

The changes of autonomic nervous function in coronary heart disease patients >60 years old with normotension and hypertension: an observational study

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Abstract

AIM The aim of our observational research was to make an in-depth analysis of the autonomic function in normotension and hypertensive patients over 60 years old with coronary artery disease. **Method** 104 patients over 60 years old with coronary heart disease (CHD) were divided into normotension group and hypertension (HT) group. 24-hour Holter monitoring was carried out to assess the autonomic function. **Result** Among the 104 patients analyzed, 52 patients had coronary heart disease with normotension, and 52 had coronary heart disease with hypertension. The 24-Holter results of time-domain methods showed that values from time-domain parameters for heart rate variability (HRV) were significantly lower in coronary heart disease patients with hypertension than coronary heart disease group. Furthermore, both during the daytime and during the nighttime, the time-domain parameters were significantly lower in coronary heart disease patients with hypertension than coronary heart disease group. We found there was no difference in autonomic function during the daytime and during the nighttime in their own group. Values from frequency-domain parameters for HRV were also significantly lower in CHD patients with hypertension than CHD group. More patients in the CHD+HT group than in the CHD group received the percutaneous coronary intervention (57.69% vs. 50% $\chi^2=0.619$, $p=0.55$). Through the 12 months of follow-up, we found no significant difference in rehospitalization for unstable angina and target lesion revascularization between CHD patients with normotension and CHD patients with hypertension. **Conclusion** The dysfunction of heart autonomic nervous in CHD patients over 60 years old with hypertension was more serious than CHD patients with normotension, and more clinical attention should be aroused.

Keywords:

Heart rate variability; coronary heart disease; hypertension; time-domain methods; frequency-domain methods

Introduction

In 1898, John Newport Langley first proposed the term “autonomic nervous system,” suggesting actions of the sympathetic and parasympathetic components.¹ Dysfunction of the autonomic nervous system tends primarily to affect the sympathetic nervous system.² Autonomic dysfunction is related to many kinds of pathological changes, including cardiovascular

disease, hypertension, hyperglycemia, high triglycerides, low high-density lipoprotein cholesterol, high body mass index, incident diabetes, and increased cardiovascular mortality. Heart rate variability (HRV) is regarded as a noninvasive electrocardiographic measure of autonomic function. Heart rate variability is a specific marker of autonomic nervous system (ANS) function, both sympathetic and parasympathetic. Cardiovascular authority commonly divide HRV measures into time-domain measurements and frequency-domain measurements.² Time-domain estimates are obtained by 24-hour directly from the patient's heart rate or the duration between successive RR intervals. Frequency-domain measures are calculated 24-hour from spectral imaging of the electrocardiology (ECG) recording. The time-domain HRV parameters included the following indicators: standard deviation of all normal to normal NN intervals (SDNN), the standard deviation of all mean 5-minute NN intervals (SDANN), mean of the standard deviation of all NN intervals for all 5-min segments of 24 hour (SDNN index), the root mean square of successive differences between adjacent normal cycles (RMSSD), percent of NN50 in the total number of NN intervals (PNN50).² Additionally, frequency-domain HRV parameters included the following indicators: low frequency (LF), high frequency (HF), LF/HF.² We found that coronary heart disease patients over 60 years old in our hospital are usually accompanied by hypertension. However, there are few clinical types of research in this field. Thus, it is necessary to better understand whether there is a significant association between circadian rhythms of autonomic nervous and coronary heart disease patients with hypertension vs. Those without hypertension. Therefore, our observational research aimed to evaluate the relationship between HRV and CHD patients over 60 years old with normotension and with hypertension. Furthermore, we also observe the autonomic nervous circadian rhythm change in each group.

