Journal of Clinical and Nursing Research, 2024, Volume 8, Issue 9
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

The Relationship Between Multiple Obesity Indices and Long-Term Prognosis in STEMI Patients: An Observational Cohort Study of 220 Cases

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Abstract: *Objective:* To investigate the association of body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHtR) with the long-term prognosis of ST-elevation myocardial infarction (STEMI) patients and to determine whether the combination of obesity indices can be used for risk stratification. *Method:* A multifactorial Cox regression analysis was performed using 3-year follow-up data from 220 STEMI patients to explore the relationship between obesity indicators and major adverse cardiovascular events (MACEs). The incidence of MACEs was also compared by combining BMI and WHtR. *Results:* WC was found to reduce the risk of MACEs within 25 months after myocardial infarction [hazard ratio (HR) = 0.95, 95% confidence interval (CI) = 0.92–0.98, $P < 0.001$]. However, this effect was not significant beyond 25 months (HR = 0.98, 95% CI = 0.97–1.07, $P = 0.49$). Neither BMI nor WHtR were significantly associated with the risk of MACEs. The incidence of MACEs was highest in patients with low body weight (BMI < 18.5 kg/m^2) and WHtR > 0.5, and lowest in obese patients (BMI ≥ 28 kg/m^2) with WHtR > 0.5. *Conclusions:* BMI, WC, and WHtR were not significantly associated with the long-term prognosis of STEMI patients. However, the combination of BMI and WHtR can be useful for further stratifying patient risk.

Keywords: ST-elevation myocardial infarction; Central obesity; Body mass index; Risk stratification

Online publication: September 27, 2024

1. Introduction

Obesity has become a major public health problem in China, with the prevalence and growth rate of overweight and obesity ranking first in the world [1]. Obesity is also closely linked to cardiovascular disease (CVD) and various complications, such as diabetes mellitus and dyslipidemia [2]. However, several studies have identified an “obesity paradox” in patients with CVD, including myocardial infarction, where patients with normal weight tend to have poorer prognoses than those who are overweight or mildly obese [3,4]. In contrast, other research indicates that, after adjusting for covariates, obesity indicators are not associated with the long-term prognosis of CVD patients [5].

While body mass index (BMI) is a widely used indicator for assessing obesity, it does not accurately reflect the type of obesity. Combining various obesity indicators may provide better risk stratification for CVD patients [5-8]. Due to inconsistent results regarding the association between obesity indices and the prognosis of CVD patients, as well as a lack of relevant research in East Asian populations, this study aimed to investigate the association between BMI, waist circumference (WC), and waist-to-height ratio (WHtR) with the long-term prognosis of ST-elevation myocardial infarction (STEMI) patients in China. Additionally, it aimed to explore whether a combination of BMI and fat distribution measurements can be used for risk stratification.

2. Method

2.1. Data sources and inclusion criteria

Two STEMI cohorts from the Heart Center of Pingjin Hospital were combined for this study. The first cohort included 100 new STEMI patients who underwent percutaneous coronary intervention (PCI) within 12 hours of symptom onset between November 2012 and May 2013. The second cohort comprised 133 new STEMI patients who underwent PCI within 12 hours of symptom onset between January 2015 and November 2015. Patients were excluded if they presented with (1) acute infection, cancer, myocardial infarction, or decompensated heart failure within the past six months; (2) were ineligible for PCI; or (3) had multi-vessel disease requiring PCI after discharge. Ultimately, 220 patients were included in the final analysis. This cohort study was approved by the Pingjin Hospital Ethics Committee, adhered to the principles of the Helsinki Declaration, and informed consent was obtained from all participants.

