
SUPPLEMENTARY DATA

Supplementary data 1. Systematic review search strategy

PubMed

1245 results

((Coronary Diseases[MeSH]) OR (Artery Disease, Coronary[MeSH]) OR (coronary artery disease[Title/Abstract]) OR (Atherosclerosis, Coronary[MeSH]) OR (coronary atherosclerosis[Title/Abstract]) OR (CAD[Title/Abstract]) OR (Angina Pectoris[MeSH]) OR (angina[Title/Abstract]) OR (Angina, Unstable[MeSH]) OR (unstable angina[Title/Abstract]) OR (Infarction, Myocardial[MeSH]) OR (Myocardial infarction[Title/Abstract]) OR (MI[Title/Abstract]) OR (chronic coronary syndrome[Title/Abstract]) OR (CCS[Title/Abstract]) OR (Coronary Syndrome, Acute[MeSH]) OR (acute coronary syndrome[Title/Abstract]) OR (Non-ST Elevation Myocardial Infarction[MeSH]) OR (Non-ST-Elevation Myocardial Infarction[Title/Abstract]) OR (Non-ST-segment elevation acute coronary syndrome[Title/Abstract]) OR (NSTEMI[Title/Abstract]) OR (NSTEMI-ACS[Title/Abstract]) OR (ST-segment elevation myocardial infarction[MeSH]) OR (ST Elevation Myocardial Infarction[Title/Abstract]) OR (STEMI[Title/Abstract])) AND ((coronary microvascular dysfunction[Title/Abstract]) OR (coronary microcirculation[Title/Abstract]) OR (coronary microcirculatory[Title/Abstract]) OR (Coronary flow reserve[Title/Abstract]) OR (coronary flow velocity reserve[Title/Abstract]) OR (coronary flow reserve velocity[Title/Abstract]) OR (CFR[Title/Abstract]) OR (CFVR[Title/Abstract]) OR (index of microvascular resistance[Title/Abstract]) OR (IMR[Title/Abstract]) OR (hyperemic microvascular resistance[Title/Abstract]) OR (HMR[Title/Abstract]) OR (resistive reserve ratio[Title/Abstract]) OR (RRR[Title/Abstract]) OR (coronary angiography-derived index[Title/Abstract]) OR (invasively-determined index[Title/Abstract]) OR (caIMR[Title/Abstract]) OR (IMRangio[Title/Abstract])) AND ((cardiovascular events[Title/Abstract]) OR (major adverse cardiovascular event[Title/Abstract]) OR (major adverse cardiovascular events[Title/Abstract]) OR (MACE[Title/Abstract]) OR (MACEs[Title/Abstract]) OR (mortality[Title/Abstract]) OR (survival[Title/Abstract]) OR (death[Title/Abstract]) OR (outcome[Title/Abstract]) OR (outcomes[Title/Abstract]) OR (prognosis[Title/Abstract]) OR (prognostic[Title/Abstract]))))

EMBASE

1753 results

('coronary artery disease'/exp OR 'coronary artery disease':ab,ti OR 'coronary artery atherosclerosis':ab,ti OR cad:ab,ti OR 'angina pectoris':ab,ti OR 'myocardial infarction':ab,ti OR mi:ab,ti OR 'chronic coronary syndrome':ab,ti OR 'acute coronary syndrome':ab,ti OR 'non ST segment elevation myocardial infarction':ab,ti OR 'non ST segment elevation acute coronary syndrome':ab,ti OR 'ST segment elevation myocardial infarction':ab,ti) AND ('coronary microvascular dysfunction'/exp OR 'coronary microvascular dysfunction':ab,ti OR 'coronary microcirculation':ab,ti OR 'coronary flow reserve':ab,ti OR 'coronary flow velocity reserve':ab,ti OR 'coronary flow reserve velocity':ab,ti OR 'cfr':ab,ti OR 'cfvr':ab,ti OR 'index of microvascular resistance':ab,ti OR 'imr':ab,ti OR 'hyperemic microvascular resistance':ab,ti OR 'hmr':ab,ti OR 'resistive reserve ratio':ab,ti OR 'rrr':ab,ti OR 'coronary

angiography-derived index':ab,ti OR 'invasively-determined index':ab,ti OR 'caimr':ab,ti OR 'imrango':ab,ti) AND ('cardiovascular events':ab,ti OR 'major adverse cardiovascular event':ab,ti OR 'mace':ab,ti OR 'mortality':ab,ti OR 'survival':ab,ti OR 'death':ab,ti OR 'outcome':ab,ti OR 'prognosis':ab,ti)

Cochrane

753 results

((MeSH descriptor: [Coronary Artery Disease] this term only) OR (coronary atherosclerosis):ti,ab,kw OR (angina pectoris):ti,ab,kw OR (myocardial infarction):ti,ab,kw OR (chronic coronary syndrome):ti,ab,kw OR (acute coronary syndrome):ti,ab,kw OR (Non-ST Elevation Myocardial Infarction):ti,ab,kw OR (Non–ST-segment elevation acute coronary syndrome):ti,ab,kw OR (ST segment elevation myocardial infarction):ti,ab,kw OR (STEMI):ti,ab,kw OR (NSTEMI):ti,ab,kw) AND ((coronary microvascular dysfunction):ti,ab,kw OR (coronary microcirculation):ti,ab,kw OR (coronary flow reserve):ti,ab,kw OR (coronary flow velocity reserve):ti,ab,kw OR (CFR):ti,ab,kw OR (CFVR):ti,ab,kw OR (index of microvascular resistance):ti,ab,kw OR (IMR):ti,ab,kw OR (hyperemic microvascular resistance):ti,ab,kw OR (HMR):ti,ab,kw OR (resistive reserve ratio):ti,ab,kw OR (RRR):ti,ab,kw OR (coronary angiography-derived index):ti,ab,kw OR (caIMR):ti,ab,kw OR (IMRango):ti,ab,kw) AND ((cardiovascular events):ti,ab,kw OR (major adverse cardiovascular event):ti,ab,kw OR (MACE):ti,ab,kw OR (mortality):ti,ab,kw OR (survival):ti,ab,kw OR (death):ti,ab,kw OR (outcome):ti,ab,kw OR (prognosis):ti,ab,kw)

Table 1 of the supplementary data. Newcastle-Ottawa scale score of included observational studies

Source	Representativeness of the exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow-up of cohorts	Total score
Takahashi et al. ¹ 2007	1	1	1	0	0	1	1	1	6
Meuwissen et al. ² 2008	1	1	1	1	1	1	0	0	7
Fearon et al. ³ 2013	1	1	1	0	1	1	1	1	7
van de Hoef et al. ⁴ 2013	1	1	1	0	1	1	1	1	7
Ahn et al. ⁵ 2017	1	1	1	1	1	1	1	0	7
de Waard et al. ⁶ 2018	1	1	1	0	1	1	1	0	7
Lee et al. ⁷ 2018	1	1	1	1	1	1	1	1	8
Murai et al. ⁸ 2018	1	1	1	0	1	1	1	0	6
Hu et al. ⁹ 2019	1	1	1	1	1	1	1	0	7
Nishi et al. ¹⁰ 2019	1	1	1	1	1	1	1	0	7
Suda et al. ¹¹ 2019	1	1	1	0	1	1	1	0	6
Joo Myung Lee et al. ¹² 2020	1	1	1	1	1	1	1	0	7
Lee et al. ¹³ 2020	1	1	1	1	1	1	1	0	7
Maznyczka et al. ¹⁴ 2020	1	1	1	0	1	1	0	1	6
Abdu et al. ¹⁵ 2021	1	1	1	0	1	1	1	1	7
Choi et al. ¹⁶ 2021	1	1	1	0	1	1	1	0	6
Johnson et al. ¹⁷ 2021	1	1	1	1	0	1	1	0	6

Kotronias et al. ¹⁸ 2021	1	1	1	0	1	1	1	1	7
Scarsini et al. ¹⁹ 2021	1	1	1	0	1	1	1	1	7
Toya et al. ²⁰ 2021	1	1	1	1	1	1	1	1	8
Dai et al. ²¹ 2022	1	1	1	1	1	1	1	0	7
Feng et al. ²² 2022	1	1	1	1	1	1	1	0	7
Liu et al. ²³ 2022	1	1	1	1	1	1	1	0	7
FISIOIAM ²⁴ 2022	1	1	1	0	1	1	1	1	7
Kim et al. ²⁵ 2022	1	1	1	1	1	1	1	0	7
Lee et al. ²⁶ 2022	1	1	1	1	1	1	1	0	7
Mejia-Renteria et al. ²⁷ 2022	1	1	1	1	0	1	1	0	6

Table 2 of the supplementary data. Definitions of MACE in included studies

Study	Definitions of MACE
Takahashi et al. ¹ 2007	Cardiac death, recurrent acute myocardial infarction, congestive heart failure requiring hospitalization
Meuwissen et al. ² 2008	Cardiac death, myocardial infarction, coronary angioplasty bypass grafting, percutaneous coronary intervention of the target artery
Fearon et al. ³ 2013	Death, re-hospitalization due to congestive heart failure
van de Hoef et al. ⁴ 2013	Cardiac mortality
Ahn et al. ⁵ 2017	Cardiac death, myocardial infarction, subsequent revascularization
de Waard et al. ⁶ 2018	Death, hospitalization for heart failure
Lee et al. ⁷ 2018	Vessel-related cardiac death, vessel-specific myocardial infarction, vessel-specific revascularization
Murai et al. ⁸ 2018	Death, myocardial infarction, clinically driven target or nontarget vessel revascularization, congestive heart failure requiring hospitalization
Hu et al. ⁹ 2019	Cardiac death, vessel-related myocardial infarction, vessel-related ischemia-driven revascularization
Nishi et al. ¹⁰ 2019	All-cause mortality, any myocardial infarction, target vessel revascularization
Suda et al. ¹¹ 2019	Cardiac death, nonfatal myocardial infarction, unstable angina
Joo Myung Lee et al. ¹² 2020	All-cause mortality, any myocardial infarction, revascularization
Lee et al. ¹³ 2020	All-cause mortality, any myocardial infarction, revascularization
Maznyczka et al. ¹⁴ 2020	Heart failure hospitalization, all-cause death, nonfatal myocardial infarction
Abdu et al. ¹⁵ 2021	Cardiovascular death, nonfatal myocardial infarction, heart failure, stroke, angina rehospitalization
Choi et al. ¹⁶ 2021	Cardiac death, readmission for heart failure
Johnson et al. ¹⁷ 2021	All-cause death, myocardial infarction, revascularization
Kotronias et al. ¹⁸ 2021	All-cause mortality, resuscitated cardiac arrest, new heart failure
Scarsini et al. ¹⁹ 2021	All-cause mortality, heart failure, resuscitated cardiac arrest, malignant ventricular arrhythmias, the need for a primary prevention implantable cardioverter-defibrillator
Toya et al. ²⁰ 2021	All-cause mortality
Dai et al. ²¹ 2022	Cardiac death, heart failure re-hospitalization

Feng et al. ²² 2022	Cardiovascular death, nonfatal myocardial infarction, heart failure, ischemia-driven revascularization
Liu et al. ²³ 2022	Cardiovascular death, nonfatal myocardial infarction, coronary revascularization, angina-related re-hospitalization, heart failure, stroke
FISIOIAM ²⁴ 2022	Cardiovascular death, myocardial infarction, coronary revascularization, hospitalization due to heart failure, unstable angina
Kim et al. ²⁵ 2022	Cardiac death, myocardial infarction, target vessel revascularization
Lee et al. ²⁶ 2022	All-cause death, target vessel myocardial infarction, clinically driven target vessel revascularization
Mejia-Renteria et al. ²⁷ 2022	Cardiac death, target vessel myocardial infarction, target vessel revascularization

MACE, major adverse cardiovascular event.

