

Tea consumption is associated with a reduced risk of coronary heart disease in female but not male populations in Guangzhou, China

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BACKGROUND/OBJECTIVES: The association between tea consumption and risk of coronary heart disease (CHD) remains controversial. This study aimed to determine whether tea consumption has an effect on CHD risk in Chinese adults.

SUBJECTS/METHODS: In this hospital-based case-control study, 267 cases of CHD and 235 non-CHD controls were enrolled. Blood samples from all cases were examined. Cardiac function indices (left ventricular ejection fraction, left ventricular end-diastolic dimension, lactate dehydrogenase, and creatine kinase of the muscle or brain type), blood lipid index (high-density lipoprotein cholesterol), and blood coagulation function indices (fibrinogen and activated partial thromboplastin time) were recorded. Tea consumption of study participants was assessed by a specifically designed questionnaire. The baseline characteristics of the study populations were recorded, and CHD-related biomarkers were detected. Differences in baseline characteristics of the study participants were examined using *t*-tests for continuous variables and chi-squared tests for categorical variables. Unconditional logistic regression was used to measure the association between tea and CHD.

RESULTS: There were significant differences in cardiac function indices, blood lipid index, and blood coagulation indices between CHD cases and controls ($P < 0.05$). We found tea consumption reduced CHD risk in female participants (adjusted odds ratio (OR) = 0.484, 95% CI: 0.242-0.968, $P = 0.0403$). Regarding the type of tea consumed, the risk of CHD was reduced in women who drank partially fermented tea (adjusted OR = 0.210, 95% CI: 0.084-0.522, $P = 0.0008$). Analytic results for the amount of tea consumed per unit time showed CHD risk was reduced in women who consumed 1-2 cups of tea per day (adjusted OR = 0.291, 95% CI: 0.131-0.643, $P = 0.0023$). A tea-drinking frequency of > 6 days/week was beneficial for CHD prevention (adjusted OR = 0.183, 95% CI: 0.049-0.679, $P = 0.0112$). When analyzed according to the duration of tea consumption, the risk of CHD was reduced in participants who had been drinking tea for 10-20 years (adjusted OR = 0.360, 95% CI: 0.137-0.946, $P = 0.0382$).

CONCLUSIONS: Tea consumption is associated with a reduced risk of CHD in female but not male populations in Guangzhou.

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INTRODUCTION

Tea is the most widely consumed beverage worldwide after water [1]. The tea plant, a species of evergreen (*Camellia sinensis*), is valued for its young leaves and leaf buds, which are used to produce the beverage. Tea types can be differentiated based on their manufacturing process, for example, 'nonfermented' green tea, 'semi-fermented' oolong tea, and 'fermented' black tea [2].

The association of tea and coronary heart disease (CHD)

prevention has been the subject of controversy [3]. Most studies have found that tea consumption reduces the risk of cardiovascular morbidity and mortality [4-6]. By contrast, some studies have shown weak or no effect of tea consumption on the risk of cardiovascular diseases [7-8]. Meta-analyses have also obtained conflicting results. Hartley reported that green and black tea consumption could prevent the morbidity of cardiovascular disease [9]. However, another meta-analysis of tea consumption in relation to stroke, myocardial infarction, and all coronary heart disease (CHD) showed that there was an

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increased risk of CHD and stroke in populations with increased tea consumption [10]. A large prospective study showed that regular green tea consumption was associated with a significantly reduced risk of death from all causes, cardiovascular disease, and cancer among Chinese adults [11]. Unanswered questions from these studies include whether sex, age, type of tea, or the amount of tea consumed can produce these different results.

In the present study, we enrolled CHD and non-CHD patients to determine the association of tea consumption with CHD risk in the study population.

SUBJECTS AND METHODS

Patient and public involvement statement

This study was approved by the Ethics Committee of Sun Yat-sen Memorial Hospital (Approval reference: 2015 No.51) and complied with the *Declaration of Helsinki*. Informed consent was obtained from all subjects. This study was carried out on 267 CHD patients and 235 non-CHD controls at Sun Yat-sen Memorial Hospital between 2013 and 2014. CHD patients were diagnosed according to the international diagnostic criteria: (1) acute chest pain; (2) ischemic changes in exercise electrocardiography (ECG); and (3) $\geq 50\%$ lumen diameter reduction in at least one major coronary artery on coronary angiography (ICA). The exclusion criteria were as follows: malignant tumor, hepatic and renal insufficiency, severe heart failure, and more than three complications. Non-CHD patients who had been hospitalized during the same period were recruited, and their exclusion criteria were similar to those for the CHD patient group.

