Research Article

Predictive Value of Post-Percutaneous Coronary Intervention Quantitative Flow Ratio for Vessel-Oriented Composite Endpoint

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Received 3 September 2022; Revised 8 August 2023; Accepted 31 August 2023; Published 9 September 2023

Academic Editor: Adam Kern

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At present, there is a lack of indicators, which can accurately predict the post-percutaneous coronary intervention (post-PCI) vessel-oriented composite endpoint (VOCE). Recent studies showed that the post-PCI quantitative flow ratio (QFR) can predict post-PCIVOCE. PubMed, Embase, and Cochrane were searched from inception to March 27, 2022, and the cohort studies about that the post-PCI QFR predicts post-PCIVOCE were screened. Meta-analysis was performed, including 6 studies involving 4518 target vessels. The results of the studies included in this meta-analysis all showed that low post-PCI QFR was an independent risk factor for post-PCI VOCE after adjusting for other factors, HR (95% CI) ranging from 2.718 (1.347–5.486) to 6.53 (2.70–15.8). Our meta-analysis showed that the risk of post-PCI VOCE was significantly higher in the lower post-PCI QFR group than in the higher post-PCI QFR group (HR: 4.14, 95% CI: 3.00–5.70, P < 0.001, I² = 27.9%). Post-PCI QFR has a good predictive value for post-PCI VOCE. Trial Registration. This trial is registered with CRD42022322001.

1. Introduction

Coronary atherosclerotic heart disease (CHD) is one of the most common cardiovascular diseases in clinical practice. Medication and percutaneous coronary intervention (PCI) can relieve symptoms and improve outcome in patients with CHD. However, some patients may still experience vessel-oriented composite endpoint (VOCE), defined as the composite of vessel-related cardiac death, vessel-related myocardial infarction, and target vessel revascularization. The incidence of post-PCI VOCE was about 7% [1, 2]. Previous studies have shown that intravascular ultrasound (IVUS), optical coherence tomography (OCT), and fractional flow reserve (FFR) can predict the long-term prognosis of the post-PCI patients [3–10]. However, these methods exert some limitations, such as invasive, high cost, and complex operation. Therefore, finding a simple method that can accurately predict the long-term prognosis of the post-PCI patients is crucial.

In 2015, Tu [11] proposed a quantitative flow ratio (QFR) based on FFR, a noninvasive and guidewire-free FFR rapid analysis system. The QFR combines a three-dimensional reconstruction technology of coronary angiography, a hemodynamic system, and artificial intelligence with respect to blood flow quantification to accurately evaluate the physiological function of the coronary artery. Recently, some studies have shown that post-PCI QFR can predict post-PCI VOCE [1, 12–19]. Among them, the
2. Materials and Methods

