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## Original Article

## Quantitative Flow Ratio in Angiography versus Intravascular Ultrasound Guided Percutaneous Coronary Intervention in Old Patients with Coronary Artery Disease

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## SUMMARY

**Background:** The impact of intracoronary imaging guidance on final coronary flow in older patients with coronary artery disease (CAD) and undergoing percutaneous coronary intervention (PCI) remains unclear.**Methods:** Older patients with chest pain and undergoing diagnostic coronary angiography (CAG) were selected. Those with significant CAD on diagnostic CAG were proceeded with CAG or intravascular ultrasound (IVUS)-guided PCI, and pre- and post-procedural coronary flow was assessed using angiography-derived quantitative flow ratio (QFR).**Results:** The analysis included 37 participants (15 healthy controls and 22 patients with significant CAD; mean age  $72 \pm 8$  and 70% male). The CAG-guided PCI was performed for 10 culprit lesions in 9 patients, while IVUS-guided PCI was performed for 14 culprit lesions in 13 patients. Pre-procedural culprit vessel QFR was comparable between lesions in CAG and IVUS-guided PCI groups ( $0.50 \pm 0.17$  vs.  $0.49 \pm 0.31$ ,  $p = 0.920$ ). Post-procedural culprit vessel QFR, however, was significantly lower in the CAG-guided PCI group compared to the IVUS group ( $0.89 \pm 0.06$  vs.  $0.95 \pm 0.02$ ,  $p = 0.003$ ). Additionally, post-procedural QFR improvement in the left anterior descending (LAD) and left circumflex (LCx) was similar to healthy controls in the IVUS-guided PCI group ( $0.89 \pm 0.15$  vs.  $0.91 \pm 0.06$ ,  $p = 0.667$  for LAD and  $0.94 \pm 0.06$  vs.  $0.96 \pm 0.03$ ,  $p = 0.221$  for LCx) but significantly lower in the CAG-guided PCI group ( $0.81 \pm 0.13$  vs.  $0.91 \pm 0.06$ ,  $p = 0.009$  for LAD and  $0.90 \pm 0.11$  vs.  $0.96 \pm 0.03$ ,  $p = 0.041$  for LCx).**Conclusion:** In older patients with stable CAD, IVUS-guided PCI provides better post-procedural QFR compared to CAG-guided PCI, with QFR values similar to healthy individuals.

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## 1. Introduction

Coronary artery disease (CAD) is a leading cause of mortality and morbidity in the aging population worldwide.<sup>1</sup> The rapid progression of atherosclerosis beyond the sixth decade of life is a main phenomenon in older patients ( $\geq 60$  years old) with CAD.<sup>2</sup> These patients often present with complex coronary lesions, such as bifurcational, calcified, diffuse and chronic total occlusion, resulting from advanced atherosclerosis and comorbid conditions, such as hypertension, chronic kidney disease (CKD) and diabetes mellitus (DM).<sup>3</sup> Due to the complexity of coronary lesions and associated comorbidities, percutaneous coronary intervention (PCI) in older patients often requires the guidance of intracoronary imaging, such as intravascular ultrasound (IVUS) or optical coherence tomography (OCT), to achieve optimal results.<sup>4,5</sup> The IVUS provides tomographic images of the coronary arteries, facilitating better stent optimization during complex PCI procedures.<sup>6</sup> However, the impact of intracoronary imaging guidance on final coronary flow in older patients with CAD re-

mains unclear. In the present study, we aimed to investigate the impact of IVUS guidance on coronary flow, as assessed by angiography-derived quantitative flow ratio (QFR), in older patients with CAD.

## 2. Materials and methods

## 2.1. Study population and data collection

Patients with stable chest pain and underwent diagnostic coronary angiography (CAG) at our institution between January 2021 and June 2024 were selected for the present study. Demographic, risk factors, comorbidity, medication, pre- and post-PCI data were prospectively collected during index hospitalization.