2.2. Variables and definitions

Data on patient demographics, clinical characteristics, and in-hospital treatments were collected. For details, please refer to a previously published study [9]. Obesity stratification criteria were as follows: BMI < 18.5 kg/m^2 was classified as underweight, 18.5–23.9 kg/m^2 as normal weight, 24–27.9 kg/m^2 as overweight, and ≥ 28 kg/m^2 as obese [10]. For adults, WC ≥ 90 cm in males or ≥ 85 cm in females indicated central obesity [10]. A WHtR greater than 0.5 was also considered indicative of central obesity [11].

2.3. Follow-up and events

The cohort was followed for approximately three years, and the follow-up process has been detailed in a previous study [9]. The endpoint events were defined as major adverse cardiovascular events (MACEs), including cardiac death, recurrent myocardial infarction, nonfatal ischemic stroke, the need for emergent or elective revascularization, and readmission due to heart failure. Death was classified as cardiac death if non-cardiovascular causes could be excluded.

2.4. Statistical analysis

Continuous variables with a normal distribution were described using mean ± standard deviation (SD), while non-normally distributed continuous variables were reported as median and quartiles. Categorical variables were described as counts and percentages. Group differences were assessed using *t*-tests, rank-sum tests, and chi-squared tests, as appropriate. The relationship between obesity indicators and MACEs was depicted using restricted cubic splines (**Supplementary Material Figure 1**). Residual proportional hazards (PH) tests were used to assess whether obesity indicators interacted with time. Multifactorial Cox regression analysis was performed to evaluate the association between obesity indicators and long-term MACEs, adjusting for variables including age, gender, 24-hour left ventricular ejection fraction (LVEF), history of hypertension, history of diabetes, smoking, infarction location, and estimated glomerular filtration rate (eGFR). Time-dependent variables were analyzed using stratified multifactorial Cox regression. The proportional risk hypothesis between obesity stratification and MACEs was assessed using inverse probability weighting and Landmark analysis. BMI and WHtR were combined for risk stratification of patients. Statistical analyses were conducted using R version 4.3.1 and Stata version 17.0, with two-sided P values less than 0.05 considered statistically significant.

2.5. Ethics statement

This cohort study was approved by the Pingjin Hospital Ethics Committee, Capital Medical University. Informed consent was obtained from all patients for inclusion in the study.

3. Results

3.1. Baseline characteristics

Based on BMI grouping, the baseline characteristics of patients are summarized in **Table 1**. Patients' age tended to decrease as BMI increased. The proportion of males was higher in the overweight and obese groups compared to the underweight and normal-weight groups. There were no significant differences in the proportion of patients with eGFR, 24-hour LVEF, or anterior wall myocardial infarction across the groups. However, the proportion of patients with both hypertension and smoking was higher in the overweight and obese groups compared to the underweight and normal-weight groups. Additionally, the proportion of patients with diabetes mellitus was higher in the obese group than in the other groups. Furthermore, the proportion of patients with both hypertension and diabetes mellitus was higher in those with central obesity compared to the control group (see **Supplementary Material Tables 1 and 2**). All patients received dual antiplatelet and statin therapy, with no significant differences in the use of other in-hospital medications within the first 24 hours among the groups.

Table 1. Characteristics based on BMI groups

Characteristics	≤ 18.5 kg/m^2 (*n* = 6)	18.6–23.9 kg/m^2 (*n* = 85)	24.0–27.9 kg/m^2 (*n* = 92)	≥ 28.0 kg/m^2 (*n* = 37)	*P*
Age (years)	70.8 ± 10.5	62.0 ± 12.1	61.2 ± 11.4	57.6 ± 10.7	0.045
Male [*n* (%)]	2 (33)	65 (76)	78 (85)	31 (84)	0.015
Height (cm)	157.5(155.0, 167.0)	170.0(165.0, 174.0)	173.0(168.0, 175.0)	172.0(165.0, 178.0)	0.046
Weight (kg)	42.5(42.0, 47.5)	65.0(60.0, 69.0)	75.0(72.0, 80.0)	90.0(85.0, 95.0)	< 0.001
eGFR (mL/min/1.73 m^2)	96.2(58.9, 122.6)	113.3(97.8, 126.0)	110.6(92.0, 131.5)	110.8(87.4, 127.7)	0.80
LVEF* (%)	48.5(37.0, 54.0)	51.0(45.0, 55.0)	50.0(41.5, 54.5)	53.0(45.0, 56.0)	0.41
Anterior infarction [*n* (%)]	5 (83)	43 (51)	46 (50)	14 (38)	0.19
Hypertension [*n* (%)]	2 (33)	32 (38)	57 (62)	26 (70)	< 0.001

