Van Tıp Dergisi: 17 (3): 89-95, 2010

Mean Platelet Volume In Acute Coronary Syndrome

Rıdvan Mercan* , Cengiz Demir*, İmdat Dilek**, Müntecep Asker***, Murat Atmaca****

Abstract

Objective: Description of risk factors in coronary heart disease has a very important place in the prevention of acute coronary syndromes as well as in predicting the prognosis. In this study, the association between acute coronary syndrome and platelet volume, which is thought to be risk factor of the former one, was investigated. Materials and methods: 214 patients were included to the study, comprising of 69 patients with acute myocardial infarction (AMI), 73 patients with unstable angina pectoris, and 72 patients with stable angina pectoris. Control group consisted of 45 subjects who had atypical chest pain with no pathological sign in coronary angiography. In cases with acute coronary syndrome, blood samples were taken at the time of hospitalization, whereas it was performed at routine follow-up visits in the other group. Statistical analysis was made through "one-way variance analysis (ANOVA)" and post-hoc Tukey HSD. A p-value of <0.05 was considered to be statistically significant Results: Mean platelet volume (MPV) and platelet counts were found to be 9,0 ± 1,0 fl and 239,6 ± 59,2 x 10^9/L in unstable angina group, respectively; 8.9 ± 0.8 fl and 228.5 ± 74.1 x 10^9/L in AMI patients, respectively; 7.5 ± 0.6 fl and 268.3 ± 73.5 x 10^9/L in stable angina pectoris group, respectively; 7.2 ± 0.6 fl and 285.5 ± 80.9 x 10^9/L in control group, respectively. Control subjects had significantly lower MPV and significantly higher platelet counts compared to each of the unstable angina and AMI groups (p<0.001, p<0.001; p=0.004, p<0.001, respectively). MPV was detected to be significantly lower in stable angina group, compared to unstable angina and AMI groups (p<0.001, p<0.001, respectively), whereas neither a significant difference was determined between stable angina and AMI groups in terms of MPV (p=0,126) nor was it between unstable angina and AMI groups (p=0.999). While no significant difference was detected between the number of platelets of stable angina group and that of control and unstable angina groups (p=0.586, p=0.076, respectively), stable angina group had significantly higher platelet counts than AMI patients (p=0.006). Such comparison between unstable angina and AMI groups also did not reach a significant level (p=0.791). Conclusion: Platelet count and mean platelet volume was detected to be increased in patients with acute coronary syndrome.

Key words: Acute coronary syndrome, mean platelet volume.

Introduction

Despite the developments regarding its diagnosis and treatment in recent years, acute coronary syndromes (ACS) keep its place of the most important reason of morbidity and mortality. Cardiac diseases have been known to be the number one cause of deaths since the beginning of twentieth century.

* Yüzüncü Yıl University Medical Faculty Division of Hematology, Van.
** Atatürk Education and Research Hospital Division of Hematology, Ankara
*** Yüksek İhtisas Hospital of Van Division of Cardiology, Van.
**** Yüzüncü Yıl University Medical Faculty Division of Endocrinology, Van.
Yazışma Adresi: Dr. Cengiz Demir, MD
Department of Internal Medicine,
Division of Hematology, Faculty of Medicine,
Yüzüncü Yıl University, Van, TURKEY.
65300 Merkez/Van/TURKEY.
Tel/Fax: +90 432 2150474
E-Mail: drcengizdemir@hotmail.com

Coronary heart diseases manifest as such clinical presentations as stable angina pectoris (AP), silent myocardial ischemia, unstable AP, myocardial infarction (MI), heart failure, and sudden cardiac death (1, 2).

Known major risk factors for coronary heart disease are age, family history, cigarette smoking, hypertension, elevated LDL cholesterol, and diabetes mellitus, the latter of which has recently been accepted as a coronary heart disease equivalent. Apart from that, endothelial dysfunction, lipoprotein (a), homocysteine, and C-reactive protein are now considered as new risk factors for coronary heart diseases (3,4).

Description of risk factors in coronary heart disease has a very important place in the prevention of acute coronary syndromes as well as in the follow-up and treatment of patients with coronary heart disease.

