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REVIEW

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Revascularization strategies for patients with established chronic coronary syndrome

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Abstract

Coronary artery disease is the most common type of cardiovascular disease, leading to high mortality rates worldwide. Although the vast majority can be treated effectively and safely by medical therapy, revascularization strategies remain essential for numerous patients. Outcomes of both percutaneous coronary intervention and coronary artery bypass grafting improve in a rapid pace, resulting from technical innovation and ongoing research. Progress has been achieved by technical improvements in coronary stents, optimal coronary target and graft selection, and the availability of minimally invasive surgical strategies. Besides technical progress, evidence-based patient-tailored decision-making by the Heart Team is the basic precondition for optimal outcome. The combination of fast innovation and long-term clinical evaluations creates a dynamic field. Research outcomes should be carefully interpreted according to the techniques used and the trial's design. Therefore, more and more trial outcomes suggest that revascularization strategies should be tailored towards the specific patient. Although the European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines on myocardial revascularization date from 2018 and a large variety of trial outcomes on revascularization strategies in chronic coronary syndrome have been published since, we aim to provide an updated overview within this review.

KEYWORDS

chronic coronary syndrome, coronary revascularization, patient-tailored

1 | INTRODUCTION

Approximately 126 million individuals suffer from coronary artery disease (CAD), resulting in 9 million annual deaths.[1,2] To reduce the high burden of coronary deaths, various algorithms and guidelines were successfully introduced. For asymptomatic patients with cardiovascular risk factors, the Systematic Coronary Risk Evaluation (SCORE) II algorithm estimates the individual's 10-year risk of cardiovascular events in order to initiate primary prevention such as lifestyle interventions and eventual drug therapy. Symptomatic patients, on the contrary, require medical therapy for symptom reduction and/or prognosis improvement, including lifestyle interventions,

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optimal medical therapy and eventual revascularization therapy (see Figure 1).[3]

Outcomes of symptomatic patients with stable CAD, recently redefined as a chronic coronary syndrome (CCS), improved rapidly due to innovations in pharmacotherapy and revascularization techniques, as well as evidence-based decision-making.[3] Yet, complete evidence on new therapies includes up to 10 years of follow-up. This combination of rapid innovation and long-term evaluation creates a dynamic field with widespread use before the completion of long-term evaluations.

Notwithstanding this fast evolution, the current 2018 European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines on myocardial revascularization are heavily debated and partly outdated.[4] Therefore, we present a brief updated overview of revascularization strategies for CCS management in order to provide cardiologists and cardiac surgeons with up-to-date information on the indications for revascularization and the revascularization strategies.

We searched various databases (MEDLINE, Embase, Cochrane and ClinicalTrials.gov) from database start-up to April 2022, as well as grey literature and cross-references. Typical search terms were coronary artery disease, revascularization, optimal medical therapy, percutaneous coronary intervention and coronary artery bypass grafting. Reporting in this literature review conforms to broad EQUATOR guidelines.[5]

Within this review, we present sections on: (1) indications for revascularization, outlining the diagnostic pathway and absolute revascularization indications compared with the strategy of optimal medical therapy; (2) selection of revascularization strategies, describing the strategy of PCI versus CABG on behalf of anatomical complexity, completeness of revascularization and comorbidities; (3) percutaneous coronary intervention, elaborating on the improvements following the introduction of drug-eluting stents and fractional flow reserve; and (4) coronary artery bypass grafting, presenting insights on donor graft materials, on- versus off-pump surgery, and minimally invasive strategies.

2 | INDICATIONS FOR REVASCULARIZATION

According to the European Society of Cardiology/European Association for Cardio-Thoracic Surgery 2018 guidelines, the main indication for revascularization is symptom reduction. Figure 1 displays the approach of diagnostic pathways for patients with suspected or established CCS. The accompanying ESC 2019 guidelines on CCS management indicate a class IA recommendation for low-risk/low-suspicious patients to undergo coronary computed tomography angiography (CCTA) to exclude CAD, for high-risk/high-suspicious patients to be treated medically with possible (non)invasive testing, and for intermediate patients to first receive medical treatment and subsequent CCTA or ischaemia detection if symptoms persist. Symptomatic patients with established CCS should undergo (non)invasive tests to determine the event risk.[3] Fractional flow reserve is frequently used as an additional functional assessment to coronary angiography and received a class IA recommendation for patients with intermediate-grade stenosis of 40%–90% on CAG without proven ischaemia on noninvasive imaging, and a class IIB recommendation for patients with multivessel CAD.[4] Thus, the guidelines recommend revascularization in patients with limited angina and insufficient response to optimal medical therapy, based on a coronary stenosis with fractional flow reserve (FFR) ≤0.80, or >90% stenosis in a major coronary artery by visual assessment on coronary angiography (class IA).[4] Multiple studies have shown that

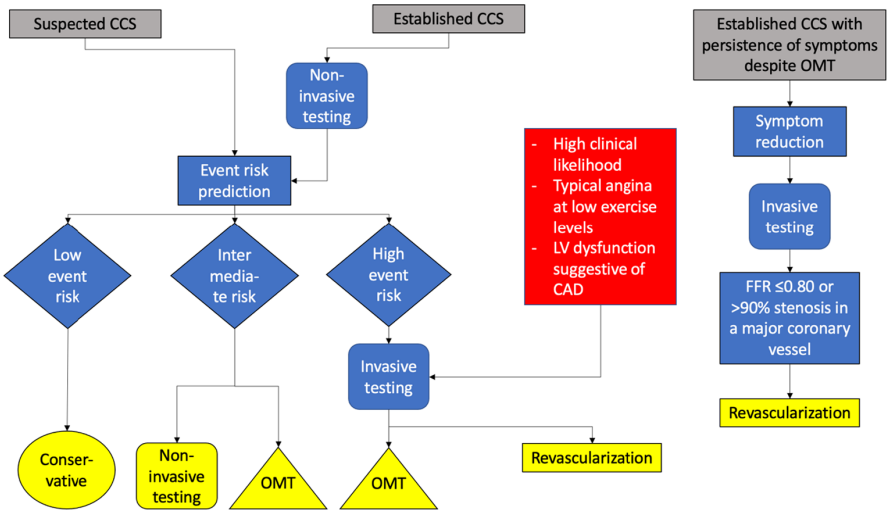

FIGURE 1 Diagnostic pathway for suspected chronic coronary syndrome. CAD, coronary artery disease; CCS, chronic coronary syndrome; LV, left ventricle; OMT, optimal medical therapy

revascularization using percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) provides a more effective reduction in angina complaints compared with optimal medical therapy alone, confirming the above-presented indication.[6–8] Evidence for prognosis improvement caused by revascularization is less profound. Nevertheless, revascularization is recommended in patients with: left main disease with stenosis >50% (class IA), proximal left anterior descending (LAD) stenosis >50% (class IA), two- or three-vessel disease with stenosis >50% combined with a left ventricular ejection fraction ≤35% (class IA) or left ventricular ischaemic area >10% detected by functional noninvasive testing or a FFR ≤0.80 (class IB), and in case of a single remaining patent coronary artery with >50% stenosis with documented ischaemia or a FFR ≤0.80 (class IC). In addition, in patients with heart failure and subsequent ventricular dysfunction and/or regional wall abnormalities, myocardial viability assessment can be performed in order to select patients suitable for coronary revascularization. The European Society of Cardiology/European Association for Cardio-Thoracic Surgery 2018 guidelines on myocardial revascularization recommend that noninvasive stress imaging may be considered for myocardial viability and ischaemia assessment in patients with heart failure and CAD to guide the decision strategy (class IIB).[4]

The recently published ISCHEMIA trial concluded that invasive strategy including revascularization by PCI or CABG in patients with CCS and moderate-to-severe ischaemia did not reduce the risk of major adverse cardiovascular events compared with conservative strategy including optimal medical therapy alone. Invasive strategy presented more procedural infarctions, yet fewer nonprocedural infarctions, than conservative strategy. Longer follow-up is expected to explain the prognostic consequences of this difference that was described for the 5-year follow-up.[9] Although there are some serious limitations in the ISCHEMIA trials regarding the statistical power, the results of the ISCHEMIA trial are in line with the previous COURAGE trial, which showed similar results for PCI and optimal medical therapy alone, and BARI 2D trial, which presented similar survival rates for revascularization and optimal medical therapy alone in diabetic patients.[8,10] Also, the investigators of the older CASS trial concluded that CABG could safely be deferred for medical treatment, in those days, beta-blockers and aspirin only, on behalf of nonsignificantly different survival rates between both groups up to 5-year follow-up. Some serious limitations in this trial should, however, be addressed. The trial applies to a limited group of CAD patients; there was a high percentage of crossover in favour of medical treatment in a trial that was already marginally powered. Therefore, the absolute numbers on mortality do not support the investigators' conclusion.[11] On the other side of the spectrum, there is the FAME-II trial, presenting a significant difference in urgent revascularizations needed in favour of FFR-guided PCI compared with optimal medical therapy alone.[12] These trials perfectly show that one should be careful in interpreting the reported results and that conclusions should be drafted in concordance with the study design, absolute therapy administered and the trial's patient selection. It is important to mention that all above trials excluded patients with left main stenosis (see Table 1). Hence, we can conclude that optimal medical therapy alone seems effective for a significant number of patients. Appropriate selection of patients eligible for this strategy, however, remains essential and should be patient-tailored.

3 | SELECTION OF REVASCULARIZATION STRATEGY

Following the indication, the appropriate revascularization strategy should be selected. Numerous trials compared PCI and CABG on a broad variety of endpoints. Meta-analyses and trials tailored to specific subgroups indicate significant differences in terms of mortality and major adverse cardiovascular events specifically for multivessel disease and diabetic patients.