Table 3 of the supplementary data. Characteristics of included studies

Source	Study design	Center	Study population	Guide wire/ software	Index	Abnormal cutoff	Follow-up duration (months)
Takahashi et al. ¹ 2007	Observational, prospective	Single-center	118	Intracoronary Doppler guide wire	CFR	≤ 1.3	62
Meuwissen et al. ² 2008	Observational, prospective	Single-center	170	Intracoronary pressure guide wire	CFR	< 2	12
Fearon et al. ³ 2013	Observational, prospective	Multicenter	253	Intracoronary pressure guide wire	IMR	> 40	33.6
van de Hoef et al. ⁴ 2013	Observational, prospective	Single-center	94	Intracoronary Doppler flow wire	CVFR	< 2.1	120
Ahn et al. ⁵ 2017	Observational, prospective	Multicenter	1837	Intracoronary pressure guide wire	pb-CFR	< 2	36
de Waard et al. ⁶ 2018	Observational, prospective	Multicenter	176	Intracoronary Doppler-pressure guide wire	HMR	HMR≥3	38.4
Lee et al. ⁷ 2018	Observational, prospective	Multicenter	519	Intracoronary pressure-temperature sensor guide wire	CFR	< 2	60
Murai et al. ⁸ 2018	Observational, prospective	Single-center	83	Intracoronary pressure guide wire	IMR	≥22.9	20.7
Hu et al. ⁹ 2019	Observational, prospective	Multicenter	283	Intracoronary pressure-temperature sensor guide wire	IMR	≥25	24
Nishi et al. ¹⁰ 2019	Observational, prospective	Multicenter	572	Intracoronary pressure-temperature sensor guide wire	CFR, IMR	CFR ≤ 2 IMR≥25	48
Suda et al. ¹¹ 2019	Observational, prospective	Single-center	187	Intracoronary pressure-temperature sensor guide wire	IMR	≥18	29

Joo Myung Lee et al. ¹² 2020	Observational, prospective	Multicenter	867	Intracoronary pressure-temperature sensor guide wire	CFR, IMR	CFR ≤ 2 IMR ≥ 23	60
Lee et al. ¹³ 2020	Observational, prospective	Multicenter	1245	Intracoronary pressure-temperature sensor guide wire	RRR	< 3.5	60
Maznyczka et al. ¹⁴ 2020	Observational, prospective	Multicenter	144	Intracoronary pressure-temperature sensor guide wire	CFR, IMR, RRR	CFR ≤ 2 IMR > 40 RRR ≤ 1.7	12
Abdu et al. ¹⁵ 2021	Observational, retrospective	Single-center	109	FlashAngio system	caIMR	> 43U	24
Choi et al. ¹⁶ 2021	Observational, retrospective	Single-center	309	FlashAngio system	Angio-IMR	> 40U	120
Johnson et al. ¹⁷ 2021	Observational, prospective	Multicenter	430	Intracoronary Doppler-pressure guide wire	CFR	< 2	24
Kotronias et al. ¹⁸ 2021	Observational, retrospective	Single-center	262	Intracoronary pressure guide wire / QAngio R® XA 3D software	CFR, IMR, NH IMRangio	CFR ≤ 2.0 IMR > 40 NH IMRangio > 43U	50.4
Scarsini et al. ¹⁹ 2021	Observational, prospective	Single-center	198	Intracoronary pressure-temperature sensor guide wire	IMR	> 40	40.1
Toya et al. ²⁰ 2021	Observational, retrospective	Single-center	1692	Intracoronary Doppler guide wire	CFR, RRR	CFR < 2.5 RRR < 2.62	135.6
Dai et al. ²¹ 2022	Observational, prospective	Single-center	138	QAngio XA software	Angio-IMR	≥ 25.1	28
Feng et al. ²² 2022	Observational,	Single-center	282	Flash Angio system	caIMR	≥ 25	35

	retrospective						
Liu et al. ²³ 2022	Observational, prospective	Single-center	151	Flash Angio system	caIMR	≥25	35
FISIOIAM ²⁴ 2022	Observational, prospective	Single-center	84	NA	CFR, IMR	CFR < 2 IMR > 25	48
Kim et al. ²⁵ 2022	Observational, prospective	Multicenter	400	Intracoronary pressure-temperature sensor guide wire	CFR	≤ 2	60
Lee et al. ²⁶ 2022	Observational, prospective	Multicenter	287	Intracoronary Doppler-pressure guide wire	CFR	≤ 2.5	60
Mejia-Renteria et al. ²⁷ 2022	Observational, prospective	Multicenter	514	Intracoronary pressure-temperature sensor guide wire	CFR	≤ 2	60

CFR, coronary flow reserve; caIMR, coronary angiography-derived index of microcirculatory resistance; HMR, hyperemic microvascular resistance; IMR, microcirculation resistance index; NA, not applicable; NH IMRangio, nonhyperemic angiography-derived index of microcirculatory resistance; pb-CFR, pressure-bounded coronary flow reserve; RRR, resistive reserve ratio.

Table 4 of the supplementary data. Main inclusion criteria

Source	Main inclusion criteria	Diagnosis
Takahashi et al. ¹ 2007	Patients with a first anterior-wall acute myocardial infarction treated with primary coronary angioplasty < 12 h after symptom onset	ACS
Meuwissen et al. ² 2008	Patients with intermediate coronary lesions (diameter stenosis 40%-70%) who deferred PCI	CCS
Fearon et al. ³ 2013	Patients presenting with STEMI after primary PCI	ACS
van de Hoef et al. ⁴ 2013	Patients presenting with STEMI after primary PCI	ACS
Ahn et al. ⁵ 2017	Patients with CAD who underwent FFR measurement	CCS*
de Waard et al. ⁶ 2018	Patients with both STEMI and NSTEMI after revascularization	ACS
Lee et al. ⁷ 2018	Patients with stable angina before coronary intervention	CCS
Murai et al. ⁸ 2018	Patients with STEMI after primary PCI	ACS
Hu et al. ⁹ 2019	Patients with 30% stenosis in a major epicardial coronary artery by visual estimation	CCS
Nishi et al. ¹⁰ 2019	Stable CAD, all patients underwent elective and successful PCI	CCS
Suda et al. ¹¹ 2019	Angina-like chest pain, nonobstructive CAD	CCS
Joo Myung Lee et al. ¹² 2020	Patients with stable angina, unstable angina, NSTEMI, or STEMI	CCS*
Lee et al. ¹³ 2020	Patients with stable angina, unstable angina, NSTEMI, or STEMI	CCS*
Maznyczka et al. ¹⁴ 2020	Patients with STEMI	ACS
Abdu et al. ¹⁵ 2021	Patients with myocardial infarction with no obstructive coronary atherosclerosis	ACS
Choi et al. ¹⁶ 2021	Patients with STEMI	ACS
Johnson et al. ¹⁷ 2021	Patients with intermediate coronary stenosis (diameter stenosis ≥50%) who underwent immediate PCI	CCS*
Kotronias et al. ¹⁸ 2021	Patients with STEMI	ACS
Scarsini et al. ¹⁹ 2021	Patients with STEMI	ACS
Toya et al. ²⁰ 2021	Patients with cardiac ischemia or angina without obstructive CAD	CCS

Dai et al. ²¹ 2022	Stable CAD patients who received PCI	CCS
Feng et al. ²² 2022	Patients with CCS	CCS
Liu et al. ²³ 2022	INOCA (all native coronary stenosis < 50% in all epicardial vessels and major branches)	CCS
FISIOIAM ²⁴ 2022	Patients with STEMI (nonculprit lesion)	ACS
Kim et al. ²⁵ 2022	CAD Patients with FFR 0.75-0.8	CCS
Lee et al. ²⁶ 2022	Patients with INOCA (typical angina symptoms and functional nonobstructive CAD)	CCS
Mejia-Renteria et al. ²⁷ 2022	Patients with stable angina, unstable angina, NSTEMI, or STEMI	CCS*

* These studies recruited all CAD population, but stable angina accounted for > 80% of the study population. Thus, they were categorized as CCS population.

ACS, acute coronary syndrome; CAD, coronary artery disease; CCS, chronic coronary syndrome; FFR, fractional flow reserve; INOCA, ischemia with no obstructive coronary atherosclerosis; NSTEMI, non–ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST segment elevation myocardial infarction.

Table 5 of the supplementary data. Baseline characteristics of included patients

Source	Age	Men No. %	BMI kg/m ²	Hypertension No. %	Diabetes mellitus No. %	Smoking history No. %	Dyslipidemia No. %
Takahashi et al. ¹ 2007	60 ± 9 (CFR ≤ 1.3) 62 ± 11 (CFR > 1.3)	81	NA	46	33	70	47
Meuwissen et al. ² 2008	61 (31 -84)	74	NA	36	17	30	61
Fearon et al. ³ 2013	56.8 ± 10.6	85.4	25.0 ± 3.7	45.1	24.1	46.6	66.8
van de Hoef et al. ⁴ 2013	56 ± 12	79	NA	22	6	51	25
Ahn et al. ⁵ 2017	64.9 ± 10.1 (CFR < 2) 62.0 ± 9.6 (CFR ≥ 2)	72	NA	65.8	31.6	24	62
de Waard et al. ⁶ 2018	60 ± 10	80	26.5 ± 3.8	41	23	51	42
Lee et al. ⁷ 2018	61.5 ± 10.2	70.9	24.5 ± 2.9	58.8	28.9	18.1	63.6
Murai et al. ⁸ 2018	63.7 ± 9.7	84	NA	68.7	33.7	37.3	44.6
Hu et al. ⁹ 2019	61.95 ± 10.02	76	NA	60.8	34.6	26.2	54.1
Nishi et al. ¹⁰ 2019	67 ± 9	82	25.6 ± 4.6	71	38	26	68
Suda et al. ¹¹ 2019	63.2 ± 12.3	60	NA	53	28	28	35
Joo Myung Lee et al. ¹² 2020	63.8 ± 10.3	74	25.0 ± 3.7	63	33.7	21.3	62.6

