Original Article

Association between the insufficient improvement of the quantitative flow ratio and worsening outcomes in ST-segment elevated myocardial infarction: a multicentre prospective cohort study

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Background: Improved coronary physiological function after percutaneous coronary intervention (PCI) has been shown to improve prognosis in stable ischaemic heart disease, but has not yet been explored in ST-segment elevated myocardial infarction (STEMI). The study sought to determine whether an improvement in the quantitative flow ratio (QFR) could improve the prognosis of STEMI patients undergoing primary PCI.

Methods: Patients diagnosed with STEMI who were receiving primary PCI were recruited for the study. Those with thrombolysis in myocardial infarction (TIMI) flow <2 after wiring were excluded. The ΔQFR was calculated using the following formula: ΔQFR = post-PCI QFR – pre-stent QFR. The primary endpoint was the composite event, including recurrent myocardial infarction (MI) and acute heart failure (AHF).

Results: In total, 515 STEMI patients with a median follow-up of 364 days were enrolled in the study. Based on the cut-off value from the receiver operator characteristic (ROC) curve, the patients were divided into the following two groups: the lower ΔQFR group (≤0.25, N=332); and the normal ΔQFR group (>0.25, N=183). Patients with a lower ΔQFR had a relatively higher rate of MI/AHF (10.5% *vs.* 4.4%, P=0.019) and AHF (7.2% *vs.* 2.7%, P=0.044). A lower ΔQFR was significantly associated with a higher incidence of MI/AHF [hazard ratio (HR) =2.962, 95% confidence interval (CI): 1.358–6.459, P=0.006, respectively] after adjusting for potential confounders. Pre-stent angiographic microvascular resistance [odds ratio (OR) =1.027, 95% CI: 1.022–1.033, P<0.001] and the stent-to-vessel diameter ratio <1.13 (OR =1.766, 95% CI: 1.027–3.071, P=0.04) were independent predictors of a lower ΔQFR.

Conclusions: An insufficient improvement in the QFR contributes to worsening outcomes and might be a useful tool for risk stratification in STEMI.

Keywords: ST-segment elevated myocardial infarction (STEMI); culprit vessels; quantitative flow ratio (QFR); outcome; risk stratification

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Introduction

Timely primary percutaneous coronary intervention (PCI) is the current preferred reperfusion strategy for treating ST-segment elevated myocardial infarction (STEMI), and stent implantation is recommended (1,2). The success of primary PCI depends on the structural re-opening of culprit vessels and the functional integrity of the coronary microcirculation (3).

Previous studies have shown that impaired intracoronary physiological function, including the wire-based fraction flow reserve (FFR), instantaneous wave-free ratio (iwFR), and vessel-based fraction flow reserve (vFFR), which can be assessed by quantitative coronary angiography after PCI, are associated with adverse cardiac events (4-7). A patient-level pooled analysis of 639 patients with multivessel disease and stable ischaemic heart disease (SIHD) found that the improvement in the FFR (calculated as: the post-PCI FFR – the pre-PCI FFR) was related to symptom relief and lower vessel-related cardiac events at the two-year follow-up (8). Coronary physiological function assessment not only depends on the severity of the target vessel but is also related to microcirculatory function, especially in acute myocardial infarction (MI) (3). Therefore, we conjectured that the higher prevalence of microvascular obstruction (MVO) in STEMI might affect coronary physiological function assessments.

The angiography-based quantitative flow ratio (QFR) is a wire-free coronary functional measurement without using drugs to induce hyperaemia and is safer and more cost-effective than the FFR (9-11). A large randomized controlled trial in China (FAVOR III, China) showed the superiority of angiographic QFR-guided coronary intervention over angiography-guided PCI (12). Recent studies have shown that a lower post-PCI QFR of the target vessel was related to adverse clinical events in different patients, including those with acute coronary syndrome, SIHD, and multivessel disease (13-15). There is increasing evidence that the QFR is comparable to other invasive coronary physiological measurements in different circumstances (16-18).

This study sought to determine whether an improvement in the QFR (ΔQFR) value, which was defined as the post-PCI QFR – the pre-stent QFR, could improve the prognosis of STEMI patients undergoing primary PCI. It also explored the risk factors leading to a lower ΔQFR in the data set. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-1518/rc).

