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Relationship between dynamic electrocardiogram and CRP, IL-6, ET-1 expression in myocardial ischemia patients with coronary heart disease

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ABSTRACT

This study aimed to observe the relationship between dynamic electrocardiogram and CRP, IL-6, and ET-1 expression in individuals with myocardial ischemia and Coronary Heart Disease (CHD). For this purpose, from January 2021 to December 2022, 80 patients with CHD were admitted to the hospital to determine the presence of myocardial ischemia according to coronary angiography. The individuals were separated into a myocardial ischemia group and a no myocardial ischemia group. Dynamic electrocardiogram (DCG), serum CRP, IL-6, and ET-1 were used in the two groups, respectively. The association between dynamic electrocardiogram indexes and serum CRP, IL-6, and ET-1 levels was discovered using a Pearson correlation analysis. Results showed that the SDNN, SDANNI, rMSSD and PNN50 of Patients with Myocardial Ischemia (PWMI) were lower than individuals with CHD without myocardial ischemia (P<0.05). CRP and IL-6 were negatively correlated with SDNN, SDANNI, rMSSD and PNN50 (P<0.001). ET-1 had a bad relationship with rMSSD and PNN50 (P<0.001). Correlation heat map analysis showed that the color difference of IL-6 was the most obvious between PWMI and Patients Without Myocardial Ischemia (POMI), and IL-6 was more strongly correlated with dynamic electrocardiogram-related indexes of myocardial ischemia. In individuals with CHD myocardial ischemia, there is a negative connection between the DCG index and the production of the inflammatory cytokines CRP, IL-6, and ET-1. In conclusion, CRP, IL-6, and ET-1 levels should be monitored in patients with decreased heart rate variability, so as to further determine the level of micro-inflammation and endothelial function.

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Introduction

More than 30% of fatalities worldwide are caused by coronary heart disease (CHD) (1). CHD is becoming the leading cause of mortality in China due to the country's aging population. CHD is often manifested by myocardial ischemia or arrhythmia. The symptoms of myocardial ischemia are occultic and often ignored in the clinic. The earlier the detection, the better the early intervention and the better the prognosis. Myocardial ischemia is mainly diagnosed by coronary angiography (2). 24h dynamic electrocardiography (DCG) can accurately record the 24h ECG changes of patients and even diagnose transient cardiac events, which is helpful to clarify the myocardial ischemia status of patients (3). However, the clinical application of DCG is limited because it needs to be worn continuously and the vascular endothelial function of PWMI cannot be clearly defined. endothelin (C-reactive protein) (4), Interleukin 6 (IL-6) (5) and endothelin 1 (ET-1) (6,7) are all important factors affecting vascular endothelial cell proliferation, neovasculogenesis and remodeling. The endothelin (C-reactive protein), endothelin (IL-6) and endothelin (ET-1) (6,7). It is also an important factor in the occurrence and development of myocardial ischemia. This research's goal is to look into the connection between dynamic electrocardiogram indexes and the expression of CRP, IL-6 and ET-1 in myocardial ischemia patients with CHD, so as to further optimize the screening route for myocardial ischemia. The report is as follows.

Materials and Methods

General information

Eighty patients with CHD admitted to our hospital from January 2021 to December 2022 were selected to determine the presence of myocardial ischemia according to coronary angiography. The suffers were separated into the myocardial ischemia group and no myocardial ischemia group. Inclusion criteria: (I) Patients with more than 50% stenosis by coronary angiography; (II) Age range from 18 to 75 years old; (III) Full clinical information. Exclusion criteria: (I) Suffers with tumor or immune deficiency; (II) Patients with infectious or infectious diseases; (III) Patients with a recent history of severe trauma or major surgery; (IV) Doubtful serological index results or abnormal sampling. Indicating comparability, there were no statistically significant differences in gender, age, illness history, systolic blood pressure, diastolic blood pressure, or BMI between the two groups (all P>0.05) (Table 1).

Research method

(I) General data acquisition: The general data questionnaire was used to gather information on the gender, age, blood pressure, body mass index, and fasting blood glucose of the patients. Demographic data in the table should be filled in by the patients themselves; Blood pressure

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Table 1. Comparison of PWMI and POMI regarding general information.

