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Association of waist circumference with long-term all-cause mortality and cardiac death in patients with a pacemaker: a retrospective study

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Abstract

Objectives To investigate the relationship between abdominal obesity and long-term prognosis in patients with a pacemaker.

Methods In the SUMMIT Study, patients were categorized by baseline waist circumference into obesity, normal, and lean groups. WC was measured at the midpoint between the last rib and hip bone after exhalation. Regular follow-ups were conducted, with all-cause mortality as the primary endpoint and cardiac death as the secondary endpoint.

Results In total, 492 patients were included in the analysis. The average baseline waist circumference was 84.2 ± 12.7 cm, and abdominal obesity was observed in 37.6% of patients. During a mean follow-up of 67.2 ± 17.5 months, 71 death due to any cause (14.40%) and 24 cardiac death (4.87%) events occurred. All-cause mortality was associated with higher waist circumference (87.6 versus 83.6 cm, $P = 0.014$), but not body mass index (23.6 versus 23.5, $P = 0.930$). Multivariate Cox analysis showed compared with patients with abdominal obesity, lean patients had a significant lower risk in both all-cause mortality (HR 0.188, 95%CI 0.070–0.505, $P = 0.001$) and cardiac death (HR 0.097, 95% CI 0.012–0.792, $P = 0.029$).

Conclusions Baseline waist circumference less than 80 cm for men and less than 75 cm for women in patients with a pacemaker had a significant lower risk in long-term all-cause mortality and cardiac death.

Keywords Waist circumference, Body mass index, All-cause mortality, Pacemaker

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What is already known?

- Obesity is related to many diseases including cardiovascular diseases.
- BMI-related obesity paradox is often observed in patients with cardiovascular disorders.

What's New?

- Abdominal obesity was quite common in patients with pacemakers.
- WC is related to long-term all-cause mortality and cardiac death in patients with a pacemaker.
- Only abdominal lean patients (male < 80 cm, female < 75 cm), but not normal group patients had significant lower risk in long-term all-cause mortality and cardiac death.

Future focus of clinical practice.

- WC might be associated with outcomes in patients with pacemaker.
- WC is helpful for early detection of cardiovascular high-risk patients and scientific research.
- Positive intervention of abdominal obesity is expected to improve the prognosis.

Introduction

The incidence of obesity, a common chronic disease worldwide, has increased in recent years, and obesity has been shown to be associated with many diseases, including cardiovascular diseases [1–5]. Obesity can be measured by determining body weight per unit height (body mass index [BMI]), waist circumference (WC), waist-hip ratio, or body fat content [6]. Although BMI is still the most commonly used index in the clinical setting, this measure is not sufficiently accurate to evaluate obesity, and a BMI-related obesity paradox is often observed in patients with cardiovascular disorders [7]. WC and BMI are critical determinants of survival rates in patients with HF. Additionally, WC and obesity are significant factors in the diagnosis and prognosis of HFpEF [8].

WC demonstrates a strong correlation with abdominal adiposity and may serve as a more accurate predictor of mortality compared to BMI [6, 9, 10]. Additionally, WC is related to cardiovascular diseases, such as hypertension, coronary heart disease, and heart failure [11–13]. In elderly patients with HFpEF and implantable cardioverter-defibrillators who are at high risk of sudden cardiac death, there is a paradoxical relationship between BMI and mortality risk due to greater metabolic reserves in overweight patients [14]. Specifically, the mortality rate among obese or overweight individuals is lower compared to those with a normal BMI (25). In patients

with a pacemaker, obesity has been extensively studied. Previous work focusing on the relationships between BMI and prognosis in patients with pacemaker implantation have been inconsistent, and the association of WC with long-term prognosis in these patients remains unclear [15–17].

This study aimed to investigate the prognostic significance of baseline WC in patients with pacemaker implantation by retrospectively analyzing its associations with long-term all-cause mortality and cardiac death.

Methods

Study population

We performed a retrospective analysis utilizing archived data from the SUMMIT registry (Study of Home Monitoring System Safety and Efficacy in Cardiac Implantable Electronic Device - Implantable Patients), which investigates the safety and efficacy of home monitoring systems in patients with cardiac implantable electronic devices in China.