Methods

Patients and ethics

We analyzed 104 consecutive patients (72.81 ± 6.72 years old) who had performed 24-hour Holter recordings after hospitalization in the first affiliated hospital of university of science and technology of China between JAN 1, 2019, and JAN 1, 2021. Key enrollment criteria were as follows: (1) Age >60 years, (2) Signed informed consent, (3) guideline-appropriate diagnosis for coronary heart disease, **(4) The patients had a past history of myocardial infarction or had undergone coronary angiography or coronary CT angiography to definitively diagnose coronary heart disease before this admission included.** **(5) Patients underwent coronary angiography or coronary CT angiography to definitively diagnose coronary heart disease during this patient's admission to the hospital.** **(6) guideline-appropriated diagnosis for hypertension.** Exclusion criteria were as follows: (1) Patients with adult congenital heart disease, (2) Patients with arrhythmia including atrial fibrillation, atrial flutter, pacing rhythm, paroxysmal supraventricular tachycardia, (3) hyperthyroidism or hypothyroidism, (4) heart failure, (5) depression or anxiety, (6) liver or kidney dysfunction, (7) malignant tumor, (8) diabetes mellitus, (9) information is not complete, et al.

Measurement of heart rate variability

Cardiovascular authority commonly divide HRV measures into time-domain and frequency-domain measurements. Time-domain estimates are obtained by 24-hour directly from the patient's heart rate or the duration between successive RR intervals. Frequency-domain

measures are obtained by 24-hour from spectral imaging of the ECG recording. The following time-domain HRV parameters were selected based on the suggestions of the Task Force and frequency of reporting: standard deviation of all normal to normal NN intervals (SDNN), the standard deviation of all mean 5-minute NN intervals (SDANN), mean of the standard deviation of all NN intervals for all 5-min segments of 24 hour (SDNN index), the root mean square of successive differences between adjacent normal cycles (RMSSD), percent of NN50 in the total number of NN intervals (PNN50). Additionally, we examined one frequency-domain measure: low frequency (LF), high frequency (HF), LF/HF were statistically recorded and analyzed. Furthermore, we analyze time-domain parameters not only during the daytime but also during the nighttime. The enrolled patients were required to avoid intense physical exercise, drinking alcohol, and smoking. They were recommended to cease movement at 10 p.m. and sleep till 6 a.m. ALL the examinations were performed in our hospital settings to limit the influences of other confounding factors, such as work stress and diet.

Clinical patient follow-up

The follow-up was 12 months for enrolled patients or until a fatal event occurred. Follow-up data were collected from patients by electronic medical records or telephone interviews. We used a mailed questionnaire if the patient could not obtain the telephone interview. The primary endpoint was cardiac death. The secondary endpoints included the recurrence of unstable angina and rehospitalization for target lesion revascularization (TLR). The methods applied follow the standard and procedure of the First Affiliated Hospital of the University of Science and Technology of China. They included data collection and follow-up under approval by the institutional review board. The local ethics committees approved our observational study, and enrolled patients signed the informed consent.

Statistical analysis

We expressed the continuous variable as mean and standard deviation. We analyze the data using a Student's *t*-test if applicable. Discrete variables and χ^2 test. We used the Shapiro-Wilk test to detect the normality of the data. All statistical tests are two-sided with a significance level of <0.05. All statistical analysis is performed using SPSS software, version 23.0 (SPSS, Inc., Chicago, IL).

Results

Between JAN 1, 2019, and JAN 1, 2021, 104 patients > 60 years old with coronary heart disease were divided into the normotension group (Group 1) and hypertension group (Group 2) in our hospital enrolled. Of the 104 subjects in our observational study, 65 were males. For enrolled patients, the male: female ratio is 1.67:1. The mean age was 72.81 years (SD 6.72). According to the obtained data (Table I), statistical analysis revealed that there was not a statistical difference in age, diastolic blood pressure (DBP), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) in these two groups. All patients followed 24-hour ambulatory electrocardiography to assess any arrhythmias, HRV, and minimum, mean, and maximum heart rate.