In the development of ACS, platelets play a critical role in the formation thrombus on the ruptured plaque and consequent progression to myocardial infarction (5). Similarly, it was

previously demonstrated that platelets had important roles in the formation of AMI and development of its complications (6-10). Therefore, acetyl salicylic acid, thienopyridine, and glycoprotein IIb/IIIa inhibitors, which all inhibit platelet functions, are used in the treatment of ACS (11-13).

Platelets are heterogeneous in size, density, and activity (14). Alterations of these parameters may be associated with pulling the trigger of acute coronary syndrome and its spread (15). Large platelets are more adhesive and tend to aggregate more than smaller ones (16). Increase of platelet volume may contribute to increased prothrombotic tendency of atherosclerotic plaque in acute coronary syndrome and increased risk of intracoronary thrombus formation in AMI cases (17).

In this study, we aimed to investigate the association between platelet volume and acute coronary syndrome in patients with the diagnosis of coronary heart disease, in comparison with control group.

Materials and Methods

The study included ACS patients admitted to coronary intensive care unit and those patients with stable AP followed in cardiology outpatients' clinic. 214 patients were included to the study, comprising of 69 patients with acute myocardial infarction (AMI), 73 patients with unstable AP, and 72 patients with stable AP. Diagnoses of ACS and stable AP were confirmed with typical symptoms, ECG findings, laboratory findings and/or coronary angiography. Control group consisted of 45 subjects who were previously presented with complaint of atypical chest pain albeit no pathological sign in consequently performed coronary angiography.

The diagnosis of AMI was established by the three criteria accepted by World Health Organization (WHO): (1) ischemic type chest pain; (2) Changes in serial ECG tracings typical for AMI; and (3) presence of at least two criteria of typical course of rise and fall of serum cardiac biomarkers (18). The diagnosis of unstable angina pectoris was established by the presence of unstable chest pain and typical electrocardiographic findings in the absence of elevated CK-MB and troponin levels.

Patients with serious hepatic and renal disease, those previously detected to have malignancy, and subjects receiving an anticoagulant, anti-inflammatory or antiplatelet therapy were not included to the study. Since the fact that acetyl salicylic acid had no influence on platelet volume as revealed by earlier studies, ACS and stable AP patients receiving acetyl salicylic acid were not excluded from the study (19).

ECG examinations of subjects were performed through an ECG device branded with Marquette Hellige. Coronary angiography was performed via a device by Siemens Axiom Artis (2002-München, Germany).

Blood samples of patients were taken at the time of hospitalization in ACS group and during routine follow-ups in other cases, both obtained via antecubital venous access. Examined biochemical markers were plasma glucose (PG), blood urea nitrogen (BUN), creatinine (Cr), cholesterol profile, creatinine kinase myocardial band (CK-MB), aspartate aminotranspherase (AST), lactate dehydrogenase (LDH), uric acid (UA), sodium (Na), potassium (K), and chloride (Cl). For this purpose, aliquot of 5 ml blood of each subject was taken to typical biochemistry tube, which was centrifuged at 2000 rpm for 10 minutes to obtain serum. Serum samples were examined via a device, branded with Hitachi modular P-P (2001 Hitachi Ltd. Tokyo, Japan). For platelet count and volume analyses, aliquots of 2 ml blood were taken to the EDTA (ethylendiamine tetraacetic acid) tubes, which were examined within 30 minutes by hemogram device, branded with Coulter STKS (1998 – New York).

Statistical analysis: Quantitative data were expressed as mean ± standard deviation. Data were tested through the method of "one-way variance analysis (ANOVA)". Probability value of $p<0.05$ was set as statistically significant. Post-hoc Tukey HSD (Tukey's honestly significant difference) test was performed in order to understand in between which groups did the significant difference exist for variables found to be significant according to ANOVA (20).

Results

259 subjects comprising of 214 patients and 45 cases as control group were included to the study. Demographic characteristics of patient and control groups are shown in Table 1.

The comparison of age of patient and control groups showed no statistically significant difference ($p>0.05$). In stable AP patients, mean platelet count was detected as 268.3 ± 73.5 x 10^9/L, and MPV as 7.5 ± 0.6 fl; which was 285.5 ± 80.9 x 10^9/L and 7.2 ± 0.6 fl in control group, respectively. Mean platelet count and MPV were

comparable between these two groups with no statistically significant difference (p=0.586 and p=0.126, respectively).