Until recently, there has been no attention to sex differences in clinical trials and these are therefore not included in the current CCS guidelines, as they assume a representative male–female distribution of the CCS population. However, there is an under-representation of women with obstructive CAD in the CCS population, which can be partly explained by the fact that women are more often symptomatic in relation to nonobstructive CAD in which vasomotor dysfunction plays an important role.[13,14] Pooled analysis of individual patient data, for example, indicated a significant difference in all-cause mortality between PCI and CABG at 5 years postoperatively (resp. 11.2% vs. 9.2%; $p = .004$). CABG was superior for patients with multivessel CAD and diabetes mellitus, indicating an absolute risk reduction of 5%.[15] Yet, for one- and two-vessel disease these outcomes did not differ, indicating that revascularization strategies should be selected on behalf of other endpoints in those cases. Aiming for a more patient-specific approach, a vast number of trials provided information on patient subcategories and risk-score determination (see Table 2). The multidisciplinary decision-making on revascularization strategies, as performed by the Heart Team, is essential and mainly focusses on anatomical

TABLE 1 Optimal medical therapy versus revascularization

Trial	Trial design	Patient population	*N*	Follow-up	MACCE	All-cause mortality	MI	CVA	Repeat revascularization
COURAGE, 2007[8]	OMT + PCI vs. OMT (RCT)	Proximal stenosis ≥70% and objective myocardial ischaemia or stenosis ≥80% in ≥1 vessel with classic angina	2287	5 years	20.0 vs. 19.5 ($p = .62$)	7.6 vs. 8.3 ($p = .38$)	13.2 vs. 12.3 ($p = .33$)	2.1 vs. 1.8 ($p = .19$)	21.1 vs. 32.6 ($p < .001$)
ISCHEMIA, 2020[9]	OMT + PCI/CABG vs. OMT (RCT)	Stable CAD (without LM disease) with moderate or severe reversible myocardial ischaemia	5179	1 year	6.9 vs. 4.9 (HR 2.0 ; 95% CI 0.7–3.2)[a]	1.7 vs. 1.0 (HR 0.7 ; 95% CI 0–1.3)	5.3 vs. 3.8 (HR 1.5 ; 95% CI 0.3–2.6)[b]	0.7 vs. 0.4 (HR 0.4 ; 95% CI 0–0.8)	NA
BARI 2D, 2009[10]	OMT + PCI/CABG vs. OMT (RCT)	Stable CAD (without LM disease) including ≥50% stenosis with positive stress test or ≥70% stenosis, all with type 2 diabetes	2368	5 years	22.8 vs. 24.1 ($p = .70$)	11.7 vs. 12.2 ($p = .97$)	NA	NA	NA
CASS, 1984[11]	OMT + CABG vs. OMT (RCT)	Patients with mild or moderate stable CAD or free of angina but with a documented history of myocardial infarction	780	2 years	NA	8 vs. 5 (p = NS)	NA	NA	NA

Note: Outcomes are presented in respective order to the trial design and are expressed in cumulative event rates and their *p*-values, or their hazard ratio's and 95% confidence interval.

Abbreviations: BARI, Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CI, confidence interval; COURAGE, Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation; HR, hazard ratio; ISCHEMIA, Initial Invasive or Conservative Strategy for Stable Coronary Disease; LM, left main; MACCE, major adverse cardiac and cerebrovascular events; MI, myocardial infarction; NA, not applicable, NS, not significant, OMT, optimal medical therapy; and PCI, percutaneous coronary intervention.

[a]Primary definition of MI based on the Third Universal Definition of Myocardial Infarction types 1, 2, 4b and 4c.

[b]MI defined as procedural MI and nonprocedural MI.

complexity of CAD, expected completeness of revascularization and the existing comorbidities.[4]

3.1 | Anatomical complexity

The coronary anatomical complexity grade is used to stratify the severity of the coronary lesion(s) and contributes to the selection in appropriate revascularization therapy. Besides indexing the anatomical location of the lesion(s), direct lesion complexity regarding, for example, in-stent restenosis (favours CABG), severe calcification (favours CABG) or extreme small distal coronary targets (favours PCI) is important too.

3.1.1 | Left main stenosis

According to the results of several randomized trials, the European Society of Cardiology/European Association for Cardio-Thoracic Surgery 2018 guidelines recommend both PCI and CABG for patients with left main stenosis and a low Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score (class IA). In patients with left main stenosis and an intermediate SYNTAX score, CABG (class IA) is preferred to PCI (class IIA), while in patients with left main stenosis and a high SYNTAX score, CABG is recommended (class IA).[4]

Yet, coronary revascularization strategies for patients with left main stenosis are still subjected to discussion. The most discussed trials, EXCEL, PRECOMBAT and NOBLE, presented different outcomes regarding the treatment preference of left main stenosis. The trial design seems the most essential difference (see Table 2 for design and outcomes). All in all, higher myocardial infarction and repeat revascularization rates have been reported following PCI compared with CABG.[20–23] A rectification of the EXCEL trial showed lower rates of myocardial infarction following CABG compared with PCI were revealed when using universal myocardial infarction definitions instead of the untested definition of periprocedural myocardial infarction. In addition, the investigators' claim that there was no between-group difference in cardiovascular death could be questioned as the adjudication of cause of death in open-label trials is prone to bias.[30]

Whereas left main stenosis is entitled a separate anatomical entity, the SYNTAX 10-year trial showed that 87% of the patients with left main disease developed lesions in other coronary arteries during follow-up.[31] Also, 81% of the EXCEL trial patients developed multiple coronary stenosis with even ≥2 vessel disease in 50% of the patients, indicating a possible bias or explanation.[20] Also regarding revascularization for left main stenosis, incomplete revascularization seems one of the most important predictors of inferior clinical outcomes.

3.1.2 | LAD stenosis

In the absence of proximal LAD stenosis, PCI is preferable to CABG in one- and two-vessel CAD (class IC recommendation). In one- and two-vessel CAD with proximal LAD stenosis, the guidelines indicate the same class of recommendation for PCI and CABG (class 1A for one-vessel CAD and 1B/C for two-vessel CAD), showing comparable results in terms of death, myocardial infarction and stroke.[4]

In contrast to the guidelines, though, Hannan et al.[17] described that CABG in two-vessel CAD, regardless of proximal LAD involvement, was associated with higher survival rates, less myocardial infarction and lower rates of repeat revascularization.

3.1.3 | Multivessel disease

Multivessel disease is defined as lesions in at least two coronary arteries. To stratify patients with multivessel disease between PCI and CABG, the guidelines recommend assessment via the SYNTAX score, estimating anatomical coronary complexity.[4,32] This estimation is performed based on the anatomical location and complexity (bi/trifurcation, ostial, total occlusion, calcium, length, tortuosity, thrombus and diffuse disease) for every lesion present. Patients with a SYNTAX score >22 should undergo CABG, and both revascularization strategies can be chosen for SYNTAX score ≤22.

Since anatomical complexity is not solely important in determining the optimal revascularization strategy, the SYNTAX score II was launched taking into account a 5-year risk of major adverse cardiovascular events based on seven prognostic factors (age, medically treated diabetes mellitus, creatinine clearance, left ventricular ejection fraction, chronic obstructive pulmonary disease, peripheral vascular disease and smoking status) combined with two effect modifiers (three-vessel disease or left main-only disease, and the anatomical SYNTAX I score).[33] For both 10-year mortality and 5-year major adverse cardiovascular events regarding those with SYNTAX score >22, superiority was outlined for PCI in the first quartile, equipoise results in the second quartile and superiority for CABG in the third and fourth quartiles (see Table 2).[18,19]

In the past decade, developments in newer generation stents, intracoronary imaging and functional testing have advanced the PCI outcomes.[34] The 5-year outcomes of the SYNTAX II trial showed that PCI is noninferior to CABG

TABLE 2 Percutaneous coronary intervention versus coronary artery bypass grafting

Trial	Trial design	Patient population	*N*	Follow-up	MACCE	All-cause mortality	MI	CVA	Repeat revascularization
I. Anatomical complexity									
Kapoor, 2008[16]	PCI vs. CABG (meta-analysis)	Single-vessel proximal LAD stenosis	1210	5 years	NA	90.6 vs. 92.8 (NS)	NA	NA	33.5 vs. 7.3 (95% CI, 20.1–33.3)
Hannan, 2008[17]	PCI vs. CABG (RCT)	Two-vessel CAD with stenosis defined as ≥70%	17400	18 months	NA	5.4 vs. 4.0 ($p = .003$)	7.5 vs. 6.5 ($p < .001$)	NA	Repeat PCI: 28.3 vs. 5.1 ($p < .001$) Repeat CABG: 2.2 vs. 0.2 ($p < .001$)
SYNTAXES II, 2020[18,19]	PCI vs. CABG (RCT)	LM disease or multivessel CAD	1800	First quartile	NA	ARD -1.4% (95% CI, −9.4 to 6.6, $p = .52$)	NA	NA	
				Second quartile	NA	ARD 0.3% (95% CI, −6.7 to 7.4, $p = .92$)	NA	NA	NA
				Third quartile	NA	ARD 6.1% (95% CI, −2.2 to 14.3, $p = .14$)	NA	NA	NA
				Fourth quartile	NA	ARD 11.4% (95% CI, −2.0 to 20.5, $p = .013$)	NA	NA	NA
		Elderly >70 years of age		5 years	39.4 vs. 35.1 (HR 1.18; 95% CI, 0.90–1.56)	(HR 1.08; 95% CI, 0.75–1.55)	(HR 2.08; 95% CI, 1.10–3.91)	(HR 0.78; 95% CI, 0.35–1.73)	(HR 2.11; 95% CI, 1.35–3.31)
		Nonelderly ≤70 years of age			36.3 vs. 23.0 (HR 1.69; 95% CI, 1.36–2.10)	(HR 1.46; 95% CI, 0.98–2.18)	(HR 2.76; 95% CI, 1.63–4.66)	(HR 0.48; 95% CI, 0.22–1.08)	(HR 2.04; 95% CI, 1.57–2.67)
		Elderly >70 years of age		10 years	NA	44.1 vs. 41.1 (HR 1.08; 95% CI, 0.84–1.40)	NA	NA	NA
		Nonelderly ≤70 years of age				21.1 vs. 16.6 (HR 1.30; 95% CI, 1.00–1.69)			
EXCEL, 2019[20]	PCI vs. CABG (RCT)	LM disease	1905	30 days	4.9 vs. 8.0 ($p < .001$)	1.0 vs. 1.1 (HR 0.90; 95% CI, 0.37–2.22, $p = .82$)	3.9 vs. 6.3 (HR 0.63; 95% CI 0.42–0.94, $p = .15$)	0.6 vs. 1.3 (HR 0.50; 95% CI 0.19–1.33, $p = .15$)	0.6 vs. 1.4 (HR 0.46; 0.18–1.21, $p = .11$)
				5 years	15.4 vs. 14.7 ($p = .02$)	8.2 vs. 5.9 (HR 1.34; 95% CI, 0.94–1.91, $p = .11$)	8.0 vs. 8.3 (HR 0.93; 95% CI, 0.67–1.28, $p = .64$)	1.0 vs. 1.1 (HR 0.90; 95% CI, 0.37–2.22, $p = .82$)	12.6 vs. 7.5 (HR 1.72; 95% CI, 1.27–2.33, $p < .001$)
				10 years	22.0 vs. 19.2 ($p = .13$)	13.0 vs. 9.0 (OR 1.38; 95% CI 1.03–1.85)[a]	9.6 vs. 4.7 (95% CI, 2.6–7.2)[a]	1.9 vs. 1.8 (HR 1.06; 95% CI, 0.52–2.15)	16.9 vs. 10.0 (95% CI, 3.7–10.0)

