Original Article

Fractional flow reserve in assessment of intermediate non-culprit lesions in acute myocardial infarction

[Reserva fraccional de flujo en la evaluación de lesiones intermedias no culpables en el infarto agudo de miocardio]

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Abstract

Context: Percutaneous coronary intervention (PCI) of intermediate non-culprit arteries can reduce death or heart attack risk in patients with acute myocardial infarction and multivessel coronary artery disease.

Aims: To compare the effectiveness of fractional flow reserve (FFR)-guided PCI with angiography-guided PCI for intermediate non-culprit lesions in patients with acute myocardial infarction and multivessel coronary artery disease.

Methods: In this cohort study, acute myocardial infarction patients with multivessel coronary artery disease who had successful percutaneous coronary intervention of the culprit artery were divided into group of patients receiving FFR-guided PCI (FFR≤0.80, n = 31) and group of patients receiving angiography-guided PCI (diameter stenosis of 50-90%, n = 62) for lesions in non-culprit arteries. These two groups were followed for at least 1 year for major adverse cardiovascular events.

Results: There was no statistically significant difference in major cardiovascular events between FFR-guided percutaneous coronary intervention group and angiography-guided percutaneous coronary intervention group. However, FFR-guided percutaneous coronary intervention group had a lower mortality rate compared to the angiography-guided percutaneous coronary intervention group (3.2% *vs.* 4.8%). Additionally, there were no reported cases of myocardial infarction in angiography-guided PCI group, while angiography-guided PCI group had a rate of 1.6%.

Conclusions: This study found that it remains uncertain whether FFR-guided PCI is superior than angiography-guided PCI for intermediate non-culprit lesions in patients with acute myocardial infarction and multivessel coronary artery disease.

Keywords: acute myocardial infarction; fractional flow reserve; intermediate non-culprit lesions; multivessel disease.

Resumen

Contexto: La intervención coronaria percutánea (ICP) de las arterias intermedias no culpables puede reducir el riesgo de muerte o infarto de miocardio en pacientes con infarto agudo de miocardio y enfermedad arterial coronaria multivaso.

Objetivos: Comparar la eficacia de la ICP guiada por la reserva fraccional de flujo (RFF) con la ICP guiada por angiografía para lesiones intermedias no culpables en pacientes con infarto agudo de miocardio y enfermedad coronaria multivaso.

Métodos: En este estudio de cohortes, los pacientes con infarto agudo de miocardio y enfermedad coronaria multivaso que se sometieron a una intervención coronaria percutánea exitosa de la arteria culpable se dividieron en grupo de pacientes que recibieron ICP guiada por FFR (FFR≤0,80, n = 31) y grupo de pacientes que recibieron ICP guiada por angiografía (estenosis del diámetro del 50-90%, n = 62) para lesiones en arterias no culpables. Estos dos grupos fueron seguidos durante al menos 1 año para detectar eventos cardiovasculares adversos mayores.

Resultados: No hubo diferencias estadísticamente significativas en los eventos cardiovasculares mayores entre el grupo de intervención coronaria percutánea guiada por FFR y el grupo de intervención coronaria percutánea guiada por angiografía. Sin embargo, la tasa de mortalidad del grupo de intervención coronaria percutánea guiada por RFF fue inferior a la del grupo de intervención coronaria percutánea guiada por angiografía (3,2% frente a 4,8%). Además, no se notificaron casos de infarto de miocardio en el grupo de ICP guiada por angiografía, mientras que el grupo de ICP guiada por angiografía tuvo una tasa del 1,6%.

Conclusiones: Este estudio reveló que sigue siendo incierto si la ICP guiada por RFF es superior a la ICP guiada por angiografía para lesiones intermedias no culpables en pacientes con infarto agudo de miocardio y enfermedad coronaria multivaso.

Palabras Clave: enfermedad multivaso; infarto agudo de miocardio; lesiones intermedias no culpables; reserva fraccional de flujo.