In unstable AP patients, mean platelet count and MPV were 239.6 ± 59.2 x 10^9 /L and 9.0 ± 1.0 fl, respectively; which was 228.5 ± 74.1 x 10^9/L and 8.9 ± 0.8 fl in AMI patients. Mean platelet count and MPV were similar between these two groups with no statistically significant difference (p=0.791 and p=0.999, respectively). When unstable angina pectoris and AMI cases were compared to each of stable angina pectoris and control groups, it was observed that platelet counts were decreased and MPV were increased.

Table 1. Baseline characteristics of patients and control group

	Number of patients	Age, mean (years)	Male (n: 185)	Female (n: 74)
Stable AP	72	57.4 ± 9.9	59	13
Unstable AP	73	58.2 ± 10.5	45	28
AMI	69	58.7 ± 11.9	51	18
CONTROL	45	56.4 ± 8.9	30	15

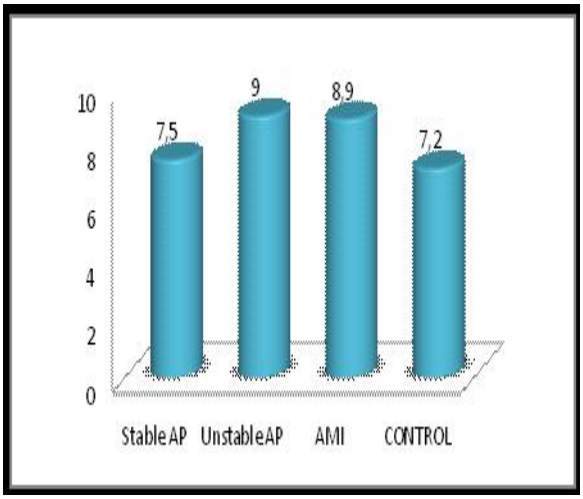
Table 2. Comparison of groups by MPV

MPV (Fl)	Stable AP group: 7.5 ± 0.6	Control group: 7.2 ± 0.6	p=0.126
	Stable AP group : 7.5 ± 0.6	Unstable AP group: 9.0 ± 1.0	p<0.001
	Stable AP group: 7.5 ± 0.6	AMI group: 8.9 ± 0.8	p<0.001
	Unstable AP group: 9.0 ± 1.0	AMI group: 8.9 ± 0.8	p=0.999
	Control group: 7.2 ± 0.6	Unstable AP group: 9.0 ± 1.0	p<0.001
	Control group: 7.2 ± 0.6	AMI group: 8.9 ± 0.8	p<0.001

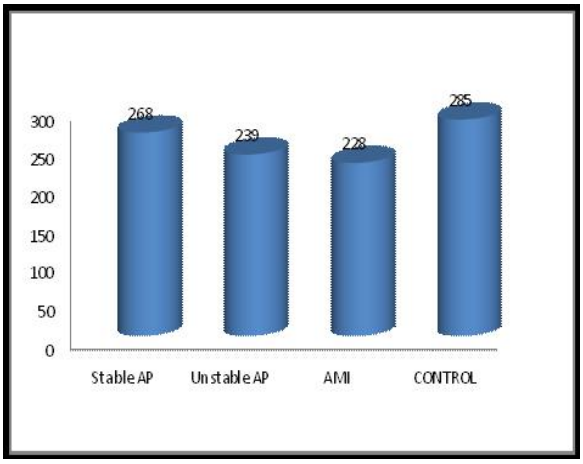
Table 3. Comparison of groups by mean platelet counts

Platelet count (x 10^9 /L)	Stable AP group: 268.3 ± 73.5	Control group: 285.5 ± 80.9	p=0.586
	Stable AP group: 268.3 ± 73.5	Unstable AP group: 239.6 ± 59.2	p=0.076
	Stable AP group: 268.3 ± 73.5	AMI group: 228.5 ± 74.1	P=0.006
	Unstable AP group: 239.6 ± 59.2	AMI group: 228.5 ± 74.1	p=0.791
	Control group: 285.5 ± 80.9	Unstable AP group: 239.6 ± 59.2	p=0.004
	Control group: 285.5 ± 80.9	AMI group: 228.5 ± 74.1	p<0.001

Comparisons of MPV and mean platelet counts are presented in Table 2 and Table 3; MPV values are shown in (Fig. 1). and mean platelet counts in (Fig. 2).