TABLE 2 (Continued)

Trial	Trial design	Patient population	*N*	Follow-up	MACCE	All-cause mortality	MI	CVA	Repeat revascularization
PRECOMBAT, 2015, 2020[21,22]	PCI vs. CABG (RCT)	LM disease	600	2 years	4.4 vs. 4.7 (HR 1.50; 95% CI, 0.90–2.52, $p = .83$)	2.4 vs. 3.4 (HR 0.69; 95% CI, 0.26–1.82, $p = .45$)	1.7 vs. 1.0 (HR 1.66; 95% CI, 0.40–6.96, $p = .49$)	0.4 vs. 0.7 (HR 0.49; 95% CI, 0.04–5.40, $p = .56$)	9.0 vs. 4.2 (HR 2.18; 95% CI, 1.10–4.32, $p = .02$)
				5 years	17.5 vs. 14.3 (HR 1.27; 95% CI, 0.84–1.90, $p = .66$)	5.7 vs. 7.9 (HR 0.73; 95% CI, 0.39–1.37, $p = .32$)	2.0 vs. 1.7 (HR 1.20; 95% CI, 0.37–3.93, $p = .76$)	0.7 vs. 0.7 (HR 0.99; 95% CI, 0.14–7.02, $p = .99$)	11.4 vs. 5.5 (HR 2.11; 95% CI, 1.16–3.84, $p = .012$)
				10 years	18.2 vs. 17.5 (HR 1.0; 95% CI, 0.70–1.40)	14.5 vs. 13.8 (HR 1.13; 95% CI, 0.75–1.70)	3.2 vs. 2.8 (HR 0.76; 95% CI, 0.32–1.82)	1.9 vs. 2.2 (HR 0.71; 95% CI, 0.22–2.23)	16.1 vs. 8.0 (HR 1.98; 95% CI, 1.21–3.21)
NOBLE, 2020[23]	PCI vs. CABG (RCT)	LM disease (stenosis ≥50% or FFR ≤0.8)	1201	1 year	7.0 vs. 7.0 (95% CI, −2.9 to 2.9, $p = 1.00$)	2.0 vs. 3.0 (95% CI, −3.0 to 0.3, $p = .11$)	2.0 vs. 1.0 (95% CI, −0.9 to 1.90, $p = .49$)[b]	<1.0 vs. 1.0 (95% CI, −1.6 to 0.3, $p = .16$)	5.0 vs. 4.0 (95% CI, −1.1 to 3.8, $p = .27$)
				5 years	28.0 vs. 18.0 (HR 1.51; 95% CI, 1.13–2.00, $p = .004$)	11.0 vs. 9.0 (HR 1.08; 95% CI, 0.67–1.74, $p = .84$)	6.0 vs. 2.0 (HR 2.87; 95% CI, 1.40–5.89, $p = .004$)[b]	5.0 vs. 2.0 (HR 2.20; 95% CI, 0.91–5.36, $p = .08$)	15.0 vs. 10.0 (HR 1.50; 95% CI, 1.04–2.17, $p = .03$)
				2 years	4.4 vs. 4.7 (HR 1.50; 95% CI, 0.90–2.52, $p = .83$)	2.4 vs. 3.4 (HR 0.69; 95% CI, 0.26–1.82, $p = .45$)	1.7 vs. 1.0 (HR 1.66; 95% CI, 0.40–6.96, $p = .49$)	0.4 vs. 0.7 (HR 0.49; 95% CI, 0.04–5.40, $p = .56$)	9.0 vs. 4.2 (HR 2.18; 95% CI, 1.10–4.32, $p = .02$)
Garcia, 2013[24]	Complete vs. incomplete revascularization (meta-analysis)	Multivessel CAD	89993	Aspecific	NA	PCI: (RR 0.72; 95% CI, 0.64–0.81, $p < .001$)	PCI: (RR 0.78; 95% CI, 0.68–0.91, $p = .001$)	NA	PCI: (RR 0.72; 95% CI, 0.63–0.81, $p < .001$)
					NA	CABG: (RR 0.70; 95% CI, 0.61–0.80, $p < .001$)	CABG: (RR 0.69; 95% CI, 0.44–1.10, $p = .12$)	NA	CABG: (RR 0.92; 95% CI, 0.67–1.28, $p = .64$)
III. Comorbidities									
FREEDOM, 2012, 2019[25,26]		PCI vs. CABG (RCT)	1900	1 year	16.8 vs. 11.8 ($p = .004$)	3.4 vs. 4.2 ($p = .35$)	5.8 vs. 3.4 ($p = .02$)	0.9 vs. 1.9 ($p = .06$)	12.6 vs. 4.8 ($p < .001$)
				5 years	26.6 vs. 18.7 ($p = .005$)	16.3 vs. 10.9 ($p = .049$)	13.9 vs. 6.0 ($p < .001$)	2.4 vs. 5.2 ($p = .03$)	NA
				7.5 years	NA	24.3 vs. 18.3 (HR 1.36; 95% CI, 1.07–1.74, $p = .01$)	NA	NA	NA

(Continues)

TABLE 2 (Continued)

Trial	Trial design	Patient population	*N*	Follow-up	MACCE	All-cause mortality	MI	CVA	Repeat revascularization
Chen, 2020[27]	Diabetes vs. no diabetes (cohort)	Single or multivessel PCI	92624	6 years	37.3 vs. 28.1 (HR 1.31; 95% CI, 1.27–1.35)[e,f]	6.2 vs. 4.7 (HR 1.34; 95% CI, 1.25–1.44)[e]	21.0 vs. 16.6 (HR 1.34; 95% CI, 1.29–1.39)[e]	NA	NA
STICHES, 2016[28]	Combined CABG and OMT vs. OMT alone	CAD suitable for CABG and LVEF ≤35%	1221	10 years	NA	58.9 vs. 66.1 (HR 0.84; 95% CI, 0.73–0.97, $p = .02$)	61.6 vs. 67.9 (HR 0.86; 95% CI, 0.74–0.98, $p = .03$)[g]	60.2 vs. 67.4 (HR 0.85; 95% CI, 0.74–0.98, $p = .03$)[g]	63.6 vs. 79.4 (HR 0.63; 95% CI, 0.55–0.73, $p < .001$)[g]
Nagendran, 2018[29]	PCI vs. CABG (propensity-matched cohort study)	Diabetics with multivessel CAD and LVEF <50%	1738	5 years	LVEF 35%–49%: 51–28 ($p < .001$)	LVEF 35%–49%: (HR 1.34; 1.07–1.68, $p = .01$)	LVEF 35%–49%: (HR 1.23; 0.87–1.76, $p = .25$)	LVEF 35%–49%: (HR 1.01; 0.57–1.78, $p = .98$)	LVEF 35%–49%: (HR 5.46; 3.80–7.78, $p < .001$)
					LVEF <35%: 61–29 ($p < .001$)	LVEF <35%: (HR 1.62; 1.20–2.22, $p = .002$)	LVEF <35%: (HR 2.27; 1.38–3.75, $p < .001$)	LVEF <35%: (HR 0.87; 0.39–1.91, $p = .72$)	LVEF<35%: (HR 7.31; 4.08–13.10, $p < .001$)

Note: Outcomes of revascularization strategies per: I. anatomical complexity; II. completeness of revascularization; and III. comorbidities. Outcomes were presented as estimated cumulative event rates, ARDs, RRs, ORs, HRs with their 95% CI, and *p*-values.

Abbreviations: ARD, absolute risk difference; BEST, Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CI, confidence interval; EXCEL, Evaluation of XIENCE versus Coronary Artery Bypass Graft Surgery for Effectiveness of Left Main Revascularization; FFR, fraction flow reserve; FREEDOM, Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease; HR, hazard ratio; LAD, left anterior descending; LM, left main; LVEF, left ventricular ejection fraction; MACCE, major adverse cardiac and cerebrovascular events; MI, myocardial infarction; NOBLE, Nordic–Baltic–British Left Main Revascularization; NS, no significance; OR, odds ratio; PCI, percutaneous coronary intervention; PRECOMBAT, Premier of Randomized Comparison of Sirolimus-Eluting Stent Implantation Versus Coronary Artery Bypass Surgery for Unprotected Left Main Coronary Artery Stenosis; RR, relative risk; STICHES, Surgical Treatment for Ischemic Heart Failure Extension Study, SYNTAX, Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery, SYNTAXES, Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery Extended Survival.

[a]After re-evaluation of the trial.

[b]Nonprocedural MI.

[c]CABG complete revascularization as reference versus incomplete PCI.

[d]CABG complete revascularization as reference versus incomplete CABG.

[e]Incidence rates per 1000 person-years.

[f]Composite outcome of MI, repeat PCI/bypass surgery and all-cause mortality.

[g]The incidence rate of this outcome is combined with death.

in patients with three-vessel CAD. These data emphasize the need for a randomized trial recruiting patients with multivessel CAD comparing PCI with CABG, using the contemporary revascularization approaches.[35]

3.2 | Completeness of revascularization

One important goal of myocardial revascularization is to minimize residual ischaemia, aiming for complete functional revascularization.[4] It has been shown that incomplete revascularization is associated with inferior long-term outcomes, which was significantly more profound following PCI than following CABG (see Table 2).[36] In addition, a meta-analysis of 89,883 multivessel disease patients reported incomplete revascularization to be more common in PCI than in CABG (resp. 56% vs. 25%; $p < .001$).[24] A complete functional revascularization strategy using FFR is preferred to improve long-term outcomes, as was presented in the FAME trial for PCI.[37] Hence, the opportunity for complete revascularization plays an important role in the selection of revascularization strategy, especially regarding multivessel disease.

