

**Clinical update**

# Coronary artery bypass grafting: Part 2— optimizing outcomes and future prospects

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Since first introduced in the mid-1960s, coronary artery bypass grafting (CABG) has become the standard of care for patients with coronary artery disease. Surprisingly, the fundamental surgical technique itself did not change much over time. Nevertheless, outcomes after CABG have dramatically improved over the first 50 years. Randomized trials comparing percutaneous coronary intervention (PCI) to CABG have shown converging outcomes for select patient populations, providing more evidence for wider use of PCI. It is increasingly important to focus on the optimization of the short- and long-term outcomes of CABG and to reduce the level of invasiveness of this procedure. This review provides an overview on how new techniques and widespread consideration of evolving strategies have the potential to optimize outcomes after CABG. Such developments include off-pump CABG, clampless/anaortic CABG, minimally invasive CABG with or without extending to hybrid procedures, arterial revascularization, endoscopic vein harvesting, intraprocedural epiaortic scanning, graft flow assessment, and improved secondary prevention measures. In addition, this review represents a framework for future studies by summarizing the areas that need more rigorous clinical (randomized) evaluation.

**Keywords**

Coronary artery bypass grafting • Off-pump • Anaortic • Minimally invasive • Hybrid revascularization • Arterial grafting • Endoscopic vein harvesting • Epiaortic scanning • Graft flow measurement • Secondary prevention • Guidelines • Heart team

## Introduction

Coronary artery bypass grafting (CABG) was first introduced in the mid-1960s and evolved rapidly as the standard of care for patients with extensive coronary artery disease.<sup>1</sup> However, the introduction of percutaneous coronary intervention (PCI) led to a reconsideration of therapeutic strategies.<sup>2</sup> Improvements in stent design, adjuvant medical therapy and technical skills quickly turned PCI into a very attractive alternative treatment option for patients with acute coronary syndromes and less complex coronary disease.<sup>3–7</sup> The broader use of PCI is reflected by declining CABG rates over the last decades,<sup>8</sup> even though recent long-term results from the SYNTAX,<sup>9</sup> ASCERT,<sup>10</sup> and FREEDOM<sup>11</sup> trials showed significantly better survival rates after CABG than after PCI. Despite converging outcomes between the two treatments in select patient populations,

coronary surgery currently remains the standard of care for most elective patients, including those with diabetes and/or complex left main or three-vessel disease.<sup>9,12</sup>

Although short-term outcomes have dramatically improved over the first 50 years, surprisingly, technical aspects of the CABG procedure did not change significantly. Particularly in an era of increasing and sometimes overuse of PCI, several aspects of CABG should be improved to further optimize short- and long-term outcomes, while at the same time improving the appeal of CABG which is regarded as an overly invasive attractive treatment option by some. A number of advancements have been proposed, but adoption rates for these techniques are low.

This review provides a summary of how CABG outcomes can be optimized by adoption of new developments. These developments include off-pump, clampless/anaortic, and minimally invasive CABG

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with or without extending to hybrid procedures, arterial revascularization, endoscopic vein harvesting, intraprocedural epi-aortic scanning and graft flow assessment and improved secondary prevention measures. Furthermore, this review represents a framework for future studies by summarizing the areas that need more rigorous clinical evaluation.

## Operative techniques

### Off-pump surgery

In 2001, ~25% of CABG procedures were performed off-pump.<sup>13</sup> In the Western world, the contemporary rate of off-pump CABG procedures is ~20%, while in Asia the majority of procedures is performed off-pump.<sup>14</sup> Theoretically off-pump CABG could reduce morbidity—particularly stroke—and even mortality by avoiding cardiopulmonary bypass that is associated with formation of microemboli, an increased blood–brain barrier permeability and aortic manipulation during cross-clamping and cannulation.<sup>15</sup>

Numerous risk-adjusted studies have found that the off-pump technique appears favourable in terms of both hard and surrogate endpoints.<sup>16,17</sup> A meta-analysis of propensity score-adjusted studies that included >120 000 patients demonstrated the superiority of the off-pump technique with respect to 11 selected short-term outcomes, particularly for mortality as the most important one (OR = 0.69; 95% CI: 0.60–0.75;  $P < 0.0001$ ) and for stroke (OR = 0.42; 95% CI: 0.33–0.54;  $P < 0.0001$ ).<sup>18</sup> In addition, the most recent meta-analysis of 59 randomized trials on a total of 8961 patients comparing on-pump with off-pump CABG demonstrated a 30% (95% CI: 1–51%) relative risk reduction for stroke.<sup>13</sup> However, some studies have shown increased rates of mortality and repeat revascularization during the follow-up;<sup>19,20</sup> probably caused by reduced graft patency after off-pump vs. on-pump CABG.<sup>21,22</sup> Although single-centre prospective angiographic studies have shown similar excellent graft patency rates with off-pump and on-pump CABG,<sup>23</sup> the 1-year results from the ROOBY trial showed a 27% higher risk of graft occlusion in the off-pump group (95% CI: 9–48%); graft patency was 87.8% in the on-pump and 82.6% in the off-pump patients ( $P < 0.001$ ).<sup>24</sup> These results were criticized for the lack of sufficient experience that contributing surgeons had with off-pump procedures.<sup>25</sup> However, several other trials involving highly experienced surgeons and a meta-analysis pointed in a similar direction as the findings from the ROOBY trial.<sup>25–27</sup> Off-pump CABG has also been associated with increased rates of incomplete revascularization, and could result in reduced long-term survival.<sup>28</sup>

The CORONARY trial showed no benefit of off-pump CABG over on-pump CABG at 30 days or 1 year in 4752 randomized patients.<sup>29,30</sup> Although there appears to be a significant benefit of off-pump over on-pump CABG in patients at high-operative risk<sup>31</sup> and in patients with atherosclerotic aortas,<sup>32</sup> the hypothesis that off-pump CABG is beneficial for ‘all-comers’ may be too optimistic.<sup>33</sup> Despite the encouragement to a general use of off-pump techniques, it has been recommended specifically for high-risk patients.<sup>34</sup> However, even this recommendation was recently challenged by the results of the GOPCABE trial, which did include elderly higher-risk patients ( $n = 2539$ ) but was still unable to confirm superiority

of the off-pump over the on-pump approach in this subset of patients.<sup>35</sup> Patient selection is critical, since the majority of patients can safely and efficiently undergo on-pump CABG without the risk of increased 30-day repeat revascularization rates associated with off-pump procedures in the latest trials.<sup>29,30,35</sup> It may therefore be cumbersome for trainees to gain experience in a procedure with a steep learning curve that is infrequently performed only in selected patients.

It is worth noting that although evidence for a survival benefit of off-pump CABG is inconsistent across the peer-reviewed literature, a preponderance of evidence suggests that it is associated with significant reductions in transfusion requirements, prolonged ventilation, ICU and hospital length of stay, new renal failure, stroke/neurocognitive decline and other clinical endpoints.<sup>36</sup>

### Clampless/anaortic off-pump surgery

If off-pump CABG is performed, the degree of aortic manipulation should be reduced to a minimum. The benefit of off-pump CABG may be limited unless partial clamping of the aorta is avoided. Aortic clamping produces a significantly higher number of solid microemboli on transcranial Doppler than clampless surgery and can therefore lead to procedural stroke.<sup>37</sup> It is to note that in most trials, including the major randomized trials, off-pump CABG was not performed using an anaortic technique, the major driver for reducing stroke.

