

# Techniques and approaches for revascularisation of left heart coronary diseases

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## Abstract

Coronary artery disease and its associated clinical sequelae are a significant medical burden to clinicians and patients. Severe coronary artery disease presenting in the context of acute myocardial ischaemia, or stable plaques causing chronic symptoms despite best conservative and pharmacological intervention, are often amenable to further intervention such as coronary artery bypass grafting. This procedure has been extensively compared to newer and less invasive techniques, such as percutaneous coronary intervention, and other minimally invasive procedures such as robotic or endoscopic techniques. This review summarises the current evidence on revascularisation of the left coronary artery system, with particular emphasis on key clinical endpoints of mortality, myocardial infarction, stroke and repeat revascularisation.

**Key words:** Coronary artery bypass grafting; Coronary revascularisation; Hybrid revascularisation; Minimally invasive; Percutaneous coronary intervention; Robotically assisted; Totally endoscopic

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## Introduction

With a prevalence of 2.3 million in the UK, coronary artery disease is a leading cause of death in the UK, as well as worldwide (British Heart Foundation, 2020). Coronary artery disease traditionally presents with angina, myocardial infarction or ischaemic heart failure, precipitated by atherosclerotic coronary vessels that may stenose or rupture resulting in vessel occlusions. The approach to myocardial revascularisation may vary depending on risk factors, vessel anatomy, and the site and extent of stenosis.

The main indication for intervention is to improve prognosis and provide symptomatic relief (Neumann et al, 2019). Many studies have compared procedures such as coronary artery bypass grafting and percutaneous coronary intervention. Additionally, novel options such as minimally invasive direct coronary artery bypass, totally endoscopic coronary artery bypass, robotically enhanced coronary artery bypass myocardial revascularisation and hybrid procedures have been gaining popularity.

The SYNTAX score (Sianos et al, 2005) was developed to grade the anatomical complexity of coronary lesions in patients with left main or three-vessel disease, and was found to be an independent predictor of long-term major adverse cardiac and cerebrovascular events and mortality following percutaneous coronary intervention. Despite all the advances in percutaneous coronary intervention, coronary artery bypass grafting remains the gold standard treatment for multi-vessel coronary artery disease. Minimally invasive and hybrid procedures are gaining popularity, and have shown similar safety and efficacy profiles to conventional coronary artery bypass grafting in selected cases, especially in the treatment of proximal stenosis of the left anterior descending artery.

This article provides an update on the current management of left-sided myocardial revascularisation with emphasis on the clinical importance of major adverse cardiac and cerebrovascular events, mortality, myocardial infarction, stroke and repeat revascularisation, as well as evaluating various revascularisation strategies.

## Current guidance and clinical practice

Current European guidelines (Neumann et al, 2019) strongly recommend coronary artery bypass grafting for revascularisation of left main stem coronary artery disease in patients of

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all SYNTAX classifications, in three-vessel coronary artery disease with/without diabetes and one-vessel coronary artery disease with proximal left anterior descending artery stenosis. Guidance is less certain for coronary artery bypass grafting in one-vessel coronary artery disease without proximal left anterior descending artery stenosis and two-vessel disease with or without proximal left anterior descending artery stenosis (Neumann et al, 2019). American guidance (Fihn et al, 2012, 2014) favours coronary artery bypass grafting, if tolerated, over percutaneous coronary intervention for patients with diabetes and those with multi-vessel coronary artery disease.

With the publication of more studies, the European guidelines now provide more definitive recommendations for coronary artery bypass grafting vs percutaneous coronary intervention, with predominantly class II recommendations and B/C levels of evidence in all classifications of coronary artery disease (Table 1) (Neumann et al, 2019). However, evidence (IIa/B recommendation) on minimally invasive techniques remains limited, so the recommendations are based on expertise. Similarly, evidence for hybrid procedures is limited to IIb/B and IIb/C in Europe and the USA.

