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Original Article

Effects of ticagrelor and clopidogrel on serum homocysteine level and neutrophil-to-lymphocyte ratio in elderly patients with coronary heart disease

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Abstract: Objective: To study the effects of ticagrelor and clopidogrel on homocysteine (Hcy) level and neutrophil-to-lymphocyte ratio (NLR) in elderly patients with coronary heart disease (CHD). Methods: A prospective study was conducted on 128 elderly patients with CHD who underwent percutaneous coronary intervention (PCI). The patients were divided into two groups according to random number table: following PCI, 64 patients treated with ticagrelor combined with aspirin were set as the observation group, and the other 64 patients treated with clopidogrel combined with aspirin were set as the control group. One case in the control group lost to follow up for the study. The clinical efficacy was observed. Serum Hcy level, NLR and left ventricular function were measured and adverse events recorded in the two groups. Results: After treatment, the total effective rate of the observation group was significantly higher than that of the control group (85.94% vs 71.43%, P<0.05). The decrease of Hcy and NLR in the observation group was more significant than that in the control group after treatment (P<0.001), and Hcy was positively correlated with NLR (r=0.224, P=0.012). Compared with the control group, the post-treatment left ventricular ejection fraction (LVEF) in the observation group was significantly higher, while the left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic diameter (LVEDD) and Left atrial diameter (LADD) were significantly lower (P<0.01 or P<0.001). The incidence of adverse events in the observation group was significantly lower than that in the control group (P<0.05). Conclusion: Ticagrelor combined with aspirin is markedly effective in the treatment of patients undergoing PCI, which can decrease Hcy and NLR, improve left ventricular function and reduce the incidence of adverse events.

Keywords: Ticagrelor, clopidogrel, coronary heart disease, Hcy, NLR

Introduction

Coronary heart disease, or CHD, is a common disease among elderly patients, presenting increasing morbidity and mortality year by year. CHD accounts for approximately 0.77-1.24% among Chinese population, and is more pervasive in elderly patients. Its mortality rate among urban Chinese population is 107.50 per 100,000 people compared with 105.37 per 100,000 people in rural areas [1]. Currently, the most effective clinical method for the treatment of CHD is to use percutaneous coronary intervention (PCI) to open the blocked blood vessels. However, postoperative thrombosis is prone to occur, causing stent re-blockage and affecting the prognosis of patients, which has become a new direction of clinical research [2, 3]. Previous studies have shown that preoperative anticoagulant therapy for PCI can effectively prevent the occurrence of no-reflow phenomenon during operation [4-6], and postoperative anticoagulant therapy is also of great significance to prevent thrombosis. Previous clinical use of clopidogrel combined with aspirin for dual-antibody therapy has been shown in studies to significantly reduce the mortality of patients and postoperative stent thrombosis, while recent studies have found that clopidogrel resistance exists in some patients, resulting in postoperative stent thrombosis [7, 8]. Therefore, clinical trials began to seek for new anticoagulants to achieve the effect of postoperative anticoagulation. Among them, ticagrelor is a new adenosine diphosphate receptor antagonist, which can inhibit platelet aggrega-

tion with rapid and strong effect [9, 10]. Evidence has shown that the formation of atherosclerotic plaques is the basis of CHD [11, 12], and elevated serum homocysteine (Hcy) is an important factor in the development of atherosclerosis. Other studies have revealed that Hcy is positively correlated with the degree of coronary artery disease [13]. The neutrophil-to-lymphocyte ratio (NLR) is a new inflammatory marker, which has been shown to be closely related to disease severity and prognosis of cancer patients [14, 15]. In recent years, researchers have identified a correlation between NLR and disease severity and prognosis in patients with CHD [16, 17]. Based on this, the purpose of this study was to explore the therapeutic effect of ticagrelor and clopidogrel on elderly patients with CHD after PCI and their effects on Hcy level and NLR.

Materials and methods

Clinical data

This study was approved by the Medical Ethics Committee of Huangshan City People's Hospital. A prospective study was conducted on 128 elderly patients with CHD who underwent-PCI in the Department of Cardiology of Huangshan City People's Hospital from January 2018 to October 2019. Using random number table method, 64 patients treated with ticagrelor-combined with aspirin were assigned to the observation group, and 64 patients treated with clopidogrel combined with aspirin were set as the control group. All the participants were aged from 60 to 86 years old, with an average age of 71.4±9.8 years old.

