POLISH HEART JOURNAL

Kardiologia Polska
The Official Peer-reviewed Journal of the Polish Cardiac Society since 1957

Online first
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ISSN 0022–9032 e-ISSN 1897–4279

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Article type: Original article

Received: July 17, 2024

Accepted: October 1, 2024

Early publication date: October 9, 2024

Fractional flow reserve versus solely angiography-guided revascularisation in coronary artery disease. Systematic review and meta-analysis

Short title: FFR vs. angiography-guided revascularisation in CAD

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WHAT'S NEW?

This is the first meta-analysis of randomized controlled trials comparing head to head fractional flow reserve (FFR) and angiography-driven revascularisation in obstructive coronary artery disease, which showed the superiority of FFR guidance. The main finding of the present analysis was that functional assessment reduced significantly the rate of myocardial infarction. Moreover, this effect was achieved with a diminished frequency of revascularisation in the FFR arm.

ABSTRACT

Background: Subsequent randomized controlled trials (RCTs) comparing the clinical outcomes of fractional flow reserve (FFR)-guided and angiography-guided revascularisation in patients with coronary artery disease yielded inconsistent results.

Aims: This study aimed to assess head to head whether FFR-guided revascularisation reduces the rates of hard clinical endpoints in comparison with the angiography-guided approach alone.

Methods: This systematic review was conducted through June 2024 at Embase, Clinicaltrials.gov, Cochrane Library, and EBSCO. Only RCTs that evaluated stable and unstable coronary artery disease and acute myocardial infarction (MI) were included. Eight RCTs involving 4713 patients were included in the meta-analysis.

Results: FFR guidance was associated with a reduction of MI (risk ratio [RR], 0.75 [95% confidence interval [CI], 0.58–0.96]; *P* = 0.02) and lower rate of revascularisation (standardised mean difference — 0.12 [95% CI, –0.14 to 0.09]; *P* <00001). There were no differences between FFR-guided and angio-guided revascularisation in major adverse cardiovascular events (RR, 0.84 [95% CI, 0.69–1.02]; *P* = 0.08), all-cause mortality (RR, 1.00 [95% CI, 0.58–1.74]; *P* = 0.99), and unplanned revascularisation (RR, 0.89 [95% CI, 0.72–1.10]; *P* = 0.28).

Conclusions: FFR-driven revascularisation was associated with a significantly lower rate of MI for entire population and also in the acute coronary syndrome subset. These results were achieved with a substantially less revascularisations compared with solely angiographic guidance.

Key words: angiography, coronary artery disease; fractional flow reserve, percutaneous coronary intervention

INTRODUCTION

Over the past decade, landmark clinical randomized trials have demonstrated the superiority of fractional flow reserve (FFR)-guided revascularisation in the reduction of hard endpoints in comparison with angiography alone [1, 2]. Consequently, functional evaluation with the use of FFR received the highest-level recommendation in the American Heart Association and European Society of Cardiology (ESC) guidelines of revascularization, class IA [3–5]. Recent ESC guidelines covering all types of acute coronary syndrome (ACS) lowered recommendation for FFR use in the ST-segment elevation myocardial infraction (STEMI) to class III [6]. Additionally, subsequent randomized controlled trials (RCTs) evaluating the clinical utility of FFR in various settings have shown inconsistent results, challenging previous reports [7, 8].

Hence, we decided to conduct a meta-analysis of RCTs comparing head to head these two techniques, focusing on endpoints such as death, nonfatal myocardial infarction (MI), and repeat revascularisation and a composite of its components in patients with obstructive coronary artery disease (CAD).

METHODS

We conducted a literature review with a meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [9]. The study design was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the number CRD42023402326. The manuscript does not contain clinical studies or patient data.

