冠状动脉微血管功能障碍的评估及其对ST段抬高型急性心肌梗死再灌注治疗的预测价值:基于QFR-AMR研究

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摘要:目的 通过联合评估冠状动脉大血管和微循环,全面预测ST段抬高型心肌梗死(STEMI)患者接受经皮冠状动脉介入治疗(PCI)治疗后发生不良心脑血管事件(MACCEs)的风险。**方法** 回顾性纳入来自两个医学中心的507例成功接受PCI的STEMI患者。基于受试者工作特征(ROC)曲线分析,确定基于血管的微血管阻力(AMR)预测MACCEs的最佳截断值为256.5 mmHg·s/m,结合既往文献确立的定量流量比(QFR)临界值0.80,采用2×2析因设计将患者分为4个亚组。第1组为心外膜血管功能正常且微循环功能良好组(QFR≥0.8且AMR<256.5,*n*=271,占53.5%);第2组为心外膜血管功能正常但微循环功能异常组(QFR≥0.8且AMR≥256.5,*n*=140,占27.6%);第3组为心外膜血管功能异常但微循环功能相对良好组(QFR<0.8且AMR<256.5,*n*=77,占15.2%);第4组为心外膜血管与微循环功能均异常组(QFR<0.8且AMR≥256.5,*n*=19,占3.7%)。主要临床结局为2年随访期间的心源性死亡或因心力衰竭再次入院的发生情况。**结果** 在507例患者中,AMR≥256.5 mmHg·s/m的患者在PCI术后2年内发生MACCEs的风险显著增加(*P*<0.001)。Kaplan-Meier生存分析表明,QFR<0.8且AMR≥256.5 mmHg·s/m的患者具有更差的生存率。多元线性回归分析显示,糖尿病(*P*<0.001)、高脂血症(*P*<0.001)、吸烟(*P*<0.014)、系统性炎症反应指数(*P*<0.007)以及血小板与淋巴细胞比值(*P*<0.001)均与AMR水平升高独立相关。此外,限制性立方样条回归分析揭示了AMR与MACCEs发生风险之间的非线性关系(non-linear *P*<0.001),当AMR阈值达到259.45 mmHg·s/m时,MACCEs的发生风险显著增加。**结论** 基于QFR与AMR的联合评估框架可有效预测STEMI患者急诊PCI术后发生MACCEs的风险。此外,AMR是PCI术后MACCEs的独立预测指标,其数值升高与MACCEs风险显著相关。
关键词:冠状动脉微循环障碍;基于血管的微血管阻力;定量血流比;急性ST段抬高型心肌梗死;主要不良心脑血管事件

Evaluation of coronary microvascular dysfunction for assessing prognosis of ST-segment elevation acute myocardial infarction following reperfusion therapy: insights from QFR-AMR

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Abstract: Objective To assess the risk of major adverse cardiovascular and cerebrovascular events (MACCEs) in patients with ST-segment elevation myocardial infarction (STEMI) following percutaneous coronary intervention (PCI) by evaluating both the large coronary vessels and coronary microcirculation. **Methods** A total of 507 patients with STEMI undergoing successful percutaneous coronary intervention (PCI) were retrospectively enrolled from two centers. The optimal cut-off value (256.5 mmHg·s·m^{-1}) of angio-based microvascular resistance (AMR) for predicting MACCEs was determined by ROC analysis. Combined with a quantitative flow ratio (QFR) threshold of 0.80, the patients were classified into 4 groups: Group 1 (QFR≥0.8, AMR<256.5; *n*=271), Group 2 (QFR≥0.8, AMR≥256.5; *n*=140), Group 3 (QFR<0.8, AMR<256.5; *n*=77), and Group 4 (QFR<0.8, AMR≥256.5; *n*=19). The primary endpoint was cardiac death or heart failure readmission within 2 years. **Results** Patients with elevated AMR (≥256.5 mmHg·s·m^{-1}) had a significantly increased risk of MACCEs within two years after PCI (P<0.001). Kaplan-Meier analysis showed the lowest survival rate in patients with both QFR<0.8 and AMR≥256.5 mmHg·s·m^{-1}. Multiple linear regression analysis suggested that diabetes (*P*<0.001), hyperlipidemia (*P*<0.001), smoking (*P*<0.014), systemic inflammation response index (*P*<0.007), and platelet to lymphocyte ratio (*P*<0.001) were independently associated with elevated AMR levels. Restricted cubic spline regression revealed a non-linear relationship between AMR and MACCEs risk (non-linear *P*<0.001), and the hazard ratio for MACCEs increased markedly for an AMR beyond the threshold of 259.45 mmHg·s·m^{-1}. **Conclusion** The integrated assessment of QFR and AMR allows effective prediction of MACCEs risk in STEMI patients after PCI, and elevated AMR is an independent predictor of significantly increased risk of MACCEs.
Keywords: coronary microcirculatory dysfunction; angio-based microvascular resistance; quantitative flow ratio; st-segment elevation myocardial infarction; major adverse cardiovascular and cerebrovascular events

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直接经皮冠状动脉介入治疗(PCI)是目前公认治疗ST段抬高型心肌梗死(STEMI)的首选策略,其主要目标在于快速恢复闭塞冠状动脉的血流灌注[1,2]。然而,部分患者在术后仍可能出现主要不良心脑血管事件(MACCEs)。有研究显示,PCI虽能改善冠状动脉血流

动力学状态，但改善微循环方面效果局限[3]。冠状动脉微血管功能障碍（CMD）可能会影响PCI的长期疗效，增加主要不良心脑血管事件（MACCEs）的发生率[4-8]。

目前测定冠状动脉微循环的金标准为微循环阻力指数（IMR），但因其操作有创性，因此在临床应用中受到一定限制[9, 10]。基于血管的为血管阻力（AMR）作为一项用于无创评估冠状动脉微循环的新技术，其优势在于操作简便、检查时间短、对患者配合依赖较低[11]。相比之下，尽管CMR在评估心肌微灌注方面具有较高的准确性，但其检查过程较为复杂，需要患者配合屏气，且部分病情严重的STEMI患者难以耐受，限制了其临床推广应用[12]。因此，AMR在临床中广受关注。作为定量血流比（QFR）的衍生指标，AMR侧重微循环层面的功能学评估；而QFR用于评估冠状动脉大血管狭窄的血流动力学意义，有助于识别可能从PCI中受益的患者，并为临床决策提供依据[13]。当前临床研究表明，当QFR值低于0.80时，通常提示冠状动脉血流受到显著限制，这可能意味着患者需要通过PCI治疗以改善血流状态。这一临界值在多项临床研究中得到了验证，并表现出较高的诊断准确性[14]。