The 24-hour Holter results of time-domain methods showed that SDNN (117.96 ± 27.56 vs. 74.75

± 16.92 , $p < 0.05$), SDANN (98.94 ± 28.40 vs. 64.79 ± 14.78 , $p < 0.05$), SDNN index (54.19 ± 17.76 vs. 32.94 ± 11.53 , $p < 0.05$), RMSSD (38.48 ± 28.90 vs. 24.02 ± 13.08 , $p < 0.05$), PNN50 (8.66 ± 11.09 vs. 4.15 ± 5.64 , $p < 0.05$) were significantly lower in CHD patients with hypertension than CHD with normotension group. Furthermore, during the daytime, Holter monitoring showed that SDNN (88.12 ± 25.94 vs. 57.25 ± 16.73 , $P < 0.05$), SDANN (65.19 ± 22.79 vs. 45.21 ± 15.23 , $P < 0.05$), SDNN index (52.21 ± 23.09 vs. 31.02 ± 10.88 , $P < 0.05$), RMSSD (38.17 ± 35.05 vs. 23.13 ± 12.44 , $P < 0.05$), PNN50 (8.91 ± 14.57 vs. 4.02 ± 5.78 , $P < 0.05$), TINN (327.92 ± 112.91 vs. 211.89 ± 70.89 , $P < 0.05$) were significantly lower in CHD patients with hypertension than CHD with normotension group. During the nighttime, Holter monitoring also showed that SDNN (91.98 ± 26.27 vs. 59.96 ± 18.84 , $P < 0.05$), SDANN (60.81 ± 17.77 vs. 44.35 ± 17.19 , $P < 0.05$), SDNN index (59.83 ± 21.73 vs. 35.25 ± 13.65 , $P < 0.05$), RMSSD (39.19 ± 26.56 vs. 23.98 ± 13.99 , $P < 0.05$), PNN50 (9.65 ± 10.24 vs. 4.46 ± 7.12 , $P < 0.05$), TINN (290.73 ± 99.96 vs. 207.19 ± 63.91 , $P < 0.05$) were significantly lower in CHD patients with hypertension than CHD with normotension group. We also point out there was no difference in autonomic function during the daytime and during the nighttime in each own group ($P > 0.05$). The 24-hour Holter recordings of frequency-domain methods showed that LF (453.33 ± 565.76 vs. 141.00 ± 143.32 , $P < 0.05$), HF (462.26 ± 902.38 vs. 179.88 ± 196.99 , $P < 0.05$), LF/HF (1.34 ± 0.77 vs. 0.96 ± 0.62 , $P < 0.05$) were also significantly lower in CHD patients with hypertension than CHD with normotension group.

The patients presented with precordial discomforts, such as chest tightness and pain. Among the 102 patients analyzed, 56 patients underwent percutaneous coronary intervention. **In the CHD+HT group, 5 patients only underwent coronary angiography, and 30 patients underwent both coronary angiography and percutaneous coronary intervention during this hospitalization. In the CHD group, 16 patients only underwent coronary angiography, and 26 patients underwent coronary angiography and percutaneous coronary intervention during this hospitalization.** More patients in the CHD+HT group than in the CHD group received PCI (57.69% vs. 50% , $\chi^2 = 0.619$, $p = 0.55$), although the result was not statistically significant. Among the 104 patients analyzed, all the patients completed 12 months of follow-up. Through the 12 months of follow-up, no patient had cardiac death; 21 patients (20.19% , $21/104$) had rehospitalization for unstable angina. Furthermore, we found no significant difference in rehospitalization for unstable angina between CHD patients with normotension and CHD patients with hypertension ($10/52$ vs. $11/52$, $\chi^2 = 0.06$, $p = 0.81$). Among the 21 patients, 33.3% ($7/21$) followed target lesion revascularization. Meanwhile, there was no significant difference in target lesion revascularization between CHD patients with normotension and CHD patients with hypertension ($3/52$ vs. $4/52$, $\chi^2 = 0.153$, $p = 0.69$).