Assessment of baseline characteristics

A pre-tested questionnaire was used to collect data for the name, place of birth, age, and sex of each participant. Hypertension, hyperlipidemia, and diabetes histories were recorded. Weight was measured to the nearest 0.01 kg using a bathroom scale (Hana, model BR9011; 120 \times 0.01 kg, China). Height was measured in meters to the nearest 0.01 m using a height meter (Seca, model 206, Germany). Body mass index (BMI) was calculated for each subject. After a 10-min rest in the sitting position, blood pressure was measured. All of the indices were recorded by a trained interviewer.

Tea consumption assessment

Tea consumption was also examined by using a questionnaire. Beverage consumption was assessed by asking: "Did you regularly consume tea, including black tea, oolong tea, or green tea, during the last year?" Participants were also asked to select how often they consumed tea. Tea consumers were asked about the type of tea consumed, the amount of tea consumed per consumption period, frequency of tea consumption per week, and duration of tea consumption.

Statistical analysis

The baseline characteristics of the study participants were examined using *t*-tests for continuous variables and chi-squared tests for categorical variables. We included the various biomarkers individually into logistic regressions to assess *p* values after

adjusting for sex, age, blood pressure, BMI, history of hypertension, history of hyperlipidemia, history of diabetes, as well as smoking, exercise, and nap behaviors, and wine consumption. An unconditional logistic regression was used to measure the association between tea and CHD. Odds ratios (ORs) were adjusted for BMI, age, blood pressure, history of hypertension, history of hyperlipidemia, history of diabetes, smoking, exercise, naps, and wine consumption. SAS software (Version 9.2, SAS Institute Inc.) was used for data analysis. A *P* < 0.05 indicated a significant difference.

RESULTS

Baseline characteristics of the study population

Out of 502 eligible participants, 267 were CHD patients and 235 were non-CHD patients (Table 1). Mean BMI was higher in CHD patients than in non-CHD patients. Moreover, the two groups' age distributions were different and compared to non-CHD patients, more CHD patients had histories of hypertension, hyperlipidemia, and diabetes.

CHD-related biomarkers in CHD and non-CHD patients

Regarding the cardiac function indices, left ventricular ejection fraction (LVEF) was worse in CHD patients than in non-CHD patients. Levels of lactate dehydrogenase (LDH) and creatine kinase of the muscle or brain type (CKMB) were higher in the CHD group than in the non-CHD group. Regarding the blood lipid index, the level of high-density lipoprotein cholesterol (HDL) was lower in CHD patients than in non-CHD patients. With

Table 1. Baseline characteristics of the two study populations¹⁾

	CHD (n = 267)	Non-CHD (n = 235)	<i>P</i> -value ²⁾
Age (yrs)	64.311 \pm 10.643	56.247 \pm 11.281	< 0.0001*
Gender (%)			
Male	64.045	45.106	
Female	35.955	54.893	
BMI (kg/m ²)	23.671 \pm 2.908	22.782 \pm 2.733	0.0006*
SBP (mmHg)	129.000 \pm 17.508	128.400 \pm 17.427	0.6621
DBP (mmHg)	75.172 \pm 10.435	76.447 \pm 10.495	0.1739
History of hypertension (%)	70.787	42.979	< 0.0001*
History of hyperlipidemia (%)	33.708	26.383	0.0747
History of diabetes (%)	22.097	11.489	0.0016*
Wine consumption (Yes / No) (%)	34.818	34.091	0.8691
Nap (Yes / No) (%)	53.252	59.545	0.1716

¹⁾ Values expressed as mean \pm SD or n (%).

²⁾ *T*-test is used to compare the values of age, BMI, SBP, DBP between CHD and Non-CHD. Chi-squared test is used to compare the categorical variables.

