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Association between skeletal muscle mass and the prognosis of patients undergoing percutaneous coronary intervention: a retrospective study

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Abstract

Background The predicted skeletal muscle mass index (pSMI) is a proven and reliable index that reflects muscle mass; however, its ability to predict major adverse cardiovascular events (MACES) in patients with coronary artery disease (CAD) undergoing percutaneous coronary intervention (PCI) remains uncertain.

Methods A total of 1340 enrolled patients were ultimately included in the study and stratified according to the pSMI tertiles. The primary endpoint was a complex set of MACEs, including all-cause mortality, nonfatal myocardial infarction, and unplanned revascularization. The Kaplan–Meier method was used to generate a cumulative incidence curve of MACEs and secondary endpoint events of all-cause mortality. Due to the competing risk relationship between all-cause mortality and cardiovascular mortality, non-fatal myocardial infarction, and unplanned revascularization events, a competing risk model was employed to analyze the cumulative event incidence curves of competing risk events.The restricted cubic spline analysis was conducted to examine the linear association between pSMI and the incidence of MACE. A univariate and multivariate Cox regression model was utilized to identify predictors of MACEs. The predictive value of the pSMI was evaluated by determining the area under the ROC curve.

Results During a median follow-up of 31.38 months, 217 patients developed MACEs. The Kaplan-Meier survival curve showed the lowest risk of MACEs and all-cause mortality in the high pSMI group(log-rank test, $P < 0.05$). After adjusting for competing risk factors for all-cause death, the cumulative events of cardiac death in the T3 group were lower than other two groups (Gray's test, $P < 0.001$), with no significant difference in the cumulative incidence of non-fatal myocardial infarction and unplanned revascularization between the pSMI groups (Gray's test, $P > 0.05$). The adjusted hazard ratio (HR) for the incidence of MACEs in the highest pSMI tertile was 0.335(95% CI 0.182–0.615; $P < 0.001$), as shown by multivariable Cox regression analysis. Subgroup analysis revealed that the pSMI was negatively correlated with the incidence of MACEs in a population of nonelderly individuals, and those without heart failure

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(all $P < 0.05$). Both the univariate and fully adjusted restriction cubic spline (RCS) curves showed a linear relationship between the pSMI and MACEs. In addition, the inclusion of the pSMI in the basic risk prediction model improved prognostic prediction (the area under the ROC curve increased from 0.647 to 0.682, $P = 0.033$).

Conclusion In patients with CAD undergoing PCI, the pSMI is a protective factor and potentially simple method for assessing the risk of MACEs independently.

Clinical trial number Not applicable.

Keywords Skeletal muscle mass index, Coronary artery disease, Percutaneous coronary intervention, Major adverse cardiovascular events, Prognosis

Introduction

Coronary artery disease (CAD) is currently one of the leading causes of hospitalization and patient death [1], and it results in high health care-related costs worldwide [2]. Percutaneous coronary intervention is currently one of the vital methods for treating coronary artery disease [3]. However, postprocedure adverse cardiovascular events remain a serious concern [4]. Thus, improving risk classification for CAD patients undergoing PCI is very important.

Skeletal muscle mass, which is an important element of body composition, is correlated with muscle strength and physical function. Recent research has suggested that low skeletal muscle mass is associated with poor prognosis of patients with cardiovascular disease [5–11]. Some studies have also indicated that a greater proportion of skeletal muscle mass is associated with increased survival and recovery rates among patients with cardiovascular disease [12, 13]. However, research on the clinical relationship between skeletal muscle mass and the prognosis of patients with coronary artery disease after PCI is limited. Previous studies have mostly used traditional anthropometric measurements, such as bioelectrical impedance analysis (BIA), dual-energy X-ray absorptiometry (DEXA), CT, and MRI, to evaluate skeletal muscle mass [14]. However, these methods require specific equipment and are expensive, which limit their use and validation among the general population. The predicted skeletal muscle mass index (pSMI) is an updated version of an approach based on the serum creatinine-to-cystatin C ratio (CCR), and this index was developed and validated in a population in East Asia [15]. A study by Jae Young Jang et al. comparing indicators based on serum creatinine and cystatin C as biomarkers for sarcopenia screening in community-dwelling older adults, indicated that pSMI is more accurate in assessing the severity of sarcopenia than other indicators such as the ratio of serum creatinine to cystatin C [16]. Several studies have indicated that the Cr/CysC ratio is associated with poor prognosis in patients undergoing PCI treatment [17, 18]. However, not all studies have reached consistent conclusions. A study by Shaochun Lu et al. showed that there was no significant correlation between the Cr/CysC ratio and the risk of mortality after discharge in patients following PCI [19]. These inconsistent research findings reflect the current lack of comprehensive understanding regarding the clinical relationship between skeletal muscle mass index and prognosis in CAD patients after PCI. The pSMI is one of the simple surrogate markers for assessing skeletal muscle mass and may facilitate dose–response analyses of the association between the pSMI and adverse outcomes of CAD after PCI; such analyses will help determine whether pSMI improves risk stratification and investigate the impact of baseline pSMI on the prognosis of patients with coronary artery disease after PCI. To our knowledge, the relationship between pSMI and clinical outcomes post-PCI has not been reported.

Methods

Study population

This study is an observational, retrospective, single-center cohort study involving patients diagnosed with CAD at the Third People's Hospital of Chengdu in Sichuan Province, China, who underwent percutaneous coronary intervention between July 2016 and December 2020. The exclusion criteria were as follows: (1) incomplete relevant clinical data and coronary angiography data; (2) missing effective follow-up information; (3) Malignant tumor, with a life expectancy of less than 1 year. Ultimately, a total of 1340 patients who met the enrollment criteria were included in the cohort.