鉴于既往关于PCI术后MACCEs的研究主要集中于微循环层面，而同时涉及冠状动脉大血管与微循环的综合性研究仍较为有限。本研究拟采用QFR与AMR，构建冠状动脉大血管联合微循环的双维度评估框架，旨在评估其对STEMI患者急诊PCI后发生MACCEs的预测效能。以提高PCI术后治疗的精确性，并为个体化治疗方案的制定提供支持。

1 资料和方法

1.1 研究对象与方案

纳入2021年1月1日~2022年7月1日，在蚌埠医科大学第一附属医院和宿州市第一人民医院因STEMI成功接受PCI的成年患者（年龄≥18岁）。根据2025年美国心脏病学会（ACC）与美国心脏协会（AHA）专家共识文件中对STEMI定义[15]。成功的PCI定义为PCI血管造影显示狭窄程度小于30%，并且伴随血流动力学改善[16]。排除标准包括：存在精神障碍性疾病的患者；冠状动脉造影质量不佳（如图像分辨率低、数据格式不规范、图像不完整、存在明显血管重叠或伪影、仅提供单一的PCI血管造影图像）；拒绝参与随访评估的患者；以及诊断为恶性肿瘤的患者。本研究遵循《赫尔辛基宣言》的指导原则及相关伦理准则，确保所有参与者均为自愿参与。本研究方案经蚌埠医科大学第一附属医院（伦理批号：2023KY046）和宿州市第一人民医院伦理委员会批准（伦理批号：SZYYLLky2024016）。本研究为回顾性研究，研究方案已获得伦理委员会批准，并获准免除知情同意书的要求。

1.2 QFR与AMR的测定

本研究评估了成功再通且血流动力学稳定后罪犯血管的QFR和AMR。采用AngioPlus系统软件（搏动医疗科技有限公司，上海 AngioPlus）计算QFR和AMR。QFR采用0.80作为风险分界值，根据此前研究所示，该阈值已被广泛接受为判断功能性狭窄的临界标准[14]。

1.3 临床结局

主要结局定义为2年内发生的心源性死亡或心力衰竭（HF）再住院事件。次要结局除了涵盖构成主要结局的各组成部分外，还进一步纳入以患者为中心的心血管结局（POCO），包括任何类型的心肌梗死、任何形式的血运重建手术、因心绞痛或卒中导致的再住院事件。心源性死亡是指由已知心脏病因、不明原因或无法明确归因的任何死亡事件。HF是一种以心输出量减少或心室充盈压升高为特征的临床综合征，相关症状可能在静息状态下或体力活动时出现。诊断依赖于详细的临床评估，并结合客观证据，例如超声心动图显示的心脏结构异常或血浆利钠肽水平升高等相关指标，以确认心脏功能或结构的异常[17]。所有事件均由经验丰富的心血管专科医师确认。随访方法包括电话回访、查阅门诊记录和分析住院记录。

1.4 实验室检查

入院时系统采集患者的临床资料，并抽取外周静脉血样本进行实验室检测。检测项目包括全血细胞计数、常规生化指标、肌钙蛋白-I（cTnI）、D-二聚体、肌酸激酶同工酶（CK-MB）以及N末端脑钠肽前体（NT-proBNP）等。根据以下公式计算中性粒细胞与淋巴细胞比值（NLR）、血小板与淋巴细胞比值（PLR）、全身免疫炎症指数（SII）和系统性炎症反应指数（SIRI）：NLR=中性粒细胞计数/淋巴细胞计数；PLR=血小板计数/淋巴细胞计数；SII=（中性粒细胞计数×血小板计数）/淋巴细胞计数；SIRI=（中性粒细胞计数×单核细胞计数）/淋巴细胞计数[18]。

1.5 统计学分析

采用SPSS 27和R 4.4.1软件进行数据分析。根据Shapiro-Wilk检验结果，对于连续性变量，根据数据分布的具体特征，其描述方式一般为均数±标准差或中位数（四分位间距）。分类变量采用频数和百分比进行描述。采用多元线性回归分析识别与AMR相关的独立危险因素。通过Kaplan-Meier分析估计结局事件的累积发生率，并采用时序检验评估组间差异。在Cox比例风险模型的框架下，采用限制性立方样条（RCS）曲线构建MACCEs的风险比（HR）曲线，探讨PCI后AMR与临床

结局之间可能存在的非线性关系。所有统计检验均为双侧，显著性水平为P<0.05。

1.6 样本量估算

实际纳入样本：507例STEMI患者。主要终点事件：60例(11.8%)。根据文献报告和预试验数据，预期低风险组(QFR≥0.8且AMR<256.5 mmHg·s/m)的2年主要终点事件发生率约为2%，高风险组(QFR<0.8且AMR≥256.5 mmHg·s/m)的事件发生率约为70%。设定双侧检验α=0.05，检验效能1-β=80%，采用Logrank检验计算样本量：$n=2[(Z\alpha/2+Z\beta)^2]/[\ln(HR)]^2\times(1/\pi_1+1/\pi_2)$，其中$\pi_1$和$\pi_2$分别为两组的预期事件比例，HR为预期风险比。计算得出本研究至少需要260例。考虑到10%的失访率，最终确定目标样本量为289例。实际纳入507例，满足研究需求。

2 结果

2.1 ROC曲线评估AMR预测MACCEs的效能

采用受试者工作特征(ROC)曲线评价AMR对MACCEs的预测效能，并确定最佳截断值。该阈值为256.5 mmHg·s/m (AUC：0.861；灵敏度：0.88；特异度：0.77)随后被用于后续分析(图1)。