The number of studies that compared clampless CABG to ‘regular’ CABG with clamping is limited (*Table 1*). In the absence of a large randomized comparison, Börgermann *et al.*<sup>38</sup> used propensity matching to compare mortality and stroke rates between patients who underwent clampless off-pump or conventional CABG. In the propensity-matched cohort of 395 pairs, clampless off-pump CABG reduced rates of death (OR = 0.25, 95% CI: 0.05–1.18;  $P = 0.080$ ) and stroke (OR = 0.36, 95% CI: 0.13–0.99;  $P = 0.048$ ). More specifically, one of the largest studies to date found significantly lower stroke rates after off-pump than on-pump CABG, if an all-arterial ‘no touch’ technique was applied or when the proximal vein-graft anastomoses were performed clampless using the HeartString device (Guidant, Indianapolis, USA).<sup>39</sup> This evidence is complemented by a meta-analysis including 11 398 patients that showed that the absence of aortic manipulation was associated with a significant reduction of neurological complications (OR = 0.46, 95% CI: 0.29–0.72;  $P = 0.0008$ ).<sup>40</sup>

### Minimally invasive coronary artery bypass grafting/hybrid revascularization

One of the drawbacks of CABG remains its invasiveness, even without the use of cardiopulmonary bypass. Quality of life scores at 30 days and patient treatment satisfaction surveys throughout the first 6 months are significantly higher after PCI than after CABG.<sup>41</sup> Moreover, CABG is sometimes referred to as a procedure where ‘the chest is cracked open’, which from a patient’s perspective presents a frightening prospect of postoperative pain and extended rehabilitation. As a result, patients often prefer PCI to CABG because of ‘temporal discounting’, i.e. disproportionately emphasize short-term results even though CABG has been shown to be superior to PCI with respect to long-term survival and angina relief.<sup>10,41–44</sup>

**Table 1** Studies comparing clampless or 'aortic no touch' off-pump coronary artery bypass grafting with conventional off-pump or on-pump surgery

Author (year)	Inclusion	Design	No. of patients	Use of devices	Unadjusted 30-day outcomes			Comment
					Mortality	Stroke	Perioperative MI	
Clampless								
Lev-Ran (2004)	2000–02	Retrospective	103 vs. 57 with clamp	No	2.9 vs. 7%	0 vs. 5.3%	3 vs. 5%	Side clamping an independent predictor of stroke or mortality: OR = 6.28, 95% CI: 1.39–28.4; <i>P</i> = 0.017
Kempfert (2008)	2003–05	RCT	51 vs. 48 with clamp	Connector: PAS-Port	0 vs. 2.1%	—	—	
Manabe (2009)	2004–07	Retrospective	109 vs. 185 no touch vs. 241 with clamp	HeartString ( <i>n</i> = 81) Enclose II ( <i>n</i> = 28)	1.8 vs. 1.1 vs. 1.2%	2.8 vs. 0.5 vs. 0.8%	—	
El Zayat (2012)	2009	RCT	29 vs. 28 with clamp	HeartString	0 vs. 0%	0 vs. 6.9%	—	
Emmert (2012)	1999–2009	Prospective	507 vs. 524 with clamp	HeartString	1.8 vs. 2.5%	0.4 vs. 2.9%	1.5 vs. 3.1%	Clampless off-pump CABG was a significant predictor of reduced stroke in a propensity-score-adjusted analysis: OR = 0.04, 95% CI: 0.003–0.48
Börgermann (2012)	2009–10	Prospective	395 vs. 887 with clamp	Connector: PAS-Port ( <i>n</i> = 310)	3.3 vs. 7.6%	—	—	In a propensity-matched cohort of 395 pairs, clampless off-pump CABG was a predictor of less death (OR = 0.25, 95% CI: 0.05–1.18; <i>P</i> = 0.080) and stroke (OR = 0.36, 95% CI: 0.13–0.99; <i>P</i> = 0.048)
Aortic no touch								
Patel (2002)	1997–2001	Prospective	597 vs. 520 off-pump with manipulation vs. 1210 on-pump	No	1.5 vs. 1.0 vs. 2.5%	0.5 vs. 0.4 vs. 1.6%	—	Aortic manipulation was not a significant predictor of neurological outcome in off-pump patients
Calafiore (2002)	1998–2000	Retrospective	1533 vs. 3290 any manipulation (on- or off-pump)	No	—	0.2 vs. 1.4%	—	In multivariable stepwise logistic regression, any aortic manipulation was associated with an OR of 8.4 (95% CI: 2.4–28.9; <i>P</i> = 0.0008) for stroke
Kim (2002)	1998–2001	Prospective	222 vs. 123 'regular' off-pump vs. 76 on-pump	No	0.9 vs. 2.4 vs. 2.6%	0 vs. 0.8 vs. 3.9%	1.4 vs. 5.7 vs. 6.6%	
Leacche (2003)	1996–2001	Retrospective	84 vs. 556 'regular' off-pump	No	1.6 vs. 1.7%	0 vs. 1%	1.3 vs. 1.8%	
Kapetanakis (2004)	1998–2002	Retrospective	476 vs. 2527 moderate vs. 4269 extensive aortic manipulation off-pump	No	1.5 vs. 1.9 vs. 2.1%	0.8 vs. 1.6 vs. 2.2%	1.1 vs. 0.7 vs. 0.5%	No touch surgery was independently associated with reduced stroke when compared with extensive (OR = 1.7, 95% CI: 1.11–2.48; <i>P</i> < 0.01) and even moderate aortic manipulation (OR = 1.8, 95% CI: 1.15–2.74; <i>P</i> < 0.01). Propensity-matched analysis failed to show similar findings
Lev-Ran (2005)	2000–03	Retrospective	471 vs. 229 off-pump with side-clamp	No	2.1 vs. 2.6%	0.2 vs. 2.2%	1.4 vs. 1.5%	The use of side-clamping was an independent predictor of stroke: OR = 28.5, 95% CI: 2.27–333.3; <i>P</i> = 0.009
Bolotin (2007)	2000–01	Prospective	110 vs. 216 on-pump CABG	No	2.7 vs. 1.9%	0 vs. 2.3%	0.9 vs. 1.4%	

Continued

**Table 1** Continued

Author (year)	Inclusion	Design	No. of patients	Use of devices	Unadjusted 30-day outcomes			Comment
					Mortality	Stroke	Perioperative MI	
Valley (2008)	2002–06	Prospective	1201 vs. 557 off-pump with aortic manipulation	No	1.4 vs. 1.3%	0.3 vs. 1.1%	0.6 vs. 0.4%	No touch surgery was an independent predictor of reduced rates of neurological events: OR = 0.23, 95% CI: 0.06–0.92; <i>P</i> = 0.037
Misfeld (2010)	2002–07	Retrospective	1346 vs. 600 'regular' off-pump vs. 1753 on-pump	No	1.0 vs. 1.0 vs. 2.3%	0.1 vs. 0.5 vs. 0.9%	0.5 vs. 0.5 vs. 0.6%	Compared to no touch off-pump CABG, on-pump CABG (OR = 12.3, 95% CI: 2.9–52.2; <i>P</i> = 0.0006) and 'regular' off-pump CABG (OR = 7.0, 95% CI: 1.4–35.0; <i>P</i> = 0.018) were independent predictors of neurological complications
Emmert (2011)	2004–09	Prospective	1365 vs. 567 off-pump with clamp	HeartString	1.8 vs. 1.6%	0.7 vs 2.3%	0.9 vs. 1.9%	No touch clampless off-pump CABG was a significant predictor of reduced stroke in a propensity score-adjusted analysis: OR = 0.39, 95% CI: 0.16–0.90; <i>P</i> = 0.04

CABG, coronary artery bypass grafting; MI, myocardial infarction; OR, odds ratio.

Less invasive surgical techniques may present an attractive alternative; minimally invasive direct coronary artery bypass (MIDCAB) does not require sternotomy and is therefore more acceptable to patients than conventional CABG.<sup>45</sup> The left minithoracotomy incision is smaller, the risk of scarring is less, and risks of deep sternal wound infection and problems with sternum healing are omitted. Although MIDCAB may be associated with slightly increased pain postoperatively due to spreading of the ribs, the length of stay is markedly reduced and there is an early postoperative quality of life benefit over conventional CABG.<sup>46–48</sup> MIDCAB was shown to be as safe and efficient as off-pump CABG, while reducing the recovery time.<sup>49</sup> Holzhey et al.<sup>50</sup> recently reported long-term results from their single-centre experience on 1768 patients. Five- and 10-year survival was 88.3 and 76.6%, respectively. The rates of freedom from major adverse cardiac or cerebrovascular events and angina were of 85.3 and 70.9%, respectively.

