VIA MEDICA

ORIGINAL ARTICLE

Cardiology Journal
2010, Vol. 17, No. 5, pp. 488–494

ISSN 1897–5593

The relationship between oxidative stress and coronary artery ectasia

Yusuf Sezen[1], Memduh Bas[1], Mustafa Polat[1], Ali Yildiz[1], Hakan Buyukhatipoglu[2], Zekeriya Kucukdurmaz[3], Zekeriya Kaya[3], Recep Demirbag[1]

[1]Department of Cardiology, Harran University, Sanliurfa, Turkey
[2]Department of Internal Medicine, Harran University, Sanliurfa, Turkey
[3]Department of Cardiology, Sanliurfa Training and Research Hospital, Sanliurfa, Turkey

Abstract

Background: *Whereas coronary artery ectasia (CAE) is a rare abnormality of the coronary arteries, co-existent coronary artery disease (CAD) is commonly seen in CAE patients. Since a causative relationship has been shown to exist between oxidative stress and CAD, we sought to determine whether any relationship exists between oxidative stress and CAE.*

Methods: *Fourty four patients with CAE (without CAD) and 86 controls (without any coronary disease) were recruited from among 1,520 patients undergoing coronary angiography. CAE subgroups were determined in accordance with the Markis classification system. Mean values for serum total oxidant status (TOS), total antioxidant status (TAS) and the oxidative stress index (OSI) were statistically compared between these two study groups and among CAE subgroups, with $p = 0.05$ set as the threshold for statistical significance.*

Results: *TOS and OSI were significantly increased ($p = 0.018$ and 0.0002) and TAS decreased ($p = 0.031$) in the CAE* versus *control group. TOS and TAS were independently related to CAE ($p = 0.037$ and 0.039), with an r^2 of 0.127. Interestingly, however, among CAE subgroups, no differences were observed.*

Conclusions: *Oxidative stress might be implicated in the pathogenesis of CAE. Clinically-defined CAE subgroups did not differ in terms of oxidative stress status. However, the clinical implications of these findings are unclear and warrant further investigation.* (Cardiol J 2010; 17, 5: 488–494)

Key words: coronary artery ectasia, oxidative stress, coronary artery disease

Introduction

Coronary artery ectasia (CAE), a rare variant of coronary artery abnormality, has been defined as a coronary artery segment that has dilated to a diameter that exceeds the diameter of adjacent segments, or the diameter of the largest coronary artery, by at least 50% [1]. The incidence of CAE has been reported as between 0.5% and 4.9% in different series [1–4].

CAE may be congenital or acquired. Acquired causes include coronary artery disease (CAD), Kawasaki disease, various infectious and inflammatory diseases, Ehlers-Danlos syndrome, Marfan syndrome, familial hypercholesterolemia, scleroderma, connective tissue disorders like SLE, and vasculi-

Address for correspondence: Assist. Prof. Yusuf Sezen, MD, Harran Universitesi Tip Fakultesi, P.K: 112 Sanliurfa, Turkey, tel: +90 505 572 62 49, fax: +90 414 315 11 81, e-mail: buyukhatipoglu@gmail.com

Received: 19.02.2010 Accepted: 29.03.2010

tides like polyarteritis nodosa, Takayasu's disease and Behcet's syndrome [5–14].

Oxidative stability is defined as a balance between the formation and elimination of free radicals. Any increase in the rate of free radical formation, or decrease in their elimination, can disrupt this balance, resulting in oxidative stress [15, 16]. Oxidative stress usually is associated with increased free radical formation, causing increased concentrations of reactive oxygen species (ROS). ROS modify phospholipids and proteins, leading to lipid peroxidation and the oxidation of thiol groups [17, 18]. These substances may lead to inflammatory responses, including complement activation, the release of cytokines, leukocyte activation, and the expression of adhesion molecules [19]. ROS also cause the depletion of plasma antioxidants, formation of several damaging metabolites, and potential DNA damage [20, 21]. Exogenous antioxidant molecules like vitamin E and C; endogenic antioxidants that include albumin, uric acid, and bilirubin; and scavenger enzymes like superoxide dismutase, glutathione peroxidase and catalase may prevent and/or inhibit the harmful effects of ROS [22].