Data sources and search strategy

Two independent reviewers (MB and SU) searched the following online databases: EBSCO (including Academic Search Ultimate, ERIC, Health Source Nursing/Academic Edition, and MEDLINE), Embase, Clinicaltrials.gov, and Cochrane Library (trials) for articles published until 15 June 2024. We considered records with no restrictions on the publication date. We used the following keywords separately and in combination to identify relevant records: (fractional flow reserve) OR (fraction flow reserve) OR (FFR) OR (physiology guide*) OR (physiology assess*) OR (physiology revasc*) OR (physiology test*) OR (functional guide*) OR (functional assess*) OR (functional revasc*) OR (functional test*) OR (invasiv* assess*) OR (invasiv* guide*) OR (invasiv* test*) OR (pressure wire) OR (hyperemic pressure ratio*) AND coronary OR (coronary artery disease) OR CAD OR angiography OR (percutaneous coronary intervention*) OR PCI OR angioplasty OR stent* OR (percutaneous transluminal coronary angioplasty) OR PTCA OR revascularisation* OR (myocardial reperfusion) OR bypass OR CABG OR (coronary artery bypass surgery) OR (coronary bypass surgery) OR (surgical revasc) OR (myocardial bridg*) OR STEMI OR (ST segment elevation) OR NSTEMI OR (non-ST segment elevation) OR (myocardial infarction) OR ACS OR (acute coronary syndrom*) OR multivessel OR multi-vessel OR three-vessel OR (triple vessel) and NOT comput* OR tomogra* OR CT. Only articles that were completed, terminated, or with results were considered. Disagreements between the two investigators during the screening process were resolved through discussion with a third reviewer (WK). For completeness, further screening by two reviewers (KF and AJ) of the references of the included records and studies which cited them was performed for the relevant publications.

Outcomes

The primary endpoints of the study were major adverse cardiovascular events (MACE) and the individual components of the composite endpoint, including all-cause mortality, nonfatal MI, and unplanned revascularization.

Eligibility criteria

Inclusion criteria were as follows: 1) RCTs comparing clinical outcomes with FFR-guided and angiography-guided myocardial revascularisation, 2) the population with obstructive CAD presented with either ACS, stable CAD or unstable angina, 3) reporting of at least one of the endpoints of interest: MACE, a composite of all-cause or cardiovascular mortality, MI, repeat revascularization, and the single components of the aforementioned endpoints, 4) hyperemic FFR as an assessment method, 5) age of patients >18, and 6) full-text articles published in English. The following publications were excluded: 1) studies evaluating FFR-guided PCI with optimal medical treatment, 2) studies comparing FFR guided revascularisation of non-culprit lesion with PCI of culprit lesion exclusively in ACS, 3) studies using physiological assessments different from FFR, 4) studies in which PCI was performed using only bare-metal stents, 5) non-randomized studies of intervention, 6) animal model studies, 7) case reports, 8) non-original studies (e.g. reviews, editorials, and commentaries), and 9) conference abstracts.

Data collection and analysis

The extracted data included: 1) year of publication, 2) size of the FFR and angiography groups, 3) enrolment criteria, 4) MACE definition, 5) length of follow-up, 6) baseline and demographic characteristics, 7) number of performed treatment strategies PCI/coronary artery bypass graft (CABG)/ optimal medical treatment, 8) proportion of used drug-eluting stents, 9) used FFR cut-off, 10) angiography percentage stenosis threshold for revascularisation, and 11) number of events for each endpoint.

Statistical analysis

Analyses were performed using a random-effects models with the Mantel-Haenszel method. The risk ratios and 95% confidence intervals (CI) were calculated for each outcome. The I^2 statistic was used to measure the heterogeneity. Heterogeneity was considered as moderate when I^2 ranged between 50% and 75% and high when I^2 was more than 75% [10]. For statistical analysis, we used Review Manager version 5.4.1 (The Cochrane Collaboration, 11–13

Cavendish Square, London, W1G 0AN, United Kingdom). The results were considered statistically significant when the *P*-value was less than 0.05.

Subgroup and sensitivity analysis

The differences in outcomes between the assessed approaches were tested by subgroup analysis. This analysis was conducted for both ACS and stable CAD subgroups. Data were sourced from clinical trials that either exclusively enrolled ACS or stable CAD patients or were derived from heterogeneous cohorts following appropriate stratification. A leave-one-out sensitivity analysis was performed to assess whether a single trial accounted for the heterogeneity.

Risk of bias assessment

The risk of bias (ROB) was assessed using the Cochrane-designed tool ROB 2, dedicated to randomized clinical trials [11]. Two independent reviewers (MG and OS) carried out a quality evaluation, and all discrepancies were resolved through discussion.

Grading the quality of evidence

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to assess the overall quality of the acquired evidence [12]. GradePRO GDT (McMaster University and Evidence Prime Inc.) was used to build a Certainty of Evidence table and Summary of Findings.

RESULTS

The initial online screening identified 11 571 records, eight of which met the inclusion criteria. The trial selection process is illustrated in Figure 1. Altogether, these studies presented data from 4713 patients, 2361 in the FFR group and 2352 in the angiography group. In the meta-analysis we decided to incorporate FAME trial with 2 years follow-up because of the presence of sub-analysis specific to ACS setting [2]. The predominant revascularisation strategy was treatment with the use of PCI exclusively in five studies, and both PCI and CABG in three studies. The dominant definitions of the composite end points were all-cause death, myocardial revascularisation, and unplanned revascularisation. The differences in the MACE components are described in Table 1. The mean follow-up period was 13.3 months. In seven trials, FFR cut-off ≤0.80 was used to detect the hemodynamic significance of the lesions, except one study, where a cut-off ≤0.75 was applied [13]. To perform the subgroup analysis, we requested the

corresponding authors to share data on the proportion of ACS and stable CAD in the investigated cohorts. The general characteristics of the included trials are listed in Table 2.