(Fig. 1). MPV values of groups



(Fig. 2). Mean platelet counts of groups

Discussion

Coronary artery diseases were the most important cause of mortality and morbidity in industrialized countries. Both endogenous and exogenous risk factors such as smoking, hypercholesterolemia, DM, and hypertension increase the risk of ACS (21). Nevertheless, these risk factors accounts for only a part of ACS cases (22). Therefore, it is needed to identify other related risk factors so as to predict individual risk in the development of ACS. While atherosclerotic plaque rupture starts the thrombogenic phenomenon in ACS, the activity of circulating platelets plays important role for the progression of thrombus (23).

Platelets were heterogeneous cells in terms of size, density, and activity (14). Platelet volume is an important indicator for platelet function and activation (24). Larger platelets contain more secretory granules and mitochondria and are known to be more active than small platelets (25,26). By leading to the formation and dissemination of intracoronary thrombus, larger and hyperactive platelets may accelerate the emergence of clinical picture called as acute coronary syndrome. Van der Loo et al., in their study, suggested that platelet volume was an important biological variable to determine platelet reactivity (27). They also suggested that elevated platelet volume measured after MI might be a determinant factor for future ischemic episodes and death. In this study, we examined the platelet volume of our cases, which we think to be likely a risk factor for ACS.

It was observed in a study that platelet volume was increased in patients with ST-elevated myocardial infarction compared to normal population (19). It was suggested that detection of increased MPV in AMI patients may be an indicator for the fact that the percentage of larger platelets was higher in these subjects and may contribute to thrombus formation (28,29). Yet, the prognostic value MPV still remained to be controversial. While a number of studies established an association between MPV and coronary artery disease or MI formation; some other studies suggested that there was not such an association (15,27,31,32,33).

Endler et al., in their study where they compared AMI patients to those with stable AP, found MPV to be increased (5). They also suggested that increased MPV was an indicator for larger and more active platelets and an independent risk factor for MI in coronary artery disease. Likewise, Park et al. also considered increased MPV to be a risk factor for platelet activation (34). Martin et al. reported that platelet volume was significantly increased within first 12 hours in post-MI period, which occurred before ACS (29). Martin et al,, in another study, suggested that increased MPV might be an independent risk factor for post-MI recurrence of coronary events and mortality (15).

In the study where they compared unstable angina pectoris and MI patients, Mathur et al. found platelet counts to be significantly lower and MPV to be higher in patients with unstable angina pectoris (35). On the other hand, we did not detect any significant difference between MI and unstable angina pectoris patients in terms of

platelet count and MPV (p=0.8 and p=0.999, respectively).

Kishk et al. compared AMI patients to stable angina pectoris and control groups and detected that the former group had lower platelet count and higher MPV (19). They suggested that it was independent of smoking, area or diameter of infarct. They also claimed that increased MPV and decreased platelet count may be a major risk factor for AMI. In consistent with these findings, we found in our study that MPV was significantly higher and platelet count was lower in AMI group, compared to stable angina pectoris and control groups.

In the study consisting of 518 chronic hemodialysis patients with concurrent coronary artery disease, Hening et al. concluded that high MPV might be associated with coronary heart disease in hemodialysed patients (36).

Puzzili et al. found MPV to be higher in unstable angina pectoris patients, compared to stable angina and control groups (31). In that study, they also detected that MPV was higher in unstable angina pectoris subjects who required emergent angioplasty, compared to the rest of unstable angina pectoris patients. These findings rendered them to claim that platelets of larger volume contributed to the formation of thrombus in coronary artery and led to reduction of platelet counts. In the same study, it was also found that platelet counts were similar in stable angina pectoris and control groups, while in stable angina pectoris group, MPV was significantly higher than that in control group. In our study, we determined MPV to be significantly higher and platelet count to be lower in unstable angina pectoris group than those in stable angina pectoris and control groups. However, we did not detect any significant difference between stable angina pectoris and control groups with respect to MPV and platelet counts (p=0.126, p=0.581).