CAE and CAD have several characteristics in common. CAE can cause ischemic heart disease, and even myocardial infarctions in patients without CAD, by means of reduced and sluggish flow, thrombus formation, and vasospasm [23, 24]. CAE and coronary atherosclerosis exhibit similar histopathological patterns [25]. Moreover, CAD is commonly seen in CAE patients and these two diseases are closely related, with 70% of CAEs co-existent with atherosclerosis and only 20–30% isolated [5, 6, 11].

In addition, a causative association between oxidative stress and CAD has been detected in several clinical studies [26–28]. Based on the common features of CAD and CAE, their frequent co-existence, and the proven association between CAD and oxidative stress, our study sought to measure oxidative status in CAE patients to determine if a relationship exists. Because CAE and CAD are so commonly observed together, to assess the independent relationship between CAE and oxidative stress, we selected CAE patients without CAD. To our knowledge, this is the first study to assess the association between oxidative stress and isolated CAE.

Methods

Subjects

The study was conducted at Harran University School of Medicine. Prior to initiating subject recruitment, the study was approved by the local ethics committee of the university, in accordance with the ethical principles for human investigations, as outlined in the second Declaration of Helsinki. All subjects provided written informed consent prior to participating.

Between 2008 and 2009, 44 CAE patients (coronary artery ectasia group; 19 females, 26 males, mean age 62 years) without coronary artery disease (defined as 50% or more narrowing in at least one coronary artery since significant CAD has been reported to be associated with the presence of increased oxidative stress) [29] were recruited from a total of 1,520 patients who underwent angiography. As a control group, 86 patients [normal coronary artery group (NCA); 52 females, 34 males, mean age 61 years] with normal coronary arteries were recruited from the same patient population. Patients were deemed ineligible for analysis if any of the following conditions were present: 1) any co-existing cardiac disease, such as heart failure or arrhythmia, a previous history of myocardial infarction, or coronary artery disease; 2) any evidence of liver, kidney or respiratory disease; 3) acute coronary syndrome; 4) malignancy; 5) any infectious, inflammatory or infiltrative disorder; 6) recent use (within 48 h) of any drug with anti-oxidant properties, such as nebivolol, carvedilol, vitamins E and C, and acetylcysteine; and 7) regular alcohol use or alcohol use within 48 hours.

Study design

This was a prospective case-control study. Before angiography, all patients were examined in detail. A medical history and detailed physical examination were recorded for each patient. The patients underwent routine laboratory workup for renal and liver function, and other routine baseline parameters. Erythrocyte sedimentation rate (ESR), C reactive protein (CRP), and urinalysis (UA) were obtained, and various numbers of electrocardiograms (ECG) were performed. A chest X-ray was obtained and echocardiography performed on each patient.

On angiography, a diagnosis of CAE was rendered if any 1.5-fold or greater dilatation was evident, relative to adjacent normal coronary segments [1]. After angiography, eligible CAE patients and controls were recruited. Potentially-eligible patients and controls were selected in such a way as to achieve a certain degree of homogeneity, in terms of age, diabetes mellitus, hypertension, smoking status and other demographic variables (Table 1). CAE patients were divided into sub-

Table 1. Demographic characteristics and laboratory parameters of subjects.

Parameters	NCA	CAE	P
Age (years)	6.106 ± 9.48	62.42 ± 11.23	0.465
Sex (female/male)	52/34	20/25	0.80
Diabetes mellitus (+/–)	25/61	14/31	0.808
Hypertension (+/–)	29/57	14/31	0.763
Dyslipidemia (+/–)	20/66	16/29	0.134
Cigarette smoking (+/–)	22/64	12/33	0.893
Heart rate [beat/min]	78.09 ± 12.94	82.93 ± 14.66	0.066
ASP [mm Hg]	132.12 ± 27.31	129.89 ± 25.36	0.667
ADP [mm Hg]	83.71 ± 14.53	81.22 ± 13.82	0.373
Waist circumference [cm]	103.85 ± 13.65	106.22 ± 13.68	0.534
BSA [m^2]	1.81 ± 0.23	1.89 ± 0.24	0.167
BMI [kg/m^2]	28.14 ± 6.12	28.83 ± 4.70	0.606
QT [ms]	392.76 ± 34.72	377.30 ± 45.74	0.065
QTc [ms]	431.08 ± 35.26	429.10 ± 36.92	0.794
Urea [mg/dL]	38.49 ± 26.11	48.64 ± 28.15	0.180
Creatinine [mg/dL]	0.89 ± 0.13	0.93 ± 0.37	0.610
Fasting glucose [mg/dL]	138.83 ± 75.26	143.81 ± 53.69	0.796
AST [U/L]	18.91 ± 4.78	44.75 ± 50.80	0.108
ALT [U/L]	29.83 ± 5.95	31.75 ± 8.97	0.544
Total cholesterol [mg/dL]	197.65 ± 48.89	200.86 ± 33.80	0.800
LDL-C [mg/dL]	118.27 ± 47.73	131.23 ± 38.42	0.315
HDL-C [mg/dL]	42.08 ± 6.02	38.13 ± 8.05	0.067
Triglyceride [mg/dL]	165.25 ± 106.88	208.71 ± 108.97	0.185

