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Murray law-based quantitative flow ratio for assessment of nonculprit lesions in patients with ST-segment elevation myocardial infarction

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Abstract

Introduction: *Revascularization of nonculprit arteries in patients with ST-segment elevation myocardial infarction (STEMI) is now recommended based on several trials. However, the optimal therapeutic strategy of nonculprit lesions remains unknown. Murray law-based quantitative flow ratio (μQFR) is a novel, non-invasive, vasodilator-free method for evaluating the functional severity of coronary artery stenosis, which has potential applications for nonculprit lesion assessment in STEMI patients.*

Methods: *Patients with STEMI who received staged PCI before hospital discharge were enrolled retrospectively. μQFR analyses of nonculprit vessels were performed based on both acute and staged angiography.*

Results: *Eighty-four patients with 110 nonculprit arteries were included. The mean acute μQFR was 0.76 ± 0.18, and the mean staged μQFR was 0.75 ± 0.19. The average period between acute and staged evaluation was 8 days. There was a good correlation ($r = 0.719$, $p < 0.001$) between acute μQFR and staged μQFR. The classification agreement was 89.09%. The area under the receiver operator characteristic (ROC) curve for detecting staged μQFR ≤ 0.80 was 0.931.*

Conclusions: *It is feasible to calculate the μQFR during the acute phase of STEMI patients. Acute μQFR and staged μQFR have a good correlation and agreement. The μQFR could be a valuable method for assessing functional significance of nonculprit arteries in STEMI patients.* (Cardiol J 2024; 31, 4: 522–527)

Keywords: quantitative flow ratio, μQFR, coronary physiology, nonculprit lesions, ST-segment elevation myocardial infarction

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Introduction

About 50% of ST-segment elevation myocardial infarction (STEMI) patients have multivessel coronary artery disease (MVD) [1]. Several randomized clinical trials (RCTs) have shown that complete revascularization can reduce the occurrence of major adverse cardiovascular events compared to culprit-only percutaneous coronary intervention (PCI) in patients with STEMI and MVD [2–7]. PCI of significant nonculprit artery stenosis is recommended to reduce cardiac event rates [8].

Revascularization of the nonculprit lesions can be based on angiographic severity or functional significance and the optimal strategy for guiding revascularization of nonculprit stenosis remains uncertain [9]. The DANAMI-3-PRIMULTI trial and the COMPARE-ACUTE trial have shown fractional flow reserve (FFR) guided complete revascularization of nonculprit arteries significantly reduces the risk of composite cardiovascular events compared with culprit-lesion-only PCI strategy in STEMI patients [4, 6]. However, its practical applicability is constrained by the need for a pressure wire and induction of hyperemia.

Quantitative flow ratio (QFR) is a novel, non-invasive, vasodilator-free method for assessing the functional severity of coronary artery stenosis and has high feasibility and diagnostic accuracy in identifying hemodynamically significant coronary stenosis [10–12]. In the FAVOR III China study, QFR-guided PCI strategy was proved to reduce major cardiac events compared with the standard angiography-guided PCI strategy [13].

Murray law-based QFR (μQFR) is a new method for computing QFR [14]. Measuring μQFR is simpler and takes less time than 3D-QFR because only one angiographic projection is required. As a result, QFR can be computed during acute angiography or afterwards, guiding the physician to perform revascularization during index PCI or to arrange phased PCI. So here, one can wonder whether μQFR has good coherence between primary PCI and staged PCI to be used in the STEMI acute phase to assess nonculprit lesions.

Methods

Study design

Patients with STEMI who had successfully undergone primary PCI and staged PCI for at least one nonculprit lesion before hospital discharge at the Peking University Third Hospital were retrospectively enrolled. Nonculprit coronary artery lesion was defined as ≥ 50% stenosis by visual estimation in a major epicardial coronary artery or major side branch measuring ≥ 2.5 mm in diameter. Patients with a chronic total occlusion (CTO) nonculprit artery were enrolled in this study only if they had at least one stenosis of 50–90% in another nonculprit artery. Patients with the following characteristics were excluded: coronary bypass graft, coronary slow flow, myocardial bridge, and coronary angiographic images unsuitable for measuring μQFR. The study was approved by the Ethics Committee of Peking University Third Hospital.

μQFR analysis

Computation of μQFR was performed offline using AngioPlus software (Pulse Medical Imaging Technology, Shanghai, China) according to the previously described protocol [14]. Acute and staged μQFR were measured for each nonculprit lesion with 50–90% diameter stenosis. In short, a single optimal angiographic image showing the whole target vessel at an appropriate projection angle was chosen for μQFR analysis. After an optimal frame was chosen, lumen contour and flow velocity were calculated automatically by artificial intelligence. When the lumen delineation was deemed inaccurate, manual edition was performed. Based on the Murray fractal law, the reference diameter was calculated along the target vessel. Then μQFR value of the target vessel lesion was calculated. Hemodynamic significance was defined as μQFR ≤ 0.80.