MACE

The composite endpoints were reported in 308 participants (13%) in the FFR group and in 368 participants (15.6%) in the angiography group. There was no difference in the trial-defined MACE (RR, 0.84 [95% CI, 0.69–1.02], *P* = 0.08) (Figure 2). The sensitivity analysis excluding the RIPCORD 2 trial showed a reduction in MACE for FFR-guided revascularisation (RR 0.80; 95% CI, 0.65–0.98; *P* = 0.04) (Supplementary material, *Figure S3*). In the subgroup analysis, the effects remained neutral for the stable CAD population (RR, 1.17 [95% CI, 0.46–2.98]; *P* = 0.74) (Supplementary material, *Figure S3*), but reduction was found in FFR arm in ACS subset (RR, 0.71 [95% CI, 0.55–0.92]; *P* = 0.01) (Supplementary material, *Figures S1* and *S2*). The sensitivity analysis excluding the FUTURE trial demonstrated a difference in favour of the FFR arm in the ACS group (RR 0.68; 95% CI, 0.50–0.92; *P* = 0.01).

All-cause mortality

Deaths occurred in 60 (2.6%) of the FFR group and in 63 (2.8%) of the angiography group. There was no difference in all-cause mortality between FFR-guided and angiography-guided revascularisation (RR, 1.00 [95% CI, 0.58–1.74]; *P* = 0.99). The effects remained neutral for stable CAD subgroup (RR, 0.72 [95% CI, 0.30–1.73]; *P* = 0.47) and for ACS subgroup (RR, 0.64 [95% CI, 0.37–1.08]; *P* = 0.10).

Myocardial infarction

The occurrence of MI was observed in 123 participants (5.4%) in the FFR-driven group and in 165 participants (7.4%) in the angiography-driven group. There was a reduction in MI for FFR-guided revascularization (RR, 0.75 [95% CI, 0.58–0.96]; *P* = 0.02). The effects remained for ACS subgroup (RR, 0.57 [95% CI, 0.41–0.81]; *P*= 0.002, but showed to be insignificant for stable CAD subgroup (RR, 1.04 [95% CI, 0.35–3.11]; *P* = 0.94).

Unplanned revascularisation

Unplanned revascularisation occurred in 155 participants (7.4%) of the FFR group and in 173 participants (8.3%) of the angiography group. There was also no difference between the FFR group and the angiography group in the rate of unplanned revascularisations (RR, 0.89 [95% CI, 0.72–1.10]; *P* = 0.28). The effects remained neutral for ACS subgroup (RR, 0.76 [95% CI,

0.55–1.05]; *P* = 0.01) and for stable CAD subgroup (RR, 0.81 [95% CI, 0.53–1.25]; *P* = 0.34). In ACS subset a sensitivity analyses demonstrated that the reduction of unplanned revascularisation in FFR arm reached statistical significance after removing the DK-CRUSH VI trial (RR, 0.76 [95% CI, 0.59–0.98]; *P* = 0.04).

Planned revascularisation during the index procedure

The number of performed revascularisations during the index procedures were accordingly 1214 (65.5%) in the FFR group and 1431 (77.1%) in the angiography group resulting in a lower rate of revascularisation in the FFR arm (standardised mean difference — 0.12, [95% CI, –0.14 to –0.09]; *P* <0.0001). The effects achieved almost statistical significance for the ACS subgroup analysis (standardised mean difference, –0.17 (95% CI, –0.34 to 0.00]; *P* = 0.05).

ROB and certainty of the evidence

The results of the ROB assessment are shown in Figure 3. The quality of evidence in RCTs was low for three endpoints and moderate for two endpoints. (Supplementary material, *Table S1*).

DISCUSSION

To our knowledge, this is the first meta-analysis of RCTs comparing head to head FFR- and angiography-driven revascularisation in obstructive CAD, which showed the superiority of FFR guidance. The main finding of the present analysis was that functional assessment reduced significantly the rate of MI. Moreover, this effect was achieved with a diminished frequency of revascularisation in the FFR arm. In comparison with other meta-analysis trials selection was performed according to the latest ESC guidelines, which do not recommend the application of physiology evaluation in multivessel disease (MVD) in STEMI [6, 14, 15]. The current guidelines recommend complete revascularisation for non-infarct related arteries based on angiographic severity in this setting. In line with this directive, we decided to exclude from the meta-analysis FLOWER MI trial, where functional measurements were conducted among STEMI patients exclusively [16].