Table 1 (Continued)

Characteristics	≤ 18.5 kg/m^2 (*n* = 6)	18.6–23.9 kg/m^2 (*n* = 85)	24.0–27.9 kg/m^2 (*n* = 92)	≥ 28.0 kg/m^2 (*n* = 37)	*P*
Diabetes [*n* (%)]	1 (17)	12 (14)	22 (24)	11 (30)	0.20
Smoking [*n* (%)]	2 (33)	48 (56)	861 (66)	31 (84)	0.011
			Medication in the first 24 hours		
ACEI/ARB [*n* (%)]	1 (17)	49 (58)	60 (65)	24 (65)	0.099
β-blocker [*n* (%)]	2 (33)	34 (40)	46 (50)	14 (38)	0.43
CCB [*n* (%)]	0 (0)	16 (19)	16 (17)	7 (19)	0.70

Note: * represents echocardiography completed within 24 hours of hospital admissions. Abbreviations: ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; β-blocker, beta-blocker; BMI, body mass index; CCB, calcium channel blocker; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction.

3.2. Association of obesity indicators with MACEs

A total of 60 MACEs occurred during the 3-year follow-up period. It was observed that WC had a negative linear relationship with the risk of MACEs, whereas BMI and WHtR did not show a linear association with MACE risk (see **Supplementary Material Figure 1**). Multivariate Cox regression analysis revealed that WC had a protective effect on the long-term prognosis of STEMI patients [hazard ratio (HR) = 0.96, 95% confidence interval (CI) = 0.94–0.99, *P* = 0.005], while no significant correlation was found between the other indicators and MACEs (**Figure 1**). Proportional hazards (PH) testing showed that WC had a time interaction effect ($P < 0.05$), and scatter plots from the PH test indicated that the correlation between WC and MACEs significantly changed after 25 months of follow-up (**Supplementary Material Figure 2**). When using the 25-month follow-up as a landmark, no significant differences were observed between the two groups from month 25 to the end of the follow-up period (*P* = 0.141) (**Figures 2a** and **2b**). Stratified Cox regression analysis showed a similar pattern, revealing that after 25 months of follow-up, WC was no longer significantly associated with MACEs (HR = 0.98, 95% CI = 0.97–1.07, *P* = 0.49) (**Figure 1**). Moreover, risk cumulative curves stratified by BMI and WHtR did not show a significant separation trend between the groups (**Figures 2c** and **2d**).

