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Original Article

Predictors of slow flow in angiographically normal coronary arteries

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Abstract: Introduction: Slow coronary flow (SCF) is a well-known angiographic finding; however, the pathophysiology of SCF remains only partially understood. In this study, we have examined the risk factors of slow coronary flow. Methods: Seventy patients with angiographically proven SCF were studied along with 60 control participants. Patients were divided into 2 groups based on the angiographic findings as with or without SCF. In both groups, clinical information was collected and laboratory parameters were measured and compared. Results: Patients with SCF had higher serum uric acid, creatinine and hemoglobin levels. They also more commonly had a history of smoking. On the other hand, C-reactive protein and hematologic parameters such as mean platelet volume (MPV), red cell distribution width (RDW), and neutrophil to lymphocyte (N/L) ratio did not differ significantly between the two groups. In the logistic regression analysis, only uric acid (odds ratio [OR]=1.583, 95% confidence interval [CI]=1.011-2.349, P=0.034) was found as an independent correlate of SCF. Conclusions: This study demonstrates that serum uric acid level is significantly correlated with SCF and may play a role in the development of the condition. These findings provide impetus for additional studies to confirm these results and treatment of SCF.

Keywords: Slow coronary flow, uric acid, hematologic parameters, C-reactive protein

Introduction

Slow coronary flow (SCF) is an angiographic finding characterized by slow progression of contrast in the coronary arteries in the absence of coronary artery obstruction [1]. The incidence of SCF ranges from 1% to 6% among patients who undergo coronary angiography [2, 3]. There are a limited number of studies focused on SCF. Therefore, the underlying pathophysiological mechanisms and the clinical importance of SCF are not known clearly. There are mechanisms that may be involved in the SCF process, including small vessel dysfunction [4], diffuse atherosclerosis [5], inflammation [6], endothelial dysfunction [7], and increased platelet aggregability [8]. Although the pathophysiological mechanisms of slow coronary flow remain uncertain, it is important to determine the main risk factors for SCF to gain insights that may allow for further study of the condition and its mechanisms. Therefore, this study focuses on investigating the risk factors of SCF.

Methods

Study population

Patients who underwent coronary angiography between August 2009 and August 2013 were evaluated for possible inclusion in the study. A total of 70 consecutive patients diagnosed with SCF along with 60 age and gender-matched patients (control group) were included in our study after the following exclusions: history of coronary artery disease or sign of coronary artery disease on coronary angiograms, coronary artery ectasia, acute coronary syndrome, valvular heart disease, congestive heart failure, renal failure (creatinine >1.5 mg/dl), hepatic and hemolytic disorders, anemia, concomitant inflammatory diseases and neoplastic diseases. Patients taking uric acid-lowering therapy were also excluded. Detailed physical examina-

tions were performed on all patients. The local ethical committee approved the study protocol.

Definitions

Hypertension was defined as a blood pressure of 140/90 mm Hg or greater, or having a history of antihypertensive drug use. Diabetes mellitus (DM) was defined as a fasting blood glucose of ≥126 mg/dl on two occasions or as being on treatment. Admission anemia was defined as a baseline hemoglobin (Hb) concentration less than 13 mg/dL in men and less than 12 mg/dL in women.

Evaluation of coronary blood flow

Coronary angiography was commonly indicated because of clinical symptoms or results of noninvasive tests that suggested myocardial ischemia. Coronary angiography was performed using the standard Judkins technique. A contrast agent was injected manually during coronary angiography (6-10 ml of contrast agent at each position using right and left, and cranial and caudal angulations). TIMI frame count (TFC) was determined for each major coronary vessel by 2 trained cardiologists with cineangiography at 25 frames per second [9]. Both investigators were blinded to the clinical details of the individual cases. The TFCs for the left anterior descending (LAD) and circumflex (Cx) arteries were assessed in either the right anterior oblique projection with caudal angulations or the left anterior oblique projection with cranial angulations and that of right coronary artery (RCA) usually in straight left anterior oblique projection. Since the LAD coronary artery is usually longer than the RCA and the CX, and the TIMI frame count for LAD is often higher, the LAD frame counts were corrected by dividing by 1.7. Patients with a TFC greater than two standard deviations from the normal published range for any 1 of the 3 vessels (40.6, 29.8 and 27.3 frames for LAD, Cx, and RCA respectively) were considered to have SCF.

