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Coronary artery bypass grafting: Practice trends and projections

ABSTRACT

Coronary artery bypass grafting, also known as CABG, is now in its sixth decade and continues to be the most frequently performed cardiac surgery in the world. This review summarizes evidence regarding the role of CABG in modern-day management of coronary artery disease and discusses the latest developments in perioperative care and outcomes. Future directions include expanding the use of multiarterial grafting, which has the potential to maximize patient longevity and lower risk for adverse events; offering patients less-invasive approaches; and enhancing operative recovery.

KEY POINTS

The collaborative multidisciplinary heart team approach should view percutaneous coronary intervention, CABG, and medical therapy as alternative and complementary treatments rather than as competing therapies; the risks and benefits of each option should be weighed for each patient.

CABG remains the standard of care for patients with complex multivessel disease and left main coronary artery disease, diabetes, or left ventricular systolic dysfunction.

Multiarterial grafting can offer better long-term survival and lower risk of adverse cardiac events for patients undergoing CABG.

Innovations that reduce the invasiveness of coronary surgery and hybrid coronary revascularization are reasonable alternatives in select patients with a preference for less-invasive revascularization procedures.

CORONARY ARTERY BYPASS GRAFTING (CABG) is performed in patients with ischemic heart disease to improve symptoms, quality of life, and life expectancy. Ischemic heart disease is a major health concern in the United States, affecting 20.5 million people and causing 371,506 deaths in 2022.^{1,2} By 2060, the number of people in the United States with ischemic heart disease is expected to exceed 29 million.³ The economic impact is substantial, with the annual cost of heart disease estimated at \$239.9 billion.²

Around 650,000 revascularization procedures are performed in the United States annually, including 450,000 percutaneous coronary interventions (PCIs) and 200,000 CABG operations.^{4,5} Although fewer revascularizations are done due to advances in medical therapy and appropriate-use criteria, progress continues in CABG applications and the refinement of techniques, including maximizing longevity with multiarterial grafting, offering patients a less-invasive approach, and improving perioperative outcomes.

Herein, we provide a review of the current indications, techniques, outcomes, and future directions of CABG surgery.

OVERVIEW OF CABG

CABG was pioneered in the 1960s by René Favaloro, MD, to improve symptoms and survival in coronary artery disease.⁶ Over the following decades, studies confirmed that CABG increases survival in patients with left main coronary artery and multivessel disease compared with medical therapy. In the early 2000s, PCI with drug-eluting stents emerged as a less-invasive

TABLE 1
Major CABG trials in multivessel disease

Study	Year	Comparison	Primary end point	Key findings
BARI-2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) ¹⁰	2009	Revascularization (CABG or PCI) plus intensive medical therapy vs intensive medical therapy in patients with diabetes	All-cause mortality at 5 years	<p>Revascularization with intensive medical therapy not superior to intensive medical therapy alone</p> <p>CABG stratum: lower prevalence of myocardial infarction (10% vs 17.6%) and MACCE (22.4% vs 30.5%), no significant difference in all-cause mortality (13.6% vs 16.4%) or cardiac death (8% vs 9%)</p> <p>PCI stratum: no significant difference in myocardial infarction, MACCE, all-cause mortality, or cardiac death</p>
FREEDOM (Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease) ¹¹	2012	CABG vs PCI	All-cause mortality, nonfatal myocardial infarction, or nonfatal stroke	CABG superior to PCI: in CABG patients, lower 5-year primary composite end point (18.7% vs 26.6%), lower prevalence of myocardial infarction (6.0% vs 13.9%) and all-cause mortality (10.9% vs 16.3%), higher prevalence of stroke (5.2% vs 2.4%)
SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) ¹²	2013	CABG vs PCI (paclitaxel-eluting stents)	Composite MACCE (all-cause mortality, stroke, myocardial infarction, and repeat revascularization)	<p>PCI inferior and not noninferior to CABG</p> <p>Lower 5-year MACCE (26.9% vs 37.3%); lower prevalence of cardiac death (5.3% vs 9%), myocardial infarction (3.8% vs 9.7%), and repeat revascularization (13.7% vs 25.9%); no significant difference in all-cause mortality (11.4% vs 13.9%) or stroke (3.7% vs 2.4%) for CABG and PCI, respectively</p>
BEST (Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients With Multivessel Coronary Artery Disease) ¹³	2015	CABG vs PCI (everolimus-eluting stents)	Composite of death, myocardial infarction, target-vessel revascularization	<p>No significant difference in primary composite end point at 2 years (PCI 11% vs CABG 7.9%)</p> <p>At longer-term follow-up (median 4.6 years), PCI had significantly higher primary end point (15.3% vs 10.6%) compared with CABG owing to repeat revascularization and spontaneous myocardial infarction</p>
STICH (Surgical Treatment for Ischemic Heart Failure) and STICHES (STICH Extension Study) ⁹	2016	CABG plus medical therapy vs medical therapy alone in patients with left ventricular ejection fraction $\leq 35\%$	All-cause mortality	<p>No significant difference in primary end point over 6 years; however, CABG with medical therapy resulted in significant improvement in long-term all-cause mortality out to 10 years compared with medical therapy alone (58.9% vs 66.1%)</p> <p>Cardiovascular mortality and morbidity were lower with CABG in both studies</p>
FAME 3 (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) ¹⁴	2021	Fractional flow reserve–guided PCI vs CABG in triple-vessel disease	MACCE (death from any cause, myocardial infarction, stroke, or repeat revascularization)	Fractional flow reserve–guided PCI not consistent with noninferiority to CABG: higher MACCE in fractional flow reserve–guided PCI arm compared with CABG (10.6% vs 6.9%) at 1 year