* *P* < 0.05

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure. History of hypertension, Hypertension can be diagnosed by measuring SBP \geq 140 mmHg and/or DBP \geq 90 mmHg three times on different days without using antihypertensive drugs, or a history of hypertension diagnosis; History of hyperlipidemia, Hyperlipidemia is a systemic disease in which either TC or LDL or TG rise beyond the normal range; History of diabetes, Diabetes is defined as fasting blood glucose equal to or greater than 7.0 mmol/L, or elevated blood glucose with medication, or a history of diabetes diagnosis. Wine consumption is defined as the drinking of beverages containing ethyl alcohol. Nap is defined as a short period of sleep, typically taken during daytime hours as an adjunct to the usual nocturnal sleep period.

Table 2. CHD-related biomarkers of the two study populations

	CHD (n = 267)	Non-CHD (n = 235)	Adjusted <i>P</i> -value ²⁾
Cardiac function indices			
LVEF (%)	63.638 ± 11.620 ¹⁾	67.817 ± 7.552	0.0023*
LAD (mm)	34.128 ± 4.457	33.340 ± 4.619	0.3154
LVEDD (mm)	48.587 ± 5.320	47.370 ± 4.830	0.5855
LDH (U/L)	279.100 ± 302.000	188.400 ± 45.047	0.0004*
CKMB (U/L)	40.071 ± 99.023	12.566 ± 4.933	0.0003*
Blood lipid indices			
TC (mmol/L)	4.693 ± 1.289	4.645 ± 1.046	0.1745
TG (mmol/L)	1.809 ± 1.338	1.540 ± 0.961	0.0121*
HDL (mmol/L)	1.086 ± 0.310	1.1254 ± 0.328	< 0.0001*
LDL (mmol/L)	2.758 ± 0.856	2.716 ± 0.839	0.1819
HDL/LDL	0.418 ± 0.142	0.509 ± 0.225	< 0.0001*
Blood coagulation indices			
PT (S)	11.393 ± 1.641	11.179 ± 0.815	0.5875
PTINR	1.024 ± 0.178	0.995 ± 0.071	0.2050
FBG (g/L)	3.318 ± 0.984	2.724 ± 0.582	< 0.0001*
APTT (S)	27.937 ± 4.703	26.890 ± 3.475	0.0168*
TT (S)	18.121 ± 1.553	18.882 ± 11.032	0.6195

¹⁾ Values expressed as mean ± SD.

²⁾ *P*-value of the biomarkers were adjusted for sex, age, blood pressure, BMI, history of hypertension, history of hyperlipidemia, history of diabetes, smoking, exercise, nap, and wine consumption.

* *P* < 0.05.

LVEF, left ventricular ejection fraction; LAD, left atrial diameter; LVEDD, left ventricular end-diastolic diameter; LDH, Lactate dehydrogenase; CKMB, creatine kinase muscle brain; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PT, prothrombin time; PTINR, prothrombin time international normalized ratio; FBG, fibrinogen; APTT, activated partial thromboplastin time; TT, Thrombin.

Table 3. Association between tea consumption and CHD risk in male patients

Tea consumption	Male CHD N (%)	Male Non-CHD N (%)	Crude OR (95% CI)	<i>P</i> -value	Adjusted OR ¹⁾ (95% CI)	<i>P</i> -value
Seldom tea consumption	36 (22.93)	36 (36.36)	1	-	1	-
Regular tea consumption	121 (77.07)	63 (63.64)	1.921 (1.104, 3.340)	0.0208	1.672 (0.909, 3.074)	0.0982
Type of tea consumption						
None	36 (22.93)	36 (36.36)	1	-	1	-
Partially fermented tea	87 (55.41)	49 (49.49)	1.776 (0.994, 3.170)	0.0522	1.592 (0.840, 3.018)	0.1544
Fully fermented tea	34 (21.66)	14 (14.14)	2.428 (1.119, 5.271)	0.0249	1.926 (0.829, 4.475)	0.1275
Amount of tea consumption per time						
None	37 (23.57)	36 (36.36)	1	-	1	-
1-2 cups ²⁾ /time	71 (45.22)	37 (37.37)	1.867 (1.018, 3.426)	0.0438	1.744 (0.890, 3.415)	0.1050
> 3 cups/time	49 (31.21)	26 (26.26)	1.834 (0.947, 3.551)	0.0721	1.477 (0.714, 3.054)	0.2928
Frequency of tea consumption per week						
None	36 (22.93)	36 (36.36)	1	-	1	-
1-3 days/week	37 (23.57)	12 (12.12)	3.083 (1.388, 6.851)	0.0057	2.884 (1.194, 6.965)	0.0185*
4-5 days/week	35 (22.29)	25 (25.25)	1.400 (0.702, 2.793)	0.3396	1.198 (0.563, 2.549)	0.6395
> 6 days/week	49 (31.21)	26 (26.26)	1.885 (0.971, 3.657)	0.0610	1.609 (0.772, 3.351)	0.2041
Duration of tea consumption (years)						
None	36 (22.93)	36 (36.36)	1	-	1	-
0-10 years	19 (12.10)	14 (14.14)	1.357 (0.591, 3.114)	0.4712	1.767 (0.676, 4.617)	0.2453
10-20 years	58 (36.94)	26 (26.26)	2.231 (1.160, 4.289)	0.0162	2.049 (1.000, 4.196)	0.0500
> 20 years	44 (28.03)	23 (23.23)	1.913 (0.965, 3.791)	0.0630	1.249 (0.584, 2.668)	0.5665