Laboratory measurements

A fasting venous blood sample was obtained in the morning before coronary angiography. Levels of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) in serum were measured using an Abbott Aeroset auto-analyzer with original kits (Abbott Laboratories. Abbott Park, Illinois, U.S.A.). Low-density lipoprotein (LDL) cholesterol levels were calculated using the Friedewald equation. Serum uric acid levels were measured using an enzymatic colorimetric test on a Roche/Hitachi analyzer. C-reactive protein (CRP) level was immunologically determined by immunoturbidimetric method (Abbott Aeroset 1600 autoanalyser, by Abbott reagents, Germany). Hemoglobin, along with other hematologic parameters, was measured on the Abbott Laboratories Cell-Dyn counter (Cell-dyn 3700 Abbott Laboratories, IL, U.S.A.). The N/L ratio was obtained by dividing the total count of neutrophils by the lymphocytes count.

Statistical analysis

All analyses were performed using SPSS V 16.0 for Windows (version 16.0, SPSS, Chicago, Illinois). All data are presented as mean ± standard deviation unless otherwise stated. The Student t test was used to compare serum uric acid levels, CRP, creatinine, LDL cholesterol and hemogram parameters in groups according to 2 groups based on the coronary flow. Chi-square test was used to compare gender, hypertension, diabetes, and smoking between 2 groups. Univariate and multivariate logistic regression analyses were applied to determine crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the relationship between uric acid levels, CRP, creatinine, LDL cholesterol, hemogram parameters and the presence of SCF. All potential (physiologically meaningful) determinants of the SCF were investigated in a univariate regression analysis. Those variables with $P<0.1$ by univariate analysis were included in the backward stepwise multivariate logistic regression analysis model and the respective odds ratios (OR) with 95% confidence intervals (CI) were calculated. All statistical tests were two-sided, and statistical significance was determined at a P value <0.05.

Results

In all of the studied patients studied, the mean age was 57.3±10 years and 49.2% of the patients were female. Among the 70 patients with slow coronary flow, 38 patients had 3-vessel involvement, 16 patients had 2-vessel involvement and 16 patients had single-vessel involvement. Moreover, SCF was most commonly

Table 1. Baseline clinical and laboratory characteristics of slow coronary flow and control groups

	Control group	SCF group	*P* value
Age, years	57.5±8.9	57.1±11.8	0.865
Male gender, n (%)	29 (48.3)	37 (52.8)	0.576
Hypertension, n (%)	18 (30)	18 (25.7)	0.468
Diabetes, n (%)	8 (13.3)	14 (20)	0.321
Smoking, n (%)	4 (6.7)	14 (20)	0.031
Heart rate (beats/min)	74.7±12.2	75.5±12.1	0.726
Total cholesterol (mg/dl)	190.7±43.4	189.9±43.1	0.927
LDL cholesterol (mg/dl)	113.9±30.8	111.8±31.4	0.759
HDL cholesterol (mg/dl)	49.3±13.6	50.4±13.4	0.704
Triglyceride (mg/dl)	135.9±73.1	145.8±103	0.608
Uric acid (mg/dl)	3.6±1.5	5.2±1.7	<0.001
Creatinine (mg/dl)	0.8±0.1	0.9±0.2	0.004
C-reactive protein, mg/l	4.1±1	4.2±1	0.654
Hemoglobin (g/dl)	13.3±1.5	14.1±1.4	0.005
Mean platelet volume (fl)	8.7±1.1	8.3±0.8	0.070
Platelet distribution width, %	16.4±0.5	16.4±0.6	0.911
Red cell distribution width, %	14.2±1.3	13.9±1.3	0.194
Neutrophil count (10^9/L)	4.4±1.8	5.1±2.1	0.061
Neutrophil/lymphocyte ratio	2.3±1.2	3±2.8	0.141
White blood cell count (10^9/L)	7.2±2.1	8.1±2.7	0.084
Beta-blocker use, n (%)	10 (16.6)	9 (15.2)	0.457
ACE inhibitor use, n (%)	16 (26.6)	12 (20.3)	0.392
Statin use, n (%)	13 (21.6)	9 (15.2)	0.233
Nitrates, n (%)	5 (8.3)	6 (10.1)	0.754
Calcium canal blockers, n (%)	4 (6.6)	6 (10.1)	0.513
TIMI frame count values			
LAD (corrected)	21.3±3.5	30.4±4.1	<0.001
LCx	20.4±3.1	28.2±3.2	<0.001
RCA	21.4±2.9	29.1±3.4	<0.001