Exposure during MIDCAB is largely limited to the left anterior descending (LAD) artery and eventually diagonal branches, and therefore almost exclusively performed in patients with isolated LAD stenosis or occlusion. An open left internal mammary artery (IMA) graft to the LAD is without doubt the single most important conduit that offers a prognostic benefit based on its proven long-term patency and improved survival. Patients with multivessel disease—especially at younger age—also derive a survival benefit from total arterial grafting with bilateral IMA (BIMA) grafts.<sup>51</sup> The added benefit of a second arterial graft in older patients is less well documented;<sup>52</sup> however, the rate of early vein-graft failure, especially to distal targets and severely diseased small vessels, is high and ranges from 10 to 26% between 12 and 18 months after surgery.<sup>21,53</sup> In some patients, a hybrid procedure can combine the benefits of an MIDCAB—providing a left IMA (LIMA) graft to the LAD—and stenting of the circumflex and/or the right coronary artery. This type of management may yield results similar to those of a full CABG procedure,<sup>54</sup> but randomized trials are still lacking (Table 2). The hospitalization costs of hybrid revascularization are similar to the costs of off-pump CABG, but the time to return to work is shorter and patient satisfaction higher.<sup>55</sup> Halkos et al.<sup>56,57</sup> showed that survival after hybrid revascularization at 5-year follow-up was comparable with off-pump CABG in patients with left main disease (88.6 vs. 83.4%, respectively; *P* = 0.55) and in patients with multivessel disease (86.8 vs. 84.3%, respectively; *P* = 0.61) (Figure 1).

Complete revascularization in patients with multivessel disease by minimally invasive CABG can also be achieved via a totally endoscopic coronary artery bypass (TECAB) procedure,<sup>58</sup> by combining an endoscopic with an open approach,<sup>59</sup> or by a hybrid endoscopic and percutaneous procedure.<sup>60</sup> Such procedures are only performed in selected patients at specialized centres and require extensive operating times. Earlier series reported unsatisfactory patency results, but with the evolution of better endoscopic stabilizers the results from these highly experienced centres are similar to conventional CABG with a reported mortality rate of 1–2%<sup>58–61</sup> and a 5-year survival in the range of 85–95%.<sup>60–62</sup>

Adoption of minimally invasive CABG procedures has been slow. For MIDCAB, this may be explained in part by the low incidence of isolated proximal LAD stenosis<sup>63</sup> and also by the high technical demands of this procedure. Hybrid revascularization for multivessel disease, theoretically, has a much larger target population. However,

a systematic search of the literature shows that the accumulated evidence is based on small non-randomized studies comprising just over 1000 patients in total (Table 3). Between October 2003 and April 2010, only 174 patients underwent hybrid revascularization in the USA.<sup>56,57</sup> Apart from technical issues, the low-adoption rate is partly due to logistic reasons; the staging of two procedures in a (hybrid) operating rooms, and/or catheterization laboratory, and the administration or discontinuation of antiplatelet therapy. A survey performed in 2002 indicated that 80% of US surgeons perform less than five MIDCAB procedures annually.<sup>64</sup> When asked about hybrid procedures, only 10% of surgeons were in favour. In contrast, 50% of 180 cardiologists were in favour of hybrid revascularization. Yet, only two cardiologists (1.1%) had referred patients for MIDCAB (with or without PCI). Stronger

evidence to support a recommendation for hybrid revascularization is expected from a number of currently on-going registries, the largest of which is the Hybrid Revascularization Observational Study (NCT01121263) that includes patients throughout the USA and is sponsored by the National Heart, Lung, and Blood Institute (NHLBI).

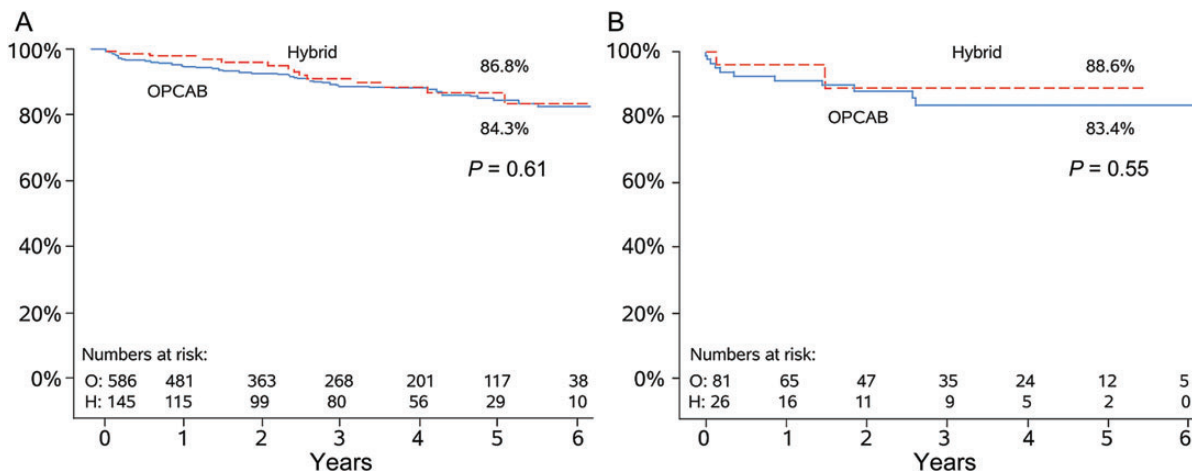
### Arterial grafting

The use of one IMA graft, most often the left IMA anastomosed to the LAD combined with venous conduits represents the standard therapy for patients undergoing CABG.<sup>65,66</sup> However, venous bypass grafts tend to fail: a recent study by Kim *et al.*<sup>67</sup> found that 11.8% of saphenous vein grafts failed within 7 days, which is similar to the failure rate reported by FitzGibbon *et al.*<sup>68</sup> Therefore, BIMA grafting should be strongly considered in patients with multivessel coronary disease, because BIMA grafting is associated with reduced mortality during the first year post-surgery and during the long-term follow-up.<sup>69</sup> A meta-analysis of seven pooled studies with 11 269 single and 4693 bilateral IMA grafts demonstrated that BIMA was associated with a reduced risk for death: HR = 0.81 (95% CI: 0.70–0.94).<sup>51</sup>

In the Arterial Revascularization Trial (ART), the only randomized trial to date comparing BIMA and single IMA (SIMA), 3102 patients were randomized in 28 centres in 7 countries.<sup>70</sup> Mortality rates at 30 days were 1.2% in both groups, and 2.3 vs. 2.5% at 1-year for SIMA and BIMA groups, respectively. There were also no differences in the incidence of stroke, MI, and repeat revascularization. While the use of a second IMA graft added 23 min to the operative procedure which in itself took 3–4 h, the trial clearly demonstrated that BIMA grafting was as safe as SIMA grafting, even though the risk of a need for later sternal reconstruction was increased: relative risk 3.24 (95% CI: 1.54–6.83). An extended follow-up (for up to 10 years) is expected for this study and will hopefully determine whether survival with BIMA grafts is indeed superior. The trial, however, also

**Table 2 Reasoning supporting hybrid revascularization**

Patients with double vessel disease and chronic total occlusion of the LAD
Patients with multivessel disease and an indication for CABG requiring complete revascularization in whom a full sternotomy is contraindicated or not desired
Patients with multivessel disease with a dominant LAD or complex proximal LAD lesion morphology and poor surgical targets in the distal CX or RCA territory amenable for PCI
Patients with multivessel disease with an indication for PCI (SYNTAX score <22) or in clinical trials comparing hybrid revascularization with PCI or CABG (SYNTAX score >23)
Patients with multivessel disease undergoing emergent PCI of a culprit lesion of a CX or RCA lesion (in the setting of STEMI, non-STEMI, or ACS) with a staged surgical revascularization of the LAD



