

# Current Practice of State-of-the-Art Surgical Coronary Revascularization

**ABSTRACT:** Coronary artery bypass grafting remains one of the most commonly performed major surgeries, with well-established symptomatic and prognostic benefits in patients with multivessel and left main coronary artery disease. This review summarizes current indications, contemporary practice, and outcomes of coronary artery bypass grafting. Despite an increasingly higher-risk profile of patients, outcomes have significantly improved over time, with significant reductions in operative mortality and perioperative complications. Five- and 10-year survival rates are ≈85% to 95% and 75%, respectively. A number of technical advances could further improve short- and long-term outcomes after coronary artery bypass grafting. Developments in off-pump and no-touch procedures; epiaortic scanning; conduit selection, including bilateral internal mammary artery and radial artery use; intraoperative graft assessment; minimally invasive procedures, including robotic-assisted surgery; and hybrid coronary revascularization are discussed.

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Coronary artery disease is one of the leading causes of death in Western countries. Since the introduction of coronary artery bypass grafting (CABG) in the 1960s,<sup>1</sup> it has rapidly become one of the most commonly performed major surgical procedures.<sup>2</sup> Outcomes have significantly improved over time, with declining rates of operative mortality and major morbidity, which may be due in part to better patient selection, improved surgical techniques, and better alternative techniques in patients presenting with cardiogenic shock (eg, mechanical support devices).<sup>3</sup> Large multicenter randomized and observational studies have reported excellent short-term outcomes.<sup>4,5</sup>

Despite the rise in rates of percutaneous coronary intervention (PCI) and the technical advances in stent design, CABG remains crucial for patients with multivessel coronary disease that is too complex to be treated optimally with PCI.<sup>6–8</sup> According to data from the Organisation for Economic Cooperation and Development, CABG is on average performed at a rate of 44 per 100 000 individuals (Figure 1).<sup>9</sup>

In this review, we discuss contemporary indications for CABG, practice patterns, and outcomes. We also discuss specific surgical techniques and a number of technical advances that have received attention over the last decade and could potentially improve short- and long-term outcomes after CABG.

## CONTEMPORARY INDICATIONS, PRACTICE, AND OUTCOMES

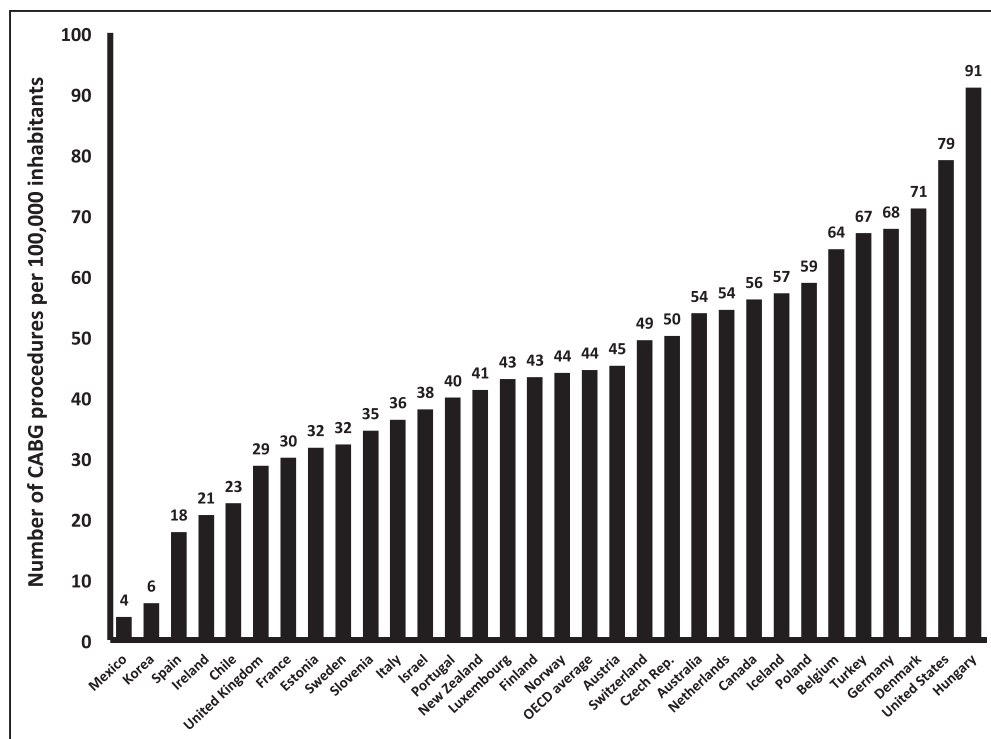
### Preoperative Risk Assessment

The choice of percutaneous or surgical revascularization depends on the risk-to-benefit ratio of procedures and should be decided by a multidisciplinary heart team

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**Figure 1. Number of coronary artery bypass graft (CABG) operations per 100 000 inhabitants.**

All data are from 2013 except for data from Hungary (2012), Belgium (2012), Australia (2012), Canada (2012), Turkey (2012), Chile (2012), the Netherlands (2010), the United States (2010), Iceland (2009), Portugal (2009), and Switzerland (2008). Data are from the Organisation for Economic Cooperation and Development (OECD).<sup>9</sup>

that includes at least an interventional cardiologist and cardiovascular surgeon but can be expanded according to the status of the patient with an anesthesiologist, nephrologist, geriatrist, etc.<sup>10</sup> To determine which treatment strategy should be favored and what the risks of surgical intervention are, preoperative risk assessment is crucial. Several risk scores have been established to estimate the surgical predicted risk of mortality. The most widely used scores are the EuroSCORE (II) and the Society of Thoracic Surgeons' risk model, with the latter also providing a calculated risk of stroke, renal failure, sternal wound infection, and length of stay.<sup>11,12</sup> Although these models include different variables, risk factors can be categorized as follows: (1) demographic variables such as age and sex; (2) previous cardiovascular events, including prior cardiovascular surgery or intervention, myocardial infarction, and stroke or transient ischemic attack; (3) cardiovascular variables, which include left ventricular function, diabetes mellitus, hypertension, arrhythmias, and peripheral vascular disease; (4) noncardiovascular variables, including renal failure and chronic obstructive pulmonary disease; (5) disease complexity and pathology, that is, the number of diseased vessels, degree of valve stenosis and regurgitation, and presence of endocarditis; and (6) the hemodynamic status of the patient and the urgency of surgery. In studies comparing the Society of Thoracic Surgeons' score and EuroSCORE II models in patients undergoing isolated CABG,

the Society of Thoracic Surgeons' score and EuroSCORE II performed similarly.<sup>13,14</sup> However, despite the comprehensiveness of these models, additional comorbid factors such as pulmonary hypertension, liver disease, previous chest radiation, and the frailty status of the patient are not included in either model but increase surgical risk and may play an important role.<sup>15</sup> The degree and complexity of coronary disease do not appear to affect short- or long-term outcomes after CABG, as shown in the SYNTAX trial (Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery). The SYNTAX score quantifies the complexity of coronary artery disease by the location and length of lesions, presence of a chronic total occlusion, bifurcation or trifurcation lesions, severe lesion calcification, vessel tortuosity, and diffuse disease and small vessels, and it has been proved to be a predictor of prognosis after PCI but not CABG. It is therefore a robust factor to differentiate which patients are candidates for CABG rather than PCI and is recommended for use in both the US and European clinical guidelines.<sup>16,17</sup> In patients in whom the risk-to-benefit ratios of percutaneous and surgical revascularization are similar, the patients' preferences should strongly influence the treatment strategy.