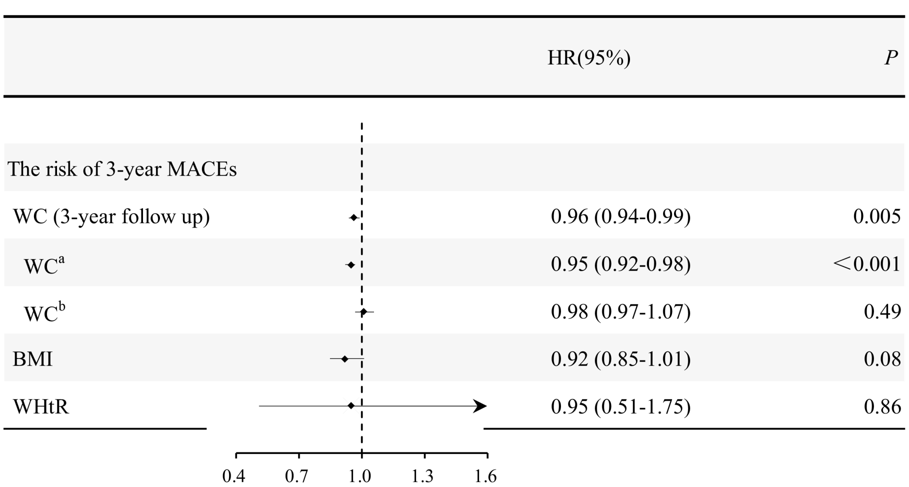

Figure 1. Association of obesity indicators with 3-year follow-up MACEs calculated by multifactorial COX regression. [a] represents the first 25-month of follow-up; [b] represents the period after 25-month follow-up

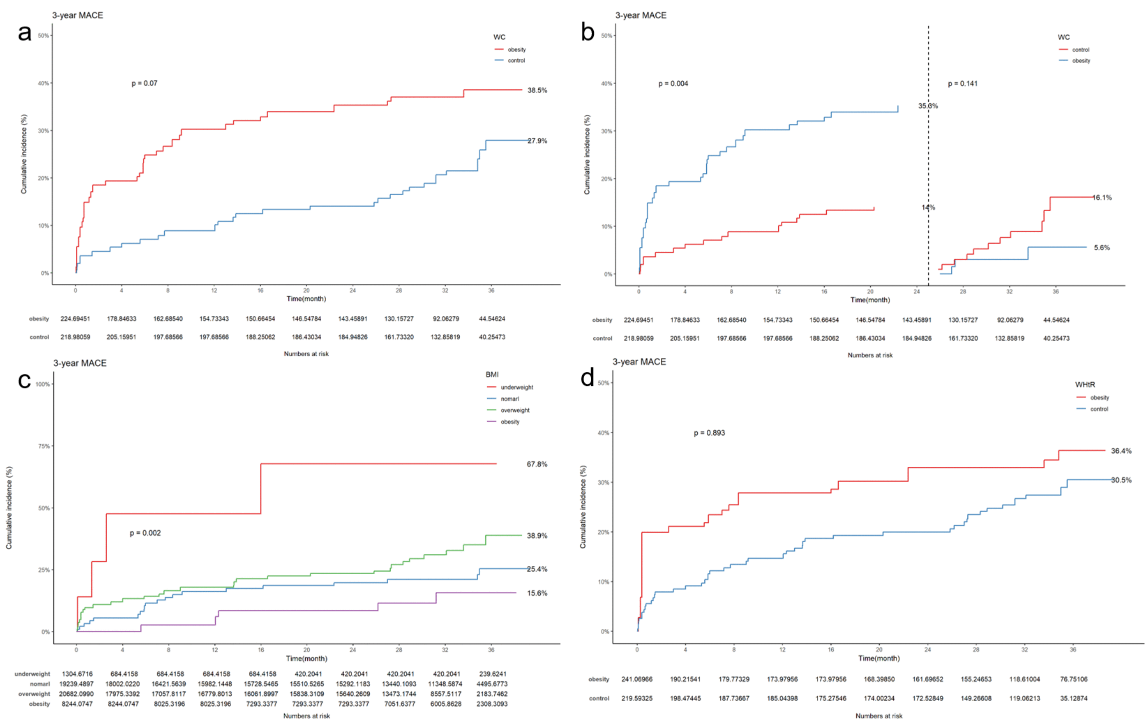

Figure 2. Cumulative risk curves for obesity indicator stratifications based on inverse probability weighting respectively. **(a)** The curve of WC stratification based on 3-year follow-up; **(b)** The landmark analysis of WC stratification of which cut-off value is the first 25 months; **(c)** The curve of BMI stratification; **(d)** The curve of WHtR stratification.