CABG = coronary artery bypass grafting; MACCE = major adverse cardiac or cerebrovascular events; PCI = percutaneous coronary intervention

TABLE 2
Major CABG trials in left main coronary artery disease

Study	Year	Comparison	Primary end point	Key findings
PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease) ¹⁵	2011	CABG vs PCI (sirolimus-eluting stents)	MACCE (death from any cause, myocardial infarction, stroke, or ischemia-driven target-vessel revascularization)	No significant difference in primary end point at 2 years Higher ischemia-driven target-vessel revascularization in PCI group (9% vs 4.2%)
SYNTAX left main coronary artery subgroup ¹⁶	2014	CABG vs PCI (paclitaxel-eluting stents)	Composite MACCE (all-cause mortality, stroke, myocardial infarction, and repeat revascularization)	No significant difference in primary end point at 5 years Increased stroke in CABG arm (4.3% vs 1.5%), higher repeat revascularization in PCI arm (26.7% vs 15.5%), and higher MACCE at 5 years in PCI with SYNTAX score ≥ 33 (46.5% vs 29.7%)
EXCEL (Evaluation of Xience Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) ¹⁷	2019	CABG vs PCI (everolimus-eluting stents)	Composite of death, stroke, myocardial infarction	PCI was noninferior to CABG for primary end point at 3 years, survival curves favored CABG at 5 years (22.0% vs 19.2%), and ischemia-driven revascularization was more frequent after PCI (16.9% vs 10%)
NOBLE (Nordic-Baltic-British Left Main Revascularization) ¹⁸	2020	CABG vs PCI	Composite MACCE (all-cause mortality, nonprocedural myocardial infarction, repeat revascularization, and stroke)	CABG superior to PCI Lower MACCE for CABG (19% vs 28%) at 5 years, driven by lower nonprocedural myocardial infarction (3% vs 8%) and lower repeat revascularization in CABG patients (10% vs 17%)

CABG = coronary artery bypass grafting; MACCE = major adverse cardiac or cerebrovascular events; PCI = percutaneous coronary intervention; SYNTAX = Synergy Between PCI With Taxus Stents and Cardiac Surgery

alternative. Despite PCI becoming more common, especially for patients with acute coronary syndromes, CABG remains the gold standard, particularly for patients with complex anatomy (ie, bifurcation disease and higher SYNTAX score—a score of coronary disease complexity, derived from the Synergy Between PCI With Taxus and Cardiac Surgery trial as criteria for treatment selection),⁷ diabetes, and left ventricular dysfunction.^{8,9} PCI is considered a valuable option for patients with fewer coronary lesions and for those who are poor surgical candidates.

CABG is one of the most studied cardiac surgical procedures, with extensive follow-up data (Table 1 and Table 2).^{9–18} Typical CABG patients are older, with more comorbidities, and often have undergone PCI. Most procedures involve multiple bypass grafts, usually

1 internal thoracic artery (ITA), and vein grafts. Arterial grafts, such as the right ITA and radial artery, can significantly improve long-term patency compared with vein grafts but are more technically challenging. Vein grafts often fail over time, leading to recurrent angina.

CURRENT INDICATIONS

The 2021 American College of Cardiology, American Heart Association, Society for Cardiovascular Angiography and Interventions guidelines⁸ on coronary artery revascularization recommend CABG along with medical therapy in various clinical and anatomic scenarios to achieve symptom relief and improve survival (Table 3). However, recent studies and trials have sparked debate about the extent of the benefits of CABG in certain patient groups.

Seminal trials from the 1970s^{19–21} confirmed the superiority of CABG over medical therapy for symptom relief and improved quality of life, with a landmark meta-analysis confirming the benefits of CABG, especially in individuals with more severe coronary artery disease.²² These data solidified CABG as the gold standard for many patients with complex coronary anatomy.

The ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) trial²³ and subsequent meta-analyses have questioned the survival advantage of CABG in patients with normal or mildly reduced left ventricular function.^{8,23} These studies often involved patients with a lower degree of disease complexity, the vast majority of whom received PCI. Additionally, a significant percentage of patients (21%) in the ISCHEMIA trial crossed over from medical therapy to intervention within a median follow-up of 3.2 years, often in the context of myocardial infarction.²³ This crossover and patient selection have complicated the direct comparison of long-term outcomes of CABG with other treatments. Recent evidence supports the safety of an initial medical approach with continued surveillance in select patients with low atherosclerotic burden. However, it does not negate the survival advantage of CABG in patients with multivessel coronary artery disease, an advantage long established by previous research.^{22,24}

CABG is also indicated for symptom relief and improvement in quality of life, particularly for patients not adequately managed with medical therapy alone.⁸

■ CABG VS PCI: WHAT THE EVIDENCE SAYS

The comparison between CABG and PCI remains a focus of study owing to the continuous advances in medical technology and techniques, need for updated long-term data, and evolving nature of patient populations and their comorbidities. This comparison has been challenging due to selection bias in clinical trials and evolving clinical practices that outpace guideline recommendations. Recent landmark trials have provided clearer insights and helped refine recommendations for the optimal use of PCI and CABG based on patient-specific factors and long-term outcomes.^{9–18}

Multivessel disease

Initial PCI vs CABG trials²⁵ primarily included patients with single- or double-vessel disease and normal left ventricular function, which had already been shown to have little prognostic benefit from surgery.²² Later trials^{9–18} shifted focus to patients with more complex conditions, such as multivessel and left main disease.