The study included patients who were hospitalized between 2010 and 2014 and met the specified inclusion criteria. The inclusion criteria for the study were as follows: [1] participants must meet the indications for the implantation of a dual-chamber pacemaker (Biotronik, Germany) [18]; [2] participants must have been implanted with a pacemaker equipped with Home Monitoring (HM) functionality and continuous connectivity; [3] participants must be capable of providing baseline data on waist circumference; and [4] participants must be over 18 years of age at the time of implantation. The exclusion criteria were as follows: [1] participants unable to complete the required follow-up; [2] participants who experienced complications during the follow-up period, including cardiac implantable electronic device (CIED)-related infective endocarditis (CDRIE) and lead dislodgment; and [3] participants diagnosed with a neoplastic disease.

The current study adhered to the principles outlined in the Declaration of Helsinki and received approval from the Ethics Committee of Fuwai Hospital (ID: 2010–296), as well as from the ethics committees of all other participating institutions. Furthermore, written informed consent was obtained from all patients prior to their participation in the study.

WC measurement and groups

WC was measured to the nearest 0.5 cm by positioning the tape at the midpoint between the last rib's lower edge and the hip bone's top, aligned with the umbilicus, after exhaling [19]. All participants in the study were local residents. Based on the baseline waist circumference (WC) measurements, the patients were categorized into three distinct groups: obese (defined as $WC \geq 90$ cm for males

and ≥ 85 cm for females), normal (WC ranging from ≥ 80 cm to < 90 cm for males and from ≥ 75 cm to < 85 cm for females), and lean (WC < 80 cm for males and < 75 cm for females) [20, 21].

Data collection

This study's baseline data for hospitalized patients are sourced from medical records and include age, gender, BMI, WC, NYHA classification, complications (ischemic cardiomyopathy, hypertension, diabetes, atrial fibrillation, stroke, syncope), and echocardiographic indexes (LVEF, LAD, LVEDD) and medications like RAS blockers, beta blockers, diuretics, calcium channel blockers, amiodarone, and statins.

Follow-up and study endpoint

The primary endpoints of the study were all-cause mortality and cardiac death. Systematic follow-up was conducted until June 2018. In cases where patient communication was disrupted, the patient's status was verified via telephone. In the event of a patient's death, the family was contacted by telephone to ascertain the cause of death, as documented on the death certificate. Cardiac death was classified as any death to which heart disease contributed, according to the International Classification of Diseases, 10th Revision (ICD-10) codes I00–I09, I11, I20–I51.

Statistical methods

Continuous variables are shown as means \pm standard deviations and analyzed with Student's *t*-tests. Categorical data are displayed as numbers (percentages) and compared using Chi-square tests. Kaplan-Meier curves and Log-rank tests were used to assess group differences in endpoints. Subsequently, Cox proportional hazards models were employed, and all variables demonstrating a statistically significant effect were incorporated into a multivariate Cox proportional hazards model. Hazard ratios (HRs) and 95% confidence intervals (CIs) were computed to assess the impact. Results with two-sided *P*-values less than 0.05 were deemed statistically significant for all tests. All statistical analyses were conducted using SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA).

Results

Baseline characteristics

In the present study, from a total of 2009 patients, 7 patients experiencing complications, including CIED-related infective endocarditis (CDRIE) and lead dislodgment during the follow-up period were excluded first, 534 patients with WC data were obtained. 40 patients with incomplete data, 2 patient with a single-chamber pacemaker were excluded further, and 492 patients were

finally included in the analysis. Men were dominant in the study cohort (55.1%). The average age was 71.9 ± 10.8 years, and the average baseline WC for all patients was 84.2 ± 12.7 cm. Abdominal obesity was observed in 37.6% of cases, abdominal normal was observed in 38.0% of cases, and 24.4% of patients were abdominal lean. Atrial pacing ($P=0.038$), LAD ($P<0.001$), and LVEDD ($P=0.001$) differed significantly between the three groups. No significant differences were found regarding other baseline characteristics (Table 1).

