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Mean platelet volume predicts embolic complications and prognosis in infective endocarditis☆

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ABSTRACT

Objectives: This study was designed to examine the change in mean platelet volume (MPV) over the course of infective endocarditis (IE) and also the association between MPV and complications including embolic events in IE.

Methods: Forty patients (26 male, mean age 46 ± 15 years) who were hospitalized with a diagnosis of IE at the Department of Cardiology, Erciyes University, from March 2005 to August 2008, were retrospectively evaluated. The diagnosis of IE was made clinically and was confirmed with Duke's criteria. The erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hs-CRP), and MPV were measured before treatment and periodically during the follow-up period, until discharge.

Results: There were 27 cases of native valve endocarditis and 13 of prosthetic valve endocarditis. While 31 patients were treated medically, an operation was performed in nine patients because of unsuccessful medical therapy. On admission, mean MPV was 10.8 ± 1.1 fl, ESR was 82 ± 26 mm/h, and hs-CRP was 110 ± 72 mg/l. Seven patients died: one intraoperatively, three patients postoperatively, and three patients during medical treatment. With the exception of these seven patients, ESR and hs-CRP were significantly reduced in all patients at discharge compared to levels at hospitalization (ESR 82 ± 26 to 32 ± 22, $p = 0.001$ and hs-CRP 110 ± 72 to 25 ± 15, $p = 0.001$). Similarly, we detected a significant decrease in MPV from hospitalization to discharge, i.e., from the active period of the disease to recovery (10.8 ± 1.1 to 9.7 ± 0.8 fl, $p = 0.002$). In addition, MPV was found to be significantly higher in patients with observed embolic complications (11.5 vs. 10.3 fl, $p = 0.001$), other complications (11.0 vs. 10.2 fl, $p = 0.001$), and death (11.1 vs. 10.4 fl, $p = 0.005$).

Conclusion: MPV can be used as an activity criterion in IE, like ESR and hs-CRP. Also, high MPV is associated with a poor prognosis and adverse outcomes, and predicts complications including embolic events.

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1. Introduction

Infective endocarditis (IE) remains a very serious health problem, afflicting 2–7 cases/100 000 person-years, with a high mortality rate despite all the improvements in diagnosis, treatment, and management.[1–3] Over the last few decades the incidence of complications has not changed much. Among these complications, embolic events occur in 20% to 43% of patients and are associated with a higher mortality.[4–6]

It is known that procoagulant changes in platelet activity may be established in patients with IE, especially in those with thromboembolic complications. This inflammation-induced hypercoagulable state can facilitate embolization, one of the major causes of death. Although clinical studies using aspirin therapy in order to prevent embolic complications have had controversial outcomes, many laboratory findings of this hypercoagulable state, such as increased platelet factor 4, increased thrombin–antithrombin complex, increased plasminogen activator inhibitor-1 levels, and elevated levels of antiphospholipid antibodies, have been confirmed.[7,8]

To date, the only approach to the prevention of embolic complications is effective antibiotic therapy. Mean platelet volume (MPV), which is generally overlooked by clinicians and is a parameter routinely provided by a full blood count analyzer, not requiring any complex or expensive technologies, correlates with platelet function and activation.[9–11] To our knowledge, no study has yet focused on MPV in patients with IE. Therefore our aim was to investigate whether or not MPV changes during effective

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antibiotic therapy in patients with IE. Additionally, we assessed the relationship between MPV and complications and disease activity in IE.

2. Methods

We retrospectively studied 40 consecutive definite IE patients hospitalized at the Department of Cardiology of our university from March 2005 to August 2008. The diagnosis of definite IE was confirmed using the modified Duke's criteria.[12]

Erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hs-CRP), and MPV were measured on admission and periodically during the follow-up period, until discharge or death. Discharge from the hospital and all-cause in-hospital mortality were end-points of the study.

Patient clinical characteristics, associated diseases predisposing to IE, culture results, echocardiographic findings, laboratory results, complications appearing during the in-hospital period, and conditions associated with mortality were obtained from the hospital registries.

In all patients hospitalized with a preliminary diagnosis of IE, blood cultures were obtained from three to four separate veins during the first hour, and transthoracic echocardiographic examinations were undertaken for both diagnosis and to establish the presence of complications. In cases of poor image quality in patients with prosthetic valves, transesophageal echocardiography was used. A Vingmed system V (Vingmed GE System 5, Horten, Norway) echocardiography device with a 2.5 MHz transducer was used for echocardiographic examinations.