Patients with a SYNTAX score of 22 or lower are generally well suited for PCI. Conversely, CABG is superior to PCI for the majority of patients with multivessel coronary artery disease with SYNTAX scores higher than 22 and for those with left main disease with SYNTAX scores of 33 or higher. In these later trials,^{9–18} patients were assessed by a collaborative multidisciplinary heart team to determine their eligibility for equivalent anatomic revascularization. Based on clinical comorbidities and disease complexity, eligible patients were then randomized to receive either PCI or CABG. The results of major trials, like FREEDOM (Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease),²² SYNTAX,²³ and BEST (Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients With Multivessel Coronary Artery Disease)²⁴ have consistently shown that CABG should be considered the primary revascularization strategy for most patients with complex multivessel disease.^{11–13}

Left main coronary artery disease

As for patients with left main coronary artery disease, the decision between choosing CABG over PCI is nuanced owing to inconsistent findings in different trials (Table 2).^{15–18} To reconcile these conflicting results, an individual patient data meta-analysis²⁶ was conducted using data from 4,394 patients from 4 randomized controlled trials—SYNTAX,^{12,16} PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease),²⁷ NOBLE (Nordic-Baltic-British Left Main Revascularization),¹⁸ and EXCEL (Evaluation of Xience Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization)²⁸—with a follow-up period of at least 5 years. In the study's time-to-event analysis, there was no statistically significant difference in 5-year all-cause mortality between patients treated with PCI using drug-eluting stents and those treated with CABG.²⁶ Although the Bayesian approach suggested that CABG may have a survival benefit over PCI, the absolute risk difference in all-cause mortality is likely less than 0.2% per year.

Furthermore, patients who underwent PCI had higher rates of spontaneous myocardial infarction (6.2%, 95% confidence interval [CI] 5.2%–7.3% vs 2.6%, 95% CI 2.0–3.4; hazard ratio [HR] 2.35, 95% CI 1.71–3.23; $P < .0001$) and repeat revascularization (18.3%, 95% CI 16.7%–20.0% vs 10.7%, 95% CI 9.4%–12.1%; HR 1.78, 95% CI 1.51–2.10; $P < .0001$).

TABLE 3

2021 American College of Cardiology, American Heart Association, Society for Cardiovascular Angiography and Interventions recommendations for CABG vs PCI

Indication	Criteria and recommendation	Class strength and level of evidence
Complex disease	Significant left main coronary artery disease with high complexity	Class 1, level B-R
	CABG is recommended over PCI to improve survival	
	Multivessel disease with complex or diffuse coronary artery disease (SYNTAX score ≥ 33)	Class 2a, level B-R
	It is reasonable to choose CABG over PCI to confer survival advantage	
Diabetes	Multivessel disease with LAD involvement	Class 1, level A
	CABG with left IMA to LAD is preferred to PCI to reduce mortality and repeat revascularizations	
	Multivessel disease amenable to PCI, indication for revascularization, and poor candidate for surgery	Class 2a, level B-NR
	PCI can be useful to reduce long-term ischemic outcomes	
	Left main coronary artery stenosis and low- or intermediate-complexity coronary artery disease in the rest of coronary anatomy	Class 2b, level B-R
	Consider PCI as alternative to CABG to reduce major adverse cardiovascular outcomes	
Previous CABG	Refractory angina on guideline-directed medical therapy attributable to LAD disease	Class 2a, level C-LD
	CABG over PCI when IMA can be used as conduit to the LAD	
	Complex coronary artery disease	Class 2b, level B-NR
	CABG over PCI when IMA can be used as a conduit to the LAD	
Nonadherence to dual antiplatelet therapy	Multivessel disease amenable to treatment with either PCI or CABG	Class 2a, level B-NR
	CABG is preferred to PCI	

CABG = coronary artery bypass grafting; IMA = internal mammary (thoracic) artery; LAD = left anterior descending coronary artery; LD = limited data; NR = nonrandomized; PCI = percutaneous coronary intervention; R = randomized; SYNTAX = Synergy Between PCI With Taxus Stents and Cardiac Surgery

Data from reference 8.

over the 5-year period compared with those who underwent CABG.²⁶ Notably, there was no difference in risk of stroke between PCI and CABG.

Eligibility

Typically, trials have limited follow-up periods, with 5 years being relatively short when long-term survival is a priority. Additionally, all trials comparing PCI and

CABG are designed around the premise of equipoise between treatments, excluding patients with very complex coronary disease, significant comorbidities, and frailty that might favor one revascularization method over the other. Patients who cannot be included in trials are often followed in registries. A study using the OPTIMUM registry (Outcomes of Percutaneous Revascularization for Management of Surgically Ineligible

Patients With Multivessel or Left Main Coronary Artery Disease) found that reasons for surgical ineligibility varied and included poor distal target or conduit (18.9%), severe left ventricular dysfunction or nonviable myocardium (16.8%), severe lung disease (10.1%), frailty or immobility, prior sternotomy, and advanced age.²⁹

There is also a large population that is ineligible for PCI. In a SYTNAX registry study in which registry patients constituted 41% of the study cohort, there were 5 times as many PCI-ineligible patients as CABG-ineligible patients.³⁰ Main reasons for PCI ineligibility included complex anatomy (70.9%), untreatable chronic total occlusion (22.0%), and inability to take antiplatelet medications (0.9%).³⁰ CABG in these patients had good outcomes. These results show a noteworthy prevalence of ineligible patients for both PCI and CABG, highlighting the importance of individualized treatment planning.