From independent samples t-test and χ^2 analysis. Values are mean ± standard deviation; NCA — normal coronary artery group; CAE — coronary artery ectasia group; ASP — arterial systolic pressure; ADP — arterial diastolic pressure; BSA — body surface area; BMI — body-mass index; QTc — corrected QT interval; AST — aspartate aminotransferase; ALT — alanine aminotransferase; LDL-C — low-density lipoprotein-cholesterol; HDL-C — high-density lipoprotein-cholesterol

groups, in accordance with the Markis classification system, as follows: Type 1 CAE, diffuse ectasia in two or three vessels; Type 2 CAE, diffuse ectasia in one vessel and localized ectasias in at least one other vessel; Type 3 CAE, diffuse ectasia in a single vessel; Type 4 CAE, localized and segmentary ectasia lesions.

Assays

All blood samples were obtained following an overnight fast, drawn from a large antecubital vein without interruption of venous flow, using a 19-gauge butterfly needle connected to a plastic syringe. Twenty milliliters [mL] of blood were drawn, with the first few ml discarded. Ten mL were used for baseline routine laboratories and ESR. The residual content of the syringe was transferred immediately to polypropylene tubes. These tubes then were centrifuged at 3,000 rpm for 10 minutes at 10––18°C. Supernatant plasma samples were stored in plastic tubes at –80°C until assayed. For serum markers of oxidant stress, total oxidant status (TOS) was measured and the oxidative stress index (OSI) calculated. Total antioxidant capacity (TAS) was measured as an indicator of antioxidant status.

Measurement of TAS

Serum TAS was determined using a novel automated measurement method, developed by Erel [30]. By this method, hydroxyl radical, the most potent biological radical, is produced. In the assay, ferrous ion solution, present in Reagent 1, is mixed with hydrogen peroxide, which is present in Reagent 2. Sequentially-produced radicals like the brown-colored dianisidinyl radical cation, produced by the hydroxyl radical, also are potent radicals. Using this method, the anti-oxidative effect of the sample against potent free-radical reactions, which are initiated by the produced hydroxyl radical, can be measured. The assay has excellent precision values, of greater than 97%. The results are expressed as mmol Trolox equiv./L.

Measurement of TOS

The TOS of serum was determined using a novel automated measurement method, also developed by Erel [31]. Oxidants present in the sample oxidize the ferrous ion-o-dianisidine complex to ferric ion. The oxidation reaction is enhanced by glycerol molecules, which are abundant in the reaction medium. The ferric ion generates a coloured complex with Xylenol Orange in an acidic medium. Colour intensity, which can be measured spectrophotometrically, is related to the quantity of oxidant molecules present in the sample. The assay is calibrated with hydrogen peroxide and the results expressed in terms of micro-molar hydrogen peroxide equivalents per liter (μmol H_2O_2 equiv./L).

Oxidative stress index

The OSI is defined as the ratio of the TOS to TAS level, expressed as a percentage. For the calculation, TAS units were changed to mmol/L, and the OSI value calculated according to the following formula (4): OSI (arbitrary unit) = TOS (μmol H_2O_2 Equiv./L)/TAS (mmol Trolox equiv./L).