Abbreviations: ACE, Angiotensin converting enzyme; LDL, Low-density lipoprotein; HDL, High density lipoprotein; LAD, Left anterior descending coronary artery; LCx, Left circumflex coronary artery; RCA, Right coronary artery; SCF, Slow coronary flow.

present in LAD in 48 participants (68.5% of SCF patients).

Demographic and clinical patient characteristics are listed in **Table 1**. There was no difference in age, gender, presence of diabetes, dyslipidemia, and hypertension, lipid profiles-including TG to HDL cholesterol-, CRP, heart rate and baseline medications between the SCF and control groups. Likewise, hematologic parameters, such as mean platelet volume (MPV), red cell distribution width (RDW), neutrophil to lymphocyte (N/L) ratio, white blood cell (WBC) and platelet distribution width (PDW), were similar between the study groups. Patients with SCF more commonly had a history of smoking. Serum uric acid (5.2±1.7 vs 3.6±1.5 mg/dl, P<0.001), creatinine (0.9±0.2 vs 0.8±0.1 mg/dl, P=0.004), and hemoglobin (14.1±1.4 vs 13.3±1.5 g/dl, P=0.005), were significantly higher in the SCF group than in the normal coronary flow group (**Table 1**).

To further explore the independent predictor(s) of slow coronary flow, various multiple regression models were analyzed based on traditional and nontraditional risk factors affecting SCF. In the multiple logistic regression analysis we adjusted for age, gender, hypertension, diabetes, LDL cholesterol, smoking, uric acid, creatinine, hemoglobin and CRP and only uric acid (odds ratio [OR]=1.583, 95% confidence interval [CI]=1.011-2.349, P=0.034) was found as an independent correlate of SCF (**Table 2**, **Figure 1**).

Discussion

Although several studies on SCF have been conducted, the precise pathophysiologic mechanisms of SCF have not yet been elucidated. Regarding control of coronary blood flow, the endothelium plays an important role by regulating coronary vascular tone [10]. It has been shown that endothelial function, measured by the brachial artery flow-mediated dilatation (FMD), is impaired in people with SCF [7]. Reduced nitric oxide (NO) bioactivity as well as impaired vascular endothelial function was also observed in patients with SCF [11]. Recently, decreased adiponectin concentrations and paraoxonase (PON) activity, two significant markers of endothelial dysfunction, have been shown to be associated with SCF [12]. High levels of serum uric acid were found to be associated with endothelial dysfunction [13]. Hyperuricemia is known to induce endothelial dysfunction via down regulation of NO production and mitochondrial $Na+/Ca^{2+}$ exchanger-mediated mitochondrial calcium overload [14]. In addition, Elbasan et al [15] demonstrated a positive independent association between serum uric acid level and SCF in

Table 2. Logistic regression analysis of the main risk factors of slow coronary flow