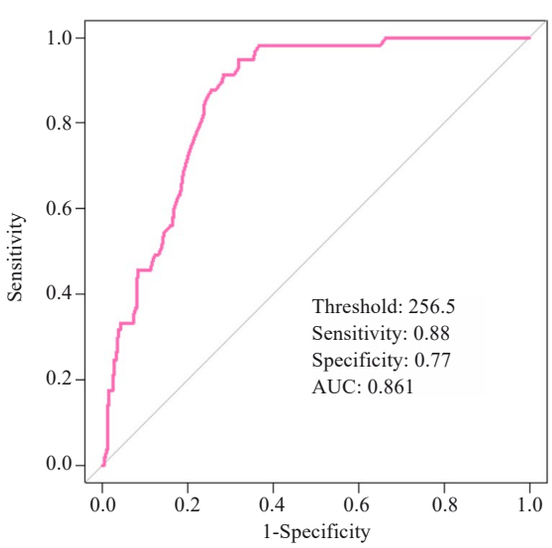

图1 STEMI患者PCI术后AMR的ROC曲线分析

Fig. 1 ROC curve analysis of angio-based microvascular resistance (AMR) in patients with ST-segment elevation myocardial infarction (STEMI) after percutaneous coronary intervention (PCI). The curve illustrates the diagnostic efficacy of AMR for identifying major adverse cardiovascular and cerebrovascular events at the optimal cutoff value of 256.5 mmHg·s/m (sensitivity: 88%; specificity: 77%; AUC: 0.861).

2.2 基线资料

本研究筛选了2021年1月1日~2022年7月1日期间接受PCI的753例患者。其中，192例患者因不符合纳入标准而被排除，另有73例患者因血管造影图像质量不满足临床评估要求而被剔除。本研究共纳入507例患者进行分析。根据QFR和AMR将患者分为4组：QFR≥0.8且AMR≥256.5 mmHg·s/m组(n=140例)；QFR≥0.8且AMR<256.5 mmHg·s/m(n=271例)；QFR<0.8且AMR≥256.5 mmHg·s/m(n=19例)；QFR<0.8且AMR<256.5 mmHg·s/m (n=77例)(图2)。

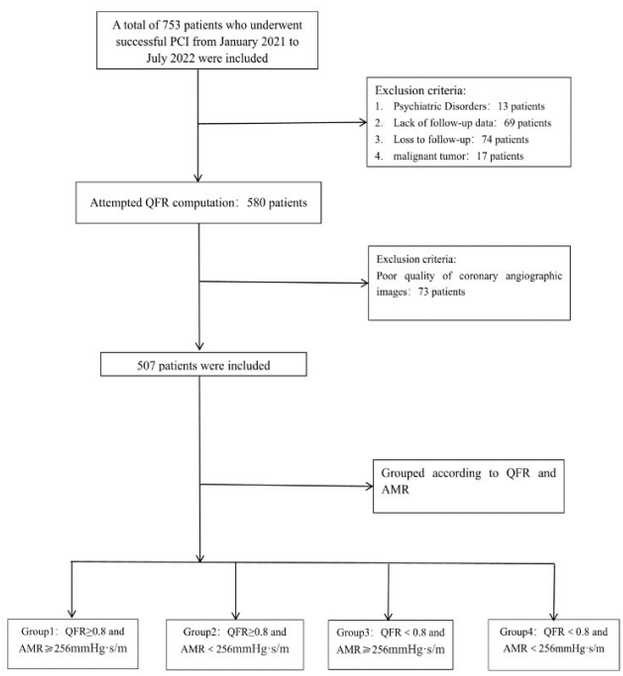

图2 患者筛选分组流程图

Fig. 2 Patient screening flowchart. A total of 753 patients who underwent PCI were screened during the period from January 1, 2021, to July 1, 2022, and 507 patients included for further analysis. According to the QFR and AMR, the patients were categorized into 4 groups.

在QFR≥0.8组(表1、2)中，组1(AMR≥256.5 mmHg·s/m)患者的平均年龄高于组2(AMR<256.5 mmHg·s/m)患者(69岁 *vs* 60岁)。此外，组1男性比例高于第2组(84.3% *vs*74.2%)。组1患者的糖尿病(55.0% *vs* 35.1%)、高脂血症(70.0% *vs* 51.7%)和吸烟(73.6% *vs* 59.0%)比例也显著高于组2。此外，组1淋巴细胞计数低于组2(1.6×10^9/L *vs* 1.9×10^9/L)，而SII水平显著高于组2 (781.9 *vs* 632.2)。组1的MACCEs发生率也显著升高(18.5% *vs* 1.4%)(P<0.05)。

在QFR<0.8组(表1、2)中，组3(AMR≥256.5 mmHg·s/m)的糖尿病(52.6% *vs* 31.1%)和高脂血症(94.7% *vs* 51.9%)患病率显著高于组4 (AMR<256.5 mmHg·s/m)。第3组血小板计数(252.0×10^9/L *vs* 204.0×10^9/L)和SII(968.0 *vs* 591.3)显著升高。此外，组3 MACCEs发生率显著高于组4(73.6% *vs* 20.7%)(P<0.05)。