On the contrary, the ISCHEMIA, BARI 2D and COURAGE trials presented that treatment with just optimal medical therapy might be as effective as revascularization in a vast number of patients.[8–10] When considering optimal medical therapy only as truly incomplete revascularization, these results lower the urge towards completeness of revascularization.

3.3 | Comorbidities

To estimate the perioperative in-hospital or 30-day mortality following cardiac surgery, both the European System for Cardiac Operative Risk Evaluation II and the Society of Thoracic Surgeons scores were developed.[4] When comparing both surgical risk scores for patients undergoing isolated CABG, similar outcomes were achieved. Yet, the European System for Cardiac Operative Risk Evaluation II is more accurate in calculating the in-hospital mortality for nonisolated CABG patients, whereas the Society of Thoracic Surgeons score calculates in-hospital or 30-day mortality following primary CABG.[4,38]

Although the risk scores are useful, none of the models provide perfect risk assessment. Furthermore, there are no established surgical mortality cut-off values for neither risk assessment scores that describe acceptable rates, so an individual approach remains necessary. For example, patients with the presence of severe comorbidities, reduced life expectancy and contraindication for surgery, or the frail (elderly) patients appear to be more eligible for PCI. On the contrary, specific comorbidities such as diabetes mellitus, contraindication for dual antiplatelet therapy and diminished left ventricular function favour CABG (see Table 2).[4]

There is an ongoing debate about the appropriate revascularization strategy for elderly patients with multivessel CAD. Recent follow-up data showed that PCI and CABG were equivalent in terms of long-term clinical outcomes and measurable outcomes including quality of life in patients aged ≥70 years with multivessel and/or left main CAD.[19] The results of this SYNTAX extended survival study contradict a set of previous observational trials that present favourability of CABG.[19,39–41] These trial results outline that revascularization strategies should be patient-tailored, with consideration of the clinical risks in the context of quality of life.

4 | PERCUTANEOUS CORONARY INTERVENTION

Before the introduction of PCI in 1977, CABG was the only revascularization therapy for CAD.[42] Currently, it is impossible to imagine CAD treatment without PCI. As mentioned before, the clinical benefit of elective PCI among patients with CCS particularly implies reduction in angina symptoms, while risk reduction for myocardial infarction and mortality is less prominent.[43] However, considerable progress in appropriate patient selection including invasive measurement of the severity of the stenosis (FFR and instantaneous flow reserve), peri- and post-procedural pharmacotherapy, intracoronary imaging techniques including optical coherence tomography and intravascular ultrasound, optimal balloon and stent deployment, and achievement of complete revascularization improves PCI outcomes.[44]

4.1 | Drug-eluting stent

The procedural success of PCI improved following the introduction of the bare-metal stent with lower repeat revascularization rates at 6 months' follow-up compared with balloon angioplasty alone (see Table 3).[45] Yet, considering the incidence of acute and subacute stent thrombosis in combination with risk of in-stent restenosis, which was still significant, the drug-eluting stent was developed.[46] These stents are coated by antiproliferative drugs in order to prevent in-stent restenosis based on intima hyperplasia. Particularly, the second-generation drug-eluting stent was associated with less repeat revascularization compared with bare-metal stent at 6 years' follow-up and outperforms the first-generation drug-eluting stent.[47,48]

Moreover, a large network analysis even reported on improved survival following second-generation drug-eluting stents compared with optimal medical treatment alone.[49] Notwithstanding the lower incidence of in-stent restenosis, the risk of acute and subacute stent thrombosis was corresponding in second-generation drug-eluting stent compared with bare-metal stent,[50,51] indicating the administration of dual antiplatelet therapy. Nevertheless, the current risk of stent thrombosis with newer drug-eluting stent is low.[52]

4.2 | Fractional flow reserve

The introduction of FFR using a coronary pressure wire further improved the indication for PCI. FFR assesses the haemodynamic significance of a coronary stenosis and is more accurate than visual assessment of the angiogram alone. The DEFER trial was the first randomized controlled trial to demonstrate that FFR-guided PCI is a suitable therapy for coronary intervention and also showed that PCI can be deferred in patients with non-FFR-significant stenosis (see Table 3).[54] The diagnostic efficacy of instantaneous flow reserve is equal to FFR for identifying myocardial perfusion abnormalities.[56] The need for angiography could be reduced by the novel technique of FFR calculations on behalf of computational fluid dynamic, computed tomography-derived FFR.[57] In the FAME study, comparing FFR-guided with coronary angiography-guided PCI in multivessel CAD, the FFR-guided PCI group showed lower major adverse cardiovascular events rates at one-year follow-up (resp. 13.2 vs. 18.3; $p = .02$) and similar rates at 5-year follow-up (resp. 28 vs. 31; $p = .31$) as compared to solely coronary angiography-guided PCI.[55] The outcomes of both trials, DEFER and FAME, indicate that FFR-guided PCI for intermediate-grade and multivessel stenoses should be the standard of care.[37,54,58]

Notwithstanding this important benefit in FFR-guided PCI, the recent FAME III trial determined CABG still superior to PCI, despite FFR usage. The routine use of FFR is primarily indicated to avoid nonflow limiting lesion stenting and their inherent complications, which is expected to be treated adequately by medical therapy alone. Patients assigned to undergo FFR-guided PCI in the FAME III trial had lower mortality and repeat revascularization rates at follow-up compared with FFR-guided PCI in the previous trials, while operative outcomes keep improving too (see Table 4).[42,58] However, incomplete revascularization related to late myocardial infarction and repeat revascularization remains one of the most important determinants explaining the superiority of CABG.

5 | CORONARY ARTERY BYPASS GRAFTING

Although CABG is more invasive than PCI, it has been proven to be superior for the outlined patient groups. In accordance with the European Society of Cardiology/European Association for Cardio-Thoracic Surgery 2018 guidelines, all coronary arteries with an epicardial target diameter ≥1.5 mm and a luminal reduction of ≥50% in at least one angiographic view have to be grafted.[4] Although FFR contributes to PCI target selection, this effect is less profound in CABG.[59,60]

5.1 | Donor graft material

The long-term outcomes of CABG seem mainly related to graft patency. Although various vessels are suitable donor grafts, the patency rates differ (see Table 4).[61,71,72] The European Society of Cardiology/European Association for Cardio-Thoracic Surgery 2018 guidelines indicate a class IB recommendation for left internal mammary artery (LIMA) in LAD grafting primarily due to the high patency rates of the IMA grafts. In addition, the guidelines indicate a class IB recommendation for arterial revascularization with the use of radial artery or right (R)IMA over saphenous vein in patients with a high-grade coronary artery stenosis and reasonable life expectancy.[4] Less frequently, the gastroepiploic artery and inferior epigastric artery are used.[73] The benefit of total arterial grafting is still extensively debated. Although bilateral (B)IMA grafting is associated with improved long-term survival compared with single (S)IMA grafting in observational trials, randomized controlled trials do not significantly underline this difference.[62,63] Although the latter might be related to study design, we now await the results of the ROMA trial comparing single arterial grafting vs. multiple arterial grafting in patients undergoing primary isolated nonemergent CABG of the left coronary system.[74] Notwithstanding the indicated superiority of arterial grafts, multiple trials stated BIMA grafting to be a predictor of sternal infections in high-risk patients (diabetics, obesity and chronic obstructive pulmonary disease).[75]

5.2 | On- versus off-pump CABG

The choice between CABG with (ONCAB) or without (OPCAB) the use of cardiopulmonary bypass is being debated for years. Again, patient-specific characteristics seem to be key in decision-making. The current guidelines indicate a class IB recommendation for OPCAB by experienced operators in patients with significant

TABLE 3 Percutaneous coronary intervention strategies

Trial	Trial design	Patient population	*N*	Follow-up	MACCE	All-cause mortality	MI	Stent thrombosis	Repeat revascularization
I. Type of stent									
Stent Restenosis Study, 1994[45]	BMS vs. balloon angioplasty (RCT)	Symptomatic CAD and new lesion of native coronary circulation with ≥70% stenosis	410	8 months	19.5 vs. 23.8 ($p = .16$)	1.5 vs. 1.5 ($p = .99$)	6.3 vs. 6.9 ($p = .81$)	NA	11.2 vs. 12.4 ($p = .72$)
Norwegian Coronary Stent, 2016[47]	DES vs. BMS (RCT)	All patients undergoing PCI	9013	6 years	16.6 vs. 17.1 (HR 0.98; 95% CI, 0.88–1.09, $p = .66$)	8.5 vs. 8.4 (HR 1.10; 95% CI, 0.94–1.32, $p = .21$)	9.8 vs. 10.5 (HR 0.89; 95% CI, 0.77–1.02, $p = .10$)[a]	0.8 vs. 1.2 (HR 0.64; 95% CI, 0.41–1.0, $p = .05$)	16.5 vs. 19.8 (HR 0.76; 95% CI, 0.69–0.85, $p < .001$)
Stone, 2007[48]	DES vs. BMS (RCT)	Single-vessel CAD suitable for PCI	1748	4 years	NA	Sirolimus: 6.7 vs. 5.3 (HR 1.27; 95% CI, 0.86–1.88, $p = .23$)	Sirolimus: 6.4 vs. 6.2 (HR 1.03; 95% CI, 0.71–1.51, $p = .86$)	Sirolimus: 1.2 vs. 0.6 (HR 2.0; 95% CI, 0.68–5.85, $p = .20$)	Sirolimus: 7.8 vs. 23.6 (HR 0.29; 95% CI, 0.22–0.39, $p < .001$)[b]
						Paclitaxel: 6.1 vs. 6.6 (HR 0.94; 95% CI, 0.70–1.26, $p = .68$)	Paclitaxel: 7.0 vs. 6.3 (HR 1.06; 95% CI, 0.81–1.39, $p = .66$)	Paclitaxel: 1.3 vs. 0.9 (HR 1.44; 95% CI, 0.73–2.84, $p = .30$)	Paclitaxel: 10.1 vs. 20.0 (HR 0.46; 95% CI, 0.38–0.55, $p < .001$)
ABSORB III, 2015[53]	Absorb scaffold vs. DES (RCT)	Patients with ischaemia and one- or two-vessel CAD undergoing PCI	2008	1 year	NA	1.1 vs. 0.4 (RR 2.58; 95% CI, 0.75–8.87, $p = .12$)	6.9 vs. 5.6 (RR 1.22; 95% CI, 0.85–1.76, $p = .28$)	1.4 vs. 0.7 (RR 1.87; 95% CI, 0.70–5.01, $p = .21$)	1.1 vs. 0.4 (RR 2.58; 95% CI, 0.75–8.87, $p = .12$)
SYNTAX II[35]	SYNTAX II vs. SYNTAX I (PCI-arm)	Three-vessel CAD without LM disease		5 years	10.8 vs. 21.8 (HR 0.47; 95% CI, 0.32–0.68)	8.1 vs. 13.8 (HR 0.57; 95% CI, 0.37–0.90)	2.7 vs. 10.4 (HR 0.26; 95% CI, 0.13–0.50)	2.3 vs. 2.7 (HR 0.83; 95% CI, 0.33–2.12)	13.8 vs. 23.8 (HR 0.56; 95% CI, 0.39–0.78)
II. FFR-guided									
DEFER, 2015[54]	FFR ≥0.75 deferred PCI vs. FFR ≥0.75 perform PCI (RCT)	Referred for elective PCI stenosis >50% of native coronary artery without documented reversible ischaemia	325	2 years	NA	Survival rate: 89.0 vs. 83.3 ($p = .27$)	NA	NA	NA
				5 years	NA	Survival: 79 vs. 73 ($p = .52$)	NA	NA	NA
				15 years	NA	33.0 vs. 31.1 (RR 1.06; 95% CI, 0.69–1.62, $p = .79$)[c]	2.2 vs. 10.0 (RR 0.22; 95% CI, 0.05–0.99, $p = .03$)	NA	42.9 vs. 34.4 ($p = .245$)