Group	*n*	Gender		Age	Course of disease (years)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	BMI (kg/m^2)
		Male	Female					
No myocardial ischemia group	51	29	22	57.90±5.10	7.98±1.10	135.80±10.58	89.39±6.49	23.45±2.15
Myocardial ischemia group	29	17	12	58.59±5.34	8.24±1.35	137.41±9.96	89.28±4.31	23.39±2.09
x^2/t		0.023		0.567	0.935	0.878	0.086	0.119
P		0.878		0.572	0.353	0.383	0.932	0.906

was sampled using Omron sphygmomanometer. For the acquisition of fasting blood glucose, fasting elbow venous blood was measured from the morning after admission and evaluated by the double-antibody sandwich method. The reagent was provided by Union Biology. (II) Holter electrocardiogram examination: LAND-STAR three-lead AECG monitoring system was used for 24h Holter electrocardiogram monitoring of all enrolled patients; The measurement results were monitored by the computer within 24h, and the relevant indicators are calculated according to the measurement results; Namely, standard deviation of all normal R-R intervals (SDNN), standard deviation of R-R intervals every 5 min (SDANNI), root mean square of normal adjacent R-R interval difference (rMSSD), and percentage of normal adjacent R-R interval difference > 50 ms (PNN50). (III) Serum CRP, IL-6 and ET-1 levels were examined: From each patient, 1~2 ml of venous fasting blood was taken; After resting for 30min, centrifuge at 4°C and 2000r/min for 10min, upper serum was taken, and CRP, IL-6, and ET-1 serum levels were identified by enzyme-linked immunoassay. The test kit was purchased from Shanghai Berger Co., LTD., and was strictly operated in accordance with the kit.

Statistical processing

Analysis was performed using SPSS 26.0. $\bar{x}\pm s$ showed the measurement information, and the count data were represented by example (%). There was a t-test, an x^2-test, and a Pearson correlation analysis. Statistics were deemed significant at P<0.05.

Results

Comparison of DCG indexes in patients

SDNN, SDANNI, rMSSD and PNN50 in PWMI were inferior to POMI, with statistically significant (P<0.05) (Table 2).

Comparison of serological indexes of patients

CRP, IL-6 and ET-1 in PWMI were higher than POMI (P<0.05) (Table 3).

Results of correlation between DCG index and serological index

CRP and IL-6 were negatively correlated with SDNN, SDANNI, rMSSD and PNN50 (P<0.001). The relationship between ET-1 and rMSSD PNN50 was unfavourable (P<0.001) (Table 4). As can be seen from Figure 1, the color difference of IL-6 was the most obvious between PWMI and POMI, and IL-6 was more strongly correlated with the dynamic electrocardiogram-related indexes of myocardial ischemia.

Table 2. Comparison of DCG indexes between PWMI and POMI.

Group	*n*	SDNN (ms)	SDANNI (ms)	rMSSD (ms)	PNN50 (%)
No myocardial ischemia group	51	53.08±6.01	33.08±3.61	22.14±3.87	22.49±6.01
Myocardial ischemia group	29	48.45±4.29	27.76±2.18	16.00±2.69	19.55±3.81
t		3.651	7.210	7.553	2.370
P		<0.001	<0.001	<0.001	0.015

Table 3. Comparison of serological indexes between PWMI and POMI.

Group	*n*	CRP (mg/L)	IL-6 (pg/ml)	ET-1 (pg/ml)
No myocardial ischemia group	51	52.36±3.40	105.56±6.53	63.06±11.10
Myocardial ischemia group	29	77.54±7.86	154.10±6.91	69.97±16.53
t		19.904	31.295	2.230
P		<0.001	<0.001	0.029

Table 4. Correlation between serological indexes and DCG indexes of patients.