A novel finding of our meta-analysis is that functional guidance can significantly reduce the number of MI for the entire population and also in the ACS subset. This outcome can likely be attributed to the capability of physiology evaluation to accurately detect the lesions, which are responsible for reversible ischemia and thereby enabling more tailored decisions to treat or not invasively. Notably, a lower rate of PCI in FFR arm contributes to the reduced risk of potential complications such as stent thrombosis, in-stent restenosis and PCI-related MI, as

convincingly showed results from FRAME-AMI trial [8]. In this study the FFR arm encountered three PCI-related MI and 11 in the angiography arm (HR 0.26 [CI, 0.07–0.94]; *P* = 0.04). It is worth noting, that complete PCI in ACS at the time of MI may lead to an underestimation of PCI-related MI due to the overlapping release of troponin from the culprit lesion and PCI-related myocardial damage. Furthermore, a sub-analysis of the FRAME-AMI trial demonstrated that FFR-driven PCI would be more cost-effective compared to the angiography-guided approach [17].

The main uncertainty of FFR use at the time of MI is that functional assessments in areas of infarction or ischemia can be unreliable due to the impossibility of achieving sufficient hyperemia. One potential mechanism is microvascular dysfunction, which can lead to false-negative FFR values. What is more, microvascular contraction can occurs also in the territory of non-culprit lesion [18]. Previously, several studies showed that complete revascularization based on angiography guidance in STEMI improves the outcomes in comparison with culprit only PCI [19–20]. Further trials demonstrated the superiority of FFR-guided complete revascularization in ACS patients with MVD [21, 22]. However, subsequent meta-analysis demonstrated that complete revascularisation among patients with STEMI and MVD is superior to culprit-only PCI when the decision for PCI is based solely on angiographic severity, rather than on FFR assessment [23]. In consequence current ESC guidelines provide robust recommendations for PCI in STEMI with MVD, advocating complete revascularisation based on angiographic assessment in class IB. Conversely, recommendations for NSTEMI patients are less solid. The debatable issue remains the optimal timing for complete PCI in MVD as well as the best guidance tool for intermediate lesions [24]. The results from observational data suggest that complete revascularisation in NSTEMI and MVD can be also superior to culprit-only PCI [25]. In FAMOUS-NSTEMI trial, a greater proportion of patients in the FFR arm had deferred PCI compared to the angiography group and it achieved almost statistical significance (71.0% in FFR group and 79.9% in angiography group; *P* = 0.057). Our hypothesis posits that delaying physiologic assessments in NSTEMI until the staged procedure would result in fewer PCIs without the risk of false-negative FFR results, while achieving equivalent or even superior clinical outcomes. Further studies are required to assess the period necessary for recovery of the vasodilatory capacity of the coronary circulation to conduct a reliable physiological evaluation.

There was a trend toward decreased rate of MACE in the FFR group compared to the angiography group (308 vs. 368 events, respectively) and this analysis reached almost statistical significance (*P* = 0.08). The sensitivity analysis demonstrated that after exclusion on the

RIPCORD 2 trial, FFR guidance decreased the incidence of MACE (RR, 0.80, 95% CI, 0.65–0.98; *P* = 0.04) [7]. This study aimed to assess whether systematic FFR measurement can improve outcomes. In fact, functional assessments were conducted in all vessels suitable for revascularisation with at least 1 stenosis of ≥30% in visual assessment. In consequence, the administration of FFR in this manner can be a bias in the interpretation of the findings. Moreover, this result underscores another issue in RCTs evaluating the utility of FFR: the heterogeneity of the population. This includes different types of ACS alongside stable CAD and the application of FFR in various context, leading to challenges in interpreting the results. We demonstrated this effect in the subgroup analysis, which focused exclusively on patients with ACS. In this cohort, FFR group exhibited a reduction in MACE (RR, 0.71 [95% CI, 0.55–0.92]; *P* = 0.01). The results of the subgroup analysis for stable CAD is questionable due to the limited available data, our findings are driven mainly by the outcomes from FAME trial.