Statistical analysis

Categorical variables are presented as counts and percentages. Continuous variables are presented as mean (± SD) or median (interquartile range) depending on their distribution. The correlation of acute μQFR and staged μQFR of target nonculprit artery was assessed by the Pearson correlation analysis. Agreement between the indices was evaluated by Bland-Altman plots depicting mean differences and corresponding 95% limits of agreement. Cohen's kappa test was used to evaluate the agreement between acute μQFR and staged μQFR results as categorical variables. Intraclass correlation coefficient for the absolute value (ICCa) analysis was used to evaluate the agreement between acute μQFR and staged μQFR values as continuous variables. Receiver operating characteristic (ROC) curve analysis was used to assess the optimal acute μQFR cut-off value to detect the staged μQFR ≤ 0.80. To explore the

acute μQFR to predict staged μQFR ≤ 0.80, sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, and diagnostic accuracy were reported. A two-sided p value < 0.05 was considered to indicate statistical significance. All statistical analyses were performed using R (4.2.2).

Results

Baseline characteristics

Baseline characteristics of patients and vessels are shown in Table 1. Eighty-four STEMI patients were included in this study. The mean age was 60 years, and 86.9% were men. The mean time interval between the index and staged angiography was 8 ± 2.3 days. Out of the 110 included nonculprit vessels, 46 (41.8%) were left anterior descending arteries (LAD), 45 (40.9%) were left circumflex arteries (LCX), and 19 (17.3%) were right coronary arteries (RCA).

μQFR assessment of nonculprit lesion

The mean value of μQFR during index angiography was 0.76 ± 0.18 and 55 (50%) of nonculprit lesions had hemodynamic significance. The mean value of μQFR during staged angiography was 0.75 ± 0.19 and 57 (51.8%) of nonculprit lesions had hemodynamic significance. There was no significant difference observed between acute μQFR and staged μQFR value (p = 0.924).

Correlation and agreement between acute μQFR and staged μQFR

The correlation between acute μQFR and staged μQFR was linear with a Pearson coefficient of 0.719 (95% CI 0.614–0.798, p < 0.001) (Figure 1). The Bland-Altman plot for acute μQFR versus staged μQFR is shown in Figure 2. On average, acute μQFR exceeds staged μQFR by 0.00127 (–0.272 to 0.274). The level of diagnostic agreement between Acute μQFR ≤ 0.80 and staged μQFR ≤ 0.80 has a kappa of 0.78 (SE 0.095, p < 0.001), and the ICCa between the acute μQFR and staged μQFR values was 0.72 (95% CI 0.62–0.80), which can be interpreted as moderate to good reliability.

Diagnostic performance of μQFR

The area under the ROC curve (C statistic) for acute μQFR to predict staged μQFR ≤ 0.80 was 0.931, which is shown in Figure 3. Based on ROC curve analysis, the optimal cutoff value of acute μQFR to predict a staged μQFR ≤ 0.80 was 0.805 (Youden index 0.783). So acute μQFR ≤ 0.80 is a reasonable cutoff value.

Fifty vessels (45%) had an acute μQFR ≤ 0.80 and a staged μQFR ≤ 0.80 (true positives). Forty-eight vessels (44%) had an acute μQFR > 0.80 and a staged μQFR > 0.80 (true negatives). Five vessels (5%) had an acute μQFR ≤ 0.80 and a staged

Table 1. Baseline characteristics of the patient population and vessels

Variables	N = 84
Age [years], mean (SD)	60 (11.2)
Male, n [%]	73 (86.9%)
Cardiovascular risk factors, n [%]	
Diabetes mellitus	22 (26.2%)
Hypertension	42 (50.0%)
Current smoker	46 (54.8%)
Hyperlipidemia	42 (50.0%)
Previous PCI, n [%]	3 (3.6%)
Previous stroke, n [%]	8 (9.5%)
Family history, n [%]	13 (15.5%)
Time from symptom onset to primary PCI, n [%]	
< 6 hours	55 (65.5%)
6–12 hours	25 (29.8%)
12 hours	4 (4.8%)
Killip class ≥ 2, n [%]	19 (22.6%)
Glycated hemoglobin [%], mean (SD)	6.6 (1.3)
LDL cholesterol [mmol/L], mean (SD)	2.9 (0.8)
Peak creatinine [μmol/L], median [IQR]	96.5 [78.0, 130.5]
LVEF [%], mean (SD)	53.2 (6.8)
TNT [ng/mL], median (IQR)	8.3 [3.0, 12.7]
NT-proBNP [pg/mL], median (IQR)	718.0 [272.3, 1636.8]
CKMB [U/L] [median (IQR)]	391.5 [216.8, 631.2]
Location of culprit lesions, n [%]	
Left anterior descending artery	23 (27.4%)
Circumflex artery	11 (13.1%)
Right coronary artery	50 (59.5%)
Location of nonculprit lesions, n [%]	
Left anterior descending artery	46 (41.8%)
Circumflex artery	45 (40.9%)
Right coronary artery	19 (17.3%)