INTRODUCTION

Acute myocardial infarction (AMI) and multivessel disease (MVD) are common cardiovascular conditions that are strongly associated with mid- and long-term risk of mortality (Dyrbuś et al., 2021). Appropriate management is crucial to prevent adverse outcomes, such as ST-segment elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI). For individuals with STEMI, primary percutaneous coronary intervention (PCI) is the preferred method for reperfusion. Various randomized trials have shown that complete revascularization improves outcomes compared to culprit lesion PCI only in terms of reducing the risk of cardiovascular death or myocardial infarction in COMPLETE trial and fewer repeat revascularizations in DANAMI 3-PRIMULTI and COMPARE ACUTE trials (Engstrøm et al., 2017). Similar results have been observed with NSTEMI (Kim et al., 2020; Sels et al., 2011). Recent major guidelines recommend complete revascularization before hospital discharge (Lawton et al., 2022; Neumann et al., 2019).

Currently, there are two main approaches to guiding PCI for non-culprit lesions, including angiography-guided PCI and fractional flow reserve (FFR)-guided PCI. Both methods have shown better outcomes in guiding complete PCI of non-culprit lesions in acute myocardial infarction compared to PCI only on culprit lesions (Gershlick et al., 2015; Mehta, 2019). Angiography-guided PCI relies on visual estimation of the degree of stenosis, while FFR-guided PCI involves measurement of the pressure gradient across the lesion to determine the functional severity of the stenosis. FFR is the ratio of maximal (hyperemic) myocardial blood flow distal to a stenotic artery to the theoretical normal hyperemic myocardial flow in the same artery (Pijls et al., 1996). FFR has been demonstrated to indicate that PCI should be performed for lesions with stenosis greater than 90%, with 96% of such lesions being functionally significant (Tonino et al., 2010). However, the best management strategy for intermediate non-culprit lesions with a stenosis of 50-90% is still controversial (Lee et al., 2023; Puymirat et al., 2021). The FLOWER-MI study did not show any significant differences in outcomes when comparing treatment outcomes between the two groups of STEMI patients who underwent complete revascularization guided by FFR and complete revascularization guided by Angiography, while the FRAME-AMI trial demonstrated that FFR-guided PCI reduced the composite endpoint of death, myo-

cardial infarction (MI), or repeat revascularization at a median follow-up of 3.5 years compared to angiography-guided PCI for patients with AMI and MVD. This reduction was primarily driven by a significantly decreased risk of death and MI in the FFR-guided PCI group.

To address this issue, this study aimed to investigate whether the use of FFR in intermediate non-culprit lesions results in better clinical outcomes than the use of angiography in AMI patients with MVD.

MATERIAL AND METHODS

Study design and settings

This was a prospective cohort study conducted at the Department of Interventional Cardiology, Gia Dinh People's Hospital in Ho Chi Minh City in Vietnam between 01 January 2020 to 03 March 2022. The Department is one of the largest interventional cardiology centers in Ho Chi Minh City.

Study population

Inclusion criteria were patients aged above 18 years old experiencing AMI and having MVD with intermediate non-culprit lesion with stenosis grade between 50-90%. Myocardial infarction was defined according to the Fourth Universal Definition of Myocardial Infarction (Thygesen et al., 2018). MVD was defined as having stenoses ≥50% in at least 2 of the 3 major epicardial coronary arteries (angiographic 2- or 3-vessel disease), which the operator deemed necessary to require stenting (Dyrbuś et al., 2021). An intermediate non-culprit lesion was defined as 50-90% stenosis with a diameter of at least 2.5 mm by visual estimation (Neumann et al., 2019). Key exclusion criteria included those with Killip class III or IV before and after PCI, left main and chronic total occlusion non-culprit lesions, collateral from non-culprit arteries, prior myocardial infarction, contraindicated to adenosine and pregnant women.