3.3. Composite BMI and WHtR to stratify STEMI patients

As shown in **Figure 3**, the incidence of MACEs was highest in the underweight group (66.7%) and decreased as BMI increased. However, patients with central obesity in all BMI groups had a worse prognosis. Underweight patients with central obesity had the worst prognosis (100% incidence of MACEs), while obese patients had the lowest incidence of MACEs (13.9%).

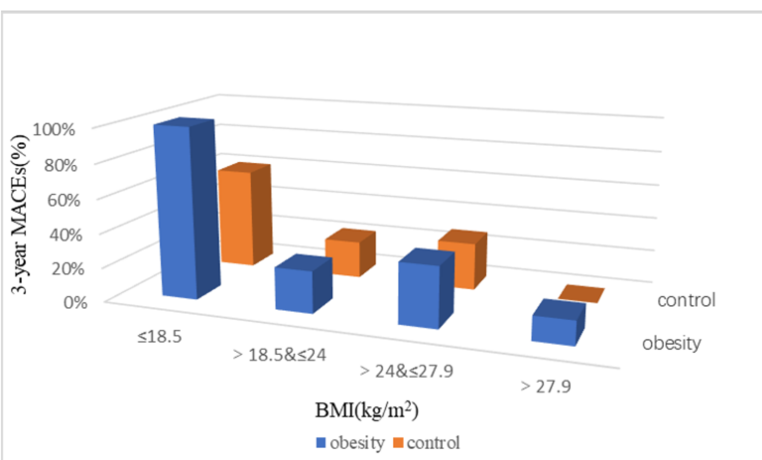

Figure 3. Combine BMI and WHtR to stratify the risk of STEMI patients. WHtR more than 0.5 is defined as central obesity, otherwise as control.

4. Discussion

In this 3-year follow-up of 220 STEMI patients, we did not observe a significant association between BMI or WHtR and long-term prognosis. However, WC showed a cardiovascular protective role during the initial 25 months, but this effect disappeared over time. When patients were categorized based on WHtR after stratification by BMI, those with central obesity had the worst prognosis. Underweight patients with central obesity had the highest incidence of MACEs, while patients with a BMI ≥ 28 kg/m^2 had the lowest incidence of MACEs.

In line with previous studies, our analysis of 220 STEMI patients revealed no significant impact of BMI, WC, or WHtR on long-term prognosis. This finding is consistent with Zeller *et al.* [5], who observed no significant correlation between BMI or WC and 1-year all-cause mortality in acute myocardial infarction patients after adjusting for multiple factors. Their landmark analysis also demonstrated that the effect of WC on prognosis changed over time. Kadakia *et al.* [7] similarly noted a cardioprotective effect of BMI or WC in patients with non-ST elevation ACS within 30 days of follow-up, but this effect was no longer significant after 1 year, and WC even increased the risk of cardiovascular events.

Although we did not find a significant correlation between BMI and MACEs, there was a decreasing trend in MACE incidence as BMI increased. The incidence of MACEs was 66.7% in the underweight population and 13.5% in the obese population. This trend aligns with the findings of Neeland *et al.* [12], who identified a U-shaped relationship between BMI categories and all-cause mortality, with the lowest risk in mildly obese patients and the highest risk in those with normal weight or severe obesity (BMI ≥ 40 kg/m^2). However, unlike our study, Neeland et al. excluded the underweight population, who may have worse prognoses due to associations with low muscle mass, frailty, tumors, and other conditions [13].

Our results suggest that relying on a single obesity index may not accurately stratify patient risk. Therefore, we combined BMI stratification with WHtR, which accounts for the influence of height on fat distribution better than WC alone [11]. When comparing different BMI subgroups, the incidence of MACEs was higher in patients with a WHtR > 0.5, particularly in the underweight group. Among all subgroups, the obese population (BMI ≥ 28 kg/m^2) had the lowest incidence of MACEs. Similarly, a study from the Korean Acute Myocardial Infarction Database found that underweight individuals (BMI < 18 kg/m^2) with a high WHR (> 1.0 in men; > 0.95 in women) had the highest mortality rate, which is consistent with our findings. They also reported a negative linear correlation between BMI and all-cause mortality, while WHR exhibited a positive linear correlation [8]. Although we did not observe a significant linear relationship between BMI and endpoint events, the incidence of MACEs tended to decrease as body weight increased (**Supplementary Material Figure 1**).