CKMB — creatine kinase isomer-MB; IQR — interquartile range; LDL — low-density lipoprotein; LVEF — left ventricular ejection fractions; NT-proBNP — N-terminal pro-B type natriuretic peptide; PCI — percutaneous coronary intervention; SD — standard deviation; TNT — troponin T

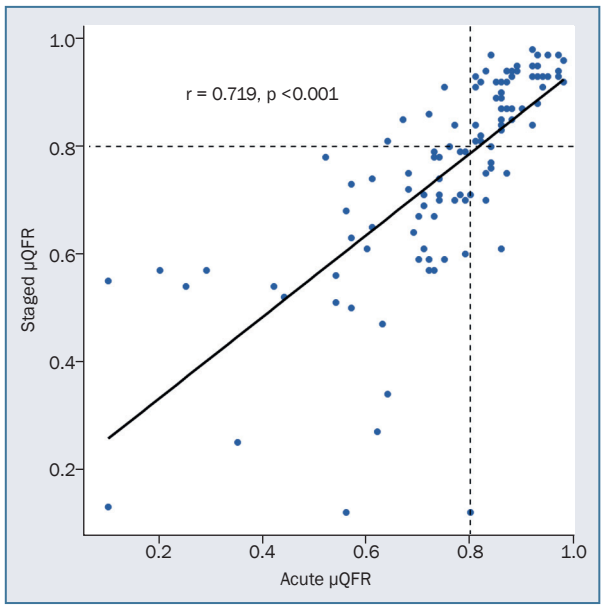

Figure 1. Plot of correlation of acute μQFR and staged μQFR; μQFR — Murray law-based quantitative flow ratio

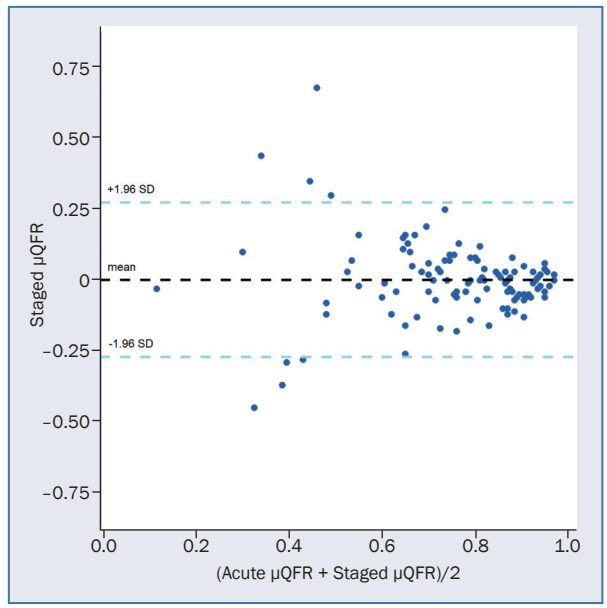

Figure 2. Bland-Altman analysis of acute μQFR and staged μQFR; μQFR — Murray law-based quantitative flow ratio; SD — standard deviation

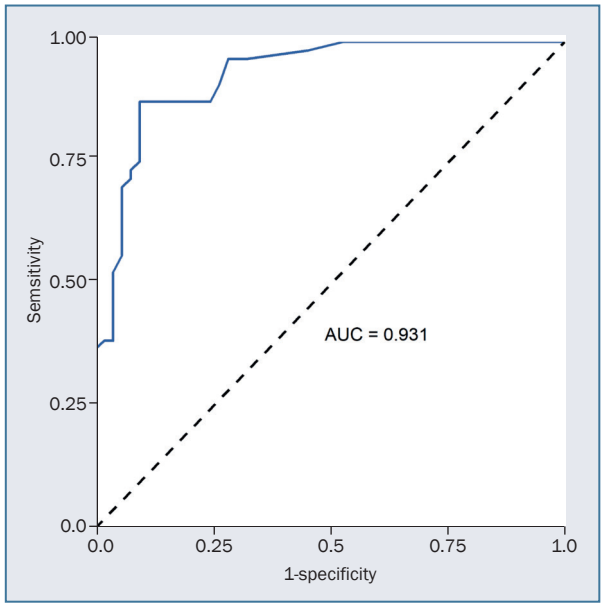

Figure 3. Receiver operating characteristic curve of acute μQFR for predicting staged μQFR, AUC — area under the curve; μQFR — Murray law-based quantitative flow ratio

μQFR > 0.80 (false positives). Seven vessels (6%) had an acute μQFR > 0.80 and a staged μQFR ≤ 0.80 (false negatives). The overall sensitivity, specificity, and positive and negative predictive value of acute μQFR versus staged μQFR were 87.72%, 90.57%, 90.91%, and 87.27%. The diagnostic accuracy was 89.09% (Table 2).