Variables	Odds Ratio	95% Confidence Interval	*P* Value
Age	1.011	0.951-1.074	0.717
Gender	2.869	0.674-15.122	0.284
Hypertension	0.785	0.178-3.465	0.750
Diabetes mellitus	0.584	0.113-3.016	0.520
Smoking	2.798	0.529-14.799	0.226
LDL cholesterol	1.002	0.981-1.023	0.875
Uric acid	1.583	1.011-2.349	0.034
Creatinine	1.405	0.016-30.741	0.902
Hemoglobin	1.004	0.569-1.769	0.990
CRP	1.099	0.690-1.750	0.692

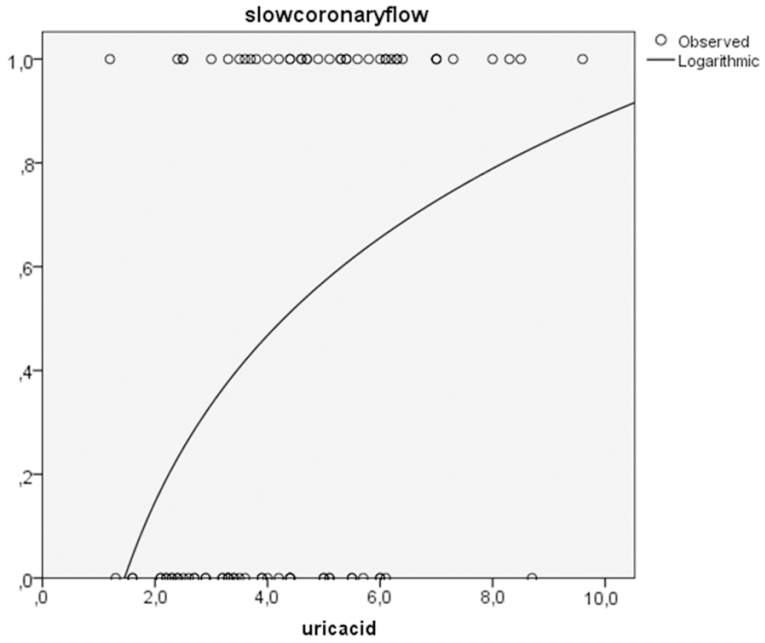

Figure 1. Uric acid as an independent corralate of SCF in logistic regression analysis.

patients with cardiac syndrome X. In this study, we consistently found that serum uric acid levels were higher in patients with SCF.

There is considerable evidence that the SCF occurs as a result of coronary microvascular dysfunction [4]. It was reported that coronary flow reserve (CFR), as an indicator coronary microvascular function, is impaired in patients with SCF [16]. Reduced CFR, has been shown to be an early manifestation of coronary atherosclerosis. Kanbay et al [17] reported that uric acid may have a role in coronary microvascular disease. Uric acid also stimulates vascular smooth muscle cell proliferation and oxidative stress via the vascular renin-angiotensin system [18]. Güllü et al [19] have also found serum uric acid level to be inversely correlated with CFR in healthy individuals and in patients with idiopathic dilated cardiomyopathy. Cin et al [20] investigated the coronary artery morphology in patients with SCF. In their coronary angiographic analysis patients with SCF had diffuse intimal thickening, atheroma which did not cause luminal irregularities and widespread calcification along the coronary vessel wall suggesting that, the SCF phenomenon may be a form of early stage coronary atherosclerosis. A growing body of evidence from experimental, clinical, and epidemiological studies suggests a possible association between elevated levels of uric acid and several indices of vascular function including the development and progression of atherosclerotic cardiovascular disease [15]. Consistent with our results, Naing et al recently found that uric acid was the most determinant factor for slow coronary flow phenomenon, whereas brain natriuretic peptide (BNP), fibrinogen, gama-glutamyl transferase (GGT) and hematologic parameters, such as MPV, RDW and hemoglobin, did not differ significantly between the SCF and control groups [21].