Data collection and definitions

Data on demographic information (age, sex, height, body weight, and body mass index), previous medical history including smoking habit, previous PCI, heart failure, previous myocardial infarction, hypertension, diabetes mellitus, stroke, atrial fibrillation, chronic obstructive pulmonary disease, and diagnostic information at admission were extracted from the electronic medical record system of the Third People's Hospital of Chengdu. Laboratory tests assessed after an 8-hour fast included triglyceride (TG), total cholesterol (TC), high-density lipoprotein-c (HDL-C), Low-density lipoprotein-c (LDL-C), fasting blood glucose (FBG), hemoglobin A1C (HbA1c), serum creatinine (Scr), cystatin C,

hemoglobin(Hb), brain natriuretic peptide (BNP) and cardiac troponin T (cTnT) levels. The left ventricular ejection fraction (LVEF) was determined via echocardiographic data. Moreover, angiographic and procedural information, such as multivessel disease (MVD), left main disease (LM), chronic total occlusion (CTO), thrombosis, long lesions, number of stents, and length of stents, was also extracted from medical records. In addition, information on medications at discharge, including aspirin, P2Y12 receptor inhibitors, statins, β-blockers, ACEI/ARB, diuretics and insulin, was obtained.

Body mass index (BMI) was calculated as follows: weight (kg)/[height (m)]2. The pSMI was calculated as follows: for men: pSMI = 4.17 – 0.012 x Age (years) + 1.24 x CCR-0.0513 x Hb (g/dL) + 0.0598 x Body weight (kg); for women: pSMI = 3.55-0.00765 x Age (years) + 0.852 x CCR – 0.0627 x Hb (g/dL) + 0.0614 x Body weight (kg). The CCR was calculated via the following formula: serum creatinine (mg/dL)/serum cystatin C (mg/L). A history of diabetes was considered to be self-reported previous diagnosis of diabetes or currently receiving treatment with diabetes medications. A history of hypertension was regarded as self-reported having hypertension or treatment with antihypertensive medications. During the follow-up period, repeated revascularization refers to undergoing PCI or coronary artery bypass grafting.

Followup and clinical endpoints

Clinical follow-up and documentation were performed at 3 months, 6 months, and 1 year, respectively, followed annually by clinical visit or telephone contact. The primary outcome was defined as MACEs, including all-cause death, nonfatal myocardial infarction (MI), and unplanned revascularization during follow-up. Secondary outcomes included all-cause death, cardiac death, nonfatal myocardial infarction, and unplanned revascularization. The endpoint events were documented and verified across relevant medical records.

Statistical analysis

The pSMI tertiles(T1、T2、T3) and the incidence of MACE during follow-up were used to divide patients. Data analyses were performed via SPSS 29.0 and RStudio 4.2.1. The continuous variables are presented as the means ± standard deviations (SDs) or medians with interquartile ranges (IQRs) and were compared via one-way analysis of variance and the Kruskal–Wallis H test. The categorical variables are presented as frequencies and percentages, and the chi-square test or Fisher's exact test was used to compare clinical data between groups, when appropriate. For comparisons across pSMI tertiles, one-way analysis of variance and the Kruskal–Wallis H test for parametric and nonparametric variables were used for continuous variables, as appropriate. For primary research indicators with missing data, we conducted a thorough exclusion based on our predefined inclusion criteria, for the secondary indicators that had missing data, we utilized mean imputation as a data processing technique.

The incidence of MACEs and secondary endpoint events of all-cause mortality was assessed by Kaplan-Meier method and the significance of differences between various groups across the log-rank test. Considering the competitive risk relationship between all-cause mortality and cardiovascular mortality, non-fatal myocardial infarction, and unplanned revascularization events, we employed a competing risks model to analyze the cumulative incidence curves of competing risk events. The significance of differences between groups was compared using Gray's test. The restricted cubic spline analysis was conducted to examine the linear association between pSMI and the incidence of MACE. If there was a nonlinear relationship, the segmented association could be estimated with a weighted Cox model with linear splines. While there was no significant nonlinear association, a univariate and multivariate Cox regression model was utilized to identify predictors of MACEs. Moreover, the analysis was used to identify any possible nonlinear associations between the pSMI adjusted for confounding factors and outcomes. We also conducted subgroup analyses to assess the associations between different populations that were modified by sex, age, hypertension, diabetes mellitus, smoking habits, heart failure, previous acute myocardial infarction (AMI), and previous PCI. Moreover, whether the inclusion of the pSMI could enhance the predictive power of models containing traditional risk indicators was assessed by the receiver operating characteristic (ROC) curve. The comparison of the area under the curve (AUC) between models was performed with the DeLong test.

Results

Baseline characteristics of the enrolled participants

A total of 1340 patients (average age of 67.28 ± 11.12 years), 387(28.90%) were female, who met the criteria and completed the follow-up were included in the study. The baseline characteristics of the research cohort stratified according to the pSMI are shown in Table 1. Compared with patients in the T1 group, patients with higher pSMIs(T3) tended to be younger, to be male, to have a history of smoking, and to use ACEIs/ARBs. Patients who exhibited greater pSMIs tended to have higher weight, BMI, TG, Scr, uric acid, cTnT, and Hb levels and lower BNP, TC, HDL-C, and LDL-C levels (all $P < 0.05$). Moreover, the baseline characteristics of the study cohort according to MACEs are summarized in Supplementary Table S1. Patients with MACEs presented higher BNP, HR, cTnT, Scr, cystatin C, and uric acid values and were