Other variables

Serum sodium (Na), potassium (K), urea, creatinine, fasting blood sugar, aspartate amino transferase (AST), alanine amino transferase (ALT), triglyceride (TG), total cholesterol (TC), HDL-cholesterol (HDL-C), and LDL-cholesterol (LDL-C) levels were determined using commercially-available assay kits (Abbott®) with an auto-analyser (Aeroset®, Germany). CRP was measured by means of nephelometric analysis (NA Latex CRP reagent: Behring Institute, Marburg, Germany). ESR was measured using a modified Westergren method (Dispette 2; Ulster Medical Products, a division of Lukens Medical Corporation, Albuquerque, New Mexico, USA).

Statistical analysis

All data analysis was conducted using SPSS version 11.5 (SPSS Inc., Chicago, Illinois, USA), with group parameters expressed as means ± standard deviations. Between-group comparisons were conducted by independent samples Student's t-tests for continuous variables, and by Pearson's χ^2 analysis for categorical variables. Subgroup analyses were performed by one-way analysis of variance (ANOVA). Because the assumption of homogeneity of variance was met and the data was approximately normally distributed, *post-hoc* comparisons were performed using Tukey's procedure. Differences at $p \leq 0.05$ were interpreted as statistically significant. For logistic regression analysis, the ENTER variable selection method, and Hosmer and Lemeshow goodness-of-fit test were used. A Nagelkerke test was utilized to calculate R square. All inferential tests were two-tailed.

Results

Demographic characteristics and routine laboratory data for the two comparison groups are shown in Table 1. There were no statistically significant differences between the two groups with regard to age (within the insignificance border), gender, body mass index, body surface area, QT and cQT interval, the rates of diabetes mellitus, hypertension, dyslipidemia, cigarette smoking, electrolytes, or other routine biochemical parameters. The serum TAS level was significantly lower in the CAE group than in the NCA group ($p = 0.018$; Fig. 1), whereas the TOS level and OSI value were significantly higher in the CAE group ($p = 0.031$ and 0.0002, respectively; Fig. 1; Table 2). On logistic regression analysis, an independent relationship was identified between the presence of CAE and both the TOS and TAS levels ($\beta = 0.875$, $\chi^2 = 4.35$, $p = 0.049$; $\beta = -0.830$, $\chi^2 = 4.35$, $p = 0.04$ respectively), with $R2 = 0.127$. Comparing the four different subgroups of CAE, there were no statistically-significant differences in TOS, TAS or OSI (Fig. 2).

Discussion

The present study generated two main results. The first is that, in patients with CAE, two oxidative parameters (TAS and OSI) were significantly elevated, while antioxidant parameters were significantly decreased, relative to normal controls without CAE or CAD. The second finding is that the serum oxidative parameters did not vary between CAE subgroups, differentiated in terms of the number and distribution of lesions. To the best of our knowledge, this is the first study to assess oxidative stress in patients with CAE.

CAE resembles atherosclerosis in several respects. One piece of supporting evidence for this statement is that the two diseases (CAE and CAD) have similar risk factors [1, 2]. Secondly, patients with CAE commonly have co-morbid CAD [5, 6, 11]. Third, the two conditions exhibit similar histopathological features [25]. Based upon these common features, we intended to research whether these two disorders share certain metabolic features. Accordingly, and since markers of oxidative stress already have been shown to be elevated in CAD