Discussion

Our observational clinical study included 104 patients with coronary heart disease following the 24-Holter monitoring. Among the 104 patients enrolled, 52 patients had coronary heart disease with normotension, and 52 had coronary heart disease with hypertension. The results showed that values from time-domain parameters (e.g., SDNN, SDANN, SDNN index, rMSSD, pNN50) for heart rate variability (HRV) were significantly lower in CHD patients with hypertension than CHD patients with normotension. Furthermore, both during the daytime and during the

nighttime, the time-domain parameters (e.g., SDNN, SDANN, SDNN index, rMSSD, pNN50) were significantly lower in CHD patients with hypertension than CHD group. We found there was no difference in autonomic function during the daytime and the nighttime in their own group. Values from frequency-domain parameters (e.g., LF, HF, LF/HF) for HRV were also significantly lower in CHD patients with hypertension than CHD group. More patients in the CHD+HT group than in the CHD group received the percutaneous coronary intervention (57.69% vs. 50% $\chi^2=0.619$, $p=0.55$), although the result was not statistically different. Moreover, through the 12 months of follow-up, we found no significant difference in rehospitalization for unstable angina and TLR between CHD patients with normotension and CHD patients with hypertension. HRV is considered as a noninvasive measure of the variability in the intervals between subsequent heartbeats and the indicator of the balance between sympathetic and parasympathetic modulation of the heart³⁻⁶. The effect of sympathetic influence on heart rate (HR) is mediated by neurotransmitter release, such as norepinephrine and epinephrine. Activation of β -adrenergic receptors results in cyclic AMP-mediated phosphorylation of the membrane proteins and increased calcium ion flux and pacemaker current (I_f)⁷⁻⁹. The final result is an increased slow diastolic depolarization. The parasympathetic influence on HR is mediated through the release of acetylcholine by the parasympathetic nerve. Then, the Muscarinic acetylcholine receptors will increase in cell membrane K^+ conductance¹⁰. Acetylcholine also inhibits the hyperpolarization-activated I_f ⁹. Autonomic dysfunction can be associated with various pathological conditions, including cardiovascular disease, high blood pressure, and high mortality et al¹²⁻¹⁷. HRV is quantified by parameters calculated from ECG data to evaluate how successfully an individual's ANS exerts a force on the heart, as indicated by the variations in time intervals between each heartbeat¹⁸. HRV data collection is noninvasive, relatively easy, and inexpensive, making it a popular and valuable tool for evaluating autonomic modulation.

Firstly, HRV measures are commonly classified into time-domain and frequency-domain measurements. In the time-domain parameters, SDNN is generally regarded as a measure of "global HRV". It indicates all cyclic components that participate in temporal variations of heartbeats¹⁹. It is essential to point out that SDNN is a measure of the total variance. In our study, the 24-Hour Holter recordings and the daytime/nighttime Holter recordings of SDNN were obvious lower in CHD patients with hypertension than in the normotension group. We concluded that the total variance decreased in CHD patients over 60 years old with hypertension compared with the normotension group. Lower HRV is closely related to a higher risk of cardiovascular events and mortality^{3,6,14}. Fang completed a meta-analysis of 28 cohort studies involving 2094 participants to analyze the relationship between HRV and cardiovascular events or the risk of all-cause death in patients with cardiovascular disease during a follow-up of at least one year²⁰. Results showed that low HRV was closely related to cardiovascular events and a higher risk of all-cause death. Previous findings reveal that patients with postmyocardial infarction syndrome with a lower standard deviation of all normal-to-normal HRV intervals (SDNN) were nearly four times to die during the subsequent three years compared to those with a higher standard deviation²¹. According to the results of SDNN (74.75 ± 16.92) in CHD patients with hypertension, we should follow up this group of patients closely. Secondly, SDANN is the standard deviation of all mean 5-minute NN intervals²³⁻²⁴. SDANN reflects the change of sympathetic tension, and the value of SDANN is negatively correlated with sympathetic activity. That is, the decrease of SDANN