2.1. Search Strategy. This study was conducted according to the PRISMA statement. PubMed, Embase, and Cochrane were searched from inception to March 27, 2022, and the cohort studies about that the post-PCI QFR predicts post-PCI VOCE were screened. Subject words plus free words were used to search the PCI. Free words were used to search QFR, because QFR has no subject words. The expression of QFR was as follows: "QFR," "quantitative flow ratio," "virtual FFR," "virtual fractional flow ratio," and "virtual pressure wire." The search strategy of PubMed was as follows: (((“Percutaneous Coronary Intervention”[Mesh]) OR (Coronary Interventions, Percutaneous*) OR (Coronary Interventions, Percutaneous*) OR (Intervention, Percutaneous Coronary*) OR (Interventions, Percutaneous Coronary*) OR (Percutaneous Coronary Interventions*) OR (Percutaneous Coronary Revascularization*) OR (Coronary Revascularization, Percutaneous*) OR (Percutaneous Coronary Revascularizations*) OR (Revascularization, Percutaneous Coronary*) OR (Revaskualrizations, Percutaneous Coronary*)) AND (((QFR* OR [Title/Abstract]) OR (quantitative flow ratio * [Title/Abstract])) OR (virtual FFR* [Title/Abstract]) OR (virtual fractional flow ratio* [Title/Abstract]) OR (virtual pressure wire* [Title/Abstract]))) OR (Percutaneous Coronary Interventions OR Coronary Interventions OR Percutaneous Coronary Interventions OR Percutaneous Coronary Revascularizations OR Revascularization, Percutaneous Coronary* OR Revascularization, Percutaneous Coronary* OR Revascularizations, Percutaneous Coronary*)). The search strategy of Embase was as follows: (“percutaneous coronary intervention”/exp OR “coronary intervention, percutaneous*”: ti, ab, kw OR “coronary interventions, percutaneous*”: ti, ab, kw OR “intervention, percutaneous coronary*”: ti, ab, kw OR “interventions, percutaneous coronary*”: ti, ab, kw OR “percutaneous coronary intervention*”: ti, ab, kw OR “percutaneous coronary interventions*”: ti, ab, kw OR “percutaneous coronary revascularization*”: ti, ab, kw OR “coronary revascularization, percutaneous*”: ti, ab, kw OR “percutaneous coronary revascularizations*”: ti, ab, kw OR “revascularization, percutaneous coronary*”: ti, ab, kw OR “revascularizations, percutaneous coronary*”: ti, ab, kw) AND (“qfr*”: ti, ab, kw OR “quantitative flow ratio*”: ti, ab, kw OR “virtual ffr*”: ti, ab, kw OR “virtual fractional flow ratio*”: ti, ab, kw OR “virtual pressure wire*”: ti, ab, kw). The search strategy of Cochrane was as follows: #1=MeSH descriptor: [Percutaneous Coronary Intervention] explode all trees; #2=(Coronary Interventions, Percutaneous*) OR (Coronary Interventions, Percutaneous*) OR (Intervention, Percutaneous Coronary*) OR (Interventions, Percutaneous Coronary*) OR (Percutaneous Coronary Interventions*) OR (Percutaneous Coronary Revascularization*) OR (Coronary Revascularization, Percutaneous*) OR (Coronary Revascularizations, Percutaneous*) OR (Revascularization, Percutaneous Coronary*) OR (Revascularizations, Percutaneous Coronary*). The search strategy of Cochrane was as follows: #1=MeSH descriptor: [Percutaneous Coronary Intervention] explode all trees; #2=(Coronary Interventions, Percutaneous*) OR (Coronary Interventions, Percutaneous*) OR (Intervention, Percutaneous Coronary*) OR (Interventions, Percutaneous Coronary*) OR (Percutaneous Coronary Interventions*) OR (Percutaneous Coronary Revascularization*) OR (Coronary Revascularization, Percutaneous*) OR (Coronary Revascularizations, Percutaneous*) OR (Revascularization, Percutaneous Coronary*) OR (Revascularizations, Percutaneous Coronary*).

2.2. Inclusion Criteria and Exclusion Criteria. The inclusion criteria were as follows: (1) cohort study; (2) the study subjects were post-PCI CHD patients; (3) QFR of the target vessels was measured after successful PCI; (4) according to the post-PCI QFR, the target vessels of all patients together were divided into two cohorts: lower post-PCI QFR group and higher post-PCI QFR group. (5) The primary endpoint of the study was post-PCI VOCE. (6) Cox regression was used for multiple-variable analysis. (7) After adjusting for other influencing factors, post-PCI QFR was analyzed as an independent risk factor for post-PCI VOCE.

Case-control studies were cross-sectional and time-independent, in which odd ratio (OR) was generally used for statistical description. Outcome measures of cohort studies were time-dependent, in which hazard ratio (HR) was generally used for statistical description. It was not appropriate to put OR and HR together for statistical merging, and case-control studies had a lower level of evidence-based medical evidence than cohort studies. Therefore, we excluded 3 case-control studies [17–19].

2.3. Data Extraction. The data, such as author, year of publication, country, data source, follow-up time, number of cases, number of target vessels, age, the proportion of males, proportion of hypertension, proportion of diabetes, proportion of smoking, the proportion of hyperlipidemia, left ventricular ejection fraction, proportion of target vessels, PCI type, post-PCI QFR cutoff value, hazard ratio (HR), 95% confidence interval (95% CI), and number of post-PCI VOCE, were independently extracted by two researchers from the finally included studies. The risk of bias was independently assessed by two researchers according to the PRISMA statement. The disagreements were resolved by discussion.

2.4. Statistical Analysis. Meta-analysis was performed using Stata 17 software. Heterogeneity was evaluated using Cochrane Q test and I² test. I² > 50% was considered evident heterogeneity. We used the random-effects model for all meta-analysis. Publication bias was assessed by funnel plots and Egger’s test. P < 0.05 was considered statistically significant.

