Russian Journal of Cardiology 2023;28(S1):5325
doi:10.15829/1560-4071-2023-5325
https://russjcardiol.elpub.ru

ISSN 1560-4071 (print)
ISSN 2618-7620 (online)
ISSN 2782-2257 (online)

Impact of assessment of fractional flow reserve and instantaneous wave-free ratio on clinical outcomes of percutaneous coronary intervention: a systematic review, meta-analysis and meta-regression analysis

Golukhova E. Z., Petrosyan K. V., Abrosimov A. V., Bulaeva N. I., Goncharova E. S., Berdibekov B. Sh.

Aim. To conduct a systematic review and meta-analysis to compare clinical outcomes in patients with coronary artery disease (CAD) undergoing percutaneous coronary intervention (PCI) using conventional coronary angiography (CAG) or fractional flow reserve (FFR)-guided PCI. In addition, FFR-guided PCI and PCI guided with instantaneous wave-free ratio (iFR) were compared.

Material and methods. PubMed, Google Scholar databases were searched for studies comparing clinical outcomes in patients with CAD undergoing CAG-guided or FFR/iFR-guided PCI. Dichotomous data analysis was presented as odds ratio (OR) with 95% confidence interval (CI). Adjusted hazard ratio (HR) values from studies with similar evaluation criteria were pooled for meta-analysis.

Results. Six randomized controlled trials (RCTs) from 184 publications were selected for this systematic review and meta-analysis. A total of 2193 patients (mean age, 64,2 years, mean follow-up, 28,0 months) were included. Analysis of RCTs showed that CAG-guided and FFR-guided PCI did not have a significant difference in the incidence of major adverse cardiovascular events (MACE) (OR: 0,78; 95% CI: 0,61-1,00; p=0,05; I^2=0%), all-cause death (OR: 0,86; 95% CI: 0,51-1,44; p=0,57; I^2=0%) or emergency revascularization (OR: 0,69, 95% CI: 0,46-1,04, p=0,08, I^2=0%). However, FFR-guided PCI was associated with a reduced risk of subsequent MI compared with CAG-guided PCI (OR: 0,70; 95% CI: 0,50-0,99; p=0,04; I^2=0%). In addition to the results of previous RCTs, we conducted a meta-analysis of 3 observational studies. In total, the CAG-guided and FFR-guided PCI groups included 165012 and 11450 patients, respectively. A meta-analysis showed that FFR-guided PCI was associated with a reduced risk of all-cause mortality (HR: 0,74; 95% CI: 0,63-0,87; P=0,0003) and MI (HR: 0,75; 95% CI: 0,61-0,94; p=0,01). In addition, there was no significant difference between iFR- and FFR-guided PCI in terms of MACE (OR: 0,97; 95% CI: 0,76-1,23; p=0,81), all-cause mortality (OR: 0,66; 95% CI: 0,40-1,10; p=0,11), MI (OR: 0,83; 95% CI: 0,56-1,24; p=0,37) or emergency repeated revascularization (OR: 1,16; 95% CI: 0,85-1,58; p=0,34).

Conclusion. FFR-guided PCI is associated with a reduced risk of all-cause mortality and subsequent MI compared with CAG-guided PCI. At the same time, the iFR-guided PCI is not inferior to the FFR-guided method in terms of MACE rate.

Keywords: percutaneous coronary intervention, coronary angiography, fractional flow reserve, instantaneous wave-free ratio.

Relationships and Activities: none.

A. N. Bakulev National Medical Research Center for Cardiovascular Surgery, Moscow, Russia.

Golukhova E. Z. ORCID: 0000-0002-6252-0322, Petrosyan K. V. ORCID: 0000-0002-3370-0295, Abrosimov A. V. ORCID: 0000-0001-5907-9508, Bulaeva N. I. ORCID: 0000-0002-5091-0518, Goncharova E. S. ORCID: 0000-0003-0038-5193, Berdibekov B. Sh.* ORCID: 0000-0001-7717-4971.

*Corresponding author:
b.berdibekov@yahoo.com

Received: 31.12.2022
Revision Received: 06.02.2023
Accepted: 14.02.2023

For citation: Golukhova E. Z., Petrosyan K. V., Abrosimov A. V., Bulaeva N. I., Goncharova E. S., Berdibekov B. Sh. Impact of assessment of fractional flow reserve and instantaneous wave-free ratio on clinical outcomes of percutaneous coronary intervention: a systematic review, meta-analysis and meta-regression analysis. *Russian Journal of Cardiology*. 2023;28(1S):5325. doi:10.15829/1560-4071-2023-5325. EDN HUTOUV

Key messages

- Fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI) versus angiography-guided PCI is associated with a reduced risk of all-cause mortality and myocardial infarction.
- PCI guided with instantaneous wave-free ratio is not inferior to FFR-guided method in terms of the rate of major adverse cardiovascular events.

Fractional flow reserve (FFR) is currently the gold standard for determining the functional significance of borderline coronary artery (CA) stenosis [1]. At the moment, the FFR ⩽0,8 is defined as a cut-off point of the hemodynamic significance of narrowing and is reflected in current guidelines for myocardial revascularization [2, 3]. However, as shown in studies, there is a frequent discrepancy between the angiographic and hemodynamic severity of coronary stenoses. Thus, according to the FAME randomized controlled trial (RCT), only 35% of stenoses of 50-70% (visual estimation) were hemodynamically significant [4]. In the visual assessment subgroup, ~20% of stenosis cases of 71-90% was not significant. Only in the case of a visual assessment of stenosis as >90%, sufficient agreement was achieved with hemodynamic severity (~96%). According to study results, myocardial revascularization by FFR-guided percutaneous coronary intervention (PCI) in addition to angiography, compared with visual assessment of CA narrowing, significantly reduced the composite endpoint rate, which included death, non-fatal myocardial infarction (MI), and repeated revascularization within 1-year follow-up. However, no significant differences were found for individual components of the primary endpoint in the form of mortality, non-fatal MI, and repeated myocardial revascularization [4]. In addition, in most subsequent small RCTs and a few observational studies, the strategy of FFR-guided PCI in addition to angiography has not demonstrated a prognosis advantage over visual assessment by coronary angiography (CAG). Notably, most of these studies had single center design with small sample sizes and few events.

Istantaneous wave-free ratio (iFR) is a recently developed method for determining the functional significance of stenosis, which does not require the administration of agents that cause hyperemia, in particular adenosine, and also has a number of advantages compared to FFR [1]. Although there are some differences between FFR and iFR in the results, according to two multicenter RCTs iFR-SWEDEHEART and DEFINE-FLAIR [5, 6], there is no significant difference in main endpoints depending on the method of stenosis assessment.

In the light of the above data, we conducted a systematic review and meta-analysis of studies where myocardial revascularization by PCI was performed under the guidance of FFR in addition to angiography compared with CAG-guided PCI, as well as a comparison of two methods of hemodynamic severity assessment (FFR and iFR).

Material and methods

Search for publications and selection of studies. The information retrieval algorithm was developed in accordance with Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) [7] in the PubMed database (Medline), Google Scholar. The last data search for inclusion in this analysis was conducted on October 15, 2022. We used the following keywords to search PubMed (Medline) databases: ((percutaneous coronary intervention) OR (PCI) OR (coronary revascularization)) AND ((coronary angiography)) AND ((ffr) OR (fractional flow reserve)) AND ((ifr) OR (instantaneous free-wave ratio) OR (wave-free ratio)). The following query was used to search the Google Scholar database: percutaneous coronary intervention, PCI, coronary angiography, ffr, fractional flow reserve, ifr, instantaneous free-wave ratio, wave-free ratio. To select eligible studies for inclusion in this systematic review and meta-analysis, two authors independently reviewed abstracts and full-text reports for inclusion criteria.

Inclusion/exclusion criteria. There were following inclusion criteria for primary studies in a systematic review followed by meta-analysis: studies with access to full texts; all participants were adults (18 years of age or older); studies with adequately presented baseline data, in particular on the incidence of endpoints. The systematic review includes both RCTs and observational studies, including registries that compared the strategy of myocardial revascularization by PCI method according to FFR/iFR data with the strategy of myocardial revascularization based on CAG data. The lower threshold for follow-up period for patients was set to 12 months. Articles in languages other than English, case reports, preclinical studies, reviews, and expert opinions were excluded from the meta-analysis.