Inclusion and exclusion criteria

Inclusion criteria: (1) Patients who met the diagnostic criteria of unstable angina pectoris formulated by the Chinese Medical Association [18], and needed PCI after coronary angiography diagnosis; (2) Patients over 60 years old; (3) Patients with first onset; (4) Patients who received and completed PCI treatment.

Exclusion criteria: (1) Patients with congenital heart disease, persistent atrial fibrillation, or cardiomyopathy; (2) Patients with malignant tumors; (3) Patients combined with hypotension shock or severe electrolyte disorder; (4) Patients with hematological diseases.

Methods

Patients in the observation group were given 300 mg aspirin (Bayer Pharmaceuticals, Italy) and 180 mg ticagrelor (Astra Zeneca AB, Sweden) before PCI. After PCI, aspirin was orally administered 100 mg once daily and ticagrelor 90 mg twice daily for 3 months. In the control group, 300 mg aspirin (Bayer Pharmaceuticals, Italy) and 300 mg clopidogrel (Sanofi Clir SNC, France) were administered before PCI, and 100 mg aspirin was taken once daily and 75 mg clopidogrel once daily orally for 3 months after PCI.

Outcome measures

Clinical efficacy evaluation [19]: Clinical efficacy was determined as markedly effective, effective and ineffective according to the frequency of angina pectoris and electrocardiogram (ECG) results after treatment. Markedly effective: the patient's clinical symptoms completely disappeared, and the ECG T wave inversion and ST segment depression basically returned to normal; effective: the patient's clinical symptoms were significantly improved, the T wave inversion became shallower by more than 50%, and the ST segment depression was partially improved; ineffective: failure to meet the above criteria. Effective rate = (markedly effective + effective)/total number of cases × 100%.

Determination of serum Hcy and NLR

Elbow venous blood (5 mL) was respectively collected from each participant before operation and 3 months after operation, and stored in sterile tubes of ethylenediaminetetraacetic acid (EDTA; Labware Technology (Shenzhen) Co., Ltd., China). After being stored in a refrigerator at 4°C for 15 minutes, the serum and plasma were separated by a centrifuge with a centrifugal force of 1106.8 (xg) and stored in a refrigerator at -80°C. Routine blood test was performed using Coulter LH750 automatic hemocyte analyzer (Beckman Coulter Company, USA), NLR = neutrophil/lymphocyte, and Hcy was determined using an automatic biochemical analyzer (Hitachi 7600-020E type).

Evaluation of left heart function before and after operation

Cardiac echocardiography: Ultrasonic cardiogram (UCG) was performed using color Doppler

Table 1. Comparison of general and baseline data ($\bar{x}$ ± sd)

Group	Observation group (n=64)	Control group (n=63)	χ^2/t	P
Gender (male/female)	42/22	39/24	0.190	0.663
Age (year)	71.7±9.3	71.3±8.9	0.248	0.805
SBP (mmHg)	152.18±7.19	152.05±8.20	0.095	0.924
DBP (mmHg)	88.18±7.19	88.20±7.82	0.015	0.988
TG (mmol/L)	1.77±0.64	1.78±0.64	0.088	0.930
TC (mmol/L)	5.56±0.76	5.60±0.78	0.293	0.770
HDL (mmol/L)	1.07±0.35	1.11±0.33	0.509	0.662
LDL (mmol/L)	3.82±0.84	3.95±0.68	0.950	0.340
HGB (g/L)	138.52±10.46	139.45±9.73	0.519	0.605
ALB (g/L)	41.78±4.76	42.81±4.86	1.027	0.230
BMI (kg/m^2)	24.07±3.98	25.14±4.12	1.489	0.139
FBG (mmol/L)	7.89±3.82	8.03±4.13	0.843	0.198

Note: SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: triglyceride; TC: total cholesterol; HDL: high density lipoprotein; LDL: low-density lipoprotein; HGB: hemoglobin; ALB: serum albumin; BMI: body mass index; FBG: fasting blood glucose.