¹⁾ ORs were adjusted for age, blood pressure, BMI, history of hypertension, history of hyperlipidemia, history of diabetes, smoking, exercise, nap, and wine consumption.

²⁾ 1 cup equals 200 mL.

* *P* < 0.05.

regard to the blood coagulation indices, fibrinogen (FBG) and activated partial thromboplastin time (ATPP) were notably higher in CHD patients than in non-CHD patients (Table 2).

Tea consumption did not reduce the CHD risk in male participants

Tea consumption (seldom or regular tea consumption), type of tea consumed (none, partially fermented tea, or fully fermented tea), amount of tea consumed per unit time (none, 1-2 cups/time, or > 3 cups/time), frequency of tea consumed per week (none, 1-3 days/week, 4-5 days/week, or > 6 days/week), and duration of tea consumption (none, 0-10 years, 10-20 years, or > 20 years) were recorded and analyzed.

The results showed that men who drank tea did not have a reduced risk of CHD (adjusted OR = 1.672, 95% CI: 0.909-3.074, *P* = 0.0982). Different types of tea, specifically, partially fermented tea (adjusted OR = 1.592, 95% CI: 0.840-3.018, *P* = 0.1544) or fully fermented tea (adjusted OR = 1.926, 95% CI: 0.829-4.475, *P* = 0.1275), did not reduce the CHD risk. A tea consumption level of > 3 cups/time (adjusted OR = 1.477, 95% CI: 0.714-3.054, *P* = 0.2928) did not influence the CHD risk. A tea consumption frequency of 4-5 days/week (adjusted OR = 1.198, 95% CI: 0.563-2.549, *P* = 0.6395) or > 6 days/week (adjusted OR = 1.609, 95% CI: 0.772-3.351, *P* = 0.2041) also did not influence the CHD risk. Male participants with a green tea consumption history of 0-10 years (adjusted OR = 1.767, 95% CI: 0.676-4.617, *P* = 0.2453), 10-20 years (adjusted OR = 2.049, 95% CI: 1.000-4.196, *P* = 0.0500) or > 20 years (adjusted OR = 1.249, 95% CI: 0.584-2.668, *P* = 0.5665) also did not have a reduced risk of CHD (Table 3).