Assessment of methodological quality. The assessment of bias risk was carried out in accordance with the Cochrane criteria for assessing the metho-

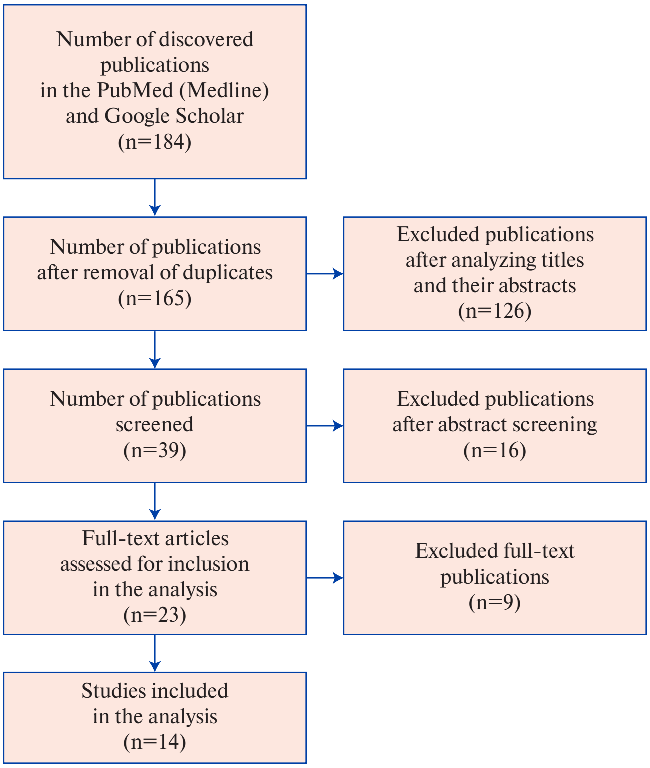


Figure 1. Flowchart for the selection of studies included in the review.

dological quality of RCTs (RoB 2 tool). In the case of observational studies, assessment was carried out according to the Newcastle-Ottawa Quality Assessment Form for Cohort Studies [8]. All inconsistencies were eliminated by discussion by the authors.

Statistical analysis. Statistical data processing was performed using Review Manager (RevMan), version 5.4.1 (The Cochrane Collaboration, 2020) and Comprehensive Meta-Analysis 3.0 (Biostat, NJ). The main results are presented as a forest plot. Testing for the statistical heterogeneity was carried out using a Q-test based on χ^2, as well as the heterogeneity index I^2. Interpretation of the assessment of statistical heterogeneity, according to the I^2 index, was carried out according the Cochrane guidelines, according to which I^2 of 0-40% corresponds to insignificant heterogeneity; 30-60% — moderate heterogeneity; 50-90% — significant heterogeneity; 75-100% — high heterogeneity. Dichotomous data were analyzed using the Mantel-Haenszel test and presented as an odds ratio (OR) with a 95% confidence interval (CI). The random effects model was adopted at $P<0,1$ in the χ^2 test and $I^2>40\%$, the fixed effect model at $P\geqslant0,1$ in the χ^2 test and $I^2\leqslant40\%$. As initial values for the survival meta-analysis, the values of the adjusted (obtained for the multivariate model, adjusted) hazard ratio (HR) was used. In this case, the meta-analysis was carried out according to the random effects model, using the inverse dispersion method. The effect was considered significant at $p<0,05$. The possible presence of bias associated with the predominant publication of positive study results was analyzed using a funnel plot. Publication bias was also assessed using the Egger test.

Results

Literature search results. Keyword search in the PubMed (Medline), Google Scholar database revealed 184 publications. The number of publications after the removal of duplicates was 165. After analyzing the titles and their abstracts, 39 publications corresponded to the goal. 23 publications passed full-text screening. Thus, 14 studies were finally included in our review, while the selection process for relevant studies is shown in Figure 1.

General characteristics of studies

The total number of patients in RCTs [4, 9-13] included in this analysis was 2193. The mean age of patients was 64,2 years. The mean follow-up period was 28 months. In three observational retrospective studies [14-16], the total number of patients was 2313. Given that observational studies are subject to the influence of confounders, these retrospective studies were excluded. However, we analyzed the results of recent large registries [17-19] regarding the impact on the prognosis of a revascularization strategy with an assessment of FFR in addition to angiography. The total number of patients in these registries was 176462. Data on study design, baseline patient characteristics are summarized in Tables 1 and 2.

Comparative analysis of FFR-guided revascularization in comparison with CAG-guided strategy according to RCT data

All of the included 6 RCTs [4, 9-13] reported on the incidence of major adverse cardiac events (MACE). The total number of patients was 2193. The average follow-up duration was 28 months. During the follow-up period, the endpoint in the form of MACE was 306 cases (13,9%). A meta-analysis showed a trend towards a lower incidence of MACE in the group of patients with FFR-guided PCI compared with CAG-guided strategy (OR: 0,78; 95% CI: 0,61-1,00; p=0,05) (Figure 2). For the individual components of MACE, data on all-cause death were reported in five studies for a total of 1964 patients in these studies. The meta-analysis showed no significant difference between groups in the incidence of all-cause death (OR: 0,86; 95% CI: 0,51-1,44; p=0,57) (Figure 2). In four studies reported data on the incidence of myocardial infarction, the total number of patients was 1895 (follow-up period, 12 months). In each of the above studies, no significant difference was found between the incidence of MI depending on the strategy of myocardial revascularization (FFR-PCI and CAG-PCI). However, their combined analysis revealed a lower incidence of myocardial infarction in the group of patients with FFR-guided PCI compared with CAG-guided strategy, and these differences were significant (OR: 0,70; 95% CI: 0,50-0,99; p=0,04) (Figure 2). Data on non-elective revascularization were presented only in two studies with the total number of 1325 patients (follow-up period, 12 months). There was no significant difference between the groups in the frequency of repeated myocardial revascularization (OR: 0,69; 95% CI: 0,46-1,04; p=0,08) (Figure 2). It is noteworthy that statistically insignificant result was obtained for homogeneity as follows: p>0,1; and heterogeneity index I^2=0%, suggesting low heterogeneity among the studies included in this analysis.

Risk of bias in included studies

The funnel plot for MACE showed some right-sided asymmetry, which indicates a publication bias (Figure 3). This conclusion was confirmed by the quantitative results of the Egger test: t=1,93; p=0,06. With respect to all-cause mortality and MI,

Table 1

General characteristics of studies included in the systematic review

First author	Year	Design	Patients	Duration, months	Inclusion criteria	Exclusion criteria
FFR vs CAG						
Tonino [4]	2009	РКИ	509/496	12	CAD (>50% stenosis in at least two large epicardial coronary arteries) that required revascularization based on angiographic and clinical findings	Recent STEMI (<5 days); NSTE-ACS with peak creatinine kinase levels >1000 U/L; CABG in history; cardiogenic shock; extremely tortuous or calcified CAs; life expectancy <2 years; pregnancy
Puymirat [14]	2012	Retrospective	222/495	60	Stable or unstable angina with small coronary vessels (diameter <3 mm)	Patients with PCI and vessel diameter ⩾3 mm; shunt stenting; STEMI or NSTEMI
Chen [9]	2015	РКИ	160/160	12	Silent myocardial ischemia, stable or unstable angina with coronary artery bifurcation lesion (stenosis ⩾50% in both the main vessel and the lateral branch, each with a reference diameter of ⩾2,5 to ⩽4,5 mm)	MI within 1 month; LVEF <30%; CABG in history; distal lesion of LCA trifurcation with non-recanalized chronic total occlusion; coronary artery calcification, requiring rotational atherectomy; elective surgery requiring interruption of antiplatelet therapy 6 months after PCI; GFR <40 ml/min/1,73 m^2; platelet count $<10\times10^9$/l; liver dysfunction; pregnancy; life expectancy <1 year; no informed consent
Layland [10]	2015	РКИ	176/174	12	Patients with a clinical diagnosis of recent NSTEMI and at least one risk factor who were eligible for randomization if emergency invasive treatment was planned within 72 hours of an episode of myocardial ischemia or if there was recurrent ischemic symptoms within 5 days	Ischemia symptoms without therapy, hemodynamic instability, STEMI, intolerance to antiplatelet agents, expected duration <1 year
Park [11]	2015	РКИ	114/115	60	Intermediate coronary stenosis	Angiographically significant LCA lesion; cardiogenic shock; CKD; life expectancy <2 years; degree 2-3 AV block; contraindications for adenosine