Table 2. Comparison of efficacy (n, %)

Group	Number of cases	Markedly effective	Effective	Ineffective	Total effective rate
Observation group	64	35 (54.69)	20 (31.25)	9 (14.06)	55 (85.94)
Control group	63	19 (30.16)	26 (41.27)	18 (28.57)	45 (71.43)
χ^2			8.516		3.996
P			0.014		0.046

echocardiography (Philips Company, USA, model: PHILPS IU22). Left ventricular ejection fraction (LVEF), left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic diameter (LVEDD) and left atrial end-diastolic dimension (LADD) were measured.

Occurrence of adverse events

The incidence of adverse events, including malignant arrhythmia, recurrent myocardial infarction, sudden cardiac death, and intractable angina pectoris, was recorded during the 3 months of treatment.

Statistical methods

The data were analyzed using SPSS 17.0 statistical software. The continuous variables were expressed as mean ± standard deviation ($\bar{x}$ ± sd), and data conforming to normal distribution and homogeneity of variance were tested by independent sample t test. The counting data were represented by number of cases (n, %), and analyzed by Pearson chi-square test. Pearson correlation analysis was used to analyze the linear correlation between two variables. P<0.05 indicated a statistically significant difference.

Results

Comparison of general and baseline data

One patient in the control group withdrew from the study due to loss of follow-up. There was no significant difference in general data and baseline data between the two groups, indicating comparability (P>0.05). See **Table 1**.

Comparison of efficacy

Comparison of the efficacy between the two groups showed that there were statistical differences in the number of markedly effective, effective and ineffective cases (P<0.05). The total effective rate of the observation group was significantly higher than that of the control group (85.94% vs 71.43%, P<0.05). See **Table 2**.

Comparison of Hcy and NLR before and after treatment

There were no significant differences in Hcy and NLR between the two groups before treatment (P>0.05). After treatment, Hcy and NLR decreased significantly in both groups (P<0.05 or P<0.001), and the decrease was more significant in the observation group (P<0.001). See **Table 3**.

Correlation between Hcy and NLR in CHD patients before PCI

A correlation study between Hcy and NLR in CHD patients before PCI treatment identified

Table 3. Comparison of Hcy and NLR before and after treatment ($\bar{x}$ ± sd)

Group	Hcy (mg/L)	NLR (%)
Before treatment		
Observation group (n=64)	16.23±2.76	4.23±2.13
Control group (n=63)	16.43±3.12	4.32±2.09
After treatment		
Observation group (n=64)	8.34±1.51$^{***,\#\#\#}$	2.17±1.89$^{***,\#\#\#}$
Control group (n=63)	14.23±2.54*	3.23±2.12***

Note: Compared with the same group before treatment, *P<0.05; ***P<0.001; Compared with the control group after treatment, $^{\#\#\#}$P<0.001. NLR: neutrophil-to-lymphocyte ratio; Hcy: homocysteine.

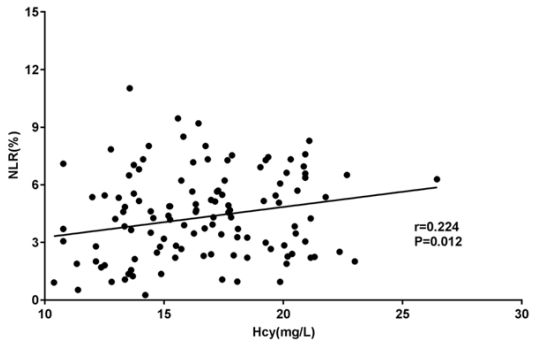

Figure 1. Correlation between Hcy and NLR in CHD patients before PCI. NLR: neutrophil-to-lymphocyte ratio; Hcy: homocysteine.

that the two were positively correlated (r=0.224, P=0.012). See **Figure 1**.

Comparison of cardiac function indexes before and after PCI treatment

The pre-treatment LVEF, LVESD, LVEDD and LADD did not differ between the two groups (P>0.05). After treatment, LVEF increased significantly (P<0.01 or P<0.001), while LVESD, LVEDD and LADD reduced significantly in both groups (P<0.01 or P<0.001), and the improvement was more obvious in the observation group (P<0.01 or P<0.001). See **Table 4**.