Current guidelines

When determining the optimal choice between PCI and CABG, several factors must be considered, including patient characteristics, disease stability, procedural risk, atherosclerotic burden and complexity, long-term efficacy, and patient preferences. The 2021 American College of Cardiology, American Heart Association, Society for Cardiovascular Angiography and Interventions guidelines⁸ for coronary revascularization provide recommendations to guide decision-making in situations where CABG or PCI may be preferred (Table 3). There seems to be consensus that when it comes to complex anatomies, heavy atherosclerotic burden, and durability, CABG is the preferred modality. When feasible, PCI is a viable alternative in those who are poor surgical candidates and those with less-extensive coronary lesions.

Ultimately, the collaborative multidisciplinary heart team approach should view PCI, CABG, and medical therapy as alternative and complementary treatments rather than competing therapies. The multidisciplinary team should carefully weigh the risks and benefits of each option for each patient. This collaborative approach is recommended to provide the best possible outcomes for patients and is considered a Class 1 indication according to current guidelines.⁸

CABG TECHNIQUES

Off-pump vs on-pump CABG

Off-pump (“beating heart”) CABG was introduced in high-risk patients to reduce the potential deleterious effects associated with cardiopulmonary bypass and aortic clamping. Despite several randomized controlled

trials, there is no consensus on which technique is superior. The choice often depends on patient characteristics and expertise of the surgeon.

Patel et al³¹ noted similar in-hospital mortality but varied longer-term outcomes in 3 of the largest contemporary trials comparing on-pump and off-pump CABG. The ROOBY (Randomized On/Off Bypass) trial reported increased 5-year all-cause mortality in the off-pump group, unlike the CORONARY (CABG Off or On Pump Revascularization) and GOPCABE (German Off-Pump Coronary Artery Bypass Grafting in Elderly Patients) studies,^{32–34} which showed no difference. Given the lack of a conclusive advantage of the off-pump approach, its use has declined in recent years, accounting for 17% of CABG procedures in 2012 but only 12% in 2021. It is favored for higher-risk patients and those with significant aortic atherosclerosis who have a high risk of perioperative stroke.^{5,35} Factors favoring on-pump over off-pump CABG include the following:

- Small or diffusely diseased coronary arteries
- Suboptimal targets
- Intramyocardial coronary arteries
- Coronary endarterectomy
- Unstable hemodynamics
- Concomitant valve surgery.

Off-pump CABG or PCI should be considered when cardiopulmonary bypass presents a prohibitive risk or when there is severe calcification of the aorta, severe ascending aortic atherosclerosis, high risk for stroke, or liver cirrhosis.

Multiarterial grafting

The long-term survival benefit provided by CABG is largely determined by the durability of the grafts used and the bypassing of multiple important targets.^{36,37} Using an ITA for bypassing the left anterior descending (LAD) artery is standard of care owing to its superior long-term outcomes compared with saphenous vein grafts, as reported in the seminal study by Loop et al.³⁸ Subsequently, in 1999, Lytle et al³⁹ found that using both left and right ITAs conferred a strong survival benefit compared with single ITA grafting. However, despite these findings, few use a second arterial conduit. Ten-year outcomes of ART (Arterial Revascularization Trial)⁴⁰ showed no difference in mortality or major adverse cardiac and cerebrovascular events. However, an as-treated analysis revealed notable 10-year survival benefit (HR 0.81, 95% CI 0.68–0.95) and a reduced composite of death, myocardial infarction, and stroke for multiarterial grafting (HR 0.80, 95% CI 0.69–0.93) compared with single-arterial grafting.⁴⁰

Current consensus supports the superiority of arterial grafts over saphenous vein grafts in appropriately selected patients undergoing CABG.⁴¹ Data from the Society of Thoracic Surgeons Adult Cardiac Surgery Database show an increasing proportion of patients undergoing multiarterial grafting, from 10.9% in 2020 to 14.3% in 2021, with both bilateral ITA and radial artery use slowly increasing.⁵

Despite evidence supporting multiarterial grafting, the saphenous vein remains the most used conduit due to the ease of harvesting and length of the conduit. However, it has lower long-term patency. The “no-touch technique,” which involves harvesting the vein with surrounding tissue to preserve its integrity, has shown comparable patency to ITA grafts but has a higher risk of wound complications given the significant prevalence of diabetes and obesity in the North American population.⁴¹ In addition, patients are more likely to prefer a less-invasive approach.

Minimally invasive techniques

Over the past 3 decades, innovations in coronary surgery have led to the development of minimally invasive coronary surgery (MICS) CABG, robotic CABG, and hybrid coronary revascularization. These techniques aim to reduce the invasiveness of procedures and improve patient outcomes.

MICS CABG combines off-pump CABG with a minimally invasive method, such as left anterior small thoracotomy to avoid sternotomy, thereby reducing possible complications related to cardiopulmonary bypass and sternotomy (**Figure 1**).^{42,43} Minimally invasive direct coronary artery bypass, the precursor of MICS, is applicable in patients with single-vessel disease in the proximal LAD or in those undergoing hybrid revascularization. MICS CABG allows multivessel grafting with various configurations and conduits, offering excellent procedural and short-term outcomes at experienced centers. The ongoing MIST (Minimally Invasive Coronary Surgery Compared to Sternotomy Coronary Artery Bypass Grafting) trial continues to evaluate whether MICS CABG leads to better recovery compared with conventional CABG.⁴³

Robotic CABG differs from traditional approaches in that it involves harvesting the ITA and performing anastomosis to the LAD and other targets endoscopically or through a small incision, thereby reducing surgical trauma and potentially shortening recovery times.^{44–46} Ideal candidates include those with single-vessel LAD disease or those being considered for hybrid revascularization, as these patients can benefit from the less-invasive nature of the procedure, leading to faster



Figure 1. Surgical incision site located on the left anterior chest wall following a small thoracotomy for minimally invasive coronary artery bypass grafting. An accompanying chest drain incision site is seen inferolaterally.

recovery and fewer perioperative complications. A systematic review reported 0.8% perioperative mortality, 11.5% conversion to larger incisions, and reduction in the morbidity associated with conventional surgical trauma.⁴⁴ High-graft patency was also reported (97.7% at < 1 month, 96.1% at < 5 years, and 93.2% at > 5 years).⁴⁵

Despite these promising results, robotic CABG is only available to a small proportion of surgical candidates at highly specialized centers. It accounts for only about 1% of total CABG procedures in the United States due to high costs, longer operative time, and the need for specialized training.⁴⁶ However, its use is likely to increase with greater procedural experience and wider availability.