The appropriate diagnostic workup of patients before revascularization should thus include a full medical history, an ECG, laboratory assessments, cardiac echocardiography, and coronary angiography. Although not

universally performed, preoperative carotid ultrasound should be routinely considered to detect carotid lesions that are linked to stroke.

## Procedural Characteristics of Contemporary CABG

The majority of CABG procedures are performed through a median sternotomy with the use of cardiopulmonary bypass so that the heart can be arrested, thereby producing ideal conditions to allow a technically less demanding procedure. During on-pump surgery, the heart is arrested with cardioplegia, a potassium-rich solution to inhibit the depolarization/repolarization cycle of myocardial cells, for myocardial preservation. Ischemic preconditioning may further reduce myocardial ischemia but has not been shown to reduce clinical outcomes.<sup>18</sup>

Off-pump coronary artery bypass (OPCAB) procedures, however, do not require cardiopulmonary bypass and cardioplegia because the heart continues to beat. It is a technically more demanding procedure but theoretically reduces complications of cardiopulmonary bypass related

to a systemic inflammatory reaction syndrome, microemboli, an increased blood-brain barrier permeability, and aortic manipulation for cross-clamping and cannulation to the heart-lung machine. An overview of CABG procedures performed in the United States showed that the percentage of procedures performed off-pump peaked at 23% in 2002 but declined to 17% in 2012.<sup>19</sup>

The choice of conduits to bypass coronary lesions has been a continuous debate since the use of a single internal mammary artery (IMA) graft proved to have superior long-term outcomes over saphenous vein grafts. However, despite 3 guidelines with recommendations for increasing the use of arterial conduits, including 1 dedicated guideline from the Society of Thoracic Surgery in 2016 on conduit selection for CABG (Table 1), rates of multiple arterial grafting with IMA grafts and/or the radial artery remain persistently low. In the United States between 2002 and 2005, the rate of bilateral IMA (BIMA) use was only 4%.<sup>21</sup> In contemporary practice, the vast majority of CABG procedures are performed with the left IMA (LIMA) anastomosed to the left anterior descending artery (LAD) and additional stenoses

**Table 1. Guideline Recommendations for Conduit Use During Coronary Artery Bypass Grafting**

	2011 ACCF/AHA <sup>17</sup>	2016 STS <sup>20</sup>	2014 ESC/EACTS <sup>16</sup>
LAD territory	<p>"If possible, the LIMA should be used to bypass the LAD artery if indicated" (Class I, Level of Evidence B)</p> <p>"The RIMA is probably indicated to bypass the LAD artery when the LIMA is unavailable or unsuitable as a bypass conduit" (Class IIa, Level of Evidence C)</p>	"The IMA should be used to bypass the LAD artery when bypass of the LAD is indicated" (Class I, Level of Evidence B)	"Arterial grafting with IMA to the LAD system is recommended" (Class I, Level of Evidence A)
BITA	"When anatomically and clinically suitable, use of a second IMA to graft the left circumflex or right coronary artery (when critically stenosed and perfusing LV myocardium) is reasonable to improve the likelihood of survival and to decrease reintervention" (Class IIa, Level of Evidence B)	"Use of BIMAs should be considered in patients who do not have an excessive risk of sternal complications" (Class IIa, Level of Evidence B)	"BIMA grafting should be considered in patients <70 yr of age" (Class IIa, Level of Evidence B)
RA	"Use of a RA graft may be reasonable when grafting left-sided coronary arteries with severe stenosis (>70%) and right-sided arteries with critical stenosis (≥90%) that perfuse LV myocardium" (Class IIb, Level of Evidence B)	"As an adjunct to LIMA to LAD (or in patients with inadequate LIMA grafts), use of a RA graft is reasonable when grafting coronary targets with severe stenosis" (Class IIa, Level of Evidence B)	"Use of the RA is recommended only for target vessels with high-degree stenosis" (Class I, Level of Evidence B)
Gastroepiploic artery	No recommendation provided	"The RGEA may be considered in patients with poor conduit options or as an adjunct to more complete arterial revascularization" (Class IIb, Level of Evidence B)	No recommendation provided
Total arterial revascularization	<p>"Complete arterial revascularization may be reasonable in patients less than or equal to 60 yr of age with few or no comorbidities" (Class IIb, Level of Evidence C)</p> <p>"Arterial grafting of the right coronary artery may be reasonable when a critical (≥90%) stenosis is present" (Class IIb, Level of Evidence B)</p>	"As an adjunct to LIMA, a second arterial graft (RIMA or RA) should be considered in appropriate patients" (Class IIa, Level of Evidence B)	<p>"Total arterial revascularization is recommended in patients with poor vein quality independently of age" (Class I, Level of Evidence C)</p> <p>"Total arterial revascularization should be considered in patients with reasonable life expectancy" (Class IIa, Level of Evidence B)</p>

ACCF indicates American College of Cardiology Foundation; AHA, American Heart Association; BIMA, bilateral internal mammary artery; BITA, bilateral internal thoracic artery; EACTS, European Association for CardioThoracic Surgeons; ESC, European Society of Cardiology; IMA, internal mammary artery; LAD, left anterior descending; LIMA, left internal mammary artery; LV, left ventricular; RA, radial artery; RGEA, right gastroepiploic artery; RIMA, right internal mammary artery; and STS, Society of Thoracic Surgeons.

bypassed with vein grafts to perform complete revascularization. However, there is significant variability in how CABG procedures are performed in different countries in terms of the use of cardiopulmonary bypass, the type of cardioplegia, and which conduits are used.<sup>22</sup>