MPV was measured in blood samples collected in EDTA tubes, which were analyzed by flow cytometry in an automated hematology analysis system (Sysmex, XT-2000i). hs-CRP was measured using a BN2 model nephelometer (Dade-Behring). The normal value range for hs-CRP in our laboratory was 0–6 mg/l and for MPV was 7.4–10.4 fl.

3. Statistical analysis

SPSS statistical software (SPSS for windows 13.0; SPSS Inc., Chicago, IL, USA) was used for all statistical calculations. Continuous variables are given as mean ± standard deviation (SD) and categorical variables as percentages. Differences between groups were tested using the Student's *t*-test for unpaired data, analysis of variance, and the Chi-square test when appropriate. A paired Student's *t*-test was used for comparison of the MPV, ESR, and hs-CRP values before and after treatment in patients with IE. Statistical significance was defined as a p-value of < 0.05.

4. Results

Between March 2005 and August 2008, 40 patients (26 male, 14 female) with a definite IE diagnosis were managed at the Department of Cardiology of our university and were included in the study. Mean patient age was 46 ± 15 years and the mean follow-up period was 24 ± 6 days. Table 1 shows the demographic and clinical characteristics of the study patients. There were 27 (67%) patients with native valve endocarditis and 13 (33%) with prosthetic valve endocarditis. The most common risk factors predisposing to IE were the presence of a prosthetic valve, rheumatic valvular disease, diabetes mellitus, and chronic renal failure.

The microorganism responsible for IE was detected in 56% of native valve endocarditis cases and 68% of prosthetic valve endocarditis cases. Coagulase-negative Staphylococcus was found to be the most common etiologic pathogen in both groups.

On echocardiographic examination, we detected a vegetation in 29 patients (73%), abscess in two patients (5%), and new dehiscence or new valvular regurgitation in seven patients (18%). The left ventricular ejection fraction was found to be 55 ± 15% (Table 2).

Table 1
Baseline characteristics of the patients

Characteristic	$N = 40$
Age (years)	46 ± 15
Gender (F/M)	14/26
Follow-up period (days)	24 ± 6
Cardiac risk factors	
Previous endocarditis	2 (5%)
Pre-existing native valve disease	13 (33%)
Prosthetic valve	13 (33%)
Non-cardiac risk factors	
Diabetes mellitus	8 (20%)
Chronic renal failure	6 (15%)
Therapy	
Surgical therapy	9 (23%)
Medical therapy	31 (78%)
Complications	
Congestive heart failure	10 (25%)
Renal failure	2 (5%)
Embolism	7 (18%)
Paravalvular abscess	2 (5%)
In-hospital death (%)	7 (18%)

Table 2
Laboratory and echocardiographic findings in patients with infective endocarditis

	$N = 40$
Laboratory findings	
Hemoglobin (g/dl)	11.2 ± 2.6
Leukocytes ($\times 10^{9/l}$)	9.8 ± 4.7
hs-CRP (mg/l)	110 ± 72
ESR (mm/h)	82 ± 26
Mean platelet volume (fl)	10.8 ± 1.1
Echocardiographic findings	
Vegetation	29 (73%)
Abscess	2 (5%)
New dehiscence or new valvular regurgitation	7 (18%)
Left ventricular ejection fraction (%)	55 ± 15

hs-CRP, high-sensitivity C-reactive protein; ESR, erythrocyte sedimentation rate.

At the time of hospitalization, mean ESR was 82 ± 26 mm/h, hs-CRP was 110 ± 72 mg/l, and MPV was 10.8 ± 1.1 fl (Table 2). Except in seven of the patients who died, ESR and hs-CRP levels decreased significantly with clinical resolution (ESR 82 ± 26 mm/h to 32 ± 22 mm/h, $p = 0.001$ and hs-CRP 110 ± 72 mg/l to 25 ± 15 mg/l, $p = 0.001$). Similarly, MPV was markedly reduced during the healing phase of IE (10.8 ± 1.1 to 9.7 ± 0.8 fl, $p = 0.002$) (Figure 1). The