Methods

Study design and patients

The study was a multicentre prospective cohort study, and the design of this study was previously described (19). The study was registered at the Chinese Clinical Trial Registry (registration number: ChiCTR1800019923). We consecutively screened potential subjects at four hospitals (Guangdong Provincial People's Hospital, Guangdong Provincial People's Hospital Zhuhai Hospital, Jiexi County Hospital, and Boluo County Hospital) from January 2018 to April 2022.

Patients were recruited for the study if they had been diagnosed with STEMI, had a symptom onset of <12 hours, and were receiving primary PCI. STEMI was defined according to the current guidelines (1,20). Patients were excluded from the study if they met any of the following exclusion criteria: (I) had a thrombolysis in myocardial infarction (TIMI) flow value <2 after wiring with or without thrombus aspiration; (II) had not undergone stent implantation of the culprit vessel; (III) had pre-stent or post-PCI angiograms that were not suitable for the QFR analysis; (IV) experienced cardiac arrest or died within 24 hours of admission; (V) were lost to follow-up; and/or (VI) did not provide informed consent. The study

was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol was reviewed and approved by the Ethics Committee of Guangdong Provincial People's Hospital [reference No: GDREC2018346H(R2)] on December 3rd, 2018. Informed consent was obtained from all the patients.

Procedure, quantitative coronary angiography (QCA), and QFR analysis

The primary PCI was performed following the best practice from the current guidelines. The interventional cardiologists from the three other centres were all trained at Guangdong Provincial People's Hospital, and the primary PCI procedures were standardized. The use of devices, including balloons and stents, intravascular ultrasound images (IVUS), procedural strategy, and peri-procedural drugs, was left to the discretion of the intervention cardiologists and physicians in charge. The location of the culprit lesion and vessel disease, size and number of stents, use of thrombectomy and glycoprotein inhibitors were recorded.

Images from index procedures were used to analyse the grades of the TIMI flow (on a scale of 0–3) and intracoronary thrombus burden (on a scale of 0–5) according to the definitions detailed in previous studies (21,22). The lesion characteristics of the culprit vessels, including the minimum lesion diameter, reference vessel diameter, lesion length, minimum lumen area, percentage of diameter stenosis, and percentage of area stenosis, were routinely calculated by QCA before stent implantation and at the end of PCI.

The angiographic image used for the QFR computation was transferred to a system that used the same algorithms for the QFR computation as previously described (10). The QFR was computed via two steps. First, a fixed QFR was computed by displaying the pullback curve of the target lesion. Second, a contrast-flow QFR (cQFR) was calculated by taking into account the flow velocity estimated by the time needed for the contrast agent to fill the segment. The cQFR was adopted as the QFR value. Angiography-derived microcirculatory resistance (AMR) was computed using the formula reported in a previous study (23). QFR and AMR were measured before stent implantation and at the end of PCI. The pre-stent QFR was defined as the QFR value of the angiogram after wiring with or without aspiration but before ballooning. The post-PCI QFR was defined as the QFR value of the angiogram at the end of PCI. The ΔQFR was calculated using the following formula: ΔQFR = the value of the post-PCI QFR – the value of the pre-stent QFR.

All the angiographic images from the four centres were copied, preserved, and sent to the academic core laboratory, where the data were assessed by the AngioPlus system (AngioPlus Core, version V3, Shanghai Pulse Medical Technology Inc., Shanghai, China) by independent analysts. The researchers were blinded to the QCA and QFR data before and after stent implantation, and the data were recorded.

Definitions and endpoints

N-terminal pro-brain natriuretic peptide (NT-pro BNP)/brain natriuretic peptide (BNP) >10-fold was defined as the peak NT-pro BNP or BNP value >10 × reference upper limit during hospitalization, which meant NT-pro BNP >3,000 pg/mL or BNP >1,000 pg/mL.

The estimated glomerular filtration rate (eGFR) was adopted by the Modification of Diet in Renal Disease equation for Chinese as follows: $186 \times Scr^{-1.154} \times age^{-0.203} \times 0.742$ (if the patient is female) × 1.233 (24).

Multivessel disease was defined as any other vessel with a stenosis >50% in the left anterior descending (LAD) artery, left circumflex artery, or right coronary artery or a stenosis >30% in the left main artery in addition to the infarct-related vessels.

A thrombus burden score >3 (22) indicated a large thrombus burden. The stent-to-vessel diameter ratio (SVDR) was defined as the maximum stent diameter (if the stent number was >1) to the reference vessel diameter (as measured by QCA) ratio.