Index	SDNN		SDANNI		rMSSD		PNN50	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
CRP	-0.329	0.003	-0.520	<0.001	-0.594	<0.001	-0.337	<0.001
IL-6	-0.400	<0.001	-0.610	<0.001	-0.619	<0.001	-0.336	<0.001
ET-1	-0.102	0.368	-0.112	0.323	-0.224	0.046	-0.717	<0.001

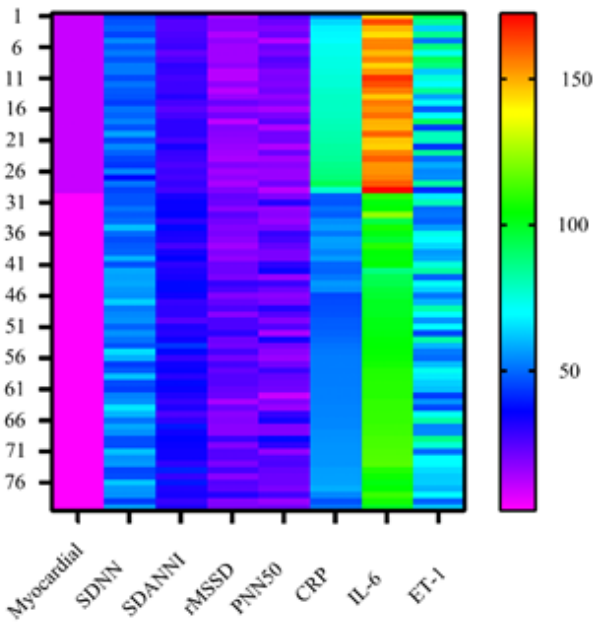

Figure 1. Correlation heat map of correlation between DCG index and serological index.

Discussion

Currently, the mortality rate of CHD is decreasing year by year, but the prevalence rate of CHD is increasing year by year, which also makes PWMI more common. The pathological manifestations of myocardial ischemia in coronary heart disease are muscle fibrillar contracture caused by the coupling of myocardial excitation and contraction, enhanced thrombotic reactions such as platelet adhesion and release, and aggravated cell membrane damage (8). Previous studies mainly used coronary angiography and electrocardiogram to screen myocardial ischemia. DCG records 24h cardiac activity of patients and then plays it back through computer technology, which can clearly show the dynamic process of myocardial ischemia of patients (such as attack frequency, time, etc.), so as to make diagnosis more accurate. In older individuals with CHD, DCG is useful for the identification of silent myocardial ischemia with arrhythmia and may increase the detection rate, giving a foundation for clinical diagnosis and therapy (9). DCG observed the shape between the ST segment and QTc by contrast scanning the ST segment trend chart and provided a 12-lead ST segment interactive 3D color trend chart. This trend chart can help physicians take note of the ST segment abnormalities that occur during myocardial ischemia episodes (9). However, in clinical practice, DCG still has certain limitations that require continuous observation of ST-T segment changes in patients and can be affected by hyperventilation, hypertension, monitoring position and other problems, leading to insufficient accuracy in monitoring myocardial ischemia. Therefore, a more accurate and non-invasive screening method for myocardial ischemia of CHD should be established for further comprehensive judgment based on patients' clinical conditions.

The endothelial function of myocardial ischemia in suffers with CHD is decreased compared with that in patients with CHD (10). Meanwhile, aberrant imaging of the myocardium under stress was associated with autonomic dysfunction in patients. Variable heart rate is an important indicator of risk stratification of myocardial ischemia (11). From the perspective of the pathological mechanism of myocardial ischemia, it is mainly related to vascular lumen stenosis or obstruction caused by vascular endothelial injury, lipid metabolism disorder, platelet aggregation and other reasons. An animal experiment found that when myocardial ischemia occurs in mice, reperfusion will cause an obvious myocardial scar and decrease of ejection fraction of the left ventricle, thus shortening the duration of QRS and decreasing heart rate variability (12). The findings of this investigation demonstrated that SDNN, SDANNI, rMSSD and PNN50 in PWMI were inferior to POMI (P<0.05). SDNN, SDANNI, rMSSD and PNN50 are common screening indicators of heart rate variation in DCG. This result may be related to the pathological mechanism of myocardial ischemia. A study on patients with ventricular fibrillation found that SDNN, SDANN, rMSSD, and PNN50 in suffer with atrial fibrillation were superior to suffers from myocardial infarction, and heart rate variability can assist in the diagnosis of atrial fibrillation (13). Myocardial ischemia is a predisposing factor for ventricular fibrillation, and its pathogenesis is similar. The heart rate variability of PWMI is decreased, and the levels of SDNN, SDANNI, rMSSD and PNN50 are lower.