Although inflammation may play a role in the pathogenesis of SCF, the association of SCF with inflammatory markers is controversial. Several studies have shown a positive relationship between SCF and inflammation [6, 22]. By contrast, CRP was not associated with SCF in a recent study [23]. Neutrophil to lymphocyte ratio provides a simple but promising method to evaluate systemic inflammation and it is

widely used as a prominent marker for cardiovascular diseases [24]. Elevated N/L ratio indicative of a systemic inflammatory response was found to be associated with SCF [25]. Elevated serum uric acid was found to be associated with inflammation [26]. A strong correlation between RDW and inflammatory markers has also been observed [27]. The RDW has also been found to be associated with reduced coronary blood flow [28]. Despite the studies mentioned above, the association between SCF and inflammation remains unclear due to the limited number of patients in these studies and conflicting data. The systemic influence hypothesis, at least for CRP, N/L ratio and RDW, is not valid in our study, as CRP, N/L ratio and RDW values were similar between the SCF and NCF groups. In the same line, Erdogan et al [29]. found no significant association between SCF and CRP. Consistent with our results, Celik et al [30] has recently shown that levels of vitamin E, a membrane protector against oxidative stress, were decreased in patients with slow coronary flow. At the same time, there was no significant difference between the two groups in terms of plasma CRP levels.

Platelet function disorder has also been implicated in the pathogenesis of the SCF phenomenon [8, 31]. Gokce et al [8] reported that the ratio of platelet aggregability was significantly higher in patients with slow coronary flow phenomenon than in control subjects. This suggests that the underlying pathophysiological mechanism of slow coronary flow may be platelet function disorder. The size of the platelets, represented by MPV, is a potentially useful marker of platelet activity. It was recently shown that MPV level is significantly associated with coronary blood flow [32]. However, in our cohort, there was no difference in MPV between the SCF and control groups.

This study has several limitations. In this study, the patients did not undergo IVUS (intravascular ultrasonography) to detect atherosclerotic changes in the coronary arteries. Although no subject presented with a doubtful appearance or wall irregularity on angiographic evaluation, atherosclerotic plaque or a lesion may only be seen by IVUS. It has been demonstrated that heart rate, nitrate use and coronary catheter size have confounding effects on frame count [33]. In the current study, coronary catheter size was the same for all participants and there was no difference in baseline medications between the SCF and control groups. Heart rate was also similar in subjects with and without SCF. In addition, we did not study the other inflammatory markers such as serum fibrinogen, and interleukins (ILs). Studying these markers may provide more informative data on the role of inflammation in the etiopathogenesis of SCF. Finally, the sample size in our study was relatively small.

In conclusion, our results suggest that endothelial dysfunction as determined by increased uric acid level, rather than inflammation, plays a role in the etiopathogenesis of SCF. Our findings provide impetus for additional studies to address the underlying mechanism and treatment of the condition.

Disclosure of conflict of interest

None.

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References

[1] Tambe AA, Demany MA, Zimmerman HA, Mascarenhas E. Angina pectoris and slow flow velocity of dye in coronary arteries: a new angiographic finding. Am Heart J 1972; 84: 66-71.

[2] Hawkins BM, Stavrakis S, Rousan TA, Abu-Fadel M, Schechter E. Coronary slow flow: Prevalence and clinical correlations. Circ J 2012; 76: 936-942.

[3] Jesuthasan LSB, Beltrame JF, Marwick TH. Incidence of coronary slow flow in a large teaching hospital. Heart Lung Circ 2009; 18: S121.

[4] Mosseri M, Yarom R, Gotsman MS, Hasin Y. Histologic evidence for small-vessel coronary artery disease in patients with angina pectoris and patent large coronary arteries. Circulation 1986; 74: 964-972.