Patients were followed-up via clinic visits or telephone calls. Loss to follow up was defined as no available medical records or the patient falling out of touch after discharge. The primary endpoint was defined as composite events, including recurrent MI and acute heart failure (AHF) in patients with at least 30 days of follow-up. Recurrent MI referred to PCI-related MI during hospitalization or a recurrent MI diagnosis after discharge according to the third universal definition of MI (20). AHF referred to the rapid onset of symptoms or signs of heart failure during hospitalization or leading to re-hospitalization or an emergency department visit after discharge (25).

Statistical analysis

A receiver operator characteristic (ROC) curve with the Youden index was used to determine the best cut-off value of the ΔQFR for the composite events of MI and AHF. Based on the ROC curve analysis, a cut-off value of 0.25

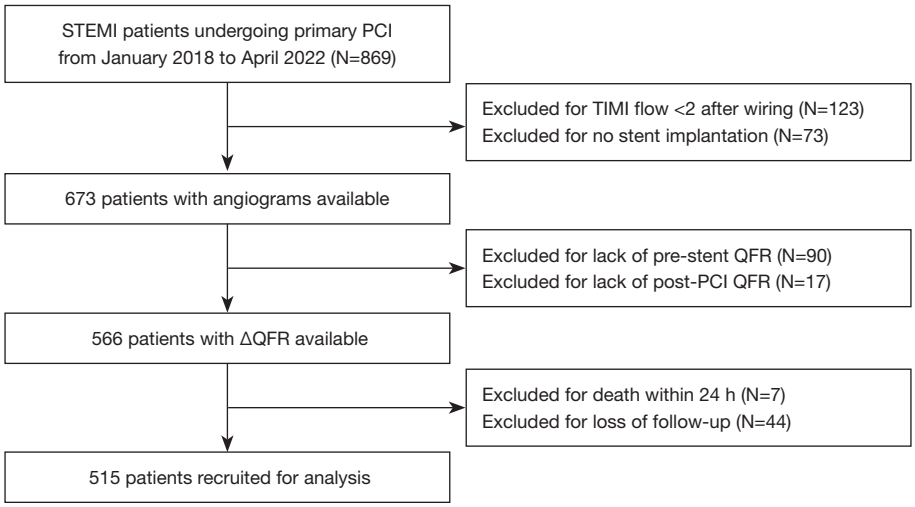

Figure 1 Study flow chart. STEMI, ST-segment elevated myocardial infarction; PCI, percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction; QFR, quantitative flow ratio.

served as the best discriminator for MI/AHF. The baseline characteristics of the ΔQFR ≤0.25 and ΔQFR >0.25 groups were compared. The continuous data are expressed as the mean ± standard deviation, and the categorical data are expressed as the frequency (percentage). The unpaired Student's *t*-test or Mann-Whitney U test was used to compare the continuous data, and the Pearson chi-square test was used to compare the categorical data. A ROC curve analysis was also conducted to determine the cut-off value of the AMR in predicting a lower ΔQFR. A linear correlation test was used to examine the correlation between the ΔQFR and pre-stent AMR, and the Pearson correlation coefficient was calculated. We used restricted cube splines (RCSs) to examine the relationship between the ΔQFR and pre-stent AMR. We also used RCSs with three knots to flexibly model the association between the ΔQFR and MI/AHF. We performed a multivariate logistic regression analysis to identify the determinants for the lowest ΔQFR, and we then carried out a multivariate logistic regression analysis in which the lower ΔQFR group was used as a dependent variable. Variables that showed a marginal difference in the comparisons between the lower ΔQFR group and normal ΔQFR group were used as the independent variables in the multivariate logistic regression analysis. The odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated. We used a Cox regression model to identify the risk factors for MI/AHF in a time-to-event analysis. Using a stepwise forwards method, all the potential parameters chosen from the baseline characteristics analysis with P values of 0.15 or less were included in the multivariable Cox regression model. The hazard ratios (HRs) and 95% CIs were calculated. Kaplan-Meier curves were used to compare the lower ΔQFR with the normal ΔQFR for MI, AHF, and the combined events. The analysis was performed using the statistical software IBM SPSS version 23.0 (Armond, NY, USA) and R studio version 4.3.2. A two-sided P value <0.05 was considered significant.