## Conventional surgical revascularisation

Traditional coronary artery bypass grafting is performed through median sternotomy, cardiopulmonary bypass and myocardial protection provided by cardioplegic arrest. Choice of conduit is determined by age, comorbidities, lesion position, suitability of targets and conduit quality. For a left anterior descending graft, the left internal mammary artery is the conduit of choice because of its high patency rate (98% at 1 year) and anatomical and histological considerations (Neumann et al, 2019). Anatomically the left internal mammary artery is more suited to be anastomosed to the left anterior descending because of its size and specific histological characteristics – it has fewer endothelial fenestrations and less intercellular permeability than saphenous vein grafts. The left internal mammary artery also offers physiological benefits in terms of its resistance to sheer stress, as well as benefits in terms of vasodilatory and antithrombotic properties and resistance to lipid

**Table 1. Levels of evidence supporting the type of revascularisation (coronary artery bypass grafting or percutaneous coronary intervention) depending on pathology in patients with coronary artery disease with suitable coronary anatomy for both procedures and low predicted surgical mortality**

Extent of coronary artery disease		Class of evidence for recommendation		
		CABG	PCI	Preferred therapy
One vessel	With proximal left anterior descending artery stenosis	I/A	I/A	–
	Without proximal left anterior descending artery stenosis	IIb/C	I/C	PCI
Two vessel	With proximal left anterior descending artery stenosis	I/B	I/C	–
	Without proximal left anterior descending artery stenosis	IIb/C	I/C	PCI
Left main stem	Low SYNTAX score (0–22)	I/A	I/A	–
	Intermediate SYNTAX score (23–32)	I/A	IIa/A	CABG
	High SYNTAX score ( $\geq 33$ )	I/A	III/B	CABG
Three vessel, without diabetes mellitus	Low SYNTAX score (0–22)	I/A	I/A	–
	Intermediate or high score ( $\geq 23$ )	I/A	III/A	CABG
Three vessel, with diabetes mellitus	Low SYNTAX score (0–22)	I/A	IIb/A	CABG
	Intermediate or high score ( $\geq 23$ )	I/A	II/A	CABG

CABG = coronary artery bypass grafting, PCI = percutaneous coronary intervention. From Neumann et al (2019)

accumulation compared to saphenous vein grafts, resulting in reduced susceptibility to atherosclerosis (Yim et al, 2020). While the radial artery and right gastroepiploic artery are well-documented alternatives, their use is currently limited by their anatomical inferiority to the left internal mammary artery, vasospastic characteristics of the radial artery specifically, and overall there is less evidence supporting these arterial conduits compared to the left internal mammary artery (Martínez-González et al, 2017).

According to the American Heart Association guidelines (Fihn et al, 2012, 2014), if the left main stem is significantly stenosed (>50%), or the proximal left anterior descending and proximal circumflex disease is significant (>70%), or the patient has one or two-vessel coronary artery disease and left ventricular ejection fraction <50%, coronary artery bypass grafting is indicated. Better survival trends were noted in patients with high SYNTAX scores or high anatomical complexity. A potential benefit of coronary artery bypass grafting is protection against disease progression in proximal segments, which may be diminished by restricting the bypass targets to functionally relevant lesions. Coronary artery bypass grafting is also recommended in patients having aortic or mitral valve surgery and whose coronary artery diameter stenosis is >70% (Neumann et al, 2019).

### Percutaneous intervention vs conventional surgery

Standard modernised percutaneous coronary intervention involves inserting a catheter into a distal (usually radial) artery. Under fluoroscopic imaging, the endoluminal access allows insertion of balloon angioplasty and arterial drug-eluting stents to consolidate coronary vessel patency. For the purposes of this review, percutaneous coronary intervention refers to percutaneous coronary intervention with drug-eluting stents only, instead of the rarer bare-metal stenting (which has less recent evidence). Other indications include ST-elevation myocardial infarction (STEMI) and non-STEMI with high-risk patients, prognostic and symptomatic management in the stable patient with stenosis >50%, and those with cardiogenic shock following recent cardiac insult (Neumann et al, 2019).