Table 1. Continuation

First author	Year	Design	Patients	Duration, months	Inclusion criteria	Exclusion criteria
De Backer [15]	2016	PSM	695/695	48	Coronary stenosis <50% or >89%	Previous CABG; life expectancy <1 year; unstable hemodynamics
Zhang [12]	2016	РКИ	110/110	12	NSTEMI over 65 of age	Cardiogenic shock or hemodynamic instability; intolerance to antiplatelet agents; technical impossibility for PCI; excessively tortuous or calcified CAs; life expectancy <1 year
Huang [16]	2017	Retrospective	101/105	14	Intermediate coronary stenosis	–
Quintella [13]	2019	РКИ	34/35	60	Patients aged 21 years and older with stable multivessel disease or on day 7 after ACS, with at least one moderate stenosis (>60%) without significant LV dysfunction and with urgent intensive care for ischemia were divided into two groups	–
Parikh [17]	2020	Observational Study (Register)	2967/15022	12	Angiographically intermediate stenoses (visually defined as 40% to 69% stenosis)	Patients with coronary artery stenoses ⩾70%, including chronic total occlusion and/or ACS
Völz [18]	2020	Observational Study (Register)	3367/20493	56	Stable angina	History of CABG
Hong [19]	2022	Observational Study (Register)	5116/129497	36	Stable angina	Acute MI, including STEMI or NSTEMI, history of CABG
iFR vs FFR						
Davies [5]	2017	РКИ	1147/1179	12	Intermediate coronary stenosis	Tandem stenosis prior to CABG, severe LCA stenosis, total coronary occlusion, restenosis, hemodynamic instability, contraindications to adenosine administration, highly calcified or tortuous vessels, severe comorbidities with a poor prognosis, pregnancy, severe valvular heart disease, recent STEMI
Götberg [6]	2017	РКИ	1012/1007	12	Stable or unstable angina, NSTEMI	Previous CABG; life expectancy <1 year; unstable hemodynamics

Abbreviations: ACS — acute coronary syndrome, AV — atrioventricular, CABG — coronary artery bypass grafting, CA — coronary artery, CAD — coronary artery disease, CAG — coronary angiography, CKD — chronic kidney disease, FFR — fractional flow reserve, GFR — glomerular filtration rate, EF — ejection fraction, iFR — instantaneous wave-free ratio, MI — myocardial infarction, STEMI — non-ST segment myocardial infarction, LV — left ventricle, LCA — left coronary artery, NSTE-ACS — non-ST elevation acute coronary syndrome, PCI — percutaneous coronary intervention, RCT — randomized clinical trial, STEMI — ST segment myocardial infarction.

funnel plots did not reveal significant asymmetry (Figure 3). When evaluating the Egger test for MI, an insignificant result was obtained: t=0,52; p=0,33. However, the Egger test for the all-cause mortality revealed a significant result: t=3,70; p=0,02.

Meta-regression analysis

Meta-regression analysis did not reveal any evidence of modification of the effect of non-ST elevation acute coronary syndrome (NSTE-ACS) rate in the included studies on MI, MACE, all-cause mortality (Q=0,09,

Table 2

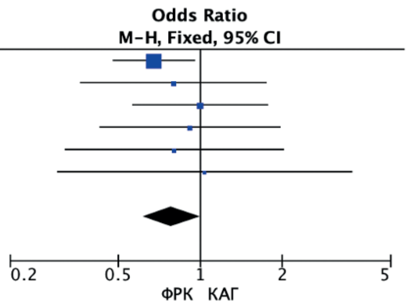
General characteristics of patients included in the systematic review

Author, year	Methodl	Patients	Age±SD	BMI (kg/m²)	Men (%)	HTN (%)	Diabetes (%)	Old myocardial infarction (%)	Multivessel CAD (%)	NSTE-ACS
Tonino, et al. 2009 [4]	FFR	509	64,6±10,3	–	384 (75,4)	312 (61,3)	123 (24,2)	187 (36,7)	509 (100)	150 (29,4)
	CA	496	64,2±10,2	–	360 (72,6)	327 (65,9)	125 (25,2)	180 (36,3)	496 (100)	178 (35,9)
Puymirat, et al. 2012 [14]	FFR	222	71,6±9,8	26,6±4,3	129 (58)	130 (59)	58 (26)	–	38 (17)	23 (10)
	CA	495	71,7±10,6	27,0±4,4	336 (68)	323 (65)	163 (33)	–	46 (9)	103 (21)
Chen, et al. 2015 [9]	FFR	160	65,2±9,6	–	121 (75,6)	116 (72,5)	48 (30,0)	12 (7,5)	112 (69,8)	98 (61,7)
	CA	160	65,4±9,2	–	116 (72,5)	106 (68,3)	43 (26,9)	19 (11,9)	110 (68,8)	99 (61,9)
Layland, et al. 2015 [10]	FFR	176	62,3±11,0	–	133 (75,6)	78 (44,3)	26 (14,8)	22 (12,5)	51 (29,0)	176 (100)
	CA	174	61,6±11,1	–	127 (73,0)	81 (46,6)	26 (14,9)	24 (13,8)	55 (31,6)	174 (100)
Park, et al. 2015 [11]	FFR	114	62±10	–	83 (72,8)	73 (64)	30 (26)	22 (19)	72 (63)	58 (51)
	CA	115	63±10	–	87 (75,7)	65 (57)	39 (34)	20 (17)	66 (57)	55 (48)
De Backer, et al. 2016 [15]	FFR	695	64,6±10,5	28,3±10,6	511 (73,5)	465 (66,9)	179 (25,8)	238 (34,2)	199 (28,7)	–
	CA	695	64,7±10,3	27,7±7,9	507 (72,9)	477 (68,6)	164 (23,6)	237 (34,1)	202 (29,1)	–
Zhang, et al. 2016 [12]	FFR	110	70±3,7	–	75 (68,2)	81 (73,6)	40 (36,4)	24 (21,8)	–	110 (100)
	CA	110	70±3,4	–	78 (70,9)	83 (75,5)	36 (32,7)	23 (20,9)	–	110 (100)
Huang, et al. 2017 [16]	FFR	101	66±9	–	74 (73)	76 (75)	35 (35)	15 (15)	73 (72)	–
	CA	105	61±11	–	82 (78)	72 (69)	39 (37)	23 (22)	72 (69)	–
Quintella, et al. 2019 [13]	FFR	34	62,7±8,4	–	25 (73,5)	25 (73,5)	12 (35,3)	8 (23,5)	34 (100)	14 (57,1)
	CA	35	59,5±9,4	–	22 (62,8)	26 (74,3)	12 (34,3)	7 (20,0)	35 (100)	13 (42,8)
Parikh, et al. 2020 [17]	FFR	2967	65,7±9,6	30,9±6,0	2624 (77,9)	2561 (76,1)	755 (22,4)	1053 (31,3)	1984 (66,8)	0 (0)
	CA	15022	67,0±9,8	30,6±6,3	15421 (75,4)	15285 (74,6)	4500 (21,9)	5694 (27,8)	9715 (64,7)	0 (0)
Völz, et al. 2020 [18]	FFR	3367	65±8,4	–	2866 (96,6)	2631 (88,7)	1294 (43,6)	686 (23,1)	1,589 (47,7)	0 (0)
	CA	20493	66±8,9	–	14615 (97,3)	13431 (89,4)	6731 (44,8)	3284 (21,9)	8,824 (43,2)	0 (0)
Hong, et al. 2022 [19]	FFR	5116	65,7±10,0	–	3557 (69,5)	3745 (73,2)	2643 (51,7)	–	–	1887 (36,9)
	CA	129497	66,9±10,3	–	85144 (65,7)	92735 (71,6)	63666 (49,2)	–	–	63302 (48,9)
Davies, et al. 2017 [5]	iFR	1250	65,2±10,6	–	929 (74,3)	884 (70,7)	376 (30,1)	376 (30,1)	519 (41,5)	186 (15,0)
	FFR	1242	65,5±10,8	–	962 (77,5)	873 (70,3)	382 (30,8)	358 (28,8)	505 (40,7)	184 (14,7)
Götberg, et al. 2017 [6]	iFR	1007	67,4±9,2	27,6±4,3	766 (75,2)	710 (69,7)	213 (20,9)	335 (32,9)	368 (36,1)	387 (38,4)
	FFR	1012	67,6±9,6	27,6±4,3	756 (74,2)	730 (71,6)	232 (22,8)	337 (33,1)	364 (35,7)	386 (37,9)

Abbreviations: HTN — hypertension, BMI — body mass index, CA — coronary angiography, iFR — instantaneous wave-free ratio, NSTE-ACS — non-ST elevation acute coronary syndrome, FFR — fractional flow reserve, PCI — percutaneous coronary intervention.