Comparison of incidence of adverse events

The incidence of adverse events was found to be lower in the observation group than in the control group, with a statistical difference (P<0.05). See **Table 5**.

Discussion

Platelet activation plays a crucial role in the occurrence and development of CHD, which is particularly true after the rupture of coronary artery plaque, so the use of anti-platelet drugs for treatment before and after PCI is of the essence for improving the prognosis of patients [20, 21]. Some studies have shown that clopidogrel resistance occurs in some patients as it is metabolized by liver enzymes and affected by CYP2C19 gene polymorphism [7, 8]. As a new type of anticoagulant, ticagrelor not only acts rapidly with strong anti-platelet effect, but is not affected by CYP2C19 gene polymorphism, and meanwhile, it is capable of dilating coronary arteries without liver enzyme metabolism [22]. And some reports have indicated that the therapeutic effect of ticagrelor is more significant than clopidogrel [23]. This study also found that ticagrelor was more effective in the treatment of CHD patients with unstable angina pectoris after PCI, which was consistent with the preceding research.

Increased Hcy is an important factor in the occurrence and development of CHD, which can damage the function of vascular cells in the body, and stimulate vascular smooth muscle and promote its proliferation, resulting in activation of platelets, imbalance of coagulation-fibrinolysis system, and eventually lead to atherosclerosis in the arteries and the occurrence of CHD [24, 25]. There is also evidence suggesting that there was a positive correlation between Hcy and the degree of coronary artery lesions [26]. Previously, it was reported that chronic inflammation was vital in the formation of atherosclerotic plaques [27]. NLR, a novel indicator of inflammation, was reported in a study that the elevation of myocardial injury markers in the low NLR group was lower than that in the high NLR group of patients with coronary artery disease undergoing PCI, and further a positive correlation was identified between NLR and CK-MB [17]. Also, research suggests that NLR can be used as an evaluation indicator for the long-term prognosis of patients with acute coronary syndrome after PCI [28], and is essential in the occurrence and development of other heart diseases [29-31]. Ticagrelor plays a certain anti-inflammatory role in the human body and promotes the release of adenosine, which, by binding to receptors, can facilitate carbon monoxide to act on coronary arteries and dilate them [32]. This study showed

Table 4. Comparison of cardiac function indexes before and after PCI treatment ($\bar{x} \pm sd$)

Group	LVEF (%)	LVESD (mm)	LVEDD (mm)	LADD (mm)
Before treatment				
Observation group (n=64)	34.62±8.56	42.98±10.72	52.63±16.02	42.65±10.54
Control group (n=63)	34.94±8.78	43.06±10.95	53.02±16.15	42.78±10.98
After treatment				
Observation group (n=64)	47.32±12.32$^{***,\#\#\#}$	33.98±7.62$^{***,\#\#\#}$	40.06±7.62$^{***,\#\#\#}$	30.82±7.89$^{***,\#\#}$
Control group (n=63)	41.21±9.69**	37.49±9.01***	45.78±10.32***	35.69±8.23**

Note: Compared with the same group before treatment, **P<0.01; ***P<0.001; Compared with the control group after treatment, $^{\#\#}$P<0.01; $^{\#\#\#}$P<0.001. LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVEDD: left ventricular end-diastolic diameter; LADD: left atrial diameter.

Table 5. Comparison of incidence of adverse events (n, %)

Group	Observation group (n=64)	Control group (n=63)	χ^2	P
Number of cases	64	63		
Malignant arrhythmia	1 (1.56)	1 (1.59)		
Myocardial infarction occurs again	1 (1.56)	2 (3.17)		
Sudden cardiac death	1 (1.56)	4 (6.35)		
Intractable angina	2 (3.13)	6 (9.52)		
Total number of cases	5 (7.81)	13 (20.63)	4.291	0.032

that the anticoagulant therapy composed of ticagrelor and aspirin reduced the Hcy level and NLR, which may be related to the anti-inflammatory effect and potent anticoagulant and anti-platelet aggregation of ticagrelor to prevent thrombosis. Further study revealed that Hcy was positively associated with NLR. Similar to our findings, previous studies showed that the higher the NLR, the more serious the coronary artery disease was [17], and there was a positive correlation between Hcy and the degree of coronary artery disease [26], which confirmed a positive correlation between NLR and Hcy.