After performing PCI for the culprit lesions, non-culprit lesions were evaluated using FFR or PCI under angiography guidance in a separate procedure during the same hospitalization. FFR was measured by PressureWire® Certus on RADI Analyzer®Xpress (St. Jude Medical Inc., St. Paul, Minnesota, United States) then Pressure wire Aeris® on QUANTIEN® machine (Abbott vascular). PCI was performed using the Siemens Axiom Artis Cath/Angio (Germany) imaging system. Intracoronary adenosine was admin-

istered to induce hyperemia during FFR procedure. The doses of adenosine used for the left coronary artery were 160 and 200 μg, respectively. The doses used for the right coronary artery were 60 and 100 μg, respectively. These doses were considered to be the most effective with the lowest possible effects (Adjedj et al., 2015). Non-culprit lesions with a stenosis greater than 90% underwent PCI without FFR. In the FFR group, FFR was used for intermediate stenosis of non-culprit lesions in 100% of patients. If FFR ≤ 0.8, the patient was performed PCI. If FFR >0.8, the patient was deferred PCI. In the angiography-guided group, PCI was performed for 100% of non-culprit lesions with a stenosis greater than or equal to 50%. All patients were treated with drug-eluting stents.

Compliance with ethical guidance

All procedures were followed in accordance with the responsible committee on human experimentation and with the Declaration of Helsinki of 1975 and subsequent revisions, and that informed consent was received from all patients involved in this study. The study was approved by the Ethical Review Committee of Hue University of Medicine and Pharmacy (No. H2019/437 dated November 28, 2019).

Measurements

The primary endpoint was major adverse cardiovascular events (MACE) – a composite of all-cause mortality, nonfatal MI, stroke, and target lesion revascularization (TLR). Secondary endpoints were all-cause mortality, cardiac mortality, non-cardiac mortality, nonfatal MI, stroke, and TLR. Cardiovascular death was defined as any death resulting from cardiovascular causes, such as non-fatal MI, congestive heart failure, fatal arrhythmias, death related to a procedure or surgery, or death with an unknown cause. Non-cardiac mortality referred to deaths resulting from non-cardiovascular causes, such as cancer, infectious diseases, or accidents. All events were assessed after discharge at 30 days, 6 and 12 months as well as at the completion of the study by hospital visits or phone interviews with the patient or their family member.

The main independent variable was method guided PCI, which was categorized as FFR- and angiography-guided PCI. Other independent variables included patient and periprocedural characteristics. Individual characteristics were age, sex, body mass index (kg/m²); current cigarette smoking; medical history (i.e., hypertension, diabetes mellitus, dyslipidemia, previous MI, prior PCI, cerebrovascular accident, peripheral arterial disease, atrial fibrillation); initial presentation (i.e., STEMI/NSTEMI, Killip class); LVEF (%); GRACE risk score (Fox et al., 2006),

risk of bleeding by PRECISE-DAPT score (Costa et al., 2017). Periprocedural details included PCI type, PCI approach (right femoral artery/ right radial artery), dominant coronary artery (right/left/co-dominant), stenosed artery ≥ 50% (2/3), location of culprit lesions and non-culprit lesions, TIMI risk score (Antman et al., 2000; Morrow et al., 2000), TIMI flow pre and post PCI; temporary pacemaker, thrombus aspiration, pre- and post-dilatation, and direct stenting. Other information including: stents characteristics [stents per patient, stent diameter (mm), stent length(mm)], volume of contrast, skin radiation (mGy).

Statistical analysis

The data were collected using paper forms and computerized using Microsoft Excel 2016 software. These data were statistically analyzed using SPSS version 20.0 software and R software version 4.2.3. We used numbers and percentages to present categorical variables, and mean and standard deviation (SD) to describe continuous variables. The Chi-squared test was used to calculate differences in the prevalence of variables between the FFR-guided or angiography-guided PCI group. Fisher's Exact Test was performed if the assumptions of the Chi-squared test were not satisfied. The t-test was used to compare means between the two groups with normal distribution variables. If the assumption of normal distribution was not satisfied, the Mann-Whitney test was used instead. Kaplan–Meier curves and Log Rank test were used to estimate the mean duration of patient living without outcomes after treatment by FFR-guided or Angio-guided PCI. All tests were two-sided, and a p-value <0.05 is considered as statistical significance.