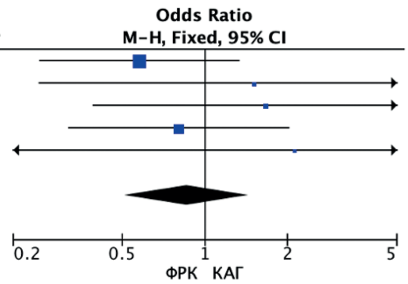
Major adverse cardiac events (MACE)

Study or Subgroup	ФРК Events	ФРК Total	КАГ Events	КАГ Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Tonino et al.	67	509	91	496	54.5%	0.67 [0.48, 0.95]	2009
Park et al.	13	114	16	115	9.6%	0.80 [0.36, 1.74]	2015
Chen et al.	29	160	29	160	16.2%	1.00 [0.57, 1.77]	2015
Layland et al.	14	176	15	174	9.5%	0.92 [0.43, 1.96]	2015
Zhang et al.	9	110	11	110	6.9%	0.80 [0.32, 2.02]	2016
Quintella et al.	6	34	6	35	3.3%	1.04 [0.30, 3.60]	2019
Total (95% CI)		**1103**		**1090**	**100.0%**	**0.78 [0.61, 1.00]**	
Total events	138		168				
Heterogeneity: $Chi^2 = 1.80$, df = 5 (P = 0.88); $I^2 = 0\%$							
Test for overall effect: Z = 1.97 (P = 0.05)							



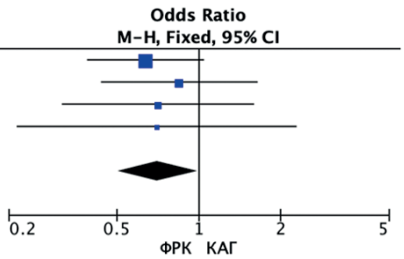
All-cause mortality

Study or Subgroup	ФРК Events	ФРК Total	КАГ Events	КАГ Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Tonino et al.	9	509	15	496	48.4%	0.58 [0.25, 1.33]	2009
Chen et al.	3	160	2	160	6.4%	1.51 [0.25, 9.16]	2015
Layland et al.	5	176	3	174	9.5%	1.67 [0.39, 7.08]	2015
Zhang et al.	9	110	11	110	32.7%	0.80 [0.32, 2.02]	2016
Quintella et al.	2	34	1	35	3.0%	2.13 [0.18, 24.59]	2019
Total (95% CI)		**989**		**975**	**100.0%**	**0.86 [0.51, 1.44]**	
Total events	28		32				
Heterogeneity: $Chi^2 = 2.60$, df = 4 (P = 0.63); $I^2 = 0\%$							
Test for overall effect: Z = 0.57 (P = 0.57)							



Myocardial infarction

Study or Subgroup	ФРК Events	ФРК Total	КАГ Events	КАГ Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Tonino et al.	29	509	43	496	50.5%	0.64 [0.39, 1.04]	2009
Chen et al.	19	160	22	160	23.9%	0.85 [0.44, 1.63]	2015
Layland et al.	11	176	15	174	17.4%	0.71 [0.32, 1.59]	2015
Zhang et al.	5	110	7	110	8.2%	0.70 [0.22, 2.28]	2016
Total (95% CI)		**955**		**940**	**100.0%**	**0.70 [0.50, 0.99]**	
Total events	64		87				
Heterogeneity: $Chi^2 = 0.46$, df = 3 (P = 0.93); $I^2 = 0\%$							
Test for overall effect: Z = 2.04 (P = 0.04)							



Emergency repeat revascularization

Study or Subgroup	ФРК Events	ФРК Total	КАГ Events	КАГ Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Tonino et al.	33	509	47	496	81.1%	0.66 [0.42, 1.05]	2009
Chen et al.	9	160	11	160	18.9%	0.81 [0.33, 2.00]	2015
Total (95% CI)		**669**		**656**	**100.0%**	**0.69 [0.46, 1.04]**	
Total events	42		58				
Heterogeneity: $Chi^2 = 0.14$, df = 1 (P = 0.70); $I^2 = 0\%$							
Test for overall effect: Z = 1.76 (P = 0.08)							

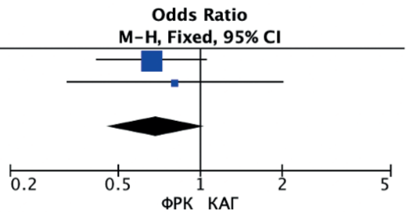


Figure 2. Forest plot of OR for endpoints depending on FFR-PCI in comparison with CA-PCI.
Abbreviations: CA — coronary angiography, FFR — fractional flow reserve.

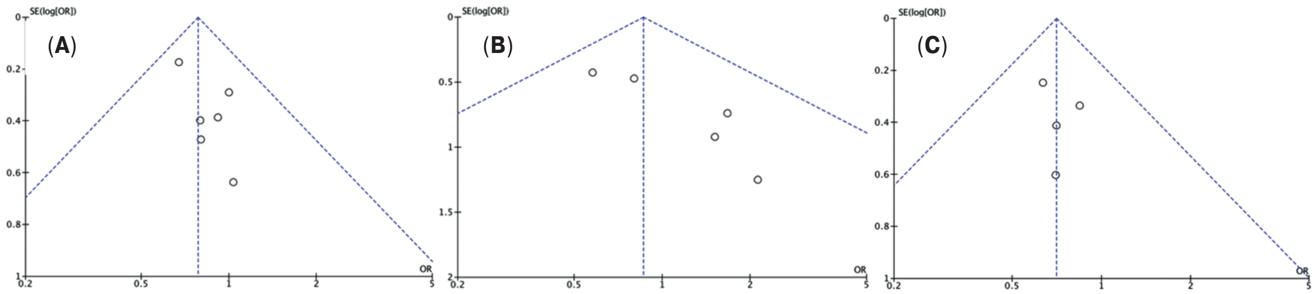


Figure 3. Funnel plot: (**A**) MACE; (**B**) all-cause mortality; (**C**) MI.

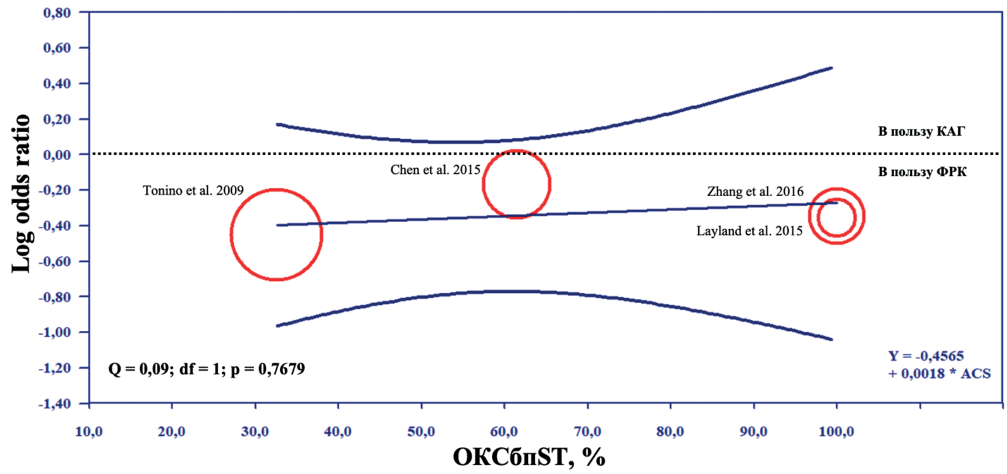


Figure 4. Random effects meta-regression analysis: association between the proportion of NSTE-ACS in the included studies with MI after myocardial revascularization.
Note: negative log OR indicate benefits of FFR. The circle size corresponds to the inverse variance of log OR and is related to the weight of individual study. Curved lines represent 95% CI.
Abbreviations: CI — confidence interval, MI — myocardial infarction, CA — coronary angiography, NSTE-ACS — non-ST elevation acute coronary syndrome, FFR — fractional flow reserve.