### Short-Term Complications and Long-Term Prognosis

Complication rates of CABG are typically measured at 30 days and include death, stroke, myocardial infarction, re-exploration for bleeding, renal failure requiring dialysis, atrial fibrillation, and deep sternal wound infection (eg, mediastinitis; Table 2). In most reports of large series of isolated CABG, early mortality rates are 1% to 2%, and higher mortality is reported for patients at higher risk in emergent scenarios or because of multiple comorbidities and advanced age. Although outcomes have improved, CABG still carries a considerable risk of morbidity.<sup>1</sup> Neurological complications include stroke in 1% to 3% and delirium in 8% to 50% of patients. The rate of myocardial infarction differs significantly among studies because of varying definitions, including changes on the ECG or cardiac enzyme elevations, but is estimated to occur at a rate of 2% to 4%. About 3% of patients with myocardial infarction have clinical hemodynamic instability resulting from early graft failure; the majority of patients will be managed by PCI, although some patients will require surgical reoperation. Reoperation is required in 2% to 4% of patients because of bleeding complications and increases the risk of other complications; bleeding can be reduced by blood conservation techniques, including cell-saver machines, antifibrinolytics use, and platelet and plasma transfusions. Some degree of renal failure is frequent after CABG, but only  $\approx$ 1% of patients require dialysis. About 15% to 30% of patients have new-onset atrial fibrillation that is usually transient. Mediastinitis develops in 0.5% to 3% of patients and causes long lengths of stay and recovery time and frequently requires sternal debridement or reconstruction. Although concerns about neurocognitive decline after CABG resulting from cardiopulmonary bypass have been raised,<sup>23</sup> large randomized studies have found preserved neurocognitive function after both on-pump or off-pump surgery.<sup>24</sup>

Length of stay after isolated CABG and combined CABG and valve procedures is  $\approx$ 7 and 10 days, respectively.<sup>25</sup> Patients are limited in their activities during the first 6 weeks after CABG because of the general effects of major surgery and anesthesia and the sternotomy, which requires time to heal. After discharge, cardiac rehabilitation optimizes physical, psychological, and social functioning of patients after CABG to increase quality of life.<sup>26</sup> Clearly, lifestyle changes, including smoking cessation, healthy food choices, and exercising, improve long-term prognosis. Moreover, educa-

tion on long-term secondary prevention compliance is essential. Compliance rates of taking antiplatelet medications,  $\beta$ -blockers, statins, and angiotensin-converting enzyme inhibitors after CABG are suboptimal, even though optimal medical therapy significantly improves long-term outcomes.<sup>27</sup> Intense or maximally tolerated statin therapy should be prescribed to reach a low-density lipoprotein cholesterol target  $<70$  mg/dL.  $\beta$ -Blockers should be initiated in patients with a preoperative myocardial infarction or reduced left ventricular ejection fraction ( $<35\%$ ). In addition, angiotensin-converting enzyme inhibitors should be given to patients with reduced left ventricular function ( $<40\%$ ) and a glomerular filtration rate  $>30$  mL $\cdot$ min $^{-1}\cdot$ 1.73 m $^{-2}$ . There is currently no consensus on the routine use of dual antiplatelet therapy after CABG.

Results of major adverse cardiac or cerebrovascular events at 5-year follow-up from large, contemporary CABG trials show that all-cause mortality at 5 years ranges between 5% and 15%, myocardial infarction between 2% and 8%, and stroke between 1% and 4%, depending on the population and definitions used (Table 3). Repeat revascularization ranges between 2% and 15% and depends on whether it is performed for anatomic or ischemic reasons. Historically, survival at 10 years is  $\approx 75\%$ <sup>35,36</sup> but may prove to be higher in contemporary practice, especially with higher use of guideline-directed medical therapy.

### Indications for CABG

CABG is indicated for both relief of symptoms and prolongation of life. Patients with stable coronary artery disease in whom medical therapy fails to significantly reduce symptoms are generally evaluated for myocardial revascularization. Evidence from the latest randomized trials showed that CABG appeared particularly beneficial for patients with more severe and complex coronary artery disease. Subgroup analyses from the SYNTAX trial showed that the difference between CABG and PCI treatment was evident only in those with intermediate or high severity of disease as determined by the SYNTAX score.<sup>37,38</sup> Diabetic patients often have diffusely diseased vessels with progressive atherosclerosis. CABG provides a improved long-term prognosis particularly in these patients.<sup>7</sup> Indeed, clinical guidelines recommend that CABG be performed in patients with complex disease, as well as in diabetic patients.<sup>16,17</sup> With continuous improvements in both CABG and PCI technology, recommendations for which revascularization strategy should be preferred for a specific patient continue to evolve on the basis of new results from randomized trials and vary significantly between different geographical regions.

Whether CABG should be performed in patients with ischemic cardiomyopathy has recently been investigated in the STICH trial (Surgical Treatment for Ischemic Heart

**Table 2. Incidence, Predictors, and Reductions of Short-Term Complications After Coronary Artery Bypass Grafting**

Complication	Incidence, %	Important Specific Predictors	How to Potentially Reduce Its Occurrence
Mortality	1–2	Cardiovascular risk factors Comorbidities: renal failure, lung disease, neurological impairment, etc Patient status Urgency of procedure	Reduce procedural invasiveness Adequate patient selection in multidisciplinary heart team meetings Delaying CABG in patients with an acute myocardial infarction whenever possible Increasing the use of mechanical support devices in patients with cardiogenic shock
Stroke	1–3	Previous stroke or transient ischemic attack Peripheral vascular disease, including carotid disease Preoperative and postoperative de novo atrial fibrillation Hypertension Severe atherosclerotic aorta	Off-pump CABG Clampless/no-touch procedures Epi-aortic scanning
Myocardial infarction	2–4	Recent myocardial infarction Urgency of procedure Procedural factors, including the graft configuration, number of distal anastomoses, incomplete revascularization, and longer cardiopulmonary bypass time Procedural problems related to insufficient myocardial protection, air embolism, and anastomoses	Sufficient myocardial protection with cardioplegia and thermal regulation Operative graft flow measurement using TTFM
Re-exploration for bleeding	2–4	Body surface area or body mass index Immunosuppressive therapy Preoperative antiplatelet or anticoagulation use Prior cardiovascular surgery Urgency of procedure Complexity of coronary disease or number of distal anastomoses	Preoperative timely discontinuation of antiplatelet or anticoagulation therapy Delaying surgery until the effect of antiplatelets has worn off Platelet function testing for optimal timing of surgery Perioperative antifibrinolytic agents, platelets, and fresh-frozen plasma
Delirium	8–50	Older age Cognitive function Prior cerebrovascular disease Duration of cardiopulmonary bypass	Preoperative screening Avoid postoperative infection Multicomponent intervention to manage cognitive impairment, sleep deprivation, immobility, visual and hearing impairment, and dehydration
Renal failure requiring dialysis	1	Preoperative renal function Diabetes mellitus Preoperative status (eg, cardiogenic shock)	Off-pump CABG
Atrial fibrillation	15–30	Peripheral vascular disease Preoperative atrial fibrillation Obesity	Medication such as amiodarone or sotalol, anti-inflammatory corticosteroids, $\beta$ -blockers, statins, antioxidant agents such as N-acetylcysteine, ACE inhibitors, and omega-3 fatty acids
Mediastinitis	0.5–3	Obesity Diabetes mellitus Hypertension Preoperative renal failure on dialysis Prior cardiovascular surgery Duration of cardiopulmonary bypass Bilateral IMA use Re-exploration for bleeding	Preoperative hygiene including preoperative antiseptic showers and hair removal Perioperative antibiotics Specific patient selection for bilateral IMA use Vancomycin paste Optimal glycemic control