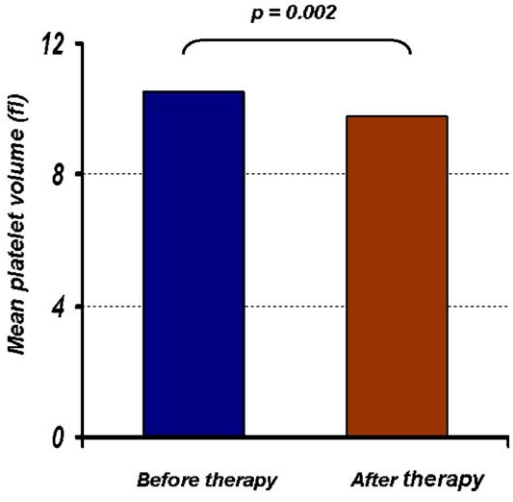


Figure 1. Mean platelet volume during the course of infective endocarditis.

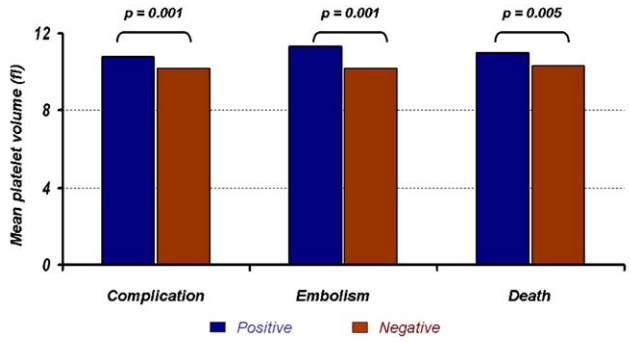


Figure 2. Association between mean platelet volume and total complications, embolic complications, and death.

decreases in ESR, hs-CRP, and MPV were established by the differences between the values at the time of hospitalization and at the time of discharge.

A prosthetic valve replacement was carried out in nine patients, and of these, four patients died (one intraoperatively and three postoperatively). Three patients in the group treated medically also died. Initial MPVs were higher in fatal cases than in those who survived (11.1 vs. 10.4 fl; $p = 0.005$). Embolic complications occurred in seven patients throughout the follow-up period. We detected higher MPVs in the patients with this catastrophic complication than in those without (11.5 vs. 10.3 fl; $p = 0.001$) (Figure 2).

A total of 21 complications, consisting of congestive heart failure, renal failure, embolism, and paravalvular abscess, were seen. These complications were associated with a high MPV (MPV in complicated patients was 11.0 fl and in uncomplicated patients was 10.2 fl, $p = 0.001$) (Figure 2).

The associations of MPV with complications, embolic events, and death were determined from measurements taken at the time of hospitalization .

Language has been changed throughout; however the following sentences have undergone more major changes. Please confirm that these are correct/advise of any changes required.

5. Discussion

IE is an uncommon but severe disease with approximately 20% in-hospital mortality.[13] In brief, its pathogenesis consists of endothelial injury and erosion caused by hemodynamic and mechanical stress, which lead to platelet deposition and the appearance of sterile thrombotic vegetations; these serve as an environment for bacterial adherence.[14] Rheumatic heart disease, congenital heart disease, degenerative heart disease, parenteral drug abuse, and prosthetic valves are major predisposing conditions. Streptococci, enterococci, *Staphylococcus aureus*, coagulase-negative staphylococci, Gram-negative bacilli, and fungi are the most common etiologic organisms.[15]

Although the incidence of acute rheumatic fever and rheumatic heart disease decrease by the day in developed countries, they remain important problems in undeveloped and developing countries.[16–18] While the incidence has declined to 20–30% in North America and Europe since the 1980s, rheumatic valvular disease is still responsible for more than 50% of IE cases in Turkey.[19–21] However, in our study, a prosthetic valve was found to be the major predisposing condition for IE.

Embolic events occur in 20% to 43% of IE cases and are one of the main causes of death.[4–6,22,23] The only established medical therapy known to reduce the risk of embolism is antimicrobial therapy.[24] To date, the use of antiplatelet agents to prevent systemic embolism has led to controversial outcomes. Chan et al.[25] demonstrated that the addition of aspirin to antibiotic treatment did not decrease the risk of embolic events in endocarditis patients; conversely, Anavekar et al.[24] showed a decrease in embolic events with antiplatelet therapy.