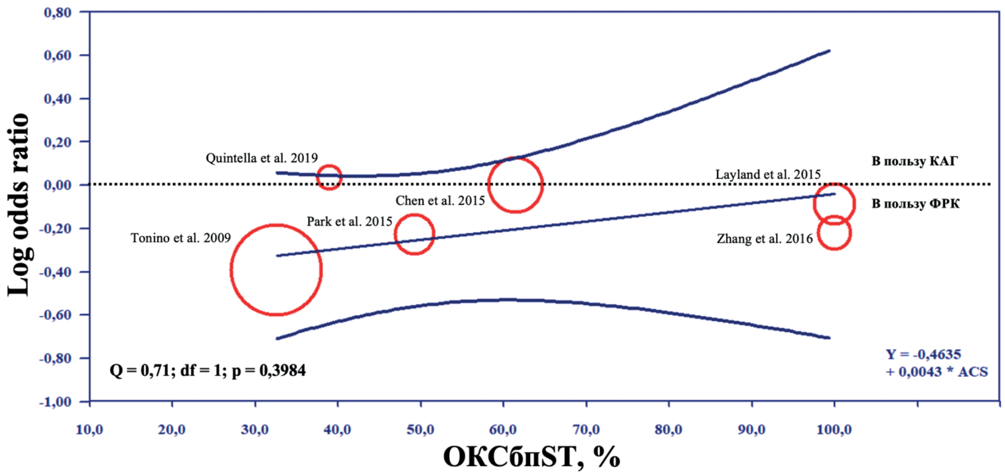


Figure 5. Random effects meta-regression analysis: association between the proportion of NSTE-ACS in the included studies with MACE after myocardial revascularization.
Note: negative log OR indicate benefits of FFR. The circle size corresponds to the inverse variance of log OR and is related to the weight of individual study. Curved lines represent 95% CI.
Abbreviations: CI — confidence interval, CA — coronary angiography, NSTE-ACS — non-ST elevation acute coronary syndrome, FFR — fractional flow reserve, MACE — major adverse cardiac events.

p=0,77; Q=0,71, p=0,40; and Q=0,52, p=0,47, respectively). Diagrams of meta-regression analysis of MI and MACE PRs depending on NSTE-ACS incidence are presented in Figures 4 and 5, respectively.

Analysis of FFR-guided PCI compared with CAG-guided strategy according to large registries

As already noted, three large registries have recently been conducted [17-19], in which the total number of patients in the group of patients with FFR-guided myocardial was 11450, while in the CAG group consisted of 165012 participants.

In contrast to the above RCTs, in these registries, the total number of patients included and the endpoint incidence made it possible to define all-cause mortality as the main primary endpoint. In addition, a study by Völz S, et al. [18] presented data on the risk of restenosis or stent thrombosis depending on myocardial revascularization strategy. In a study by Parikh RV, et al. [17], in addition to data on the risk of all-cause mortality, MI, repeated myocardial revascularization, and a composite point including the above events were presented. Finally, recently

Table 3

Main endpoints of studies included in the systematic review

Author, year	Method	Patients	All-cause mortality (%)	MI (%)	Emergency repeat revascularization (%)	MACE (%)
Tonino, et al. 2009 [4]	FFR	509	9 (1,8)	29 (5,7)	33 (6,5)	67 (13,2)
	CA	496	15 (3,0)	43 (8,7)	47 (9,5)	91 (18,3)
Puymirat, et al. 2012 [14]	FFR	222	3 (1,4)	NR	10 (4,5)	13 (5,9)
	CA	479	13 (2,7)	NR	59 (12,3)	90 (18,8)
Chen, et al. 2015 [9]	FFR	160	3 (1,9)	19 (11,9)	9 (5,6)	29 (18,1)
	CA	160	2 (1,3)	22 (13,8)	11 (6,9)	29 (18,1)
Layland, et al. 2015 [10]	FFR	176	5 (2,8)	11 (6,2)	–	14 (8,0)
	CA	174	3 (1,7)	15 (8,6)	–	15 (8,6)
Park, et al. 2015 [11]	FFR	114	–	–	–	13 (11,4)
	CA	115	–	–	–	16 (13,9)
De Backer, et al. 2016 [15]	FFR	695	110 (15,8)	217 (31,2)	254 (36,5)	255 (36,7)
	CA	695	191 (27,5)	210 (30,2)	231 (33,2)	236 (34,0)
Zhang, et al. 2016 [12]	FFR	110	9 (8,2)	5 (4,5)	–	9 (8,2)
	CA	110	11 (10,0)	7 (6,4)	–	11 (10,0)
Huang, et al. 2017 [16]	FFR	101	1 (1)	0 (0)	–	3 (3)
	CA	105	0 (0)	1 (1)	–	6 (6)
Quintella, et al. 2019 [13]	FFR	34	2 (5,8)	–	–	6 (17,6)
	CA	35	1 (2,8)	–	–	6 (17,1)
Parikh, et al. 2020 [17]	FFR	2967	82 (2,8)	19 (0,64)	112 (3,8)	203 (6,8)
	CA	15022	890 (5,9)	111 (0,79)	510 (3,4)	1403 (9,3)
Völz, et al. 2020 [18]	FFR	3367	275 (8,2)	–	–	–
	CA	20493	2916 (14,2)	–	–	–
Hong, et al. 2022 [19]	FFR	5116	205 (5,8)	64 (1,6)	586 (15,7)	–
	CA	129497	7532 (7,7)	2115 (2,2)	15147 (15,2)	–
Davies, et al. 2017 [5]	iFR	1148	22 (1,9)	31 (2,7)	46 (4,0)	78 (6,8)
	FFR	1182	13 (1,1)	28 (2,4)	63 (5,3)	83 (7,0)
Götberg, et al. 2017 [6]	iFR	1012	15 (1,5)	22 (2,2)	47 (4,6)	68 (6,7)
	FFR	1007	12 (1,2)	17 (1,7)	46 (4,6)	61 (6,1)

Abbreviations: MI — myocardial infarction, CA — coronary angiography, iFR — instantaneous wave-free ratio, FFR — fractional flow reserve, PCI — percutaneous coronary intervention, MACE — major adverse cardiac events.

published registry by Hong D, et al. [19] presented data on the risk of MI, non-elective myocardial revascularization, and the combination of MI and mortality depending on myocardial revascularization strategy (Table 3).

The above studies presented HR data from multivariate Cox regression analysis (Table 4). These HR values by study endpoint were further pooled in a meta-analysis. A meta-analysis showed that FFR-guided PCI was associated with a significantly lower risk of all-cause death (HR: 0,74; 95% CI: 0,63-0,87; p=0,0003) compared with CAG-guided strategy (Figure 6). When evaluating the Egger test, a statistically insignificant result was obtained (t=2,33; p=0,129).

However, the first two registries SCAAR and VA failed to show concrete results that could contribute to the reduction of mortality in a FFR-based approach [17, 18]. MI, as a key outcome that could affect mortality, was not studied in the SCAAR registry [18], and did not differ depending on FFR use in the VA registry [17] (0,64% vs 0,79% for FFR-PCI and CAG-PCI, respectively; HR: 0,77; 95% CI: 0,47-1,27; p=0,31). Only in the recent largest registry, Hong D, et al. managed to demonstrate a significantly lower risk of MI with FFR-PCI (HR: 0,75; 95% CI: 0,59-0,96; p=0,02) compared with CAG-PCI [19].