Despite the data supporting FFR utilization for guiding revascularization the adoption of this technique in clinical practice remains relatively low [26]. This can be attributed to several factors, including longer procedural time, additional costs and reimbursement problems. A recent study showed that FFR adoption slowly raised between 2009 and 2017 from 14.8% to 18.5% in CAD with intermediate lesions and from 44% to 75% among patients who underwent PCI [27]. In the context ACS, physiological assessments can be particularly valuable in NSTEMI patients for identifying the culprit lesion, especially when coronary angiography images are inconclusive or ambiguous. Alternatively, a novel angiography-derived index calculating FFR values without the need for pressure wires and hyperemic agents could overcome these barriers. However, its diagnostic accuracy still requires improvements [28–31].

Limitations

This meta-analysis had several limitations. First, the definition of MACE differed among the studies. Most RCTs used composite endpoints consisting of all-cause death, MI, and unplanned revascularisation, although the inclusion of stroke varied. Second, there were differences in the durations of follow-ups and clinical heterogeneity of the study participants across the RCTs. Third, this was not a patient-level meta-analysis, and we were unable to extract cohorts treated with a uniform method (either PCI or CABG). However, since the majority of the trials utilized PCI exclusively for revascularization, we decided to exclude the FARGO and GRAFFITI trials, where CABG was employed exclusively [32, 33]. For similar reasons, we were unable to exclude patients with STEMI in the FRAME-AMI trial. Nevertheless, the majority of the study

population, exceeding 50%, consisted of patients with NSTEMI and sensitivity analysis indicated that this trial did not impact the outcomes.

CONCLUSIONS

The adoption of FFR in myocardial revascularisation among patients with CAD has been associated with significant reduction of MI across the entire study population and also in ACS subset. Moreover, these results were achieved with a significantly lower rate of revascularisation compared with solely angiographic guidance. Functional assessment can accurately identifies epicardial stenosis that is hemodynamically significant and requires revascularisation. These results are likely attributable to the occurrence of PCI-related events and necessary stenting in the angiography arm. We believe that the results of our meta-analysis including the potential for improvement of outcomes will encourage interventional cardiologists to more routinely integrate functional assessments in catheterization laboratories. Additional RCTs are necessary to elucidate the best timing and assessment tool to perform multivessel PCI in the NSTEMI setting.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/polish_heart_journal.

Article information

Conflict of interest: None declared.

Funding: This work was supported by the subsidy no. SUBZ.A460.24.040 for the Institute of Heart Diseases, Wroclaw Medical University, Poland.

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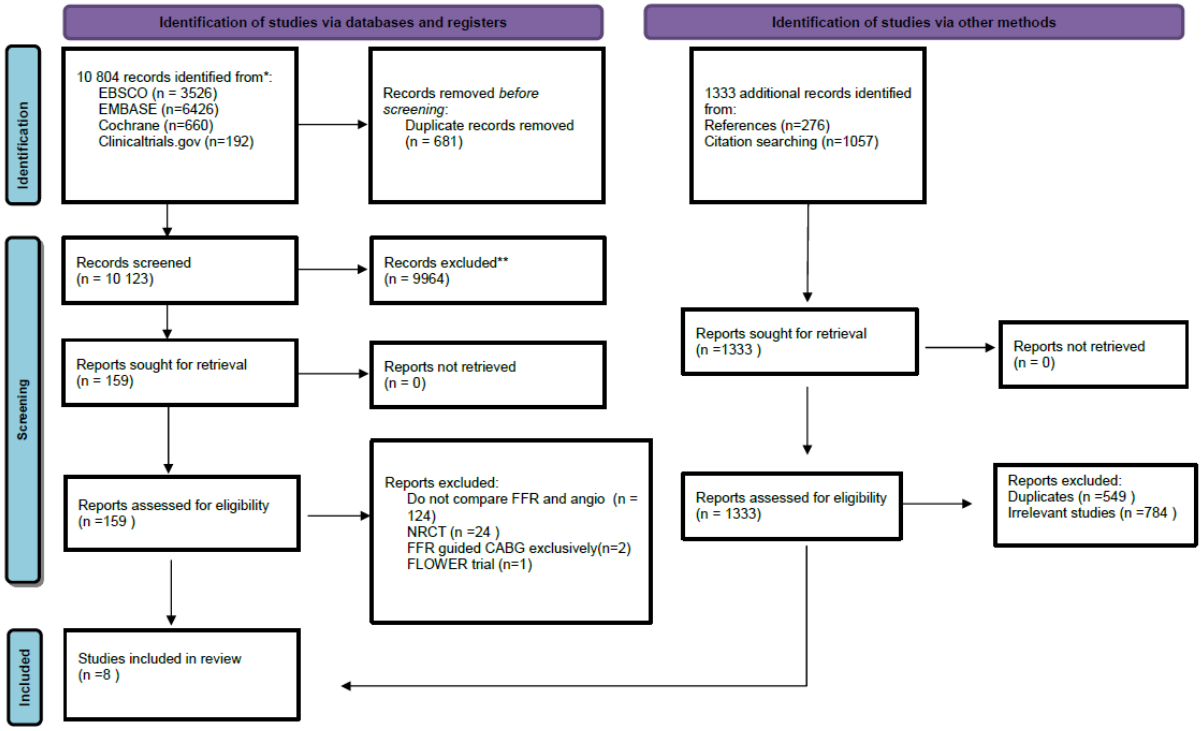