In some investigations, even in the absence of cardiac involvement, systemic bacterial infections have been demonstrated as an independent risk factor for an embolic event.[26–28] Inflammation-induced procoagulant changes may be responsible for this scenario. Kupferwasser et al. showed that infection-associated elevated antiphosphoplipid antibodies are associated with thrombin generation, endothelial cell activation, and major embolic events in IE.[8] Ileri at al. confirmed an inflammation-induced hypercoagulable state in IE patients with embolic complications, showing increased platelet factor 4, increased thrombin–antithrombin complex, and increased plasminogen activator inhibitor-1 levels.[7]

MPV is a marker of platelet activation, i.e., a larger platelet volume means both an enzymatically and metabolically more active platelet than a smaller one. Because these larger platelets have higher intracellular thromboxane A_2 levels and increased levels of procoagulant surface proteins such as P selectin and GpIIb/IIIa, they have a greater prothrombotic potential.[29] Since the risk of embolism in IE decreases with antimicrobial therapy, we hypothesized that MPV would reduce gradually with effective therapy. Data regarding the association between MPV and embolic complications in IE do not exist in the literature. If such an association is discovered, MPV might be helpful in recognizing patients at increased risk of embolic complications. In this report, a significant decrease in MPV with clinical resolution and improvements in known laboratory markers associated with disease activity, such as ESR and hs-CRP, was detected. In addition, MPV in the IE patients with embolic complications was higher than in those patients without these complications. This slight but significant positive association between MPV level and embolic complications supports our hypothesis.

On the other hand, inflammation, a well-known stimulant of platelets, plays a critical role in the pathogenesis of many diseases such as ankylosing spondylitis, psoriasis, and rheumatoid arthritis.[30–32] To date, only few data are available on MPV and the interaction between MPV and inflammatory markers and disease activity in inflammatory and infectious diseases. Yazici et al.[30] demonstrated that patients with ankylosing spondylitis have significantly higher baseline MPV than healthy controls. They were also the first to report that MPV is closely correlated with clinical disease activity in ankylosing spondylitis. After 6 months of therapy, they found that MPV was markedly decreased, as well as white blood cell count, ESR, and CRP levels. Consequently, although they considered that further studies were required, they anticipated that MPV could be used as a follow-up marker during the management of ankylosing spondylitis in the future. Similar results were observed in another clinical trial investigating MPV in rheumatoid arthritis, which is another chronic inflammatory disease.[32] It has also been shown that MPV is positively associated with inflammatory markers and disease activity in this rheumatic disease. With regard to psoriasis, a chronic, recurrent inflammatory skin disease, Karabudak et al.[31] emphasized that the hypercoagulable state in psoriasis may be associated with systemic inflammation, and they showed an increased MPV in psoriasis patients compared to controls.

Tozkoparan et al. showed that active tuberculosis patients had high MPVs with considerable correlation with the radiological extent of tuberculosis.[33] Van der Lelie et al., in patients with septicemia, showed that MPV was high and reached normal values after one week of treatment in patients who responded favorably to antibiotic treatment.[34] High MPV has also been demonstrated in patients with septic shock by Dastugue et al.[35] In addition, Becchi

et al. demonstrated that MPV gradually decreased in survivors of sepsis, as it increased in non-survivors.[36]

From all this research we came to the conclusion that MPV does not only represent platelet activation, but also infection and inflammation status. This was another hypothesis that led us to investigate MPV in IE patients. We wondered if this parameter could be used in IE as a marker of recovery, in the same way as ESR and hs-CRP, and we found this to be the case.

Although Wallace et al.[37] found that high hs-CRP levels and ESRs did not have any prognostic implication and did not predict in-hospital mortality or 6-month mortality, in many studies, linear relationships between these parameters and prognosis have been demonstrated .[38] Similarly, we have shown significantly higher hs-CRP levels and ESRs in fatal cases of IE than in non-fatal cases. We also confirm that high MPV levels are associated with a poor prognosis in IE because of the higher levels in fatal and complicated cases.

To our knowledge, this is the first research in the literature to evaluate MPV in IE patients. From this research we are aware that there is significant overlap between the MPV values in patients with and without emboli. We are also aware that hs-CRP and ESRs are reliable, well-known disease activity markers. However, the measurement of MPV as a routinely studied parameter by most full blood count analyzers is very easy and cheap. Consequently, it can be used as a practical disease activity marker in the follow-up period, like hs-CRP and ESR. Clinicians should be alert to high MPV values in IE patients because of the high complications rate. Confirmation of our results in future studies would be valuable for the management of IE.