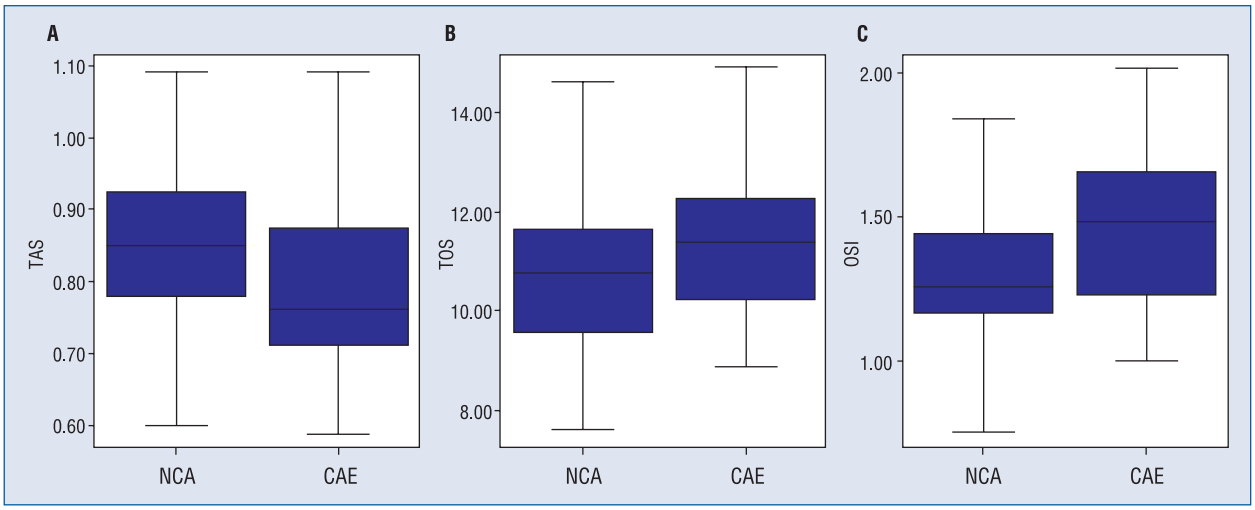

Figure 1. A. Total antioxidant status (TAS) values by subject group; **B.** Total oxidant status (TOS) values by subject group; **C.** Oxidative stress index (OSI) values by subject group; NCA — normal coronary artery group; CAE — coronary artery ectasia group.

Table 2. Oxidative/anti-oxidative markers in coronary artery ectasia group (CAE) and normal coronary artery group (NCA).

Parameters	NCA	CAE	P
Total antioxidant status [mmol Trolox equiv./L]	0.85 ± 0.11	0.80 ± 0.13	0.018
Total oxidant status [μmol H_2O_2 equiv./L]	10.82 ± 1.50	11.41 ± 1.43	0.031
Oxidative stress index [arbitrary unit]	1.30 ± 0.23	1.46 ± 0.27	0.00002

From independent samples t-test. Values are mean ± standard deviation.

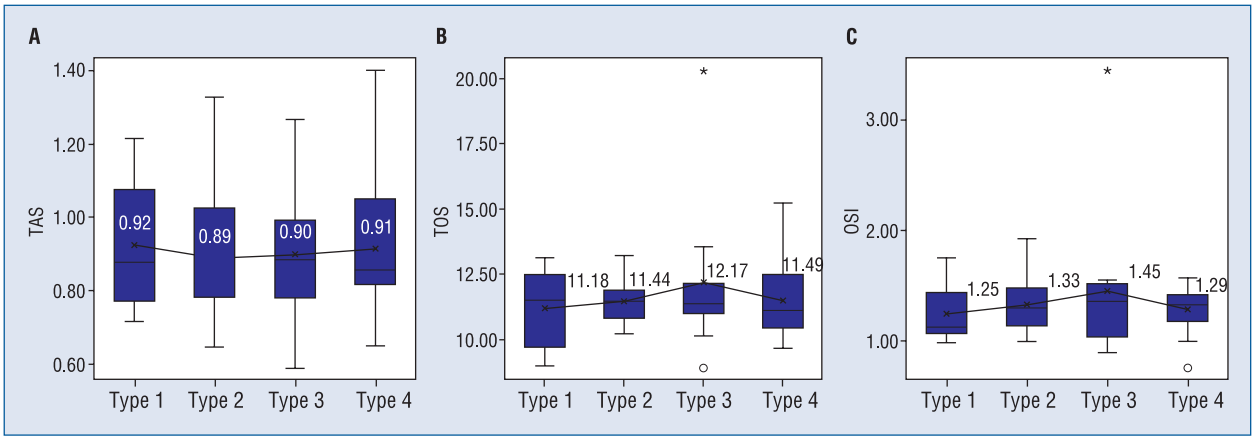

Figure 2. A. Total antioxidant status (TAS) values by coronary artery ectasia group (CAE) subgroup; **B.** Total oxidant status (TOS) values by CAE subgroup; **C.** Oxidative stress index (OSI) values by CAE subgroup; Type 1, 2, 3 and 4 — subgroups. Mean values are shown in the figure.

patients [26–28], we sought to determine whether such markers also are high in patients with isolated CAE.

Recently-published studies have revealed oxidative stress to be independently related to CAD in regression models. However, it is not clear

whether oxidative stress is a direct cause of CAD or the result of several metabolic pathways. Nevertheless, irrespective of how it happens, it has been concluded that oxidative stress has some causative role in atherosclerosis formation, though the net effect might be small [26–28, 32].