RESULTS

Participants

From January 2020 to March 2022, a total of 667 AMI patients (434 STEMI patients and 233 NSTEMI patients) with MVD were treated with PCI at the Department of Interventional Cardiology, Gia Dinh People's Hospital in Ho Chi Minh City in Vietnam. The study population was divided into FFR-guided PCI group and angiography-guided PCI group. This study cohort included 93 patients, in which 31 (33.3%) patients underwent non-culprit PCI guided by FFR, while 62 patients underwent non-culprit PCI guided by angiography.

Baseline characteristics

There were no significant differences in baseline demographic and clinical characteristics between the groups, except for a higher smoking rate in the angio-

Table 1. Demography and baseline characteristics of study patients.

Variables	Total (n = 93)	FFR group (n = 31)	Angiography group (n = 62)	p-value
Characteristics				
Age, years (mean (SD))	63.2 (10.0)	64.4 (9.8)	62.6 (10.1)	0.411[a]
Male, n (%)	63 (67.7%)	19 (61.3%)	44 (71.0%)	0.347[b]
Body mass index, kg/m^2 (mean (SD))	23.05 (3.01)	22.44 (3.2)	23.4 (2.9)	0.169[a]
Current cigarette smoking	50 (53.8%)	11 (35.5%)	39 (62.9%)	0.012[b]
Medical history				
Hypertension	70 (75.3%)	24 (77.4%)	46 (74.2%)	0.734[b]
Diabetes mellitus	29 (31.2%)	10 (32.3%)	19 (30.6%)	0.874[b]
Dyslipidemia	68 (73.1%)	23 (74.2%)	45 (72.6%)	0.869[b]
Prior MI	3 (3.2%)	1 (3.2%)	2 (3.2%)	1.000[c]
Prior PCI	2 (2.2%)	1 (3.2%)	1 (1.6%)	1.000[c]
Cerebrovascular accident	4 (4.3%)	0 (0%)	4 (6.5%)	N/A
Peripheral arterial disease	1 (1.1%)	0 (0%)	1 (1.6%)	N/A
Atrial fibrillation	1 (1.1%)	0 (0%)	1 (1.6%)	N/A
Clinical and paraclinical features				
Initial presentation				
STEMI	56 (60.2%)	17 (54.8%)	39 (62.9%)	0.454[b]
NSTEMI	37 (39.8%)	14 (45.2%)	23 (37.1%)	
Killip class on admission				
I	90 (96.8%)	30 (96.8%)	60 (96.8%)	1.000[c]
II	3 (3.2%)	1 (3.2%)	2 (3.2%)	
LVEF, % (mean (SD))	51.9 (10.6)	51.7 (9.3)	51.9 (11.2)	0.912[a]
Creatinine (mean (SD))	88.7 (22.8)	84.6 (23.5)	90.7 (22.4)	0.159[d]
GRACE (mean (SD))	144.3 (26.1)	142.2 (30.3)	146.2 (23.8)	0.493[a]
PRECISE-DAPT score (mean (SD))	16.3 (9.6)	15.1 (7.1)	16.9 (10.6)	0.781[d]

[a] t-test, [b] Chi-square test, [c] Fisher's Exact Test, [d] Mann-Whitney test.

graphy group (Table 1). Details of treatment procedure for study participants are presented in Table 2. Patients in the FFR group received fewer stents and had shorter total stent length. The LAD was the most studied non-culprit lesion in the FFR group, with a significantly higher proportion of LAD lesions in the FFR group compared to the Angio-guided group. According to Table 3, among those with non-culprit lesions, the FFR-guided group had significantly fewer stents, shorter stent length, and lower doses of skin than the angiography-guided group. In those with culprit lesions, only the use of Volume of contrast was significantly lower in the angiography-guided group compared to the FFR-guided group.

Clinical study endpoints

All patients were followed for a mean duration of 22.66 ± 7.72 months (ranged from 12 to 36 months). The average follow-up time in the FFR group was 21.8 ± 8.3 months, and angiography group was 23.1 ± 7.5 months. During the follow-up period, there was 2 MACE (6.5%), 1 target lesion revascularization stroke (3.2%), 1 non-cardiac death (3.2%) in FFR group; and 5 MACE (8.1%), 1 stroke (1.6%), 1 myocardial infarction (MI) (1.6%), 1 stroke (1.6%), 3 death (4.8%) in angiography guided group (Table 4). There were no statistically significant differences in those clinical endpoints between the two groups (Table 4, Fig. 1).