3. Results

A total of 203 articles were retrieved: 82 from PubMed, 78 from Embase database, 41 from Cochrane database, and 2 from manual search. After these articles were imported into
NoteExpress reference management software (https://www.inoteexpress.com/aegean/), 61 duplicates, 12 reviews, 2 meta-analysis, and systematic reviews were excluded. After reading the abstract of the remaining 128 articles, 115 articles were further excluded. After reading the full text of the remaining 13 articles, 6 articles were finally included in this meta-analysis [1, 12–16]. The flowchart of literature screening is shown in Figure 1.

The characteristics of the included 6 studies were summarized in Table 1. There were 3332 patients involving 4518 target vessels. These studies were published from 2019 to 2022. Four of six studies included in this meta-analysis were from China [13–16], and two of six studies included in this meta-analysis were from other countries [1, 12]. Biscaglia et al.’s study was from Italy and Spain. Kogame et al.’s study was from the Netherlands, Japan, Poland, United Kingdom, Northern Ireland, and Spain. Biscaglia et al.’s [1] study was a registered prospective clinical trial. Three studies, Kogame [12], Zhang [16] and Liu and Ding [15], were retrospective analysis of previously registered prospective clinical trials. Two studies, Tang et al. [13] and Tang [14], were retrospective analysis of previously unregistered prospective data. The follow-up duration was approximately 1-2 years. The PCI type in 4 studies was drug-eluting stent (DES) implantation [1, 12, 13, 16], and the PCI type in the other 2 studies was drug-coated balloon (DCB) expansion [14, 15].

The quality of the included studies was evaluated according to the Newcastle-Ottawa scale (NOS), Table 2. Five studies were of high quality with scores of 8 or 9, and one study was of general quality with a score of 6.

The post-PCI QFR cutoff value was not completely same, which ranged from 0.89 to 0.94, Table 3. The target vessel numbers in lower post-PCI QFR group and higher post-PCI QFR group were 1019 and 3499, respectively. The post-PCI VOCE numbers in lower post-PCI QFR group and higher post-PCI QFR group were 168 (16.49%) and 105 (3.00%), respectively. The results of the studies included in this meta-analysis all showed that low post-PCI QFR was an independent risk factor for post-PCI VOCE after adjusting for other factors, HR (95% CI) ranging from 2.718 (1.347–5.486) to 6.53 (2.70–15.8). The factors adjusted for in the 6 studies were as follows: (1) Biscaglia et al.: diabetes, prior MI, lesion length, post-PCI %DS, left anterior descending coronary artery location, and baseline SYNTAX score; (2) Kogame et al.: creatinine clearance, LAD stenosis, and SYNTAX score; (3) Tang and Chu et al.: peak troponin I, diffuse disease, culprit lesion, and diabetes mellitus; (4) Tang and Hou et al.: diabetes mellitus and diameter stenosis (post-procedural in-stent); (5) Liu et al.: diabetes mellitus, difference of drug-coated balloon diameter, and reference vessel diameter (per 0.10-mm increase); (6) Zhang et al.: age, sex, body mass index, hypertension, family history of coronary artery disease, creatine clearance, left ventricular ejection fraction, acute myocardial infarction, vessel SYNTAX score, total occlusion, baseline diameter stenosis, and post-PCI in-stent diameter stenosis. Our meta-analysis showed that the risk of post-PCI VOCE was significantly higher in the lower post-PCI QFR group than in the higher post-PCI QFR group (HR: 4.14, 95% CI: 3.00–5.70, P < 0.001, I² = 27.9%; Figure 2). Funnel plots were almost symmetric, indicating that there was no evident publication bias, Figure 3. Egger’s test also showed no publication bias (P = 0.804).