(Continues)

TABLE 3 (Continued)

Trial	Trial design	Patient population	*N*	Follow-up	MACCE	All-cause mortality	MI	Stent thrombosis	Repeat revascularization
FAME trial, 2009, 2015[37,55]	FFR-guided vs. CAG-guided PCI (RCT)	Multivessel CAD defined as ≥50% stenosis in ≥2 of the major epicardial coronary arteries	1005	1 year	13.2 vs. 18.3 ($p = .02$)[d]	1.8 vs. 3.0 ($p = .19$)	5.7 vs. 8.0 ($p = .07$)	NA	6.5 vs. 9.5 ($p = .08$)
				5 years	28.0 vs. 31.0 ($p = .31$)[d]	9.0 vs. 10.0 ($p = .50$)	9.6 vs. 12.1 (NA)	NA	15.0 vs. 17.0 ($p = .39$)

Note: Outcomes of I. different coronary stents and II. FFR-guided PCI.

Abbreviations: AIDA, Amsterdam Investigator-Initiated Absorb Strategy All-Comers; ABSORB, A Bioresorbable Everolimus-Eluting Scaffold Versus a Metallic Everolimus-Eluting Stent; BMS, bare-metal stent; CAD, coronary artery disease; CI, confidence interval; DEFER, Deferral versus Performance of PTCA in Patients Without Documented Ischemia; DES, drug-eluting stent; FAME, Fractional Flow Reserve versus Angiography for Multivessel Evaluation; FFR, fractional flow reserve; HR, hazard ratio; MACCE, major adverse cardiac and cerebrovascular events; MI, myocardial infarction; OMT, optimal medical therapy; PCI, percutaneous coronary intervention; RR, relative risk.

[a]Nonprocedural MI.

[b]Repeat target lesion revascularization.

[c]Composite outcome of cardiac death and MI.

[d]Composite outcome of all-cause death, MI and repeat revascularization. Outcomes are presented as estimated cumulative event rates, RRs, HRs with their 95% CI and *p*-values.

atherosclerotic aortic disease and a class IIA recommendation in subgroups of high-risk patients.[4] In the main randomized controlled trials comparing ONCAB and OPCAB, no differences were observed in long-term event rates (see Table 4).[64–66] Subsequently, meta-analyses revealed incomplete revascularization and the surgeon's experience as predictors of higher late mortality rates in OPCAB.[76] On the contrary, several analyses indicated that patients could benefit from OPCAB on the short term because of reduction in prolonged ventilation, intensive care unit and hospital length of stay, transfusion requirements, new renal failure, and stroke or neurocognitive decline.[77] This suggests that OPCAB should be considered in the elderly and in high-risk populations if performed by experienced operators.[78,79] Notwithstanding these short-term successes, specifically no-aortic touch OPCAB procedures are associated with reduced stroke rates and a reduced risk of early morbidity.[80] The European Society of Cardiology/European Association for Cardio-Thoracic Surgery 2018 guidelines therefore indicate a class IB recommendation for no-touch techniques on the ascending aorta in patients with significant atherosclerotic aortic disease.[4]

5.3 | Minimally invasive approaches

Minimally invasive direct coronary artery bypass and totally endoscopic coronary artery bypass are two alternative options to reduce surgical access, by avoiding sternotomy. Both procedures can be performed with or without robotic assistance. The current guidelines indicate a class IIB recommendation for minimally invasive direct coronary artery bypass by experienced operators in patients with isolated LAD lesions.[4] Although minimally invasive direct coronary artery bypass procedures mainly suit anterior wall revascularizations, totally endoscopic coronary artery bypass procedures allow complete revascularization. The vast downsides of totally endoscopic coronary artery bypass are represented by an extended learning curve, procedure duration and high equipment costs.[81] The outcomes of minimally invasive direct coronary artery bypass and totally endoscopic coronary artery bypass surgery improved over time and are currently excellent; however, direct comparison with conventional CABG in large trials is still lacking (see Tables 4 and 5).[67–69,81,82]

A hybrid coronary revascularization combines minimally invasive anterior or eventually lateral wall bypass surgery with PCI of the remaining targets. The European Society of Cardiology/European Association for Cardio-Thoracic Surgery 2018 guidelines indicate a class IIB recommendation for hybrid coronary revascularization

TABLE 4 Coronary artery bypass grafting strategies

Trial	Trial design	Patient population	*N*	Follow-up	MACCE	All-cause mortality	MI	CVA	Repeat revascularization	Graft patency
I. FFR-guided										
FARGO, 2018[59]	FFR-guided vs. CAG-guided CABG (RCT)	≥1 lesion defined as visually assessed ≥50% stenosis with a proximal reference segment diameter >2.5 mm	100	6 months	12.0 vs. 12.0 ($p = .97$)	vs. 4.0 ($p = .24$)	2.0 vs. 0.0 ($p = .50$)	NA	6.0 vs. 6.0 ($p = 1.0$)	72.0 vs. 67.0 ($p = .64$)
GRAFFITI, 2019[60]	FFR-guided vs. CAG-guided CABG (RCT)	Significant LM disease or proximal LAD stenosis plus ≥1 intermediate lesion 30%–90% in one other major coronary artery	172	1 year	5.7 vs. 7.1 ($p = .69$)	NA	NA	NA	NA	81.0 vs. 80.0 ($p = .89$)
FAME III, 2021[58]	FFR-PCI vs. CABG (RCT)	Three-vessel CAD without LM disease	1500	1 year	10.6 vs. 6.9 (HR 1.5; 95% CI, 1.1–2.2)	1.6 vs. 0.9 (HR 1.7; 95% CI 0.7–4.3)	5.2 vs. 3.5 (HR 1.5; 95% CI, 0.9–2.5)	NA	5.9 vs. 3.9 (HR 1.5; 95% CI, 0.9–2.3)	0.8 vs. 1.3 (NA)
II. Graft choice										
Cao, 2013[61]	Radial artery vs. Saphenous vein (meta-analysis)	Multivessel disease with proximal lesion >70% stenosis of native coronary artery	1840	1 year	20.0 vs. 19.5 ($p = .62$)	7.6 vs. 8.3 ($p = .38$)	13.2 vs. 12.3 ($p = .33$)	NA	NA	79.2 vs. 82.5 (OR 0.79; 95% CI, 0.50–1.26, $p = .33$)
				4 years	NA	NA	NA	NA	NA	89.9 vs. 63.1 (OR 5.19; 95% CI, 2.35–11.47, $p < .001$)
Buttar, 2017[62]	BIMA vs. SIMA (meta-analysis)	Patients with CAD undergoing CABG	89399	Short-term[a]	NA	1.2 vs. 2.1 ($p = .04$)	2.02 vs. 2.00 ($p = .006$)	NA	4.8 vs. 10.0 ($p = .005$)	NA
				Long-term[b]	NA	HR 0.78; 95% CI, 0.72–0.84, $p < .001$	HR 0.73; 95% CI, 0.64–0.83, $p < .001$	NA	NA	NA
ART, 2019[63]	BIMA- vs. SIMA (RCT)	Multivessel disease	3102	1 year	NA	2.5 vs. 2.3 (RR 1.06; 95% CI, 0.68–1.67)	2.0 vs. 2.0 (RR 0.97; 95% CI, 0.59–1.60)	NA	1.5 vs. 1.8 (RR 1.36; 95% CI, 0.77–2.41)	NA
					12.2 vs. 12.7 ($p = .69$)	8.7 vs. 8.4 ($p = .77$)	3.4 vs. 3.5 ($p = .86$)	NA	6.5 vs. 6.6 ($p = .91$)	NA
					24.9 vs. 27.3 (HR 0.90; 95% CI, 0.79–1.03, $p = .12$)	20.3 vs. 21.2 (HR 0.96; 95% CI, 0.82–1.12, $p = .62$)	4.6 vs. 5.0 (HR 0.92; 95% CI, 0.66–1.26)	NA	10.3 vs. 10.0 (HR 1.02; 95% CI, 0.83–1.26)	NA

(Continues)

TABLE 4 (Continued)