## 2.2. Diagnostic CAG and QFR measurement

The diagnostic CAG procedure was conducted in accordance with current guidelines and local best practices.<sup>7,8</sup> In brief, left and right coronary ostia were engaged with standard JL 4.0 and JR 4.0 diagnostic catheters and intracoronary nitroglycerine was adminis-

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tered before capturing CAG images. Contrast media was injected manually with a long and brisk injection to ensure good contrast filling. For each region of interest, two CAG images were taken at angles at least 25 degrees apart. To ensure optimal QFR analysis, foreshortening and overlapping were minimized as much as possible and zooming was avoided. All CAG images were archived in DICOM format for subsequent QFR measurement. Both pre and post-procedural QFR was measured offline using commercially available QAngio XA 3D software (Medis Medical Imaging System by, The Netherlands) by certified users who were blinded to types of PCI (Figure 1).<sup>9</sup>

2.3. CAG and IVUS-guided PCI

After diagnostic CAG, patients who were diagnosed with significant CAD, defined as luminal stenosis  $\geq 50\%$ , were treated with CAG or IVUS-guided PCI. All lesions were pre-dilated using a non-compliant balloon (semi-compliant balloon in case of balloon uncrossable lesions) sized 1:1 to vessel diameter before stenting. For patients undergoing CAG-guided PCI, the stent sizing was left at operator's discretion.<sup>8</sup> While, stent sizing was based on IVUS measurements including minimal lumen area and diameter and reference lumen area and diameter in patients who underwent IVUS-guided PCI. Following initial stent deployment, post-dilatation with a non-compliant balloon was performed. In IVUS-guided PCI group, final stent optimization with IVUS was performed to ensure stent apposition less than 400  $\mu\text{m}$ , minimal stent area reaching 90–100% of the distal reference lumen area and absence of stent edge dissection (Figure 1).<sup>6</sup>

2.4. Statistical analysis

Continuous variables are presented as mean  $\pm$  standard deviation when normally distributed (assessed by the Shapiro–Wilk test and distribution histograms) and as median [and interquartile range (IQR)] when not normally distributed. Categorical variables are presented as frequencies and percentages. Based on initial CAG and PCI decision, patients were divided into three subgroups as healthy control, CAG and IVUS-guided PCI groups. Differences in continuous variables across the study groups were evaluated using one-way ANOVA with LSD correction when normally distributed or Kruskal Wallis test when not normally distributed, while differences in categorical variables were compared by  $\chi^2$  tests (Fisher's exact test when indicated). Changes in pre- and post-procedural QFR were evaluated by linear mixed models with random intercepts. Predictors of post-procedural QFR improvement were evaluated using univariable and multivariable linear regression analysis. Variables with significant association in the univariable analysis were selected for the multivariable analysis. To prevent multiple collinearity, forward selection method was used in the multivariable analysis. All statistical tests were two-sided, and a p-value of  $< 0.05$  was considered to be statistically significant. Statistical analysis was performed using SPSS for Windows version 25.0 (IBM Corporation, Armonk, New York, USA).