Lee et al. ¹³ 2020	64.7 ± 10.3	76.9	24.9 ± 3.7 (RRR ≥ 5) 24.9 ± 3.4 (RRR 3.5-4.9) 24.7 ± 3.5 (RRR 2.5-3.4) 24.8 ± 3.6 (RRR < 2.5)	65.6	35.7	21.4	63
Maznyczka et al. ¹⁴ 2020	59 ± 111	80	28.1 (24.6-31.0)	28.5	11.1	47.2	NA
Abdu et al. ¹⁵ 2021	64.47 ± 13.15 (calMR > 43U) 63.13 ± 12.98 (calMR ≤ 43U)	51.4	23.55 ± 3.77 (calMR > 43U) 23.78 ± 4.20 (calMR ≤ 43U)	50.5	17.4	46.8	18.3
Choi et al. ¹⁶ 2021	61.4 ± 11.2	74.8	24.1 ± 3.1	47.2	50.2	26.9	34.3
Johnson et al. ¹⁷ 2021	67 ± 10	74	NA	68	27	56	88
Kotronias et al. ¹⁸ 2021	62 ± 11	82	NA	46	16	42	84
Scarsini et al. ¹⁹ 2021	60.2 ± 10.7	85.9	NA	44.9	19.8	36.7	38.5
Toya et al. ²⁰ 2021	51.4 ± 12.5	34	28.1 (24.5-32.7)	43	11	47	55
Dai et al. ²¹ 2022	65.0 ± 8.7	69.6	24.6 ± 3.0	72.5	36.2	26.1	8.0
Feng et al. ²² 2022	64.95 ± 9.46	69.1	22.49 (21.33-23.28) (normal weight) 26.45 (25.08-27.98) (overweight)	70.6	34	24.1	20.9
Liu et al. ²³ 2022	60.6 ± 9.5	41.1	25.00 ± 3.38	50.3	14.6	15.2	10.6

FISIOIAM ²⁴ 2022	62 ± 10	87	28.77 ± 4.5 (CFR ≥ 2) 27.01 ± 3.54 (CFR < 2)	50.6	13.3	67.5	38.6
Kim <i>et al.</i> ²⁵ 2022	63.9 ± 10.2	79.1	26.3 ± 3.8	66.2	32.7	21.8	71.2
Lee <i>et al.</i> ²⁶ 2022	63.0 ± 10.6 (CFR ≤ 2.5) 59.7 ± 9.4 (CFR > 2.5) 62.7 ± 9.5 (INOCA, CFR ≤ 2.5) 63.0 ± 10.5 (INOCA, CFR > 2.5)	64.1	25.9 ± 4.9 (CFR ≤ 2.5) 26.6 ± 3.8 (CFR > 2.5) 26.6 ± 4.2 (INOCA, CFR ≤ 2.5) 26.6 ± 4.2 (INOCA, CFR > 2.5)	48.8	16.7	25.8	56.1
Mejia-Renteria <i>et al.</i> ²⁷ 2022	63 (57-70)	76	24.6 (22.8-26.3)	64	33	20	68

Values are expressed as mean ± standard deviation or median (P₂₅, P₇₅) or No. (%).

BMI, body mass index; CFR, coronary flow reserve; caIMR, coronary angiography-derived index of microcirculatory resistance; INOCA, ischemia with

no obstructive coronary atherosclerosis; NA, not applicable; RRR, resistive reserve ratio.

Figure 1 of the supplementary data. Flow diagram. Preferred reporting items for systematic reviews and meta-analyses 2020 demonstrating search results and study selection.

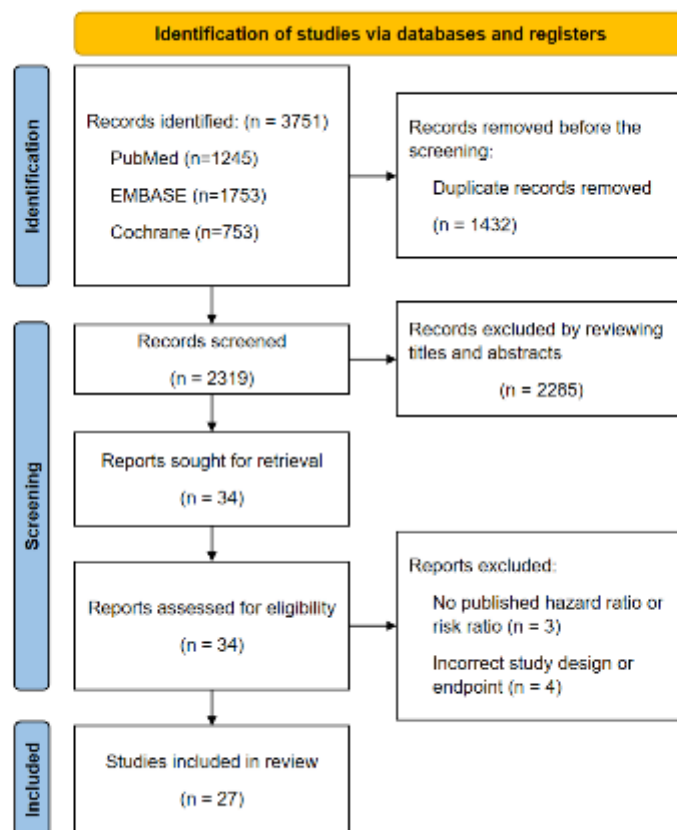
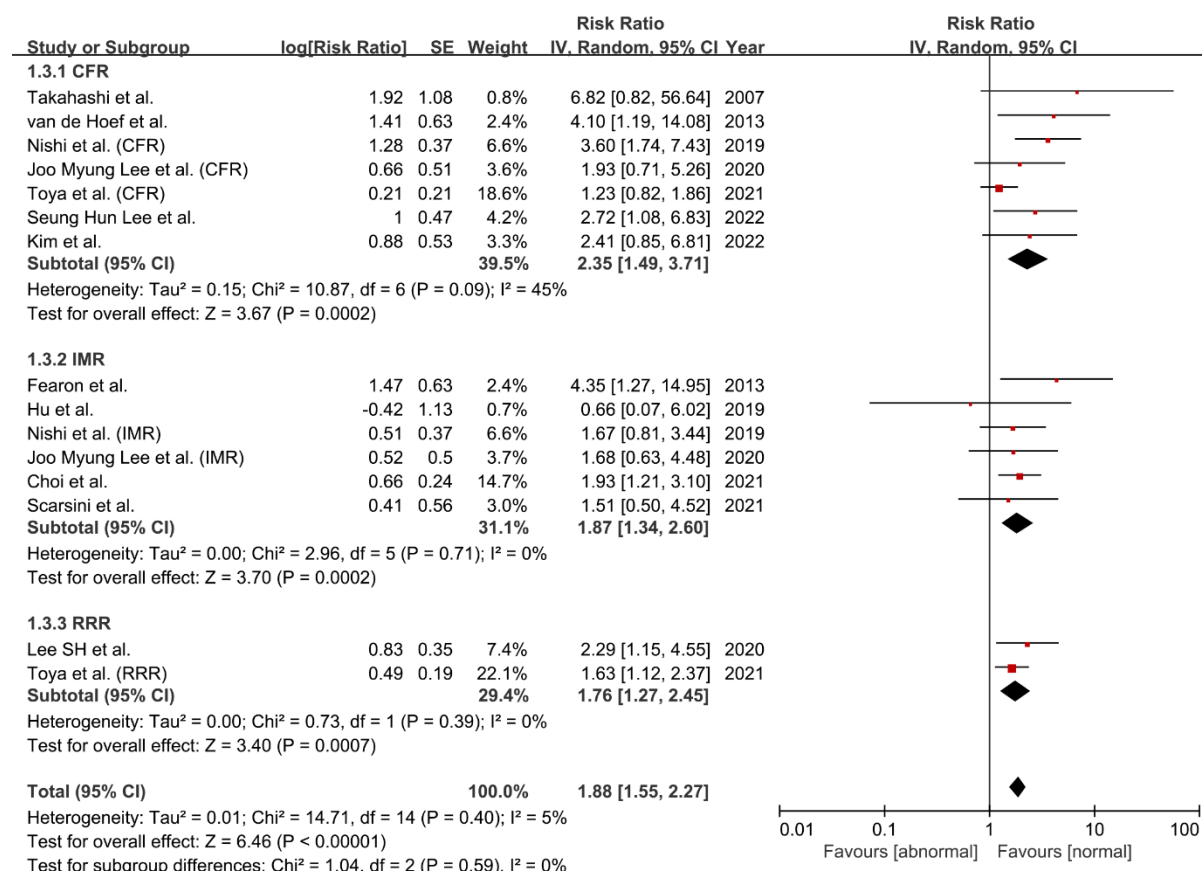


Figure 2 of the supplementary data. Subgroup analysis for all-cause death stratified by measurement modalities.



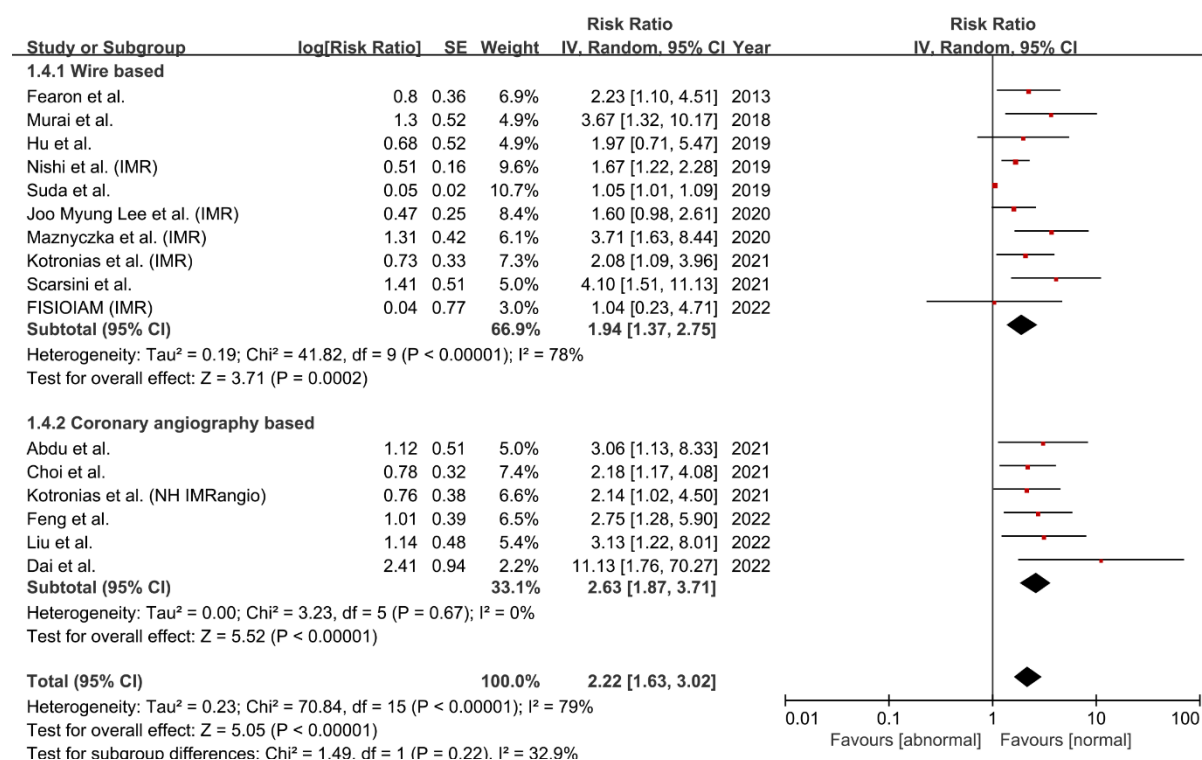
Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines.

Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

CFR, coronary flow reserve; 95%CI, 95% confidence intervals; IMR, index of microvascular resistance; IV, inverse-variance; RRR, resistive reserve ratio; SE, standard error.