Hybrid revascularization combines grafting the LAD with the left ITA using CABG (preferably MICS or robotic CABG) and PCI of non-LAD coronary stenoses.⁴⁷ The rationale includes the survival advantage of the left ITA-to-LAD graft, benefits of avoiding cardiopulmonary bypass and sternotomy, and restenosis rates of PCI-treated, non-LAD vessels comparable to occlusion rates of saphenous vein grafts. Limited data suggest hybrid revascularization offers durability,

symptom relief, and survival benefits over triple-vessel stenting, but may result in higher repeat revascularization rates in PCI-treated vessels.

In summary, minimally invasive techniques are promising but are limited to specialized centers. Further research is warranted to evaluate long-term outcomes and identify optimal patient selection for each technique.

Intraoperative management

The evolution of cardiopulmonary bypass has centered on enhancing biocompatibility and reducing hemodilution, leading to significant advances over prior cardiopulmonary bypass setups.⁴⁸ These newer systems provide considerable clinical benefits, such as significant reduction in postoperative atrial fibrillation, enhanced renal and myocardial protection, decreased systemic inflammatory responses, reduced cerebral gaseous microembolization, and better preservation of end-organ function. Concurrently, cardioplegia administration, using high-dose potassium to induce depolarized cardiac arrest, is essential to protect myocardial function and prevent ischemic damage during cardiopulmonary bypass. Cold potassium cardioplegia is used most often and has proven effective even in cases of severe ischemic cardiomyopathy.

Epiaortic ultrasonography and computed tomography are valuable tools for screening select patients for major atherosclerosis and calcifications in the ascending aorta. These methods greatly influence intraoperative management by allowing adjustments in the location of the aortic cannula to reduce the risk of atheroembolization. Additionally, specialized cannulas are used to minimize the risk of perioperative stroke or aortic dissection by reducing dislodgement of atheromatous debris during aortic manipulation.

Cerebral monitoring tools like near-infrared spectroscopy and electroencephalographic-based anesthesia depth monitoring are integrated to detect and manage potential neurologic complications, with ongoing research of their effectiveness.⁴⁸ Furthermore, transit time flow measurement serves as an essential intraoperative quality control measure, confirming graft patency and thereby enhancing both short- and long-term outcomes of CABG.

These developments highlight the continuous evolution of the CABG procedure and the optimization of surgical outcomes.

OUTCOMES CONTINUE TO IMPROVE

CABG is a safe procedure, with national in-hospital mortality below 2.1%, operative mortality below 2.7%, and centers of excellence maintaining operative mortality less than 1% for more than a decade.^{5,49} These

outcomes are consistent with global trends. Recent attention has been given to improving perioperative outcomes, which has driven differences between contemporary and early comparisons of CABG and PCI and has impacted early- and long-term mortality. In the FAME 3 (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) trial,²² 30-day mortality for CABG was 0.3%, identical to that of PCI¹⁴ and 10 times less than what was reported in earlier trials.

Of all consecutively enrolled patients eligible for CABG (n = 153,208) documented in the Society of Thoracic Surgeons Adult Cardiac Surgery Database in 2021, including patients who underwent emergency and salvage CABG, the following major morbidities were reported: reoperation, 2.6%; deep sternal wound infection or mediastinitis, 0.8%; permanent stroke, 1.5%; prolonged ventilation (> 24 hours), 6.7%; renal failure (defined as a 3-fold increase in serum creatinine, serum creatinine > 4 mg/dL, or initiation of dialysis), 2.2%; new-onset atrial fibrillation, 26%; 30-day readmission, 9.1%; and postoperative hospital length of stay, 6 days (range 4–7).⁵ Outcomes have improved over time, and centers of excellence are able to offer CABG with low morbidity and mortality despite referrals of older and sicker patients.

IMPORTANCE OF MEDICAL THERAPY AS AN ADJUNCT TO CABG

Optimal medical therapy affects postoperative outcomes, and adherence is important. Statins lower the risk of readmissions and late mortality from myocardial infarction or stroke. Furthermore, the adoption of modern nonstatin agents is expected to further reduce the risk of major adverse cardiovascular events in high-risk patients.⁵⁰

The optimal antithrombotic therapy regimen after CABG is a topic of ongoing research. A recent meta-analysis of 38 studies involving 77,447 patients aimed to evaluate efficacy and risks of different antiplatelet regimens after CABG.⁵¹ It compared dual antiplatelet therapy (DAPT) with single antiplatelet therapy and DAPT with clopidogrel vs DAPT with ticagrelor or prasugrel. The analysis demonstrated that, while DAPT is superior to single antiplatelet therapy in reducing mortality and major adverse events, it increases bleeding risks. Notably, DAPT with ticagrelor or prasugrel was found to be more effective than DAPT with clopidogrel in reducing mortality without affecting other outcomes. These findings suggest a need for personalized antiplatelet regimens after CABG based on individual risk profiles.