By reviewing previous studies, we found that the NLR of patients undergoing PCI was negatively correlated with LVEF [17]. Another study suggested that NLR was significantly increased in patients with acute coronary syndrome when the LVEF value was less than 50%, suggesting that the higher the NLR level, the more severe the myocardial injury, the decreased cardiac function, and the more prone to the left ventricular dysfunction. In this study, the improvement of left ventricular function in patients treated with ticagrelor was superior to those treated with clopidogrel, which may be related to ticagrelor's anti-inflammatory effect to reduce NLR and improve left ventricular function of patients.

According to some researches, monitoring the NLR of patients with acute coronary syndrome can predict their long-term prognosis and the occurrence of adverse events. The lower the NLR, the better the prognosis is and the lower the incidence of adverse events [33]. Studies have shown that when the NLR value is 3.39, it predicts the 2-year all-cause mortality and the incidence of adverse events in patients with acute coronary syndrome with a sensitivity of 70% and a specificity of 77% [34]. Another study showed that NLR can also predict all-cause mortality and cardiogenic death after PCI in patients with stable coronary artery disease [35]. In this study, the incidence of adverse events in patients treated with ticagrelor combined with aspirin after PCI was lower than that intervened by clopidogrel and aspirin, which was related to the ticagrelor-induced reduction of NLR and the resulting decline of incidence of adverse events in patients.

Deficiency and prospect: As a single-center study with a small sample size, this study can be further expanded by multicenter randomized controlled trial in future studies. In addition, the short follow-up time in this study can be further increased to observe the 2-year all-cause mortality of patients and the incidence of adverse events.

To sum up, ticagrelor combined with aspirin exert marked effects on patients undergoing

PCI, and can reduce Hcy and NLR, improve left ventricular function with a low incidence of adverse events, which is worthy of clinical promotion.

Disclosure of conflict of interest

None.

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References

[1] Chen WW, Gao RL, Liu LS, Zhu ML, Wang W, Wang YJ, Wu ZS, Li HJ, Gu DF, Yang YJ, Zheng Z, Jiang LX and Hu SS. China cardiovascular diseases report 2015: a summary. J Geriatr Cardiol 2017; 14: 1-10.

[2] Cardi T, Kayali A, Ristorto J and Morel O. Prognostic value of incomplete revascularization after PCI following acute coronary syndrome. Focus on CKD patients. Arch Cardiovasc Dis Suppl 2018; 10: 21-22.

[3] Zhao S, Tang Y, Cai HR, Liu WF, Zhang LY, Chen DJ and Chen BJ. Treatment of danhong injection combined with naoxintong capsule in acute coronary syndrome patients undergoing PCI operation: study for a randomized controlled and double-blind trial. Evid Based Complement Alternat Med 2018; 8485472.

[4] Mahmood MM, Qureshi MA, Morley R, Austin D, Carter J, de Belder MA, Hall JA, Muir DF, Swanson N, Sutton AGC, Williams P and Wright RA. 27 Use of rotational atherectomy in primary pci for st-elevation myocardial infarction- a single centre 10-year experience. Heart 2017; 103 Suppl 5: A22-A23.

[5] Dong Z and Zheng JG. Anticoagulation after coronary stenting: a systemic review. Br Med Bull 2017; 123: 79-89.

[6] Deharo P, Rahbi H and Cuisset T. Optimizing adjunctive antithrombotic and anticoagulant therapy in primary PCI for STEMI. Minerva Cardioangiol 2017; 64: 238-255.

[7] Amabile N, Malergue MC, Achkouty G, Czitrom D and Caussin C. How to detect myocardial ischemia in patients following acute coronary syndrome treated by PCI. Presse Med 2017; 46: 719-723.

[8] Antoniou S, Colicchia M, Guttmann OP, Rathod KS, Wright P, Fhadil S, Knight CJ, Jain AK, Smith EJ, Mathur A, Weerackody R, Wragg A and Jones DA. Risk scoring to guide anti-platelet therapy post percutaneous coronary intervention (PCI) for acute-coronary syndrome (ACS) results in improved clinical outcomes. Eur Heart J Qual Care Clin Outcomes 2018; 14: 283-289.