Table 1 Baseline characteristics based on pSMI tertiles

Variable	T1(pSMI ≤ 6.95; *n*=447)	T2(6.95< pSMI≤ 7.77; *n*=447)	T3 (pSMI> 7.77; *n*=446)	*P* value
pSMI	6.25 ± 0.47	7.4 ± 0.24	8.35 ± 0.51	< 0.001
Age, years	73.91 ± 8.3	69.29 ± 9.55	61.42 ± 11.28	< 0.001
Female, n (%)	325(72.70)	54(12.10)	8(1.80)	< 0.001
Body weight, kg	54.22 ± 6.5	65.21 ± 5.34	76.63 ± 8.66	< 0.001
BMI, kg/m2	22.52 ± 2.9	24.45 ± 2.63	26.79 ± 3.01	< 0.001
Smoking, n (%)	100(22.40)	282(63.10)	310(69.50)	< 0.001
Heart failure, n (%)	23(5.10)	18(4.00)	17(3.80)	0.575
Previous AMI, n (%)	11(2.5)	20(4.5)	17(3.8)	0.256
Previous PCI, n (%)	34(7.60)	46(10.30)	41(9.2. 0)	0.371
COPD, n (%)	18(4.00)	19(4.3.00)	9(2.00)	0.131
Hypertension, n (%)	325(72.70)	308(68.90)	302(67.70)	0.237
Diabetes mellitus, n (%)	177(39.60)	180(40.30)	202(45.30)	0.169
Atrial fibrillation, n (%)	20(4.50)	19(4.30)	10(2.20)	0.147
Previous Stroke, n(%)	20(4.50)	29(6.50)	14(3.10)	0.059
Laboratory data				
SBP, mmHg	135.36 ± 22.39	133.35 ± 21.09	132.06 ± 20.00	0.064
Heart rate, bpm	78.57 ± 15.69	77.15 ± 13.99	77.75 ± 13.38	0.056
cTnT, pg/ml	21.95(9.41,278.23)	32.66(11.38, 625.25)	26.61(11.17, 502.25)	0.029
BNP, pg/ml	115.00(49.80, 318.10)	104.00(39.10, 301.60)	80.75(25.10, 219.38)	< 0.001
Scr, mg/dl	0.78(0.65, 0.96)	0.91(0.78, 1.09)	0.92(0.81, 1.05)	< 0.001
Cystatin C, mg/L	1.32 ± 0.62	1.35 ± 0.73	1.29 ± 0.90	0.414
Uric acid, umol/L	364.96 ± 119.15	378.71 ± 123.99	421.34 ± 127.99	< 0.001
FBG, mmol/L	1.35 ± 0.42	1.39 ± 0.7	1.28 ± 0.86	0.414
HbA1c	7.22 ± 1.55	7.22 ± 1.73	7.36 ± 1.69	0.620
TG, mmol/L	2.05 ± 1.51	1.62 ± 0.92	2.22 ± 1.76	< 0.001
TC, mmol/L	4.83 ± 1.33	4.29 ± 1.32	4.39 ± 1.27	< 0.001
HDL-C, mmol/L	1.29 ± 0.36	1.13 ± 0.31	1.04 ± 0.25	< 0.001
LDL-C, mmol/L)	2.89 ± 0.94	2.61 ± 0.98	2.7 ± 0.96	0.037
Haemoglobin, g/dL	12.58 ± 1.73	13.50 ± 1.84	14.12 ± 1.87	< 0.001
LVEF	55.92 ± 9.99	55.06 ± 9.89	53.66 ± 9.34	0.074
Clinical presentation, n (%)				0.055
CCS	38(8.50)	42(9.40)	31(7.00)	
UA	231(51.70)	203(45.40)	212(47.50)	
NSTEMI	83(18.60)	97(21.70)	74(16.60)	
STEMI	95(21.30)	105(23.50)	129(28.90)	
Treatment				
Aspirin, n (%)	432(97.10)	429(96.40)	438(98.90)	0.055
P2Y12 receptor inhibitor, n(%)	440(98.70)	435(97.50)	441(99.10)	0.153
Statins, n (%)	440(98.40)	434(97.10)	434(97.30)	0.370
β-blockers, n (%)	298(66.70)	297(66.40)	315(70.60)	0.321
ACEI/ARB, n (%)	211(47.20)	194(43.40)	234(52.50)	0.025
Diuretics, n (%)	88(19.70)	80(17.90)	69(15.50)	0.253
Insulin, n (%)	49(1.10)	50(11.20)	41(9.20)	0.566
MVD, n (%)	309(69.10)	300(67.10)	277(62.10)	0.074
LM, n (%)	27(6.00)	13(2.90)	24(5.40)	0.069
Thrombosis, n (%)	6(5.70)	9(9.00)	16(1.50)	0.071
Long lesion, n (%)	75(68.20)	71(66.40)	75(65.20)	0.894
CTO, n (%)	25(23.60)	17(16.80)	27(24.80)	0.329
Number of stents	1.46 ± 0.82	1.47 ± 0.97	1.53 ± 0.93	0.695
Length of stents, mm	38.1 ± 24.3	39.67 ± 29.93	40.58 ± 28.32	0.948

more likely to have MVD, to use diuretics, to take insulin, to be NSTEMI and STEMI, to have a higher prevalence of diabetes mellitus and heart failure, and lower levels of pSMI, weight, BMI, Hb, LVEF (all $P<0.05$).

Skeletal muscle mass, estimated by the pSMI, and the risk of adverse cardiovascular events

The occurrence of MACEs and individual incidents are summarized in Table 2. Over a median follow-up duration of 31.38 months (IQR, 27.58–35.57 months), 217 patients (16.2%) experienced MACEs during the follow-up period, including 94(7.0%) all-cause deaths, 54(4.0%) cardiac deaths, 36(2.7%) nonfatal MIs, and 119(8.9%) unplanned revascularizations. As the pSMI increased among the three groups, the risk of compound MACEs, all-cause deaths, and cardiac deaths decreased (all $P<0.05$). No significant differences in the incidence of nonfatal myocardial infarction and unplanned revascularization were observed between three groups.