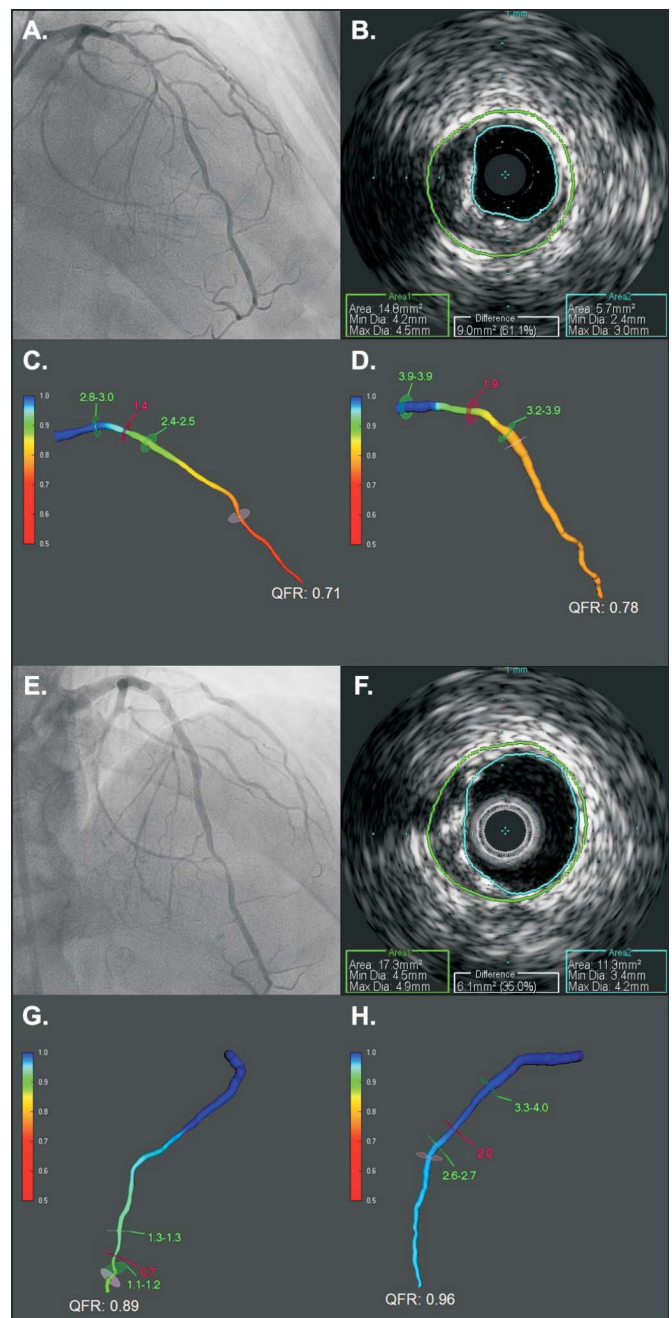
2.5. Ethical approval

Study design and protocol was approved by the Ethical Committee of the Ministry of Health of Mongolia (approval number is 23/014) and a signed informed consent was taken from all participants. The investigation in the present study conformed with principles of the "Declaration of Helsinki".<sup>10</sup>

3. Results

3.1. Baseline characteristics

Baseline patient characteristics were summarized in Table 1. A total of 37 patients who were suspected chest pain and underwent diagnostic CAG were included in the present study (mean age  $72 \pm 8$  and 70% male). Based on diagnostic CAG, 15 patients without significant CAD (luminal diameter  $< 50\%$ ) were classified as healthy controls, while 9 and 13 patients who had significant CAD underwent for CAG and IVUS-guided PCI, respectively. Patients in CAG and IVUS-guided PCI groups were more likely smokers (67% and 39%), compared to healthy controls (0%,  $p < 0.05$  vs. other groups). The preva-



**Figure 1.** The measurement of pre- (panel A and C for CAG-guided PCI group and panel B and D for IVUS-guided PCI group) and post-procedural (panel E and G for CAG-guided PCI group and panel F and H for IVUS-guided PCI group) QFR. CAG, coronary angiography; IVUS, intravascular ultrasound; PCI, percutaneous coronary intervention; QFR, quantitative flow ratio.

lence of stable angina was higher in CAG and IVUS-guided PCI groups (56% and 85%) than healthy controls (13%,  $p < 0.05$  vs. other groups) and the prevalence of dyslipidemia was lower in healthy controls and IVUS-guided PCI groups (47% and 15%) compared to CAG-guided PCI group (89%,  $p < 0.05$  vs. other groups). Usage of beta-blocker and antiplatelet were higher in CAG and IVUS-guided PCI groups (89% and 75% for beta blocker and 67% and 92% for antiplatelet, respectively) than healthy controls (33% for beta-blocker and 27% for antiplatelet,  $p < 0.05$  vs. other groups).

### 3.2. CAG findings

Baseline diagnostic CAG results were described in Table 2. A total of 24 significant CAD lesions were evaluated and 15, 6 and 3 lesions occurred in LAD, LCx and RCA, respectively. In CAG-guided PCI group, 5 lesions in left anterior descending (LAD), 2 lesions in left circumflex (LCx) and 3 lesions in right coronary artery (RCA) and while, 10 lesions in LAD, 4 lesions in LCx and no lesion in RCA for IVUS-guided PCI group ( $p = 0.091$ ). The prevalence of multivessel dis-