This study had several limitations. Firstly, the small sample size resulted in low statistical power, especially due to the limited number of obese individuals, which hindered further stratification within this group. Secondly, as an observational study, it was vulnerable to residual confounding factors, which may have contributed to the low occurrence of endpoint events. Over-adjustment for confounders could also lead to issues of overfitting. Thirdly, we did not record changes in BMI, WC, or WHtR over time, making it difficult to establish a clear association between changes in obesity indicators and patient prognosis. Lastly, although WHtR is considered a better measure of fat distribution than WC, it may still lack precision. Future research should focus on using more objective measures, such as body fat content or visceral fat area, to assess the impact of obesity on the prognosis of CVD patients.

In conclusion, our 3-year follow-up of 220 STEMI patients from China revealed no significant association between BMI, WC, or WHtR and long-term prognosis. However, patients with low body weight and central obesity had the worst prognosis, suggesting that the combination of BMI and WHtR can be used for risk stratification in STEMI patients. Clinically, patients should be encouraged to maintain a healthy diet and normal body shape, with particular attention to the cardiovascular risks associated with central obesity.

Funding

(1) National Natural Science Foundation of China (Grant/Award Number: 81970304);

(2) Tianjin Municipal Science and Technology Commission (Grant/Award Numbers: 18ZXZNSY00290 and 19JCQNJC11500).

Disclosure statement

The authors declare no conflict of interest.

Author contributions

Conceptualization: All authors
Methodology: All authors
Formal analysis: Xiwen Song, Zhuoqun Wang
Investigation: Xiwen Song, Zhuoqun Wang
Writing – original draft: Xiwen Song
Writing – review & editing: All authors

Ethics approval and consent to participate

This study involved human participants, and informed consent was obtained from all patients who participated in this study.

Consent for publication

All patients in this study consent for publication.

Availability of data

The data and study materials are made available for onsite audits by third parties for the purposes of reproducing the results or replicating the procedure.