Clinical outcomes

With an average follow-up of 67.2 ± 17.5 months, 71 death due to any cause (14.40%) and 24 cardiac death (4.87%) events occurred. Patients who died of all-cause mortality showed higher WC values (87.6 versus 83.6 cm, $P=0.014$) than those survived; however, there were no differences in BMI (23.6 versus 23.5, $P=0.930$). Compared with patients with abdominal obesity and normal patients, lean patients had lower rates of all-cause mortality (17.83% versus 17.65% versus 4.17%, respectively; $P=0.001$). Lean patients also tended to have lower cardiac death rates (6.47% versus 5.88% versus 0.83%, respectively; $P=0.059$) (Table 2).

Kaplan-Meier survival curves

Estimated Kaplan-Meier survival curves showed that lean patients but not normal patients had better survival in terms of both all-cause mortality (log-rank $P<0.001$; Fig. 1a) and cardiac death (log-rank $P=0.017$) than patients with obesity (Fig. 1b).

Relationship between WC and endpoints

In the univariate Cox regression models, lean patients had a lower risk for all-cause mortality (HR 0.217, 95% CI: 0.085–0.556, $P=0.001$). After the model was adjusted for confounders, including age, NYHA class, BMI, ventricular pacing percentage, the presence of cardiomyopathy, the presence of hypertension, the presence of DM, the presence of stroke, the presence of AF, LVEF, LVEDD, β -blocker, CCB and statins consumption, the multivariate Cox regression modelling results showed that only lean patients, but not normal patients (HR: 0.188, 95% CI: 0.570–1.574; $P=0.835$), had significant lower risk for all-cause mortality (HR: 0.188, 95% CI: 0.070–0.505, $P=0.001$; Table 3).

Additionally, lean patients were found to be negatively associated with cardiac death (HR 0.125, 95% CI: 0.016–0.963, $P=0.046$). After the model was adjusted for confounders, including age, NYHA class, BMI, ventricular pacing percentage, the presence of cardiomyopathy, the presence of hypertension, the presence of DM, the presence of stroke, the presence of AF, LVEF, LVEDD, β -blocker and CCB consumption, the multivariate Cox

Table 1 Baseline characteristics of pacemaker patients in different waist circumference groups

Variables	Total (N = 492)	Abdominal obesity (n = 185)	Abdominal normal (n = 187)	Abdominal lean (n = 120)	P value
Demographic					
Age, years	71.89 ± 10.80	72.19 ± 9.53	71.62 ± 11.83	71.87 ± 11.05	0.879
Male, (%)	271(55.1)	113(61.1)	98(52.4)	60(50.0)	0.106
Height, cm	165.97 ± 7.82	167.45 ± 7.60	165.50 ± 7.89	164.41 ± 7.70	0.112
BMI, kg/m ²	23.55 ± 2.71	24.80 ± 2.85	23.37 ± 2.14	21.90 ± 2.32	<0.001
WC, cm	84.15 ± 12.70	96.56 ± 9.36	81.35 ± 3.45	69.38 ± 6.32	<0.001
NYHA, class I–II	461(93.7)	175(94.6)	175(93.6)	111(92.5)	0.760
Pacing parameters					
Atrial pacing, (%)	41.17 ± 36.21	46.29 ± 38.80	36.81 ± 34.22	40.08 ± 34.37	0.038
Ventricular pacing, (%)	59.67 ± 41.61	59.74 ± 41.74	59.10 ± 41.68	60.45 ± 41.65	0.962
Comorbidities					
Structural heart disease, (%)	235(47.8)	89(48.1)	97(41.3)	49(40.8)	0.167
Hypertension, (%)	253(51.4)	99(53.5)	102(54.5)	52(43.3)	0.123
DM, (%)	67(13.6)	23(12.4)	27(14.4)	17(14.2)	0.836
Stroke, (%)	27(5.5)	10(5.4)	14(7.5)	3(2.5)	0.173
AF, (%)	70(14.2)	29(15.7)	27(14.4)	14(11.7)	0.616
Echocardiography					
LVEF, (%)	60.24 ± 10.45	59.95 ± 11.35	60.83 ± 9.47	59.78 ± 10.49	0.617
LAD, (mm)	35.07 ± 6.96	35.69 ± 6.83	36.07 ± 6.83	32.54 ± 6.82	<0.001
LVEDD, (mm)	48.88 ± 7.54	50.48 ± 7.31	48.36 ± 8.21	47.23 ± 6.31	0.001
Medications					
β-blockers	143(29.1)	65(35.1)	49(26.2)	29(24.2)	0.066
ACEI/ARB	126(25.6)	47(25.4)	43(23.0)	36(30.0)	0.389
Amiodarone	40(8.1)	18(9.7)	13(7.0)	9(7.5)	0.593
Diuretics	58(11.8)	23(12.4)	24(12.8)	11(9.2)	0.588
CCBs	109(22.2)	44(23.8)	42(22.5)	23(19.2)	0.633
Statins	115(23.4)	46(24.9)	50(26.7)	19(15.8)	0.074