[9] Khayata M, Gabra JN, Nasser MF, Litman GI, Bhakta S and Raina R. Comparison of clopidogrel with prasugrel and ticagrelor in patients with acute coronary syndrome: clinical outcomes from the national cardiovascular database ACTION registry. Cardiol Res 2017; 8: 105-110.

[10] Rezaei SS, Geroldinger A, Heinze G, Reichardt B and Wolzt M. Clopidogrel, prasugrel, or ticagrelor use and clinical outcome in patients with acute coronary syndrome: a nationwide long-term registry analysis from 2009 to 2014. Int J Cardiol 2017; 235: 61-66.

[11] Döring Y, van der Vorst EPC, Duchene J, Jansen Y, Gencer S, Bidzhekov K, Atzler D, Santovito D, Rader DJ, Saleheen D and Weber C. CXCL12 derived from endothelial cells promotes atherosclerosis to drive coronary artery disease. Circulation 2019; 139: 1338-1340.

[12] Titov VN, Rozhkova TA, Kaminnaya VA and Alchinova IB. Atherosclerosis and atheromatosis are consequtive metabolic disordes. Pathology of the biological functions of trophology and endoecology is the basis for ischemic heart diseaseprevention. Klin Lab Diagn 2018; 63: 196-204.

[13] Nian SY, Feng L, Zhao Y, Luo F, Zhang S, Li D, Xu WB, Zhang XF, Ye D and Bai XJ. Combination of susceptibility gene and traditional risk factors might enhance the performance ofcoronary heart disease screening strategy. Oncotarget 2017; 8: 69005-69011.

[14] Elyasinia F, Keramati MR, Ahmadi F, Rezaei S, Ashouri M, Parsaei R, Yaghoubi M, Elyasinia F, Aboutorabi A and Kaviani A. Neutrophil-lymphocyte ratio in different stages of breast cancer. Acta Med Iran 2017; 55: 228-232.

[15] Ethier JL, Desautels D, Templeton A, Shah PS and Amir E. Prognostic role of neutrophil-to-lymphocyte ratio in breast cancer: a systematic review and meta-analysis. Breast Cancer Res 2017; 19: 2.

[16] Diniz LR, de Lima SG, de Amorim Garcia JM and de Oliveira Diniz KL. Neutrophil to lymphocyte ratio as a prognostic predictor in older people with acute coronary syndrome. Angiology 2018; 3319718796565.

[17] Chen C, Cong BL, Wang M, Abdullah M, Wang XL, Zhang YH, Xu SJ and Cui L. Neutrophil to lymphocyte ratio as a predictor of myocardial damage and cardiac dysfunction in acute coronary syndrome patients. Integr Med Res 2018; 7: 192-199.

[18] Wang B, Li Y and Han YL. Guidelines for the diagnosis and treatment of stable coronary