There are two main limitations to our study. Firstly, our results are retrospective; secondly, the number of patients included in the study is too few to draw definite conclusions from the results.

In conclusion, MPV can be used as an activity criterion in IE, like ESR and hs-CRP. Also, a high MPV is associated with a poor prognosis and adverse outcomes, and predicts complications including embolic complications and death. Further studies, including prospective, randomized studies involving a greater number of patients are needed to clarify the usefulness of MPV in the management of IE.

Conflict of interest: No conflict of interest to declare.

References

1. Hoen B, Alla F, Selton-Suty C, Béguinot I, Bouvet A, Briançon S, et al. Changing profile of infective endocarditis: results of a 1-year survey in France. *JAMA* 2002;**288**:75–81.
2. Moreillon P, Que YA. Infective endocarditis. *Lancet* 2004;**363**:139–49.
3. Tleyjeh IM, Steckelberg JM, Murad HS, Anavekar NS, Ghomrawi HM, Mirzoyev Z, et al. Temporal trends in infective endocarditis: a population-based study in Olmsted County, Minnesota. *JAMA* 2005;**293**:3022–8.
4. Nissen H, Nielsen PF, Frederiksen M, Helleberg C, Nielsen JS. Native valve infective endocarditis in the general population: a 10-year survey of the clinical picture during the 1980s. *Eur Heart J* 1992;**13**:872–7.
5. Hart RG, Foster JW, Luther MF, Kanter MC. Stroke in infective endocarditis. *Stroke* 1990;**21**:695–700.
6. Stewart JA, Silimperi D, Harris P, Wise NK, Fraker Jr TD, Kisslo JA. Echocardiographic documentation of vegetative lesions in infective endocarditis: clinical implications. *Circulation* 1980;**61**:374–80.
7. Ileri M, Alper A, Senen K, Durmaz T, Atak R, Hisar I, et al. Effect of infective endocarditis on blood coagulation and platelet activation and comparison of patients with to those without embolic events. *Am J Cardiol* 2003;**91**:689–92.
8. Kupferwasser LI, Hafner G, Mohr-Kahaly S, Erbel R, Meyer J, Darius H. The presence of infection-related antiphospholipid antibodies in infective endocarditis determines a major risk factor for embolic events. *J Am Coll Cardiol* 1999;**33**:1365–71.
9. Sandhaus LM, Meyer P. How useful are CBC and reticulocyte reports to clinicians? *Am J Clin Pathol* 2002;**118**:787–93.
10. Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. *Blood Coagul Fibrinolysis* 1996;**7**:157–61.
11. Kapsoritakis AN, Koukourakis MI, Sfiridaki A, Potamianos SP, Kosmadaki MG, Koutroubakis IE, et al. Mean platelet volume: a useful marker of inflammatory bowel disease activity. *Am J Gastroenterol* 2001;**96**:776–81.
12. Li JS, Sexton DJ, Mick N, Nettles R, Fowler Jr VG, Ryan T, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000;**30**:633–8.
13. Duval X, Leport C. Prophylaxis of infective endocarditis: current tendencies, continuing controversies. *Lancet Infect Dis* 2008;**8**:225–32.
14. Thiene G, Basso C. Pathology and pathogenesis of infective endocarditis in native heart valves. *Cardiovasc Pathol* 2006;**15**:256–63.
15. Bashore TM, Cabell C, Fowler Jr V. Update on infective endocarditis. *Curr Probl Cardiol* 2006;**31**:274–352.
16. Yavuz SS, Eren M, Yavuz A, Biçer Y, Koçak F, Bilgen F, et al. Infective endocarditis: evaluation of 58 cases (in Turkish). *Klimik Dergisi* 2003;**16**:55–62.
17. Hoesley CJ, Cobbs CG. Endocarditis at the millennium. *J Infect Dis* 1999;**179**(Suppl 2):360–3.
18. Moreillon P. Endocarditis and endarteritis. In: Armstrong D, Cohen J, editors. *Infectious diseases*. London: Mosby; 1999. p. 2.50.1–2.50.10.