Table 4. Association between tea consumption and CHD risk in female patients

Tea consumption	Female CHD N (%)	Female Non-CHD N (%)	Crude OR (95% CI)	P-value	Adjusted OR ¹⁾ (95% CI)	P-value
Seldom tea consumption	61 (68.54)	58 (48.33)	1	-	1	-
Regular tea consumption	29 (32.22)	63 (52.07)	0.438 (0.248, 0.772)	0.0044	0.484 (0.242, 0.968)	0.0403*
Type of tea consumption						
None	61 (67.78)	58 (49.93)	1	-	1	-
Partially fermented tea	13 (14.44)	47 (38.84)	0.263 (0.129, 0.536)	0.0002	0.210 (0.084, 0.522)	0.0008*
Fully fermented tea	16 (17.78)	16 (13.22)	0.951 (0.436, 2.076)	0.8992	1.480 (0.578, 3.789)	0.4137
Amount of tea consumption per time						
None	62 (68.89)	58 (47.93)	1	-	1	-
1-2 cups ²⁾ /time	20 (22.22)	58 (47.93)	0.323 (0.173, 0.601)	0.0004	0.291 (0.131, 0.643)	0.0023*
> 3 cups/time	8 (8.89)	5 (4.13)	1.497 (0.436, 0.439)	0.5005	3.014 (0.788, 11.533)	0.1071
Frequency of tea consumption per week						
None	61 (67.78)	58 (48.33)	1	-	1	-
1-3 days/week	18 (20.00)	39 (32.50)	0.439 (0.226, 0.853)	0.0151	0.634 (0.283, 1.419)	0.2674
4-5 days/week	5 (5.56)	7 (5.83)	0.679 (0.204, 0.261)	0.5283	0.723 (0.182, 2.875)	0.6455
> 6 days/week	6 (6.67)	16 (13.33)	0.357 (0.131, 0.971)	0.0443	0.183 (0.049, 0.679)	0.0112*
Duration of tea consumption (years)						
None	61 (68.54)	58 (48.33)	1	-	1	-
0-10 years	9 (10.11)	23 (19.17)	0.372 (0.159, 0.871)	0.2227	0.383 (0.133, 1.103)	0.0753
10-20 years	9 (10.11)	30 (25.00)	0.285 (0.125, 0.652)	0.0030	0.360 (0.137, 0.946)	0.0382*
> 20 years	10 (11.24)	9 (7.50)	1.056 (0.401, 2.786)	0.9116	1.045 (0.334, 3.264)	0.9398

¹⁾ ORs were adjusted for age, blood pressure, BMI, history of hypertension, history of hyperlipidemia, history of diabetes, smoking, exercise, nap, and wine consumption.

²⁾ 1 cup equals 200 mL.

* $P < 0.05$.

Tea consumption reduced the CHD risk in female participants

In contrast to the male results, the risk of CHD was reduced in women who drank tea (adjusted OR = 0.484, 95% CI: 0.242-0.968, $P = 0.0403$). The risk of CHD was also reduced in women who drank partially fermented tea (adjusted OR = 0.210, 95% CI: 0.084-0.522, $P = 0.0008$). Moreover, female participants who consumed 1-2 cups/day of tea had a reduced CHD risk (adjusted OR = 0.291, 95% CI: 0.131-0.643, $P = 0.0023$). A tea consumption frequency of > 6 days/week was also beneficial for CHD prevention (adjusted OR = 0.183, 95% CI: 0.049-0.679, $P = 0.0112$). In addition, female participants who had been drinking tea for 10-20 years (adjusted OR = 0.360, 95% CI: 0.137-0.946, $P = 0.0382$) had a reduced risk of CHD (Table 4).

DISCUSSION

Tea consumption has been shown to be useful for the prevention of many debilitating human diseases. Several published studies have reported similar results to those reported herein, showing that tea consumption can reduce CHD risk [11,12]. In our study, we observed that tea consumption was associated with a reduced risk of CHD in female participants, but not in male participants, in Guangzhou, China. The protective association was related to the type of tea, the amount of tea consumed per unit time, the frequency of tea consumption per week, and the duration of tea consumption, as shown by the reduced CHD risks for partially fermented tea, 1-2 cups/time, > 6 days/week, and 10-20 years of tea consumption, respectively.

There is evidence indicating that catechins, which are the main polyphenolic compounds in tea, are responsible for the

inverse association between tea consumption and CHD in women. Previously, tea catechins were shown to be associated with a reduced risk of CHD [13]. It was also shown that a tea catechin extract significantly reduced the circulating total cholesterol (TC) and LDL-cholesterol concentrations in women [14,15]. Higher catechin antioxidant activities have been observed in female animals compared to that in male animals [16]. Catechins have conferred cardio-protection in the case of ischemia/reperfusion injury [17] and have provided vascular benefits that influence both CHD and cerebrovascular diseases. In our study, we found that tea consumption was associated with a reduced risk of CHD in female participants but not in male participants in Guangzhou, which was consistent with a previous canonical study [18].