The Kaplan–Meier analysis revealed that patients in the 3rd pSMI tertile tended to experience the lowest cumulative incidence of MACEs, while patients in the 1st and 2nd pSMI tertiles had a similar incidence of MACEs (log-rank test, $P=0.001$) (Fig. 1A). The differences were driven mainly by the decrease in all-cause mortality (log-rank test, $P<0.001$)(Fig. 1B). After adjusting for competing risk factors for all-cause death, the cumulative events of cardiac death in the T3 group were lower than other two groups (Gray's test, $P<0.001$)(Fig. 2A), with no significant difference in the cumulative incidence of non-fatal myocardial infarction and unplanned revascularization between the pSMI groups (Gray's test, $P>0.05$). Moreover, the incidences of recurrent myocardial infarction (Gray's test, $P=0.50$) and unplanned revascularization (Gray's test, $P=0.30$) during the follow-up time were similar (Fig. 2B and C). Additionally, the pSMI showed a linear association with the incidence of MACEs (Pnonlinearity = 0.060; Fig. 3A). Among all the participants, those with higher pSMIs had a lower incidence of MACEs. Then, univariate and multivariate Cox proportional hazards analyses identified the association between pSMI and MACEs during follow-up, and the results are shown in Supplementary Table S2. Univariate Cox regression analysis revealed that the pSMI, heart failure, atrial fibrillation, COPD, diabetes mellitus, BNP, uric acid, HbA1c, LVEF, MVD, and use of diuretics were strongly associated with MACE occurrence in patients after PCI (all $P<0.05$). Significant variables in the univariate Cox analysis and traditional risk factors (previous AMI, previous PCI, and previous stroke) were included in the multivariate Cox proportional hazards regression analysis. After controlling for the covariates, the multivariate Cox regression analysis showed that the continuous variable pSMI was still negatively correlated with the occurrence of the MACEs. Additionally, multivariate Cox proportional risk regression analysis was further constructed to demonstrate that the pSMI tertiles were significantly associated with MACE occurrences ($P<0.05$, Table 3). After adjusting Model I (accounting for heart failure, diabetes mellitus, BNP and uric acid) and Model II (comprehensive adjustments for above risk factors), the highest tertile of the pSMI was associated with a statistically significant reduction in the incidence of MACEs compared with the 1st tertile (all $P<0.05$). According to the fully adjusted model, the adjusted HR for the incidence of MACEs in the 3rd pSMI tertile compared with the lowest tertile was 0.335(95% CI 0.182–0.615). Additionally, the RCS analysis also revealed a linear association between the pSMI and the risk of MACEs in the fully adjusted model (Pnonlinearity = 0.113; Fig. 3B). The diagnostic performance of the pSMI for MACEs in patients after PCI was assessed via ROC analysis (Fig. 4). The areas under the ROC curves of the baseline risk model, baseline risk model + pSMI for predicting the occurrence of MACEs after PCI were 0.647 (95%CI 0.604 to 0.690; $P<0.001$), 0.682 (95%CI 0.641 to 0.722; $P<0.001$), respectively. The area under the ROC curve increased from 0.647 to 0.682($p=0.033$), a statistically significant predicted incremental value can be observed in the ROC curve. The addition of the CCR had an increase in the AUC from 0.647 (95%CI 0.604 to 0.690; $P<0.001$) to 0.677 (95%CI 0.635 to 0.719; $P<0.001$), but no statistically significant predicted incremental value was observed($P=0.052$). The model incorporating pSMI showed an increase in AUC compared to the model incorporating CCR(from 0.677 to 0.682, $p=0.640$), but no statistically significant improvement was noted.

Table 2 Adverse cardiovascular events in the study population during follow-up

Variable	Total (n=1340)	T1 (*n*=447)	T2 (*n*=447)	T3 (*n*=446)	*P* value
MACE, n (%)	217(16.2)	84(18.8)	83(18.3)	51(11.4)	**0.004**
All-cause death, n (%)	94(7.0)	45(10.1)	37(8.3)	12(2.7)	**<0.001**
Cardiac death, n (%)	54(4.0)	23(5.1)	26(5.8)	5(1.1)	**<0.001**
Non-fatal MI, n (%)	36(2.7)	13(2.9)	14(3.1)	9(2.0)	0.553
Unplanned revascularization, n (%)	119(8.9)	35(7.8)	47(10.5)	37(8.3)	0.321

The data are presented as n (%)