表1 基线资料

Tab.1 Baseline characteristics of the patients included

Characteristics	QFR≥0.8		*P*	QFR<0.8		*P*
	AMR≥256.5 mmHg·s/m (*n*=140, group 1)	AMR<256.5 mmHg·s/m (*n*=271, group 2)		AMR≥256.5 mmHg·s/m (*n*=19, group 3)	AMR<256.5 mmHg·s/m (*n*=77, group 4)	
Study population						
Age (year)	69 (60, 77)	60 (53, 72)	<0.001	69 (56, 76.00)	67.00 (57, 78)	0.873
Male [*n* (%)]	118 (84.3)	201 (74.2)	0.024	18 (94.7)	53 (68.8)	0.021
Cardiovascular risk factors						
Hypertension [*n* (%)]	93 (66.4)	160 (59.1)	0.165	17 (89.5)	54 (70.1)	0.142
Diabetes [*n* (%)]	77 (55.0)	95 (35.1)	<0.001	10 (52.6)	24 (31.1)	0.036
Hyperlipemia [*n* (%)]	98 (70.0)	140 (51.7)	<0.001	18 (94.7)	40 (51.9)	<0.001
Stroke [*n* (%)]	29 (20.7)	45 (16.6)	0.343	2 (10.5)	12 (15.6)	0.729
Smoking [*n* (%)]	103 (73.6)	160 (59.0)	0.005	12 (63.1)	47 (61.0)	0.875
Previous CHD [*n* (%)]	16 (11.4)	46 (16.9)	0.148	2 (10.5)	11 (14.3)	0.397
Previous PCI [*n* (%)]	10 (7.1)	16 (5.9)	0.671	0 (0)	2 (2.6)	0.682
Pain-to-balloon time (min)	246 (140.8, 362.5)	219 (129.5, 387.0)	0.110	489 (247.0, 690.0)	454.0 (254.0, 900.0)	0.457
Laboratory index						
cTnI (ng/L)	1.1 (0.1, 8.7)	0.6 (0.1, 7.6)	0.443	12.6 (1.3, 36.6)	9.4 (1.2, 27.9)	0.608
NT-proBNP (pg/mL)	241.0 (97.2, 1019.2)	220.1 (70.7, 731.5)	0.724	852.0 (407.1, 1600.0)	356.0 (158.0, 1877.0)	0.300
Creatinine (μmol/L)	69.0 (56.0, 82.0)	66.0 (55.0, 79.0)	0.232	69.0 (59.5, 85.0)	69.0 (58.0, 86.0)	0.835
CK/CKMB	7.4 (5.5, 9.6)	7.3 (5.6, 9.5)	0.755	6.1 (5.0, 8.2)	8.2 (5.2, 9.9)	0.124
TC-C (mmol/L)	4.7 (3.8, 5.4)	4.7 (3.8, 5.6)	0.472	4.3 (3.6, 4.7)	4.4 (3.7, 5.2)	0.561
TG (mmol/L)	1.6 (1.0, 2.3)	1.5 (1.0, 2.2)	0.339	1.2 (0.8, 1.8)	1.2 (0.7, 1.9)	0.846
HDL-C (mmol/L)	1.0 (0.9, 1.2)	1.0 (0.8, 1.2)	0.472	1.0 (0.9, 1.2)	1.0 (0.8, 1.2)	0.896
LDL-C (mmol/L)	2.6 (2.2, 3.3)	2.7 (2.1, 3.4)	0.508	2.6 (2.3, 3.0)	2.6 (2.2, 3.1)	0.935
Inflammatory index						
Neutrophil (10^9/L)	6.2 (4.8, 7.2)	6.0 (4.6, 7.4)	0.728	6.3 (5.8, 8.3)	7.1 (5.4, 9.2)	0.306
Monocyte (10^9/L)	0.5 (0.3, 0.6)	0.4 (0.3, 0.6)	0.263	0.5 (0.4, 0.8)	0.5 (0.4, 0.7)	0.919
Platelet (10^9/L)	223.0 (187.2, 255.2)	201.0 (164.0, 235.0)	0.005	252.0 (240.5, 265.5)	204.0 (155.0, 227.0)	0.001
Lymphocyte (10^9/L)	1.6 (1.2, 2.0)	1.9 (1.5, 2.4)	<0.001	1.4 (1.2, 2.3)	2.4 (1.9, 2.6)	0.051
SII	781.9 (651.9, 942.6)	632.2 (466.0, 769.8)	<0.001	968.0 (773.6, 1466.5)	591.3 (422.6, 812.3)	0.002
SIRI	1.7 (1.1, 2.8)	1.49 (0.9, 2.1)	0.061	1.87 (1.1, 3.8)	1.57 (1.0, 2.8)	0.609
PLR	3.6 (2.9, 4.0)	3.2 (2.3, 4.0)	0.005	3.9 (2.9, 5.6)	3.0 (2.2, 4.0)	0.124
NLR	130.3 (105.4, 165.1)	100.8 (74.9, 125.8)	<0.001	152.3 (99.1, 224.3)	83.0 (64.4, 100.7)	<0.001
Discharge medications						
Aspirin [*n* (%)]	134 (95.7)	265 (97.7)	0.306	14 (73.6)	63 (96.9)	0.468
Ticagrelor [*n* (%)]	80 (57.1)	174 (64.2)	0.381	11 (57.8)	55 (84.6)	0.286
Clopidogrel [*n* (%)]	52 (37.1)	95 (35.0)	0.511	3 (15.7)	10 (15.3)	0.702
Statins [*n* (%)]	133 (95.0)	266 (98.1)	1.000	14 (73.6)	62 (95.3)	0.572
ACEI/ARB [*n* (%)]	65 (46.4)	139 (51.2)	0.597	4 (21.0)	20 (30.7)	0.511
Beta-blocker [*n* (%)]	107 (76.4)	219 (80.8)	0.788	10 (52.6)	44 (67.6)	0.488
ARNi [*n* (%)]	24 (17.1)	57 (21.0)	0.135	5 (26.3)	24 (36.9)	0.304
SGLT2i [*n* (%)]	1 (0.7)	13 (4.8)	0.041	1 (5.2)	10 (15.3)	0.392
Spirolactone [*n* (%)]	64 (45.7)	102 (37.6)	0.068	6 (31.5)	22 (33.8)	0.180
Furosemide [*n* (%)]	57 (40.7)	92 (33.9)	0.125	6 (31.5)	19 (29.2)	0.259

QFR: Quantitative flow ratio; AMR: Angio-based microvascular resistance; CHD: Coronary Heart Disease; PCI: Percutaneous coronary intervention; cTnI: Cardiac troponin I; NT-proBNP: N-terminal pro b-type natriuretic peptide; CK/CKMB: Creatine kinase/creatine kinase-MB; TC-C: Total cholesterol; TG: Triglycerides; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; SII: Systemic immune-inflammation index; SIRI: Systemic inflammation response index; PLR: Platelet-lymphocyte ratio; NLR: Neutrophil-lymphocyte ratio.