Results

A total of 515 patients were recruited for this study according to the inclusion and exclusion criteria (*Figure 1*). The mean age of the patients was 60.8 years, and 437 (84.9%) of the patients were male. The mean value of the ΔQFR was 0.231, and the median value was 0.16. The maximum and minimum values of the ΔQFR were 0.88 and –0.41, respectively. The proportion of patients with a ΔQFR <0 was 2.7% (14/515).

Baseline characteristics

The patients were divided into the following two groups based on the ΔQFR: the lower group (ΔQFR ≤0.25, N=332) and the normal group (ΔQFR >0.25, N=183). There were no significant differences between the two groups in terms of age, left ventricular fraction ejection (LVEF), and eGFR. The proportions of patients with previous MI, hypertension, diabetes mellitus, current smokers, NT-pro

BNP/BNP >10-fold, multivessel disease, a large thrombus burden, thrombus aspiration, an intra-aortic balloon pump, and a final TIMI flow <3 did not differ significantly between the lower ΔQFR group and the normal ΔQFR group. The lower ΔQFR group had a lower rate of culprit lesion LAD and IVUS use, while the normal ΔQFR group had higher stent numbers, longer stent lengths, and a higher rate of an initial TIMI flow ≤1. The patients in the lower ΔQFR group had a smaller SVDR and a higher pre-stent QFR and pre-stent AMR than those in the normal ΔQFR group. The maximum stent diameter, reference vessel diameter, diameter stenosis, area of stenosis, lesion length, minimum lumen area, post-PCI QFR and post-PCI AMR did not differ significantly between the two groups (*Table 1*).

Predictors of a lower ΔQFR

Pre-stent AMR showed a good correlation with the ΔQFR (r=–0.724, P<0.001), and the RCSs also showed a negative relationship between ΔQFR and pre-stent AMR (*Figure 2*); thus, the higher the microcirculatory resistance index of the culprit lesion, the lower the ΔQFR.

The multivariable logistic regression showed that pre-stent AMR (OR =1.027 for every increment, 95% CI: 1.022–1.033, P<0.001) and the SVDR <1.13 (OR =1.766, 95% CI: 1.027–3.071, P=0.04) were independent risk factors for a lower ΔQFR after adjusting for IVUS use and an initial TIMI ≤1 (*Table 2*).

Lower ΔQFR and clinical outcomes

The median period of follow-up was 364 days. The patients with a lower ΔQFR had a relatively higher rate of MI/AHF (10.5% *vs.* 4.4%, P=0.019) and AHF (7.2% *vs.* 2.7%, P=0.044). There was no significant difference between the two groups in terms of all-cause mortality, cardiac death, MI, target vessel revascularization (TVR), cardiac death/MI, cardiac death/MI/TVR, and cardiac death/MI/AHF (*Table 3*). The RCSs revealed a reverse J shaped association between the ΔQFR and MI/AHF (*Figure 3*). The HR of major adverse cardiac events decreased more quickly as the ΔQFR increased when the ΔQFR <0.4, but more smoothly when the ΔQFR >0.4. The cut-off point of the ΔQFR was 0.16 in the RCSs, which differed to the cut-off point of the ROC curve.

The Cox regression model revealed that a lower ΔQFR was significantly associated with a higher incidence of MI/AHF (HR =2.962, 95% CI: 1.358–6.459, P=0.006, respectively) after adjusting for age ≥75 years, LVEF <40%, multivessel disease, and NT-pro BNP/BNP >10-fold (*Table 4*). The Kaplan-Meier curve showed that a lower ΔQFR had a similar rate of MI (4.8% *vs.* 1.6%, log-rank P=0.07, *Figure 4A*). The lower ΔQFR group had a significantly higher rate of AHF (7.2% *vs.* 2.7%, log-rank P=0.047, *Figure 4B*) and composite events of MI/AHF (10.5% *vs.* 4.4%, log-rank P=0.018, *Figure 4C*) than the normal ΔQFR group. The lower ΔQFR group did not differ significantly from the normal ΔQFR group in terms of the composite events of cardiac death/MI/AHF (13.0% *vs.* 8.2%, log-rank P=0.127, *Figure 4D*).