Table 2. Periprocedural details among study participants.

Variables	Total (n = 93)	FFR group (n = 31)	Angiography group (n = 62)	p-value
PCI type				
Primary	56 (60.2%)	17 (54.8%)	39 (62.9%)	N/A
Delayed	34 (36.6%)	13 (41.9%)	21 (33.9%)	
Urgent	1 (1.1%)	0 (0%)	1 (1.6%)	
Early	2 (2.2%)	1 (3.2%)	1 (1.6%)	
TIMI risk score				
STEMI (n=56)	3.2 (1.4)	3.4 (1.5)	3.2 (1.3)	0.564[a]
NSTEMI (n=37)	3.1 (1.3)	3.1 (1.3)	3.0 (1.4)	0.817[a]
Time frame (STEMI) (min)				
Diagnostic – Wire*	79.1 (33.9)	88.5 (28.1)	75.3 (35.6)	0.204[b]
Door to balloon time**	101.1 (56.4)	103.7 (32.6)	100.1 (64.0)	0.203[a]
Culprit artery PCI				
Access site				
Right femoral artery	22 (23.7%)	7 (22.6%)	15 (24.2%)	0.863[c]
Right radial artery	71 (76.3%)	24 (77.4%)	47 (75.8%)	
Dominant coronary artery				
Right	88 (94.6%)	29 (93.5%)	59 (95.2%)	N/A
Left	3 (3.2%)	2 (6.5%)	1 (1.6%)	
Co-dominant	2 (2.2%)	0 (0%)	2 (3.2%)	
Number of stenosed arteries ≥ 50%				
2	39 (41.9%)	17 (54.8%)	22 (35.5%)	0.075[c]
3	54 (58.1%)	14 (45.2%)	40 (64.5%)	
Location of culprit lesions				
LAD	37 (39.8%)	10 (32.3%)	27 (43.5%)	0.575[c]
LCx	13 (14.0%)	5 (16.1%)	8 (12.9%)	
RCA	43 (46.2%)	16 (51.6%)	27 (43.5%)	
Location of non-culprit lesions				
LAD	48/115 (41.7%)	21/32 (65.6%)	27/83 (32.5%)	0.003[c]
LCx	37/115 (32.2%)	4/32 (12.5%)	23/83 (27.7%)	
RCA	30/115 (26.1%)	7/32 (21.9%)	33/83 (39.8%)	
TIMI flow before PCI (culprit lesions)				
0	40 (43.0%)	13 (41.9%)	27 (43.5%)	0.538[c]
I	8 (8.6%)	2 (6.5%)	6 (9.7%)	
II	20 (21.5%)	5 (16.1%)	15 (24.2%)	
III	25 (26.9%)	11 (35.5%)	14 (22.6%)	
TIMI flow after PCI (culprit lesions)				
II	2 (2.2%)	1 (3.2%)	1 (1.6%)	1.000c
III	91 (97.8%)	30 (96.8%)	61 (98.4%)	
Temporary Pacemaker	3 (3.2%)	0 (0%)	3 (4.8%)	N/A

Table 2. Periprocedural details among study participants (continued...)

Variables	Total (n = 93)	FFR group (n = 31)	Angiography group (n = 62)	p-value
Thrombus aspiration	31 (33.3%)	11 (35.5%)	20 (32.3%)	0.756[c]
Pre-dilatation	63 (67.7%)	18 (58.1%)	45 (72.6%)	0.158[c]
Direct stenting	21 (22.6%)	6 (19.4%)	15 (24.2%)	0.599[c]
Post-dilatation	89 (95.7%)	30 (96.8%)	59 (95.2%)	1.000[d]
TIMI flow (non-culprit lesions)				
Before PCI – TIMI III	79/79 (100.0%)	16/16 (100.0%)	63/63 (100.0%)	N/A
After PCI – TIMI III	79/79 (100.0%)	16/16 (100.0%)	63/63 (100.0%)	N/A

[a]Mann-Whitney test, [b]t-test, [c]Chi-square test, [d]Fisher's Exact Test; *n = 53, **n=52.