ACE indicates angiotensin-converting enzyme; CABG, coronary artery bypass grafting; IMA, internal mammary artery; and TTFM, transit-time flow measurement. Modified from Head et al<sup>1</sup> with permission of the publisher. © 2013, Oxford University Press.

Failure). Among 1212 patients with a left ventricular ejection fraction <35% who were randomly assigned to CABG or medical therapy, 10-year outcomes favored CABG over medical therapy for all-cause death (58.9% versus 66.1%, respectively;  $P=0.02$ ) and cardiovascular

death (40.5% versus 49.3%, respectively;  $P=0.006$ ).<sup>39</sup> The impact of CABG on cardiovascular death remained consistent over all ages.<sup>40</sup> From these results, an evidence basis for the indication of CABG in patients with poor ejection fraction is substantiated.

**Table 3. Five-Year Outcomes After Contemporary Coronary Artery Bypass Grafting**

Trial	Patient Inclusion	Trial Setup	Inclusion and Patients, n	5-Year Outcomes of CABG, %					
				Death	MI	Stroke	Death+ Stroke+MI	Repeat Revascularization	MACCEs
SYNTAX trial <sup>6</sup>	Multivessel or left main disease	PCI vs CABG	2005–2007 n=1800	11.4	3.8	3.7	16.7	13.7	26.9
MASS III trial <sup>28</sup>	Multivessel disease	On- vs off-pump	2001–2006 n=308	5.2–8.4	1.9–6.5	1.9–3.2	...	5.9–6.5	...
FREEDOM trial <sup>7</sup>	Multivessel disease, diabetics	PCI vs CABG	2005–2010 n=1900	10.9	6.0	5.2	...	...	...
PRECOMBAT trial <sup>29</sup>	Left main disease	PCI vs CABG	2004–2009 n=600	7.9	1.7	0.7	9.6	5.5 (Ischemia driven)	14.3
PREVENT IV trial <sup>30</sup>	All coronary artery disease	Prevention of graft failure with edifoligide	2002–2003 n=3014	10.9–12.5	...	...	...	...	...
BEST trial <sup>31</sup>	Multivessel disease	PCI vs CABG	2008–2013 n=880	5.0	2.7	2.9	9.5	5.4	13.3
NOBLE trial <sup>32</sup>	Left main disease	PCI vs CABG	2008–2015 n=1201	9	2 (Nonprocedural)	2	...	10	19
CORONARY trial <sup>33</sup>	All coronary artery disease	On- vs off-pump	2006–2011 n=4752	13.5–14.6	7.5–8.2	2.3–2.8	...	2.3–2.8	...
ART Trial <sup>34</sup>	Multivessel disease	Single vs double IMA use	2004–2007 n=3102	8.4–8.7	3.4–3.5	2.5–3.2	12.2–12.7	6.5–6.6	

ART indicates Arterial Revascularization Trial; BEST, Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease; CABG, coronary artery bypass grafting; CORONARY, Coronary Artery Bypass Surgery (CABG) Off or On Pump Revascularization Study; FREEDOM, Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease; IMA, internal mammary artery; MACCE, major adverse cardiac or cerebrovascular event; MASS, Medicine, Angioplasty, or Surgery Study; MI, myocardial infarction; NOBLE, Nordic-Baltic-British Left Main Revascularization Study; PCI, percutaneous coronary intervention; PRECOMBAT, Premier of Randomized Comparison of Bypass Surgery Versus Angioplasty Using *Sirolimus*-Eluting Stent in Patients With Left Main Coronary Artery Disease; PREVENT IV, Project of Ex-Vivo Vein Graft Engineering via Transfection IV; and SYNTAX, Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery.

When patients are evaluated for revascularization, results from a coronary angiogram provide necessary information on which vessels require revascularization. Because visual inspection of coronary angiograms can be subjective and cannot always estimate the functional significance of a lesion to flow, fractional flow reserve (FFR) is frequently used to quantify the degree of stenosis in terms of a pressure drop across a coronary lesion. An  $FFR \leq 0.80$  is generally considered to be a significant stenosis.<sup>41</sup> Although FFR-guided revascularization has been shown to be associated with significantly improved outcomes after PCI,<sup>42</sup> evidence from studies evaluating FFR-guided CABG is scarce. Toth and coauthors<sup>43</sup> compared angiography- and FFR-guided CABG and reported that FFR-guided CABG was associated with fewer anastomoses and a higher rate of off-pump procedures but with comparable rates of the composite of death, myocardial infarction, and target vessel revascularization at 3-year follow-up in the largest study to date.

## CONDUITS

### BIMA Use

A large body of clinical and angiographic evidence supports the use of BIMA instead of a single IMA graft with additional venous conduits. Particularly in younger

patients, the benefit of BIMA use is apparent, with the age cutoff estimated at 60 to 70 years.<sup>44,45</sup> This may be the result of the combination of a longer life expectancy of younger patients and diverging survival curves between single IMA and BIMA use with longer follow-up. A meta-analysis of studies with a follow-up duration of >9 years found that among 15 583 patients enrolled in 9 observational studies, survival was significantly improved in patients in whom BIMA grafts were used as opposed to a single IMA graft, with a hazard ratio (HR) of 0.79 (95% confidence interval [CI], 0.75–0.84).<sup>46</sup> However, some surgeons may be reluctant to perform BIMA grafting because of fear of an increased risk of deep sternal wound infections; this risk is most apparent in female patients with obesity, diabetes mellitus (particularly those with poorly regulated diabetes mellitus), renal failure, and chronic obstructive pulmonary disease. To limit the risk of sternal wound infections, skeletonized rather than pedicled harvesting of IMA grafts is preferred because it maintains sternal vasculature, which significantly reduced the risk of sternal wound complications in a recent analysis.<sup>47</sup>