Guideline-directed medical therapy is critical in patients with reduced ejection fraction to enhance cardiac function, improve quality of life, and prevent further complications. This therapy includes renin-angiotensin-aldosterone system antagonists, beta-blockers, mineralocorticoid receptor antagonists, and sodium-glucose cotransporter 2 inhibitors.⁵²

Last, starting and reinforcing other secondary prevention measures, including lifestyle changes, after CABG surgery are recommended.⁸ Such measures include cardiac rehabilitation programs, personalized diet and exercise plans, and aggressive management of risk factors such as hypertension, diabetes, smoking, and chronic kidney disease. These changes, augmented by optimal medical therapies, help maintain long-term graft patency, enhance quality of life, and improve long-term prognosis.

■ FUTURE DIRECTIONS

The future of CABG depends on removing barriers to adopting beneficial practices and broadening access. Addressing discrepancies between current guidelines and actual practice and expanding the use of multiarterial grafting strategies and minimally invasive techniques in carefully selected patients are key. The clear volume-outcome relationships, especially with multiarterial grafting strategies, indicate a rapidly approaching era of coronary subspecialization.^{53,54} Additionally, enhanced recovery protocols involving multidisciplinary teamwork, best practices implementation, continuous audits, and change readiness can accelerate recovery, shorten hospital length of stay, lower costs, and potentially increase survival rates.⁵⁵

The public reporting scorecard needs revision to more accurately capture the scope and complexity of cardiac surgery practices, encouraging more hospitals to adopt best practices while minimizing risk aversion.⁵⁶ Accordingly, the American Association for Thoracic Surgery Quality Gateway aims to efficiently address gaps in outcomes reporting and quality assurance. By using advanced machine learning algorithms and high-performance computing, the American Association for Thoracic Surgery Quality Gateway provides real-time, risk-adjusted outcome predictions for all types of cardiac surgery, regardless of complexity, with lean data collection.⁵⁷

Addressing disparities in access to CABG is also paramount. Current inequalities in healthcare call

for strategies to make CABG more available and affordable, particularly in developing nations. This includes training local surgeons in advanced techniques, improving local healthcare infrastructures, and establishing collaborations with international cardiac surgery centers.⁵⁸ These factors will improve the care of many more patients requiring CABG.

In 2021, guidelines for CABG in patients with ischemic cardiomyopathy and heart failure were issued by the American Association for Thoracic Surgery expert consensus group.⁵² They recommended a structured approach to revascularization, including use of mechanical cardiac support when necessary. The guidelines noted a lack of high-level evidence and emphasized the need for future research, particularly in optimizing perioperative mechanical cardiac support use, including right ventricular support, in this high-risk population.

Future research should prioritize optimizing treatment approaches for older patients, particularly because frailty is not currently integrated into risk-scoring models.

Last, newer medical therapies hold promise for stabilizing atherosclerotic lesions in the native coronary arteries, potentially improving long-term patency of bypass grafts.

■ TAKE-HOME MESSAGE

CABG remains the standard of care for patients with complex multivessel disease, left main coronary artery disease, diabetes, or left ventricular systolic dysfunction, offering durable long-term symptomatic relief and survival. PCI is a valuable alternative for poor surgical candidates and those with less extensive coronary lesions. Multiarterial grafting promises to maximize longevity, and less-invasive approaches have been developed. Ultimately, it is important for the collaborative multidisciplinary heart team to weigh the risks and benefits of each option for the individual patient to provide the best outcome. ■