**Table 1**  
Baseline characteristics.

Variables	All patients (n = 37)	Healthy controls (n = 15)	CAG-guided PCI (n = 9)	IVUS-guided PCI (n = 13)	p-value
Age (years)	72 ± 8	71 ± 7	69 ± 7	74 ± 10	0.365
Gender, n (%)					0.080
Female	11 (30%)	6 (40%)	0 (0%)	5 (39%)	
Male	26 (70%)	9 (60%)	9 (100%)	8 (61%)	
BMI (kg/m <sup>2</sup> )	28.5 ± 4.3	29.5 ± 5.2	29.5 ± 3.2	26.5 ± 3.3	0.148
Smoking status, n (%)					0.002
Non smoker	26 (70%)	15 (100%)	3 (33%) <sup>a</sup>	8 (61%) <sup>a</sup>	
Current smoker	11 (30%)	0 (0%)	6 (67%) <sup>a</sup>	5 (39%) <sup>a</sup>	
Co-morbidities					
Hypertension, n (%)	29 (78%)	10 (67%)	6 (67%)	13 (100%)	0.063
Stable angina, n (%)	18 (49%)	2 (13%)	5 (56%) <sup>a</sup>	11 (85%) <sup>a</sup>	0.001
MI, n (%)	7 (19%)	0 (0%)	3 (33%)	4 (31%)	0.052
HF, n (%)	2 (5%)	0 (0%)	1 (11%)	1 (8%)	0.458
DM, n (%)	12 (32%)	4 (27%)	5 (56%)	3 (23%)	0.230
CKD, n (%)	1 (3%)	0 (0%)	1 (11%)	0 (0%)	0.202
Dyslipidemia, n (%)	17 (46%)	7 (47%)	8 (89%) <sup>a,c</sup>	2 (15%) <sup>b</sup>	0.003
Medications					
ACEi/ARB, n (%)	25 (68%)	10 (67%)	5 (56%)	10 (77%)	0.572
ARNI, n (%)	5 (14%)	0 (0%)	3 (33%)	2 (15%)	0.067
Beta-blocker, n (%)	22 (60%)	5 (33%)	8 (89%) <sup>a</sup>	9 (75%) <sup>a</sup>	0.012
Aspirin, n (%)	32 (87%)	14 (93%)	9 (100%)	9 (75%)	0.152
Other antiplatelet, n (%)	22 (60%)	4 (27%)	6 (67%)	12 (92%) <sup>a</sup>	0.002
Statin, n (%)	23 (62%)	9 (60%)	8 (89%)	6 (55%)	0.226
VKA, n (%)	1 (3%)	0 (0%)	1 (11%)	0 (0%)	0.202
OAK, n (%)	1 (3%)	1 (7%)	0 (0%)	0 (0%)	0.471

ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BMI, body mass index; CAG, coronary angiography; CKD, chronic kidney disease; DM, diabetes mellitus; HF, heart failure; IVUS, intravascular ultrasound; MI, myocardial infarction; OAC, oral anticoagulant; VKA, vitamin K antagonist.

<sup>a</sup>  $p < 0.05$  vs. Healthy control, <sup>b</sup>  $p < 0.05$  vs. CAG guided PCI, <sup>c</sup>  $p < 0.05$  vs. IVUS guided PCI.

**Table 2**  
Coronary angiography and QFR findings.

Variables	All lesions (n = 24)	Healthy controls (n = 0)	Lesions treated with CAG-guided PCI (n = 10)	Lesions treated with IVUS-guided PCI (n = 14)	p-value
Culprit vessel, n (%)					0.091
LAD	15 (63%)	-	5 (50%)	10 (71%)	
LCx	6 (25%)	-	2 (20%)	4 (29%)	
RCA	3 (12%)	-	3 (30%)	0 (0%)	
Multivessel disease, n (%)	21 (88%)	-	9 (90%)	12 (86%)	0.754
SYNTAX score	16 (15-34)	-	16 (12-29)	19 (16-34)	0.276
Pre-procedural QFR					
Culprit vessel	0.49 ± 0.26	-	0.50 ± 0.17	0.49 ± 0.31	0.920
LAD	0.70 ± 0.27	0.91 ± 0.06	0.62 ± 0.19 <sup>a</sup>	0.53 ± 0.31 <sup>a</sup>	< 0.001
LCx	0.80 ± 0.31	0.96 ± 0.03	0.73 ± 0.30	0.67 ± 0.42 <sup>a</sup>	0.032
RCA	0.90 ± 0.14	0.95 ± 0.04	0.80 ± 0.22 <sup>a,c</sup>	0.94 ± 0.05 <sup>b</sup>	0.009
Post-procedural QFR					
Culprit vessel	0.92 ± 0.05	-	0.89 ± 0.06	0.95 ± 0.02	0.003
LAD	0.88 ± 0.12	0.91 ± 0.06	0.81 ± 0.13 <sup>a</sup>	0.89 ± 0.15	0.090
LCx	0.94 ± 0.07	0.96 ± 0.03	0.90 ± 0.11 <sup>a</sup>	0.94 ± 0.06	0.090
RCA	0.94 ± 0.05	0.95 ± 0.04	0.94 ± 0.05	0.94 ± 0.05	0.607

CAG, coronary angiography; IVUS, intravascular ultrasound; LAD, left anterior descending; LCx, left circumflex; PCI, percutaneous coronary intervention; QFR, quantitative flow ratio; RCA, right coronary artery.