mainly indicates the increase of sympathetic activity. In our study, both the 24-hour Holter recordings and the daytime/nighttime Holter recordings of SDANN were significantly lower in CHD patients with hypertension than in the normotension group. So, we concluded that increased sympathetic activity in CHD patients over 60 years old with hypertension compared with the normotension group. Fantoni found that SDANN can be a well-established marker to evaluate cardiac resynchronization treatment in patients with heart failure. The results of SDANN also pointed out that we should pay more attention to CHD patients with hypertension. Thirdly, RMSSD is calculated by taking the square root of the mean of the squared differences between consecutive NN intervals. PNN50 presents the proportion of NN50 divided by the whole number of normal QRS complexes (i.e., $NN50/NN$). Both RMSSD and PNN50 reflect the change of parasympathetic tone. Their values are positively correlated with parasympathetic activity. That is, the decrease of RMSSD and pNN50 indicates the decrease of parasympathetic activity. In our study, both the 24-hour Holter recordings and the daytime/nighttime Holter recordings of RMSSD and PNN50 decreased in CHD patients with hypertension than the normotension group. So, we concluded that decrease in parasympathetic tone in CHD patients with hypertension compared with the normotension group. Fourthly, the triangular interpolation of the NN interval histogram (TINN), approximating the NN interval distribution, is the baseline width of the distribution. TINN is regarded as a measure of HRV. In our study, both the daytime and the nighttime Holter recordings of TINN were significantly decreased in CHD patients with hypertension than in the normotension group. These results also proved that HRV decreased in CHD patients > 60 years old with hypertension than the normotension group. Fifthly, The power variables widely applied to analyze HRV are LF and HF. Historically, LF oscillations were applied to assess sympathetic nervous system activation. Recently, the interpretation of LF oscillations was proven to be more complicated. It has been pointed out that both parasympathetic activation and sympathetic activation affect this oscillatory region. The result of LF was also significantly lower in CHD patients with hypertension than CHD with normotension group also pointed out dysfunction of sympathetic and parasympathetic function. High frequency indicates parasympathetic nervous system activation. The 24-hours Holter recordings of frequency-domain methods showed that HF was significantly lower in CHD patients with hypertension than CHD with the normotension group. The results of high frequency again proved the decreased parasympathetic tone. **Furthermore, the autonomic nervous system plays a crucial role in developing hypertension. The HRV was significantly lower in coronary heart disease patients with hypertension than in coronary heart disease with the normotension group. Lower levels of heart rate variability mean dysfunction of autonomic control. More patients in the CHD+HT group than in the CHD group received PCI (57.69% vs. 50%, $p=0.55$), although the result was not statistically significant. However, we found no significant difference in the outcome of follow-up. These results suggest early intervention treatment might improve patients' prognoses with seriously decreased HRV. The clinical utility of HRV as a means of the adequacy of therapy in secondary prevention, especially in coronary heart disease patients combined with hypertension, can improve the prognosis.**

Above all, from the result of the time-domain and frequency-domain, the dysfunction of heart autonomic in CHD patients > 60 years old with hypertension was more serious than in CHD patients > 60 years old without hypertension. From the relationship between the parameter of

HRV and ANS function, we conclude the increased activity of the sympathetic nervous and the decreased activity of the parasympathetic nervous. Furthermore, from the relationship between the parameter of HRV and the adverse event among the clinical patient follow-up, we can draw the conclusion that both the time-domain parameters and the frequency domain parameters of heart rate variability may be a target marker of dysfunction of the ANS in CHD patients with hypertension and more clinical attention should be aroused. It also suggested that more interventions are required to improve the prognosis in patients with abnormal heart rate variability.