表2 冠状动脉血管相关特征

Tab. 2 Characteristics related to coronary artery vessels in different groups of patients

Characteristics	QFR≥0.8		*P*	QFR<0.8		*P*
	AMR≥256.5 mmHg·s/m (*n*=140, Group 1)	AMR<256.5 mmHg·s/m (*n*=271, Group 2)		AMR≥256.5 mmHg·s/m (*n*=19, Group 3)	AMR<256.5 mmHg·s/m (*n*=77, Group 4)	
Infarct-related artery						
LAD [*n* (%)]	65 (46.4)	105 (38.7)	0.408	13 (68.4)	45 (58.4)	0.744
AMR	269 (263, 302)	220 (195, 235)	<0.001	297 [269, 329]	199 (161, 225)	<0.001
LCX [*n* (%)]	81 (57.8)	172 (63.4)	0.473	3 (15.7)	9 (11.6)	0.833
AMR	296 (274, 310)	227 (211, 242)	<0.001	257 [256, 260]	195 (186, 233)	0.182
RCA [*n* (%)]	59.0 (42.1)	118.0 (43.5)	0.987	3 (15.7)	23 (29.8)	0.679
AMR	272 (261, 303)	221.5 (198, 239)	<0.001	306 [299, 327]	194 (180, 215)	0.220
Multivessel disease						
1 [*n* (%)]	65 (46.4)	65 (23.9)	0.013	7 (36.8)	14 (18.1)	0.689
2 [*n* (%)]	24 (17.1)	114 (42.0)	0.040	7 (36.8)	38 (49.3)	0.844
3 [*n* (%)]	51 (36.4)	92 (33.9)	0.908	5 (26.3)	25 (32.4)	0.689
TIMI flow grade (inital)						
0	124 (88.5)	229 (84.5)	0.374	15 (78.9)	46 (59.7)	0.338
1	12 (8.5)	32 (11.8)	0.898	2 (10.5)	24 (31.1)	0.784
2	2 (1.4)	4 (1.4)	0.933	0 (0)	7 (7.7)	1.000
3	2 (1.4)	6 (2.2)	0.947	2 (10.5)	1 (1.3)	0.863
TIMI flow grade (post)			0.776			0.645
0	0	0		0	0	
1	0	0		0	0	
2	0	0		0	0	
3	140 (100)	271 (100)		19 (100)	77 (100)	
QFR	0.94 (0.91, 0.97)	0.94 (0.89, 0.97)	0.382	0.74 (0.70, 0.77)	0.74 (0.70, 0.77)	0.885
AMR (mmHg·s/m)	274.00 (262.75, 308.00)	221.00 (197.50, 238.00)	<0.001	293.00 (268.00, 327.00)	195.00 (169.00, 225.00)	<0.001
MACCEs [*n* (%)]	26 (18.57)	4 (1.48)	<0.001	14 (73.68)	16 (20.78)	<0.001
Non-culprit vessel						
QFR	0.90 (0.85, 0.96)	0.85 (0.83,0.94)	0.452	0.83 (0.81,0.91)	0.88 (0.82, 0.94)	0.521
AMR (mmHg·s/m)	232.00 (204.00, 241.00)	227.00 (200.00, 239.00)	0.326	239.00 (217.50, 249.00)	225.00 (214.00, 234.00)	0.428

QFR: Quantitative flow ratio; AMR: Angio-based microvascular resistance; LAD: Left anterior descending artery; LCX: Left circumflex artery; RCA: Right coronary artery; TIMI: Thrombolysis in myocardial infarction; MACCEs: Major adverse cardiovascular and cerebrovascular event.

2.3 AMR的线性回归分析

对AMR指标进行线性回归分析(表3)。AMR与糖尿病、高脂血症、吸烟、SIRI、PLR呈正相关(P<0.05)。糖尿病(β=16.970)和高脂血症(β=15.071)对AMR的影响最大。

2.4 2年随访结局

在2年随访期间,4个研究组共有60例患者发生了由全因死亡或心力衰竭相关再入院构成的复合终点(表4)。Cox比例风险模型分析显示,AMR是MACCEs的独立预测因素,HR为1.247(95% *CI*: 1.185-3.583, P<0.001,表5)。多因素分析显示AMR、高血压、糖尿病和吸烟状态是STEMI患者复合结局的独立预测因素。ROC曲线分析显示,高血压(AUC=0.648)、糖尿病(AUC=0.685)和吸烟(AUC=0.622)在预测MACCEs方面均具有一定的判别能力(图3)。Kaplan-Meier生存分析显示4组之间的生存率有显著的统计学差异(P<0.0001),其中组3显示出最低的生存率(图4)。尽管使用逆处理概率加权法方法校正了潜在的混杂因素,包括年龄、高血压、糖尿病、高脂血症、吸烟状态、血管再通时间、SIRI和AMR,四组的生存率仍然存在显著差异(P<0.0001,图5)。在整个观察期间,第3组的生存率始终最低。Kaplan-Meier生存曲线分析显示4组间全因死亡率和HF发生率均有统计学差异(P<0.0001)。组3的主要结局发生率最高(图6)。

表3 AMR的多元线性回归分析

Tab.3 Multivariate linear regression analysis of AMR of the patients

Characteristics	Regression coefficient β	Standard error	*t*	*P*
Diabetes	16.970	5.014	3.384	<0.001
Hyperlipemia	15.071	4.531	3.326	<0.001
Smoking	11.457	4.645	2.466	0.014
SIRI	5.677	2.081	2.728	0.007
PLR	0.261	0.064	4.072	<0.001

SIRI: systemic inflammation response index; PLR: Platelet-lymphocyte ratio.

表4 不同组别的临床结果

Tab.4 Clinical outcomes across different groups of patients

Characteristics	Total	Group1	Group2	Group3	Group4	*P*
Primary outcome	60 (11.83%)	26 (18.57%)	4 (1.48%)	14 (73.68%)	16 (20.78%)	<0.001
All-cause mortality	24 (4.73%)	9 (6.43%)	2 (0.74%)	6 (31.57%)	7 (9.09%)	<0.001
Cardiac failure	36 (7.10%)	17 (12.14%)	2 (0.74%)	8 (42.11%)	9 (11.69%)	0.005
Any myocardial infarction	7 (1.38%)	3 (2.14%)	0 (0.00%)	2 (10.52%)	2 (2.59%)	0.438
IRA myocardial infarction	4 (0.79%)	2 (1.43%)	0 (0.00%)	1 (5.26%)	1 (1.29%)	0.572
Non-IRA myocardial infarction	3 (0.59%)	1 (0.71%)	0 (0.00%)	1 (5.26%)	1 (1.29%)	0.801
Readmission for angina	18 (3.55%)	8 (5.71%)	1 (0.37%)	3 (15.78%)	6 (7.79%)	0.092
Any revascularization	10 (1.97%)	4 (2.86%)	0 (0.00%)	2 (10.52%)	4 (5.19%)	0.221
Stroke	5 (0.98%)	3 (2.14%)	1 (0.37%)	1 (5.26%)	0 (0.00%)	0.284

IRA: Infarct-related artery.