<sup>a</sup>  $p < 0.05$  vs. Healthy control, <sup>b</sup>  $p < 0.05$  vs. CAG guided PCI, <sup>c</sup>  $p < 0.05$  vs. IVUS guided PCI.

ease was 88% for entire study population, and 90% and 86% for CAG and IVUS-guided PCI groups, respectively ( $p = 0.754$ ). The SYNTAX score indicating severity of coronary lesions were similar between CAG and IVUS-guided PCI groups (16, IQR 12–29 and 19, IQR 16–34,  $p = 0.276$ ).

**3.3. Pre- and post-procedural changes in QFR between study groups**

The vessel level pre- and post-procedural QFR was measured for culprit vessels and each of the LAD, LCx and RCA, in study groups. The culprit vessel pre-procedural QFR between CAG and IVUS-guided groups were comparable ( $0.50 \pm 0.17$  vs.  $0.49 \pm 0.31$ ,  $p = 0.920$ ). Pre-procedural QFR was lower in CAG and IVUS-guided groups ( $0.62 \pm 0.19$  and  $0.53 \pm 0.31$ ) than healthy controls ( $0.91 \pm 0.06$ ,  $p < 0.05$  vs. the other groups) for LAD. Pre-procedural QFR was significantly lower in IVUS-guided PCI group compared to healthy controls ( $0.67 \pm 0.42$  vs.  $0.96 \pm 0.03$ ,  $p < 0.05$ ) for LCx, while it was significantly lower in CAG-guided PCI group ( $0.80 \pm 0.22$ ,  $p < 0.05$  vs. the other groups) than healthy controls ( $0.95 \pm 0.04$ ) and IVUS-guided PCI group ( $0.94 \pm 0.05$ ) for RCA (Table 2).