A meta-analysis of two recent studies [17, 19] showed that a FFR-guided approach to myocardial

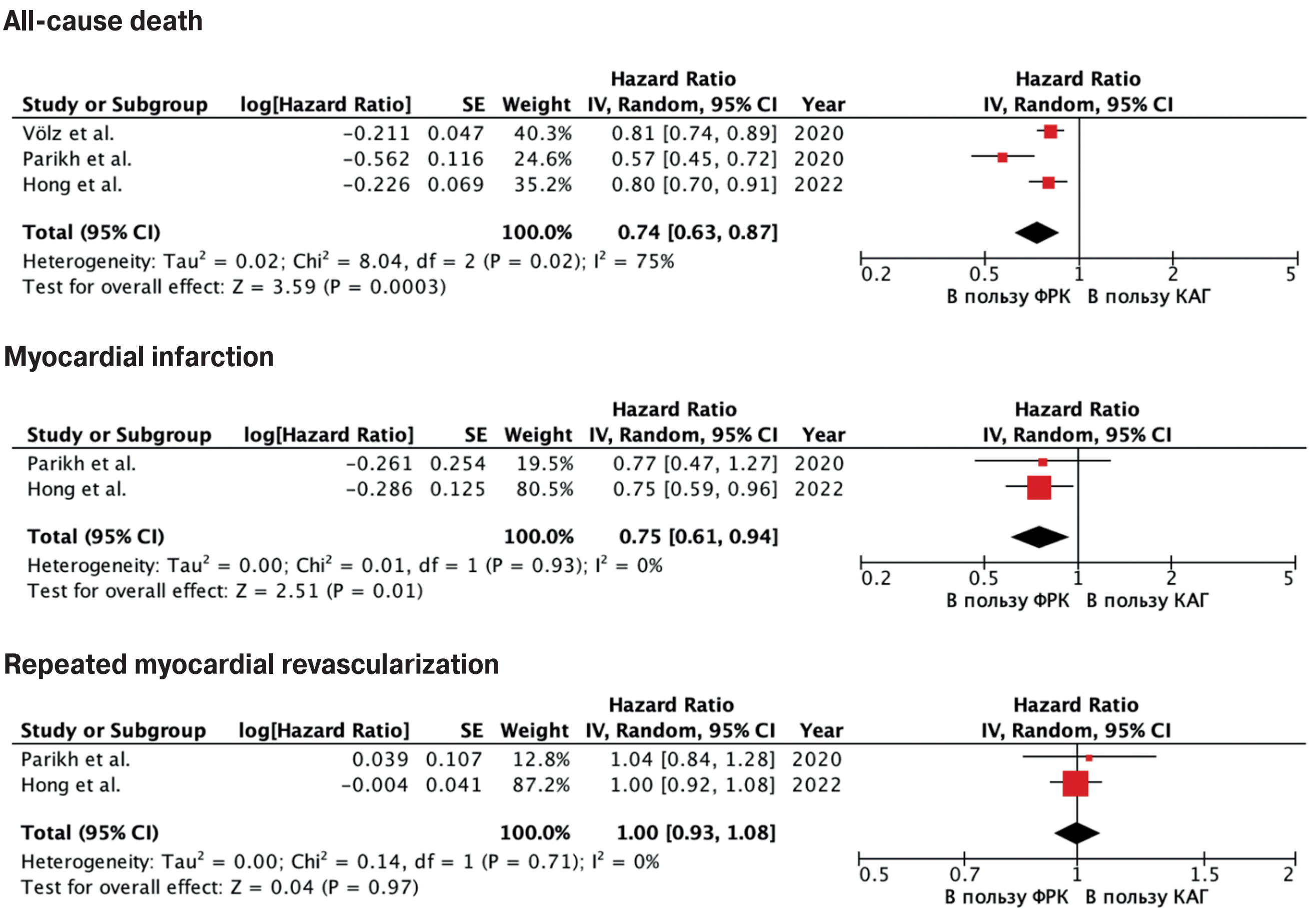


Figure 6. Forest plot of clinical outcomes after FFR-guided PCI according to registers.
Abbreviations: CA — coronary angiography, FFR — fractional flow reserve.

Table 4

OR according to multivariate Cox regression

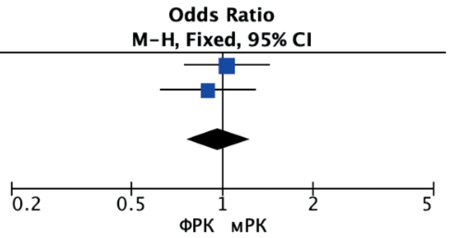
Study	End point	HR	95% CI	p	Log OP	SE
Völz, et al. 2020 [18]	All-cause mortality	0,81	0,73-0,89	<0,001	-0,211	0,047
	Restenosis or stent thrombosis	0,74	0,57-0,96	0,022	–	–
	Stent restenosis	0,71	0,54-0,94	0,016	–	–
	Stent thrombosis	0,98	0,45-2,14	0,958	–	–
Parikh, et al. 2020 [17]	All-cause death	0,57	0,45-0,71	<0,0001	-0,562	0,116
	MI	0,77	0,47-1,27	0,31	-0,261	0,254
	Repeated myocardial revascularization	1,04	0,84-1,28	0,74	0,039	0,107
	Composite point: all-cause mortality, MI, repeat myocardial revascularization	0,80	0,69-0,93	0,004	-0,223	0,076
	Stroke	0,68	0,38-1,21	0,19	–	–
Hong, et al. 2022 [19]	All-cause death	0,798	0,698-0,913	0,001	-0,226	0,069
	MI	0,751	0,587-0,959	0,022	-0,286	0,125
	Emergency repeated myocardial revascularization	0,996	0,918-1,080	0,922	-0,004	0,041
	Death or spontaneous MI	0,773	0,685-0,872	<0,001	-0,257	0,062

Abbreviations: CI — confidence interval, MI — myocardial infarction, HR — hazard ratio.

Major adverse cardiac events (MACE)

Study or Subgroup	ФРК Events	ФРК Total	мРК Events	мРК Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Davies et al.	83	1182	78	1148	53.6%	1.04 [0.75, 1.43]	2017
Götberg et al.	61	1007	68	1012	46.4%	0.90 [0.63, 1.28]	2017
Total (95% CI)		**2189**		**2160**	**100.0%**	**0.97 [0.76, 1.23]**	
Total events	144		146				

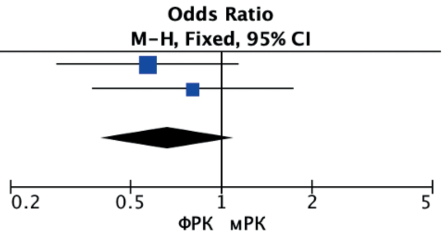
Heterogeneity: Chi^2 = 0.36, df = 1 (P = 0.55); I^2 = 0%
Test for overall effect: Z = 0.24 (P = 0.81)



All-cause mortality

Study or Subgroup	ФРК Events	ФРК Total	мРК Events	мРК Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Davies et al.	13	1182	22	1148	59.9%	0.57 [0.29, 1.14]	2017
Götberg et al.	12	1007	15	1012	40.1%	0.80 [0.37, 1.72]	2017
Total (95% CI)		**2189**		**2160**	**100.0%**	**0.66 [0.40, 1.10]**	
Total events	25		37				

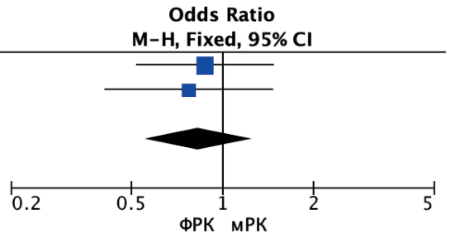
Heterogeneity: Chi^2 = 0.42, df = 1 (P = 0.51); I^2 = 0%
Test for overall effect: Z = 1.58 (P = 0.11)



Myocardial infarction

Study or Subgroup	ФРК Events	ФРК Total	мРК Events	мРК Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Davies et al.	28	1182	31	1148	58.7%	0.87 [0.52, 1.47]	2017
Götberg et al.	17	1007	22	1012	41.3%	0.77 [0.41, 1.46]	2017
Total (95% CI)		**2189**		**2160**	**100.0%**	**0.83 [0.56, 1.24]**	
Total events	45		53				

Heterogeneity: Chi^2 = 0.09, df = 1 (P = 0.77); I^2 = 0%
Test for overall effect: Z = 0.89 (P = 0.37)