Abbreviations: ACEIs, angiotensin-converting enzyme inhibitors; AF, atrial fibrillation; ARBs, angiotensin receptor blockers; BMI, Body Mass Index; CCB, calcium channel blockers; DM, diabetes mellitus; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; NYHA class, New York Heart Association class; WC, waist circumference

Categorical data were presented as numbers (percentages) and compared with Chi-square tests

Table 2 Clinical outcomes of patients depended on waist circumference

Variables	Total (N = 492)	Abdominal Obesity (n = 185)	Abdominal Normal (n = 187)	Abdominal Lean (n = 120)	P value
All-cause mortality	71(14.43%)	33(17.83%)	33(17.65%)	5(4.17%)	0.001
Cardiac death	24(4.88%)	12(6.47%)	11(5.88%)	1(0.83%)	0.059

Categorical data were presented as numbers (percentages) and compared with Chi-square tests

regression modelling results showed that lean patients, but not normal patients (HR: 0.796, 95% CI: 0.333–1.903; $P=0.608$), had significant lower risk for cardiac death (HR: 0.097, 95% CI: 0.012–0.792; $P=0.029$; Table 4).

Discussion

In this study, we investigated the relationships of abdominal obesity with outcomes in patients with a pacemaker. We found that abdominal obesity was quite common in patients with a pacemaker (nearly 40% of patients in the current study). Additionally, WC, as a simple, convenient, economical, and harmless measurement method, was related to long-term all-cause mortality and cardiac

death in patients with a pacemaker. Finally, we also found that lean patients had significantly lower all-cause mortality and cardiac death rates.

Obesity is prevalent worldwide, including China. Gao et al. found that the proportion of abdominal obesity in healthy Chinese individuals was 29.1% in a cross-sectional study of nearly half a million participants [19]. The abdominal obesity rate in patients with pacemaker implantation was higher than that in the general Chinese population. This may be because these patients are also more likely to have metabolic diseases. Indeed, Jensen et al. found that higher BMI was a risk factor of sick sinus syndrome in a large sample of people [22].