19. Hogevik H, Olaison L, Andersson R, Lindberg J, Alestig K. Epidemiologic aspects of infective endocarditis in an urban population. A 5-year prospective study. *Medicine (Baltimore)* 1995;**74**:324–39.
20. Cetinkaya Y, Akova M, Akalin HE, Aşçioğlu S, Hayran M, Uzuns O, et al. A retrospective review of 228 episodes of infective endocarditis where rheumatic valvular disease is still common. *Int J Antimicrob Agents* 2001;**18**:1–7.
21. Çaylan R, Aydın K, Kaygusuz S, Köksal I, Orem C. Otuziki infektif endokardit atağının değerlendirilmesi. *Flora* 2001;**6**:267–73.
22. Jones Jr HR, Siekert RG. Neurological manifestations of infective endocarditis: review of clinical and therapeutic challenges. *Brain* 1989;**112**:1295–315.
23. Jaffe WM, Morgan DE, Pearlman AS, Otto CM. Infective endocarditis, 1983-1988: echocardiographic findings and factors influencing morbidity and mortality. *J Am Coll Cardiol* 1990;**15**:1227–33.
24. Anavekar NS, Tleyjeh IM, Anavekar NS, Mirzoyev Z, Steckelberg JM, Haddad C, et al. Impact of prior antiplatelet therapy on risk of embolism in infective endocarditis. *Clin Infect Dis* 2007;**44**:1180–6.
25. Chan KL, Dumesnil JG, Cujec B, Sanfilippo AJ, Jue J, Turek MA, et al. Investigators of the Multicenter Aspirin Study in Infective Endocarditis. A randomized trial of aspirin on the risk of embolic events in patients with infective endocarditis. *J Am Coll Cardiol* 2003;**42**:775–80.
26. Valtonen V, Kuikka A, Syrjänen J. Thrombo-embolic complications in bacteraemic infections. *Eur Heart J* 1993;**14**:20–3.
27. Macko RF, Ameriso SF, Barndt R, Clough W, Weiner JM, Fisher M. Precipitants of brain infarction: roles of preceding infection/inflammation and recent psychological stress. *Stroke* 1996;**27**:1999–2004.
28. Syrjänen J, Valtonen VV, Iivanainen M. Preceding infection as an important risk factor for ischemic brain infarction in young and middle aged patients. *Br Med J* 1988;**296**:1156–60.
29. Kamath S, Blann AD, Lip GY. Platelet activation: assessment and quantification. *Eur Heart J* 2001;**22**:1561–71.
30. Yazici S, Yazici M, Erer B, Erer B, Calik Y, Bulur S, et al. The platelet functions in patients with ankylosing spondylitis: anti-TNF-alpha therapy decreases the mean platelet volume and platelet mass. *Platelets* 2010;**21**:126–31.
31. Karabudak O, Ulusoy RE, Erikci AA, Solmazgul E, Dogan B, Harmanyeri Y. Inflammation and hypercoagulable state in adult psoriatic men. *Acta Derm Venereol* 2008;**88**:337–40.
32. Yazici S, Yazici M, Erer B, Erer B, Calik Y, Ozhan H, et al. The platelet indices in patients with rheumatoid arthritis: mean platelet volume reflects disease activity. *Platelets* 2010;**21**:122–5.
33. Tozkoparan E, Deniz O, Ucar E, Bilgic H, Ekiz K. Changes in platelet count and indices in pulmonary tuberculosis. *Clin Chem Lab Med* 2007;**45**:1009–13.
34. Van der Lelie J, Von dem Borne AK. Increased mean platelet volume in septicaemia. *J Clin Pathol* 1983;**36**:693–6.
35. Dastugue N, Picheloup F, Sie P, Genestal M, Cathala B, Boneu B. Increase in mean platelet volume in shock-related thrombocytopenia. *Nouv Presse Med* 1982;**11**:2899–901.
36. Becchi C, Al Malyan M, Fabbri LP, Marsili M, Boddi V, Boncinelli S. Mean platelet volume trend in sepsis: is it a useful parameter? *Minerva Anestesiol* 2006;**72**:749–56.
37. Wallace SM, Walton BI, Kharbanda RK, Hardy R, Wilson AP, Swanton RH. Mortality from infective endocarditis: clinical predictors of outcome. *Heart* 2002;**88**:53–60.
38. Inanç T, Kaya MG, Kaya EG, Doğan A, Ardıç I, Doğdu O, et al. Infective endocarditis: retrospective evaluation of 27 patients (in Turkish). *Tıp Araştırmaları Dergisi* 2007;**5**:91–9.