Table 2. Diagnostic performance of acute μQFR for predicting staged μQFR

	Value	95% CI
Sensitivity	87.72%	76.32%–94.92%
Specificity	90.75%	79.34%–96.87%
Positive predictive value	90.91%	80.05%–96.98%
Negative predictive value	87.27%	75.52%–94.73%
Diagnostic accuracy	89.09%	81.72%–94.23%
Positive likelihood ratio	9.30	4.02, 21.53
Negative likelihood ratio	0.14	0.07, 0.27

μQFR — Murray law-based quantitative flow ratio

Discussion

The present study investigated the feasibility and diagnostic reliability of μQFR assessment of nonculprit lesions in STEMI patients with MVD. μQFR shows good diagnostic performance in assessing nonculprit lesions, regardless of whether the images were acquired during primary PCI or a few days subsequent during a staged procedure. This suggests that μQFR can reliably assess the functional severity of nonculprit stenosis in STEMI patients during the acute phase.

QFR is a novel angiography-based technique for assessing the functional significance of coronary artery and has a good correlation with FFR [11]. Several previous studies investigated the application of 3D-QFR based on contrast-flow in the acute stage of STEMI patients. These studies have demonstrated a good correlation between acute 3D-QFR and staged 3D-QFR [15–18]. However, 3D-QFR requires two angiographic projections (at least 25° apart), which may restrict its application during the acute phase. μQFR requires only one angiographic projection and has perfect agreement with standard 3D-QFR [19], so it will take less time to acquire images and calculate, and may be better applied to assess the function of a nonculprit artery in the acute phase.

In STEMI patients, complete revascularization is currently recommended based on many well-designed RCTs. The optimal method for evaluating the nonculprit lesions remains uncertain. Coronary arteriography may overestimate the severity of the lesions, resulting in overtreatment, with additional costs and risks [20]. As for pressure wire-based functional diagnostics, FFR may underestimate functional significance in the acute setting [21]. This may be due to microvascular resistance and incomplete adenosine-induced vasodilation. The significance of instantaneous wave-free ratio (iFR) may be underestimated in the acute setting [22]. In the present study, μQFR shows a good correlation between acute and staged settings, which is consistent with previous QFR studies. Furthermore, μQFR does not require pressure wire or pharmacological agents to induce hyperemia, which makes it easier and faster to perform during the acute phase. In STEMI patients, μQFR may be a quick, reliable, and noninvasive way to assess the functional significance of nonculprit stenosis.

Despite its good diagnostic accuracy, μQFR occasionally yields false negatives or false positives, indicating the possibility of it overestimating or underestimating the severity of non-culprit lesions during the acute phase. It was believed herein, that several factors may contribute to these discrepancies. Firstly, due to the retrospective nature of the study, disparities were observed in the angiographic projections used for μQFR computation between the acute and staged settings. Utilizing consistent angiographic projections may enhance accuracy. Secondly, the μQFR is based on coronary arteriography, any variations in coronary arteriography could impact μQFR results and may lead to false positives. Lastly, when the μQFR value gets close to the cutoff threshold, minor fluctuations in functional assessments may result in a change in the outcome.

Limitations

The present study has several limitations. First, because this was a retrospective study, the coronary angiographies were not obtained for μQFR analysis. As a result, a few angiographies were not obtained optimally according to the μQFR acquisition guide. Furthermore, μQFR was retrospectively computed offline in this study. Online computation may improve the feasibility because operators could get optimal angiographies and direct feedback during the primary PCI, which may offer more functional information in clinical practice. Finally, the prognostic value of μQFR-guided revascularization of nonculprit lesions in STEMI patients with MVD should be confirmed in further prospective studies. Randomized clinical trials are needed to ascertain whether or not revascularization of nonculprit lesions can be safely deferred based on μQFR value.

Conclusion

The current study suggests that μQFR assessment appears to be feasible and relatively reliable during the acute phase in STEMI patients. The findings provide a practical basis for using μQFR to assess functional significance of nonculprit lesions in STEMI with MVD patients. The prognostic value of μQFR-guided revascularization in STEMI patients should be confirmed in further prospective studies.

Conflict of interest: The authors report no competing interests.

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