Myocardial ischemia is also considered to be a metabolic disorder, and inflammation theory is an important hypothesis for its pathogenesis. Elevated levels of serum CRP and IL-6 will lead to increased levels of chronic microinflammation in the body, and also increase the risk of exacerbating patients' disease. At the same time, this study further found that PWMI had increased amounts of CRP, IL-6 and ET-1. Mechanism analysis shows that myocardial apoptosis can lead to an inflammatory response, and myocardial ischemia-reperfusion injury is the main cause of myocardial apoptosis (14). Macrophages and dendritic cells are the main cells that promote and inhibit myocardial inflammation (15). Genetically, the IL-6 signalling pathway raises the risk of cardiovascular disease. Inhibition of the IL-6 signaling pathway can reduce the risk of coronary heart disease, and this phenomenon is considered to be related to the synchronous decline of hs-CRP level and IL-6 (16). CRP can trigger the cell death of ischemic cells (17), and ischemic cell apoptosis is also found in myocardial ischemia. ET-1, as a potent vasoconstricting peptide, shared intron gene enhancer (rs9349379-G allele) and chromosome 6 (PHACTR1/EDN1) link ET-1 to vascular disorders (18). Myocardial ischemia is a typical disease of poor vasoconstriction. The level of ET-1 in patients was increased, which further aggravated vasoconstriction and increased the chance of myocardial ischemia. This outcome is comparable to the research result of Liu Y et al. (19). Meanwhile, the time of arterial reperfusion in patients with CHD is closely related to ET-1, which is involved in the process of myocardial ischemia in CHD (20). It can be seen that the relationship between myocardial ischemia and CRP, IL-6 and ET-1 provides certain clues for the early detection and targeted therapy of myocardial ischemia.

Correlation studies showed that CRP and IL-6 in those suffering from CHD were negatively associated with SDNN, SDANNI, rMSSD and PNN50 (P<0.001). SDNN and SDANNI had a negative correlation with ET-1 (P<0.001). Correlation heat map analysis showed that the

color difference of IL-6 was the most obvious between PWMI and POMI, and IL-6 was more strongly correlated with dynamic electrocardiogram-related indexes of myocardial ischemia. Myocardial cells in PWMI are often in a state of insufficient energy, which can lead to the disturbance of electrophysiological parameters. Meanwhile, electrophysiological parameters, especially heart rate variability-related indicators SDNN, PNN50, SDANN, RMSSD and Hypersensitive C-reactive protein (hs-CRP), were significantly correlated with the degree of tubular artery lesions. Patients with elevated hs-CRP may have the chance of stable coronary artery disease (21). Studies have shown that CRP in acute coronary syndrome suffers is negatively correlated with SDNN and RMSSD, and ET-1 is negatively associated with low-frequency power components of TP and LF (22). Alen (23) once found that heart rate variability significantly correlated negatively with IL-6, CRP, and fibrinogen. Serum hs-CRP was also found in a study of systemic inflammatory responses in sufferers who suffer from obstructive sleep apnea syndrome. Hs-CRP is significantly negatively correlated with PNN50. This study's findings were comparable to those of Xie J et al. (24), but the examination method in this study was based on a routine electrocardiogram. In this study, DCG was used as the examination method, and there were some differences in the observation indicators.

In summary, DCG indexes in CHD patients are negatively correlated with the expression of inflammatory cytokines CRP, IL-6 and ET-1. The levels of CRP, IL-6 and ET-1 should be monitored in patients with decreased heart rate variability, so as to further determine the level of microinflammation and endothelial function. Due to the limitations of the research time and the inclusion of sample data, this study did not include healthy people for control, and there were few relevant indicators in the study, which inevitably resulted in data bias. In the later stage, our research group will use a multi-center study to increase the sample size and investigate the data disparities of various serological factors in myocardial infarction, myocardial ischemia and other heart diseases, so as to provide help for early screening and diagnosis of disease progression in patients with CHD.

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