infection, it was 0.22 still falling into normal range. Finally in this study, we did not specifically investigate the relationship between viral infections and disease flare-up.

In conclusion, the serum procalcitonin level may not be affected by IBD activity, but by combined infection. Measurement of serum procalcitonin level can be useful in differentiating infectious complications in IBD and intestinal BD patients experiencing disease flare up. A higher serum procalcitonin level may reflect the severity of infection. Therefore, serum procalcitonin level can be a candidate biomarker for assessing the infection stage in IBD or intestinal BD patients.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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REFERENCES

1. Jung YS, Kim SW, Yoon JY, et al. Expression of a soluble triggering receptor expressed on myeloid cells-1 (sTREM-1) correlates with clinical disease activity in intestinal Behcet's disease. Inflamm Bowel Dis 2011;17:2130-2137.
2. Park JJ, Cheon JH, Kim BY, et al. Correlation of serum-soluble triggering receptor expressed on myeloid cells-1 with clinical disease activity in inflammatory bowel disease. Dig Dis Sci 2009;54:1525-1531.
3. Kim KO, Jang BI, Lee SH. Does carotid intima-media thickness increase in patients with inflammatory bowel disease? Intest Res 2014;12:293-298.
4. Lidar M, Langevitz P, Shoenfeld Y. The role of infection in inflammatory bowel disease: initiation, exacerbation and protection. Isr Med Assoc J 2009;11:558-563.
5. Park JJ, Kim WH, Cheon JH. Outcome predictors for intestinal Behçet's disease. Yonsei Med J 2013;54:1084-1090.
6. Joo K, Park W, Lim MJ, Kwon SR, Yoon J. Serum procalcitonin

for differentiating bacterial infection from disease flares in patients with autoimmune diseases. J Korean Med Sci 2011;26:1147-1151.
7. Le Moullec JM, Jullienne A, Chenais J, et al. The complete sequence of human preprocalcitonin. FEBS Lett 1984;167:93-97.
8. Whicher J, Bienvenu J, Monneret G. Procalcitonin as an acute phase marker. Ann Clin Biochem 2001;38(Pt 5):483-493.
9. Müller CA, Uhl W, Printzen G, et al. Role of procalcitonin and granulocyte colony stimulating factor in the early prediction of infected necrosis in severe acute pancreatitis. Gut 2000;46:233-238.
10. Uzzan B, Cohen R, Nicolas P, Cucherat M, Perret GY. Procalcitonin as a diagnostic test for sepsis in critically ill adults and after surgery or trauma: a systematic review and meta-analysis. Crit Care Med 2006;34:1996-2003.
11. Oruç N, Ozütemiz O, Osmanoğlu N, Ilter T. Diagnostic value of serum procalcitonin in determining the activity of inflammatory bowel disease. Turk J Gastroenterol 2009;20:9-12.
12. Floriańczyk B. Structure and diagnostic value of procalcitonin. Ann Univ Mariae Curie Sklodowska Med 2003;58:338-342.
13. Cheon JH, Kim ES, Shin SJ, et al. Development and validation of novel diagnostic criteria for intestinal Behçet's disease in Korean patients with ileocolonic ulcers. Am J Gastroenterol 2009;104:2492-2499.
14. Lennard-Jonesa JE. Classification of inflammatory bowel disease. Scand J Gastroenterol 1989;24 Suppl 170:2-6.
15. Kornbluth A, Sachar DB; Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults (update): American College of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol 2004;99:1371-1385.
16. Hanauer SB, Sandborn W; The Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's disease in adults. Am J Gastroenterol 2001;96:635-643.
17. Cheon JH, Han DS, Park JY, et al. Development, validation, and responsiveness of a novel disease activity index for intestinal Behçet's disease. Inflamm Bowel Dis 2011;17:605-613.
18. Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. Chest 1992;101:1644-1655.
19. Gibot S, Kolopp-Sarda MN, Béné MC, et al. Plasma level of a triggering receptor expressed on myeloid cells-1: its diagnostic accuracy in patients with suspected sepsis. Ann Intern Med 2004;141:9-15.
20. Nijsten MW, Olinga P, The TH, et al. Procalcitonin behaves as a fast responding acute phase protein in vivo and in vitro. Crit Care Med 2000;28:458-461.
21. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med 1999;340:448-54.
22. Eberhard OK, Haubitz M, Brunkhorst FM, Kliem V, Koch KM, Brunkhorst R. Usefulness of procalcitonin for differentiation between activity of systemic autoimmune disease (systemic lupus erythematosus/systemic antineutrophil cytoplasmic antibody-associated vasculitis) and invasive bacterial infection. Arthritis Rheum 1997;40:1250-1256.
23. Oczenski W, Fitzgerald RD, Schwarz S. Procalcitonin: a new parameter for the diagnosis of bacterial infection in the peri-operative period. Eur J Anaesthesiol 1998;15:202-209.
24. Korczowski B, Szybist W. Serum procalcitonin and C-reactive protein in children with diarrhoea of various aetiologies. Acta Paediatr 2004;93:169-173.
25. Gattas DJ, Cook DJ. Procalcitonin as a diagnostic test for sepsis: health technology assessment in the ICU. J Crit Care 2003;18:52-58.
26. Limper M, de Kruif MD, Duits AJ, Brandjes DP, van Gorp EC. The diagnostic role of procalcitonin and other biomarkers in discriminating infectious from non-infectious fever. J Infect 2010;60:409-416.
27. Delèvaux I, André M, Colombier M, et al. Can procalcitonin measurement help in differentiating between bacterial infection and other kinds of inflammatory processes? Ann Rheum Dis 2003;62:337-340.
28. Meynaar IA, Droog W, Batstra M, Vreede R, Herbrink P. In critically ill patients, serum procalcitonin is more useful in differentiating between sepsis and SIRS than CRP, IL-6, or LBP. Crit Care Res Pract 2011;2011:594645.
29. Simon L, Gauvin F, Amre DK, Saint-Louis P, Lacroix J. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. Clin Infect Dis 2004;39:206-217.
30. Herrlinger KR, Dittmann R, Weitz G, et al. Serum procalcitonin differentiates inflammatory bowel disease and self-limited colitis. Inflamm Bowel Dis 2004;10:229-233.
31. Oussalah A, Laurent V, Bruot O, et al. Additional benefit of procalcitonin to C-reactive protein to assess disease activity and severity in Crohn's disease. Aliment Pharmacol Ther 2010;32:1135-1144.
32. Koido S, Ohkusa T, Takakura K, et al. Clinical significance of serum procalcitonin in patients with ulcerative colitis. World J Gastroenterol 2013;19:8335-8341.
33. Thia KT, Chan ES, Ling KL, Ng WY, Jacob E, Ooi CJ. Role of procalcitonin in infectious gastroenteritis and inflammatory bowel disease. Dig Dis Sci 2008;53:2960-2968.
34. Adam B, Calikoglu E. Serum interleukin-6, procalcitonin and C-reactive protein levels in subjects with active Behçet's disease. J Eur Acad Dermatol Venereol 2004;18:318-320.