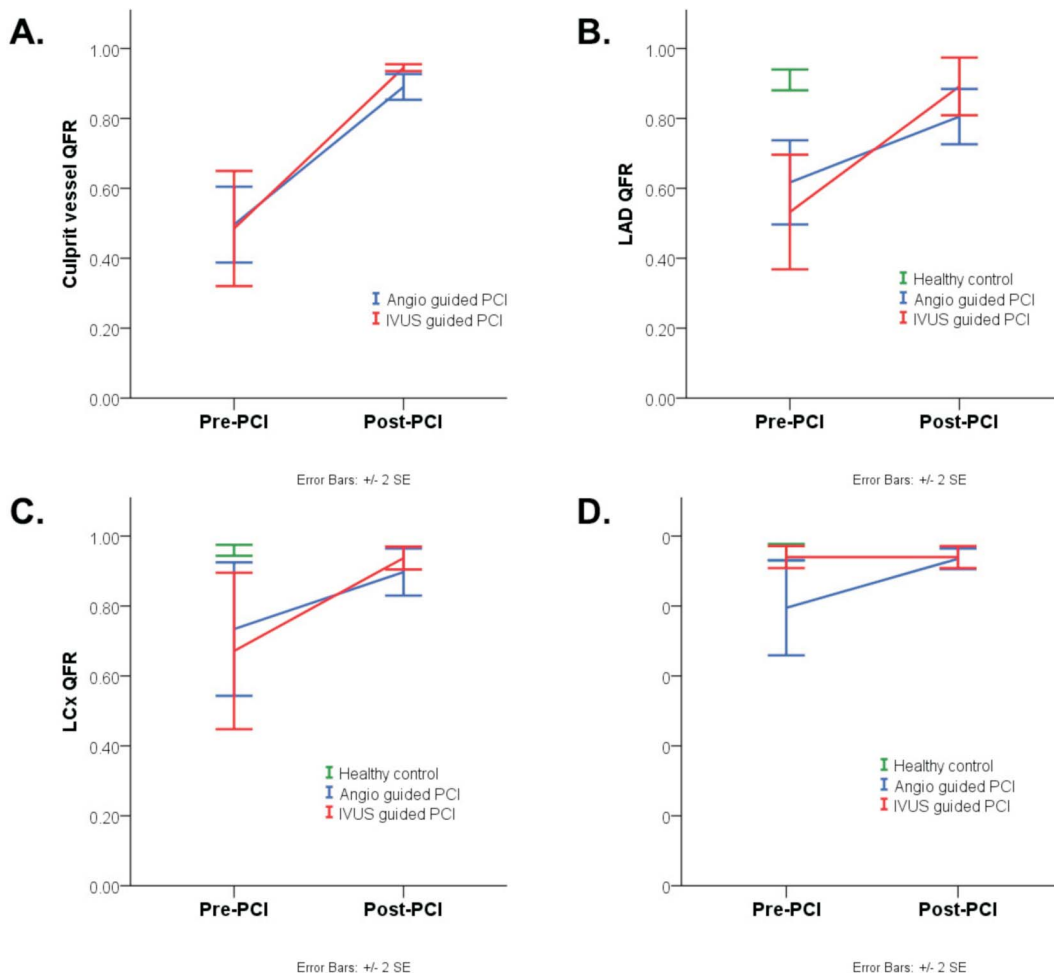
The culprit vessel QFR was improved in both CAG ( $0.50 \pm 0.17$  vs.  $0.89 \pm 0.06$ ,  $p < 0.001$ ) and IVUS-guided PCI groups ( $0.49 \pm 0.31$  vs.  $0.95 \pm 0.02$ ,  $p < 0.001$ ) after PCI (Figure 2A). For LAD, post-procedural QFR was significantly increased in both CAG ( $0.62 \pm 0.19$  vs.  $0.81 \pm 0.13$ ,  $p = 0.022$ ) and IVUS-guided PCI groups ( $0.53 \pm 0.31$  vs.

$0.89 \pm 0.15$ ,  $p = 0.001$ ) (Figure 2B). For LCx, post-procedural changes in QFR was not significant in CAG-guided PCI group ( $0.73 \pm 0.30$  vs.  $0.90 \pm 0.11$ ,  $p = 0.087$ ) (Figure 2C, blue line), while it was significantly increased in IVUS-guided PCI group ( $0.67 \pm 0.42$  vs.  $0.94 \pm 0.06$ ,  $p = 0.027$ ) (Figure 2C, red line). For RCA, there was no significant difference before and after PCI in both CAG ( $0.80 \pm 0.22$  vs.  $0.94 \pm 0.05$ ,  $p = 0.05$ ) and IVUS-guided PCI ( $0.94 \pm 0.05$  vs.  $0.94 \pm 0.05$ ,  $p > 0.99$ ) groups (Figure 2D).

The post-procedural comparison of vessel level QFR has been shown in Table 2. The culprit vessel QFR improvement was lower in CAG-guided PCI group than IVUS-guided PCI group ( $0.89 \pm 0.06$  vs.  $0.95 \pm 0.02$ ,  $p = 0.003$ ). For LAD, improvement of QFR in IVUS-guided PCI group was similar to healthy controls ( $0.89 \pm 0.15$  vs.  $0.91 \pm 0.06$ ,  $p = 0.667$ ), while it was significantly lower in CAG-guided PCI group ( $0.81 \pm 0.13$  vs.  $0.91 \pm 0.06$ ,  $p = 0.009$ ). The post-procedural QFR in IVUS-guided PCI groups was similar to healthy controls ( $0.94 \pm 0.06$  vs.  $0.96 \pm 0.03$ ,  $p = 0.221$ ) in LCx, however, it was significantly lower in CAG-guided PCI group ( $0.90 \pm 0.11$  vs.  $0.96 \pm 0.03$ ,  $p = 0.041$ ). There was no significant difference in post-procedural QFR between study groups for RCA.