Subgroup analyses showed that the post-PCI VOCE risk of the drug-eluting stent (DES) subgroup was significantly higher in the lower post-PCI QFR group than in the higher post-PCI QFR (HR: 3.70, 95% CI: 2.52–5.42, P < 0.001, I² = 40.3%), Figure 4. The post-PCI VOCE risk of the drug-coated balloon (DCB) subgroup was significantly higher in the lower post-PCI QFR group than in the higher post-PCI QFR (HR: 6.24, 95% CI: 3.29–11.86, P < 0.001, I² = 0.0%). The post-PCI VOCE risk of post-PCI 1 year subgroup was significantly higher in the lower post-PCI QFR group than in the higher post-PCI QFR group (HR: 4.97, 95% CI: 3.31–7.47, P < 0.001, I² = 40.3%). The post-PCI VOCE risk in China subgroup was significantly higher in the lower post-PCI QFR group than in the higher post-PCI QFR group (HR: 3.13, 95% CI: 2.06–4.75, P < 0.001, I² = 0%). The post-PCI VOCE risk in registred studies subgroup was significantly higher in the lower post-PCI QFR group than in the higher post-PCI QFR group (HR: 4.23, 95% CI: 2.88–6.20, P < 0.001, I² = 33.5%). The post-PCI VOCE risk in unregistered studies subgroup was significantly higher in the lower post-PCI QFR group than in the higher post-PCI QFR group (HR: 4.04, 95% CI: 1.72–9.49, P = 0.001, I² = 56.9%).

4. Discussion

Since Pijs et al. [20] proposed FFR in 1993, it had become the gold standard for functional evaluation of coronary artery stenosis over long-term basic and clinical research [21]. It involves sending a guidewire with a pressure sensor to the distal end of the coronary artery and measuring the ratio of the pressure at the distal end to the pressure at the proximal end. It requires the use of adenosine, which some patients are intolerant of. Therefore, Tu [11] proposed QFR in 2015, which involves reconstructing the three-dimensional model of the coronary artery and calculating the process of blood flow pressure changes in the whole vessel according to the coronary angiography image. QFR does not require the use of drugs and does not require the use of guidewire. Compared with FFR, QFR has the advantages of simpler operation and better security. Both FFR and QFR belong to functional indicators, which can more accurately reflect the impact of lesions on cardiac function than the pure degree of vascular stenosis. FFR is a direct measurement of pressure and can only be performed during the operation. As long as there is past or present coronary angiography image, QFR can be performed at any
time. Therefore, post-PCI QFR can be calculated based on post-PCI coronary angiography images from past prospective databases, and the relationship between post-PCI QFR and long-term prognosis of patients can be analyzed. In this meta-analysis, five studies were retrospective analyses of previous prospective data [12–16], and the other one was a prospective clinical trial [1].

2014 ESC/EACTS Guidelines had clearly stated that it was beneficial to guide PCI based on FFR values measured before PCI [21]. In recent years, studies had shown that QFR and FFR had a very high diagnostic consistency [22, 23]. It was also beneficial to guide PCI based on the QFR values measured before PCI [24]. In addition, it was found that FFR values measured after PCI could predict the long-term outcome of patients [25]. Systematic reviews and meta-analysis had also reached similar conclusions [10, 26]. In recent years, studies had shown that QFR could also predict post-PCI VOCE [1, 12–16]. However, there has been no relevant systematic review and meta-analysis. Therefore, we conducted this meta-analysis, and the results showed that the hazard ratio of post-PCI VOCE was significantly higher in the lower post-PCI QFR group than in the higher post-PCI QFR group.

After successful PCI, many patients still had residual disease, stent underexpansion, and stent edge dissection, which were very important reasons for the occurrence of post-PCI VOCE. Post-PCI QFR measured the stenosis function of target vessels after PCI, which could reflect not only the stented segment but also the nonstented segment. Biscaglia et al.’s [1] study showed that 13% of suboptimal post-PCI QFR was due to PCI segments. For these patients with suboptimal post-PCI QFR, further stent optimization during PCI might could reduce the occurrence of post-PCI VOCE. This meta-analysis showed that mean or median of QFR after angiographically successful PCI were higher than 0.9, and that post-PCI QFR of 5.9% to 7.4% target vessels were still lower than 0.8. Post-PCI QFR could help identify patients at high risk for post-PCI VOCE. In addition, it was noteworthy whether the suboptimal QFR was derived from the PCI segment.