Figure 1 Flowchart of the systematic review process

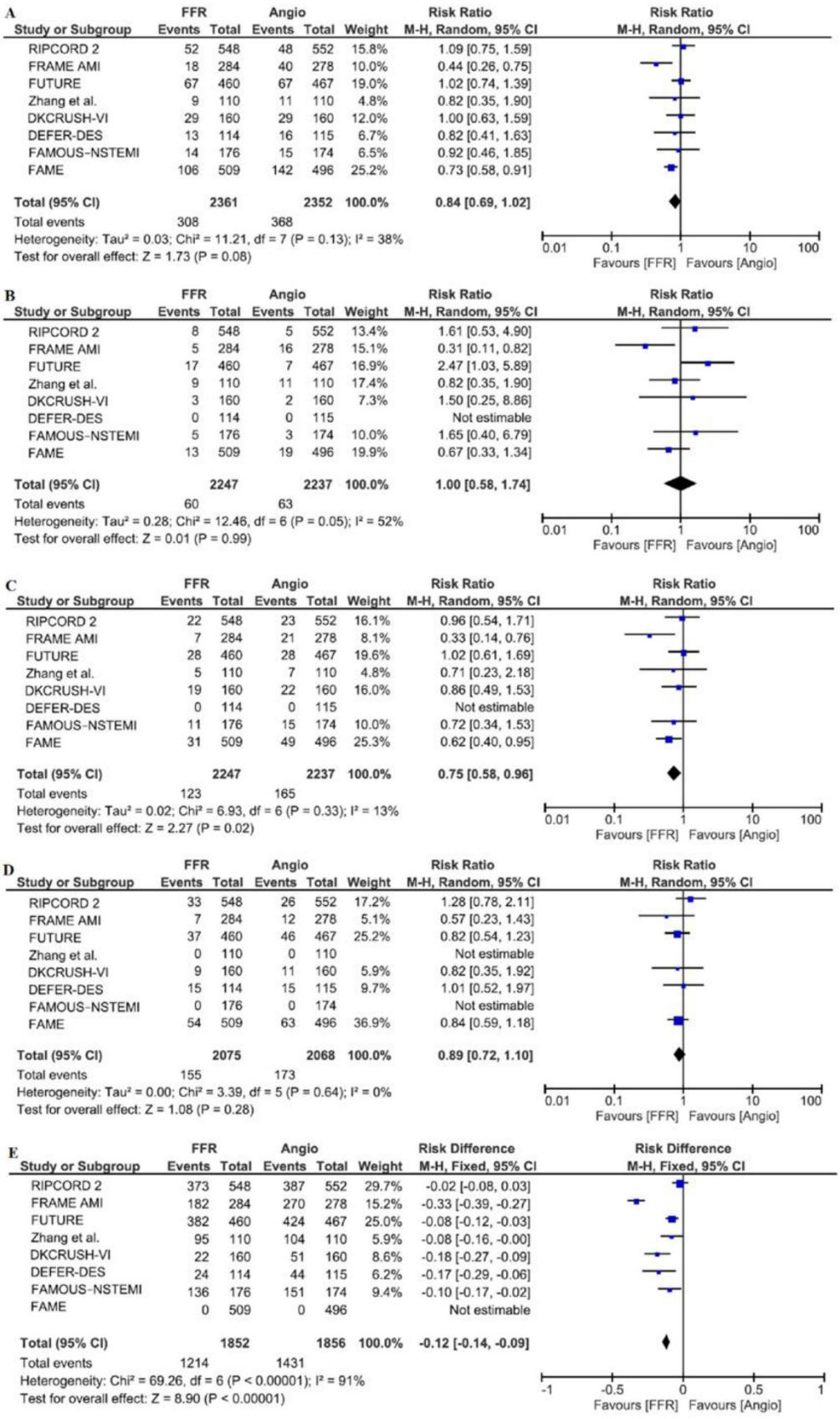

Figure 2 Forest plots of **A.** MACE. **B.** All-cause mortality. **C.** MI. **D.** Unplanned revascularization. **E.** Planned revascularization during index procedure (by PCI + CABG).