In this study, we identified a similar effect in CAE patients. We found two markers of oxidative stress to be significantly higher in those with CAE than in controls without either CAE or CAD. Furthermore, upon regression analysis, TAS was found to be independently related to CAE, predicting roughly 13% of the variance in CAE presence, providing evidence implicating oxidative stress in CAE pathogenesis. However, as mentioned above, this relationship might be the result of various unknown relationships and interactions. Consequently, though the results of this study might not explain why CAD and CAE share certain features, they provide evidence that certain common pathophysiological pathways might be at play [3–5].

On the other hand, the second main finding of the current study was the lack of any of the differences that we might have anticipated between CAE subgroups classified according to lesion number and distribution. And, although the subgroup samples admittedly were relatively small, the average subgroup oxidant/antioxidant levels were nearly the same, and the data was distributed normally, suggesting that larger samples may not alter these negative results. This means that oxidative status might have a role in the pathogenesis of CAE. This is an important finding because, as mentioned above, the relationship of oxidative stress with CAE could be causative, or it could be that oxidative stress is a result of CAE. It was not possible for us to clarify this effect in the current study. However, we can conclude that oxidative stress is either a cause, or a result, of various metabolic pathways.

This study is worth reporting for several reasons. To begin with, the method by which we evaluated antioxidant status is relatively new and had not been validated previously. Measuring total oxidative status is more valid and reliable, since there are a great number of oxidants and antioxidants in the body. When you measure only a few parameters, you may find their levels unchanged or decreased, even when actual oxidant status is increased, or vice versa. Secondly, isolated CAE is relatively rare; and, in terms of evaluating oxidative status, this study was the first. As mentioned above, CAD is common in patients with CAE. However, we only recruited CAE patients without CAD. Therefore, we clearly observed oxidative stress increased in CAE separate from CAD, though different severities of CAE appeared to exert no influence.

Conclusions

The clinical implications of these results are elusive, and whether increased oxidative stress might respond to antioxidant treatment also is elusive. However, if drug management is needed for CAE (as in the cases of co-existing CAD, coronary symptoms, or hypertension) using drugs with antioxidant properties (e.g. nebivolol for hypertension instead of other beta-blockers) might be preferred. However, further studies are needed to draw clear-cut conclusions.

Acknowledgements

The authors do not report any conflict of interest regarding this work.

References

1. Swaye PS, Fisher LD, Litwin P et al. Aneurysmal coronary artery disease. Circulation, 1983; 67: 134–138.
2. Pinar Bermudaz E, Lopez Palop R, Lozano Martinez-Luengaz I et al. Coronary ectasia: Prevalence, and clinical and angiographic characteristic. Rev Esp Cardiol, 2003; 56: 473–479.
3. Leschka S, Stolzmann P, Scheffel H et al. Prevalence and morphology of coronary artery ectasia with dual-source CT coronary angiography. Eur Radiol, 2008; 18: 2776–2784.
4. Yilmaz H, Sayar N, Yilmaz M et al. Coronary artery ectasia: Clinical and angiographical evaluation. Turk Kardiyol Dern Ars, 2008; 36: 530–535.
5. Swanton RH, Thomas ML, Coltart DJ et al. Coronary artery ectasia: A variant of occlusive coronary arteriosclerosis. Br Heart J, 1978; 40: 393–400.
6. Markis JE, Joffe CD, Cohn PF et al. Clinical significance of coronary arterial ectasia. Am J Cardiol, 1976; 37: 217–222.
7. Dieter RS, Murtaugh T, Black J et al. Coronary arteriomegaly in a patient with Ehlers-Danlos syndrome and multiple aneurysms: A case report. Angiology, 2003; 54: 733–736.
8. Chaithiraphan S, Goldberg E, O'Reilly M et al. Multiple aneurysms of coronary artery in sclerodermal heart disease. Angiology, 1973; 24: 86–93.
9. Sumino H, Kanda T, Sasaki T et al. Myocardial infarction secondary to coronary aneurysm in systemic lupus erythematosus. An autopsy case. Angiology, 1995; 46: 527–530.
10. Altinbas A, Nazli C, Kinay O et al. Predictors of exercise induced myocardial ischemia in patients with isolated coronary artery ectasia. Int J Cardiovasc Imag, 2004; 20: 3–17.
11. Suzuki H, Daida H, Tanaka M et al. Giant aneurysm of the left main coronary artery in Takayasu aortitis. Heart, 1999; 81: 214–217.
12. Yilmaz H, Sayar N, Yilmaz M et al. Coronary artery ectasia: Clinical and angiographical evaluation. Turk Kardiyol Dern Ars, 2008; 36: 530–535.
13. Sezen Y, Buyukhatipoglu H, Kucukdurmaz Z, Geyik R. Cardiovscular involvement in Behcet's disease. Clin Rheumatol, 2010; 29: 7–12.