There are also studies conflicting with above-mentioned results implying an association between increased platelet volume and acute coronary syndrome. Halbmayer et al, in their study comparing those patients waiting for coronary artery bypass graft surgery to the control group, did not detect any difference in terms of MPV (32). They claimed that MPV could not be used as risk indicator for coronary artery disease or MI. Likewise, no significant difference was found between unstable angina pectoris and control arms in terms of MPV, in the study consisted of 54 patients with unstable AP and performed by Butkiewicz and his colleagues (33). In this study, platelet counts were decreased when unstable AP patients were compared to the control group, yet this difference failed to reach a statistically significant level (33). In other two studies, platelet counts were found to be reduced in atherosclerosis cases (24,37). We detected that platelet count was significantly lower in AMI and unstable angina group vs. control group, and that it was significantly higher in stable angina group than AMI group. These findings imply that a declining of platelet count may ensue along with disease progression in acute coronary events. Seneran et al. found platelet counts of ACS patients to be higher than that of control group, though this was statistically non-significant (38).

In conclusion, we detected that platelet counts were decreased and mean platelet volumes were increased in patients presenting with acute coronary syndrome. Based on these findings, we have concluded that larger platelet volumes may constitute a high risk for acute coronary syndrome and ischemic complications. For this purpose, we think that MPV measurement, which is a non-invasive and easy-to-perform method, may be an important tool for the follow-up of these patients. Nonetheless, conflicting results of other studies make this issue controversial, which warrants performing of more comprehensive studies in future.

Akut Koroner Sendromda Ortalama Trombosit Hacmi

Özet

Amaç: Koroner kalp hastalığında risk faktörlerinin tanımlanması gerek akut koroner sendromların önlenmesinde, gerekse prognozu tahmin etmede büyük önem taşımaktadır. Bu çalışmada akut koroner sendrom ile risk faktörü olabileceği düşünülen trombosit hacmi arasındaki ilişki araştırıldı.

Materyal ve metod: Çalışmaya, 69 akut miyokard infarktüslü (AMİ), 73 kararsız angina pektoris ve 72 kararlı angina pektorisli olmak üzere toplam 214 hasta dahil edildi. Atipik göğüs ağrısı olan ve koroner anjiyografilerinde patolojik bulgu saptanmayan 45 olgu ise kontrol grubu olarak seçildi. Akut koroner sendromlu hasta grubunun kan örnekleri hastaneye yatışlarında, diğer olgularda ise hastaların rutin takiplerinde alındı. İstatistiksel analiz "Tek yönlü varyans analizi (ANOVA)" ve post-hoc Tukey HSD ile yapıldı. P< 0.05 istatistiksel olarak anlamlı kabul edildi.

Bulgular: Ortalama trombosit hacmi (TH) ve trombosit sayıları sırasıyla; kararsız angina grubunda 9,0 1,0 fl ve 239,6 ± 59,2 x 10^9/L, AMİ grubunda 8.9 ± 0.8 fl ve 228.5 ± 74.1 x 10^9/L, kararlı angina grubunda 7.5 ± 0.6 fl ve 268.3 ± 73.5 x 10^9/L, kontrol grubunda ise 7.2 ± 0.6 fl ve 285.5 ± 80.9 x 10^9/L olarak bulundu. Kontrol grubu ile kararsız angina ve AMİ grubu karşılaştırıldığında ortalama

TH anlamlı olarak düşük, trombosit sayısı daha yüksek saptandı (sırasıyla p<0.001, p<0.001, p=0.004, p<0.001). Ortalama TH açısından; kararlı angina grubu, kararsız angina ve AMİ grubu ile karşılaştırıldığında TH anlamlı olarak daha düşük saptandı (sırasıyla p<0.001, p<0.001), kararlı angina grubu ile kontrol grubu karşılaştırıldığında anlamlı fark saptanmadı (p=0,126), kararsız angina grubu ile AMİ grubu karşılaştırıldığında anlamlı fark saptanmadı (p=0.999). Trombosit sayıları açısından; kararlı angina grubu ile kontrol grubu ve kararsız angina grubu karşılaştırıldığında trombosit sayıları anlamlı olarak farklı bulunmadı (sırasıyla p=0.586, p=0.076), kararlı angina grubu ile AMİ grubu karşılaştırıldığında trombosit sayısı anlamlı olarak yüksek saptandı (p= 0.006). Kararsız angina ile AMİ grubu karşılaştırıldığında anlamlı fark saptanmadı (p= 0.791).