References: Takahashi et al.¹ van de Hoef et al.⁴ Fearon et al.³ Nishi et al.¹⁰ Hu et al.⁹ Joo Myung Lee et al.¹² Lee SH et al.¹³ Scarsini et al.¹⁹ Toya et al.²⁰ Choi et al.¹⁶ Kim et al.²⁵ Seung Hun Lee et al.²⁶

Figure 3 of the supplementary data. Subgroup analysis for MACE stratified by the measurement method of IMR



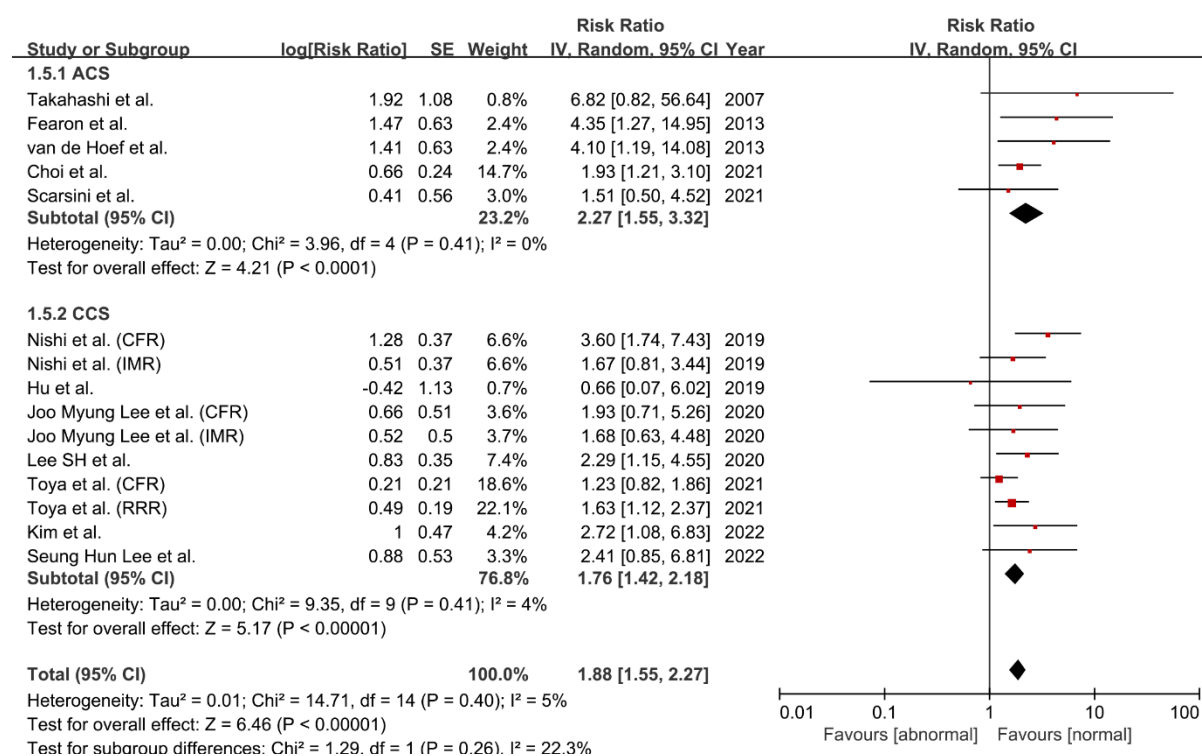
Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines.

Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

95%CI, 95% confidence intervals; IMR, index of microvascular resistance; IV, inverse-variance; MACE, major adverse cardiovascular event; NH IMRangio, nonhyperemic angiography-derived index of microcirculatory resistance; SE, standard error.

References: Fearon et al.³ Murai et al.⁸ Hu et al.⁹ Nishi et al.¹⁰ Suda et al.¹¹ Joo Myung Lee et al.¹² Maznyczka et al.¹⁴ Kotronias et al.¹⁸ Scarsini et al.¹⁹ FISIOIAM.²⁴ Abdu et al.¹⁵ Choi et al.¹⁶ Feng et al.²² Liu et al.²³ Dai et al.²¹

Figure 4 of the supplementary data. Subgroup analysis for all-cause death stratified by CAD populations



Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines.

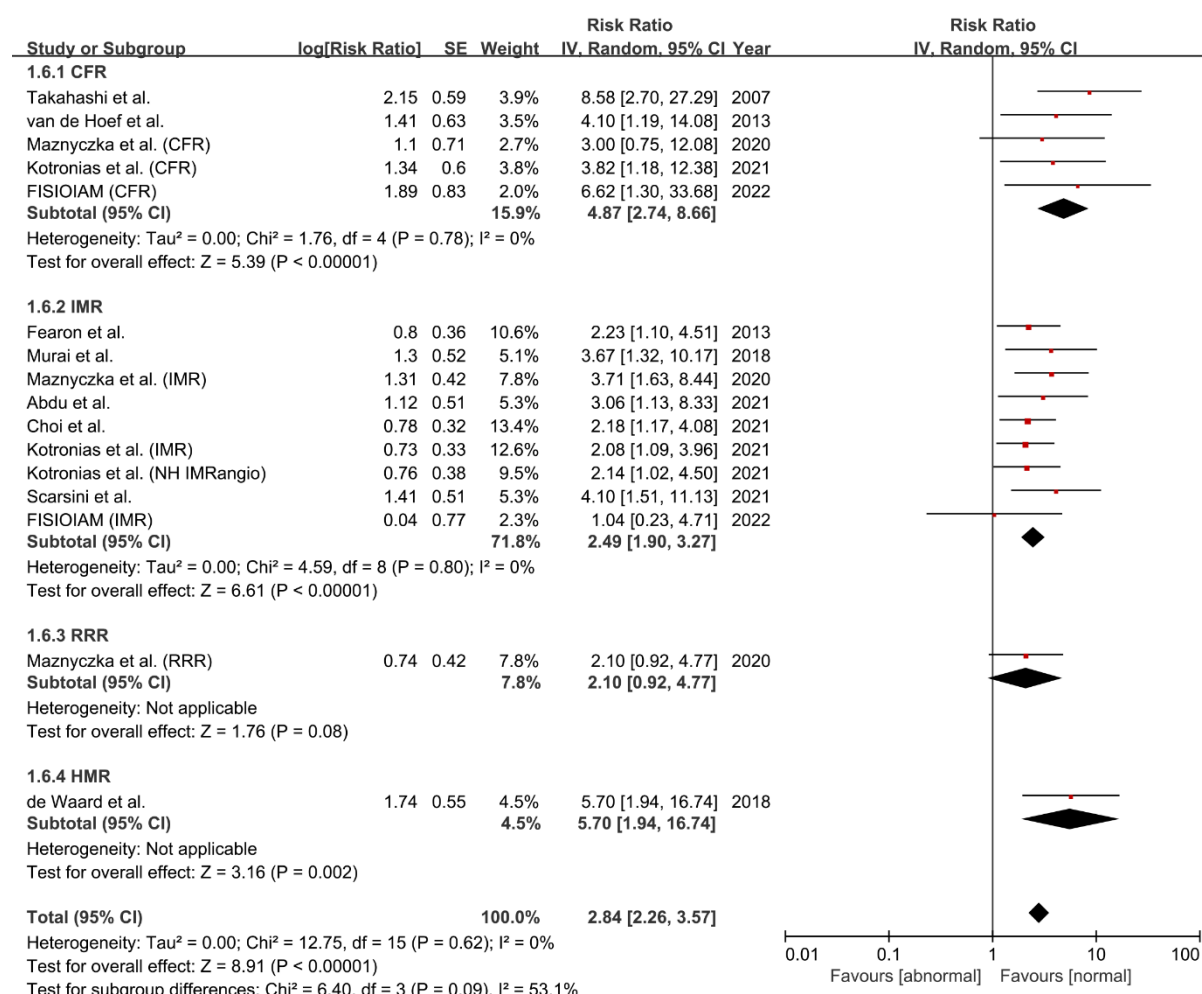
Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

CAD, coronary artery disease; CFR, coronary flow reserve; 95%CI, 95% confidence interval; IV, inverse-variance; IMR, index of microvascular resistance; RRR, resistive reserve ratio; SE, standard error.

References: Takahashi et al.¹ Fearon et al.³ van de Hoef et al.⁴ Choi et al.¹⁶ Scarsini et al.¹⁹ Nishi et al.¹⁰

Hu et al.⁹ Joo Myung Lee et al.¹² Lee SH et al.¹³ Toya et al.²⁰ Kim et al.²⁵ Seung Hun Lee et al.²⁶

Figure 5 of the supplementary data. Subgroup analysis for MACE stratified by measurement modalities in ACS population



Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines.

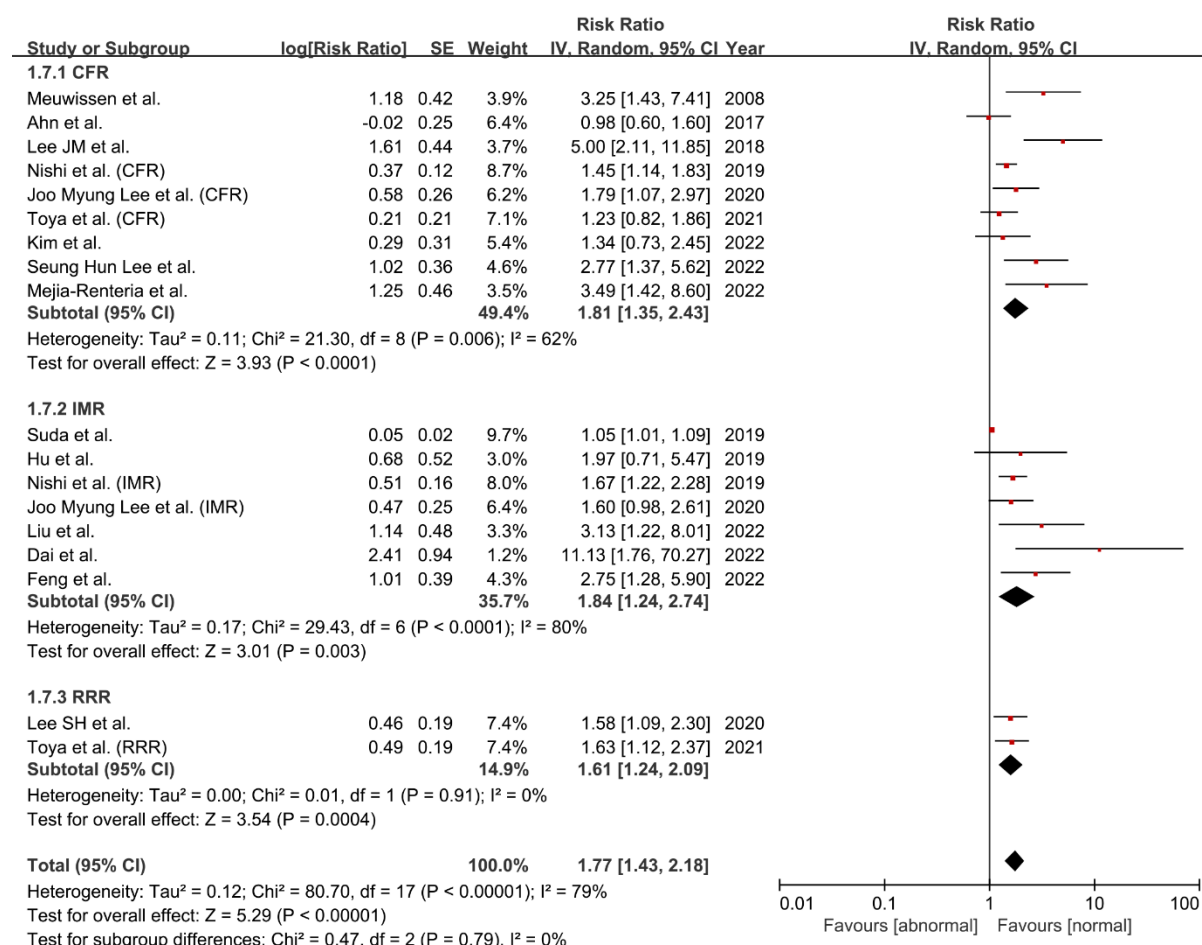
Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

ACS, acute coronary syndrome; CFR, coronary flow reserve; 95%CI, 95% confidence intervals; HMR, hyperemic microvascular resistance; IMR, index of microvascular resistance; IV, inverse-variance; MACE, major adverse cardiovascular event; NH IMRangio, nonhyperemic angiography-derived index of microcirculatory resistance; RRR, resistive reserve ratio; SE, standard error.