**3.4. Predictors of post-procedural QFR improvement**

The association between possible predictors and post-procedural QFR improvement was assessed using univariable and multivariable linear regression analysis (Table 3). In the univariable analysis, dys-



**Figure 2.** The changes in QFR at pre and post-PCI for culprit vessel (panel A), LAD (panel B), LCx (panel C) and RCA (panel D) in patients who underwent for CAG-guided PCI (blue line) and who underwent for IVUS-guided PCI (red line) compared to healthy control (green line). Data presented as mean  $\pm$  2SE. CAG, coronary angiography; IVUS, intravascular ultrasound; LAD, left anterior descending; LCx, left circumflex; PCI, percutaneous coronary intervention; QFR, quantitative flow ratio; RCA, right coronary artery.

lipidemia ( $\beta = -0.052$ , 95% CI  $-0.087$  to  $-0.016$ ,  $p = 0.006$ ), ARNI ( $\beta = -0.056$ , 95% CI  $-0.100$  to  $-0.011$ ,  $p = 0.017$ ) and statin ( $\beta = -0.050$ , 95% CI  $-0.095$  to  $-0.005$ ,  $p = 0.033$ ) use were found to have a negative association with post-procedural QFR, and while IVUS-guided PCI ( $\beta = 0.055$ , 95% CI  $0.021$  to  $0.089$ ,  $p = 0.003$ ) demonstrated positive association with post-procedural QFR. In the multivariable analysis using forward selection, ARNI use ( $\beta = -0.055$ , 95% CI  $-0.099$  to  $-0.011$ ,  $p = 0.018$ ) and IVUS-guided PCI ( $\beta = 0.044$ , 95% CI  $0.010$  to  $0.078$ ,  $p = 0.015$ ) were identified as independent predictors of post-procedural QFR.

#### 4. Discussion

The results of the current study can be summarized as follows: IVUS-guided PCI results in better coronary flow restoration following complex PCI procedures, and coronary flow restoration achieved with IVUS-guided PCI in old patients is comparable to those of similar age without angiography-defined CAD.

Performing PCI in old patients with CAD is often challenging due to the complexity of coronary stenosis, multiple comorbidity and frailty.<sup>3,7</sup> Therefore, intracoronary imaging is recommended to achieve optimal results and avoid unnecessary complications.<sup>8</sup> Among available techniques, IVUS is the preferred method for intravascular imaging because of its wider availability, cost-effectiveness, and reduced contrast media usage compared to OCT.<sup>11–13</sup>

##### 4.1. Stenotic vessel luminal restoration and prognosis

In principle, optimal PCI outcomes should involve both luminal and flow restoration in stenotic vessels. Major clinical trials have shown that IVUS-guided PCI provides lower target vessel failure than CAG-guided PCI, indicating better luminal restoration in stenotic vessels.<sup>14–16</sup> The investigators of the Intravascular Ultrasound Guided Drug Eluting Stents Implantation in “All-Comers” Coronary Lesions trial have demonstrated that the IVUS-guided drug eluting stent im-

plantation is associated with lower target vessel failure compared to angiography guided group at 1 and 3 year follow-up.<sup>14,15</sup> In a large Korean bifurcation registry, IVUS-guided PCI was associated with larger minimal stent area and better prognosis compared to angiography guided PCI group.<sup>17</sup> Authors from the Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents trial observed superiority of IVUS guidance in terms of cardiac death, myocardial infarction or stent thrombosis compared to angiography guidance for drug eluting stent optimization.<sup>16</sup> However, these trials were underrepresented old patients who may have higher underlying risks than younger patients.

##### 4.2. Coronary flow restoration and clinical importance

The restoring coronary flow in old patients can be significantly more complex than restoration of luminal stenosis. Compared to younger patients, old individuals are more likely to present with bifurcational, calcified, and diffuse coronary lesions.<sup>18–20</sup> Therefore, complex PCI is increasingly common in old patients than their younger counterparts.<sup>20,21</sup>

These complex lesion types pose unique challenges, such as plaque and carina shift in bifurcational stenosis,<sup>22,23</sup> arterial wall injury from unmatched high-pressure ballooning in calcified lesions,<sup>24</sup> and microvascular occlusion caused by extensive debris during large-scale angioplasty in long lesions<sup>25</sup> can all compromise coronary flow restoration. Intracoronary imaging offers operators the ability to mitigate these risks, which may not be fully preventable with CAG-guided PCI. Voigtlander et al. have shown that the calcification detected with IVUS in coronary stenosis is an independent predictor of dissection after balloon angioplasty.<sup>26</sup> In a systematic review and network meta-analysis of 24 randomized trials, intracoronary imaging-guided PCI was associated with significantly lower ischemia driven target lesion revascularization compared to angiography-guided PCI.<sup>27</sup> In the present study, we demonstrated that the IVUS guidance