14. Kucukdurmaz Z, Buyukhatipoglu H, Sezen Y, Kaya Z. Polycystic kidney disease with coronary aneurysm and acute coronary syndrome. Intern Med, 2009; 48: 1989–1991.
15. Halliwell B. Free radicals, antioxidants, and human disease: Curiosity, cause, or consequence. Lancet, 1994; 344: 721–724.
16. Halliwell B, Gutteridge JM. Lipid peroxidation, oxygen radicals, cell damage, and antioxidant therapy. Lancet, 1984; 1: 396––397.
17. Elmoselhi AB, Lukas A, Ostadal P et al. Preconditioning attenuates ischemia-reperfusion-induced remodeling of Na+-K+- ATPase in hearts. Am J Physiol Heart Circ Physiol, 2003; 285: 1055–1063.
18. Suzuki S, Kaneko M, Chapman DC et al. Alterations in cardiac contractile proteins due to oxygen free radicals. Biochim Biophys Acta, 1991; 24: 95–100.
19. Biglioli P, Cannata A, Alamanni F et al. Biological effects of off--pump vs. on-pump coronary artery surgery: Focus on inflammation, hemostasis and oxidative stress. Eur J Cardiothorac Surg, 2003; 24: 260–269.
20. Dhalla NS, Elmoselhi AB, Hata T, Makino N. Status of myocardial antioxidants in ischemia-reperfusion injury. Cardiovasc Res, 2000; 47: 446–456.
21. Toivonen HJ, Ahotupa M. Free radical reaction products and antioxidant capacity in arterial plasma during coronary artery bypass grafting. J Thorac Cardiovasc Surg, 1994; 108: 140–147.
22. Young IS, Woodside JV. Antioxidants in health and disease. J Clin Pathol, 2001; 54: 176–186.
23. Papadakis MC, Manginas A, Cotileas P et al. Documentation of slow coronary flow by the TIMI frame count in patients with coronary ectasia. Am J Cardiol, 2001; 88: 1030–1032.
24. Kruger D, Stierle U, Herrmann G, Simon R, Sheikhzadeh A. Exercise-induced myocardial ischemia in isolated coronary artery ectasias and aneurysms ("dilated coronopathy"). J Am Coll Cardiol, 1999; 34: 1461–1470.
25. Antoniadis AP, Chatzizisis YS, Giannoglou GD. Pathogenetic mechanisms of coronary ectasia. Int J Cardiol, 2008; 28; 130: 335–343.
26. Georgiadou P, Iliodromitis EK, Varounis C et al. Relationship between plasma osteopontin and oxidative stress in patients with coronary artery disease. Expert Opin Ther Targets, 2008; 12: 917–920.
27. Vassalle C, Pratali L, Boni C, Mercuri A, Ndreu R. An oxidative stress score as a combined measure of the pro-oxidant and anti--oxidant counterparts in patients with coronary artery disease. Clin Biochem, 2008; 41: 1162–1167.
28. Demirbag R, Yilmaz R, Kocyigit A. Relationship between DNA damage, total antioxidant capacity and coronary artery disease. Mutat Res, 2005; 570: 197–203.
29. Gur M, Aslan M, Yildiz A et al. Paraoxonase and arylesterase activities in coronary artery disease. Eur J Clin Invest, 2006; 36: 779–787.
30. Erel O. A novel automated method to measure total antioxidant response against potent free radical reactions. Clin Biochem, 2004; 37: 112–119.
31. Erel O. A new automated colorimetric method for measuring total oxidant status. Clin Biochem, 2005; 38: 1103–1111.
32. Yildiz A, Gur M, Yilmaz R et al. Association of paraoxonase activity and coronary blood flow. Atherosclerosis, 2008; 197: 257–263.