MACEs, major adverse cardiovascular events; MI, myocardial infarction

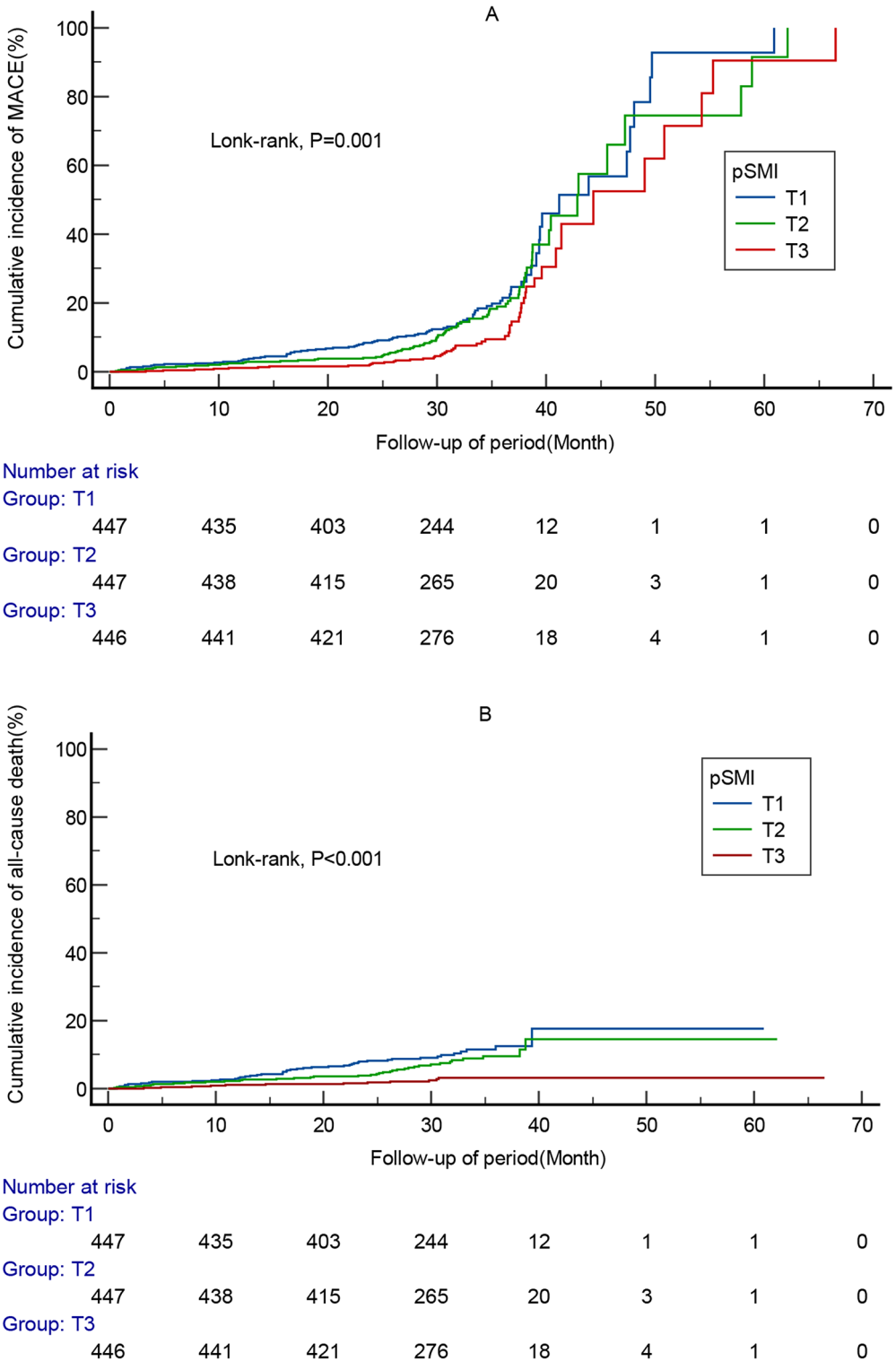

Fig. 1 Kaplan–Meier survival curve for the cumulative incidence of MACEs and all-cause death according to the pSMI tertiles. Significant differences in the cumulative risks of MACEs, and all-cause mortality among the three groups of pSMI ($P < 0.05$). Kaplan–Meier curves for the incidence of MACEs (**A**), all-cause death (**B**)