The SYNTAX trial (Serruys et al, 2009) remains one of the largest randomised controlled trials comparing percutaneous coronary intervention and coronary artery bypass grafting. In this non-inferiority study, the authors randomised 1800 patients into the two treatment arms to compare the 12-month composite primary outcome of major adverse cardiac and cerebrovascular events, repeat revascularisation and all-cause mortality. However, as this involved patients with predominantly multi-vessel disease (61.2% coronary artery bypass grafting, 60.5% percutaneous coronary intervention), results are not specific to coronary artery disease alone. Overall, percutaneous coronary intervention underperformed in major adverse cardiac and cerebrovascular events, with a higher incidence of 17.8% compared to 12.4% in the coronary artery bypass grafting group (95% confidence interval 1.15–1.81,  $P=0.002$ ). With the 5-year follow-up also showing consistency with earlier studies, coronary artery bypass grafting should remain the strategy of choice, particularly in patients with complex or severe disease and those with diabetes.

Boudriot et al (2011) randomised 201 patients and assessed the primary endpoint at 12-month follow up (which, unlike SYNTAX, did not include cerebrovascular events). They found overall that percutaneous coronary intervention was inferior to coronary artery bypass grafting (95% confidence interval 5.3–15.7,  $P=0.19$  for non-inferiority), and suggested higher requirements for repeated revascularisation in the percutaneous coronary intervention group. The authors cited inferiority compared to coronary artery bypass grafting in the primary endpoint, given percutaneous coronary intervention actually performed non-inferiorly to coronary artery bypass grafting with regards to major adverse cardiovascular events and mortality (95% confidence interval 10.6–4.4,  $P<0.001$  for non-inferiority).

The Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) Trial (Stone et al, 2016) is the largest randomised controlled trial to date, randomising 1905 patients into two interventions, compared non-inferiority of the primary composite endpoint of 3-year mortality or major adverse cardiac and cerebrovascular events. Percutaneous coronary intervention was non-inferior to coronary artery bypass grafting with an event percentage rate difference of 0.7 ( $P=0.02$ ) and a higher revascularisation rate (hazard ratio 1.72,  $P<0.001$ ).

Contrarily, the Nordic-Baltic-British Left Main Revascularisation (NOBLE) study (Mäkikallio et al, 2016) concluded coronary artery bypass grafting as superior. Their cohort of 1201 demonstrated higher rates of major adverse cardiac and cerebrovascular events (hazard ratio 1.51, 95% confidence interval 1.13–2.00,  $P=0.0044$ ), equivocal all-cause mortality ( $P=0.84$ ) and higher rates of repeat revascularisation (hazard ratio 1.50, 95% confidence interval 1.04–2.17,  $P=0.0304$ ) at Kaplan–Meier 5-year estimates for intention-to-treat. Additionally, unlike SYNTAX, the NOBLE study found no association between SYNTAX score and adverse outcomes. Since these studies, no further randomised controlled trials have compared these interventions.

A meta-analysis (Garg et al, 2017) included the aforementioned studies and reconfirmed the association between percutaneous coronary intervention and an equivocal risk of all-cause mortality ( $P=0.95$ ), cardiovascular mortality ( $P=0.93$ ), myocardial infarction ( $P=0.15$ ) and stroke ( $P=0.74$ ), but an increased risk of repeat revascularisation (odds ratio 1.82, 95% confidence interval 1.51–2.21,  $P<0.00001$ ). Crucially, the study included sensitivity analyses, and favoured individual over composite endpoints, allowing more precise and objective assessment of clinical outcomes. While this study may be limited by variable trial designs and stent models, it does highlight trends seen in individual randomised controlled trials. The relevant studies used in this review are summarised in [Table 2](#).

## Minimally invasive techniques

While the long-term outcomes of coronary artery bypass grafting remain superior to percutaneous coronary intervention (Mäkikallio et al, 2016) in patients with multi-vessel disease, this comes with increased invasiveness as a result of sternotomy and longer hospital stay than percutaneous coronary intervention (Cohen et al, 2011). An alternative, minimally invasive direct coronary artery bypass, uses smaller incisions via mini-thoracotomy, and despite worse postoperative pain, is superior to traditional median sternotomy in terms of overall quality of life (Diegeler et al, 1999).