**Figure 1** Long-term survival of hybrid revascularization in comparison with off-pump coronary artery bypass grafting. A comparison between treatment strategies shows no differences in 5-year survival in patients with multivessel disease (A), nor in patients with left main disease (B). Adapted with permission from Halkos *et al.*<sup>56,57</sup>

**Table 3** Systematic review of studies evaluating hybrid revascularization

Author (year)	Inclusion	Design	No. of patients	Type of lesions	Strategy	30-day outcomes			Long-term outcomes		
						Conversion	Death	Revascularization	Mean follow-up	Mortality	Revascularization
Lloyd (1999)	1996–98	Prospective	18	Multivessel	Simultaneous, <i>n</i> = 4 PCI following MIDCAB, <i>n</i> = 14	0	0	5.6%	At 18 months	0	5.6%
Zenati (1999)	1996–98	Retrospective	31	Multivessel	Staged	0	0	3.2%	11 months	0	9.6%
Wittwer (2000)	1996–99	—	35	Multivessel	PCI following MIDCAB	0	0	0	11 ± 8 months	0	6.5% (of 31 patients)
de Canniere (2001)	1997–97	Retrospective	20	Two-vessel	MIDCAB following PCI, <i>n</i> = 9 PCI following MIDCAB, <i>n</i> = 11	0	0	0	At 2 years	0	15%
Cisowski (2002)	1999–2001	Retrospective	50	Two-vessel	PCI following MIDCAB	0	0	0	—	0	12.7%
Riess (2002)	1997–2001	Retrospective	57	Multivessel	PCI following MIDCAB	0	0	0	101 ± 38 weeks	1.8%	—
Stahl (2002)	—	Retrospective	54	Multivessel	PCI following MIDCAB, <i>n</i> = 35 MIDCAB following PCI, <i>n</i> = 19	0	0	0	12 months	0	—
Davidavicius (2005)	2001–03	Prospective	20	Multivessel	MIDCAB following PCI, <i>n</i> = 14 PCI following MIDCAB, <i>n</i> = 6	0	0	0	19 ± 10 months	0	0
Katz (2006)	—	Prospective	27	Two-vessel	Simultaneous, <i>n</i> = 4 PCI following MIDCAB, <i>n</i> = 12 MIDCAB following PCI, <i>n</i> = 11	0	0	0	At 3 months	0	18.5%
Us (2006)	2002–04	Prospective	17	Multivessel	MIDCAB following PCI	0	0	0	21 ± 7 months	0	17.6%
Gilard (2007)	2000–...	Prospective	70	Multivessel	MIDCAB following PCI	0	1.4%	2.9%	33 months	1.4%	0
Holzhey (2008)	1996–2007	Retrospective	117	Multivessel	Simultaneous, <i>n</i> = 5 PCI following MIDCAB, <i>n</i> = 59 MIDCAB following PCI, <i>n</i> = 53	0	1.9%	1.9%	208 patient-years	92.5% at 1 year 84.8% at 5 years	—
Kiaii (2008)	2004–07	Prospective	58	Two-vessel	Simultaneous	1.7%	0	0	20 months	0	—
Kon (2008)	2005–06	Prospective	15	Multivessel	Simultaneous	0	0	0	At 1 year	0	6.7%
Gao (2009)	2007–08	Prospective	10	Multivessel	PCI following MIDCAB	0	0	0	5 months	0	0
Vassiliades (2009)	2003–07	Prospective	91	Multivessel	Staged	2.0%	0	0	—	94% at 3 years	5.5% at 1 year
Zhao (2009)	2005–07	Retrospective	112	Multivessel	Simultaneous	N/A	2.6%	0	—	—	—
Delhaye (2010)	2006–08	Prospective	18	Multivessel	PCI following MIDCAB	0	0	0	At 1 year	0	5.6% (TVR)
Halkos (2011)	2003–10	Retrospective	27	LM	PCI following MIDCAB	0	0	0	Median 3.2 years	88.6% at 5 years	7.4%
Halkos (2011)	2003–10	Retrospective	147	Multivessel	Simultaneous <i>n</i> < 10 Staged for the remaining	0	0.7%	0	Median 3.2 years	86.8% at 5 years	12.2% 8.8% (TVR)
Hu (2011)	2007–09	Retrospective	104	Multivessel	Simultaneous	1.0%	0	0	18 months	0	1.9%
Rab (2012)	2003–...	Retrospective	22	LM	PCI following MIDCAB	0	0	0	39 ± 23	4.5%	0

The PubMed database was searched from its inception through June 2012, which yielded the included studies.

CABG, coronary artery bypass grafting; MIDCAB, minimally invasive coronary artery bypass; N/A, not applicable; LM, left main; PCI, percutaneous coronary intervention; TVR, target vessel revascularization.

highlighted the difficulties with BIMA grafting; 16.4% of patients randomized to BIMA did not receive the allocated treatment compared with 3.3% patients not receiving SIMA grafting.<sup>71</sup>

The proportion of procedures that are performed with IMA grafts is increasing, but a large inter-hospital variance remains. The use of at least one IMA can be as low as 45–65% in some centres, failing to provide optimal care to patients.<sup>72</sup> It is disconcerting that in the USA the use of BIMA grafts was only 4.0% among 541 368 patients.<sup>72</sup> The respective figures are 12% in Europe and 30% in Japan.<sup>73</sup> Among 1541 procedures performed in the SYNTAX trial and registry, 97.1% included a single arterial conduit while 22.7% received a second IMA graft. Owing to the technically more challenging and time-consuming nature of BIMA grafting, the fear of higher morbidity (i.e. sternal wound complications) and mortality, and the absence of clear randomized data showing a survival benefit, some surgeons may be reluctant to use BIMA grafts. Nevertheless, in order to improve CABG outcomes, the use of both IMA grafts should be considered more frequently.

When unilateral IMA grafting is performed, the saphenous vein is the most frequently chosen conduit for additional graft(s). Because of high failure rates of venous grafts, the radial artery has been investigated as an alternative. The long-term results from the RSVP trial ( $n = 142$ ) suggested favourable radial artery graft patency rates.<sup>74</sup> More recent 5-year results from the larger randomized RAPS trial ( $n = 510$ ) showed that, compared with the saphenous vein grafts, the radial artery had lower rates of functional graft occlusion (12.0 vs. 19.7%, respectively;  $P = 0.03$ ) and complete occlusion (8.9 vs. 18.6%, respectively;  $P = 0.002$ ), although the string sign was observed more frequently in radial artery grafts (3.4 vs. 0%,  $P = 0.01$ ).<sup>75</sup> Several large observational studies have confirmed excellent graft patency and have even reported superior long-term survival rates,<sup>76,77</sup> also after applying propensity matching.<sup>78–80</sup> However, widespread utilization of the radial artery has been hampered by concerns regarding vessel spasm, graft atherosclerosis, and unfavourable results from a number of studies. The largest trial ( $n = 733$ ) to date found no differences in graft patency at 1-year follow-up;<sup>81</sup> similar results have been reported from a number of observational studies.<sup>79,82</sup> At least one study has shown radial artery graft patency to be significantly worse than right IMA graft patency.<sup>83</sup> To ensure good graft patency, the radial artery should be used preferably in high-grade lesions.<sup>84</sup> Data from the STS database suggest that only 9% of CABG procedures are performed with the radial artery.<sup>85</sup>

A higher rate of disease progression to total occlusion in native coronaries has been reported after CABG than after PCI.<sup>86</sup> Patent arterial grafts, by virtue of their nitric oxide secreting properties, may protect against future atherosclerotic lesions. Therefore, arterial grafting can be viewed as a preventive measure that goes beyond pure treatment.<sup>87,88</sup>