Xu Y et al. *Invasive assessment of coronary microvascular dysfunction and cardiovascular outcomes across the full spectrum of CAD: a meta-analysis.* Rev Esp Cardiol. 2024.

References: Takahashi et al.¹ van de Hoef et al.⁴ Maznyczka et al.¹⁴ Kotronias et al.¹⁸ FISIOIAM.²⁴ Fearon et al.³ Murai et al.⁸ Abdu et al.¹⁵ Choi et al.¹⁶ Scarsini et al.¹⁹ de Waard et al.⁶

Figure 6 of the supplementary data. Subgroup analysis for MACE stratified by measurement modalities in CCS population

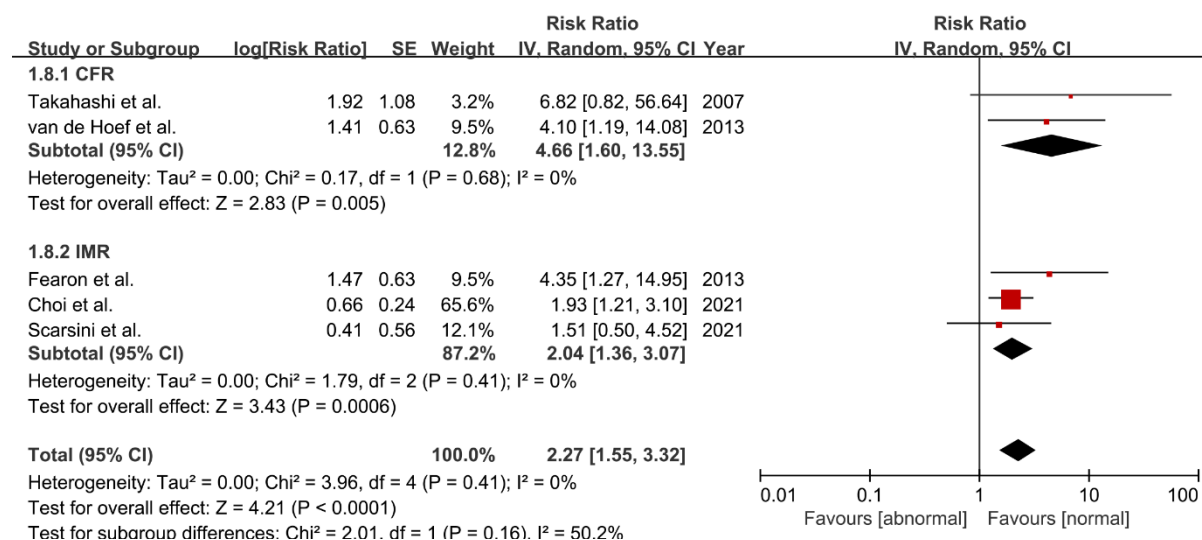


Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines. Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

CCS, chronic coronary syndrome; CFR, coronary flow reserve; 95%CI, 95% confidence intervals; IMR, index of microvascular resistance; IV, inverse-variance; MACE, major adverse cardiovascular event; RRR, resistive reserve ratio; SE, standard error.

Reference: Meuwissen et al.² Ahn et al.⁵ Lee JM et al.⁷ Nishi et al.¹⁰ Joo Myung Lee et al.¹² Toya et al.²⁰ Kim et al.²⁵ Seung Hun Lee et al.²⁶ Mejia-Renteria et al.²⁷ Suda et al.¹¹ Hu et al.⁹ Liu et al.²³ Dai et al.²¹ Feng et al.²² Lee SH et al.¹³ Toya et al.²⁰

Figure 7 of the supplementary data. Subgroup analysis for all-cause death stratified by measurement modalities in ACS population



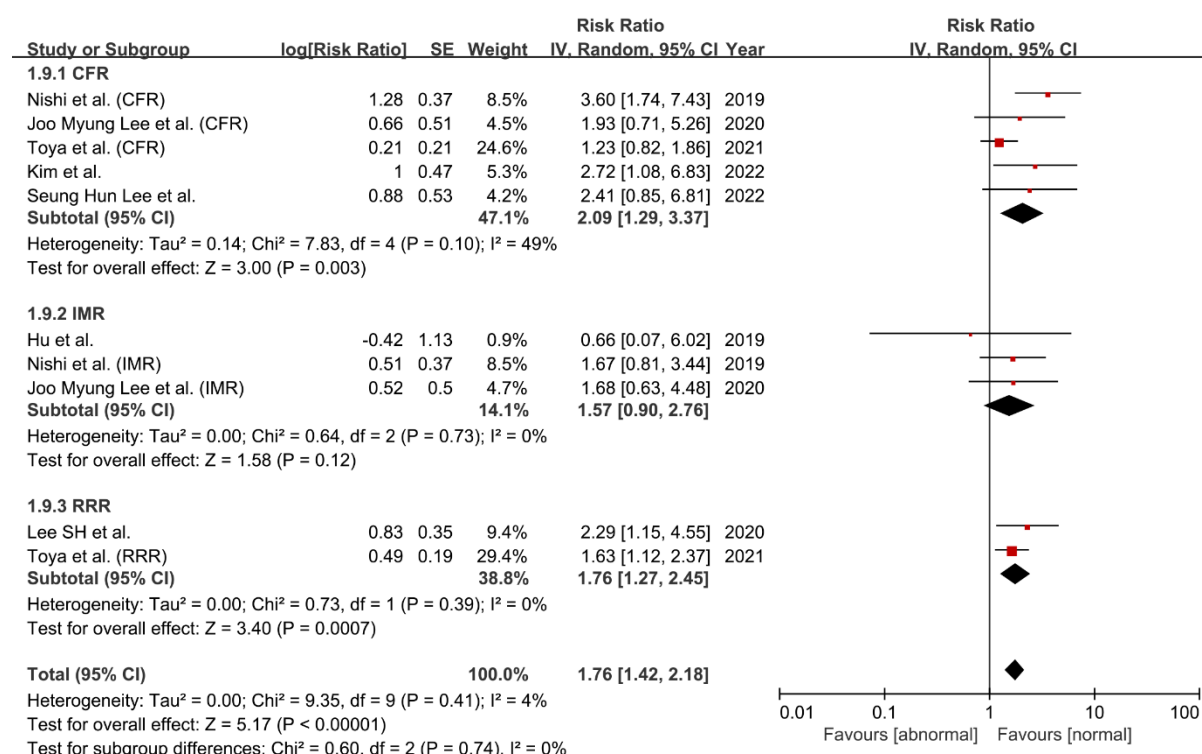
Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines.

Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

ACS, acute coronary syndrome; CFR, coronary flow reserve; 95%CI, 95% confidence intervals; IMR, index of microvascular resistance; IV, inverse-variance; SE, standard error.

References: Takahashi et al.¹ van de Hoef et al.⁴ Fearon et al.³ Choi et al.¹⁶ Scarsini et al.¹⁹

Figure 8 of the supplementary data. Subgroup analysis for all-cause death stratified by measurement modalities in CCS population



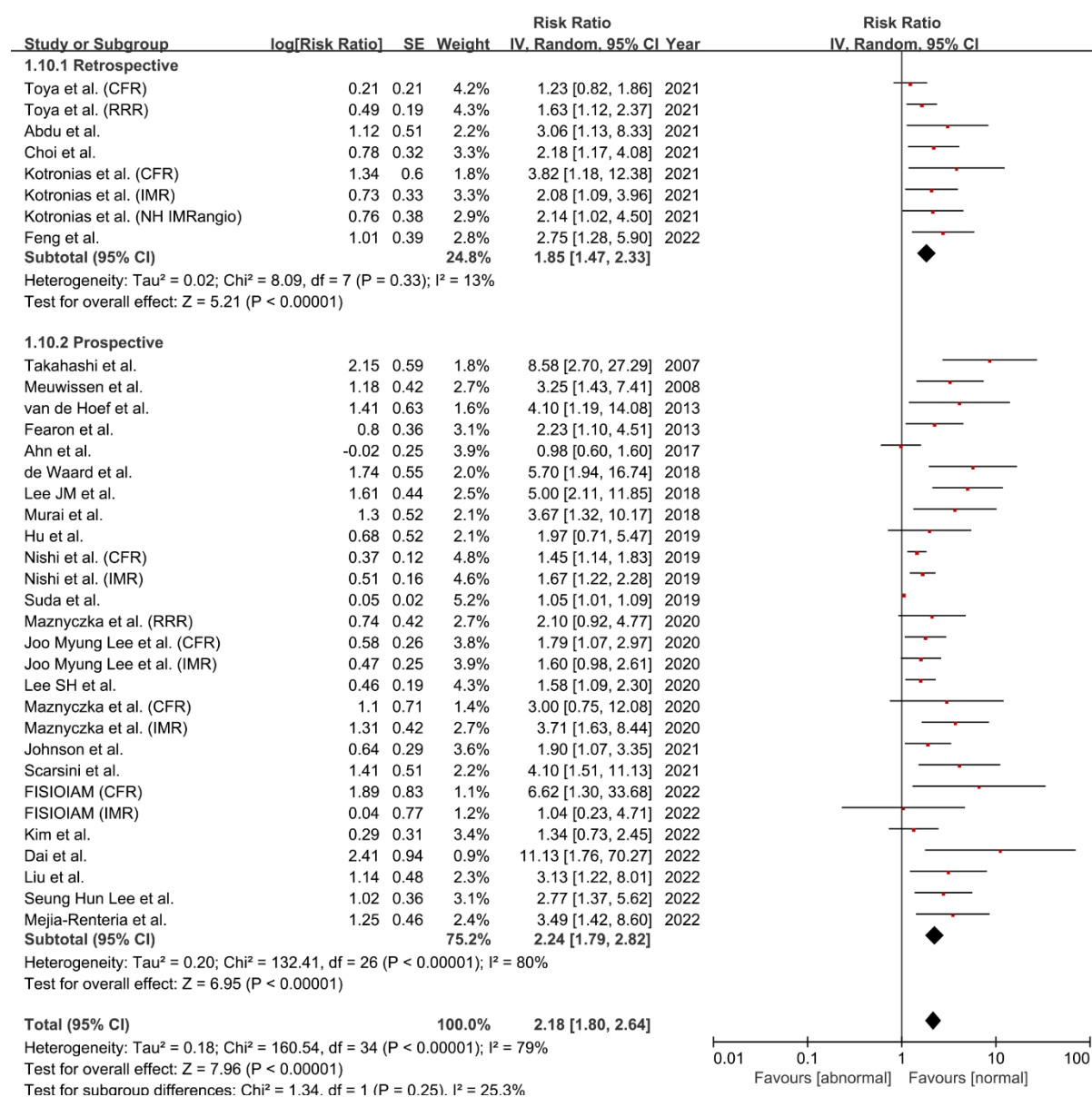
Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines.

Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

CCS, chronic coronary syndrome; CFR, coronary flow reserve; 95%CI, 95% confidence interval; IMR, index of microvascular resistance; IV, inverse-variance; RRR, resistive reserve ratio; SE, standard error.

References: Nishi et al.¹⁰ Joo Myung Lee et al.¹² Toya et al.²⁰ Kim et al.²⁵ Seung Hun Lee et al.²⁶ Hu et al.⁹ Lee SH et al.¹³

Figure 9 of the supplementary data. Subgroup analysis for MACE stratified by study design

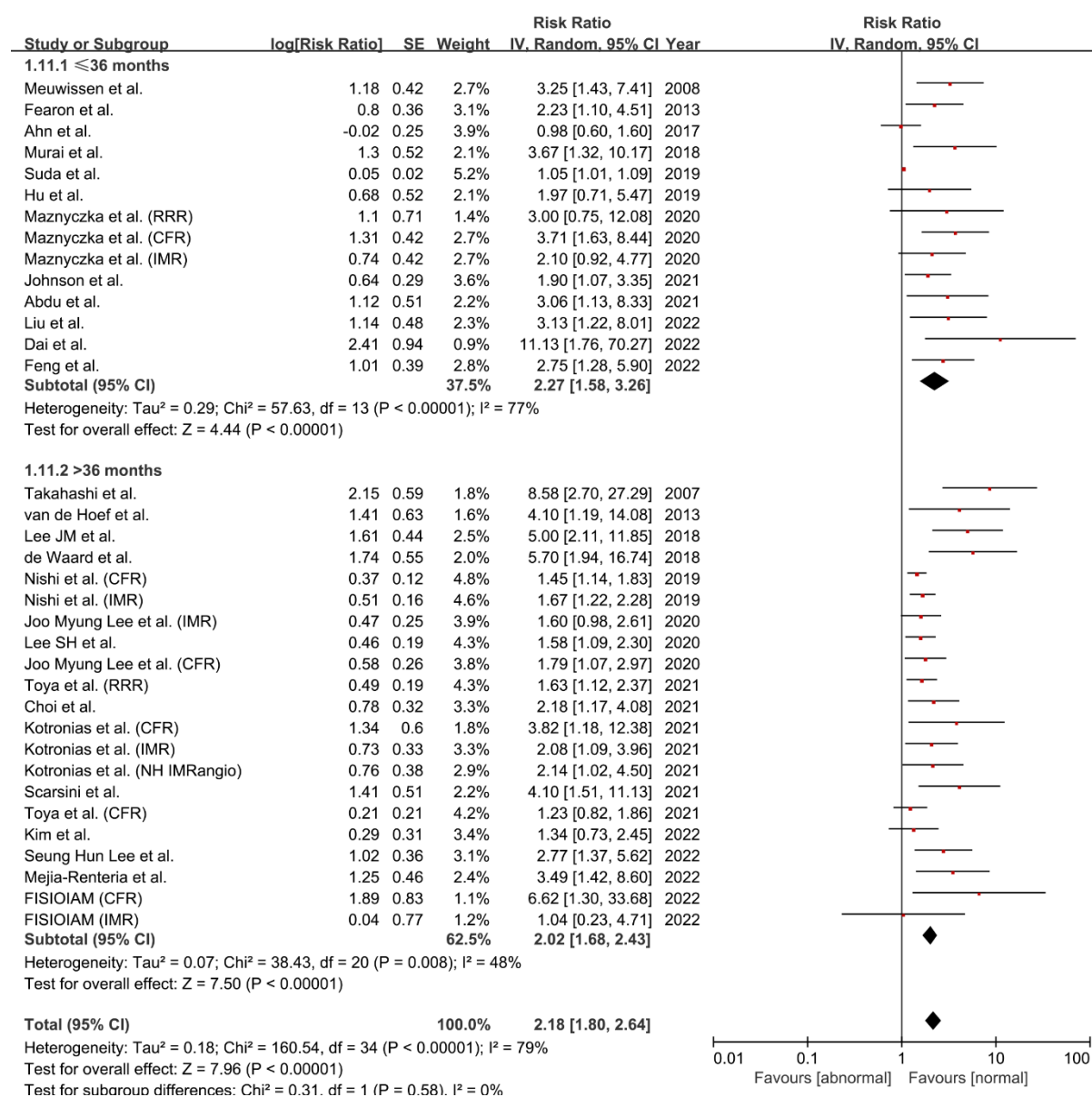


Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines. Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

CFR, coronary flow reserve; 95%CI, 95% confidence interval; IMR, index of microvascular resistance; IV, inverse-variance; MACE, major adverse cardiovascular event; NH IMRangio, nonhyperemic angiography-derived index of microcirculatory resistance; RRR, resistive reserve ratio; SE, standard error.

References: Takahashi et al.¹ Meuwissen et al.² Fearon et al.³ van de Hoef et al.⁴ Ahn et al.⁵ Murai et al.⁸ de Waard et al.⁶ Lee JM et al.⁷ Nishi et al.¹⁰ Suda et al.¹¹ Hu et al.⁹ Joo Myung Lee et al.¹² Lee SH et al.¹³ Maznyczka et al.¹⁴ Abdu et al.¹⁵ Choi et al.¹⁶ Johnson et al.¹⁷ Kotronias et al.¹⁸ Scarsini et al.¹⁹ Toya et al.²⁰ FISIOIAM.²⁴ Kim et al.²⁵ Seung Hun Lee et al.²⁶ Dai et al.²¹ Feng et al.²² Liu et al.²³ Mejia-Renteria et al.²⁷

Figure 10 of the supplementary data. Subgroup analysis for MACE stratified by follow-up duration



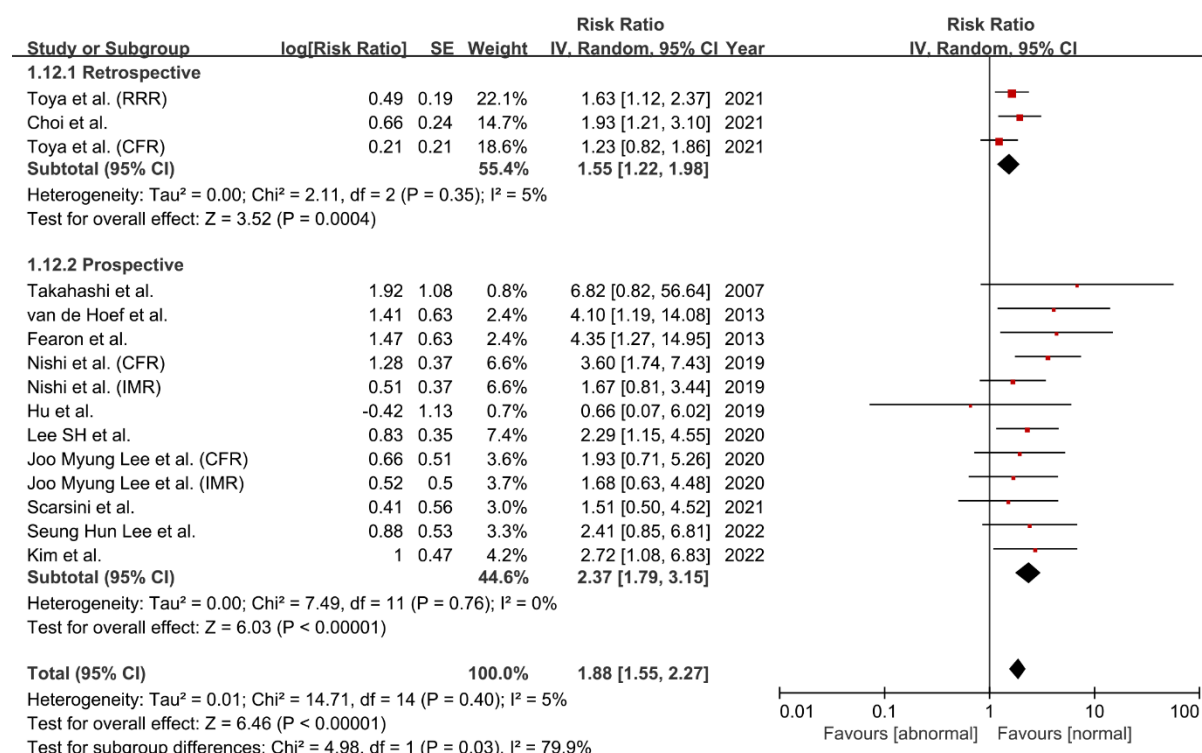
Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines.

Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

95%CI, 95% confidence interval; CCS, chronic coronary syndrome; CFR, coronary flow reserve; IMR, index of microvascular resistance; IV, inverse-variance; RRR, resistive reserve ratio; SE, standard error.

References: Takahashi et al.¹ Meuwissen et al.² Fearon et al.³ van de Hoef et al.⁴ Ahn et al.⁵ Murai et al.⁸ de Waard et al.⁶ Lee JM et al.⁷ Nishi et al.¹⁰ Suda et al.¹¹ Hu et al.⁹ Joo Myung Lee et al.¹² Lee SH et al.¹³ Maznyczka et al.¹⁴ Abdu et al.¹⁵ Choi et al.¹⁶ Johnson et al.¹⁷ Kotronias et al.¹⁸ Scarsini et al.¹⁹ Toya et al.²⁰ FISIOIAM.²⁴ Kim et al.²⁵ Seung Hun Lee et al.²⁶ Dai et al.²¹ Feng et al.²² Liu et al.²³ Mejia-Renteria et al.²⁷

Figure 11 of the supplementary data. Subgroup analysis for all-cause death stratified by study design