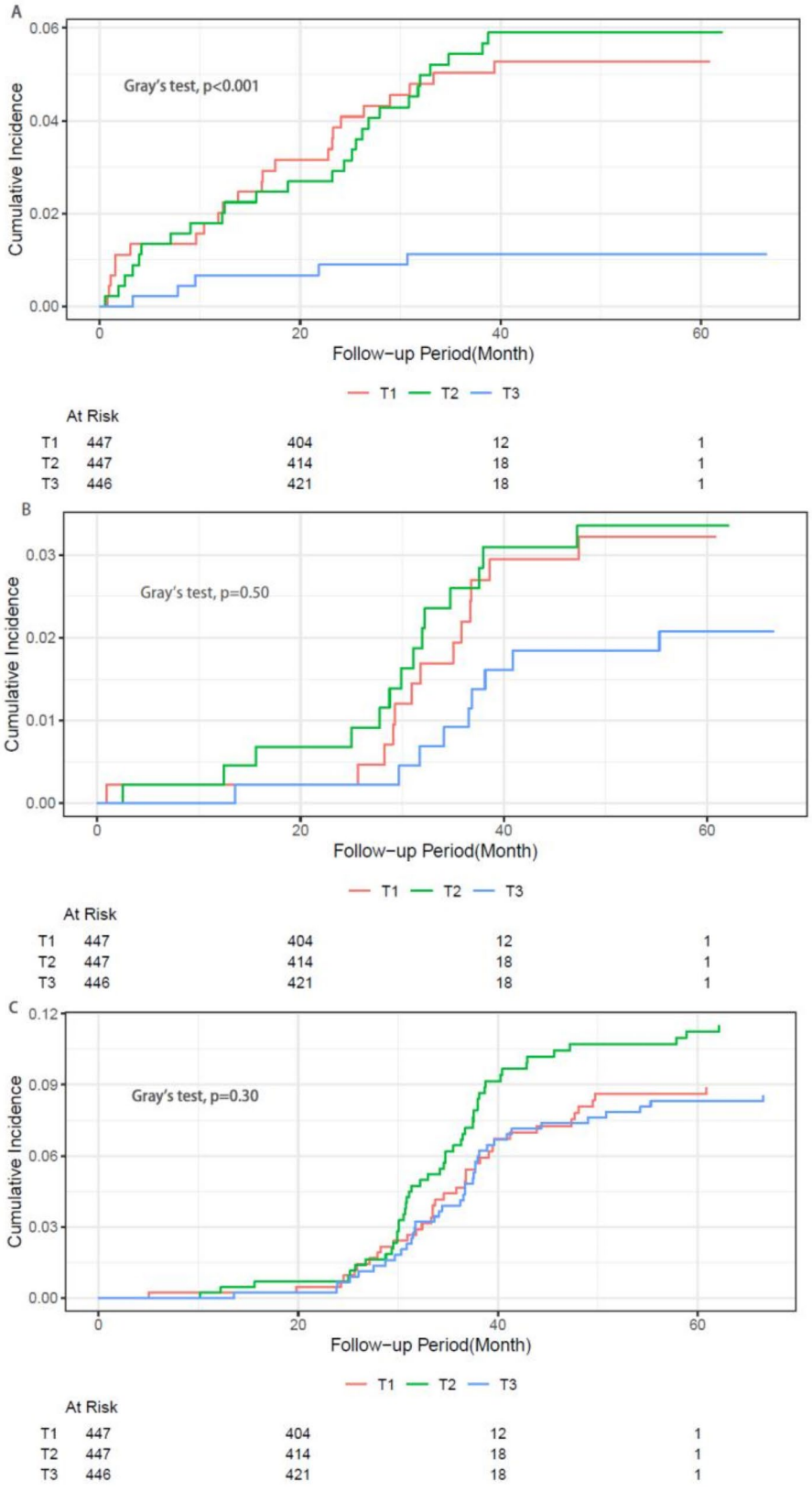

Fig. 2 Competitive risk analysis for competitive risk endpoint events based on different pSMI tertiles. After controlling for competing risk events, significant differences in the cumulative incidence of cardiovascular mortality among the three groups of pSMI ($P < 0.05$), no significant differences were observed among the three groups in non-fatal myocardial infarction and unplanned revascularization events ($P > 0.05$). Competitive risk analysis for the incidence of cardiovascular death (**A**), nonfatal myocardial infarction (**B**), and unplanned repeat revascularization (**C**)

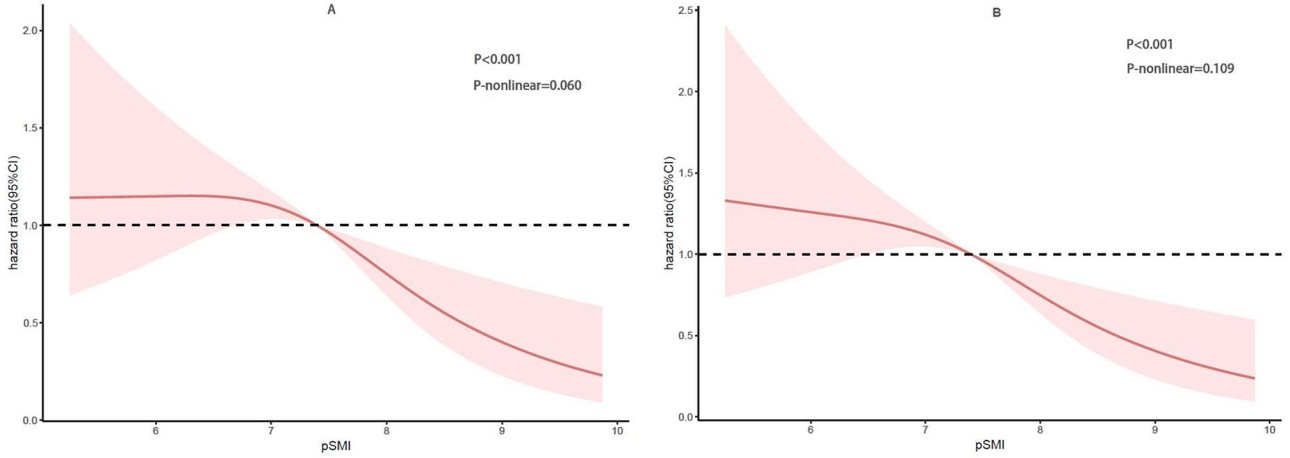

Fig. 3 Relationships between the pSMI and MACEs. **A** Penalized spline curve in patients (unadjusted). **B** Penalized spline curve in patients with fully adjusted variables (previous AMI, previous PCI, previous stroke, heart failure, atrial fibrillation, COPD, diabetes mellitus, BNP, uric acid, HbA1c, LVEF, MVD, and diuretics). CI, confidence interval

Table 3 Multivariate Cox regression analyses for MACE in the study population

	Non-adjusted		Model I		Model II	
	HR (95% CI)	***P* value**	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
pSMI	0.760(0.655–0.883)	< 0.001	0.726(0.618–0.853)	< 0.001	0.681(0.535–0.866)	0.002
T1	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
T2	0.887(0.653–1.204)	0.441	0.826(0.600-1.137)	0.241	0.800(0.487–1.314)	0.378
T3	0.529(0.372–0.751)	< 0.001	0.469(0.321–0.684)	< 0.001	0.335(0.182–0.615)	< 0.001

None, non-adjusted model

Model I: adjusted for heart failure, diabetes mellitus, BNP and uric acid

Model II: Model I + further adjusted for previous AMI, previous PCI, previous stroke, COPD, atrial fibrillation, HbA1c, LVEF, MVD, and diuretics

Subgroup analyses

Next, we conducted subgroup analyses stratified by sex, age, hypertension, diabetes mellitus, smoking habits, heart failure, previous AMI, and previous PCI. As shown in Fig. 5, the results indicated an apparent interaction between age and the effect of the pSMI on the incidence of MACEs (P for interaction < 0.001). Similar results were also observed in the heart failure subgroup (P for interaction < 0.001). Furthermore, we found that each 1.0-SD increase in the pSMI was negatively correlated with the incidence of MACEs in a population of nonelderly individuals (HR: 0.67, 95% CI: 0.49 – 0.91, $P < 0.01$), and those without heart failure (HR: 0.77, 95% CI: 0.66–0.90, $P = 0.001$). However, no statistical interaction was observed among the gender, hypertension, diabetes mellitus, smoking habits, previous AMI, and previous PCI(all P for interaction > 0.05).

Discussion

This study is the first, to our knowledge, to investigate the association between the pSMI and the incidence of long-term adverse events in patients undergoing PCI for CAD. In this study, we observed a negative correlation between the pSMI and the risk of MACEs in patients after PCI. The group with the highest pSMIs had a significantly decreased risk of MACEs, which was mainly driven by all-cause death. Even after adjusting for potential confounding factors, the pSMI remained independently associated with the incidence of MACEs. A series of subgroup analyses revealed that individuals whose pSMI was most strongly associated with MACEs were those with nonelderly individuals, and patients with no history of heart failure. The results also demonstrated a consistent fundamental linear relationship, both unadjusted and after multivariable adjustment. In summary, our research confirms that the pSMI has predictive value for MACEs in patients with CAD following PCI.