Emergency repeat revascularization

Study or Subgroup	ФРК Events	ФРК Total	мРК Events	мРК Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Davies et al.	63	1182	46	1148	49.7%	1.35 [0.91, 1.99]	2017
Götberg et al.	46	1007	47	1012	50.3%	0.98 [0.65, 1.49]	2017
Total (95% CI)		**2189**		**2160**	**100.0%**	**1.16 [0.88, 1.55]**	
Total events	109		93				

Heterogeneity: Chi^2 = 1.19, df = 1 (P = 0.28); I^2 = 16%
Test for overall effect: Z = 1.05 (P = 0.29)

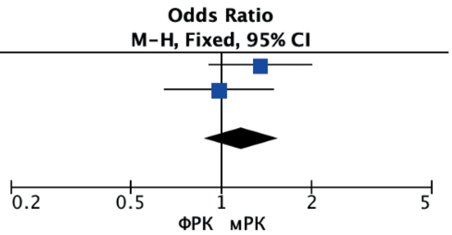


Figure 7. Forest plot of clinical outcomes within 12 months after FFR- and iFR-guided PCI.
Abbreviations: iFR — instantaneous wave-free ratio, FFR — fractional flow reserve.

revascularization was associated with a significantly lower risk of MI (HR: 0,75; 95% CI: 0,61-0,94; p=0,01) (Figure 6). When assessing the homogeneity of studies, an insignificant result was obtained: p=0,93; and heterogeneity index I^2=0%. At the same time, there was no significant association between the risk of recurrent myocardial revascularization depending on FFR-PCI or CAG-PCI (HR: 1,00; 95% CI: 0,93-1,08; p=0,97) (Figure 6).

Analysis of iFR-strategy myocardial revascularization compared with FFR-guided strategy

The DEFINE-FLAIR [5] and iFR-SWEDEHEART [6] randomized trials compared the iFR- and PCI-guided myocardial revascularization in terms of adverse outcomes over 12 months. The primary endpoint in the studies was the composite endpoint (MACE), which included all-cause mortality, non-fatal MI, and non-elective myocardial revascularization 12 months after the procedure. The primary secondary endpoints were the frequency of each component of the primary endpoint over 12 months after PCI. Meta-analysis showed no significant difference between groups in the incidence of the combined endpoint (MACE) (OR: 0,97; 95% CI: 0,76-1,23; p=0,81). There was also no significant difference between groups in the incidence of each component of the primary endpoint, namely the development of all-cause mortality (OR: 0,66; 95% CI: 0,40-1,10; p=0,11), MI (OR: 0,83; 95% CI: 0,56-1,24; p=0,37) and non-elective myocardial revascularization (OR: 1,16; 95% CI: 0,88-1,55; p=0,29) (Figure 7).

Thus, according to two large randomized trials, the iFR-guided myocardial revascularization demonstrated a similar clinical result compared to the FFR-guided strategy in patients with chronic and NSTE-ACS within 12-month follow-up period.

Discussion

In our study, a pooled RCT analysis of patients with FFR-guided PCI, in addition to angiography, revealed significantly lower incidence of MI compared with single CAG. In addition, MACE and repeat myocardial revascularization also tended to have lower event rates in the FFR-PCI group (p<0,1).

Over the past few years, a number of meta-analyses have been published, but they have shown conflicting results. For example, Verardi R, et al. analyzed in 2018 conducted a network meta-analysis to evaluate the effectiveness and safety of FFR and iFR strategies compared to CAG. The authors showed that after 12 months MACE and all-cause mortality rates did not differ between groups. At the same time, in patients with stable coronary artery disease (CAD), both FFR and iFR reduced the risk of subsequent MI compared with CAG [20].

A meta-analysis by Baumann S, et al. published in 2019 found no significant differences for the main endpoints: MACE (OR: 0,78; 95% CI: 0,59-1,04; I^2=73%), all-cause mortality (OR: 0,74; 95% CI: 0,46-1,18; I^2=74%), MI (OR: 0,93; 95% CI: 0,81-1,07; I^2=0%) and non-elective revascularization (OR: 0,71; 95% CI: 0,41-1,23; I^2=79%) [21]. However, this meta-analysis also included three small retrospective observational studies, which most likely resulted in high heterogeneity (I^2>70%) and indicated the need for careful interpretation of the pooled OR estimates for all studies.

In our study, we performed a meta-analysis of individual RCTs, while excluding retrospective studies from the pooled analysis in order to exclude the influence of confounders and reduce study heterogeneity. So, when assessing the homogeneity of studies in relation to all four endpoints, we obtained an insignificant result (p>0,1) and heterogeneity index I^2 of 0%, suggesting low heterogeneity among the studies included in the analysis.

In a systematic review and meta-analysis published in December 2022 [22], the authors found no differences in all-cause mortality, MI, or non-elective myocardial revascularization. However, the number of patients undergoing elective revascularization with PCI with coronary artery stenting or coronary artery bypass grafting was significantly lower with the FFR-guided strategy compared with the CAG-guided strategy (p<0,001). In addition, it should be noted that, in the case of PCI with coronary stenting, the average number of implanted stents was significantly lower also when using the FFR-guided revascularization strategy (weighted mean difference -0,45 (95% CI -0,70 to -0,20), p=0,004). However, eight RCTs were included in this analysis, of which two studies performed myocardial revascularization exclusively by coronary artery bypass grafting [23, 24]. In addition, two RCTs were included in patients with ST-segment elevation ACS and multivessel CAD who underwent successful PCI of an infarct-related artery and who underwent total myocardial revascularization guided by FFR or CAG [22, 25]. Perhaps the above factors are responsible for the differences between the results of this meta-analysis and our study. Recall that our meta-analysis included patients with stable CAD or NSTE-ACS who underwent myocardial revascularization exclusively or to a greater extent by PCI with coronary stenting.

Another distinguishing feature of our study was the meta-regression analysis performed, since the RCTs included patients with NSTE-ACS along with patients with stable CAD, and the frequency of inclusion of these patients in the studies varied. The analysis did not reveal any evidence of an effect modification of NSTE-ACS incidence in the included studies on the development of MI, MACE, or all-cause mortality.

RCTs are still the "gold standard" in the hierarchy of evidence-based medicine research. However, they are characterized by strict inclusion and exclusion criteria, which, on the one hand, allows minimizing the risk of the influence of uncontrolled factors on the RCT results, and, on the other hand, limits the application of obtained results to entire population. This is due to the fact that entire groups of patients that are present in clinical practice do not pass the strict inclusion and exclusion criteria for RCTs [26]. Healthcare registries complement the information obtained in RCTs, provide objective data on the efficacy and safety of therapy in patients who were not included in RCTs according to exclusion criteria.

As noted, over the past few years, large registries have been published on the impact on prognosis and cost-effectiveness of a revascularization strategy with FFR in addition to angiography. We performed the first meta-analysis based on the above registries and showed that a FFR-guided myocardial revascularization was associated with a significantly lower risk of all-cause death. When analyzing the factors that could contribute to a reduction in mortality with a FFR-guided approach, we found that this approach is associated with a significantly lower risk of MI. At the same time, there was no significant association between the risk of repeated myocardial revascularization depending on FFR-PCI or CAG-PCI.

Finally, another aspect of our meta-analysis was to assess the difference between iFR- and FFR-guided PCI. In 2017, the results of two multicenter RCTs iFR-SWEDEHEART and DEFINE-FLAIR [5, 6] were published, according to which no significant difference was found in relation to the main endpoints depending on the method selected. Our meta-analysis also demonstrated that there was no significant difference between groups in the incidence of the composite endpoint, MACE, and in the incidence of each component of the primary endpoint, namely all-cause death, MI, and non-elective myocardial revascularization. Thus, according to two large randomized trials, iFR-guided myocardial revascularization showed a FFR strategy for 12 months. Nevertheless, the question of the effectiveness and safety of this strategy in the long-term period (>12 months) remained unclear. However, more recently, the JAAC published the results of a 5-year follow-up of patients from the iFR-SWEDEHEART study [27]. The authors showed that the frequency of the primary composite endpoint at 5 years did not differ significantly between the groups and was 21,5% in the iFR group and 19,9% in the FFR group (HR: 1,09; 95% CI: 0,90 -1,33). All-cause death (9,4% vs 7,9%; HR: 1,20; 95% CI: 0,89-1,62), non-fatal MI (5,7% vs 5,8%; HR: 1,00; 95% CI: 0,70-1,44) and non-elective myocardial revascularization (11,6% vs 11,3%; HR: 1,02; 95% CI: 0,79-1,32) also did not differ between the two groups.