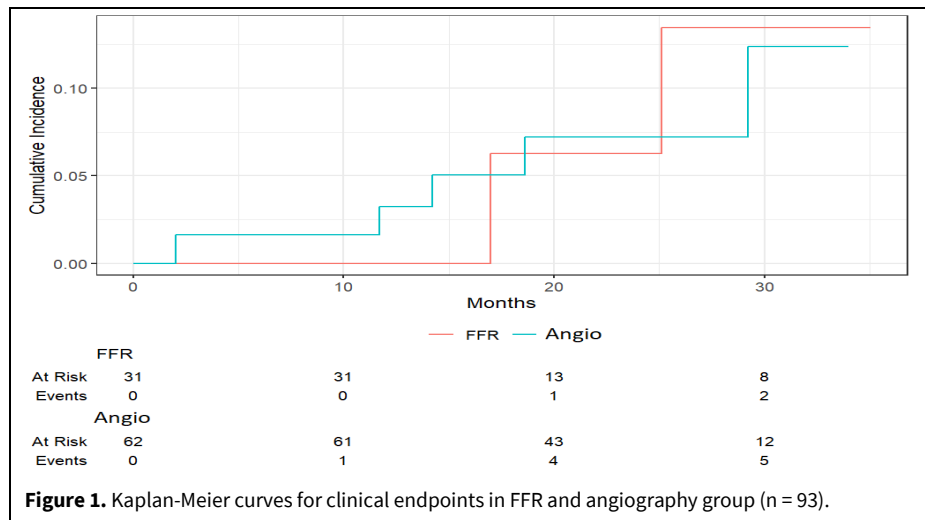**Table 3.** Outcomes of PCI procedure in culprit and non-culprit lesions.

Factors	Total			Culprit lesions			Non-culprit lesions		
	FFR (n = 31)	Angiography (n = 62)	p-value	FFR (n = 31)	Angiography (n = 62)	p-value	FFR (n = 31)	Angiography (n = 62)	p-value
Number of stents per patient	2.0 (1.1)	2.7 (0.8)	<0.001[a]	1.3 (0.5)	1.3 (0.5)	0.963[a]	0.7 (1.0)	1.3 (0.7)	<0.001[a]
Stent diameter (mm)	3.2 (0.4)	3.1 (0.4)	0.787[a]	3.3 (0.5)	3.2 (0.4)	0.592[a]	3.0 (0.4)*	3.0 (0.4)**	0.465[a]
Stent length(mm)	30.4 (6.6)	28.1 (5.3)	0.067[b]	31.2 (7.7)	29.2 (8.7)	0.221[a]	11.9 (14.1)	26.0 (9.1)	<0.001[b]
V contrast	309.0 (92.0)	292.1 (71.6)	0.246[a]	169.0 (38.2)	155.2 (36.8)	0.036[a]	121.5 (61.4)	136.1 (38.6)**	0.078[a]
Skin radiation - mGy	1583.2 (859.7)	1855.1 (1292.9)	0.259[a]	1914.7 (1173.8)	2067.6 (2117.4)	0.909[a]	1247.2 (1196.4)	1554.1 (854.1)	0.009[a]
Procedural success	47/47 (100%)	125/125 (100%)	N/A	31/31 (100.0%)	62/62 (100%)	N/A	16/16 (100%)	63/63 (85.7%)	N/A

[a]Mann-Whitney test, t-test; *n = 14, **n = 59.

Table 4. Clinical endpoints at follow-up.

Endpoints	Total (n = 93)	FFR group (n = 31)	Angiography group (n = 62)	p-value
Primary endpoint				
Major adverse cardiovascular events (MACE)	7 (7.5%)	2 (6.5%)	5 (8.1%)	1.000 [a]
Secondary outcome				
All-cause mortality	4 (4.3%)	1 (3.2%)	3 (4.8%)	1.000 [a]
Cardiac mortality	1 (1.1%)	0 (0%)	1 (1.6%)	N/A
Non-cardiac mortality	3 (3.2%)	1 (3.2%)	2 (3.2%)	N/A
Nonfatal Myocardial infarction	1 (1.1%)	0 (0%)	1 (1.6%)	N/A
Stroke	1 (1.1%)	0 (0%)	1 (1.6%)	N/A
Target lesion revascularization	1 (1.1%)	1 (3.2%)	0 (0%)	N/A

[a]Fisher's exact test.