Sonuç: Akut koroner sendromlu hastalarda, trombosit sayılarının azaldığı ve ortalama trombosit hacimlerinin arttığı saptandı.

Anahtar kelimeler: Akut koroner sendrom, ortalama trombosit hacmi.

References

1. Van de Werf F, Ardissino D, Betriu A, Cokkinos DV, Falk E, Fox KA, et al. Management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J 2003; 24(1):28-66.
2. Bertrand ME, Simoons ML, Fox KA, Wallentin LC, Hamm CW, McFadden E, et al. Task Force on the Management of Acute Coronary Syndromes of the European Society of Cardiology. Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2002; 23: 1809-1840.
3. Pahor M, Elam MB, Garrison RJ, Kritchevsky SB, Applegate WB. Emerging noninvasive biochemical measures to predict cardiovascular risk. Arch Intern Med 1999; 159(3):237-245.
4. Onat A, Hergenç G, Yıldırım B, Uysal Ö, Keleş İ, Çetinkaya A, et al. Türk erişkinlerinde kanda fibrinojen düzeyi ve bazı risk parametreleri ile ilişkisi. Türk Kardiyol Dern Arş. 2000; 28:115-120.
5. Endler G, Klimesch A, Sunder-Plassmann H, Schillinger M, Exner M, Mannhalter C, et al. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. Br. J. Haematol 2002; 117:399-404.
6. Weinberger I, Fuchs J, Davidson E, Rotenberg Z. Circulating Aggregated Platelets, Number of Platelets per Aggregate, and Platelet Size During Acute Myocardial Infarction. Am J Cardiol 1992; 70:981-983.
7. Fuchs J, Weinberger I, Rotenberg Z, Joshua H, Almozlino A, Agmon J. Circulating Aggregated Platelets in Coronary Artery Disease. Am J Cardiol 1987; 60:534-537.
8. Fuster V, Badimon L, Cohen M, Ambrose JA, Badimon JJ, Chesebro J. Insights into the patogenesis of acute ischemic syndromes. Circulation 1988; 77:1213-1220.
9. Fuster V, Jang IK. Role of Platelet- Inhibitor Agents in Coroner Artery Disease. ln Topol EJ (ed). Textbook of interventional cardiology. Philadelphia, W.B.Saunders Company 1994; 3-22
10. Davies MJ, Thomas AC, Knapman PA, Hangartner JR. Intramyocardial platelet aggregation in patients with unstable angina suffering sudden ischemic cardiac death. Circulation 1986; 73:418-427.
11. Antiplatelet Trialists Collaboration. Collaborative over view of randomized trials of antiplatelet therapy. I: Prevention of death, myocardial infarction and stroke by prolonged antiplatelet therapy in various categories of patients. BMJ 1994; 308:81-106.
12. Mehta SR, Yusuf S. Clopidogrel in Unstable angina to prevent Recurrent Events Study Investigators. The Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial program; rationale, design and baseline characteristics including a meta-analysis of the effects of thienopyridines in vascular disease. Eur Heart J 2000; 21:2033-2041.
13. Inhibition of the platelet glycoprotein IIb/IIIa receptor with tirofiban in unstable angina and non-Q-wave myocardial infarction. Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) Study Investigators. N Engl J Med 1998; 338:1488-1497.
14. Karpatkin S. Heterogeneity of human platelets. II. Functional evidence suggestive of young and old platelets. J Clin Invest 1969; 48:1083-1087.
15. Martin JF, Bath PM, Burr ML. Influence of platelet size on outcome after myocardial infarction. Lancet 1991; 338:1409-1411.
16. Schoene NW. Design Criteria: tests used to assess platelet function. Am J Clin Nutr. 1997; 65(Sup):1665-1685.
17. Davies MJ, Thomas AC. Thrombosis and acute coronary artery lesions in sudden cardiac ischemic death. N Engl J Med 1984; 310:1137-1140.
18. Tunstall-Pedoe H, Kuulasmaa K, Mähönen M, Tolonen H, Ruokokoski E, Amouyel P. for the WHO MONICA (monitoring trends and determinants in cardiovascular disease) Project. Contribution of trends in survival and

coronary-event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA Project populations. Lancet 1999; 353:1547-1557.