表5 MACCEs的独立预测因子

Tab.5 Independent predictors of MACCEs in patients with STEMI

Characteristics	HR (univariable)	*P*	HR (multivariable)	*P*
Age	1.033 (1.010-1.056)	0.045	1.043 (1.010-1.078)	0.069
Hypertension	3.625 (1.486-6.085)	<0.001	3.412 (1.178-6.328)	0.002
Diabetes	4.838 (2.645-8.849)	<0.001	2.948 (1.326-6.557)	0.008
Hyperlipemia	5.408 (2.511-11.648)	0.032	5.434 (2.121-13.923)	0.079
Smoking	3.680 (1.767-7.664)	<0.001	3.021 (1.187-7.687)	0.020
Pain-to-balloon time	1.458 (1.235-3.454)	0.033	1.001 (0.701-1.012)	0.041
SIRI	1.582 (1.335-1.874)	0.065	1.665 (1.370-2.023)	0.082
AMR	1.247 (1.185-3.583)	<0.001	1.145 (1.046-2.638)	<0.001

HR: Hazard Ratio; SIRI: Systemic inflammation response index; AMR: Angio-based microvascular resistance.

2.5 RCS曲线分析

图7显示了AMR值和MACE发生率风险比之间的非线性关联。当AMR>259.45 mmHg·s/m时，HR>1，呈上升趋势。AMR值升高与MACCEs发生率呈正相关。统计学分析表明，AMR值与MACCEs风险之间存在显著的非线性关系，总体*P*值和非线性*P*值均<0.001。

3 讨论

本研究旨在探讨联合应用QFR和AMR在评估STEMI患者PCI术后发生CMD的预后价值。本研究的主要结果如下：不同人群的预后存在显著差异，尤其是QFR≤0.8且AMR>为256.5 mmHg·s/m的患者，其总体预后更差。AMR与MACCEs之间呈非线性关系。当AMR>259.45 mmHg·s/m时，发生MACCEs的风险显著增加。AMR是STEMI患者PCI术后MACCEs发生的独立影响因素。

STEMI罪犯血管中CMD的发生已被多项研究证实[19]。尽管PCI能够有效恢复冠状动脉大血管的血流，但由动脉粥样硬化引发的血栓栓塞所导致的微血管损伤可能仍然持续存在。微栓子不仅通过诱导微循环闭

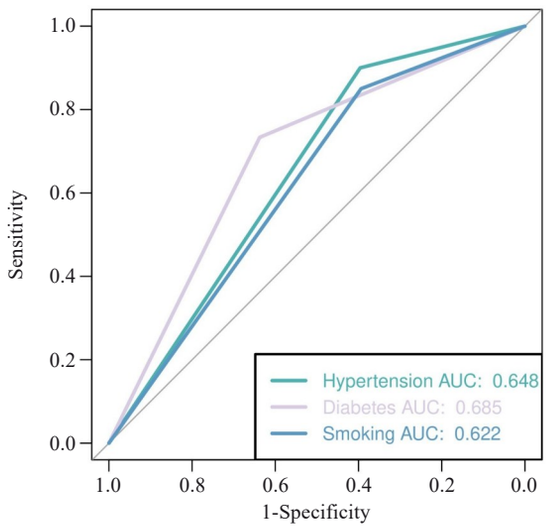

图3 多因素风险模型的判别性能评估图

Fig.3 ROC curve analysis for evaluating the performance of the multivariate model for predicting MACCEs.

塞加重局部血流灌注障碍，还可激活凝血级联系统，从而促进微血管内血栓的形成。此外，血栓可诱发局部炎症反应，进而损害微血管壁的完整性，导致血流灌注受限[20]。随着CMD的逐步进展，冠状动脉血流灌注能力逐渐减弱，导致氧气和营养物质供应无法满足心肌代谢的代谢需求。这种情况不仅会导致心肌缺血和收缩功能障碍，还可能显著增加严重心力衰竭及心脏性猝死的风险[21]。基于我们的研究结果，进一步证实了CMD可显著增加初次PCI后MACCEs的发生风险。此外，AMR水平升高的患者，其MACCEs的发生风险也有所增加。

该研究揭示了AMR与多种临床因素之间存在独立相关性。糖尿病、高脂血症、吸烟、SIRI、PLR与AMR发生风险独立相关。糖尿病患者持续的高血糖状态可促进晚期糖基化终末产物的生成[22, 23]，进而导致微血管内皮细胞的损伤。内皮功能障碍不仅会损害血管的舒张能力，还会增加微血管壁的通透性，进一步促进炎症反应和血栓形成。这最终会加重冠状动脉微循环的阻力[24]。血脂水平升高显著促进CMD的进展，并显著增加高危心血管疾病患者的死亡风险[25]。SIRI和PLR是反映体内炎症状态和免疫反应的重要生物标志物。其水平升高通常表明体内存在慢性低度炎症。现有研究表明，慢性炎症在心血管疾病的发病机制及疾病进展中发挥着关键作用[26]。慢性炎症通过多种机制对心血管健康产生不利影响，包括加速动脉粥样硬化进展、损害血管内皮细胞功能、增强氧化应激反应以及促进血栓形成[27]。综上所述，这些病理生理过程显著增加了MACCEs的风险。

尽管大量研究显示AMR与STEMI患者总死亡率和心力衰竭再入院风险的增加密切相关，但关于AMR的具体阈值界定，学术界尚未形成统一共识。Qian等[28]研究表明，AMR值为255 mmHg·s/m可作为STEMI后发生MACCEs的预测指标的阈值。其研究所报告的AMR值与本研究获取的AMR值存在一定差异。这种差异可能源于样本量的差异。Qian等[28]的研究纳入了232例患者，而本次研究涵盖了507例患者。此外，本研究中患者平均年龄较高且合并症患病率较高，这些因素可能在一定程度上影响了AMR值的测定与解释。Da Luo等[29]研究显示，当AMR≥250 mmHg·s/m时，新发心力衰竭的风险显著增加。而Jie Ma等[30]报道AMR≥704 mmHg·s/m与三支病变患的不良预后之间存在显著相关。然而，特定的AMR数据还需要通过大规模、多中心的临床研究加以验证，进一步提高其科学性与可靠性。