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Supplementary materials

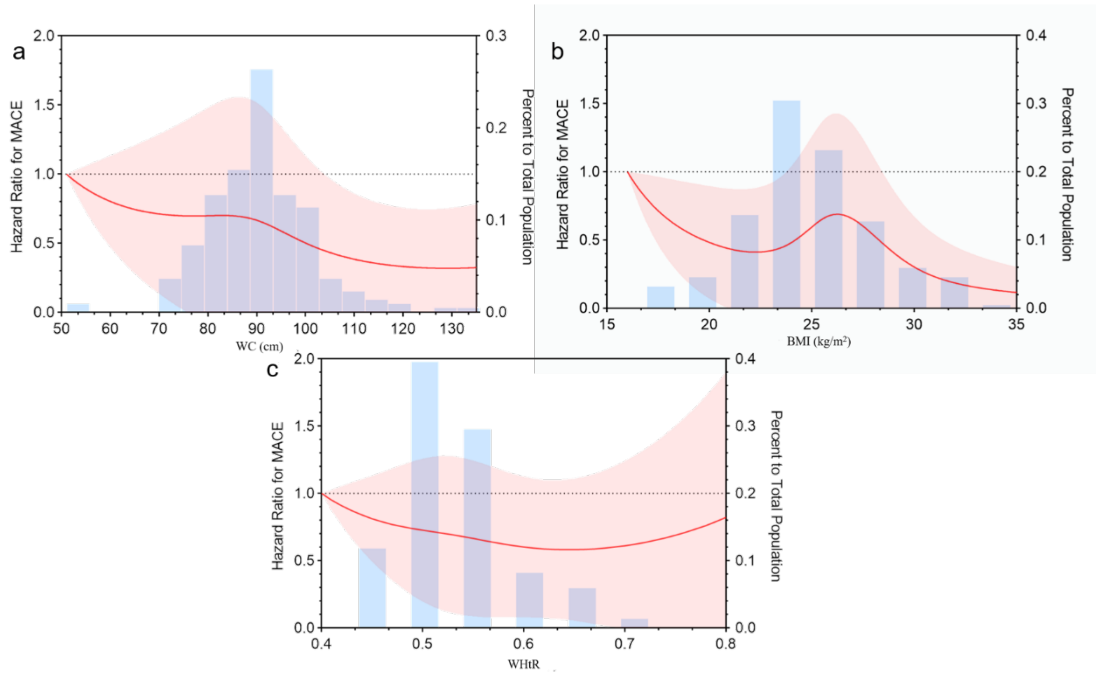

Figure 1. Restricted cubic sample bars demonstrating the association of obesity indicators with the risk of MACEs in STEMI patients at 3-year follow-up. The solid red line represents the risk of incident MACEs; the red shading represents the 95% confidence interval for the risk of incident MACEs; and the blue histogram represents the percent density distribution of each indicator in the population.

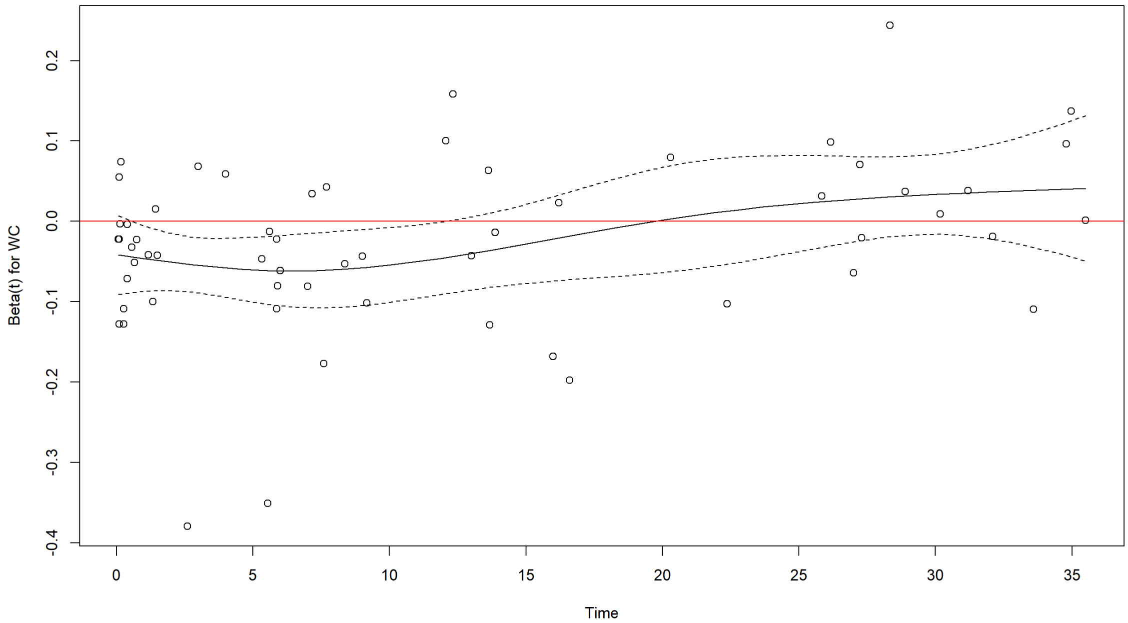

Figure 2. The residual PH test plots scatter plots to show the trend of variable correlation coefficients over time. Circles represent the distribution of the correlation coefficients of the variables; black realizations represent the curves fitted to the correlation coefficients; black dashed lines represent the 95% confidence intervals of the correlation coefficients.