Discussion

The main findings of our study are summarized as follows: (I) an insufficient improvement in the QFR (calculated as the post-PCI QFR – the pre-stent PCI) was associated with worsening outcomes, including recurrent MI and AHF in the long-term follow-up of STEMI patients; and (II) the presence of microcirculatory dysfunction and the selection of an inadequate stent size were predictors of a lower ΔQFR in primary PCI.

Lower ΔQFR and clinical outcomes

A large body of evidence has confirmed that post-PCI, coronary physiological assessments can optimize procedure outcomes (4-7). Agarwal *et al.* used the post-PCI FFR to re-classify 20% of angiographically satisfactory lesions that required procedure optimization (4). Our study found that a sufficient improvement in the QFR in culprit lesions reduced long-term cardiac events (i.e., MI and AHF). This finding is consistent with the findings of previous studies that in terms of coronary physiological function, "the higher QFR, the better".

Fournier *et al.* reported that a larger improvement in FFR values after PCI tended to be associated with more complete symptomatic relief and a lower rate of vessel-oriented cardiac events (VOCEs) (8). They classified their study population into three groups based on the value of the ΔFFR, and the lowest tertile of the ΔFFR had the highest rate of VOCEs (7.2% *vs.* 5.0% *vs.* 2.5%, P=0.002). Lee *et al.* reported that the percentage FFR increase [(post-PCI FFR – pre-PCI FFR)/pre-PCI FFR × 100%] had similar prognostic implications as the post-PCI FFR, and adding the relative increase in the FFR to the post-PCI FFR would enable clinicians to better identify high-

Table 1 Baseline patient and vessel characteristics according to the ΔQFR divided by ΔQFR ≤0.25 and >0.25

Baseline characteristics	ΔQFR ≤0.25 (N=332)	ΔQFR >0.25 (N=183)	P value
Patient characteristics			
Age, years	61±13	60±14	0.364
Male, %	281 (84.6)	156 (85.2)	0.898
History of MI, %	19 (5.7)	13 (7.1)	0.569
Hypertension, %	154 (46.4)	82 (44.8)	0.782
DM, %	92 (27.7)	45 (24.6)	0.467
Current smoker, %	181 (54.5)	110 (60.1)	0.229
NT-pro BNP or BNP >10-fold, %	54 (16.3)	36 (19.7)	0.396
LVEF, %	51.8±13.6	49.8±11.8	0.079
eGFR at admission, mL/min/1.73 m^2	97.8±40.0	97.9±47.3	0.977
Vessel characteristics			
Culprit lesion			0.002
LAD, %	155 (46.7)	107 (58.5)	
LCX, %	22 (6.6)	19 (10.4)	
RCA, %	155 (46.7)	57 (31.1)	
Multivessel disease, %	201 (60.5)	112 (61.2)	0.925
Initial TIMI flow ≤1, %	237 (71.4)	107 (58.5)	0.003
Final TIMI <3, %	64 (19.3)	33 (18.0)	0.814
Large thrombus burden, %	239 (72.0)	122 (66.7)	0.228
Thrombus aspiration, %	64 (19.3)	31 (16.9)	0.554
Stent numbers	1.06±0.60	1.24±0.68	0.003
Max SD, mm	2.79±1.12	2.98±0.95	0.053
RLD, mm	2.93±0.59	2.88±0.51	0.30
SVDR	0.98±0.46	1.07±0.39	0.032
SVDR <1.13, %	228 (68.7)	97 (53.0)	0.001
Precent diameter stenosis, %	24.4±13.2	24.1±10.1	0.792
Precent area stenosis, %	40.9±18.1	40.9±14.3	0.982
Minimum lumen area, mm^2	4.55±2.10	4.43±1.61	0.486
Pre-stent QFR	0.82±0.09	0.46±0.17	<0.001
Post-PCI QFR	0.92±0.07	0.93±0.06	0.316
Pre-stent AMR, mmHg·s/m	208.9±67.1	120.2±50.6	<0.001
Post-PCI AMR, mmHg·s/m	251.0±66.5	252.8±61.1	0.764
Stent length, mm	30.3±14.1	35.1±17.1	0.001
IABP, %	20 (6.0)	14 (7.7)	0.465
IVUS, %	80 (24.1)	63 (34.4)	0.014

The data are expressed as the mean ± standard deviation or number (percentage) [n (%)]. QFR, quantitative flow ratio; MI, myocardial infarction; DM, diabetes mellitus; NT-pro BNP, N-terminal pro-brain natriuretic peptide; BNP, brain natriuretic peptide; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction; Max SD, maximum stent diameter; RLD, reference luminal diameter; SVDR, stent to vessel diameter ratio; PCI, percutaneous coronary intervention; AMR, angiographic microvascular resistance; IABP, intra-aortic balloon pump; IVUS, intravascular ultrasound.