Trial	Trial design	Patient population	*N*	Follow-up	MACCE	All-cause mortality	MI	CVA	Repeat revascularization	Graft patency
III. On- versus off-pump										
CORONARY, 2016[64]	Off-pump vs. On-pump CABG (RCT)	All CAD	4752	30 days	9.8 vs. 10.3 (HR 0.95; 95% CI, 0.79–1.14, $p = .59$)	2.5 vs. 2.5 (HR 1.02; 95% CI, 0.71–1.46)	6.7 vs. 7.2 (HR 0.93; 95% CI, 0.75–1.15)	1.0 vs. 1.1 (HR 0.89; 95% CI, 0.51–1.54)	0.7 vs. 0.2 (HR 4.01; 95% CI, 1.34–12.0, $p = .01$)	NA
				1 year	12.1 vs. 13.3 (HR 0.91; 95% CI, 0.77–1.07, $p = .24$)	5.1 vs. 5.0(HR 1.03; 95% CI, 0.80–1.32)	6.8 vs. 7.5 (HR 0.90; 95% CI, 0.73–1.12)	1.5 vs. 1.7 (HR 0.90; 95% CI, 0.57–1.41)	1.4 vs. 0.8 (HR 1.66; 95% CI, 0.95–2.89, $p = .07$)	NA
				4.8 years	23.1 vs. 23.6 (HR 0.98; 95% CI, 0.87–1.10, $p = .72$)	14.6 vs. 13.5 (HR 1.08; 95% CI, 0.93–1.26, $p = .30$)	7.5 vs. 8.2 (HR 0.92; 95% CI, 0.75–1.13, $p = .41$)	2.3 vs. 2.8 (HR 0.83; 95% CI, 0.58–1.19, $p = .32$)	2.8 vs. 2.3 (HR 1.21; 95% CI, 0.85–1.73, $p = .29$)	NA
ROOBY, 2017[65]	Off-pump vs. on-pump CABG (RCT)	All CAD	2203	30 days	5.6 vs. 7.0 (RR 1.26; 95% CI, 0.91–1.74, $p = .19$)	1.6 vs. 1.2 (RR 1.38; 95% CI, 0.68–2.80, $p = .47$)	NA	1.3 vs. 0.7 (RR 1.75; 95% CI, 0.74–4.14, $p = .28$)	NA	NA
				1 year	9.9 vs. 7.4 (RR 1.33; 95% CI, 1.01–1.76, $p = .04$)	4.1 vs. 2.9 (RR 1.41; 95% CI, 0.90–2.24, $p = .15$)	2.0 vs. 2.2 (RR 0.90; 95% CI, 0.50–1.62, $p = .76$)	NA	4.6 vs. 3.4 (RR 1.35; 95% CI, 0.88–2.05, $p = .18$)	NA
				5 years	31.0 vs. 27.1 (RR 1.14; 95% CI, 1.00–1.30, $p = .046$)	15.2 vs. 11.9 (RR 1.28; 95% CI, 1.03–158, $p = .02$)	12.1 vs. 9.6 (RR 1.27; 95% CI, 1.00–1.62, $p = .05$)	NA	13.4 vs. 12.0 (RR 1.12; 95% CI, 0.89–1.41, $p = .33$)	NA
GOPCABE, 2019[66]	Off-pump vs. on-pump CABG (RCT)	Patients ≥75 years of age with CAD, scheduled for first-time CABG	2394	30 days	7.8 vs. 8.2 (OR 0.95; 95% CI, 0.71–1.28, $p = .74$)[c]	2.6 vs. 2.8 (OR 0.92; 95% CI, 0.57–1.51, $p = .75$)	1.5 vs. 1.7 (OR 0.92; 95% CI, 0.51–1.66, $p = .79$)	2.2 vs. 2.7 (OR 0.83; 95% CI, 0.50–1.38, $p = .47$)	1.3 vs. 0.4 (OR 2.42; 95% CI, 1.03–5.72, $p = .04$)	NA
				1 year	13.1 vs. 14.0 (HR 0.93; 95% CI, 0.76–1.16, $p = .48$)[c]	7.0 vs. 8.0 (HR 0.88; 95% CI, 0.65–1.18, $p = .38$)	2.1 vs. 2.4 (HR 0.90; 95% CI, 0.53–1.54, $p = .70$)	3.5 vs. 4.4 (HR 0.79; 95% CI, 0.53–1.19, $p = .26$)	3.1 vs. 2.0 (HR 1.52; 95% CI, 0.90–2.54, $p = .11$)	NA
				5 years	34 vs. 33 (HR 1.03; 95% CI, 0.89–1.18, $p = .704$)[d]	31 vs. 30 (HR 1.03; 95% CI, 0.89–1.19, $p = .71$)	2.1 vs. 1.5 (HR 1.69; 95% CI, 0.78–3.70, $p = .181$)	NA	4.1 vs. 3.2 (HR 1.34; 95% CI, 0.83–2.15, $p = .228$)	NA

TABLE 4 (Continued)

Trial	Trial design	Patient population	*N*	Follow-up	MACCE	All-cause mortality	MI	CVA	Repeat revascularization	Graft patency
IV. Minimally invasive approaches										
Stanbridge, 1999[67]	MIDCAB vs. sternotomy (meta-analysis)	Patients who underwent CABG by either MIDCAB or sternotomy	6364	Short-term	NA	1.6 vs. 2.2 (NS)	NA	NA	NA	89.5 vs. 93.6 ($p = .08$)
Ruel, 2014[68]	MIDCAB (prospective cohort)	Patients referred for first-time single or multivessel CABG suitable for MIDCAB	91	6 months	NA	NA	NA	NA	NA	92%
Kitahara, 2019[69]	MIDCAB vs. TECAB (meta-analysis)	Patients referred for CABG by either MIDCAB or TECAB	4000	<1 month	NA	NA	NA	NA	NA	97.7% vs. 98.9%
				<5 months	NA	NA	NA	NA	NA	96.1% vs. 95.8%
				>5 years	NA	NA	NA	NA	NA	93.2% vs. 93.6%
POL-MIDES, 2018[70]	HCR vs. CABG (RCT)	Patients with multivessel CAD involving >70% LAD lesion, referred for CABG	200	5 years	45.2 vs. 53.4 ($p = .39$)[e]	6.4 vs. 9.2 ($p = .69$)	NA	NA	NA	NA

Note: Outcomes following CABG: I. FFR-guided; II. per specific donor graft; III. off- versus on-pump; and IV. minimally invasive approaches. Outcomes were presented as estimated cumulative event rates, RRs, ORs, with their 95% CI, and *p*-values.

Abbreviations: ART, arterial revascularization trial; BIMA, bilateral internal mammary artery; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CAG, coronary angiogram; CI, confidence interval; CORONARY, CABG Off or On Pump Revascularization Study; FFR, fractional flow reserve; FARGO, Fractional Flow Reserve versus Angiography Randomization for Graft Optimization; GOPCABE, German Off-Pump Coronary Artery Bypass Grafting in Elderly Patients; GRAFFITI, Graft Patency After FFR-Guided versus Angiography-Guided CABG; HCR, hybrid coronary revascularization; HR, hazard ratio; LAD, left anterior descending; MACCE, major adverse cardiac and cerebrovascular events; MD, mean difference; MI, myocardial infarction; MIDCAB, minimally invasive coronary artery bypass; NA, not applicable; NS, not significant; OR, odds ratio; POL-MIDES, Safety and Efficacy Study of Hybrid Revascularization in Multivessel Coronary Artery Disease; ROOBY, Randomization Off-Pump versus On-Pump Bypass; RR, relative risk; SIMA, single internal mammary artery; and TECAB, totally endoscopic coronary artery bypass.

[a]In-hospital rates.

[b]Event-free rates.

[c]The composite outcome of all-cause death, MI, stroke, repeat revascularization and new renal-replacement therapy.

[d]The composite outcome of all-cause death, MI and repeat revascularization.

[e]The composite outcome of all-cause death, MI, stroke and repeat revascularization.

TABLE 5 Perioperative outcomes of minimally invasive CABG approaches

Trial	Trial design	Patient population	*N*	Redo thoracotomy	Conversion to sternotomy	Blood transfusion	Ventilation time	Hospital length of stay
Ruel, 2014[68]	MIDCAB (prospective cohort)	Patients referred for first-time single or multivessel CABG suitable for MIDCAB	91	2.2%	0%	23%	538 ± 255 min	NA
Argenziano, 2006[82]	TECAB (prospective cohort)	Patients referred for first-time single-vessel LIMA to LAD	85	3.5%	5.9%	31%	14 ± 28 h	5.1 ± 3.4 days
Reynolds, 2018[83]	HCR vs. sternotomy (meta-analysis)	Patients referred for CABG by either HCR or sternotomy	4260	NA	NA	22.8 vs. 46.1 (OR 0.38; 95% CI, 0.31–0.46, $p < .001$)	MD −8.99 (95% CI, −15.85 to −2.13, $p = .01$)	MD −1.48 (95% CI, −2.61 to −0.36, $p = .010$)
Dong, 2018[84]	HCR vs. sternotomy (meta-analysis)	Patients with multivessel CAD or LM disease referred for CABG	6121	NA	NA	MD 0.57 (95% CI, 0.49–0.67, $p < .001$)	MD −0.36 (95% CI, −0.55 to −0.16, $p < .001$)	MD −0.29 (95% CI, −0.50 to −0.07, $p < .05$)

Note: Perioperative outcomes of minimally invasive CABG. Outcomes were presented as estimated cumulative event rates, MD, RR, ORs with their 95% CI, and *p*-values.

Abbreviations: CABG, coronary artery bypass grafting; CAD, coronary artery disease; CI, confidence interval; HCR, hybrid coronary revascularization; HR, hazard ratio; LIMA, left internal mammary artery; LM, left main; MD, mean difference; MIDCAB, minimally invasive coronary artery bypass; OR, odds ratio; RR, relative risk; TECAB, totally endoscopic coronary artery bypass.

in specific patient subsets at experienced centres. Hybrid coronary revascularization is a staged approach that is either indicated to avoid sternotomy in multivessel CAD patients or to graft single LAD lesions potentially following emergency PCI of the other targets.[4] It has been indicated that the outcomes of hybrid coronary revascularization align with those of MIDCAB and conventional CABG, with especially short-term outcomes in favour of hybrid coronary revascularization (see Tables 4 and 5).[70,83,84] Although minimally invasive approaches are expensive and require dedicated surgical teams, they could be alternative treatment plans for multivessel CAD patients with high risk of sternotomy-related complications, diabetic and obese patients, and those suffering from chronic obstructive pulmonary disease.[83]

6 | CONCLUSION

Revascularization outcomes rapidly improve due to new techniques and patient-tailored strategies. Following up on the 2018 ESC/EACTS guidelines of myocardial revascularization, important trial outcomes are published. The ISCHEMIA trial suggests medical therapy alone should suffice in CCS patients without left main involvement. A rectification of the EXCEL trial showed significant lower rates of MI and mortality in CABG than in PCI. The recently published FAME III results did report inferiority of FFR-guided PCI compared to CABG in multivessel disease. All indicates that to further improve revascularization outcomes, the decision-making process should be increasingly patient-tailored.