Comparisons between percutaneous coronary intervention and minimally invasive direct coronary artery bypass plus drug-eluting stents have only been trialled in smaller studies, with additional data from observational or retrospective studies. First published evidence comparing percutaneous coronary intervention and minimally invasive direct coronary artery bypass plus drug-eluting stents (Hong et al, 2005) examined a small cohort ( $n=189$ ) from South Korea. In a 6-month follow-up period, the authors found similar risks between percutaneous coronary intervention and minimally invasive direct coronary artery bypass: 0% vs 2.9% mortality ( $P=0.135$ ), 1.7% vs 2.9% myocardial infarction ( $P=0.627$ ) and 1.7% vs 5.9% repeat revascularisation ( $P=0.196$ ). While percutaneous coronary intervention outperformed in-hospital outcomes, their conclusions on conventional clinical endpoints suggested comparable outcomes for isolated left anterior descending stenosis.

A study also compared percutaneous coronary intervention plus drug-eluting stents against minimally invasive direct coronary artery bypass at 12-month follow up, with non-inferiority results in mortality and myocardial infarction (Thiele et al, 2009). The 7-year outcomes of this cohort (Blazek et al, 2015) recorded no significant differences in endpoints of mortality ( $P=0.81$ ), myocardial infarction ( $P=0.74$ ) or quality of life, but the risk of needing repeat revascularisation is increased with percutaneous coronary intervention ( $P<0.001$ ).

A meta-analysis (Raja et al, 2018) combined three randomised controlled trials totalling 7710 patients and showed no significant differences in major adverse cardiac and cerebrovascular events (pooled odds ratio 1.31, 95% confidence interval 0.58–2.95,  $P=0.52$ ), mortality (pooled odds ratio 0.92, 95% confidence interval 0.65–1.32,  $P=0.66$ ) or myocardial infarction (pooled odds ratio 1.13, 95% confidence interval 0.62–2.06,  $P=0.69$ ). Minimally invasive direct coronary artery bypass showed a reduced risk of repeat revascularisation (odds ratio 0.27, 95% confidence interval 0.16–0.45,  $P<0.0001$ ) but did not include stroke risks. These findings corroborate with other meta-analyses, but cautious comparison is needed as patients undergoing percutaneous coronary intervention tend to have more complex vessel disease than those undergoing minimally invasive direct coronary artery bypass.

**Table 2. Studies comparing coronary artery bypass grafting, percutaneous coronary intervention, minimally invasive direct coronary artery bypass and hybrid coronary revascularisation**

Comp- arison	Study (reference)	Study design	Total patients	Follow up (months)	Inter- vention	Sample size	MACCE	Mortality	MI	Stroke	RR	Conclusions
CABG vs PCI	SYNTAX (Serruys et al, 2009)	RCT	1800	12	CABG	897	12.4	3.5	3.3	2.2	5.9	PCI not non-inferior to CABG, in a large part because of a significant difference in repeat revascularisation rates
					PCI-PES	903	17.8*	4.4	4.8	0.6*	13.5*	
	Boudroit et al (2011)	RCT	201	12	CABG	101	13.9	5.0	3.0	NA	4.0	PCI not non-inferior to CABG, in a large part due to a significant difference in repeat revascularisation rates
					PCI-SES	100	19.0	2.0	3.0		13.0	
	PRECOM- BAT (Ahn et al, 2015)	RCT	600	60	CABG	300	14.3	7.9	1.7	0.7	7.3	PCI non-inferior to CABG regarding MACCE, despite a significantly increased risk of revascularisation with PCI
					PCI-SES	300	17.5	5.7	2.0	0.7	13*	
	EXCEL (Stone et al, 2016)	RCT	1905	36	CABG	947	19.1	5.9	8.3	2.9	7.6	PCI non-inferior to CABG regarding MACCE, not including repeat revascularisation data
					PCI-EES	948	23.1	8.2	8.0	2.3	12.9*	
	NOBLE (Mäkikallio et al, 2016)	RCT	1201	60†	CABG	603	18.0	9.0	2.0	2.0	10.0	CABG better than PCI
					PCI-BES	598	28.0*	11.0	6.0*	5.0	15*	
	Garg et al (2017)	Meta- analysis	4595	60	CABG	2298	NA	7.1	4.9	2.3	8.4	PCI viable alternative to CABG, with similar risk of mortality, myocardial infarction and stroke, but increased risk of repeat revascularisation
					PCI-DES	2297	NA	7.5	6.0	2.0	14.3*	
MIDCAB	Hong et al (2005)	RCT	189	6	PCI-DES	119	NA	0	1.7	NA	1.7	Similar rates of mortality, myocardial infarction and repeat revascularisation
					MIDCAB	70		2.9	2.9	5.9		