Limitation

There might be limitations inherent in our study. Because age is a risk factor for CHD. We included patients are all over 60 years old. So we did not create a group as hypertensive patients without coronary artery disease. In our further research, we will include large number of patients and compare these three groups: CHD group, CHD group+hypertension group and hypertension group. We will deal with these problems in our future study.

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AUTHOR CONTRIBUTION

Jing-Xiu Li and Jing Wang contributed significantly to data collection and manuscript preparation. Bei-Bei Ding and Min Gao performed the analysis with discussion. All authors agree on the order in which their names will be listed in the manuscript.

CONFLICTS OF INTEREST

Founders did not play any role in this study design, data collection, analysis, the decision to publish, or preparation of the manuscript.

DATA AVAILABILITY STATEMENT

Data sharing does not apply to this article.

ETHICS STATEMENT

We identify that the ethics committee of The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China has approved the case and that this case conforms to recognized standards, the Declaration of Helsinki.

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REFERENCE

1. Maehle AH. "Receptive substances": John Newport Langley (1852-1925) and his path to a receptor theory of drug action. *Med Hist.* 2004;48(2):153-74.
2. Karim S, Chahal A, Khanji MY, Petersen SE, Somers VK. Autonomic Cardiovascular Control in

Health and Disease. *Compr Physiol.* 2023;13(2):4493-4511.

3. Huikuri H V, Stein P K. Heart rate variability in risk stratification of cardiac patients[J]. *Progress in cardiovascular diseases*, 2013, 56(2): 153-159.
4. Hon EH, Lee ST. Electronic evaluation of the fetal heart rate.VIII. Patterns preceding fetal death, further observations[J].*Am J Obstet Gynecol*, 1963, 87:814-826.
5. Kawano H, Okada R, Yano K. Histological study on the distribution of autonomic nerves in the human heart[J].*Heart Vessels*,2003,18(1):32-39.
6. Schiweck C, Piette D, Berckmans D, et al. Heart rate and high frequency heart rate variability during stress as biomarker for clinical depression. a systematic review[J].*Psychol Med*,2019,49(2):200-211.
7. Trautwein W, Kameyama M. Intracellular control of calcium and potassium currents in cardiac cells. *Jpn Heart J.* 1986;27 Suppl 1:31-50.
8. Brown HF, DiFrancesco D, Noble SJ. How does adrenaline accelerate the heart?. *Nature.* 1979;280(5719):235-236.
9. DiFrancesco D, Ferroni A, Mazzanti M, Tromba C. Properties of the hyperpolarizing-activated current (if) in cells isolated from the rabbit sino-atrial node. *J Physiol.* 1986;377:61-88.
10. Sakmann B, Noma A, Trautwein W. Acetylcholine activation of single muscarinic K⁺ channels in isolated pacemaker cells of the mammalian heart. *Nature.* 1983;303(5914):250-253.
11. DiFrancesco D, Tromba C. Muscarinic control of the hyperpolarization-activated current (if) in rabbit sino-atrial node myocytes. *J Physiol.* 1988;405:493-510.
12. Askin L, Cetin M, Turkmen S. Ambulatory blood pressure results and heart rate variability in patients with premature ventricular contractions[J]. *Clinical and Experimental Hypertension*, 2018, 40(3): 251-256.
13. Patel V N, Pierce B R, Bodapati R K, et al. Association of holter-derived heart rate variability parameters with the development of congestive heart failure in the cardiovascular health study[J]. *JACC: Heart failure*, 2017, 5(6): 423-431.
14. Wu L, Jiang Z, Li C, et al. Prediction of heart rate variability on cardiac sudden death in heart failure patients: a systematic review[J]. *International journal of cardiology*, 2014, 174(3): 857-860.
15. Moors S, Staaks KJJ, Westerhuis MEMH, et al. Heart rate variability in hypertensive pregnancy disorders: A systematic review. *Pregnancy Hypertens.* 2020;20:56-68.
16. Maciorowska M, Krzesiński P, Wierzbowski R, et al. Heart Rate Variability in Patients with Hypertension: the Effect of Metabolic Syndrome and Antihypertensive Treatment. *Cardiovasc Ther.* 2020;2020:8563135.
17. Vesela J, Osmancik P, Herman D, et al. Changes in heart rate variability in patients with atrial fibrillation after pulmonary vein isolation and ganglionated plexus ablation. *Physiol Res.* 2019;68(1):49-57.
18. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology[J].*Circulation*,1996,93(5):1043-1065.
19. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology[J]. *Eur Heart J.* 1996;17(3):354-381.
20. Fang SC, Wu YL, Tsai PS. Heart rate variability and risk of all-cause death and cardiovascular events in patients with Cardiovascular disease: a Meta-analysis of cohort studies[J].*Biol Res*