Table 1. Baseline characteristics of the WHtR groups

Characteristics	Total (n = 220)	Central obesity (n = 164)	Control (n = 56)	*P*
Age (years)	61.2±11.7	61.2±11.6	61.0±12.1	0.93
Male [*n* (%)]	176 (80.0)	134 (81.7)	42 (75.0)	0.28
Height (cm)	172.0 (165.5, 175.0)	172.0 (165.5, 175.0)	170.0 (166.0, 175.0)	0.92
Weight (kg)	72.0 (65.0, 80.0)	75.0 (66.0, 80.0)	65.0 (60.0, 75.0)	< 0.001
eGFR (mL/min/1.73 m^2)	111.7 (91.9, 127.3)	108.6 (88.2, 126.1)	116.7 (107.1, 130.4)	0.017
LVEF* (%)	51.0 (43.5, 55.0)	50.0 (43.5, 55.0)	52.0 (44.0, 55.5)	0.22
Anterior infarction [*n* (%)]	108 (49.1)	76 (46.3)	32 (57.1)	0.16
Hypertension [*n* (%)]	117 (53.2)	94 (57.3)	23 (41.1)	0.035
Diabetes [*n* (%)]	46 (20.9)	40 (24.4)	6 (10.7)	0.030
Smoking [*n* (%)]	142 (64.5)	106 (64.6)	36 (64.3)	0.96
		Medication in the first 24 hours		
ACEI/ARB [*n* (%)]	134 (60.9)	102 (62.2)	32 (57.1)	0.50
β-blocker [*n* (%)]	96 (43.6)	69 (42.1)	27 (48.2)	0.42
CCB [*n* (%)]	39 (17.7)	29 (17.7)	10 (17.9)	0.98

Note: * represents echocardiography completed within 24 hours of hospital admissions. Abbreviations: ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; β-blocker, beta-blocker; BMI, body mass index; CCB, calcium channel blocker; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; WHtR, weight-to-height ratio.

Table 2. Baseline characteristics of the WC groups

Characteristics	Total (n = 220)	Central obesity (n = 164)	Control (n = 56)	*P*
Age (years)	61.2±11.7	61.5±12.0	60.7±11.3	0.63
Male [*n* (%)]	176 (80.0)	98 (80.3)	78 (79.6)	0.89
Height (cm)	172.0 (165.5, 175.0)	173.0 (167.0, 176.0)	170.0 (165.0, 174.0)	0.013
Weight (kg)	72.0 (65.0, 80.0)	75.0 (70.0, 85.0)	65.5 (60.0, 72.5)	<0.001
eGFR (mL/min/1.73 m^2)	111.7 (91.9, 127.3)	108.6 (87.4, 126.4)	115.5 (100.2, 127.9)	0.066
LVEF* (%)	51.0 (43.5, 55.0)	50.0 (42.0, 55.0)	51.5 (45.0, 55.0)	0.23
Anterior infarction [*n* (%)]	108 (49.1)	60 (49.2)	48 (49.0)	0.98
Hypertension [*n* (%)]	117 (53.2)	71 (58.2)	46 (46.9)	0.096
Diabetes [*n* (%)]	46 (20.9)	31 (25.4)	15 (15.3%)	0.067
Smoking [*n* (%)]	142 (64.5)	81 (66.4)	61 (62.2)	0.52
		Medication in the first 24 hours		
ACEI/ARB [*n* (%)]	134 (60.9)	82 (67.2)	52 (53.1)	0.033
β-blocker [*n* (%)]	96 (43.6)	52 (42.6)	44 (44.9)	0.74
CCB [*n* (%)]	39 (17.7)	21 (17.2)	18 (18.4)	0.82

Note: * represents echocardiography completed within 24 hours of hospital admissions. Abbreviations: ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; β-blocker, beta-blocker; BMI, body mass index; CCB, calcium channel blocker; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; WC, waist circumference.