## Endoscopic vein harvesting

Traditional open saphenous vein-graft harvesting requires a large incision, resulting in a large scar and a risk of postoperative wound complications. Endoscopic vein harvesting was introduced in the mid-1990s as an alternative.<sup>89</sup> This method has the advantages of reduced scarring, less pain, decreased postoperative complications, and shorter length of stay.<sup>90</sup>

Several randomized studies and meta-analyses have shown that endoscopic harvesting significantly reduces rates of wound infection, wound dehiscence, and overall complications.<sup>91</sup> However, subgroup analyses from the PREVENT IV and ROOBY randomized trials suggested that endoscopic vein harvesting resulted in reduced graft patency during the follow-up.<sup>92,93</sup> In PREVENT IV, there even were significantly higher rates of death. Although this is of potential concern, long-term follow-up analyses from large observational studies have not been able to confirm that clinical outcomes are worse in patients that underwent endoscopic vein harvesting.<sup>94,95</sup> A recent study that included 235 394 patients with 3-year follow-up showed no increased risk of mortality [adjusted HR = 1.00 (95% CI: 0.97–1.04)  $P < 0.99$ ] or the composite of mortality, myocardial infarction, and repeat revascularization [adjusted HR = 1.00 (95% CI: 0.98–1.05)  $P = 0.34$ ].<sup>95</sup>

Current data indicate a paradigm shift towards endoscopic harvesting as opposed to open vein graft harvesting. Between 2003 and 2008, 52% of grafts were harvested endoscopically at 989 sites in the USA; in 2008, the rate was already 70%.<sup>95</sup> Trainees in the USA now almost exclusively learn how to perform endoscopic harvesting.<sup>90</sup> It is important to start using this technique at an early stage, especially because inexperienced surgeons are known to cause significantly more vein injury.<sup>96</sup> The International Society of Minimally Invasive Cardiothoracic Surgery Consensus statement has given a Class IB recommendation for endoscopic vein harvesting.<sup>97</sup> Still, endoscopic harvesting is performed in only a minority of cases in Europe. A recent single-centre study showed that only 12.4% of veins were harvested endoscopically between 2008 and 2010.<sup>98</sup> Unfortunately, large-scale real-world data from European centres are scarce.

## Intra-operative assessments

### Epi-aortic scanning

Atherosclerosis of the ascending aorta is present in >50% of patients undergoing CABG.<sup>99</sup> Aortic atherosclerosis was found to be a significant predictor of postoperative neurological events and renal failure, both caused by atheroembolism.<sup>100,101</sup> Palpation of the aorta is frequently employed prior to cannulation and/or aortic manipulation, but the sensitivity of this technique is very limited.<sup>102</sup> Therefore, imaging is advocated to detect atherosclerosis if an anaortic technique cannot be applied. Depending on the findings, the operative technique can be modified as needed.<sup>103</sup> Both transoesophageal echocardiography and epi-aortic ultrasonography were introduced as methods for detecting severe atherosclerosis. While transoesophageal echocardiography severely underestimates the degree of atherosclerosis, epi-aortic scanning is an easy, safe and efficient procedure and is preferred.<sup>104</sup>

Epi-aortic scanning is not routinely used probably because of the cost of the machine (>€100 000) and the fact that there have been no direct randomized comparisons between CABG with and without epi-aortic scanning that demonstrate a benefit. Such a study would be problematic because of the large sample size required. However, although one small study indicated no reduction in transcranial Doppler-detected cerebral emboli,<sup>105</sup> several studies have suggested that early postoperative stroke is significantly reduced when the operative technique is modified in accordance with

results of epiaortic scanning.<sup>106–109</sup> Wareing et al.<sup>110</sup> reported that in 14% of elderly patients undergoing cardiac procedures (CABG in 89%), the site of aortic cannulation and/or clamping, the sites for attaching vein grafts, and/or the sites for instillation of cardioplegic solution were altered. The precise rates of such modifications provided in the literature vary, between 4 and 31%.<sup>99</sup> A recent study by Daniel et al.<sup>111</sup> showed that epiaortic scanning was increasingly performed from 2002 to 2009 (45 and 90%, respectively) and coincided with less frequent aortic clamping (98 and 73%, respectively).

## Graft flow measurement

Data from the PREVENT IV trial showed a suboptimal rate of saphenous vein-graft failure after on- and off-pump CABG at 1 year;<sup>112</sup> a meta-analysis reported a failure rate of ~5 and 25% at 3 and 12 months, respectively.<sup>113</sup> Several mechanisms of graft failure have been described. Early graft failure can occur as a result of anastomotic problems, limited outflow, graft kinking upon chest closure, and thrombosis. Late failure is the result of thrombosis and processes of intimal hyperplasia and atherosclerosis. Intra-operative graft assessment has been introduced to evaluate grafts and identify anastomotic problems and limited outflow. Disturbingly, Balacumaraswami et al.<sup>114</sup> demonstrated that intra-operative graft assessment identified 9% of grafts with inadequate flow in 25% of CABG patients, which led to revision in 3% of grafts and 8% of patients. Multiple techniques for intra-operative graft assessment have been proposed: coronary angiography, transit time flow measurement (TTFM), high-frequency epicardial echocardiography, thermal coronary angiography and intra-operative fluorescence imaging (IFI).<sup>115</sup> Although angiography is thought to be the best and most reliable method for assessing flow,<sup>116</sup> the infrastructure required for coronary angiography is rarely available in standard operating rooms. Wider implementation of hybrid operating rooms could potentially facilitate the use of coronary angiography. Currently, intra-operative graft assessment is most frequently performed by TTFM or IFI.

Both TTFM and IFI have strengths and weaknesses and have been criticized for their inability to identify grafts with minor abnormalities that present a risk for failure. Furthermore, inconsistent and variable measurements may lead to unnecessary graft revisions.<sup>114</sup> Two parameters, graft function and anatomy, are required for the complete assessment of bypass grafts. Transit time flow measurement assesses function and can very accurately detect truly poor and truly good grafts (true positives, true negatives), but there is an issue with respect to detecting poor grafts with a low pulsatility index (PI) (false negatives). False positives (good graft, high PI) rarely occur. Intra-operative fluorescence imaging evaluates anatomy but is associated with more inter-observer error than standard angiography. Comparisons between TTFM and IFI suggest that IFI is more sensitive.<sup>113,114,117</sup> Transit time flow measurement combined with epicardial ultrasonic scanning is a recently introduced approach that may provide both a functional as well as anatomic assessment.

Despite issues, the clinical value of TTFM has been demonstrated in studies that found that TTFM predicted graft failure at 3, 6, and/or 12 months post-CABG.<sup>118–120</sup> Inadequate graft flow as defined by PI >5 on TTFM was found to be an independent predictor of major adverse cardiac events, operative death in particular.<sup>121</sup> No studies have yet explored the impact of IFI measurements on clinical outcomes during the follow-up. In general, randomized comparisons

between CABG with and without graft flow measurement remain absent. Such studies would be required to evaluate the true benefit their routine intra-operative use would have on early and late rates of reintervention, myocardial infarction and death. One issue that remains, however, is that long-term graft failure would still occur as caused by other mechanisms than those controlled by intra-operative graft assessment. This could be one of the reasons why surgeons doubt its clinical impact and consequently why routine use has been limited.