Nurs,2020,22(1):45-56.

21. Goldenberg I, Goldkorn R, Shlomo N, et al. Heart Rate Variability for Risk Assessment of Myocardial Ischemia in Patients Without Known Coronary Artery Disease: The HRV-DETECT (Heart Rate Variability for the Detection of Myocardial Ischemia) Study. J Am Heart Assoc. 2019 17;8(24):e014540.

22. Li Jingxiu, Zhang Fujun and Wei Xijin et al. Using Three-Dimensional Lorenz Scatter Plots to Detect Patients with Atrioventricular Node Double Path Caused by Interpolated Ventricular Premature Systoles: A Case Study. CVIA. Vol. 5(4):301-306.

23. Jing-xiu Li, Ling Weng and Xue-qi Li et al. An Observational Study of the Relationship Between Outcome and Platelet Reactivity in Chinese Patients Undergoing PCI Loading with 600 mg Clopidogrel. CVIA. Vol. 5(1):27-35.

24. Bai X, Li J, Zhou L, Li X. Influence of the menstrual cycle on nonlinear properties of heart rate variability in young women. Am J Physiol Heart Circ Physiol. 2009;297(2):H765-H774.

Table1. Baseline characteristics of the included patients enrolled in this study (n=104)

| | Group 1 | Group 2 | T-test/ χ^2 test | P 值 |
|-------------|--------------|--------------|--------------------------|-------|
| male (n,%) | 39 (75 %) | 26 (50%) | 6.93 | 0.015 |
| age (year) | 72.31±6.59 | 73.33±6.88 | 0.772 | 0.442 |
| SBP (mmHg) | 129.37±14.97 | 137.46±21.47 | 2.231 | 0.028 |
| DBP (mmHg) | 78.17±10.25 | 80.54±12.24 | 1.068 | 0.288 |
| TC (mmol/L) | 4.26±1.09 | 4.23±1.09 | 0.116 | 0.908 |
| TG (mmol/L) | 1.53±1.59 | 1.57±0.84 | 0.159 | 0.874 |
| HDL-C | 1.09±0.24 | 1.05±0.26 | 0.952 | 0.343 |
| LDL-C | 2.32±0.81 | 2.32±0.87 | 0.007 | 0.994 |

Group 1: patients over 60 years old in coronary heart disease with normotension. Group 2: patients over 60 years old in coronary heart disease with hypertension. SBP: systolic blood pressure, diastolic blood pressure (DBP), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C)

Table 2: Time-domain HRV parameters during 24-hour in coronary heart disease patients with normotension and hypertension

| | N | SDNN | SDANN | SDNN index | rMSSD | pNN50 |
|---------|----|------------------|-----------------|-----------------|-----------------|----------------|
| Group 1 | 52 | 117.96 ±27.56 | 98.94 ±28.4 | 54.19 ±17.76 | 38.48 ±28.90 | 8.66 ±11.09 |
| Group 2 | 52 | 74.75 ±16.92 | 64.79 ±14.78 | 32.94 ±11.53 | 24.02 ±13.08 | 4.15 ±5.64 |
| t value | | 9.636 | 7.689 | 7.238 | 3.287 | 2.619 |
| P value | | <0.01 | <0.01 | <0.01 | <0.01 | 0.011 |