Furthermore, in this study, the inverse association between tea consumption in women and CHD risk was related to the type, amount, frequency, and duration of tea consumed, which were partially fermented tea, 1-2 cups/time, > 6 days/week, and 10-20 years of tea consumption, respectively. Fully fermented tea (black tea) contains fewer antioxidant compounds, such as caffeine or catechins, than those in partially fermented and nonfermented teas (green tea and oolong tea). In addition, most catechins are oxidized by fermentation to thearubigins and theaflavins, which have reduced antioxidant properties, and black tea (fully fermented) has lower antioxidant properties than green tea or oolong tea (partially fermented) [19]. Our results show that 1-2 cups/time and > 6 days/week consumption of partially fermented tea has a lowering effect on CHD risk in women.

The results suggest that drinking tea is a good habit for CHD

prevention. However, drinking too much tea might cause insomnia, which is a risk hazard for CHD [20]. In our study, consumption of > 3 cups/time contributed to the absence of an inverse association between tea consumption and CHD. However, we did observe that only 10-20 years of tea consumption could reduce CHD risk.

The underlying reason for the differences between our results for men and women might be the presence of a “critical time window” for the prevention of CHD in women. In our study, we observed a similar temporal phenomenon. Women who had been drinking tea for 10-20 years but not those who had been drinking tea for more than 20 years had a reduced risk of CHD. The mechanisms involved in this “critical time window” need to be clarified in the future.

We also observed that CHD-related biomarkers, namely, cardiac function indices (LVEF, LDH, and CKMB), blood lipid index (HDL), and blood coagulation indices (FBG and APTT), were worse in the CHD group than in the non-CHD control group. When analyzing the reasons behind these differences, we first detected that the cardiac function indices (LVEF, LDH, and CKMB) were worse in the CHD group than in the non-CHD control group. Studies have shown that tea polyphenols promote cardiac function and energy metabolism in *ex vivo* rat heart with ischemic/reperfusion injury. Second, tea consumption could decrease triglyceride and cholesterol levels to reduce serum lipid concentrations. Third, the blood coagulation indices (FBG and APTT) were worse in the CHD group than in the non-CHD control group. Studies have shown that the green tea polyphenol epigallocatechin has notable dose-dependent anti-platelet activity and blood anticoagulation effects. The above reasons might indicate some aspects of the mechanisms behind the beneficial effects of tea consumption.

There are a few limitations associated with this study. First, the number of patients in our study was limited; thus, larger scale studies are needed. Second, the proportion of the Guangzhou population that consumes tea may not be representative of that of the average population across China. Third, our study had a retrospective design. Prospective studies could better illustrate the association between tea consumption and CHD incidence. Moreover, we did not consider other potential confounding factors that may affect the outcome of CHD, such as consumption of wine and coffee, daily calorie intake, and CHD family history. Therefore, prospective studies are needed, and we suggest that future studies include an extended follow-up period for individuals who consume tea (because tea consumption pertains to CHD incidence) to ascertain long-term outcomes.

In summary, found that tea consumption was associated with a reduced risk of CHD in women (but in not men) in Guangzhou, China. The association was related to the type of tea consumed (partially fermented tea), the amount of tea consumed per unit time (1-2 cups/time), the frequency of tea consumed per week (> 6 days/week), and the duration of tea consumption (10-20 years of tea consumption).

CONFLICT OF INTEREST

The authors declare no potential conflicts of interests.

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AUTHORS' CONTRIBUTIONS

QLX and SXZ contributed to the study design as well as to manuscript writing and editing. YC and CZ contributed to the study design and data collection. YFY and JP contributed to data analysis. ZZ and MYC contributed to data collection. All of the authors critically reviewed the manuscript for scientific content and approved the final version.

ABBREVIATIONS

CVD, Cardiovascular disease; CHD, Coronary heart disease; ECG, Electrocardiography; ICA, Coronary angiography; BMI, Body mass index; ORs, Odds ratios; LAD, Left atrial diameter; LVEF, Left ventricular ejection fraction; LVEDD, Left ventricular end-diastolic dimension; LDH, Lactate dehydrogenase; CKMB, Creatine kinase of the muscle or brain type; TC, Total cholesterol; TG, Triglyceride; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; PT, Prothrombin time; PTINR, Prothrombin time international normalized ratio; FBG, Fibrinogen; APTT, Activated partial thromboplastin time; TT, Thrombin.

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