**Table 3**  
Predictors of post-procedural QFR improvement.

Variables	Univariable analysis			Multivariable analysis		
	B coefficient	95% CI	p-value	B coefficient	95% CI	p-value
Age	0.001	-0.002 to 0.003	0.554			
Gender	-0.028	-0.077 to 0.022	0.258			
BMI	-0.001	-0.007 to 0.004	0.600			
Smoking	-0.013	-0.054 to 0.028	0.521			
Hypertension	0.021	-0.040 to 0.083	0.480			
Stable angina	0.025	-0.019 to 0.069	0.251			
MI	-0.003	-0.048 to 0.043	0.895			
HF	-0.019	-0.093 to 0.056	0.609			
DM	-0.012	-0.055 to 0.030	0.556			
CKD	-0.065	-0.164 to 0.035	0.191			
Dyslipidemia	-0.052	-0.087 to -0.016	0.006			
ACEi/ARB	0.020	-0.023 to 0.063	0.345			
ARNI	-0.056	-0.100 to -0.011	0.017	-0.055	-0.099 to -0.011	0.018
Beta-blocker	-0.035	-0.085 to 0.014	0.152			
Aspirin	-0.033	-0.087 to 0.022	0.224			
Antiplatelet	0.002	-0.053 to 0.058	0.926			
Statin	-0.050	-0.095 to -0.005	0.033			
VKA	0.029	-0.074 to 0.132	0.563			
Multivessel disease	0.002	-0.060 to 0.065	0.938			
SYNTAX score	0.001	-0.001 to 0.003	0.419			
Pre-procedural QFR	0.031	-0.050 to 0.113	0.435			
IVUS guided PCI	0.055	0.021 to 0.089	0.003	0.044	0.010 to 0.078	0.015

ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor, BMI, body mass index; CAG, coronary angiography; CKD, chronic kidney disease; DM, diabetes mellitus; HF, heart failure; IVUS, intravascular ultrasound; LAD, left anterior descending; LCx, left circumflex; MI, myocardial infarction; PCI, percutaneous coronary intervention; QFR, quantitative flow ratio; RCA, right coronary artery; VKA, vitamin K antagonist.

during PCI in old patients is independently associated improvement of post-procedural QFR compared to CAG-guided PCI. The superiority of IVUS guidance in terms of coronary flow restoration could be explained as more precise stent optimization than conventional CAG-guided PCI.

#### 4.3. Clinical implications

The application of IVUS in complex coronary lesions allow more precise visualization of lesion morphology than CAG in patients with stable CAD who undergoing for complex PCI. However, currently available evidences in intracoronary imaging-guided PCI are mostly derived from relatively young patients. Old patients often have more advanced coronary lesions due to aging and therefore, those patients frequently requires complex PCI compared to young patients. The results from current study are supporting IVUS-guided PCI to achieve optimal coronary flow compared to conventional CAG-guided PCI in old patients with CAD.

#### 4.4. Study limitations

The present study has several limitations. First, the data used in this investigation was obtained from the same interventional team at single center, making it essential to conduct confirmatory analyses using data from other institutions. Second, the patient cohort was relatively small due to the limited number of old patients included in the study. Third, the procedures in the current study were performed by multiple operators, and operator expertise may have influenced the final outcome. Lastly, the multivariable analysis relied on the forward variable selection method due to small sample size.

### 5. Conclusions

The IVUS-guided PCI in old patients with CAD is associated with significant improvement in coronary flow compared to those of similar age who were underwent with CAG-guided PCI. Notably, the improvement in coronary flow is comparable to healthy controls without angiography-defined CAD.

#### Consent for publication

None.

#### Availability of data and material

The data which was used for the present study is available from corresponding author by reasonable request.

#### Competing interest

The authors declare no conflict of interest.

#### Author's contributions

ED, MB, SC and BK designed and conceptualized the present study. ED, OB, BB, GC, AL and BK performed procedures and collected data. SC performed statistical analysis and wrote manuscript together with BK. All authors reviewed and approved the manuscript.

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All individuals who contributed to this publication have been included as authors.

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