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**Table 2. Studies comparing coronary artery bypass grafting, percutaneous coronary intervention, minimally invasive direct coronary artery bypass and hybrid coronary revascularisation (continued)**

MIDCAB	Thiele et al (2009)	RCT	130	12	PCI-SES	65	7.7	0 <sup>¶</sup>	1.5	NA	6.2	MIDCAB non-inferior to PCI-SES with respect to MACE
					MIDCAB	65	7.7	0 <sup>¶</sup>	7.7*		0	
	Blazek et al (2015)	RCT	130	86	PCI-SES	65	22	14	6	NA	13	Similar outcomes in regard to primary composite endpoint between MIDCAB and PCI-SES but repeat revascularisation risk higher with stenting
					MIDCAB	65	12	17	9		1*	
	Raja et al (2018)	Meta-analysis	7710	6-86	PCI-DES	5157	14.8	5.6	3.1	NA	15.5	MIDCAB offers benefit over PCI-DES in regard to repeat revascularisation, with similar rates of MACCE, mortality and myocardial infarction
					MIDCAB	2553	13.4	4.9	3.8		10.4*	
	MIST (Guo et al, 2019)	RCT	~180	-	CABG	-	-	-	-	-	-	Estimated to be available in 2025
					MIDCAB	-	-	-	-	-	-	
HCR	Harskamp et al (2015)	Retro-spective cohort	1224	1	CABG	918	3.1	1.1	0.9	1.7	NA	HCR is safe, with a faster recovery yet similar outcomes to CABG
					HCR	306	3.3	1.6	0.7	1		
	POLMIDES (Tajstra et al, 2018)	RCT	200	60	CABG	102	53.4	9.2	7.2	4.1	45.4	HCR has similar outcomes to CABG in respect to all conventional endpoints
					HCR	98	45.2	6.4	4.3	2.1	37.2	
	Puskas et al (2016)	Observational	298	17.6	PCI-DES	98	13.3	2	3.1	0	10	No significant difference in MACCE rates between HCR and PCI-DES
					HCR	200	11.5	1.5*	2*	2.5	7	
	Sardar et al (2018)	Meta-analysis	2245	1-36	CABG	1510	5.4 <sup>‡</sup>	1.5	1.9	1.9	4.5	HCR safe with similar outcomes to CABG
					HCR	735	3.6 <sup>‡</sup>	1.3	1.4	1	3.8	
	Hybrid Coronary Revascularisation Trial**	RCT	~2300	60	PCI DES	-	-	-	-	-	-	Awaited – estimated 2024
					HCR	-	-	-	-	-	-	

CABG = coronary artery bypass grafting; HCR = hybrid coronary revascularisation; MACCE = major cardiovascular and cerebrovascular events (not including cerebrovascular events or repeat revascularisation if data unavailable); MI = myocardial infarction; NA = not available or not reported; PCI-PES = percutaneous coronary intervention with paclitaxel-eluting stent; PCI-BES = percutaneous coronary intervention with Biolimus-eluting stent; PCI-DES: percutaneous coronary intervention with drug eluting stent (various); PCI-EES: percutaneous coronary intervention with everolimus-eluting stent; PCI-SES: percutaneous coronary intervention with sirolimus-eluting stent; RCT = randomised control trial; RR = Repeat revascularisation; TBC = to be confirmed; \* = statistically significant result (difference)  $p \leq 0.05$ ; † = Kaplan-Meier 5-year estimates; ‡ = MACCE does not include repeat revascularisation data; ¶ = reported as cardiac death \*\* = (ClinicalTrials.gov NCT03089398)

The MIST trial (Guo et al, 2019) is the first randomised controlled trial directly comparing minimally invasive direct coronary artery bypass with coronary artery bypass grafting, examining quality of life of a targeted 180 patients at 1-month post-coronary artery bypass grafting or post-minimally invasive direct coronary artery bypass. Results are awaited, with an estimated study completion date of 2025, and may offer insight into the relative benefits of minimally invasive direct coronary artery bypass compared to other management strategies with respect to major adverse cardiac and cerebrovascular events and other secondary outcomes.