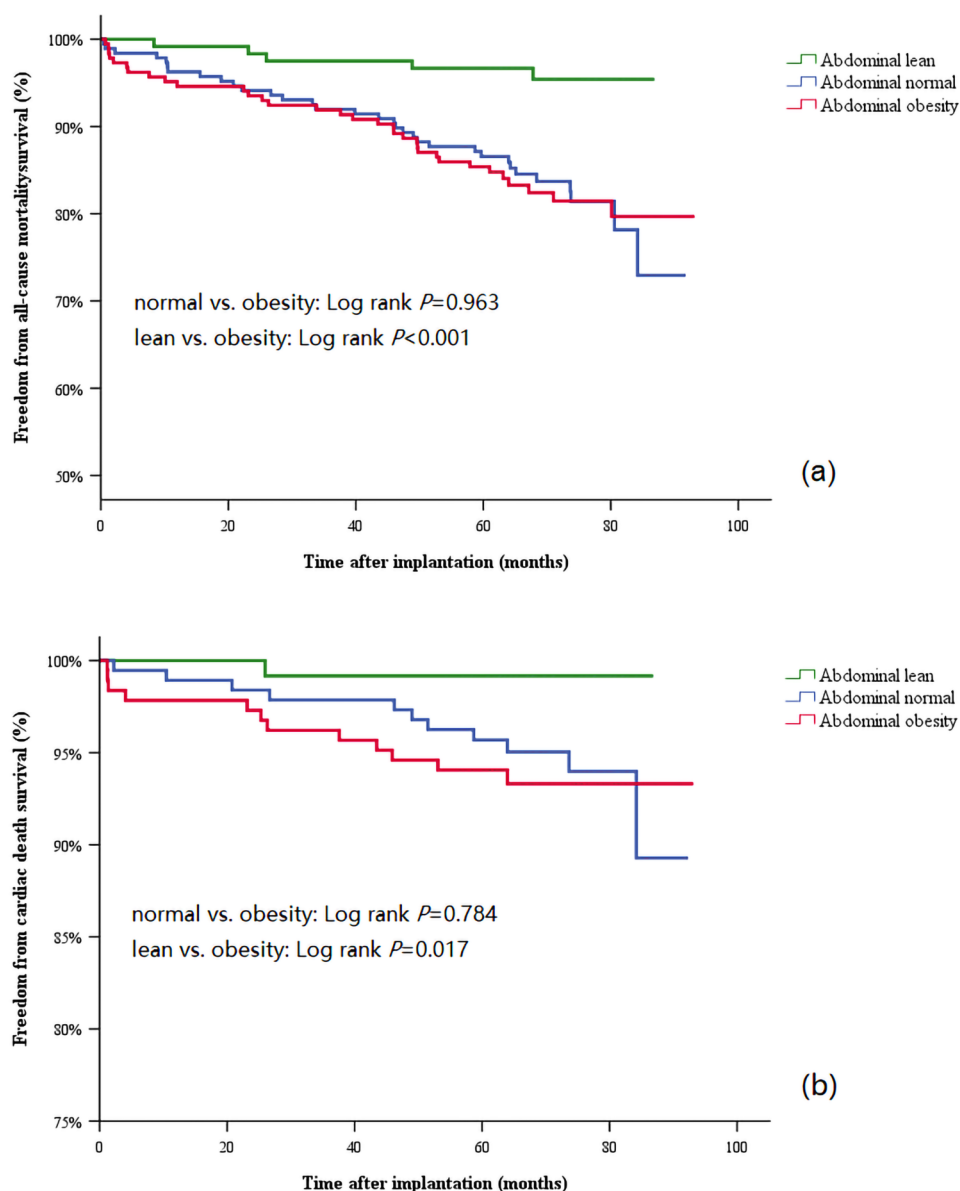


Fig. 1 Kaplan-Meier estimates of freedom from all-cause mortality (a) and cardiac death (b) survival in the 3 groups

The relationship between WC and mortality has been verified in many studies. Sobiczewski observed a direct relationship of WC with both total mortality and cardiovascular mortality in hypertensive patients with coronary heart disease [11]. Additionally, Tsujimoto found that abdominal obesity was associated with an increased risk of all-cause mortality in patients with heart failure with preserved ejection fraction [12]. Moreover, Xing concluded that higher WC is associated with increased risks of major adverse cardiac events in male but not female patients with type 2 DM [13]. However, none of these studies included patients with pacemakers. We found that WC had predictive value in patients with a dual-chamber pacemaker with long-term follow-up. Moreover, remote

monitoring systems that classify transmissions based on the predefined criteria are able to promptly identify abnormal transmissions from patients, facilitating the determination of patient mortality and the underlying causes through proactive follow-up. We found that compared with the abdominal obesity group, lean patients, but not normal patients, had a significant lower risk in both all-cause mortality and cardiac death. In addition, we found that age and percentage of ventricular pacing were related to mortality in patients with a pacemaker, consistent with previous research results [23].

The relationship between obesity and cardiovascular disease and the potential mechanisms are listed as follows. Research has demonstrated that adipose tissue

Table 3 Predictors of all-cause mortality risk, uni- and multivariate Cox proportional hazards models

Variables	Univariate		Multivariate	
	HR(95% CI)	P-value	HR(95% CI)	P-value
Age, years	1.097(1.064–1.132)	< 0.001	1.090(1.054–1.126)	< 0.001
NYHA III/IV	1.496(0.648–3.452)	0.345		
BMI	0.994(0.913–1.082)	0.994		
WC, cm (Abdominal obesity as reference)		0.005		0.003
Abdominal Normal	0.986(0.608–1.599)	0.955	0.948(0.570–1.574)	0.835
Abdominal Lean	0.217(0.085–0.556)	0.001	0.188(0.070–0.505)	0.001
Ventricular pacing	1.008(1.002–1.014)	0.014	1.008(1.001–1.015)	0.016
Cardiomyopathy	1.455(0.908–2.332)	0.119		
Hypertension	1.477(0.918–2.377)	0.108		
DM	1.614(0.899–2.897)	0.109		
Stroke	2.430(1.163–5.074)	0.018		
AF	1.296(0.710–2.366)	0.398		
LVEF, %	0.978(0.959–0.997)	0.024		
LVEDD, mm	0.992(0.959–1.026)	0.622		
β-blockers	1.427(0.881–2.314)	0.149		
CCBs	1.778(1.087–2.909)	0.022		
Stains	1.724(1.054–2.820)	0.030		