Group 1: patients over 60 years old in coronary heart disease with normotension. Group 2: patients over 60 years old in coronary heart disease with hypertension. The standard deviation of

all normal to normal NN intervals (SDNN), the standard deviation of all mean 5-minute NN intervals (SDANN), mean of the standard deviation of all NN intervals for all 5-min segments of 24 hour (SDNN index), the root mean square of successive differences between adjacent normal cycles (RMSSD), percent of NN50 in the total number of NN intervals (PNN50).

Table 3: Frequency-domain parameters during 24-hour in coronary heart disease patients with normotension and hypertensive

| | N | LF/HF | LF | HF |
|---------|----|-----------|---------------|---------------|
| Group 1 | 52 | 1.34±0.77 | 453.33±565.76 | 462.26±902.38 |
| Group 2 | 52 | 0.96±0.62 | 141.00±143.32 | 179.88±196.99 |
| t value | | 2.72 | 3.786 | 2.164 |
| P value | | 0.008 | <0.01 | 0.035 |

Group 1: patients over 60 years old in coronary heart disease with normotension. Group 2: patients over 60 years old in coronary heart disease with hypertension. LF: low frequency, HF: high frequency, LF/HF: the ratio of low frequency and high frequency.

Table 4: Time-domain parameters during the daytime in coronary heart disease patients with normotension and hypertensive

| | N | SDNN | SDANN | SDNN index | rMSSD | pNN50 | TINN |
|---------|----|-----------------|-----------------|-----------------|-----------------|----------------|-------------------|
| Group 1 | 52 | 88.12 ±25.94 | 65.19 ±22.79 | 52.21 ±23.09 | 38.17 ±35.05 | 8.91 ±14.57 | 327.92 ±112.91 |
| Group 2 | 52 | 57.25 ±16.73 | 45.21 ±15.23 | 31.02 ±10.88 | 23.13 ±12.44 | 4.02 ±5.78 | 211.89 ±70.89 |
| t value | | 7.21 | 5.26 | 5.99 | 2.916 | 2.25 | 6.28 |
| P value | | <0.01 | <0.01 | <0.01 | <0.05 | <0.05 | <0.01 |

Group 1: patients over 60 years old in coronary heart disease with normotension. Group 2: patients over 60 years old in coronary heart disease with hypertension. TINN: the triangular interpolation of NN interval histogram.

Table 5: Time-domain parameters during the nighttime in coronary heart disease patients with normotension and hypertensive

| | N | SDNN | SDANN | SDNN index | rMSSD | pNN50 | TINN |
|---------|----|-----------------|-----------------|-----------------|-----------------|----------------|------------------|
| Group 1 | 52 | 91.98 ±26.27 | 60.81 ±17.77 | 59.83 ±21.73 | 39.19 ±26.56 | 9.65 ±10.24 | 290.73 ±99.96 |
| Group 2 | 52 | 59.96 ±18.84 | 44.35 ±17.19 | 35.25 ±13.65 | 23.98 ±13.99 | 4.46 ±7.12 | 207.19 ±63.91 |
| t value | | 7.142 | 4.802 | 6.907 | 3.654 | 2.995 | 5.077 |
| P value | | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 |

Group 1: patients over 60 years old in coronary heart disease with normotension. Group 2: patients over 60 years old in coronary heart disease with hypertension. The standard deviation of all normal to normal NN intervals (SDNN), the standard deviation of all mean 5-minute NN intervals (SDANN), mean of the standard deviation of all NN intervals for all 5-min segments of 24

hour (SDNN index), the root mean square of successive differences between adjacent normal cycles (RMSSD), percent of NN50 in the total number of NN intervals (PNN50), TINN: the triangular interpolation of NN interval histogram.