Figure 1. Kaplan-Meier curves for clinical endpoints in FFR and angiography group (n = 93).

In the FFR group, the average amounts of adenosine administered for the left coronary artery were 165 ± 13.51 μg and 200 μg, respectively. The mean doses used for the right coronary artery were 60 μg and 94.29 ± 15.12 μg, respectively. The average amounts of adenosine administered during the initial and subsequent attempts within the FFR group were 141.29 ± 46.17 μg and 175.33 ± 45.99 μg, respectively. Adverse events observed in this patient group included third-degree atrioventricular block (25.8%), bradycardia (9.7%), sinus arrest (3.2%), and chest discomfort (3.2%).

DISCUSSION

This study found that using FFR to guide PCI for intermediate non-culprit vessels did not result in a significant difference in the risk of the composite primary outcome (death from any cause, nonfatal myocardial infarction, or target revascularization at 1 year) compared to using angiography. Individual factors also did not show statistically significant differences.

In patients with STEMI and MVD, complete revascularization has been shown to have better outcomes than performing PCI only on culprit lesions. The randomized trials PRAMI and CvLPRIT demonstrated that performing PCI to achieve complete revascularization under the guidance of coronary angiography results in better outcomes compared to only performing PCI on culprit coronary lesions (McCann et al., 2015; Wald et al., 2013). This difference came from the significantly fewer repeat revascularizations.

When applying FFR to guide interventions on non-culprit coronary lesions, randomized studies have also shown positive results. Complete revascularization of non-culprit lesions guided by FFR showed better outcomes compared to PCI only on

culprit lesions (Mehta et al., 2019). The COMPLETE trial demonstrated better outcomes in terms of reducing the risk of cardiovascular death or myocardial infarction, as well as the risk of cardiovascular death, myocardial infarction, or ischemia-driven revascularization, compared to the FFR-guided group (Mehta et al., 2019). Randomized trials DANAMI 3-PRIMULTI and COMPARE ACUTE showed significantly fewer repeat revascularizations (Engstrøm et al., 2015; Smits et al., 2017). Hence, patients can safely have all of their lesions treated during the index admission to prevent the need for subsequent revascularization. The study also contributes positive results towards the complete revascularization strategy on AMI patients with MVD, whether guided by angiography or FFR.

When comparing the effectiveness of complete revascularization guided by FFR and complete revascularization guided by angiography, the RCT study FLOWER-MI found inconclusive results when only looking at the group of STEMI patients (Puymirat et al., 2021). This finding is somewhat similar to the results of the present study. However, since the present study was conducted on both STEMI and NSTEMI patients, caution should be exercised in drawing conclusions. The present study indicated that it was inconclusive when comparing treatment outcomes between the two groups of STEMI patients who underwent complete revascularization guided by FFR and angiography.

When comparing treatment outcomes between two groups of patients with AMI, including both STEMI and NSTEMI, who underwent complete revascularization guided by FFR and angiography, the FRAME-AMI study shared many similarities in patient population with the present study, which included patients with AMI (STEMI and NSTEMI) (Lee et al., 2023). The FRAME-AMI trial demonstrated that FFR-guided PCI reduced the composite endpoint of

death, MI, or repeat revascularization at a median follow-up of 3.5 years compared to angiography-guided PCI for patients with AMI and MVD. This reduction was primarily driven by a significantly decreased risk of death and MI in the FFR-guided PCI group. The present study did not observe any differences in treatment outcomes between the two groups, which may be due to the small sample size and the follow-up time not being long enough compared to the FRAME-AMI study.