ART (Arterial Revascularization Trial) randomly assigned 3102 patients to BIMA or single IMA use and is likely to provide a definitive answer on whether BIMA should be performed more routinely. Short-term safety rates were comparable for groups with single IMA and BIMA use, with 30-day mortality rates of 1.2% in both

groups and comparable rates of stroke, myocardial infarction, and repeat revascularization, although there was an increased risk for sternal reconstruction with BIMA use.<sup>5</sup> Recent completion of a 5-year midterm follow-up showed that there was no difference between BIMA and single IMA use for the primary end point of death (8.7% versus 8.4%, respectively;  $P=0.77$ ) or in terms of mortality, myocardial infarction, and stroke (12.2% versus 12.7%, respectively;  $P=0.69$ ).<sup>34</sup> This may be the result of the use of a radial graft in 20% of patients in the single IMA group, which could have improved outcomes in that group by providing a second arterial conduit. Moreover, rates of adherence to optimal medical therapy for secondary prevention were excellent in both groups, perhaps limiting early vein graft failure. The study was not powered to detect a difference at 5-year follow-up and will continue to 10 years. Indeed, the benefit of BIMA is often seen with increased follow-up because vein graft failure accelerates after 5 years.

When CABG with BIMAs is performed, whether to use both arteries in situ or in a Y or T configuration remains a matter of debate. A recent randomized controlled trial of 304 randomized patients concluded that the primary end point of graft patency at 3-year follow-up was comparable for composite grafting and in situ grafts, and there were no differences in the rates of all-cause survival and myocardial infarction.<sup>48</sup> However, composite grafting significantly reduced the rate of repeat revascularization over 7-year follow-up, probably because of more complete arterial revascularization with composite grafts:  $3.2\pm 0.8$  distal anastomoses were placed versus  $2.4\pm 0.5$  with in situ grafts ( $P<0.01$ ).

## Radial Artery Use

The radial artery is often used in patients in whom BIMA use is not feasible or advised or to augment the number of arterial grafts performed in addition to BIMA grafting to accomplish total arterial revascularization. Numerous randomized controlled trials have compared graft patency of radial arteries and vein grafts. A meta-analysis of 5 trials found that radial artery grafts were associated with significantly better graft patency than vein grafts<sup>49</sup> but without reductions in all-cause death in underpowered analyses.<sup>50,51</sup> Several propensity-matched observational studies showed that the radial artery improved long-term survival over the use of vein grafts.<sup>52,53</sup> The radial artery has furthermore been compared with the right IMA (RIMA) in addition to a LIMA to the LAD. In the RAPCO trial (Radial Artery Patency and Clinical Outcomes), a total of 394 patients <70 years of age were assigned to receiving a radial artery or free RIMA; at a mean follow-up of 5.5 years, the Kaplan-Meier estimates of graft patency were 89.8% and 83.2%, respectively ( $P=0.06$ ), although 10-year

follow-up is awaited.<sup>54</sup> A meta-analysis of 8 propensity-matched analyses including 15 374 patients reported a significantly better survival with a RIMA graft than with a radial artery, with a HR of 0.75 (95% CI, 0.58–0.97;  $P=0.03$ ).<sup>55</sup> Therefore, it has been proposed that the radial artery be used as an alternative to the RIMA in patients with a high risk of mediastinitis or to graft the highly stenosed right coronary artery or distal circumflex territory.

Recent interest has been directed to determining whether the radial artery as an adjunct to BIMA use is superior to additional vein grafts. Benedetto and colleagues<sup>56</sup> reported that survival of 275 propensity-matched pairs, after a mean follow-up of 10.6 years, was comparable between patients receiving a radial artery and those receiving a vein graft in addition to BIMA use ( $P=0.54$ ). Grau and colleagues,<sup>57</sup> however, reported that, although 15-year survival was comparable between BIMA with radial or vein grafting, survival beyond the 10-year follow-up appeared to be significantly better with a radial artery. Impressively, Shi and colleagues<sup>58</sup> reported that 15-year survival was 82% versus 72% in patients receiving a radial versus vein graft as a third conduit ( $P=0.021$ ) in an analysis of 262 propensity-matched pairs.

If a radial artery is used, it should be anastomosed only to coronaries with a high-grade stenosis (>90%) to avoid competitive flow that may otherwise lead to a “string sign” of the conduit. In the RAPS trial (Radial Artery Patency Study;  $n=440$ ), the rate of graft occlusion was 11.8% in patients with 70% to 89% stenosis in the native vessel but only 5.9% in patients with  $\geq 90\%$  stenosis ( $P=0.03$ ).<sup>59</sup>

## Saphenous Vein Graft Optimization

In current practice, almost 80% of all bypass conduits are saphenous veins because of their ease of harvesting and the lesser technical challenge of vein grafting compared with multiple arterial grafting. Although recent studies have shown excellent outcomes with vein grafts compared with the RIMA as part of a Y configuration with LIMA inflow,<sup>60</sup> the major disadvantage of the saphenous vein is its tendency for progressive failure during follow-up.<sup>61</sup> Despite the higher use of optimal medication in recent studies, particularly antiplatelet therapy and statins, saphenous vein grafts still show a significant failure rate.<sup>62</sup> However, vein graft patency could be improved. First, Samano and colleagues<sup>63</sup> have now reported a 16-year follow-up of a no-touch technique for vein graft harvest that resulted in significantly better patency than conventional skeletonized vein harvesting, which may be the result of reduced intimal hyperplasia and protection against distension-induced damage that preserves vessel morphology and nitric oxide secreting activity.<sup>64</sup> The use of endoscopic vein harvesting to re-

duce the rate of wound infections, wound dehiscence, and overall complications compared with open vein harvesting raised concerns about reduced graft patency because of the potential for increased damage to the conduit with endoscopic techniques. However, 2 large observational studies reported no long-term excess of all-cause mortality or myocardial infarction with endoscopic vein harvesting compared with open vein harvesting.<sup>65,66</sup> Second, exploratory work from the PREVENT IV trial (Project of Ex-Vivo Vein Graft Engineering via Transfection) reported that storage of vein grafts in a buffered solution provided significantly improved graft patency and tended to reduce the rate of adverse clinical outcomes at 5 years compared with vein grafts stored in normal saline or blood.<sup>67</sup> Although many solutions have been developed, large-scale studies are not yet available. Third, both Taggart and colleagues<sup>68</sup> and Meirson and colleagues<sup>69</sup> have reported that the use of an external stent for saphenous vein grafts significantly reduced intimal hyperplasia at the 1-year follow-up, perhaps as a consequence of a lower oscillatory shear index that results in less turbulent flow. Larger studies with longer follow-up are required to determine whether this translates into improved vein graft patency and ultimately improved clinical outcomes.