Abbreviations: AF, atrial fibrillation; BMI, Body Mass Index; CCBs, calcium channel blockers; DM, diabetes mellitus; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; NYHA class, New York Heart Association class; WC, waist circumference

Table 4 Predictors of cardiac death risk, uni- and multivariate Cox proportional hazards models

Variables	Univariate		Multivariate	
	HR(95% CI)	P-value	HR(95% CI)	P-value
Age, years	1.061(1.012–1.113)	0.014		
NYHA III/IV	2.295(0.684–7.699)	0.179		
BMI	0.971(0.836–1.128)	0.699		
WC, cm (Abdominal obesity as reference)		0.135		0.093
Abdominal Normal	0.892(0.393–2.022)	0.784	0.796(0.333–1.903)	0.608
Abdominal Lean	0.125(0.016–0.963)	0.046	0.097(0.012–0.792)	0.029
Ventricular pacing	1.012(1.001–1.024)	0.040	1.013(1.000–1.026)	0.045
Cardiomyopathy	1.770(0.774–4.048)	0.176		
Hypertension	1.581(0.692–3.614)	0.277		
DM	2.172(0.862–5.476)	0.100		
Stroke	2.657(0.792–8.913)	0.113		
AF	1.536(0.573–4.118)	0.393		
LVEF, %	0.968(0.938–0.999)	0.042	0.960(0.924–0.999)	0.043
LVEDD, mm	0.999(0.947–1.055)	0.985		
β-blockers	1.741(0.773–3.920)	0.181		
CCBs	2.497(1.109–5.625)	0.027		

Abbreviations: AF, atrial fibrillation; BMI, Body Mass Index; CCBs, calcium channel blockers; DM, diabetes mellitus; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; NYHA class, New York Heart Association class; WC, waist circumference

possesses extensive endocrine functions, with cytokines such as leptin, adiponectin, and interleukin-6 exhibiting diverse biological roles [24]. Adipose tissue-derived molecules are involved in several biological processes in the myocardium, such as hypertrophy, redox balance, contractility, inflammation, and fibrosis, and in clinical conditions, such as arrhythmogenesis and heart failure [25].

As cardiovascular physicians, in addition to height and weight, we should evaluate the WC of patients. The ratio of patients admitted to the cardiovascular department who have their WC measured is low, i.e., only about

one-quarter of patients in the database used in this study. In patients with pacemakers, waist circumference is significantly correlated with all-cause mortality.

Limitations

In the present study, despite its multi-center design, the investigation is limited to a single pacemaker model (Bio-tronik) and exclusively includes dual-chamber pacemakers. Moreover, only baseline WC was collected, other parameters of visceral obesity and the dynamic observation of WC was not performed. Additionally, intervening

variables as lipid profile and other cardiometabolic variables were missing. Finally, the conclusions were based on results of retrospective analysis; thus, more prospective studies with larger sample sizes are needed to further validate our findings.

Conclusions

WC can be used as a simple and practical predictor of long-term prognosis in patients with a pacemaker. This should be considered and applied by clinicians in practice.

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None.

Author contributions

XYL and SZ2 contributed to the conception or design of the work. XYL and SZ1 contributed to the acquisition, analysis, and interpretation of data for the work. XYL drafted the manuscript. KPC, WH, YGS, JFY, ZGL, WX, HXN, SZ2 critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Data availability

The datasets generated and analyzed during the current study are not publicly available due to the Fuwai Hospital regulations, but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The present study complied with the Declaration of Helsinki and was approved by the ethics committee of Fuwai Hospital (ID: 2010–296) and all other participating organizations, and all patients provided written informed consent before entering this study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Disclosure

The authors declared no conflict of interest.

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