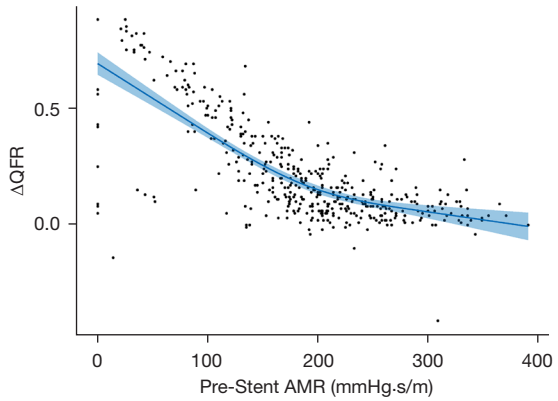

Figure 2 Restricted cube splines of the ΔQFR and pre-stent AMR. Pre-stent AMR showed a negative correlation with the ΔQFR (r=−0.724, P<0.001). QFR, quantitative flow ratio; AMR, angiographic microvascular resistance.

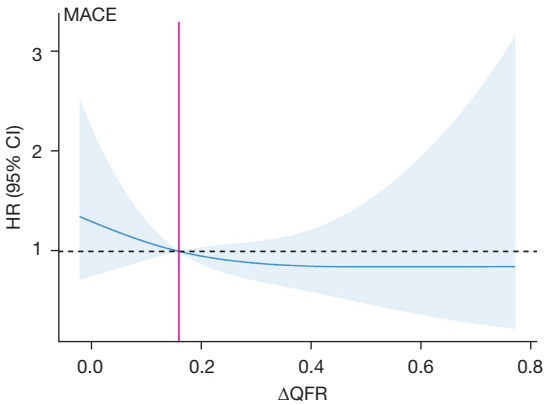

Figure 3 Association of the ΔQFR with MI/AHF by restricted cube splines. The dashed line represents HR =1, and the red line represents the cut-off value of the ΔQFR (0.16). MACE, major adverse cardiac event; HR, hazard ratio; CI, confidence interval; QFR, quantitative flow ratio; MI, myocardial infarction; AHF, acute heart failure.

Table 2 Predictive variables for a lower ΔQFR by multivariable logistic regression

Independent variables	OR	95% CI	P
IVUS	1.168	0.626–2.179	0.626
Pre stent AMR (every increment)	1.027	1.022–1.033	<0.001
Initial TIMI ≤1	0.666	0.372–1.192	0.172
SVDR <1.13	1.766	1.027–3.071	0.04

QFR, quantitative flow ratio; OR, odds ratio; CI, confidence interval; IVUS, intravascular ultrasound; AMR, angiographic microvascular resistance; TIMI, thrombolysis in myocardial infarction; SVDR, stent to vessel diameter ratio.

Table 3 Long-term follow-up of cardiac events between the lower ΔQFR and normal ΔQFR groups

Outcome	ΔQFR ≤0.25 (N=332)	ΔQFR >0.25 (N=183)	P
All-cause mortality	17 (5.1%)	8 (4.4%)	0.832
Cardiac death	15 (4.5%)	7 (3.8%)	0.822
MI	16 (4.8%)	3 (1.6%)	0.087
TVR	1 (0.3%)	1 (0.5%)	1
AHF	24 (7.2%)	5 (2.7%)	0.044
Cardiac death/MI	28 (8.4%)	10 (5.5%)	0.290
Cardiac death/MI/TVR	29 (8.7%)	10 (5.5%)	0.224
Cardiac death/MI/AHF	43 (13.0%)	15 (8.2%)	0.111
MI/AHF	35 (10.5%)	8 (4.4%)	0.019

QFR, quantitative flow ratio; MI, myocardial infarction; TVR, target vessel revascularization; AHF, acute heart failure.