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REFERENCES

1. CDC Centers for Disease Control and Prevention and National Center for Health Statistics. National Vital Statistics System: public use data file documentation: mortality multiple cause-of-death micro-data files. https://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/DVS/mortality/Multiple-Cause-of-Death-Public-Use-File-Control-Total-Table-2022.pdf. Accessed February 14, 2025.
2. Tsao CW, Aday AW, Almarazooq ZI, et al. Heart disease and stroke statistics—2023 update: a report from the American Heart Association [published correction appears in *Circulation* 2023; 147(8):e622] [published correction appears in *Circulation* 2023; 148(4):e4]. *Circulation* 2023; 147(8):e93–e621. doi:10.1161/CIR.0000000000001123
3. Mohebi R, Chen C, Ibrahim NE, et al. Cardiovascular disease projections in the United States based on the 2020 census estimates. *J Amer Coll Cardiol* 2022; 80(6):565–578. doi:10.1016/j.jacc.2022.05.033
4. Alkhouli M, Alqahtani F, Kalra A, et al. Trends in characteristics and outcomes of patients undergoing coronary revascularization in the United States, 2003–2016. *JAMA Netw Open* 2020; 3(2):e1921326. doi:10.1001/jamanetworkopen.2019.21326
5. Kim KM, Arghami A, Habib R, et al. The Society of Thoracic Surgeons Adult Cardiac Surgery Database: 2022 update on outcomes and research. *Ann Thorac Surg* 2023; 115(3):566–574. doi:10.1016/j.athoracsurg.2022.12.033
6. Bakaeen FG, Blackstone EH, Pettersson GB, Gillinov AM, Svensson LG. The father of coronary artery bypass grafting: René Favaloro and the 50th anniversary of coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2018; 155(6):2324–2328. doi:10.1016/j.jtcvs.2017.09.167
7. Sianos G, Morel M-A, Kappetein AP, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention* 2005; 1:219–227. PMID:19758907
8. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines [published correction appears in *Circulation* 2022; 145(11):e771]. *Circulation* 2022; 145(3):e4–e17. doi:10.1161/CIR.0000000000001039
9. 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
10. Chaitman BR, Hardison RM, Adler D, et al. The Bypass Angioplasty Revascularization Investigation 2 diabetes randomized trial of different treatment strategies in type 2 diabetes mellitus with stable ischemic heart disease: impact of treatment strategy on cardiac mortality and myocardial infarction [published correction appears in *Circulation* 2010; 121(12):e254]. *Circulation* 2009; 120(25):2529–2540. doi:10.1161/CIRCULATIONAHA.109.913111
11. Farkouh ME, Domanski M, Sleeper LA, et al. Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med* 2012; 367(25):2375–2384. doi:10.1056/NEJMoa1211585
12. Mohr FW, Morice MC, Kappetein AP, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. *Lancet* 2013; 381(9867):629–638. doi:10.1016/S0140-6736(13)60141-5
13. Park SJ, Ahn JM, Kim YH, et al. Trial of everolimus-eluting stents or bypass surgery for coronary disease. *N Engl J Med* 2015; 372(13):1204–1212. doi:10.1056/NEJMoa1415447
14. Fearon WF, Zimmermann FM, De Bruyne B, et al. Fractional flow reserve-guided PCI as compared with coronary bypass surgery. *N Engl J Med* 2022; 386(2):128–137. doi:10.1056/NEJMoa2112299
15. Park SJ, Kim YH, Park DW, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease. *N Engl J Med* 2011; 364(18):1718–1727. doi:10.1056/NEJMoa1100452
16. Morice MC, Serruys PW, Kappetein AP, et al. Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the synergy between percutaneous coronary intervention with taxus and cardiac surgery trial. *Circulation* 2014; 129(23):2388–2394. doi:10.1161/CIRCULATIONAHA.113.006689
17. Stone GW, Kappetein AP, Sabik JF, et al. Five-year outcomes after PCI or CABG for left main coronary disease [published correction appears in *N Engl J Med* 2020; 382(11):1078]. *N Engl J Med* 2019; 381(19):1820–1830. doi:10.1056/NEJMoa1909406
18. Holm NR, Mäkilä 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
19. Veterans Administration Coronary Artery Bypass Surgery Cooperative Study Group. Eleven-year survival in the Veterans Administration randomized trial of coronary bypass surgery for stable angina. *N Engl J Med* 1984; 311:1333–1339. doi:10.1056/NEJM198411223112102
20. Varnauskas E; European Coronary Surgery Study Group. Twelve-year follow-up of survival in the randomized European Coronary Surgery Study. *N Engl J Med* 1988; 319:332–337. doi:10.1056/NEJM198808113190603
21. CASS principal investigators and their associates. Coronary Artery Surgery Study (CASS): a randomized trial of coronary bypass surgery. Survival data. *Circulation* 1983; 68:939–950. doi:10.1161/01.cir.68.5.939
22. Yusuf S, Zucker D, Peduzzi P, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration [published correction appears in *Lancet* 1994; 344(8934):1446]. *Lancet* 1994; 344(8922):563–570. doi:10.1016/S0140-6736(94)91963-1
23. 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
24. Bakaeen FG, Ruel M, Calhoun JH, et al. STS/AATS-endorsed rebuttal to 2023 ACC/AHA chronic coronary disease guideline: a missed opportunity to present accurate and comprehensive revascularization recommendations. *J Thorac Cardiovasc Surg* 2023; 166(4):1115–1118. doi:10.1016/j.jtcvs.2023.03.001
25. Hoffman SN, TenBrook JA, Wolf MP, Pauker SG, Salem DN, Wong JB. A meta-analysis of randomized controlled trials comparing coronary artery bypass graft with percutaneous transluminal coronary angioplasty: one- to eight-year outcomes. *J Am Coll Cardiol* 2003; 41:1293–1304. doi:10.1016/S0735-1097(03)00157-8
26. Sabatine MS, Bergmark BA, Murphy SA, et al. Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: an individual patient data meta-analysis [published correction appears in *Lancet* 2022; 399(10335):1606.] [published correction appears in *Lancet* 2022; 400(10360):1304]. *Lancet* 2021; 398(10318):2247–2257. doi:10.1016/S0140-6736(21)00233-5
27. 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; 65:2198–2206. doi:10.1016/j.jacc.2015.03.033
28. 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; 381:1820–1830. doi:10.1056/NEJMoa1909406
29. Salisbury AC, Grantham JA, Brown WM, et al. Outcomes of medical therapy plus PCI for multivessel or left main CAD ineligible for surgery. *JACC Cardiovasc Interv* 2023; 16(3):261–273. doi:10.1016/j.jcin.2023.01.003
30. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease [published correction appears in *N Engl J Med* 2013; 368(6):584]. *N Engl J Med* 2009; 360(10):961–972. doi:10.1056/NEJMoa0804626
31. Patel V, Unai S, Gaudino M, Bakaeen F. Current readings on outcomes after off-pump coronary artery bypass grafting. *Semin Thorac Cardiovasc Surg* 2019; 31(4):726–733. doi:10.1053/j.semtcvs.2019.05.012