### Intraoperative Graft Assessment

CABG is the only major vascular surgical procedure that is not routinely assessed with a "completion angiogram" or other imaging study at the time of surgery. In all other vascular surgical procedures, this intraoperative quality assessment is considered routine and necessary. Although intraoperative angiography remains impractical on a routine basis for CABG except in a hybrid operating room, some quantitative and qualitative assessment of graft flow and function may be considered in CABG.

Suboptimal rates of graft patency may be potentially related to operative technical issues such as anastomotic imprecision, graft kinking, and limited graft outflow. Therefore, several methods have been introduced as intraoperative graft assessment tools to check for technical issues that could be resolved during the operation. Transit-time flow measurement (TTFM) is the most widely used technique because of its user-friendliness and comprehensive validation. Among studies that applied TTFM during CABG, 2% to 4% of grafts required revision.<sup>70,71</sup> Studies that have related TTFM findings to short- and longer-term outcomes have been controversial, although the majority of studies found that either graft flow or pulsatility index was a predictor of short-term complications, as well as death and graft failure during follow-up.<sup>71</sup> Although TTFM is valuable to identify truly poor and truly good grafts, its value is limited in identifying grafts with minor abnormalities

that may present false-negative values of pulsatility index and flow. As a result, recent studies have suggested that 2 parameters, graft flow and anastomotic patency, are required for the complete assessment of bypass grafts. TTFM combined with epicardial echocardiography is an approach that provides both a functional and an anatomic assessment of bypass grafts. In a recent article by Di Giammarco and coauthors,<sup>72</sup> the positive predictive value of TTFM was increased from 10% to almost 100% if epicardial echocardiography was also performed to directly image flow through the graft-coronary anastomosis.

## OFF-PUMP AND AORTIC MANIPULATION

### Off-Pump Surgery

More than 60 randomized trials have compared off-pump with on-pump CABG. Several meta-analyses of these trials performed at different time points and with different inclusion criteria all come to a uniform conclusion: OPCAB significantly reduced short-term rates of stroke and renal failure but did not reduce the risk of mortality or myocardial infarction in low- and mixed-risk patients.<sup>73,74</sup> Specific studies in high-risk patients found a significant reduction in mortality with OPCAB compared with on-pump CABG in high-risk patients, although at the price of higher rates of repeat revascularization.<sup>74,75</sup>

Two of the largest contemporary trials (CORONARY trial [CABG Off or On Pump Revascularization Study], n=4752, and GOPCABE trial [German Off Pump Coronary Artery Bypass in Elderly Study], n=2539) noted that there were comparable 1-year rates of mortality, stroke, myocardial infarction, renal failure requiring dialysis, and repeat revascularization, as well as composite end points of these events.<sup>76</sup> The CORONARY trial recently reported results at the 5-year follow-up; there were still no differences in any of the clinical end points, with identical survival between the 2 techniques at 5 years.<sup>33</sup> Concerns about OPCAB procedures are particularly related to the potential for a lower rate of complete revascularization and compromised graft patency. Whether there is an impact of on- or off-pump surgery on survival remains highly controversial. In a recent single-center analysis of 13 226 patients, 10-year risk-adjusted survival was nearly identical between on- and off-pump CABG (72.8% versus 72.1%, respectively;  $P=0.56$ ), as was the freedom from death and reintervention ( $P=0.23$ ).<sup>77</sup> Routine intraoperative TTFM may be of particular value to the OPCAB surgeon to ensure optimal graft patency during challenging cases.

One of the fundamental issues with OPCAB remains the experience and expertise of the surgeon. The multi-



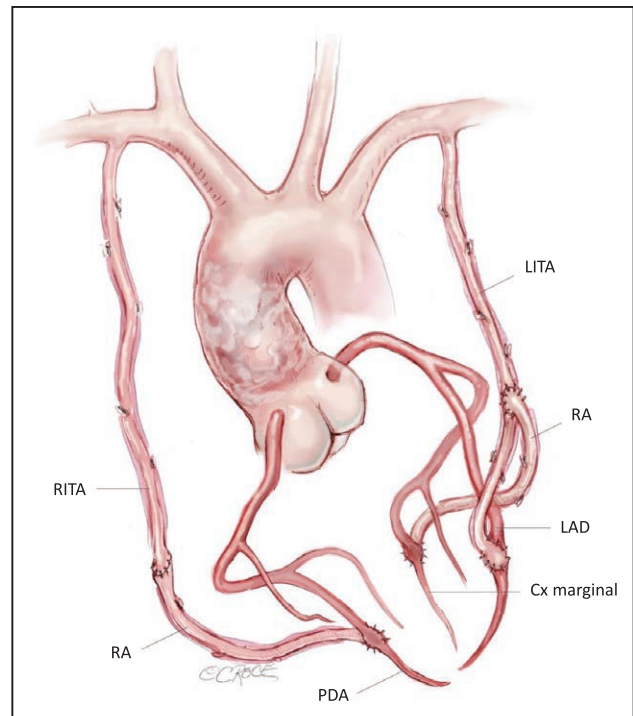
center ROOBY trial (Randomized On/Off Bypass) reported significantly better outcomes with on-pump CABG but was severely criticized because of strikingly asymmetrical experience with on-pump versus off-pump CABG among the enrolling surgeons.<sup>78</sup> In trials that required substantial experience of participating surgeons such as CORONARY and GOPCABE, outcomes of OPCAB have not been inferior.<sup>33,76</sup> A recent study found that OPCAB outcomes were best if a surgeon performed >50 OPCAB procedures annually,<sup>79</sup> although another study suggested that outcomes were not dependent on the level of the operator being a trainee or attending.<sup>80</sup> It has become clear that the experience of not only a specific surgeon but also the entire hospital matters in optimizing outcomes with OPCAB.<sup>81</sup> For this reason, clinical guidelines recommend that OPCAB be performed in high-volume off-pump centers.<sup>16</sup>

### Clampless and No-Touch Surgery

One particular potential benefit of OPCAB procedures is the possibility of avoiding manipulation of the aorta. However, OPCAB has most commonly been performed with the use of a side clamp for proximal anastomoses, which increases the risk of hard and soft plaque emboli that could cause neurological events. Some critique has been directed to studies comparing OPCAB and on-pump CABG for not specifically avoiding any manipulation of the aorta by using either proximal anastomosis devices or a conduit configuration that still requires a proximal anastomosis. This may explain why perioperative stroke reduction with OPCAB has not been more impressive. A propensity-matched analysis reported a trend toward a significant reduction in in-hospital all-cause mortality associated with avoiding aortic clamping in addition to a significantly lower rate of stroke.<sup>82</sup> Indeed, aortic manipulation has been found to be associated with postoperative major adverse events, and any reduction of aortic manipulation, by clamping only once instead of multiple times, reduces the risk of stroke. Therefore, the weight of evidence suggests that the surgical approach associated with the lowest risk of perioperative stroke appears to be a no-touch, total arterial off-pump CABG (Figure 2); a network meta-analysis of 13 studies and 37 720 patients supports this recommendation by showing significant reductions in mortality, stroke, and renal failure when this technique is applied.<sup>83</sup> Even if on-pump surgery is performed and the aorta is cross-clamped, stroke rates can be reduced by not performing multiple clamping or avoiding side-biting clamp techniques.