## Secondary prevention

Apart from technical and procedural considerations, further optimization of long-term outcomes after CABG can be achieved through a strict medical regimen. Progression of atherosclerosis in the native coronary arteries continues after CABG and is associated with deterioration of left ventricular function. However, this can be prevented by the administration of antiplatelet agents,<sup>122</sup>  $\beta$ -blockers,<sup>123</sup> angiotensin-converting enzyme inhibitors (ACE-I),<sup>124</sup> statins<sup>125,126</sup> and fatty acids,<sup>127</sup> all of which have been identified as independent predictors of survival after CABG. The PREVENT IV trial found that secondary prevention medications were associated with significantly reduced rates of death or myocardial infarction after CABG.<sup>128</sup> Moreover, data suggest that graft patency may be better in patients taking statins,<sup>129</sup> fatty acids,<sup>130</sup> aspirin,<sup>65</sup> and possibly dual antiplatelet therapy.<sup>131</sup> Administration of secondary prevention medications has increased remarkably,<sup>132,133</sup> and differences between PCI and CABG have shown to converge (Table 4). Nevertheless, some data have shown that differences between PCI and CABG still remain and again stressed the need for further progress (Figure 2).<sup>134–136</sup>

Furthermore, the effect of lifestyle interventions on outcomes may be underestimated. A plethora of data exists on the impact of lifestyle intervention on outcomes after CABG. Van Domburg et al.,<sup>137</sup> for example, reported that patients who quit smoking had significantly improved 30-year survival when compared with persistent smokers after CABG [HR = 0.60 (95% CI: 0.48–0.72)]. Education and counselling on eliminating risk factors, healthy food choices, stress relief and exercise provide substantial benefit for patients.<sup>138</sup> A meta-analysis that combined 63 randomized clinical trials with follow-up data on 21 295 patients found that implementation of secondary prevention programmes significantly reduced all-cause mortality [risk ratio (RR) = 0.85 (95% CI: 0.77–0.94)] and myocardial infarction [RR = 0.83 (95% CI: 0.74–0.94)].<sup>139</sup> Notably, specific patient subgroups may benefit most from rigorous behavioural modifications: young (age <60 years) or old (age  $\geq$ 75 years) patients, patients with a sedentary lifestyle and/or a smoking habit, patients with a low Mediterranean diet score and those who live alone.<sup>140</sup> However, data from three EUROASPIRE surveys showed that there was a clear need for more effective lifestyle management among patients with previous coronary revascularization.<sup>141</sup> The authors rightfully stated that treatment of coronary artery disease 'without addressing the underlying causes of the disease is futile; we need to invest in prevention'.

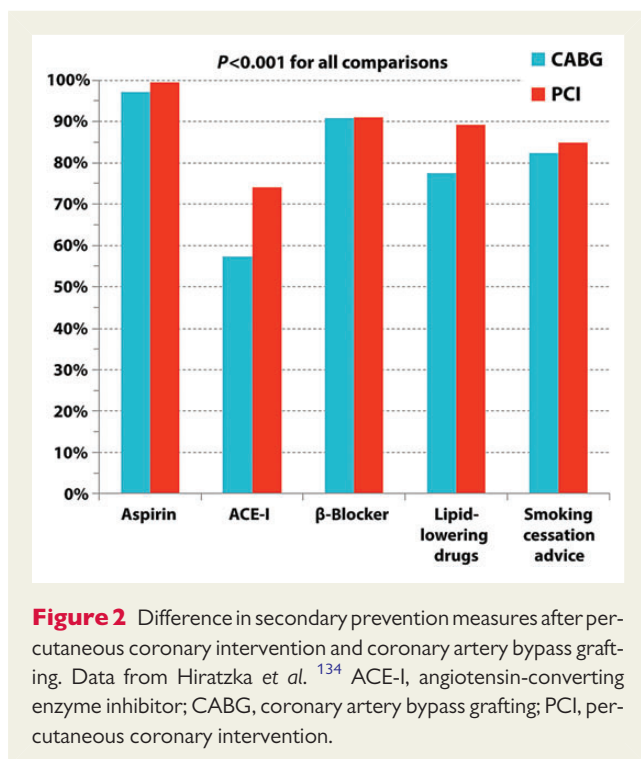
Initiatives should be undertaken to increase the rate of prescribing appropriate discharge medications and to emphasize the need for long-term medication compliance and lifestyle changes. In particular, home-based programmes may be efficient and more acceptable to



**Table 4** Trends in the use of secondary preventive medication and the difference between coronary artery bypass grafting and percutaneous coronary intervention

	EUROASPIRE I 1995–96, n = 9 countries	EUROASPIRE II 1999–2000, n = 15 countries	EUROASPIRE III 2006–07, n = 22 countries
<b>Antiplatelets (%)</b>			
CABG	87.9	86.8	92.9
PCI	89.4	90.0	94.9
Δ	–1.5	–3.2	–2.0
<b>Beta-blockers (%)</b>			
CABG	56.5	68.0	90.7
PCI	61.7	73.6	84.4
Δ	–5.2	–5.6	+6.3
<b>Blood pressure-lowering drugs (%)</b>			
CABG	86.2	90.1	98.7
PCI	87.4	91.3	95.9
Δ	–1.2	–1.2	+2.8
<b>Lipid-lowering drugs (%)</b>			
CABG	36.7	67.6	90.5
PCI	42.2	69.9	89.4
Δ	–5.5	–2.3	+1.1

Data from Kotseva et al.<sup>133</sup>  
 CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.



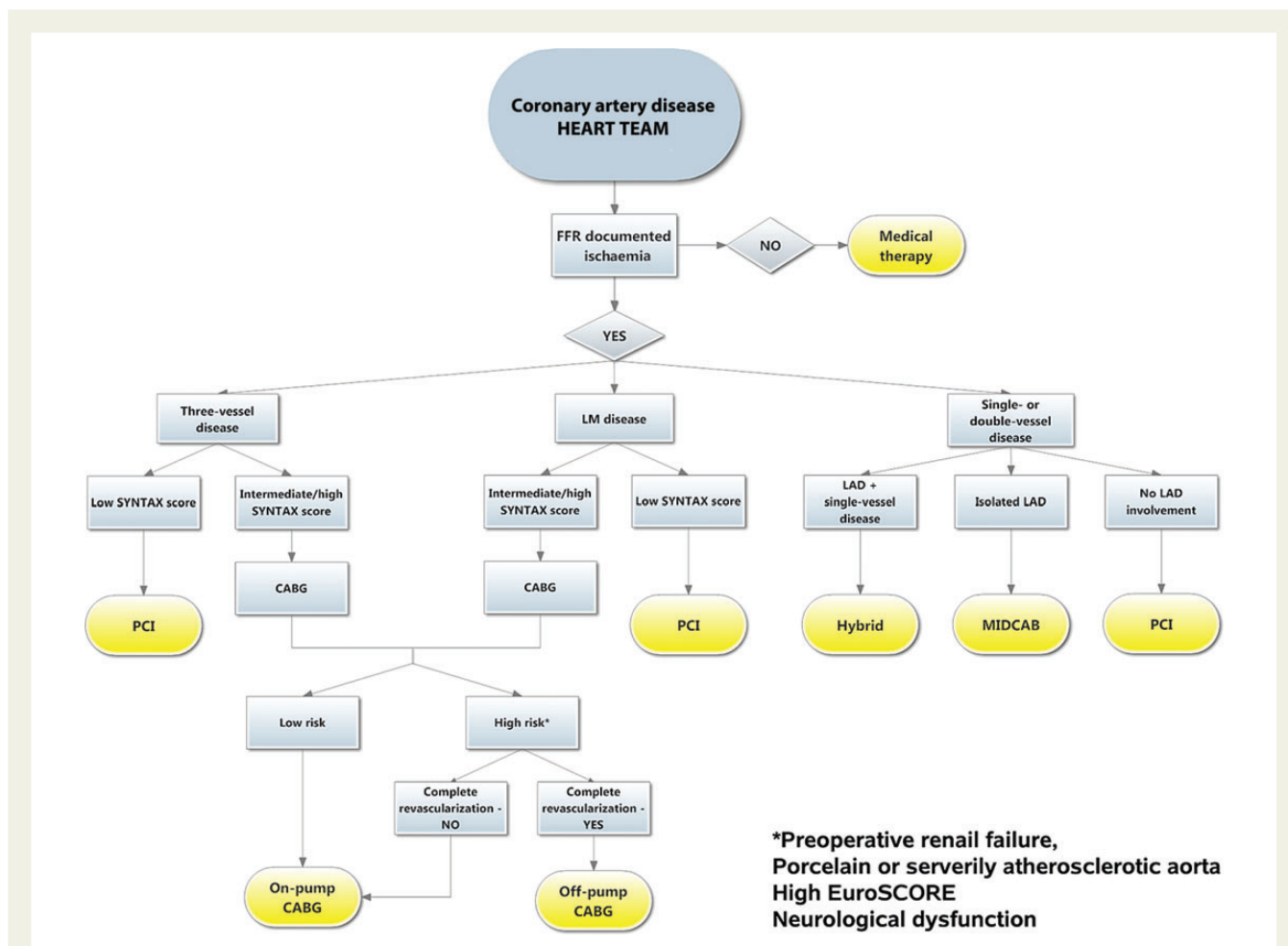
**Figure 2** Difference in secondary prevention measures after percutaneous coronary intervention and coronary artery bypass grafting. Data from Hiratzka et al.<sup>134</sup> ACE-I, angiotensin-converting enzyme inhibitor; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

patients—with the additional benefit of lower costs.<sup>142</sup> Such quality improvement programmes can be easily instated and could potentially improve patient care significantly.