heart disease. Chin J Cardiol 2018; 46: 680-694.
[19] Zheng XY. Guiding Principles of Clinical Research on New Drugs of Traditional Chinese Medicine (Trial). Beijing: Chin Med Sci Technol Press 2002; 29-35.
[20] Sibbing D, Aradi D, Jacobshagen C, Gross L, Trenk D, Geisler T, Orban M, Hadamitzky M, Merkely B, Kiss RG, Komócsi A, Dézsi CA, Holdt L, Felix SB, Parma R, Klopotowski M, Schwinger RHG, Rieber J, Huber K, Neumann FG, Koltowski L, Mehilli J, Huczek Z and Massberg S; TROPICAL-ACS Investigators. Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention (TROPICAL-ACS): a randomised, open-label, multicentre trial. Lancet 2017; 390: 1747-1757.
[21] Wilson SJ, Newby DE, Dawson D, Irving J and Berry C. Duration of dual antiplatelet therapy in acute coronary syndrome. Heart 2017; 103: 573-580.
[22] Goto S, Huang CH, Park SJ, Emanuelsson H and Kimura T. Ticagrelor vs. clopidogrel in Japanese, Korean and Taiwanese patients with acute coronary syndrome--randomized, double-blind, phase III PHILO study. Circ J 2015; 79: 2452-2460.
[23] Zhong ZX, Hou JY, Zhang QF, Li B, Li CR, Liu ZD, Yang M, Zhong W, He XB, Wu HS, Zhong MC and Zhao PS. Effect of cytochrome P450 2C19 polymorphism on adverse cardiovascular events after drug-eluting stent implantation in a large Hakka population with acute coronary syndrome receiving clopidogrel in southern China. Eur J Clin Pharmacol 2018; 74: 423-431.
[24] Feng C, Ji T, Liu Y, Chen DF, Dai J, Ni XS, Zhu JQ, Liu XB and Zhao XX. Role of depression in secondary prevention of Chinese coronary heart disease patients receiving percutaneous coronary intervention. PLoS One 2017; 12: e0187016.
[25] Burge MR, Eaton RP, Comerci G, Cavanaugh B, Ramo B and Schade DS. Management of asymptomatic patients with positive coronary artery calcium scans. J Endocr Soc 2017; 1: 588-599.
[26] Piccolo R, Franzone A and Pilgrim T. Coronary artery disease and myocardial revascularization in patients undergoing transcatheter aortic valve replacement. J Thorac Dis 2017; 9: 4219-4221.
[27] Budzianowski J, Pieszko K, Burchardt P, Rzeźniczak J and Hiczkiewicz J. The role of hematological indices in patients with acute coronary syndrome. Dis Markers 2017; 2017: 3041565.
[28] Zhang S, Diao J, Qi CM, Jin JJ, Li L, Gao XJ, Gong L and Wu WH. Predictive value of neutrophil to lymphocyte ratio in patients with acute ST segment elevation myocardial infarction after percutaneous coronary intervention: a meta-analysis. BMC Cardiovasc Disord 2018; 18: 75.
[29] Wan GX, Ji LH, Xia WB, Cheng L and Zhang YG. Screening genes associated with elevated neutrophil-to-lymphocyte ratio in chronic heart failure. Mol Med Rep 2018; 18: 1415-1422.
[30] Berkovitch A, Younis A, Grossman Y, Segev S, Kivity S, Sidi Y, Beinart R, Goldenberg I and Maor E. Relation of neutrophil to lymphocyte ratio to risk of incident atrial fibrillation. Am J Cardiol 2019; 123: 396-401.
[31] Khalil C, Pham M, Sawant AC, Sinibaldi E, Bhardwaj A, Ramanan T, Qureshi R, Khan S, Ibrahim A, Gowda SN, Pomakov A, Sadawarte P, Lahoti A, Hansen R, Baldo S, Colern G, Pershad A and Iyer V. Neutrophil-to-lymphocyte ratio predicts heart failure readmissions and outcomes in patients undergoing transcatheter aortic valve replacement. Indian Heart J 2018; 70 Suppl 3: S313-S318.
[32] Watti H, Dahal K, Zabher HG, Katikaneni P, Modi K and Abdulbaki A. Comparison of prasugrel and ticagrelor in patients with acute coronary syndrome undergoing percutaneous coronary intervention: a meta-analysis of randomized and non-randomized studies. Int J Cardiol 2017; 249: 66-72.
[33] Dong CH, Wang ZM and Chen SY. Neutrophil to lymphocyte ratio predict mortality and major adverse cardiac events in acute coronary syndrome: a systematic review and meta-analysis. Clin Biochem 2018; 52: 131-136.
[34] Xu N, Tang XF, Yao Y, Zhao XY, Chen J, Gao Z, Yang YJ, Gao RL, Xu B and Yuan JQ. Predictive value of neutrophil to lymphocyte ratio in long-term outcomes of left main and/or three-vessel disease in patients with acute myocardial infarction. Catheter Cardiovasc Interv 2018; 91: 551-557.
[35] Wada H, Dohi T, Miyauchi K, Shitara J, Endo H, Doi S, Konishi H, Naito R, Tsuboi S, Ogita M, Kasai T, Hassan A, Okazaki S, Isoda K, Suwa S and Daida H. Pre-proceduralneutrophil-to-lymphocyte ratio and long-term cardiac outcomes after percutaneous coronary intervention for stable coronary artery disease. Atherosclerosis 2017; 265: 35-40.