Table 4 Independent predictors for MI/AHF by Cox regression analysis

Independent variables	HR	95% CI	P
ΔQFR ≤0.25	2.962	1.358–6.459	0.006
Age ≥75 years	2.867	1.458–5.635	0.002
LVEF <40%	2.092	1.037–4.222	0.039
Multivessel disease	1.875	0.914–3.845	0.086
NT-pro BNP/BNP >10-fold	2.611	1.266–5.383	0.009

MI, myocardial infarction; AHF, acute heart failure; HR, hazard ratio; CI, confidence interval; QFR, quantitative flow ratio; LVEF, left ventricular ejection fraction; NT-pro BNP, N-terminal pro-brain natriuretic peptide; BNP, brain natriuretic peptide.

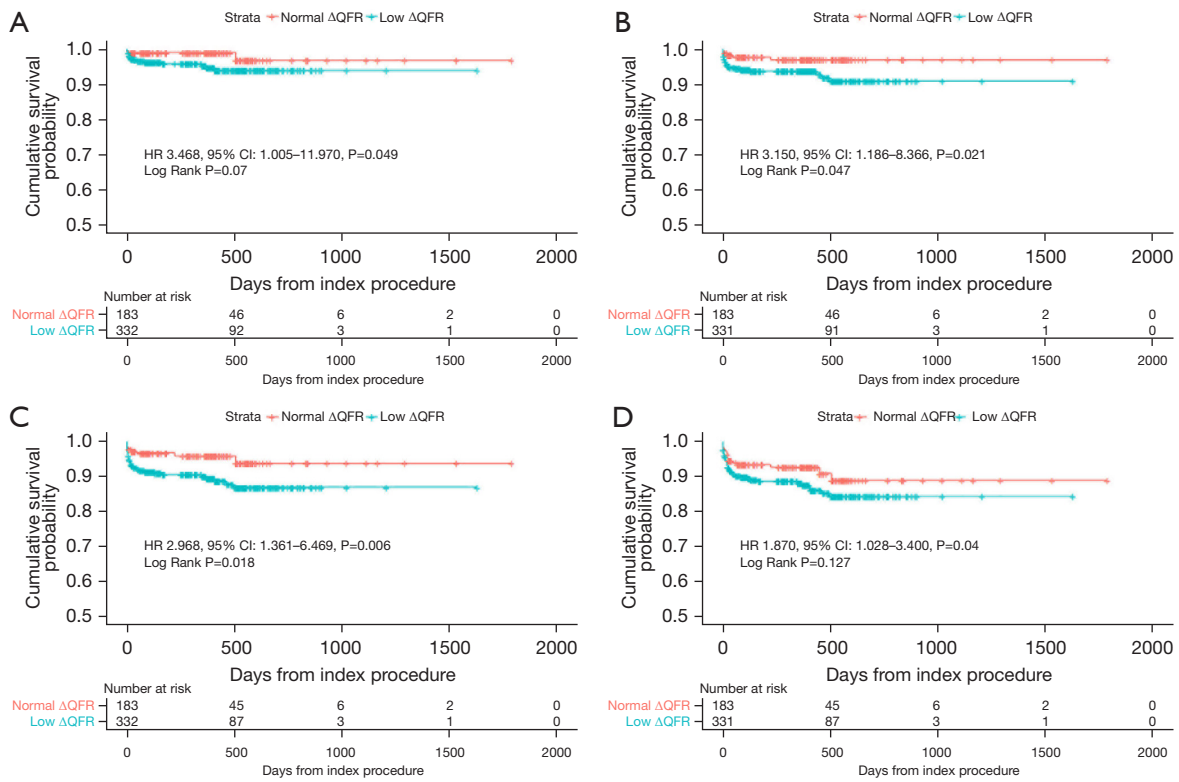

Figure 4 Kaplan-Meier curves of different cardiac events based on the groups of lower ΔQFR (≤0.25) and normal ΔQFR (>0.25). (A) MI, (B) AHF, (C) MI/AHF, and (D) cardiac death/MI/AHF. HR, hazard ratio; CI, confidence interval; QFR, quantitative flow ratio; MI, myocardial infarction; AHF, acute heart failure.

risk patients after stent implantation (26). Lee *et al.*'s study defined the composition events of cardiac death, target vessel-related MI, and TVR as target vessel failure (TVF), and reported that a low post-PCI FFR and low %FFR increase were independent predictors of TVF (HR: 5.384; 95% CI: 2.168–13.370; P<0.001). In the two studies above, the difference was mainly driven by TVR. Conversely, in our study, recurrent MI (4.8% *vs.* 1.6%, P=0.087) and AHF (7.2% *vs.* 2.7%, P=0.044) were the main contributors of cardiac events. We discuss the potential mechanism below. First, the study population was different. Patients diagnosed with STEMI have a higher risk of AHF than those with SHID because of a broader range of myocardial damage and reperfusion injury (3). Similar to previous studies, we

found that patients with a lower ΔQFR and a higher rate of MVO were more likely to suffer AHF. Moreover, the median follow-up was 364 days, which is a relatively short period in which to detect late TVR.