## Decision-making

Despite the potential for further optimization of CABG outcomes, PCI will remain an excellent alternative in specific patients. Evidence suggests that there is overuse, underuse and inappropriate selection of revascularization strategies.<sup>143</sup> Inappropriate use and underuse may partly explain the preferences expressed by patients,<sup>144</sup> who prefer less invasive techniques with minimized pain over the long-term prospect of improved survival. In that respect, MIDCAB or hybrid procedures may present an alternative, but often patients are not even informed about the survival advantage with CABG.<sup>145</sup> Naturally, if two treatments are considered to produce similar results, patients will opt for the least invasive.

Reflecting on the current revascularization guidelines, recent trial results and weighting risk–benefit ratios of (new) developments, Figure 3 provides a proposal for a decision-tree for revascularization. The myriad of treatment options emphasize the need for targeted patient selection, and the mix of surgical and interventional therapies provides rationale for multidisciplinary Heart Team decision-making to discuss all potential treatment options and obtain informed consent. Clinical cardiologists, interventional cardiologists and cardiovascular surgeons should convene on a regular basis to recommend the most appropriate treatment strategy for individual patients.<sup>143,146</sup> The importance of a Heart Team was once more stressed in the SYNTAX trial<sup>147</sup> and was subsequently included in the European and American guidelines.<sup>3,148</sup> Practice may be different across centres and countries, and a local protocol should be established to define patient populations that are candidates for certain



**Figure 3** Proposal for a decision-tree for revascularization. Some of these recommendations have not yet been validated and still require randomized evaluation. CABG, coronary artery bypass grafting; LAD, left anterior descending; LM, left main; MIDCAB, minimally invasive coronary artery bypass; PCI, percutaneous coronary intervention.

therapies. The various pros and cons of surgical revascularization strategies should then be considered by the Heart Team (Table 5).

## Future studies

Rigorous evaluation of potential advancements remains crucial before they are introduced on a wide scale. Even an extensive body of evidence supporting some interventions is not necessarily sufficient to provide evidence-based recommendations. This is exemplified by the >60 randomized trials comparing off-pump with on-pump surgery:<sup>13,30,35</sup> a benefit of off-pump CABG has been suggested in many studies that included different patient populations. Nevertheless, the two latest and largest randomized trials that included low- and high-risk patients found no difference between the two treatment options.<sup>30,35</sup>

In contrast, data on some new therapeutic strategies remain scarce, but the existing data may demonstrate excellent safety and efficacy. Such results often represent outcomes from highly selected patients treated by experienced surgeons in high-volume centres. This introduces a bias; the generalizability of such results is limited

and caution is advised. An example of this is the evaluation of TECAB procedures.

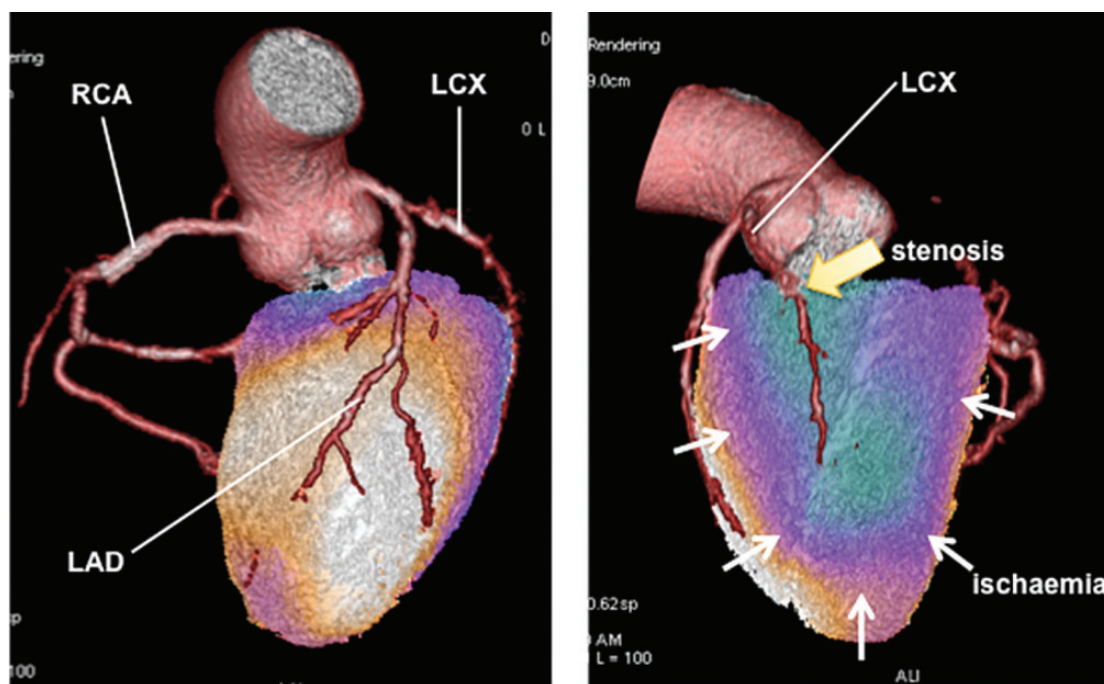
## Percutaneous coronary intervention vs. coronary artery bypass grafting studies

Continuous evaluation of PCI vs. CABG calls for a specific focus on new developments in both interventions. For PCI patients, new stents will become available and the use of fractional flow reserve to assess the need and completeness of revascularization is emphasized.<sup>149,150</sup> Equivalent data on FFR-guided CABG are scarce.<sup>151</sup> Future studies should explore the use and differences of FFR-guided revascularization between PCI and CABG.<sup>152</sup> The impact of the degree of ischaemia and viability on the outcomes of both CABG and PCI in patients with stable angina is still under debate. Whether image-guided revascularization that is based on a combination of functional and anatomical imaging—for example, position emission tomography computed tomography (Figure 4)—can improve the outcomes as compared with the traditional occlusostotic approach warrants further trials.

**Table 5** Pros and cons of different surgical revascularization techniques

	Conventional CABG	Off-pump CABG	MIDCAB	TECAB	Hybrid revascularization
Lesions	Multivessel disease (+)	Multivessel disease (+)	Isolated LAD stenosis (+/-)	Multivessel disease (+)	Multivessel disease (+)
Technical difficulty	None (+)	Moderate (+/-)	Moderate (+/-)	Difficult (-)	Moderate (+/-)
Incision	Sternotomy (-)	Sternotomy (-)	J-incision (+/-)	Endoscopic (+)	J-incision (+/-)
Cardiopulmonary bypass	Yes (-)	No (+)	No (+)	No (+)	No (+)
Procedure time	Short (+)	Prolonged (+/-)	Long (-)	Long (-)	Long (-)
Blood products	Many (-)	Less (+/-)	Few (+)	Few (+)	Few (+)
Completeness of revascularization	Complete (+)	Complete (+) or incomplete (+/-)	Complete (+) or incomplete (+/-)	Complete (+) or incomplete (+/-)	Complete (+)
Postoperative length of stay	Long (-)	Prolonged (+/-)	Short (+)	Short (+)	Short (+)
Postoperative pain	Yes (-)	Yes (-)	Yes (-)	Less (+/-)	Yes (-)
Recovery time	Long (-)	Long (-)	Short (+)	Short (+)	Short (+)
Rate of stroke	High (-)	Less (+/-)	Less (+/-)	Less (+/-)	Less (+/-)
Rate of repeat revascularization	Good (+)	Moderate (+/-)	Good (+)	Moderate (+/-)	Moderate (+/-)

The various features are scored as following: in favour of the technique (+), reasonable in favour (+/-), detrimental for the technique (-). CABG, coronary artery bypass grafting; LAD, left anterior descending; MIDCAB, minimally invasive coronary artery bypass.