[5] Pekdemir H, Cin VG, Cicek D, Camsari A, Akkus N, Doven O, Parmaksiz HT. Slow coronary flow may be a sign of diffuse atherosclerosis. Contribution of FFR and IVUS. Acta Cardiol 2004; 59: 127-133.

[6] Turhan H, Saydam GS, Erbay AR, Ayaz S, Yasar AS, Aksoy Y, Basar N, Yetkin E. Increased plasma soluble adhesion molecules: ICAM-1,

VCAM-1, and E-selectin levels in patients with slow coronary flow. Int J Cardiol 2006; 108: 224-230.
[7] Damaske A, Muxel S, Fasola F, Radmacher MC, Schaefer S, Jabs A, Orphal D, Wild P, Parker JD, Fineschi M, Munzel T, Forconi S, Gori T. Peripheral hemorheological and vascular correlates of coronary blood flow. Clin Hemorheol Microcirc 2011; 49: 261-269.
[8] Gokce M, Kaplan S, Tekelioglu Y, Erdogan T, Kucukosmanoglu M. Platelet function disorder in patients with coronary slow flow. Clin Cardiol 2005; 28: 145-148.
[9] Gibson CM, Cannon CP, Daley WL, Dodge JT Jr, Alexander B Jr, Marble SJ, McCabe CH, Raymond L, Fortin T, Poole WK, Braunwald E. TIMI frame count: a quantitative method of assessing coronary artery flow. Circulation 1996; 93: 879-888.
[10] Lücher TF, Richard V, Tschudi M, Yang ZH, Boulanger C. Endothelial control of vascular tone in large and small coronary arteries. J Am Coll Cardiol 1990; 15: 519-527.
[11] Sezgin N, Barutcu I, Sezgin AT, Gullu H, Turkmen M, Esen AM, Karakaya O. Plasma nitric oxide level and its role in slow coronary flow phenomenon. Int Heart J 2005; 46: 373-382.
[12] Selcuk H, Selcuk MT, Temizhan A, Maden O, Saydam GS, Ulupinar H, Dogan M, Aydin C, Topcu DI, Sasmaz AH. Decreased plasma concentrations of adiponectin in patients with slow coronary flow. Heart Vessels 2009; 24: 1-7.
[13] Kanbay M, Segal M, Afsar B, Kang DH, Rodriguez-Iturbe B, Johnson RJ. The role of uric acid in the pathogenesis of human cardiovascular disease. Heart 2013; 99: 759-766.
[14] Papežíková I, Pekarová M, Kolářová H, Klinke A, Lau D, Baldus S, Lojek A, Kubala L. Uric acid modulates vascular endothelial function through the down regulation of nitric oxide production. Free Radic Res 2013; 47: 82-88.
[15] Elbasan Z, Sahin DY, Gür M, Seker T, Kıvrak A, Akyol S, Sümbül Z, Kuloğlu O, Caylı M. Serum uric acid and slow coronary flow in cardiac syndrome X. Herz 2013; 38: 544-548.
[16] Erdogan D, Caliskan M, Gullu H, Sezgin AT, Yildirir A, Muderrisoglu H. Coronary flow reserve is impaired in patients with slow coronary flow. Atherosclerosis 2007; 191: 168-174.
[17] Kanbay M, Sánchez-Lozada LG, Franco M, Madero M, Solak Y, Rodriguez-Iturbe B, Covic A, Johnson RJ. Microvascular disease and its role in the brain and cardiovascular system: a potential role for uric acid as a cardiorenal toxin. Nephrol Dial Transplant 2011; 26: 430-437.
[18] Corry DB, Eslami P, Yamamoto K, Nyby MD, Makino H, Tuck ML. Uric acid stimulates vascular smooth muscle cell proliferation and oxidative stress via the vascular renin-angiotensin system. J Hypertens 2008; 26: 269-275.