In all 6 studies included in this meta-analysis, post-PCI QFR was used as a binary variable for Cox regression.
**Table 1: Characteristics of included studies.**

<table>
<thead>
<tr>
<th>Studies</th>
<th>Year</th>
<th>Country</th>
<th>Data source</th>
<th>Follow-up (months)</th>
<th>Patients</th>
<th>Target vessel numbers</th>
<th>Age (years)</th>
<th>Male (%)</th>
<th>Hypertension (%)</th>
<th>Diabetes (%)</th>
<th>Smoke (%)</th>
<th>Hyperlipidemia (%)</th>
<th>LVEF (%)</th>
<th>Target vessel proportion</th>
<th>PCI type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biscaglia et al. [1]</td>
<td>2019</td>
<td>Other countries</td>
<td>HAWKEYE study</td>
<td>21</td>
<td>602</td>
<td>751</td>
<td>68</td>
<td>74</td>
<td>74</td>
<td>23</td>
<td>19</td>
<td>56</td>
<td>NA</td>
<td>47</td>
<td>25</td>
</tr>
<tr>
<td>Kogame [12]</td>
<td>2019</td>
<td>Other countries</td>
<td>SYNTAX II trial</td>
<td>24</td>
<td>393</td>
<td>771</td>
<td>66.6</td>
<td>92.6</td>
<td>75.4</td>
<td>29.7</td>
<td>14.7</td>
<td>77.1</td>
<td>58.3</td>
<td>45.7</td>
<td>31.5</td>
</tr>
<tr>
<td>Tang et al. [13]</td>
<td>2021</td>
<td>China</td>
<td>Unregistered study</td>
<td>24</td>
<td>186</td>
<td>415</td>
<td>63.1</td>
<td>75.3</td>
<td>61.8</td>
<td>34.9</td>
<td>67.7</td>
<td>18.8</td>
<td>56.2</td>
<td>40.7</td>
<td>25.5</td>
</tr>
<tr>
<td>Tang et al. [14]</td>
<td>2021</td>
<td>China</td>
<td>Unregistered study</td>
<td>12</td>
<td>177</td>
<td>185</td>
<td>68</td>
<td>81</td>
<td>NA</td>
<td>46</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>50</td>
<td>20</td>
</tr>
<tr>
<td>Liu and Ding [15]</td>
<td>2021</td>
<td>China</td>
<td>DCB-ISR trial</td>
<td>12</td>
<td>169</td>
<td>169</td>
<td>62.5</td>
<td>76</td>
<td>73</td>
<td>41</td>
<td>23</td>
<td>34</td>
<td>60.66</td>
<td>48</td>
<td>15</td>
</tr>
<tr>
<td>Zhang [16]</td>
<td>2022</td>
<td>China</td>
<td>PANDA III trial</td>
<td>24</td>
<td>1805</td>
<td>2227</td>
<td>60.9</td>
<td>70.2</td>
<td>62</td>
<td>23.9</td>
<td>50.8</td>
<td>32</td>
<td>59.2</td>
<td>48.4</td>
<td>21.6</td>
</tr>
</tbody>
</table>

LVEF, left ventricular ejection fraction; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; PCI, percutaneous coronary intervention; DES, drug-eluting stent; DCB, drug-coated balloon; NA, not available. Biscaglia et al.’s study was from Italy and Spain. Kogame et al.’s study was from the Netherlands, Japan, Poland, United Kingdom, Northern Ireland, and Spain. Hawkeye Study (ClinicalTrials.gov, NCT02811796); SYNTAX II Trial (ClinicalTrials.gov, NCT02015832); PANDA III Trial (ClinicalTrials.gov, NCT02017275).
Table 2: Quality evaluation of included studies (the Newcastle-Ottawa scale, NOS).

<table>
<thead>
<tr>
<th>Studies</th>
<th>Representativeness of the exposed cohort</th>
<th>Selection of the nonexposed cohort</th>
<th>Ascertainment of exposure</th>
<th>Outcomes of interest was not present at start of study</th>
<th>Comparability of cohorts on the basis of the design or analysis</th>
<th>Assessment of outcomes</th>
<th>Follow-up duration was sufficient for outcomes to occur</th>
<th>Adequacy of follow-up of cohorts</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biscaglia et al. [1]</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Kogame [12]</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Tang et al. [13]</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Tang [14]</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Liu and Ding [15]</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Zhang [16]</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>8</td>
</tr>
</tbody>
</table>