PCI has become one of the important treatment modalities for CAD, and increasing attention is being paid to the MACEs occurring after PCI. Previous studies have focused primarily on traditional cardiovascular risk factors, leaving significant room for optimizing risk classification. Early research has indicated that a reduction in muscle mass is an important risk factor for cardiovascular disease and other diseases. The pSMI reflects muscle mass on the basis of the serum creatinine/cystatin C ratio, which was developed and validated in a population study in Japan and demonstrated better diagnostic performance than the serum creatinine/cystatin C ratio did [15, 20]. A large-scale cohort study also revealed a

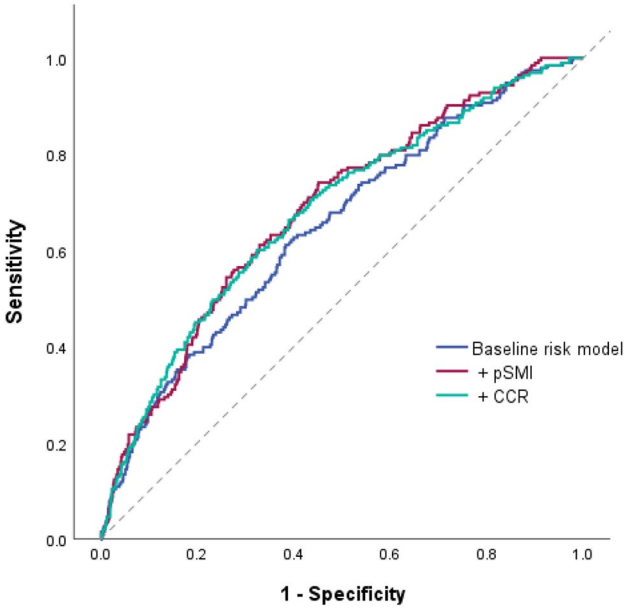

Fig. 4 The receiver operating characteristic (ROC) curves of the pSMI. The areas under the ROC curves of the baseline risk model, baseline risk model + pSMI, and baseline risk model + CCR for predicting the occurrence of MACEs after PCI were 0.647 (95%CI 0.604 to 0.690; $P < 0.001$), 0.682 (95%CI 0.641 to 0.722; $P < 0.001$), and 0.677 (95%CI 0.635 to 0.719; $P < 0.001$), respectively. P for comparison between the baseline model and the baseline model + pSMI is 0.033. P for comparison between the baseline model and the baseline model + CCR is 0.052, and P for comparison between the baseline model and + pSMI and the baseline model + CCR is 0.640. The baseline risk model includes previous AMI, previous PCI, previous stroke, heart failure, atrial fibrillation, COPD, diabetes mellitus, BNP, uric acid, HbA1c, LVEF, MVD, and diuretics

correlation between skeletal muscle mass and diabetes [21]. However, research on using pSMI as a predictor of skeletal muscle mass is limited, and the development of this index is based on the Japanese population. Its applicability to the Chinese population is still unclear, and currently, there are no studies correlating pSMI with the prognosis of coronary heart disease patients after PCI. Thus, we performed an analysis to obtain an association between the pSMI and the risk of MACEs in patients who underwent PCI. Our study revealed a negative correlation between the pSMI and MACEs. A single-center, prospective cohort study in Korea revealed that a lower SMI based on the CT measurement of L1 is closely associated with an increased risk of all-cause mortality and MACEs over three years [22]. Two other studies indicated that a lower SMI (calculated based on the serum creatinine/cystatin C ratio) was associated with an increase in MACE endpoints [17, 18]. These findings confirmed that a lower SMI is an independent predictor of adverse clinical outcomes. Our study indicated that a higher pSMI was associated with a decreased risk of MACEs in CAD patients who underwent PCI, this disparity may be due to differences in follow-up time and mortality. This research revealed that high skeletal muscle mass may protect against cardiovascular events, and consistent with previously published findings. Carl J. Lavie MD et al. suggested that patients with greater skeletal muscle mass may have improved heart failure prognoses [12]. The model incorporating pSMI showed an increase in AUC compared to the model incorporating CCR, However, there is no statistically significant improvement.

In this study, traditional risk factors such as previous AMI, previous PCI, and stroke did not show statistically significant effects in the univariate Cox regression analysis. The potential reasons for this may include limitations due to insufficient sample size and not enough follow-up time, as well as the interference of confounding factors within the demographic characteristics that were not adequately controlled in the analysis. Additionally, the limitations of univariate analysis itself, which does not account for interactions between factors and the influence of other variables, may have contributed to the lack of significant impact of previous AMI, prior PCI, and stroke in the univariate Cox regression analysis. However, due to the strong clinical relevance of these variables, we included previous AMI, previous PCI, and stroke in a multivariable Cox proportional hazards model for analysis, but still no significant effect was observed. A larger sample size may be needed for further analysis.

Subgroup analysis revealed an interaction between pSMI and its effect on the incidence of MACEs across age and heart failure subgroups. In the non-elderly population and individuals without a history of heart failure, pSMI showed a significant negative correlation with the incidence of MACEs. The following reasons may explain the results. In the elderly population, the decline in physical function and the increased likelihood of multiple chronic diseases may weaken the protective effect of skeletal muscle mass on the cardiovascular system. In contrast, good skeletal muscle quality may more effectively exert its metabolic regulation and cardiovascular protective functions in younger patients, thereby significantly reducing the risk of MACEs. Research shows heart failure may induce a reduction in muscle mass through common pathophysiological mechanisms such as hormonal changes, malnutrition, and lack of physical activity. Conversely, the reduction in muscle mass may promote the development of Heart failure through different mechanisms, including pathological myoclonus. High skeletal muscle mass may play a compensatory and protective role in cardiac function by improving the interaction between the heart and skeletal muscle, thereby further reducing the occurrence of MACEs. However, the organic decline in cardiac function may diminish the protective effect of high skeletal muscle mass in heart failure populations [11].