### Epiaortic Scanning

Surgeons generally palpate the aorta before cannulating or constructing a proximal anastomosis to detect



**Figure 2.** Example of a complete arterial no-touch coronary artery bypass graft configuration.

Cx indicates circumflex; LAD, left anterior descending; LITA, left internal thoracic artery; PDA, posterior descending artery; RA, radial artery; and RITA, right internal thoracic artery.

atherosclerotic burden that is present in >50% of patients who undergo CABG. However, aortic palpation has limited sensitivity because of the inability to palpate the complete circumference of the aorta and to detect soft plaques. Consequently, epiaortic ultrasonography has been recommended to detect plaque, and several large retrospective studies of all cardiac surgery operations and specifically CABG procedures found that the use of epiaortic ultrasound significantly reduced the incidence of stroke.<sup>84,85</sup> This reduction in stroke is achieved by modifying the surgical technique when significant plaque is detected. The need for technique modifications based on epiaortic ultrasonography ranges between 4% and 31%,<sup>85,86</sup> depending on the type of modification and the definitions used. On the basis of these findings, intraoperative epiaortic scanning should be considered before aortic manipulation.

## REDUCING INVASIVENESS

### Minimally Invasive CABG

An alternative approach to a sternotomy for CABG may be to perform minimally invasive direct coronary artery bypass (MIDCAB) via a small (5–10 cm) left anterior thoracotomy. The LIMA can then be harvested by direct vision or with robotic endoscopic techniques. The largest series by Holzhey and colleagues<sup>87</sup> of 1768 patients undergo-

ing MIDCAB from 1996 to 2009 reported a postoperative mortality of 0.8% and a 95.5% graft patency at routine postoperative angiography (n=712). Survival at 5 and 10 years was 88.3% and 76.6%, respectively. A number of small studies have compared MIDCAB procedures with conventional CABG. A recent propensity-matched analysis of 159 pairs showed comparable rates of procedural complications and similar lengths of hospital stay after LAD revascularization via MIDCAB and sternotomy.<sup>88</sup> However, postoperative pain is often increased after a MIDCAB approach. Despite this, full recovery after a MIDCAB procedure appears to be quicker than after sternotomy, with potential improvements in quality of life.

## Robotic CABG

In most centers, the term robotic CABG is used to describe a robotic LIMA harvest technique, followed by a hand-sewn off-pump LIMA-LAD anastomosis via a very small (3–4 cm) left anterior thoracotomy without rib excision or spreading. Operative times are generally longer than for CABG procedures through sternotomy, but short-term outcomes are comparable.<sup>89</sup> A meta-analysis showed excellent safety and only a 2.5% rate of conversion to sternotomy.<sup>90</sup> Concerns about the quality of anastomoses have been raised, but a series of 307 patients showed that 95% of LIMA-LAD conduits were patent among 199 patients with an angiogram before discharge.<sup>91</sup> At longer follow-up, graft patency has been in the range of 92% to 97% for LIMA-to-LAD anastomoses through 8 years of follow-up.<sup>92,93</sup>

The term robotic CABG may also refer to a robotic totally endoscopic CABG procedure in which the LIMA is both harvested and anastomosed to the LAD by robotic endoscopic techniques. Totally endoscopic CABG procedures have been used to treat isolated LAD lesions and multivessel disease. However, in a single-arm multicenter registry, 13 of 98 patients (13%) with the intention of totally endoscopic CABG needed to be excluded intraoperatively because of failed femoral cannulation or inadequate working space, emphasizing that appropriate patient selection is essential for this very demanding technical procedure.<sup>94</sup> Because it is so technically challenging and has a high rate of conversion to sternotomy of ≈15% to 20%,<sup>90</sup> widespread adoption of totally endoscopic CABG procedures awaits the development of easily maneuverable anastomotic devices.

## Hybrid Coronary Revascularization

Hybrid coronary revascularization (HCR) consisting of a LIMA-LAD anastomosis through (robotic) MIDCAB plus stenting of remaining non-LAD lesions for patients with multivessel disease has received much attention in recent years. A small randomized trial to assess the safety of the procedure included 200 patients who were randomly as-

signed to undergo either HCR or CABG. There were no differences in the rates of death, myocardial infarction, stroke, major bleeding, or repeat revascularization at the 1-year follow-up.<sup>95</sup> Among centers in the United States, overall short-term complication rates were low and comparable to those of conventional CABG.<sup>96</sup> However, particular benefits include higher patient satisfaction and shorter times for patients to return to work. Midterm results over the first years of follow-up have been promising, with reports of rates of major adverse cardiac or cerebrovascular events and survival comparable to those of CABG, although higher rates of repeat revascularization associated with HCR are a potential concern.<sup>97,98</sup>

Only carefully selected patients are currently considered candidates for HCR, as shown by a recent analysis of 198 622 patients treated with CABG in the United States between 2011 and 2013, of whom only 0.5% underwent HCR.<sup>96</sup> Criteria for HCR therefore include a proximal LAD lesion graftable with a MIDCAB or robotic MIDCAB procedure; a complexity of residual lesions feasible for PCI, for example, intermediate SYNTAX score at most; and no contraindication to dual antiplatelet therapy. Because there is currently no substantiated evidence from large-scale randomized controlled trials to support widespread use of HCR as opposed to multiarterial CABG, HCR is currently limited to patients with specific indications (Table 4). Moreover, HCR may be technically and logistically more demanding than CABG or PCI alone, with the option of PCI before CABG, which introduces the issue of preoperative continuation of dual antiplatelet therapy; the option of CABG before PCI, with the potential risk of ischemia in non-LAD lesions; or the option of simultaneous PCI and CABG, which requires a hybrid operating

**Table 4. Proposed Current Indications for Hybrid Revascularization in Patients With Multivessel Disease**

Patients with a low SYNTAX score but an LAD lesion not amenable to PCI
Patients with an indication for CABG requiring complete revascularization but with a contraindication for sternotomy
Patients with a graftable proximal LAD lesion but poor surgical targets in the Cx or RCA that are amenable to PCI
Patients undergoing emergent PCI of a culprit Cx or RCA lesion but with residual disease requiring staged surgical revascularization of the LAD
Patients with a porcelain aorta and no ability to achieve complete revascularization without the use of a proximal anastomosis in whom off-pump revascularization of the LAD can take place with residual lesions being treated by delayed PCI
Patients with a history of pericarditis in whom non-LAD surgical targets are difficult to identify
Patients requiring a redo sternotomy after a previous noncoronary cardiac operation in whom grafting surgical targets in the Cx is high risk for lateral wall dissection

CABG indicates coronary artery bypass grafting; Cx, circumflex; LAD, left anterior descending artery; PCI, percutaneous coronary intervention; RCA, right coronary artery; and SYNTAX, Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery.