The full score is nine.
<table>
<thead>
<tr>
<th>Studies</th>
<th>Post-PCI QFR mean or median</th>
<th>Post-PCI QFR ≤ 0.8</th>
<th>QFR cutoff</th>
<th>Lower post-PCI QFR group</th>
<th>Higher post-PCI QFR group</th>
<th>Lower post-PCI VOCE group (%)</th>
<th>Higher post-PCI VOCE group (%)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biscaglia et al. [1]</td>
<td>0.97 (0.92, 0.99)</td>
<td>NA</td>
<td>0.89</td>
<td>123</td>
<td>628</td>
<td>31 (25.20%)</td>
<td>22 (3.50%)</td>
<td>2.91 (1.63–5.19)</td>
</tr>
<tr>
<td>Kogame [12]</td>
<td>0.91 ± 0.07</td>
<td>7.4%</td>
<td>0.91</td>
<td>284</td>
<td>487</td>
<td>34 (11.97%)</td>
<td>18 (3.70%)</td>
<td>3.38 (1.85–6.20)</td>
</tr>
<tr>
<td>Tang et al. [13]</td>
<td>0.94 ± 0.09</td>
<td>NA</td>
<td>0.91</td>
<td>101</td>
<td>314</td>
<td>21 (20.79%)</td>
<td>18 (5.73%)</td>
<td>2.718 (1.347–5.486)</td>
</tr>
<tr>
<td>Tang [14]</td>
<td>NA</td>
<td>5.9%</td>
<td>0.94</td>
<td>59</td>
<td>126</td>
<td>20 (33.90%)</td>
<td>7 (5.56%)</td>
<td>6.53 (2.70–15.8)</td>
</tr>
<tr>
<td>Liu and Ding [15]</td>
<td>NA</td>
<td>7.1%</td>
<td>0.89</td>
<td>36</td>
<td>133</td>
<td>11 (30.56%)</td>
<td>9 (6.77%)</td>
<td>5.94 (2.33–15.09)</td>
</tr>
<tr>
<td>Zhang [16]</td>
<td>0.98 (0.95, 1.00)</td>
<td>NA</td>
<td>0.92</td>
<td>416</td>
<td>181</td>
<td>51 (12.26%)</td>
<td>31 (1.71%)</td>
<td>6.007 (3.634–9.930)</td>
</tr>
</tbody>
</table>

QFR, quantitative flow ratio; VOCE, vessel-oriented composite endpoint; HR (95% CI), hazard ratio (95% confidence interval); NA, not available. The factors adjusted for in the 6 studies were as follows: (1) Biscaglia et al.: diabetes, prior MI, lesion length, post-PCI %DS, left anterior descending coronary artery location, and baseline SYNTAX score; (2) Kogame et al.: creatinine clearance, LAD stenosis, and SYNTAX score; (3) Tang and Chu et al.: peak troponin I, diffuse disease, culprit lesion, and diabetes mellitus; (4) Tang and Hou et al.: diabetes mellitus, diameter stenosis (post-procedural in-stent); (5) Liu et al.: diabetes mellitus, difference of drug-coated balloon diameter and reference vessel diameter (per 0.10 mm increase); (6) Zhang et al.: age, sex, body mass index, hypertension, family history of coronary artery disease, creatine clearance, left ventricular ejection fraction, acute myocardial infarction, vessel SYNTAX score, total occlusion, baseline diameter stenosis, post-PCI in-stent diameter stenosis.
In addition, post-PCI QFR was also used as a continuous variable for Cox regression analysis in 3 studies. Biscaglia et al.’s [1] study showed that hazard ratio of post-PCI VOCE fell by 0.56 for every 0.1 increase of post-PCI QFR (HR 0.56; 95% CI 0.46–0.68, \( P < 0.001 \)). Tang’s [14] study showed that hazard ratio of post-PCI VOCE fell by 0.36 for every 0.1 increase of post-PCI QFR (HR 0.36; 95% CI 0.22–0.59, \( P < 0.001 \)). Liu and Ding’s [15] study showed that hazard ratio of post-PCI VOCE fell by 0.34 for every 0.1 increase of post-PCI QFR (HR 0.34; 95% CI 0.23–0.51, \( P < 0.001 \)). These results also showed that the risk of post-PCI VOCE decreases with the increase of post-PCI QFR.

Although the heterogeneity of this meta-analysis was not evident, we still conducted subgroup analyses. The results of subgroup analyses showed that we might need to pay more attention to those who underwent DCB than to those who underwent DES. We might need to pay more attention to the period of post-PCI 1 year than post-PCI 2 year. Biscaglia et al.’s [1] study seems to focus on European participants. Kogame [12] study seems to have diverse ethnic backgrounds. Tang et al.’s [13], Tang’s [14], Liu and Ding’s [15] and Zhang [16] studies seem to focus on Chinese participants. Post-PCI QFR might have a better predictive value for post-PCI VOCE in Chinese population than other populations. Genetical and cultural implication may be one of the reasons for the difference between Chinese population and other populations. Further investigations are needed to find the pathological cause.