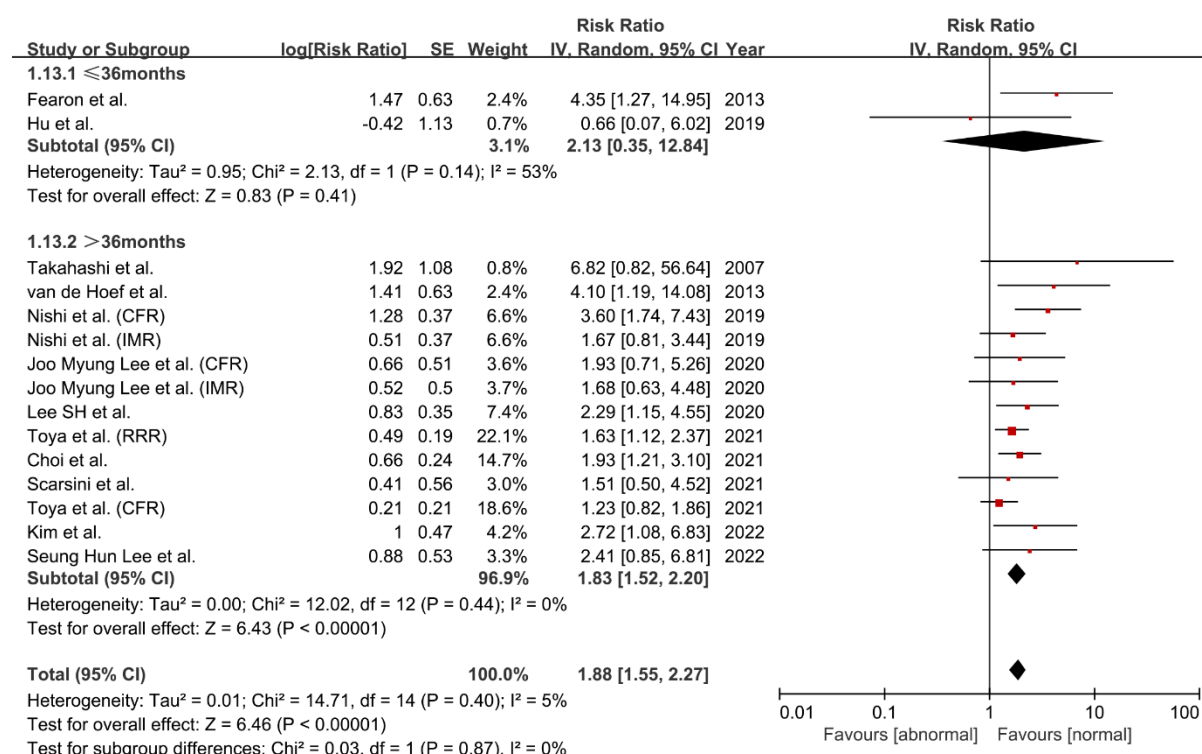
Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines.

Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

CFR, coronary flow reserve; 95%CI, 95% confidence interval; IMR, index of microvascular resistance; IV, inverse-variance; RRR, resistive reserve ratio; SE, standard error.

References: Takahashi et al.¹ van de Hoef et al.⁴ Fearon et al.³ Nishi et al.¹⁰ Hu et al.⁹ Joo Myung Lee et al.¹² Lee SH et al.¹³ Scarsini et al.¹⁹ Toya et al.²⁰ Choi et al.¹⁶ Kim et al.²⁵ Seung Hun Lee et al.²⁶

Figure 12 of the supplementary data. Subgroup analysis for all-cause death stratified by follow-up duration



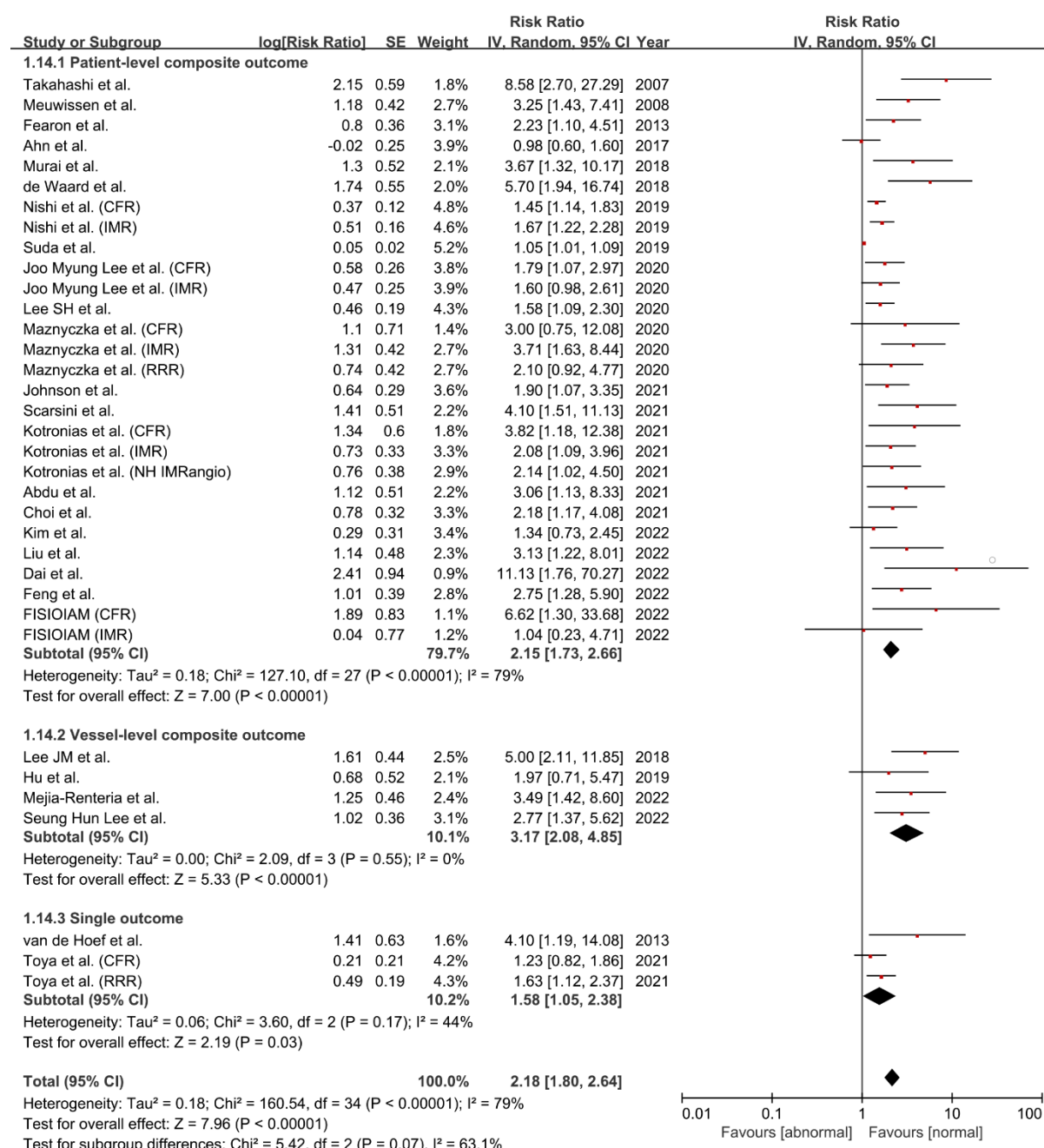
Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines.

Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

CCS, chronic coronary syndrome; CFR, coronary flow reserve; 95%CI, 95% confidence interval; IMR, index of microvascular resistance; IV, inverse-variance; RRR, resistive reserve ratio; SE, standard error.

References: Takahashi et al.¹ van de Hoef et al.⁴ Fearon et al.³ Nishi et al.¹⁰ Hu et al.⁹ Joo Myung Lee et al.¹² Lee SH et al.¹³ Scarsini et al.¹⁹ Toya et al.²⁰ Choi et al.¹⁶ Kim et al.²⁵ Seung Hun Lee et al.²⁶

Figure 13 of the supplementary data. Subgroup analysis for MACE stratified by the definition of outcomes

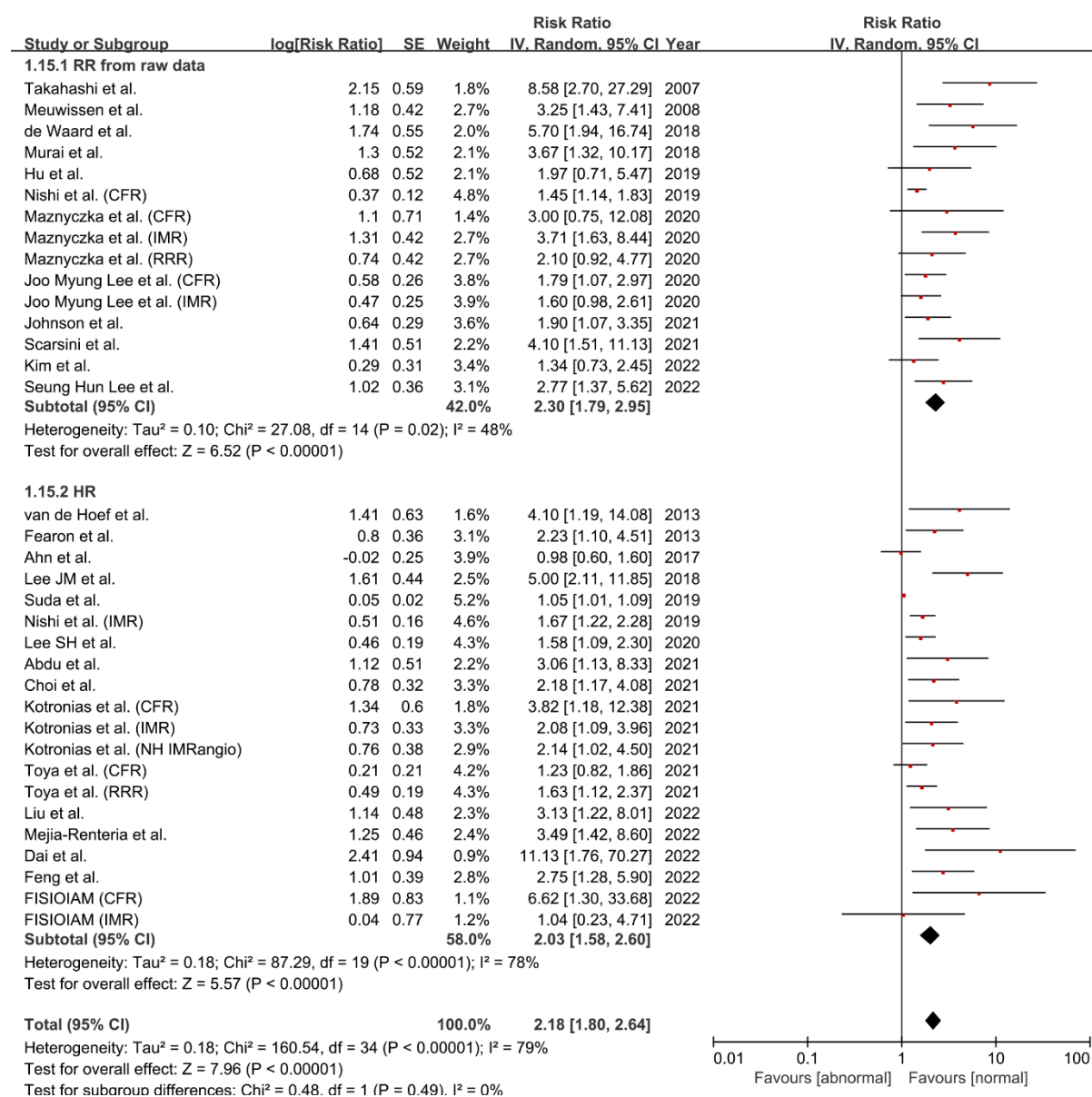


Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines. Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

CCS, chronic coronary syndrome; CFR, coronary flow reserve; 95%CI, 95% confidence intervals; IMR, index of microvascular resistance; IV, inverse-variance; RRR, resistive reserve ratio; SE, standard error.