QFR通过整合三维定量CAG与血流动力学算法，

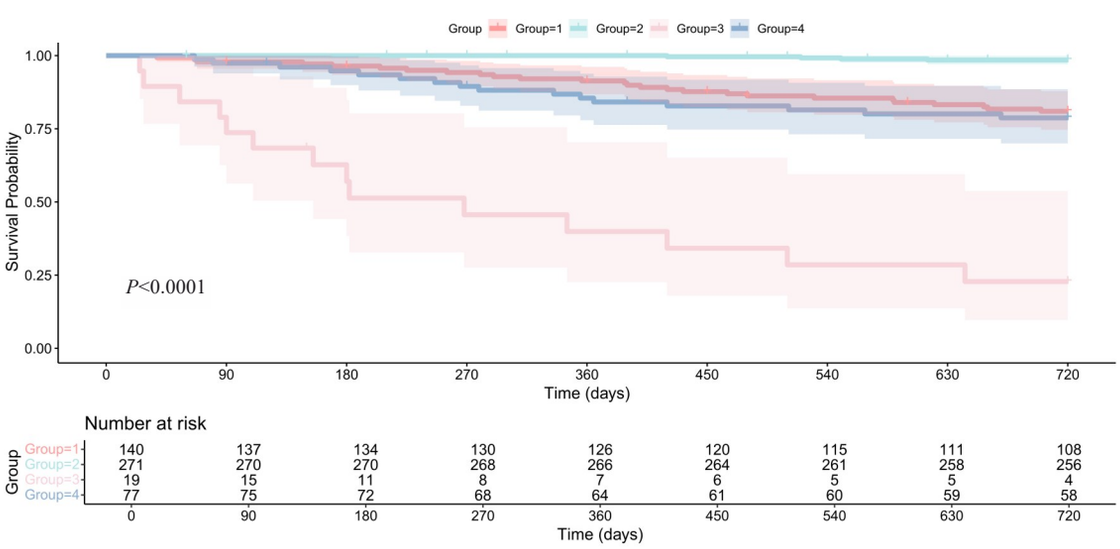

图4 根据QFR-AMR分层的Kaplan-Meier生存曲线

Fig.4 Kaplan-Meier survival curves of the primary outcome in patients with STEMI stratified by QFR-AMR. The survival outcomes vary significantly across the groups (P<0.0001).

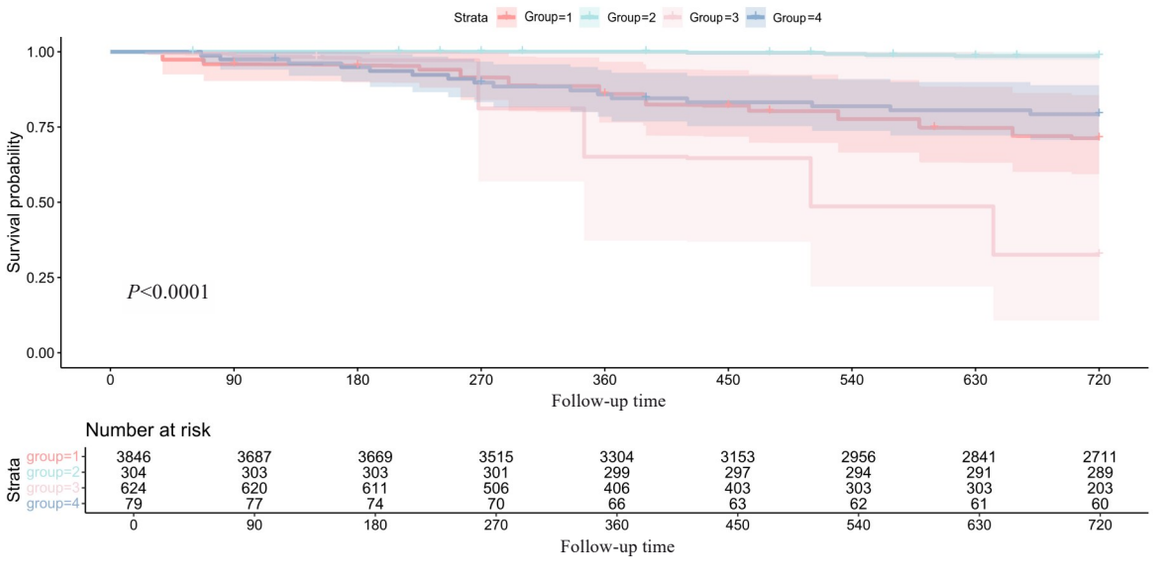

图5 根据逆概率加权方法调整后的Kaplan-Meier生存曲线

Fig.5 Outcomes of the patients after adjustment with the IPTW method (*P*<0.0001).