CONFLICT OF INTEREST

We have no conflicts of interest to disclose.

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REFERENCES

1. Khan MA, Hashim MJ, Mustafa H, et al. Global epidemiology of ischemic heart disease: results from the global burden of disease study. *Cureus*. 2020;12(7):e9349. doi:10.7759/cureus.9349
2. Wang F, Yu Y, Mubarik S, et al. Global burden of ischemic heart disease and attributable risk factors, 1990–2017: a secondary analysis based on the global burden of disease study 2017. *Clin Epidemiol*. 2021;13:859–870. doi:10.2147/clep.S317787
3. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J*. 2020;41(3):407–477. doi:10.1093/eurheartj/ehz425
4. 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

5. Simera I, Moher D, Hoey J, Schulz KF, Altman DG. A catalogue of reporting guidelines for health research. *Eur J Clin Invest*. 2010;40(1):35–53. doi:10.1111/j.1365-2362.2009.02234.x
6. Henderson RA, Pocock SJ, Clayton TC, et al. Seven-year outcome in the RITA-2 trial: coronary angioplasty versus medical therapy. *J Am Coll Cardiol*. 2003;42(7):1161–70. doi:10.1016/s0735-1097(03)00951-3
7. Hueb W, Soares PR, Gersh BJ, et al. The medicine, angioplasty, or surgery study (MASS-II): a randomized, controlled clinical trial of three therapeutic strategies for multivessel coronary artery disease: one-year results. *J Am Coll Cardiol*. 2004;43(10):1743–51. doi:10.1016/j.jacc.2003.08.065
8. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med*. 2007;356(15):1503–16. doi:10.1056/NEJMoa070829
9. Maron DJ, Hochman JS, Reynolds HR, et al. Initial invasive or conservative strategy for stable coronary disease. *N Engl J Med*. 2020;382(15):1395–1407. doi:10.1056/NEJMoa1915922
10. BARI 2D Study Group, Frye RL, August P et al. A randomized trial of therapies for type 2 diabetes and coronary artery disease. *N Engl J Med*. 2009;360(24):2503-2515. doi:10.1056/NEJMoa0805796
11. Coronary artery surgery study (CASS): a randomized trial of coronary artery bypass surgery. Comparability of entry characteristics and survival in randomized patients and nonrandomized patients meeting randomization criteria. *J Am Coll Cardiol*. 1984;3(1):114–28.
12. De Bruyne B, Pijls NH, Kalesan B, et al. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N Engl J Med*. 2012;367(11):991–1001. doi:10.1056/NEJMoa1205361
13. Meyer MR. Chronic coronary syndromes in women: challenges in diagnosis and management. *Mayo Clin Proc*. 2021;96(4):1058–1070. doi:10.1016/j.mayocp.2020.09.023
14. Kunadian V, Chieffo A, Camici PG, et al. An EAPCI Expert Consensus Document on Ischaemia with Non-Obstructive Coronary Arteries in Collaboration with European Society of Cardiology Working Group on Coronary Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group. *EuroIntervention*. 2021;16(13):1049–1069. doi:10.4244/eijy20m07_01
15. Head SJ, Milojevic M, Daemen J, et al. Mortality after coronary artery bypass grafting versus percutaneous coronary intervention with stenting for coronary artery disease: a pooled analysis of individual patient data. *Lancet*. 2018;391(10124):939–948. doi:10.1016/s0140-6736(18)30423-9
16. Kapoor JR, Gienger AL, Ardehali R, et al. Isolated disease of the proximal left anterior descending artery comparing the effectiveness of percutaneous coronary interventions and coronary artery bypass surgery. *JACC Cardiovasc Interv*. 2008;1(5):483–91. doi:10.1016/j.jcin.2008.07.001
17. Hannan EL, Wu C, Walford G, et al. Drug-eluting stents vs. coronary-artery bypass grafting in multivessel coronary disease. *N Engl J Med*. 2008;358(4):331–41. doi:10.1056/NEJMoa071804
18. Takahashi K, Serruys PW, Fuster V, et al. Redevelopment and validation of the SYNTAX score II to individualise decision making between percutaneous and surgical revascularisation in patients with complex coronary artery disease: secondary analysis of the multicentre randomised controlled SYNTAXES trial with external cohort validation. *Lancet*. 2020;396(10260):1399–1412. doi:10.1016/s0140-6736(20)32114-0
19. Ono M, Serruys PW, Hara H, et al. 10-year follow-up after revascularization in elderly patients with complex coronary artery disease. *J Am Coll Cardiol*. 2021;77(22):2761–2773. doi:10.1016/j.jacc.2021.04.016
20. Stone GW, Kappetein AP, Sabik JF, et al. Five-year outcomes after PCI or CABG for left main coronary disease. *N Engl J Med*. 2019;381(19):1820–1830. doi:10.1056/NEJMoa1909406
21. Park DW, Ahn JM, Park H, et al. Ten-year outcomes after drug-eluting stents versus coronary artery bypass grafting for left main coronary disease: extended follow-up of the PRECOMBAT trial. *Circulation*. 2020;141(18):1437–1446. doi:10.1161/circulationaha.120.046039
22. Ahn JM, Roh JH, Kim YH, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease: 5-year outcomes of the PRECOMBAT study. *J Am Coll Cardiol*. 2015;65(20):2198–206. doi:10.1016/j.jacc.2015.03.033
23. Holm NR, Mäkikallio T, Lindsay MM, et al. Percutaneous coronary angioplasty versus coronary artery bypass grafting in the treatment of unprotected left main stenosis: updated 5-year outcomes from the randomised, non-inferiority NOBLE trial. *Lancet*. 2020;395(10219):191–199. doi:10.1016/s0140-6736(19)32972-1
24. Garcia S, Sandoval Y, Roukoz H, et al. Outcomes after complete versus incomplete revascularization of patients with multivessel coronary artery disease: a meta-analysis of 89,883 patients enrolled in randomized clinical trials and observational studies. *J Am Coll Cardiol*. 2013;62(16):1421–31. doi:10.1016/j.jacc.2013.05.033
25. Farkouh ME, Domanski M, Sleeper LA, et al. Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med*. 2012;367(25):2375–84. doi:10.1056/NEJMoa1211585
26. Farkouh ME, Domanski M, Dangas GD, et al. Long-term survival following multivessel revascularization in patients with diabetes: the FREEDOM follow-on study. *J Am Coll Cardiol*. 2019;73(6):629–638. doi:10.1016/j.jacc.2018.11.001
27. Chen WW, Chen JY, Li CI, et al. Diabetes mellitus associated with an increased risk of percutaneous coronary intervention long-term adverse outcomes in Taiwan: a nationwide population-based cohort study. *J Diabetes Complications*. 2020;34(11):107689. doi:10.1016/j.jdiacomp.2020.107689
28. Velazquez EJ, Lee KL, Jones RH, et al. Coronary-artery bypass surgery in patients with ischemic cardiomyopathy. *N Engl J Med*. 2016;374(16):1511–1520. doi:10.1056/NEJMoa1602001
29. Nagendran J, Bozso SJ, Norris CM, et al. Coronary artery bypass surgery improves outcomes in patients with diabetes and left ventricular dysfunction. *J Am Coll Cardiol*. 2018;71(8):819–827. doi:10.1016/j.jacc.2017.12.024
30. Stone GW, Serruys PW, Sabik JF. PCI or CABG for left main coronary artery disease. Reply. *N Engl J Med*. 2020;383(3):292–294. doi:10.1056/NEJMc2000645
31. Thuijs D, Kappetein AP, Serruys PW, et al. Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial. *Lancet*. 2019;394(10206):1325–1334. doi:10.1016/s0140-6736(19)31997-x
32. Kang J, Han JK, Kang DY, et al. SYNTAX score and SYNTAX score II can predict the clinical outcomes of patients with left main and/or 3-vessel disease undergoing percutaneous coronary intervention in the contemporary cobalt-chromium everolimus-eluting stent era. *Korean Circ J*. 2020;50(1):22–34. doi:10.4070/kcj.2019.0097