With further technological advancements, the development of totally endoscopic coronary artery bypass allows even less invasive techniques than minimally invasive direct coronary artery bypass. Pure minimally invasive direct coronary artery bypass (without robotic enhancement) has been performed and described but as evidence remains limited, its relative efficacy is uncertain.

A meta-analysis of 17 cohort studies, totalling 3721 patients with a mean follow up of 3.3 years, examined totally endoscopic coronary artery bypass (Leonard et al, 2018). Their pooled results showed rates of 0.80% intraoperative mortality, 2.28% myocardial infarction, 1.5% stroke, 2.99% repeat revascularisation and 94% patency at follow up. While the results are acceptable, the authors recognised the relatively high rate of intraoperative myocardial infarction and provided possible explanations. Pair-wise meta-analysis provided equivocal odds ratio of intraoperative mortality (0.25, 95% confidence interval 0.02–2.83), myocardial infarction (3.09, 95% confidence interval 0.37–26.12) and stroke (1.33, 95% confidence interval 0.17–10.26), but insufficient data prevented comparisons of repeat revascularisation and graft patency. In 376 patients, across two studies where direct comparison of totally endoscopic coronary artery bypass (69.9%) to minimally invasive direct coronary artery bypass was available, no differences were seen in operative mortality, myocardial infarction, stroke or 30-day mortality. Their conclusions are limited by the nature of selection bias in low-risk cohorts of the included studies.

The da Vinci Surgical System, or robotically enhanced minimally invasive direct coronary bypass, has also been extended to include coronary artery disease (Argenziano et al, 2006). Mixed conclusions have been drawn from the small studies investigating perioperative risks, duration, early graft patency and its economic, personnel and infrastructural requirements compared to more traditional techniques (Harky et al, 2020). The paucity of robust evidence has limited the ability to draw useful conclusions regarding robotically enhanced coronary artery bypass, particularly regarding longer-term technical efficacy. Another systematic review of off-pump totally endoscopic coronary artery bypass and minimally invasive direct coronary artery bypass showed similar intraoperative complications as traditional techniques, but long-term mortality was not assessed because of discrepancies in follow-up interval between studies. These results (Cao et al, 2016) support findings from the literature and conclude that there are relatively safe outcomes, suggesting a useful basis for further studies. Studies evaluating totally endoscopic and robotically enhanced coronary artery bypass are summarised in [Table 3](#).

**Table 3. Studies evaluating totally endoscopic and robotically enhanced minimally invasive direct coronary bypass**

Reference	Study design	Total patients	Intervention	Follow up (months)	Conclusions
Leonard et al (2018)	Meta-analysis	3721	Mostly single-arm evaluating totally endoscopic coronary artery bypass. A portion of 376 patients compared totally endoscopic coronary artery bypass (69.9%) to minimally invasive direct coronary artery bypass	40	Totally endoscopic coronary artery bypass has acceptably low operative risks, a good early patency rate, with evidence of increased incidence of perioperative myocardial infarction
Cao et al (2016)	Systematic review	8034 (44 studies)	A selection of robotically-assisted totally endoscopic coronary artery bypass (on/off pump), and robotically-assisted minimally invasive direct coronary artery bypass (on/off pump)	<1–96	Acceptable perioperative mortality rates demonstrated. Conclusions limited by lack of robust clinical data

## The hybrid approach

While minimally invasive approaches confer multiple benefits over coronary artery bypass grafting, these techniques may limit access to the proximal left anterior descending. Therefore, hybrid coronary revascularisation combines a minimally invasive procedure, such as minimally invasive direct coronary artery bypass or totally endoscopic coronary artery bypass treating the proximal left anterior descending, with percutaneous coronary intervention in other coronary arteries either simultaneously or within 60 days post intervention (Saha et al, 2018). This specific management, although having fairly specific patient indications, may widen the use of minimally invasive direct coronary artery bypass or totally endoscopic coronary artery bypass and avoid coronary artery bypass grafting.