The determinants of a lower ΔQFR

The calculation of the QFR is related to the lesion location, lesion length, reference vessel diameter, degree of vessel stenosis, microcirculatory resistance, and range of myocardium target vessel supply. Our data showed that the difference in the ΔQFR between the two groups mainly contributed to the difference in the pre-stent QFR (0.82 *vs.* 0.42, P<0.001). The logistic regression analysis showed that pre-stent AMR (OR =1.027, P<0.001) and the SVDR (OR =1.766, P=0.04) were the two determinants of a lower ΔQFR. AMR is derived solely from a single angiographic view. A recent study confirmed that AMR with a pressure-based index of microvascular resistance (IMR) had good diagnostic accuracy in assessing MVO (23). The study examined 163 patients with 257 vessels (27% of whom were STEMI patients) and reported a good correlation between AMR and IMR. Our AMR data were analysed independently by staff members from the same core laboratory who were blinded to the study. In our study, the patients with a lower ΔQFR had a higher pre-stent QFR while the percentage of diameter stenosis was similar between two groups. It may be that those with a higher burden of thrombus and mild residual stenosis after wiring had a pseudo-higher pre-stent QFR but were more likely to develop MVO. The higher pre-stent AMR in the lower ΔQFR group, which represented pre-stent MVO, confirmed our hypothesis (27). Thus, more attention should be paid to microvascular function after wiring to improve prognosis even in patients with minimal residual stenosis and a normal pre-stent QFR.

Treating MVO

As the European Society of Cardiology guidelines do not recommend the routine use of thrombus aspiration (1), the use of thrombus aspiration in our study was relatively low (<20%) despite the high prevalence of a large thrombus burden (nearly 70%). However, a small-scale study found that deferring stenting in primary PCI would reduce MVO and preserve microcirculatory function (28). Another study suggested that pre-PCI QFR computation (defined as the contrast-flow QFR – the fix-flow QFR) with culprit lesions presenting with TIMI flow grade 2–3 may be a useful tool for predicting MVO, which was measured by contrast-enhanced cardiac magnetic resonance imaging (MRI) after STEMI (29). Thus, we inferred that for those patients with a TIMI flow grade 2–3 after wiring and before stent implantation, the occurrence of MVO might weaken the benefit of stent implantation in improving post-intervention physiological function. Those with pre-stent MVO might benefit from sufficient thrombus aspiration or delayed stent implantation to minimize the effect of MVO and maximize myocardial salvage.

Our study also found that the choice of a larger stent diameter to vessel diameter ratio improved the ΔQFR, but the post-PCI QFR did not differ significantly between the two groups. A larger stent size with adequate post-dilation would no doubt enlarge the lumen area after stenting, which is associated with a better improvement in coronary physiological function, which in turn leads to a lower rate of vessel-related cardiac events (30).

Study limitations

This study had a number of limitations. First, the pre-stent QFR might be overestimated in culprit vessels due to the rare use of thrombus aspiration, which might affect the calculation of the ΔQFR (see discussion above). Second, we used AMR instead of cardiac MRI, which is not the gold standard for distinguishing MVO. Third, this was not a randomized controlled trial, therefore, selection bias was unavoidable.

Conclusions

The ΔQFR is a promising predictor for worsening outcomes in STEMI patients undergoing primary PCI. The pre-stent MVO and the inadequate size of stents might contribute to a lower ΔQFR in culprit lesions. Based on these findings, attention should be paid to microcirculatory function, and the strategy of stent implantation after the recovery of blood flow in primary PCI settings should be optimized.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work, including ensuring that any questions related to the accuracy or integrity of any part of the work have been appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol was reviewed and approved by the Ethics Committee of Guangdong Provincial People's Hospital (reference No: GDREC2018346H(R2)). Informed consent was obtained from all the patients.

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