For non-culprit lesions, if the degree of stenosis is above 90%, it typically causes localized ischemia and may warrant direct PCI. For intermediate stenosis (50-90%) assessed by visual estimation, most lesions do not have functional stenosis. The severity of stenosis in non-culprit lesions may be overestimated during the acute phase, leading to unnecessary stent placement (Neumann et al., 2019). Unnecessary stent placement can result in procedural complications, such as stent thrombosis, restenosis within the stent, and may require repeat revascularization, increasing the risk of myocardial infarction and procedure-related mortality (Puymirat et al., 2021). Although the rate of stent thrombosis is not high, the higher number of stents used in the control group in the study may be associated with increased risk of stent thrombosis in the future (Reejhsinghani and Lotfi, 2015). Therefore, the decision to place a stent in cases of intermediate stenosis (50-90%) on angiography without functional stenosis needs to be carefully considered, taking into account all relevant clinical factors, based on available clinical evidence and treatment guidelines. Moreover, reducing the number of stents used can potentially decrease the overall cost for the patient (Pijls et al., 2010). Monitoring and evaluating outcomes after intervention are also crucial for making optimal treatment decisions for patients. While FFR may underestimate the severity of lesions in the infarct-related artery (IRA) of patients with STEMI, it has been deemed valuable in assessing the functional significance of non-culprit stenosis according to studies, and the efficacy of FFR in non-IRA remains relatively stable during both the index procedure and the follow-up phase (Ntalianis et al., 2010a).

The significantly lower number of stents used in the FFR-guided group compared to the angiography-guided group in the present study suggests the potential for reducing future cardiovascular events due to lower rates of restenosis and revascularization-related events. This finding was similar to the results of FLOWER-MI and FRAME-AMI trials (Lee et al., 2023; Puymirat et al., 2021).

There was a numerical reduction in the amount of contrast dye used between the FFR group and the control group. When performing FFR on non-culprit lesions, the skin radiation dose in the FFR group were significantly lower. When performing FFR, if the result is negative (FFR > 0.80), the patient may not need to undergo PCI. Compared to other cardiovascular imaging modalities, the additional radiation dose, procedural time, and contrast medium used to obtain FFR measurements are generally low (Ntalianis et al., 2010b). As a result, factors related to intervention procedure such as the amount of contrast agents and radiation exposure dose and time are reduced, which can lower the risks of renal impairment and skin ulcer in patients.

Limitations

While this study provides valuable insights, it is important to consider its limitations in evaluating the results. These limitations are as follows: Firstly, the sample size in this study was small, which may limit the ability to evaluate major cardiovascular events due to a low number of events. Therefore, it is important to carefully evaluate the results of the study and avoid drawing strong conclusions based solely on a small sample size. Secondly, this study was non-randomized, which may result in asymmetry in sample selection between treatment groups. Thirdly, this study was a single-center study, which may limit the generalizability of the results to other healthcare facilities or larger populations. Therefore, it is important to exercise caution when applying the results of this study to other situations and seek confirmation from larger studies or multicenter studies. Finally, this study was lack of medication data. Medication can be an important prognostic factor affecting patient outcomes, and incomplete information on medications may compromise the integrity and generalizability of the results. Furthermore, a low incidence of MACE might limit the overall interpretation of study's findings.

CONCLUSION

This study found no substantial differences in major adverse cardiovascular events between patients with acute myocardial infarction and multivessel coronary artery disease who underwent FFR-guided intervention and those who underwent angiography-guided intervention after one year of follow-up. However, this study may not have provided sufficient evidence to make a definitive statement. Since most non-culprit lesions are stable, future studies will require longer follow-up times and larger sample sizes to gain a more accurate understanding of the effectiveness of each treatment method.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Contribution	Chau DTS	Truong QB	Nguyen DA	Le MT	Nguyen DD	Hoang AT
Concepts or ideas	x	x	x	x	x	x
Design	x	x	x	x	x	x
Definition of intellectual content	x	x				x
Literature search	x					x
Clinical trial	x					x
Experimental studies						
Data acquisition	x			x	x	x
Data analysis	x					x
Statistical analysis	x					x
Manuscript preparation	x					x
Manuscript editing	x	x	x			x
Manuscript review	x	x	x	x	x	x