A retrospective cohort study of 1224 patients, with 306 undergoing hybrid coronary revascularisation, compared short- and long-term outcomes with coronary artery bypass grafting (Harskamp et al, 2015). At 30-day follow up, composite endpoints (mortality, myocardial infarction, stroke) between the two groups were similar (odds ratio 0.86, 95% confidence interval 0.42–1.73,  $P=0.67$ ) and again at 3.7 years follow up (hazard ratio 0.90, 95% confidence interval 0.55–1.47,  $P=0.69$ ). There were no significant differences associated with disease severity. It should be noted that not all patients had specifically left main coronary artery disease, but subgroup analysis yielded similar results across comparisons.

The prospective randomised pilot study evaluating the safety and efficacy of hybrid revascularisation in patients with multi-vessel coronary artery disease evaluated 12-month outcomes comparing hybrid coronary revascularisation and coronary artery bypass grafting (Gaşior et al, 2014). In their 200-patient cohort, there were no significant differences in mortality, myocardial infarction, major bleeding or repeat revascularisation rates. In their 5-year outcomes (Tajstra et al, 2018), 191 patient outcomes (94 hybrid coronary revascularisation) were available for analysis. Similar to 12-month outcomes, hybrid coronary revascularisation and coronary artery bypass grafting performed equivocally in all major outcomes of mortality ( $P=0.69$ ), myocardial infarction ( $P=0.30$ ), stroke ( $P=0.38$ ), repeat revascularisation ( $P=0.38$ ) and any major adverse cardiac and cerebrovascular events ( $P=0.39$ ), which included no significant change associated with EuroSCORE/SYNTAX severity.

The first multicentre observational study comparing hybrid coronary revascularisation to multi-vessel percutaneous coronary intervention (Puskas et al, 2016) evaluated 298 patients (200 hybrid coronary revascularisation), comparing the composite endpoint of major adverse cardiac and cerebrovascular events at 12-months follow up. Hybrid coronary revascularisation was non-inferior to percutaneous coronary intervention at 12-month follow up (hazard ratio 1.063, 95% confidence interval 0.666–1.697), but also at the end of the study (hazard ratio 0.868, 95% confidence interval 0.556–1.355) at a median of 17.6 months follow up. More notable are the propensity-score adjusted Kaplan–Meier major adverse cardiac and cerebrovascular events-free survival curve results, demonstrating an increased risk associated with hybrid coronary revascularisation at only 0–6 months. The authors highlight a seemingly significant widening of risk reduction in favour of hybrid coronary revascularisation until the end of their study and emphasise the need for more robust trials and better comparisons. As such, the completion of the multicentre prospective randomised controlled Hybrid Coronary Revascularisation Trial in 2024 (ClinicalTrials.gov NCT03089398), which compares primary endpoints in over 2000 patients, is awaited.

Of note, results from the HREVS trial (Ganyukov et al, 2020) showed similar outcomes of residual myocardial ischaemia and major adverse cardiac and cerebrovascular events following treatment with coronary artery bypass grafting, percutaneous coronary intervention or hybrid coronary revascularisation. The study has a relatively short 12-month follow up and was not appropriately powered for assessment of major adverse cardiac and cerebrovascular events, mortality, myocardial infarction, stroke and revascularisation, thus its main outcomes were in favour of percutaneous coronary intervention because of the  $\geq 50\%$  shorter hospital stays and total sick leave compared to other interventions. The results further highlight the need for adequately designed trials to elucidate any potential benefits of hybrid coronary revascularisation.

The most up-to-date meta-analysis (Sardar et al, 2018) compared hybrid coronary revascularisation vs coronary artery bypass grafting across 2245 patients (one randomised controlled trial and seven observational studies). The study found no significant differences in major adverse cardiac and cerebrovascular events (odds ratio 0.53 without repeat

revascularisation, 95% confidence interval 0.24–1.16), myocardial infarction (odds ratio 0.72, 95% confidence interval 0.31–1.64), stroke (odds ratio 0.53, 95% confidence interval 0.23–1.20) and repeat revascularisation (odds ratio 1.28, 95% confidence interval 0.58–2.83), but reduced transfusion needs and hospital stay in patients undergoing hybrid coronary revascularisation. While the findings, particularly short-term results, corroborate with the literature, this highlights the lack of well-designed randomised controlled trials.