Forrest plots of the subgroup analysis and sensitivity analysis are available in Supplementary material

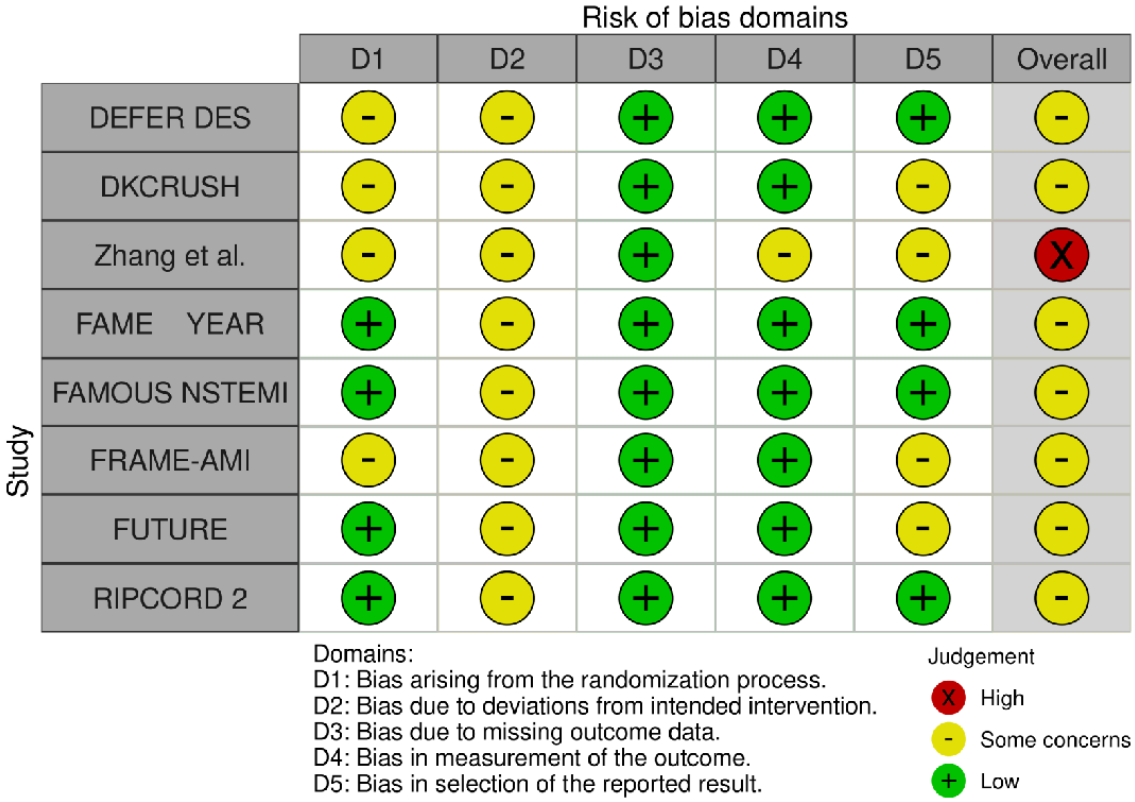

Figure 3 Risk of bias (ROB) of the included studies

Table 1. Characteristics of included RCTs

Study	Year	Angio group	FFR group	Enrolment criteria	MACE definition	Follow-up	Main findings
RIPCORD 2	2022	552	548	Stable angina or NSTEMI	All-cause mortality, stroke, MI and unplanned revascularization	1 year	No difference in MACE between FFR group and Angio group (9.5% vs. 8.7%; *P* = 0.064).
FRAME-AMI	2022	278	284	STEMI or NSTEMI	Death, MI, or unplanned revascularisation	3.5 years	Lower composite rates of MACE were observed in FFR group in comparison to the Angio group (7.4% vs. 19.7%; *P* = 0.003).
FUTURE	2021	467	460	ACS or stable angina or silent ischemia or atypical chest pain	Death from any cause, nonfatal MI, stroke, unplanned revascularization	1 year	No difference in MACE between FFR group and Angio group (14.6% vs. 14.4%; *P* = 0.85).
Zhang et al.	2016	110	110	NSTEMI	Cardiovascular death, nonfatal MI, or unplanned hospitalization for heart failure	1 year	No difference in MACE and MACCE between FFR guided group angiography-guided group — MACE (8.2% vs. 10%; *P* = 0.639), MACCE (9.1% vs. 11.8%; *P* = 0.509)
DKCRUSH-VI	2015	160	160	Stable or unstable angina	Cardiac death, MI, or ischemia-driven target vessel revascularization	1 year	No differences between FFR group and Angio group according to: MACE (18.1% in both groups; *P* = 1.00)