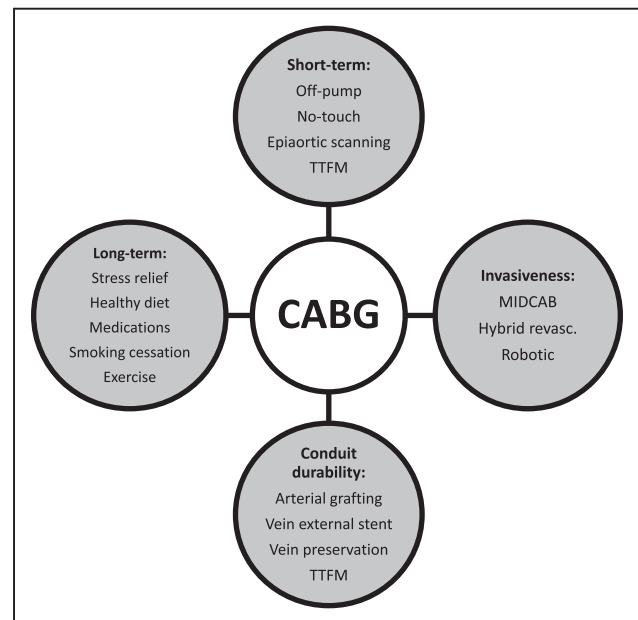
Adapted from Head and colleagues<sup>99</sup> with permission of the publisher. © 2013, Oxford University Press.

room. The recent National Institutes of Health–funded Hybrid Observational Trial by Puskas and colleagues<sup>100</sup> demonstrated a wide variation in current practice across a network of 11 premier US cardiac surgical centers for patients with hybrid-eligible coronary lesions. There was general agreement among cardiologists and surgeons at these sites as to which of 6669 consecutive patients who underwent diagnostic coronary angiography could be considered eligible for HCR (454, 12.2%). Moreover, among 200 patients who had HCR and 98 who had multivessel PCI, major adverse cardiac or cerebrovascular events were statistically similar through 17.6 months of follow-up, with a nonsignificant trend toward more adverse events in the PCI group during the later months of follow-up. Thus, equipoise is established for a larger prospective randomized trial of HCR versus multivessel PCI in patients with low-SYNTAX-score, hybrid-eligible coronary artery disease. Such a trial has been recently funded by the National Heart, Lung, and Blood Institute and will begin enrollment in late 2017.

In a survey of surgeons in the United States, only 10% were in favor of HCR,<sup>101</sup> although a more recent survey among 200 cardiologists and surgeons found that three quarters of responders (n=90) believed adoption of HCR will expand in the next decade.<sup>102</sup> Therefore, a heart team should weigh the benefits and risks of PCI, CABG, and HCR to decide which treatment is most appropriate for each individual patient with multivessel disease.<sup>10</sup> With the most recent randomized trials and large observational studies of PCI with drug-eluting stents versus CABG in multivessel disease showing improved outcomes with CABG,<sup>7,31,37,103</sup> surgeons will be reassured and confident that CABG is effective and offers increased longevity. Before HCR becomes a standard procedure at centers around the world, surgeons will have to commit to MIDCAB procedures.

## Conclusions

Although patients referred for CABG bear increasing cardiovascular risk factors and comorbidities, actual outcomes have significantly improved over the last decades, with low rates of 30-day complications. Although many developments in operative techniques and devices have been established to further improve both short- and long-term outcomes, adoption rates often remain low. The use of multiple arterial conduits remains scarce, mostly because of fear of sternal wound complications and the lack of data from randomized trials; the ART trial, which is currently completing 10 years of follow-up, will provide necessary and long-awaited insights. The weight of data shows similar mortality outcomes with on- and off-pump surgery among low- and mixed-risk patients; patients at high risk of morbidity and mortality with conventional CABG benefit most from OPCAB. Minimizing aortic manipulation is directly related to lower rates of stroke after CABG, and no-



**Figure 3. Developments for state-of-the-art coronary artery bypass graft (CABG).**

MIDCAB indicates minimally invasive coronary artery bypass; revasc., revascularization; and TTFM, transit-time flow measurement.

touch OPCAB may provide the lowest stroke risk. Intraoperative Doppler graft assessment should be routine, especially in OPCAB. One of the most exciting developments is hybrid revascularization, although evidence for widespread use is not currently available and surgical experience with MIDCAB procedures is still limited. These and other developments have provided the contemporary state-of-the-art CABG procedure (Figure 3).

## DISCLOSURES

Dr Taggart discloses that he is an investigator in the REQUEST Registry study (Registry for Quality Assessment with Ultrasound Imaging and Transit-Time Flow Measurement in Cardiac Bypass Surgery), funded by Medistim, Inc, Oslo, Norway, and has received traveling and speaking fees from Medistim, Inc. He is a paid consultant to Vascular Graft Solutions and principal investigator of the VEST I and VEST II trials (Venous External Stent Trial), funded by Vascular Graft Solutions, Tel Aviv, Israel. He has received research funding and traveling and speaking fees and has share options in Vascular Graft Solutions. He is the international principal investigator of the ART trial (Arterial Revascularization Trial), a prospective randomized multicenter trial of single versus bilateral internal thoracic artery grafting, funded by the British National Institutes of Health and the British Heart Foundation. Dr Puskas discloses that he is the unpaid principal investigator for the international REQUEST Registry study of the use of intraoperative transit-time Doppler graft assessment, funded by Medistim, Inc. He is also national coprincipal investigator for the Hybrid Coronary Revascularization Trial, a prospective randomized study funded by the US National Heart, Lung, and Blood Institute (UO1 HL125488-01A1). He serves as the

unpaid national principal investigator for the upcoming US Food and Drug Administration Investigational Drug Exemption trial of external stenting for saphenous vein graft conduits, funded by Vascular Graft Solutions. He receives royalty payments from the sale by Scanlan Inc. of surgical instruments he designed. Dr Head reports he is an investigator in the international REQUEST Registry study. Dr Milojevic reports no conflicts of interest.

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## FOOTNOTES

*Circulation* is available at <http://circ.ahajournals.org>.

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