Study limitations. First, a small number of studies were included in our systematic review and meta-analysis. Secondly, the inclusion and exclusion criteria in the studies in most cases differed. In particular, the incidence of NSTE-ACS and the number of coronary lesions in the studies were different. In addition, registries as a variant of observational studies are also susceptible to confounders and selection bias.

Conclusion

This systematic review and meta-analysis based on RCTs showed that a FFR-guided PCI in patients with CAD is associated with a reduced risk of MI compared with single CAG strategy. In addition, real-world data from large registries have shown that a FFR-based approach to PCI is associated with a reduction in the mortality risk, and this is primarily based on a reduction in the MI risk. The iFR-guided myocardial revascularization strategy demonstrated a similar clinical outcome compared to the FFR-guided strategy.

The results of our analysis support the current clinical guidelines that FFR/iFR should be used to assess the functional significance of borderline coronary stenosis in order to make decision about the need for myocardial revascularization.

Relationships and Activities: none.

References

1. Golukhova EZ, Petrosian KV, Abrosimov AV, Losev VV. Current state of practical application of invasive methods for assessing intracoronary physiology. Creative Cardiology. 2020;14(3):272-9. (In Russ.) doi:10.24022/1997-3187-2020-14-3-272-279.
2. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J. 2019;40(2):87-165. doi:10.1093/eurheartj/ehy394.
3. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145(3):e4-e17. doi:10.1161/CIR.0000000000001039.
4. Tonino PA, De Bruyne B, Pijls NH, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med. 2009;360(3):213-24. doi:10.1056/NEJMoa0807611.
5. Davies JE, Sen S, Dehbi HM, et al. Use of the Instantaneous Wave-free Ratio or Fractional Flow Reserve in PCI. N Engl J Med. 2017;376(19):1824-34. doi:10.1056/NEJMoa1700445.
6. Götberg M, Christiansen EH, Gudmundsdottir IJ, et al. Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI. N Engl J Med. 2017;376(19):1813-23. doi:10.1056/NEJMoa1616540.
7. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev. 2021;10(1):89. doi:10.1186/s13643-021-01626-4.
8. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25(9):603-5. doi:10.1007/s10654-010-9491-z.
9. Chen SL, Ye F, Zhang JJ, et al. Randomized Comparison of FFR-Guided and Angiography-Guided Provisional Stenting of True Coronary Bifurcation Lesions: The DKCRUSH-VI Trial (Double Kissing Crush Versus Provisional Stenting Technique for Treatment of Coronary Bifurcation Lesions VI). JACC Cardiovasc Interv. 2015;8(4):536-46. doi:10.1016/j.jcin.2014.12.221.
10. Layland J, Oldroyd KG, Curzen N, et al. Fractional flow reserve vs. angiography in guiding management to optimize outcomes in non-ST-segment elevation myocardial infarction: the British Heart Foun-

dation FAMOUS-NSTEMI randomized trial. Eur Heart J. 2015; 36(2):100-11. doi:10.1093/eurheartj/ehu338.
11. Park SH, Jeon KH, Lee JM, et al. Long-Term Clinical Outcomes of Fractional Flow Reserve-Guided Versus Routine Drug-Eluting Stent Implantation in Patients With Intermediate Coronary Stenosis: Five-Year Clinical Outcomes of DEFER-DES Trial. Circ Cardiovasc Interv. 2015;8(12):e002442. doi:10.1161/CIRCINTERVENTIONS.115.002442.
12. Zhang Z, Li K, Tian J. Efficacy and safety outcomes of fractional flow reserve in guiding clinical therapy of non-ST-segment elevation myocardial infarction compared with angiography alone in elderly Chinese patients. Clin Interv Aging. 2016;11:1751-4. doi:10.2147/CIA.S123735.
13. Quintella EF, Ferreira E, Azevedo VMP, et al. Clinical Outcomes and Cost-Effectiveness Analysis of FFR Compared with Angiography in Multivessel Disease Patient. Arq Bras Cardiol. 2019;112(1):40-7. doi:10.5935/abc.20180262.
14. Puymirat E, Peace A, Mangiacapra F, et al. Long-term clinical outcome after fractional flow reserve-guided percutaneous coronary revascularization in patients with small-vessel disease. Circ Cardiovasc Interv. 2012;5(1):62-8. doi:10.1161/CIRCINTERVENTIONS.111.966937.
15. De Backer O, Biasco L, Lønborg J, et al. Long-term outcome of FFR-guided PCI for stable coronary artery disease in daily clinical practice: a propensity score-matched landmark analysis. EuroIntervention. 2016;11(11):e1257-66. doi:10.4244/EIJV11I11A247.
16. Huang CL, Jen HL, Huang WP, et al. The Impact of Fractional Flow Reserve-Guided Coronary Revascularization in Patients with Coronary Stenoses of Intermediate Severity. Acta Cardiol Sin. 2017; 33(4):353-61. doi:10.6515/acs20170202b.
17. Parikh RV, Liu G, Plomondon ME, et al. Utilization and Outcomes of Measuring Fractional Flow Reserve in Patients With Stable Ischemic Heart Disease. J Am Coll Cardiol. 2020;75(4):409-19. doi:10.1016/j.jacc.2019.10.060.
18. Völz S, Dworeck C, Redfors B, et al. Survival of Patients With Angina Pectoris Undergoing Percutaneous Coronary Intervention With Intracoronary Pressure Wire Guidance. J Am Coll Cardiol. 2020;75(22):2785-99. doi:10.1016/j.jacc.2020.04.018.
19. Hong D, Lee SH, Shin D, et al. Prognosis and Medical Cost of Measuring Fractional Flow Reserve in Percutaneous Coronary Intervention. JACC Asia. 2022;2:590-603. doi:10.1016/j.jacasi.2022.04.006.
20. Verardi R, Fioravanti F, Barbero U, et al. Network meta-analysis comparing iFR versus FFR versus coronary angiography to drive coronary revascularization. J Interv Cardiol. 2018;31(6):725-30. doi:10.1111/joic.12551.
21. Baumann S, Mueller KSE, Hetjens S, et al. One-year clinical outcome of angiography, fractional flow reserve and instantaneous wave-free ratio guided percutaneous coronary intervention: A PRISMA-compliant meta-analysis. Exp Ther Med. 2019;17(3):1939-51. doi:10.3892/etm.2019.7156.
22. Maznyczka AM, Matthews CJ, Blaxill JM, et al. Fractional Flow Reserve versus Angiography-Guided Management of Coronary Artery Disease: A Meta-Analysis of Contemporary Randomised Controlled Trials. J Clin Med. 2022;11(23):7092. doi:10.3390/jcm11237092.
23. Thuesen AL, Riber L, Veien KT, et al. Fractional Flow Reserve Versus Angiographically-Guided Coronary Artery Bypass Grafting. J. Am. Coll. Cardiol. 2018;72:2732-43. doi:10.1016/j.jacc.2018.09.043.
24. Toth GG, De Bruyne B, Kala P, et al. Graft patency after FFR-guided versus angiography-guided coronary artery bypass grafting: The GRAFFITI trial. EuroIntervention. 2019;15:e999-e1005. doi:10.4244/EIJ-D-19-00463.
25. Puymirat E, Cayla G, Simon T, et al. Multivessel PCI Guided by FFR or Angiography for Myocardial Infarction. N. Engl. J. Med. 2021;385: 297-308. doi:10.1056/NEJMoa2104650.
26. Schastlivtsev IV, Navasardyan AR, Lobastov KV. Registers, Their Place in Scientific Hierarchy and Clinical Significance on the Example of the RIETE Register. Flebologiya. 2022;16(3):227-37. (In Russ.) doi:10.17116/flebo202216031227.
27. Götberg M, Berntorp K, Rylance R, et al. 5-Year Outcomes of PCI Guided by Measurement of Instantaneous Wave-Free Ratio Versus Fractional Flow Reserve. J Am Coll Cardiol. 2022;79(10):965-74. doi:10.1016/j.jacc.2021.12.030.