[19] Gullu H, Erdogan D, Caliskan M, Tok D, Kulaksizoglu S, Yildirir A, Muderrisoglu H. Elevated serum uric acid levels impair coronary microvascular function in patients with idiopathic dilated cardiomyopathy. Eur J Heart Fail 2007; 9: 466-488.
[20] Cin VG, Pekdemir H, Camsar A, Cicek D, Akkus MN, Parmaksýz T, Katýrcýbaý T, Doven O. Diffuse intimal thickening of coronary arteries in slow coronary flow. Jpn Heart J 2003; 44: 907-919.
[21] Naing Z, Qiu CG. Dawn of the most influential mechanism from the nightmare of slow coronary flow phenomenon: a randomized controlled study. Int J Cardiol 2013; 168: 4951-4953.
[22] Barutcu I, Sezgin AT, Sezgin N, Gullu H, Esen AM, Topal E, Ozdemir R, Kosar F, Cehreli S. Increased high sensitive CRP level and its significance in pathogenesis of slow coronary flow. Angiology 2007; 58: 401-407.
[23] Arı H, Arı S, Erdoğan E, Tiryakioğlu O, Huysal K, Koca V, Bozat T. The effects of endothelial dysfunction and inflammation on slow coronary flow. Turk Kardiyol Dern Ars 2010; 38: 327-333.
[24] Arbel Y, Finkelstein A, Halkin A, Birati EY, Revivo M, Zuzut M, Shevach A, Berliner S, Herz I, Keren G, Banai S. Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography. Atherosclerosis 2012; 225: 456-460.
[25] Cingoz F, Iyisoy A, Demirkol S, Sahin MA, Balta S, Celik T, Unlu M, Arslan Z, Cakar M, Kucuk U, Demirbas S, Kocak N. Carotid intima-media thickness in patients with slow coronary flow and its association with neutrophil-to-lymphocyte ratio: a preliminary report. Clin Appl Thromb Hemost 2014; 20: 393-399.
[26] Lyngdoh T, Marques-Vidal P, Paccaud F, Preisig M, Waeber G, Bochud M, Vollenweider P. Elevated serum uric acid is associated with high circulating inflammatory cytokines in the population-based Colaus study. PLoS One 2011; 6: e19901.
[27] Patel KV, Ferrucci L, Ershler WB, Longo DL, Guralnik JM. Red blood cell distribution width and the risk of death in middle-aged and older adults. Arch Intern Med 2009; 169: 515-523.
[28] Luo SH, Jia YJ, Nie SP, Qing P, Guo YL, Liu J, Xu RX, Zhu CG, Wu NQ, Jiang LX, Dong Q, Liu G, Li JJ. Increased red cell distribution width in patients with slow coronary flow syndrome. Clinics (Sao Paulo) 2013; 68: 732-737.

[29] Erdogan T, Canga A, Kocaman SA, Cetin M, Durakoglugil ME, Cicek Y, Ugurlu Y, Bozok S. Increased epicardial adipose tissue in patients with slow coronary flow phenomenon. Kardiol Pol 2012; 70: 903-909.
[30] Celik VK, Eken IE, Yildiz G, Yilmaz MB, Gurlek A, Aydin H. Vitamin E and antioxidant activity; its role in slow coronary flow. Cardiovasc J Afr 2013; 24: 360-363.
[31] Lanza GA, Andreotti F, Sestito A, Sciahbasi A, Crea F, Maseri A. Platelet aggregability in cardiac syndrome X. Eur Heart J 2001; 22: 1924-1930.
[32] Isik T, Ayhan E, Uyarel H, Ergelen M, Tanboga IH, Kurt M, Korkmaz AF, Kaya A, Aksakal E, Sevimli S. Increased mean platelet volume associated with extent of slow coronary flow. Cardiol J 2012; 19: 355-362.
[33] Abaci A, Oguzhan A, Eryol NK, Ergin A. Effect of potential confounding factors on the thrombolysis in myocardial infarction trial frame count and its reproducibility. Circulation 1999; 100: 2219-2223.