33. Farooq V, van Klaveren D, Steyerberg EW, et al. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. *Lancet*. 2013;381(9867):639–50. doi:10.1016/s0140-6736(13)60108-7
34. Almarzooq ZI, Yeh RW. 'State of the Art' PCI: bridging the implementation gap. *Eur Heart J*. 2022;43(13):1317–1319. doi:10.1093/eurheartj/ehab855
35. Banning AP, Serruys P, De Maria GL, et al. Five-year outcomes after state-of-the-art percutaneous coronary revascularization in patients with de novo three-vessel disease: final results of the SYNTAX II study. *Eur Heart J*. 2022;43(13):1307–1316. doi:10.1093/eurheartj/ehab703
36. Ahn JM, Park DW, Lee CW, et al. Comparison of stenting versus bypass surgery according to the completeness of revascularization in severe coronary artery disease: patient-level pooled analysis of the SYNTAX, PRECOMBAT, and BEST trials. *JACC Cardiovasc Interv*. 2017;10(14):1415–1424. doi:10.1016/j.jcin.2017.04.037
37. van Nunen LX, Zimmermann FM, Tonino PA, et al. Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial. *Lancet*. 2015;386(10006):1853–60. doi:10.1016/s0140-6736(15)00057-4
38. Ad N, Holmes SD, Patel J, Pritchard G, Shuman DJ, Halpin L. Comparison of EuroSCORE II, Original EuroSCORE, and The Society of Thoracic Surgeons Risk Score in Cardiac Surgery Patients. *Ann Thorac Surg*. 2016;102(2):573–9. doi:10.1016/j.athoracsur.2016.01.105
39. Graham MM, Norris CM, Galbraith PD, Knudtson ML, Ghali WA. Quality of life after coronary revascularization in the elderly. *Eur Heart J*. 2006;27(14):1690–8. doi:10.1093/eurheartj/ehl038
40. Nicolini F, Contini GA, Fortuna D, et al. Coronary artery surgery versus percutaneous coronary intervention in octogenarians: long-term results. *Ann Thorac Surg*. 2015;99(2):567–74. doi:10.1016/j.athoracsur.2014.09.019
41. Weintraub WS, Grau-Sepulveda MV, Weiss JM, et al. Comparative effectiveness of revascularization strategies. *N Engl J Med*. 2012;366(16):1467–1476. doi:10.1056/NEJMoa1110717
42. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360(10):961–72. doi:10.1056/NEJMoa0804626
43. Shaw LJ, Berman DS, Maron DJ, et al. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy. *Circulation*. 2008;117(10):1283–91. doi:10.1161/circulationaha.107.743963
44. Patel DB, Shah R, Jovin IS. Improving outcomes of percutaneous coronary interventions in patients with stable ischemic heart disease. *J Thorac Dis*. 2020;12(4):1740–1749. doi:10.21037/jtd.2019.11.17
45. Fischman DL, Leon MB, Baim DS, et al. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. Stent Restenosis Study Investigators. *N Engl J Med*. 1994;331(8):496–501. doi:10.1056/nejm199408253310802
46. Morice MC, Serruys PW, Sousa JE, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med*. 2002;346(23):1773–80. doi:10.1056/NEJMoa012843
47. Bønaa KH, Mannsverk J, Wiseth R, et al. Drug-eluting or bare-metal stents for coronary artery disease. *N Engl J Med*. 2016;375(13):1242–52. doi:10.1056/NEJMoa1607991
48. Stone GW, Moses JW, Ellis SG, et al. Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. *N Engl J Med*. 2007;356(10):998–1008. doi:10.1056/NEJMoa067193
49. Windecker S, Stortecky S, Stefanini GG, et al. Revascularisation versus medical treatment in patients with stable coronary artery disease: network meta-analysis. *BMJ*. 2014;348:g3859. doi:10.1136/bmj.g3859
50. Tada T, Byrne RA, Simunovic I, et al. Risk of stent thrombosis among bare-metal stents, first-generation drug-eluting stents, and second-generation drug-eluting stents: results from a registry of 18,334 patients. *JACC Cardiovasc Interv*. 2013;6(12):1267–74. doi:10.1016/j.jcin.2013.06.015
51. Changal KH, Mir T, Khan S, et al. Drug-eluting stents versus bare-metal stents in large coronary artery revascularization: systematic review and meta-analysis. *Cardiovasc Revasc Med*. 2021;23:42–49. doi:10.1016/j.carrev.2020.07.018
52. Stevens JR, Zamani A, Osborne JIA, Zamani R, Akrami M. Critical evaluation of stents in coronary angioplasty: a systematic review. *Biomed Eng Online*. 2021;20(1):46. doi:10.1186/s12938-021-00883-7
53. Ellis SG, Kereiakes DJ, Metzger DC, et al. Everolimus-eluting bioresorbable scaffolds for coronary artery disease. *N Engl J Med*. 2015;373(20):1905–15. doi:10.1056/NEJMoa1509038
54. Zimmermann FM, Ferrara A, Johnson NP, et al. Deferral vs. performance of percutaneous coronary intervention of functionally non-significant coronary stenosis: 15-year follow-up of the DEFER trial. *Eur Heart J*. 2015;36(45):3182–8. doi:10.1093/eurheartj/ehv452
55. 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
56. van de Hoef TP, Lee JM, Echavarria-Pinto M, et al. Non-hyperaemic coronary pressure measurements to guide coronary interventions. *Nat Rev Cardiol*. 2020;17(10):629–640. doi:10.1038/s41569-020-0374-z
57. Wardziak Ł, Kruk M, Pleban W, et al. Coronary CTA enhanced with CTA based FFR analysis provides higher diagnostic value than invasive coronary angiography in patients with intermediate coronary stenosis. *J Cardiovasc Comput Tomogr*. 2019;13(1):62–67. doi:10.1016/j.jcct.2018.10.004
58. Fearon WF, Zimmermann FM, De Bruyne B, et al. Fractional flow reserve-guided PCI as compared with coronary bypass surgery. *N Engl J Med*. 2021;386:128–137. doi:10.1056/NEJMoa2112299
59. Thuesen AL, Riber LP, Veien KT, et al. Fractional flow reserve versus angiographically-guided coronary artery bypass grafting. *J Am Coll Cardiol*. 2018;72(22):2732–2743. doi:10.1016/j.jacc.2018.09.043
60. 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(11):e999–e1005. doi:10.4244/eij-d-19-00463

61. Cao C, Manganas C, Horton M, et al. Angiographic outcomes of radial artery versus saphenous vein in coronary artery bypass graft surgery: a meta-analysis of randomized controlled trials. *J Thorac Cardiovasc Surg*. 2013;146(2):255–61. doi:10.1016/j.jtcvs.2012.07.014
62. Buttar SN, Yan TD, Taggart DP, Tian DH. Long-term and short-term outcomes of using bilateral internal mammary artery grafting versus left internal mammary artery grafting: a meta-analysis. *Heart*. 2017;103(18):1419–1426. doi:10.1136/heartjnl-2016-310864
63. Taggart DP. Implications of the 10-year outcomes of the Arterial Revascularization Trial (ART) for multiple arterial grafts during coronary artery bypass graft. *Eur J Cardiothorac Surg*. 2019;56(3):427–428. doi:10.1093/ejcts/ezz174
64. Lamy A, Devereaux PJ, Prabhakaran D, et al. Five-year outcomes after off-pump or on-pump coronary-artery bypass grafting. *N Engl J Med*. 2016;375(24):2359–2368. doi:10.1056/NEJMoa1601564
65. Shroyer AL, Hattler B, Wagner TH, et al. Five-year outcomes after on-pump and off-pump coronary-artery bypass. *N Engl J Med*. 2017;377(7):623–632. doi:10.1056/NEJMoa1614341
66. Diegeler A, Börgermann J, Kappert U, et al. Five-year outcome after off-pump or on-pump coronary artery bypass grafting in elderly patients. *Circulation*. 2019;139(16):1865–1871. doi:10.1161/circulationaha.118.035857
67. Stanbridge RD, Hadjinikolaou LK. Technical adjuncts in beating heart surgery comparison of MIDCAB to off-pump sternotomy: a meta-analysis. *Eur J Cardiothorac Surg*. 1999;16(Suppl 2):S24–33.
68. Ruel M, Shariff MA, Lapierre H, et al. Results of the minimally invasive coronary artery bypass grafting angiographic patency study. *J Thorac Cardiovasc Surg*. 2014;147(1):203–8. doi:10.1016/j.jtcvs.2013.09.016
69. Kitahara H, Nisivaco S, Balkhy HH. Graft patency after robotically assisted coronary artery bypass surgery. *Innovations (Phila)*. 2019;14(2):117–123. doi:10.1177/1556984519836896
70. Tajstra M, Hrapkowicz T, Hawranek M, et al. Hybrid coronary revascularization in selected patients with multivessel disease: 5-year clinical outcomes of the prospective randomized pilot study. *JACC Cardiovasc Interv*. 2018;11(9):847–852. doi:10.1016/j.jcin.2018.01.271
71. Mack MJ, Osborne JA, Shennib H. Arterial graft patency in coronary artery bypass grafting: what do we really know? *Ann Thorac Surg*. 1998;66(3):1055–9. doi:10.1016/s0003-4975(98)00815-7
72. FitzGibbon GM, Burton JR, Leach AJ. Coronary bypass graft fate: angiographic grading of 1400 consecutive grafts early after operation and of 1132 after one year. *Circulation*. 1978;57(6):1070–74. doi:10.1161/01.cir.57.6.1070
73. Izzat MB, West RR, Bryan AJ, Angelini GD. Coronary artery bypass surgery: current practice in the United Kingdom. *Br Heart J*. 1994;71(4):382–5. doi:10.1136/hrt.71.4.382
74. Taggart DP. The role of multiple arterial grafts in CABG: all roads lead to ROMA. *J Am Coll Cardiol*. 2019;74(18):2249–2253. doi:10.1016/j.jacc.2019.09.016
75. Itagaki S, Cavallaro P, Adams DH, Chikwe J. Bilateral internal mammary artery grafts, mortality and morbidity: an analysis of 1 526 360 coronary bypass operations. *Heart*. 2013;99(12):849–53. doi:10.1136/heartjnl-2013-303672
76. Gaudino M, Benedetto U, Bakaeen F, et al. Off- versus on-pump coronary surgery and the effect of follow-up length and surgeons' experience: a meta-analysis. *J Am Heart Assoc*. 2018;7(21):e010034. doi:10.1161/JAHA.118.010034
77. Dieberg G, Smart NA, King N. On- vs. off-pump coronary artery bypass grafting: a systematic review and meta-analysis. *Int J Cardiol*. 2016;223:201–211. doi:10.1016/j.ijcard.2016.08.250
78. Altarabsheh SE, Deo SV, Rababa'h AM, et al. Off-pump coronary artery bypass reduces early stroke in octogenarians: a meta-analysis of 18,000 patients. *Ann Thorac Surg*. 2015;99(5):1568–75. doi:10.1016/j.athoracsur.2014.12.057
79. Benedetto U, Caputo M, Vohra H, et al. Off-pump versus on-pump coronary artery bypass surgery in patients with actively treated diabetes and multivessel coronary disease. *J Thorac Cardiovasc Surg*. 2016;152(5):1321–1330.e12. doi:10.1016/j.jtcvs.2016.06.038
80. Emmert MY, Seifert B, Wilhelm M, Grünenfelder J, Falk V, Salzberg SP. Aortic no-touch technique makes the difference in off-pump coronary artery bypass grafting. *J Thorac Cardiovasc Surg*. 2011;142(6):1499–506. doi:10.1016/j.jtcvs.2011.04.031
81. Bonatti J, Lee JD, Bonaros N, Schachner T, Lehr EJ. Robotic totally endoscopic multivessel coronary artery bypass grafting: procedure development, challenges, results. *Innovations (Phila)*. 2012;7(1):3–8. doi:10.1097/IMI.0b013e3182552ea8
82. Argenziano M, Katz M, Bonatti J, et al. Results of the prospective multicenter trial of robotically assisted totally endoscopic coronary artery bypass grafting. *Ann Thorac Surg*. 2006;81(5):1666–74; discussion 1674-5. doi:10.1016/j.athoracsur.2005.11.007
83. Reynolds AC, King N. Hybrid coronary revascularization versus conventional coronary artery bypass grafting: systematic review and meta-analysis. *Medicine*. 2018;97(33):e11941. doi:10.1097/md.0000000000011941
84. Dong L, Kang YK, An XG. Short-term and mid-term clinical outcomes following hybrid coronary revascularization versus off-pump coronary artery bypass: a meta-analysis. *Arq Bras Cardiol*. 2018;110(4):321–330. doi:10.5935/abc.20180044

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