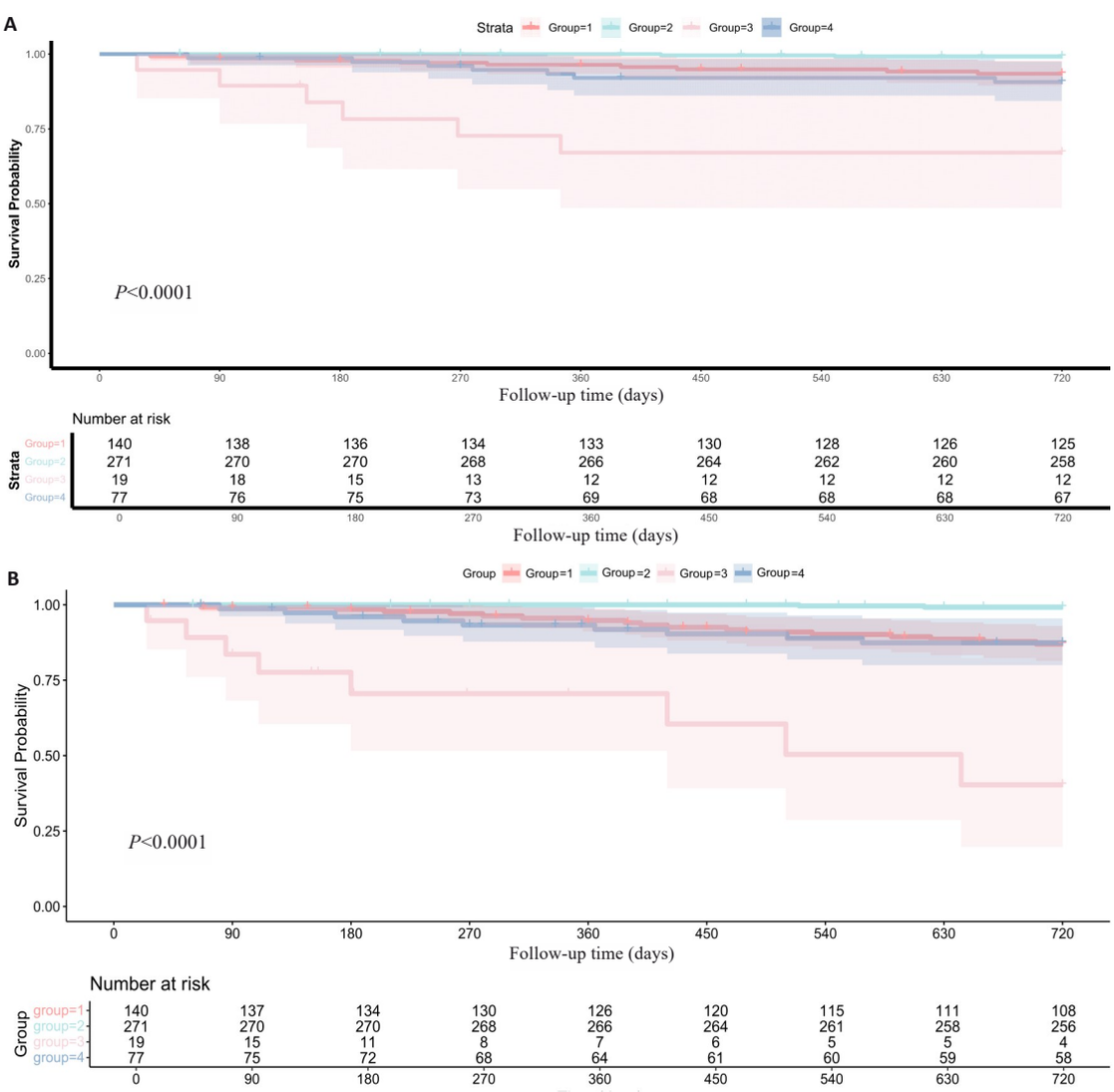

图6 根据AMR-QFR分组的全因死亡和心力衰竭结局的Kaplan-Meier生存曲线

Fig. 6 Kaplan-Meier analyses reveal significant differences in all-cause mortality rates (**A**) and heart failure incidence (**B**) among the 4 groups stratified based on AMR-QFR.

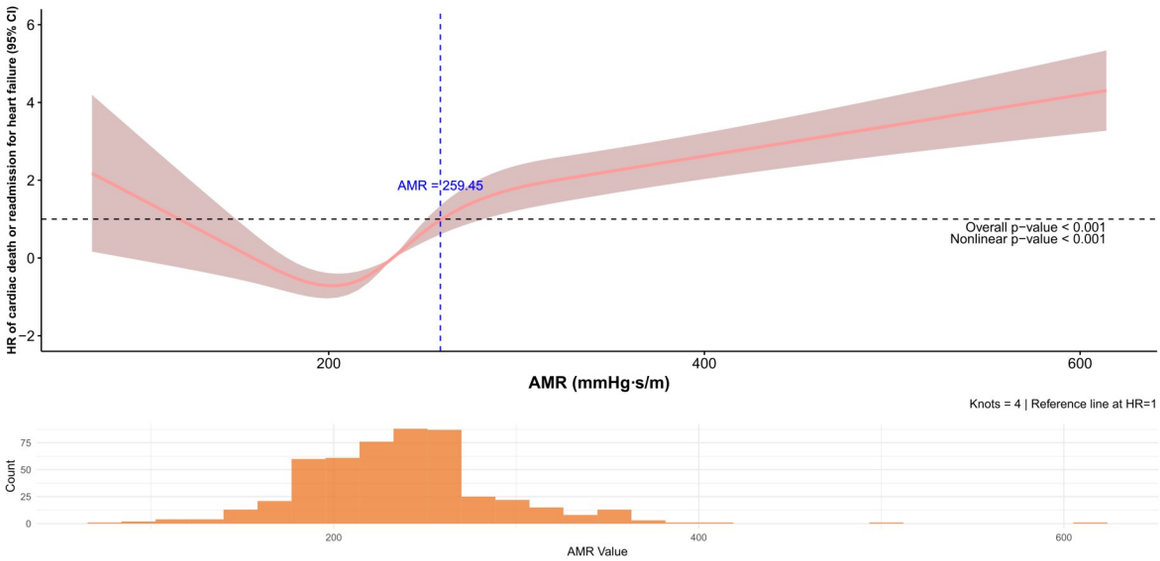

图7 限制三次样条分析

Fig.7 Relationships between MAR and the risk of cardiac death or readmission for heart failure according to the restricted cubic spline analysis.

能够精准评估狭窄病变的血流动力学影响。此外,其准确性已经通过与FFR对比的研究中得到了充分验证[31, 32]。多项研究一致表明,当QFR低于0.80时,冠状动脉血流显著受限,需要考虑PCI以改善血流状态。AMR作为一种潜在的冠状动脉微循环指标,可作为评估冠状动脉微血管功能状态的客观指标。其核心价值在于能够精准评估微血管损伤程度及血流灌注状态。通过联合应用QFR和AMR进行危险分层,可以全面评估冠心病相关的血流动力学特征。综合评估不仅有助于治疗决策,而且为患者提供可靠的预后支持。

本研究存在若干局限性。首先,作为一项回顾性观察性研究,其结果需通过前瞻性研究进一步验证。其次,部分患者由于血管造影图像质量不达标而未纳入分析,这可能导致潜在的选择性偏倚。此外,相对较小的样本量可能降低了统计学功效,从而导致某些具有临床意义的结果未能达到统计学显著性。最后,有限的随访时间无法全面评估疾病的长期进展或治疗效果,从而对长期结局的分析造成一定限制。

综上所述,基于QFR与AMR的联合评估框架可有效预测STEMI患者急诊PCI术后发生MACCEs的风险。此外,AMR是PCI术后MACCEs的独立预测指标,其数值升高与MACCEs风险显著相关。

Declaration of interests: The authors declare no competing interests.

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