References: Takahashi et al.¹ Meuwissen et al.² Fearon et al.³ van de Hoef et al.⁴ Ahn et al.⁵ Murai et al.⁸ de Waard et al.⁶ Lee JM et al.⁷ Nishi et al.¹⁰ Suda et al.¹¹ Hu et al.⁹ Joo Myung Lee et al.¹² Lee SH et al.¹³ Maznyczka et al.¹⁴ Abdu et al.¹⁵ Choi et al.¹⁶ Johnson et al.¹⁷ Kotronias et al.¹⁸ Scarsini et al.¹⁹ Toya et al.²⁰ FISIOIAM.²⁴ Kim et al.²⁵ Seung Hun Lee et al.²⁶ Dai et al.²¹ Feng et al.²² Liu et al.²³ Mejia-Renteria et al.²⁷

Figure 14 of the supplementary data. Subgroup analysis for MACE stratified by the data type



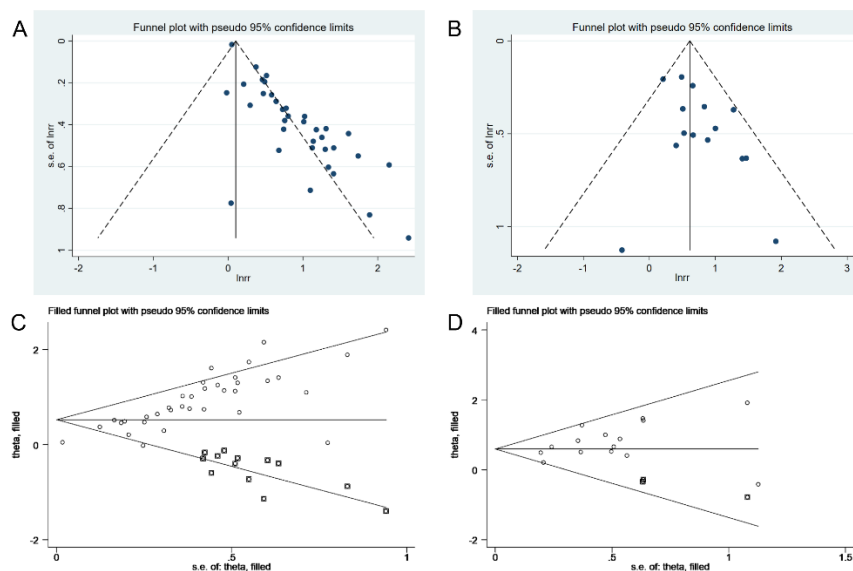
Risk ratios for individual studies are indicated by squares, and 95% CIs are indicated by horizontal lines.

Pooled estimates and their 95% CIs are represented by diamonds. The sizes of the squares and the diamonds are proportional to the weight assigned to the relative effect sizes.

CCS, chronic coronary syndrome; CFR, coronary flow reserve; 95%CI, 95% confidence interval; IMR, index of microvascular resistance; IV, inverse-variance; RRR, resistive reserve ratio; SE, standard error.

References: Takahashi et al.¹ Meuwissen et al.² Fearon et al.³ van de Hoef et al.⁴ Ahn et al.⁵ Murai et al.⁸
de Waard et al.⁶ Lee JM et al.⁷ Nishi et al.¹⁰ Suda et al.¹¹ Hu et al.⁹ Joo Myung Lee et al.¹² Lee SH et al.¹³
Maznyczka et al.¹⁴ Abdu et al.¹⁵ Choi et al.¹⁶ Johnson et al.¹⁷ Kotronias et al.¹⁸ Scarsini et al.¹⁹ Toya et
al.²⁰ FISIOIAM.²⁴ Kim et al.²⁵ Seung Hun Lee et al.²⁶ Dai et al.²¹ Feng et al.²² Liu et al.²³ Mejia-Renteria et
al.²⁷

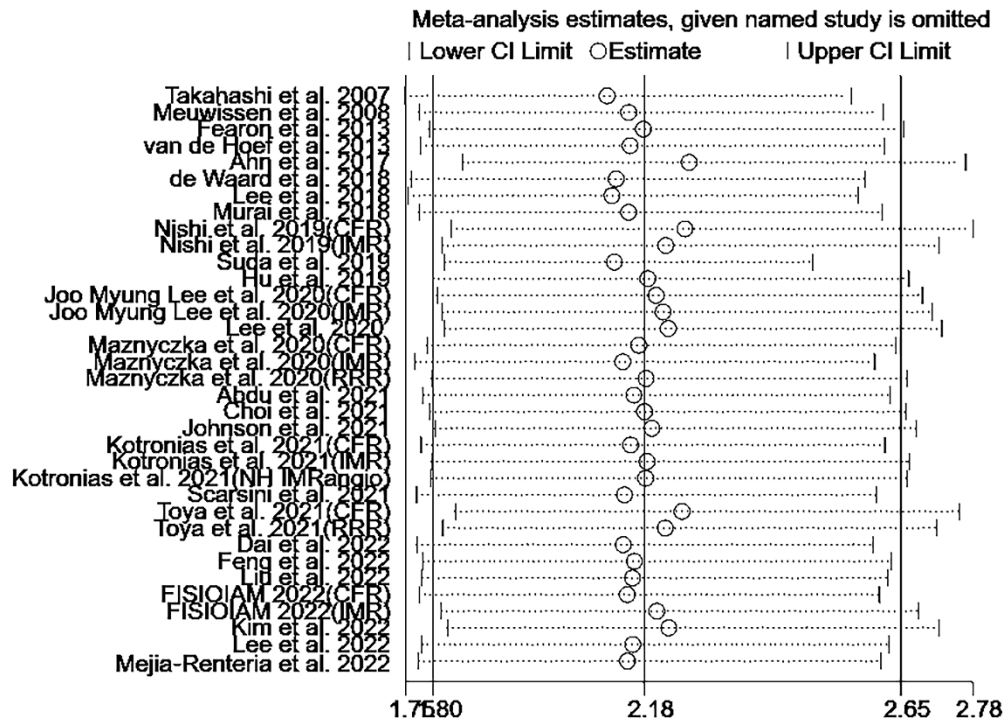
Figure 15 of the supplementary data. Publication bias for MACE and all-cause death



A: funnel plot assesses publication bias for MACE. The asymmetry on both sides of the funnel plot suggested the existence of publication bias. Egger’s test demonstrated the possibility of publication bias ($P < .05$). B: funnel plot assesses publication bias for all-cause death. The asymmetry on both sides of the funnel plot suggested the existence of publication bias. Egger’s test demonstrated the possibility of publication bias ($P = .05$). C: publication bias for MACE was corrected by the trim-and-fill method. The square below represents supplementary studies by trim-and-fill method. Thirteen additional studies were added to control for publication bias, and the result showed that patients with CMD had a higher risk of MACE (RR, 1.69; 95%CI, 1.43-1.99; $P < .01$). D: publication bias for all-cause death was corrected by the trim-and-fill method. The square below represents supplementary studies by the trim-and-fill method. Three additional studies were added to control for publication bias, and the result showed that patients with CMD had a higher risk of all-cause death (RR, 1.81; 95%CI, 1.46-2.23; $P < .01$).

CMD, coronary microvascular dysfunction; lnrr, natural logarithm of the risk ratio MACE, major adverse cardiovascular event; RR, risk ratio; SE, standard error.

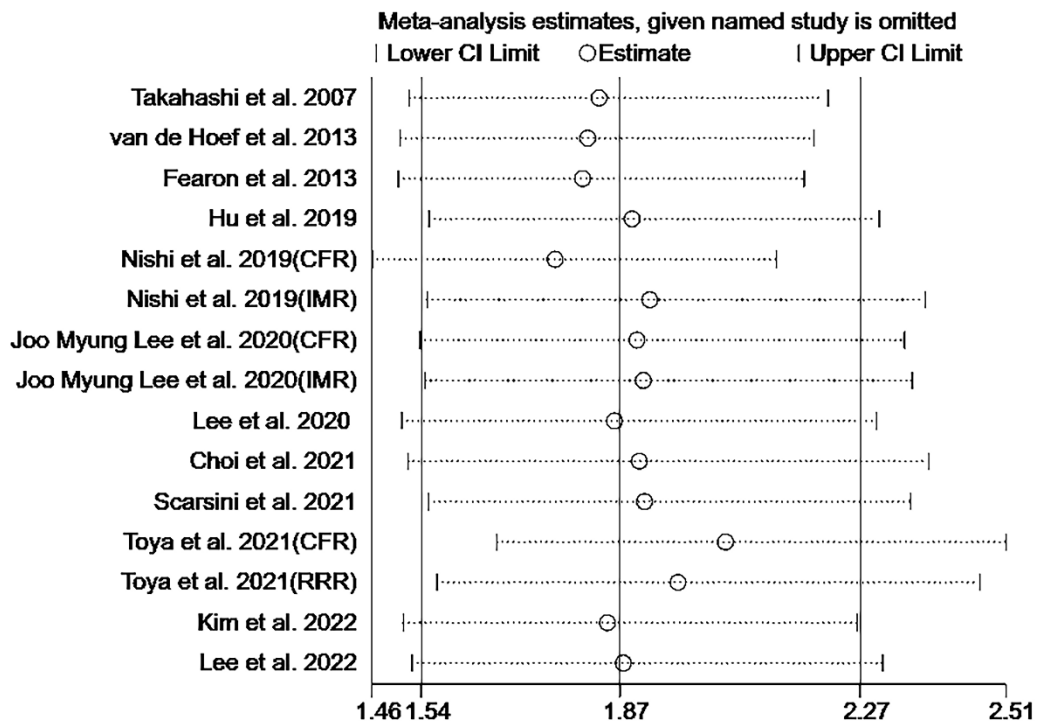
Figure 16 of the supplementary data. Sensitivity analysis for MACE



CFR, coronary flow reserve; CI, confidence intervals; IMR, index of microvascular resistance; MACE, major adverse cardiovascular event; NH IMRangio, nonhyperemic angiography-derived index of microcirculatory resistance; RRR, resistive reserve ratio.

References: Takahashi et al.¹Meuwissen et al.² Fearon et al.³ van de Hoef et al.⁴ Ahn et al.⁵ Murai et al.⁸ de Waard et al.⁶ Lee et al. 2018⁷ Nishi et al.¹⁰ Suda et al.¹¹ Hu et al.⁹ Joo Myung Lee et al.¹² Lee et al. 2020¹³ Maznyczka et al.¹⁴ Abdu et al.¹⁵ Choi et al.¹⁶ Johnson et al.¹⁷ Kotronias et al.¹⁸ Scarsini et al.¹⁹ Toya et al.²⁰ FISIOIAM.²⁴ Kim et al.²⁵ Lee et al. 2022²⁶ Dai et al.²¹ Feng et al.²² Liu et al.²³ Mejia-Renteria et al.²⁷

Figure 17 of the supplementary data. Sensitivity analysis for all-cause death



CFR, coronary flow reserve; CI, confidence intervals; IMR, index of microvascular resistance; RRR, resistive reserve ratio.

References: Takahashi et al.¹ van de Hoef et al.⁴ Fearon et al.³ Nishi et al.¹⁰ Hu et al.⁹ Joo Myung Lee et al.¹² Lee et al. 2020¹³ Scarsini et al.¹⁹ Toya et al.²⁰ Choi et al.¹⁶ Kim et al.²⁵ Lee et al. 2022²⁶

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