19. Kishk YT, Trowbridge EA, Martin JF. Platelet volume subpopulations in acute myocardial infarction: an investigation of their homogeneity for smoking, infarct size and site. Clin Sci 1985; 68:419-425.
20. Sümbüloğlu K, Sümbüloğlu V. Biyoistatistik. Hatiboğlu Yayınevi. Ankara, 1998.
21. McKarns SC, Smith CJ, Payne VM, Doolittle DJ. Blood parameters associated with atherogenic and thrombogenic risk in smokers and nonsmokers with similar life-styles. Mod Pathol 1995; 8:434-440.
22. Koenig W. Epidemiology of coronary heart disease. Z Kardiol 1998; 87:3-7.
23. Karpatkin S. Heterogeneity of human platelets. VI. Correlation of platelet function with platelet volume. Blood 1978; 51:307-316.
24. Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. Blood Coagul Fibrinolysis 1996; 7: 157-161.
25. Thompson CB, Jakubowski JA, Quinn PG, Deykin D, Valeri CR. Platelet size as a determinant of platelet function. J Lab Clin Med 1983; 101:205-213.
26. Martin JF, Trowbridge EA, Salmon GL, Plumb J. The biological significance of platelet volume: its relationship to bleeding time, platelet thromboxane B2 production and megakaryocyte nuclear DNA concentration. Thromb Res 1983; 32:443-460.
27. Van der Loo B, Martin JF. A role for changes in platelet production in the cause of acute coronary syndromes. Arterioscler Thromb Vasc Biol 1999; 19:672–679.
28. Erne P, Wardle J, Sanders K, Lewis SM, Maseri A. Mean platelet volume and size distribution and their sensitivity to agonists in patients with coronary artery disease and congestive heart failure. Thromb Haemost 1988; 59:259-263.
29. Martin JF, Plumb J, Kilbely RS, Kishk YT. Changes in volume and density of platelets in myocardial infarction. Br Med J 1983; 287: 456-459.
30. Martin JF, Trowbridge T, Slater D. Mean platelet volume in MI. Br Med J 1983; 287: 1798.
31. Pizzulli L, Yang A, Martin JF, Luderitz B. Changes in platelet size and count in unstable angina compared to stable angina or non cardiac chest pain. Eur Heart J 1998; 19:80-84.
32. Halbmayer WM, Haushofer A, Radek J, Schon R, Deutsch M, Fischer M. Platelet size, fibrinogen and lipoprotein (a) in coronary heart disease. Coron Artery Dis 1995; 6:397-402.
33. Butkiewicz AM, Kemona H, Dymicka-Piekarska V, Bychowski J. Beta-thromboglobulin and platelets in unstable angina. Kardiol Pol 2003; 58:449-455.
34. Park Y, Schoene N, Harris W. Mean platelet volume as an indicator of platelet activation: methodological issues. Platelets 2002; 13: 301-306.
35. Mathur A, Robinson MS, Cotton J, Martin JF, Erusalimsky JD. Platelet reactivity in acute coronary syndromes: evidence for differences in platelet behaviour between unstable angina and myocardial infarction. Thrombosis and Haemostasis 2001; 85:989-994.
36. Henning BF, Zidek W, Linder B, Tepel M. Mean platelet volume and coronary heart disease in hemodialysis patients. Kidney Blood Press Res 2002; 25:103-108.
37. Brown AS, Martin JF. The megacaryocyte platelet system and vascular disease. Eur J Clin Invest 1994; 24(Suppl) 1:9-15.
38. Senaran H, Ileri M, Altinbas A, Kosar A, Yetkin E, Ozturk M, ve ark. Thrombopoietin and mean platelet volume in coronary artery disease. Clin Cardiol 2001; 24:405-408.