32. 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
33. 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
34. 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
35. Bakaeen FG, Shroyer AL, Gammie JS, et al. Trends in use of off-pump coronary artery bypass grafting: results from the Society of Thoracic Surgeons Adult Cardiac Surgery Database. *J Thorac Cardiovasc Surg* 2014; 148(3):856–864. doi:10.1016/j.jtcvs.2013.12.047
36. Bakaeen FG, Ravichandren K, Blackstone EH, et al. Coronary artery target selection and survival after bilateral internal thoracic artery grafting. *J Am Coll Cardiol* 2020; 75(3):258–268. doi:10.1016/j.jacc.2019.11.026
37. Bakaeen FG, Ghandour H, Ravichandren K, et al. Right internal thoracic artery patency is affected more by target choice than conduit configuration. *Ann Thorac Surg* 2022; 114(2):458–466. doi:10.1016/j.athoracsur.2021.09.015
38. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. *N Engl J Med* 1986; 314(1):1–6. doi:10.1056/NEJM198601023140101
39. Lytle BW, Blackstone EH, Loop FD, et al. Two internal thoracic artery grafts are better than one. *J Thorac Cardiovasc Surg* 1999; 117(5):855–872. doi:10.1016/S0022-5223(99)70365-X
40. Taggart DP, Benedetto U, Gerry S, et al. Bilateral versus single internal-thoracic-artery grafts at 10 years. *N Engl J Med* 2019; 380(5):437–446. doi:10.1056/NEJMoa1808783
41. Gaudino M, Bakaeen FG, Sandner S, et al. Expert systematic review on the choice of conduits for coronary artery bypass grafting: endorsed by the European Association for Cardio-Thoracic Surgery (EACTS) and the Society of Thoracic Surgeons (STS). *Eur J Cardiothorac Surg* 2023; 64(2):ezad163. doi:10.1093/ejcts/ezad163
42. McGinn JT Jr, Usman S, Lapierre H, Pothula VR, Mesana TG, Ruel M. Minimally invasive coronary artery bypass grafting: dual-center experience in 450 consecutive patients. *Circulation* 2009; 120(11 suppl):S78–S84. doi:10.1161/CIRCULATIONAHA.108.840041
43. Guo MH, Wells GA, Glineur D, et al. Minimally Invasive coronary surgery compared to STernotomy coronary artery bypass grafting: the MIST trial. *Contemp Clin Trials* 2019; 78:140–145. doi:10.1016/j.cct.2019.01.006
44. Göbölös L, Ramahi J, Obeso A, et al. Robotic totally endoscopic coronary artery bypass grafting: systematic review of clinical outcomes from the past two decades. *Innovations (Phila)* 2019; 14(1):5–16. doi:10.1177/1556984519827703
45. 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
46. Whellan DJ, McCarey MM, Taylor BS, et al. Trends in robotic-assisted coronary artery bypass grafts: a study of The Society of Thoracic Surgeons Adult Cardiac Surgery Database, 2006 to 2012. *Ann Thorac Surg* 2016; 102(1):140–146. doi:10.1016/j.athoracsur.2015.12.059
47. Puskas JD, Halkos ME, DeRose JJ, et al. Hybrid coronary revascularization for the treatment of multivessel coronary artery disease: a multicenter observational study. *J Am Coll Cardiol* 2016; 68(4):356–365. doi:10.1016/j.jacc.2016.05.032
48. Wahba A, Milojevic M, Boer C, et al. 2019 EACTS/EACTA/EBCP guidelines on cardiopulmonary bypass in adult cardiac surgery. *Eur J Cardiothorac Surg* 2020; 57(2):210–251. doi:10.1093/ejcts/ezz267
49. **Vital Stats in Adult Cardiac Surgery, Valve Surgery and Aorta Surgery.** Consult QD. February 24, 2023. <https://consultqd.clevelandclinic.org/vital-stats-in-adult-cardiac-surgery-valve-surgery-and-aorta-surgery>. Accessed February 14, 2025.
50. Deo SV, Al-Kindi S, Virani SS, Fremes S. Novel therapies to achieve the recommended low-density lipoprotein cholesterol concentration (LDL-C) targets for patients after coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2024; 167(2):723–730.e4. doi:10.1016/j.jtcvs.2023.05.028
51. Agrawal A, Kumar A, Majid M, et al. Optimal antiplatelet strategy following coronary artery bypass grafting: a meta-analysis. *Heart* 2024; 110(5):323–330. doi:10.1136/heartjnl-2023-323097
52. Bakaeen FG, Gaudino M, Whitman G, et al. 2021: The American Association for Thoracic Surgery expert consensus document: coronary artery bypass grafting in patients with ischemic cardiomyopathy and heart failure. *J Thorac Cardiovasc Surg* 2021; 162(3):829–850.e1. doi:10.1016/j.jtcvs.2021.04.052
53. Gaudino M, Bakaeen F, Benedetto U, et al. Use rate and outcome in bilateral internal thoracic artery grafting: insights from a systematic review and meta-analysis. *J Am Heart Assoc Cardiovasc Cerebrovasc Dis* 2018; 7(11):e009361. doi:10.1161/JAHA.118.009361
54. Watkins AC, Ghoreishi M, Maassel NL, et al. Programmatic and surgeon specialization improves mortality in isolated coronary bypass grafting. *Ann Thorac Surg* 2018; 106(4):1150–1158. doi:10.1016/j.athoracsur.2018.05.032
55. Ljungqvist O. The enhanced recovery after surgery in cardiac surgery revolution. *JAMA Surg* 2019; 154(8):767. doi:10.1001/jamasurg.2019.1154
56. Ghandour H, Weiss AJ, Gaudino M, et al. Public reporting for coronary artery bypass graft surgery: the quest for the optimal scorecard. *J Thorac Cardiovasc Surg* 2023; 166(3):805–815.e1. doi:10.1016/j.jtcvs.2022.01.051
57. Svensson LG, Jones DR. American Association for Thoracic Surgery Quality Gateway (AQG): interim report. *J Thorac Cardiovasc Surg* 2024; 167(1):1–2. doi:10.1016/j.jtcvs.2023.10.036
58. Angelini GD, Ramsingh RAE, Rahaman NC, et al. Developing a cardiac surgery unit in the Caribbean: a reflection. *J Card Surg* 2020; 35(11):3017–3024. doi:10.1111/jocs.14965

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