## Conservative treatment strategies

While this review focuses upon invasive revascularisation strategies, the ISCHAEMIA trial results comparing conservative ( $n=2591$ ) to invasive ( $n=2588$ ) management in those with moderate or severe ischaemia based on non-invasive testing, suggests equivocal clinical outcomes in these treatment groups (ISCHEMIA Trial Research Group et al, 2018). Of those undergoing invasive intervention, 74% underwent percutaneous coronary intervention, with the rest undergoing coronary artery bypass grafting. Their composite primary endpoint of time to cardiovascular death, myocardial infarction, hospitalisation for unstable angina, heart failure and cardiac arrest showed no significant difference between treatment strategies at final follow up (adjusted hazard ratio 0.93, 95% confidence interval 0.80–1.08,  $P=0.34$ ). In terms of quality of life outcome measures, while the invasive intervention offered benefit in those suffering from daily–monthly angina pre-randomisation, this benefit was negligible in those who had minimal or no angina. The non-inferiority of conservative therapy compared to invasive strategies in these patients suggests careful consideration is needed before embarking on invasive intervention, and perhaps invasive revascularisation should be avoided in those without significant frequency of angina at presentation.

## Discussion

Current guidelines support percutaneous coronary intervention for treatment of STEMI and revascularisation in simple and intermediate complexity vessel disease in certain populations, but coronary artery bypass grafting remains the standard in patients with complex disease and those with diabetes. With a large evidence base, and no further comparative trials intervention at the time of writing, current findings will remain the background of decision making for now. While comparison of the two methods show largely non-significant differences in mortality and cardiovascular morbidity, the recurrent evidence for increased revascularisation risks in patients undergoing percutaneous coronary intervention, may limit the technique's claim to non-inferiority over coronary artery bypass grafting. While patients can benefit from a less invasive procedure and faster postoperative recovery, patients and clinicians might hesitate to choose percutaneous coronary intervention if their symptoms are more likely to recur, with potential repeated intervention and coronary artery bypass grafting in the future.

Modern approaches, such as minimally invasive direct coronary artery bypass, totally endoscopic coronary artery bypass, robotically enhanced coronary artery bypass and hybrid coronary revascularisation, offer promising outcomes, especially given their comparability to coronary artery bypass grafting and percutaneous coronary intervention. There is therefore particular interest in comparing these specific procedures to standard interventions. However, the high technical demand and lower availability of these procedures may limit the possibility of undertaking large randomised controlled trials. Less rigorous evidence, in the form of case series or cohort studies, may form the basis of further interest and collaboration between specialist centres to better assess these under-investigated revascularisation approaches.

## Conclusions

Overall, in selected patients, comparisons of coronary artery bypass grafting and percutaneous coronary intervention support equivocal risk in mortality, myocardial infarction and stroke, but increased repeat revascularisation risks with percutaneous coronary intervention. Less invasive procedures, such as robotic or hybrid approaches, could allow the benefits of coronary artery bypass grafting – an exciting but under-elucidated prospect as a true alternative. Further study into these techniques for management of left coronary artery disease is warranted.

## Key points

- Left-sided coronary artery disease is a significant clinical burden, the management of which often extends beyond standard medical treatment towards surgical intervention.
- Evidence comparing coronary artery bypass grafting to percutaneous coronary intervention in certain populations supports equivocal risk of mortality and cardiovascular morbidity but shows an increased risk of further revascularisation with percutaneous coronary intervention.
- More modern procedures, such as minimally invasive, totally endoscopic, robotically enhanced and hybrid revascularisation techniques offer promising and comparable outcomes to more traditional techniques, but are less widely available as a result of increased technical demand, contributing to a less robust, albeit expanding, evidence base.

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### Conflicts of interest

The authors declare no conflicts of interest.

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