5. Limitations

There were some limitations to this meta-analysis. Data recording might be subject to bias, because data of some included studies was from previously unregistered database.

**Figure 2: Forest plot (meta-analysis of the hazard ratio of post-PCI VOCE in the lower post-PCI QFR group than in the higher post-PCI QFR group).**

<table>
<thead>
<tr>
<th>Study ID</th>
<th>HR (95% CI)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biscaglia et al. (2019)</td>
<td>2.91 (1.63, 5.19)</td>
<td>20.33</td>
</tr>
<tr>
<td>Kogame et al. (2019)</td>
<td>3.38 (1.85, 6.20)</td>
<td>19.18</td>
</tr>
<tr>
<td>Tang and Chu et al. (2021)</td>
<td>2.72 (1.35, 5.49)</td>
<td>15.50</td>
</tr>
<tr>
<td>Tang and Hou et al. (2021)</td>
<td>6.53 (2.70, 15.80)</td>
<td>10.82</td>
</tr>
<tr>
<td>Liu et al. (2021)</td>
<td>5.94 (2.33, 15.09)</td>
<td>9.86</td>
</tr>
<tr>
<td>Zhang et al. (2022)</td>
<td>6.01 (3.63, 9.93)</td>
<td>24.31</td>
</tr>
<tr>
<td>Overall ( (I^2 = 27.9%, \ p = 0.225) )</td>
<td>4.14 (3.00, 5.70)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

**Figure 3: Funnel plots (the hazard ratio of post-PCI VOCE in the lower post-PCI QFR group than in the higher post-PCI QFR group).**

In the studies included in this meta-analysis, follow-up time, PCI types, post-PCI QFR cutoff values, and adjusted factors were not completely consistent, which might affect the results of this meta-analysis to some extent. Our meta-analysis would be more convincing if we could obtain the raw data of all studies included in our meta-analysis, reanalyze them, and obtain an optimal cutoff value for post-PCI QFR. To some extent correlation among vessels in a patient may affect results. However, the purpose of our study is to study the predictive value of post-PCI QFR for post-PCI VOCE. Both subjects (post-PCI QFR) and outcomes (post-PCI VOCE) were analyzed based on the number of vessels. This method should be feasible. This is also the case with other meta-analysis, such as the meta-analysis published by Hwang [26] in JAMA in 2022. Hence, the results of this study should be considered exploratory.
6. Conclusion

In summary, this meta-analysis showed that post-PCI QFR had a good predictive value for post-PCI VOCE. Large sample prospective studies with carefully controlling for confounders are needed to confirm this conclusion.

Abbreviations

CHD: Coronary atherosclerotic heart disease
IVUS: Intravascular ultrasound
OCT: Optical coherence tomography
FFR: Fractional flow reserve
VOCE: Vessel-oriented composite endpoint

PCI: Percutaneous coronary intervention
QFR: Quantitative flow ratio
DES: Drug-eluting stent
DCB: Drug-coated balloon.

Data Availability

All the data generated or analysed during this study are included in this published article.

Disclosure

Weibin Liu, Huaxiu Cai, and Yin Zheng are co-first authors.
Conflicts of Interest
The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors’ Contributions
Jun Cao and Gang Cao jointly designed this meta-analysis, and they jointly searched and screened the literature. Yongkang Wen and Sicheng Chen independently extracted the data from the finally included studies. Xiuying Xie and Huan Zeng independently assessed the risk of bias. Gang Cao and Huaxiu Cai jointly completed the statistical analysis. Weibin Liu, Huaxiu Cai, Yin Zheng, Hengqing Zhu, Fang Pei, and Zhongan Ni jointly wrote this manuscript. All the authors read and approved the final manuscript. Weibin Liu, Huaxiu Cai, and Yin Zheng are co-first authors. Gang Cao and Jun Cao are co-corresponding authors.

Supplementary Materials
Table 4: occurrences of CV death, TVMI, and TVR 312.
Figure 5: Forest plot (CV death, TVMI, and TVR). (Supplementary Materials)

References