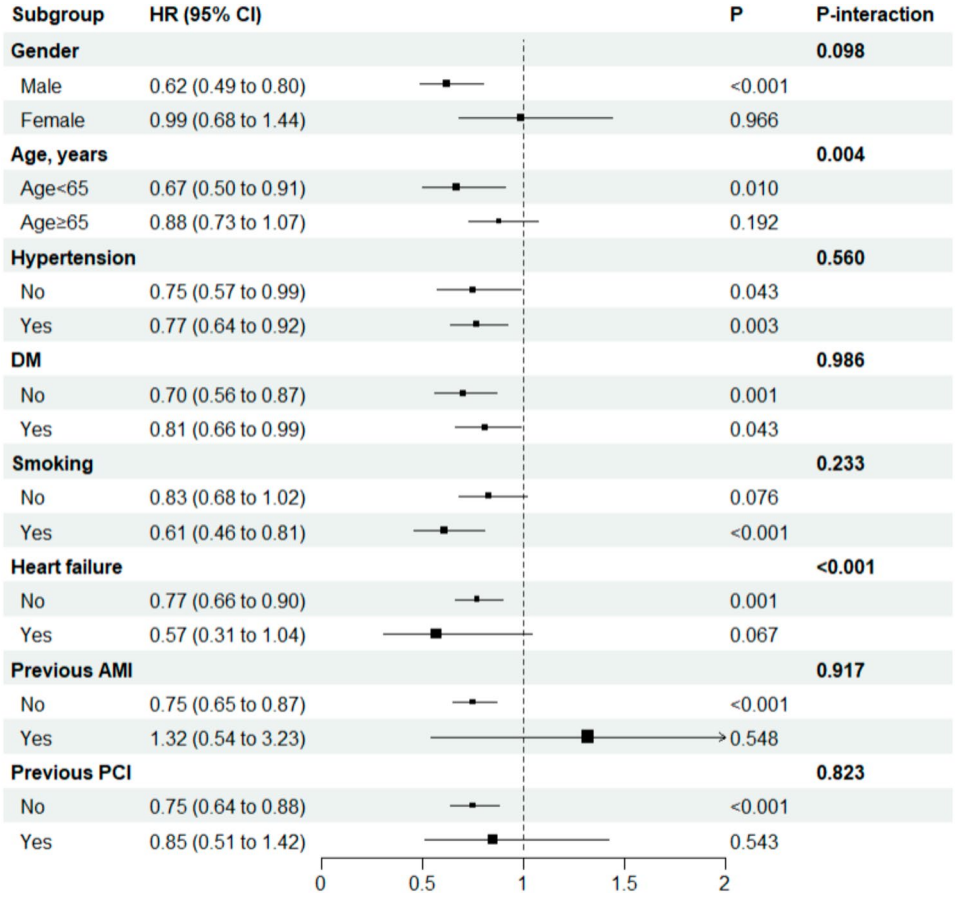

Fig. 5 Subgroup analysis between the pSMI and MACEs in various subgroups (sex, age, hypertension, diabetes mellitus, smoking habits, heart failure, previous AMI, and previous PCI)

These findings highlight increased muscle mass as a preventive measure for poor cardiovascular outcomes. In patients with low muscle mass, along with older age, preexisting chronic comorbidities, frailty, or muscle loss, these factors may contribute to an increased mortality rate [23–27]. The strong evidence for increasing muscle mass, strength, and physical function comes from studies of exercise intervention programs, such as resistance and aerobic training [28–31]. A study also indicated that elderly men and women benefit equally from progressive resistance exercise [32]. Some studies have shown that a diet rich in protein and amino acids may be an important measure for increasing muscle mass [33–35]. Combining resistance training with protein supplementation may yield better results. These findings collectively emphasized the critical role of resistance exercise and nutrition in preventing major adverse cardiovascular endpoint events.

Study limitations

First, the present investigation was a single-center retrospective analysis, therefore, it is limited in directly drawing causal inferences between skeletal muscle mass and MACEs in individuals after PCI. Further randomized, multicenter, and large cohort studies are necessary to explore the potential of increased muscle mass for preventing major cardiovascular events in patients undergoing PCI. Second, while the reliability and accuracy of the pSMI have recently been validated in Asian populations, the pSMI is a surrogate marker of muscle mass, not a direct measure, and the pSMI is a composite index that includes only baseline serum creatinine, cystatin C, and Hb values; however, these values may change during follow-up due to participants' lifestyles and medications. Therefore, more research is needed to validate this approach. Third, the exclusion of a considerable number of patients due to missing data and the relatively small number of hard endpoints observed in our cohort might have led to an underestimation of the effect. Longer follow-up times and larger cohort studies are needed. Finally, the development of the pSMI indicator is based on elderly individuals living in the community in Japan, with different calculation formulas for males and females. However, our study is from a Chinese population, and it is unclear whether an accurate analysis can be conducted. Uncontrolled confounding factors may limit the

conclusions that can be drawn. Therefore, the application of the pSMI indicator in population-based studies requires further research.

Conclusion

The pSMI, which is a surrogate indicator of muscle mass, is an independent prognostic factor for MACEs in patients undergoing PCI. Patients with a higher pSMI have a reduced risk of MACEs, suggesting the pSMI is a protective factor. Therefore, these patients may benefit from targeted prevention or aggressive treatment to improve their clinical outcomes.

Supplementary Information

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Supplementary Material 1

Author contributions

Xf.P drafted the manuscript, Xf.P and Sq.X were major contributors to the collection, analysis, and interpretation of data. Cy.C, T.Y, X.C, Sq. Y, Ly.Q, Q.F, MI.J, and L.T contributed to the data collection. L.C and Z.Z designed the study and finally approved the manuscript submitted. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval and consent to participate

The cohort study strictly adhered to the Declaration of Helsinki and received approval from the Research Ethics Committee of Chengdu Third People's Hospital. Patients who participated in the study provided written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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