DEFER-DES	2015	115	114	Stable angina and ACS	Cardiac death, MI, and target lesion revascularization	5 year	No difference in MACE rates between FFR group and Angio group (11.6 ± 3.0% vs. 14.2 ± 3.3%; *P* = 0.55)
FAMOUS –NSTEMI	2015	174	176	NSTEMI	Cardiac death, hospitalization for MI or heart failure	1 year	No difference in MACE between FFR and Angio group (8% vs. 8.6%; *P* = 0.89)
FAME	2009	496	509	Stable, unstable angina and NSTEMI	Death, myocardial infarction, and repeat revascularization	2 year	No difference in MACE between FFR and Angio group (22.4% in angio group and 17.9% in FFR group, *P* = 0.08)

Abbreviations: ACS, acute coronary syndrome; angio, angiography; CABG, coronary-artery bypass grafting; FFR, fractional flow reserve; MACCE, major adverse cardiac and cerebral event; MACE, major adverse cardiac events; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction

Table 2. Patient and procedural characteristics from included RCTs

Study	Strategy	Age, mean ± SD, or median (IQR)	Male, %	Diabetes mellitus, %	Tabacco user, %	LVEF, mean ± SD	ACS, %	Left main disease, %	Three vessel disease, %	Heart failure, %	Proportion of PCI, %	Proportion of CABG, %	Second generation DES, %	FFR cut-off	Angiography stenosis thresholds for PCI/CABG

RIPCORD 2	Angio group	64.3 ± 10.2	77.2	17.6	65.0	N/A	53.1	8.7	6.5	23.4	60.9	9.2	N/A	≤0.8	≥30
	FFR group	64.3 ± 10.0	73.5	20.6	58.5	N/A	50.4	7.8	11.3	21.4	56.2	11.9	N/A		
FRAME–AMI	Angio group	62.7 ± 11.5	84.2	30.9	37.8	53.6 ± 10.2	100	N/A	32.4	N/A	100	0	94.8	≤0.8	≥50
	FFR group	63.9 ± 11.4	84.5	34.2	32.0	53.2 ± 9.8	100	N/A	44.7	N/A	100	0	97.3		
FUTURE	Angio group	66 ± 11	82.0	32.0	26.0	56 ± 11	45.61	11	50	N/A	79	12	94	≤0.80	≥50
	FFR group	65 ± 10	85.0	31.0	24.0	55 ± 12	46.96	13	54	N/A	71	12	95		
Zhang et al.	Angio group	70 ± 3.4	70.9	32.7	28.2	N/A	100	N/A	N/A	1.0	100	0	N/A	≤0.8	≥70 [≥50 for left main]
	FFR group	70 ± 3.7	68.2	36.4	26.4	N/A	100	N/A	N/A	2.0	100	0	N/A		
DKCRUSH-VI	Angio group	65.4 ± 9.2	72.5	26.9	40.0	60.6 ± 8.7	77.5	8.8	36.3	N/A	100	0	100	≤0.8	≥70
	FFR group	65.2 ± 9.6	75.6	30.0	41.3	61.3 ± 7.4	79.4	9.4	39.6	N/A	100	0	100		
DEFER-	Angio	63 ±	75.0	34.0	33.0	61 ± 9	48	0	23	N/A	100	0	100	≤0.75	40–70

DES	group	10													
	FFR group	62 ± 10	73.0	26.0	26.0	62 ± 9	51	0	20	N/A	100	0	100		
FAMOUS–NSTEMI	Angio group	61.6 ± 11.1	73.0	14.9	40.8	N/A	100	3.4	7.5	N/A	79.9	6.9	N/A	≤0.8	≥30
	FFR group	62.3 ± 11	75.6	14.8	40.9	N/A	100	1.1	6.8	N/A	71	6.2	N/A		
FAME	Angio group	64.2 ± 10.2	72.6	25.2	31.5	57.1 ± 12.0	35.89	0	N/A	N/A	100	0	100	≤0.8	≥50
	FFR group	64.6 ± 10.3	75.4	24.2	27.1	57.2 ± 11.0	29.47	0	N/A	N/A	100	0	100		

Abbreviations: DES, drug-eluting stent; LVEF, left ventricular ejection fraction; N/A, not applicable; other — see Table 1