**Figure 4** Functional and anatomical imaging using position emission tomography computed tomography. Case: 70-year-old male had atypical symptoms of three-vessel coronary artery disease for which he underwent stenting of the right coronary artery in 2012. Scan is positive for inferolateral wall ischaemia (purple). LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

Traditionally, trials are limited to their internal validity, i.e. the results are only applicable to the included patient cohort; large 'real-world' registries are required to demonstrate whether trial results

are also applicable to the general population.<sup>10</sup> Alternatively, an 'all-comers' trial design with none to limited patient exclusion criteria increases external validation, and presents a more balanced trade-off

**Table 6** American and European guideline recommendations

	Guidelines	
	American	European
Off-pump CABG	'In patients with preoperative renal dysfunction (creatinine clearance < 60 mL/min), off-pump CABG may be reasonable to reduce the risk of acute kidney injury' <b>IIb B</b> 'It is reasonable to consider off-pump CABG to reduce perioperative bleeding and allogeneic blood transfusion' <b>IIa A</b>	'Off-pump CABG may be considered, rather than on-pump CABG for patients with mild-to-moderate chronic kidney disease' <b>IIb B</b>
MIDCAB	No recommendation	No recommendation
Hybrid revascularization	'Hybrid coronary revascularisation is reasonable in patients with 1 or more of the following: limitations to traditional CABG, such as heavily calcified proximal aorta or poor target vessels for CABG (but amenable to PCI); lack of suitable graft conduits; unfavourable LAD artery for PCI (i.e. excessive vessel tortuosity or chronic total occlusion)' <b>IIa B</b> 'Hybrid coronary revascularization may be reasonable as an alternative to multivessel PCI or CABG in an attempt to improve the overall risk–benefit ratio of the procedures' <b>IIb C</b>	'Hybrid procedure, defined as consecutive or combined surgical and interventional revascularization may be considered in specific patient subsets at experienced centres' <b>IIb B</b>
Clampless/'no touch'	'Patients with extensive disease of the ascending aorta pose a special challenge for on-pump CABG; for these patients, cannulation or cross-clamping of the aorta may create an unacceptably high risk of stroke. In such individuals, off-pump CABG in conjunction with avoidance of manipulation of the ascending aorta (including placement of proximal anastomoses) may be beneficial' ( <b>no formal recommendation, no level of evidence</b> )	No recommendation
Endoscopic vein harvesting	No recommendation	'Endoscopic vein-graft harvesting cannot be recommended at present as it has been associated with vein-graft failure and adverse clinical outcomes' ( <b>no formal recommendation, no level of evidence</b> )
Epiaortic scanning	'Routine epiaortic ultrasound scanning is reasonable to evaluate the presence, location, and severity of plaque in the ascending aorta to reduce the incidence of atheroembolic complications' <b>IIa B</b>	No recommendation
Graft flow assessment	No recommendation	'Graft evaluation is recommended before leaving the operating theatre' <b>I C</b>
Arterial revascularization	'If possible, the LIMA should be used to bypass the LAD artery when bypass of the LAD artery is indicated' <b>I B</b> 'When anatomically and clinically suitable, use of a second IMA to graft the left circumflex or right coronary artery (when critically stenosed and perusing LV myocardium) is reasonable to improve the likelihood of survival and to decrease reintervention' <b>IIa B</b> 'Complete arterial revascularization may be reasonable in patients ≤ 60 years of age with few or no comorbidities' <b>IIb C</b>	'Arterial grafting to the LAD system is indicated' <b>I A</b> 'Complete revascularization with arterial grafting to non-LAD coronary systems is indicated in patients with reasonable life expectancy' <b>I A</b>

<p>Secondary prevention</p> <p>'All smokers should receive in-hospital educational counselling and be offered smoking cessation therapy during CABG hospitalization' <b>IA</b></p> <p>'[Aspirin] should be initiated within 6 h postoperatively and then continued indefinitely to reduce the occurrence of SVG closure and adverse cardiovascular events' <b>IA</b></p> <p>'All patients undergoing CABG should receive statin therapy, unless contraindicated' <b>IA</b></p> <p>'<math>\beta</math>-blockers should be prescribed to all CABG patients without contraindications at the time of hospital discharge' <b>IC</b></p> <p>'ACE inhibitors and ARBs should be initiated postoperatively and continued indefinitely in CABG patients who were not receiving them preoperatively, who are stable, and who have an LVEF <math>\leq</math> 40%, hypertension, diabetes mellitus, or CKD, unless contraindicated' <b>IA</b></p>	<p>In general, an 'ABCDE' approach is proposed: 'A' for antiplatelet therapy, anticoagulation, ACE inhibition, or angiotensin receptor blockade; 'B' for beta-blockade and blood pressure control; 'C' for cholesterol treatment and cigarette smoking cessation; 'D' for diabetes management and diet; and 'E' for exercise.</p> <p>Several recommendations are provided with regard to lifestyle and risk factor management (e.g. counselling on physical activity and exercise training, <b>IA</b>; diet and weight control management, <b>IB</b>; smoking cessation, <b>IB</b>).</p> <p>'Secondary prevention demands lifelong antiplatelet therapy with 75–325 mg acetylsalicylic acid daily'</p> <p>'ACE inhibitors should be started and continued indefinitely in all patients with LVEF <math>\leq</math> 40% and for those with hypertension, diabetes, or CKD, unless contraindicated' <b>IA</b></p> <p>'It is indicated to start and continue <math>\beta</math>-blocker therapy in all patients after MI or ACS or left ventricular dysfunction, unless contraindicated' <b>IA</b></p> <p>'High-dose lipid lowering drugs are indicated in all patients regardless of lipid levels, unless contraindicated' <b>IA</b></p> <p>'Fibrates and omega-3 fatty acids (1 g/day) should be considered in combination with statins and in patients intolerant of statins' <b>IIb B</b></p>
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The level of evidence is shown in bold. ACE, angiotensin-converting enzyme; ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; LAD, left anterior descending; LVEF, left ventricular ejection fraction; (L) IMA, (left) internal mammary artery; MI, myocardial infarction; PCI, percutaneous coronary intervention.

between internal and external validation.<sup>153</sup> Furthermore, reporting the experience of centres and operators will also contribute to the internal and external validity of trial results: superior outcomes in experienced centres as opposed to inexperienced centres unveils limited external validity and should restrict one from over-extrapolating trial results to real-world clinical settings.

In the SYNTAX trial a new angiographic score was validated—the SYNTAX score—for grading the complexity of coronary artery disease.<sup>154</sup> This score appears to be a very promising tool for deciding if PCI or CABG would be preferable. Use of the score is therefore recommended for decision-making. Recently, the SYNTAX II score was introduced and showed an improvement in guiding decision-making.<sup>155</sup> Yet, further validation of these hypothesis-generating data is needed and future studies should provide a larger body of evidence about the SYNTAX (II) score.

Pharmacological management of patients after PCI and CABG differs significantly and has an impact on long-term results. It would be interesting to see the results of PCI and CABG if the pharmacological management and treatment adherence after PCI and CABG would be identical.

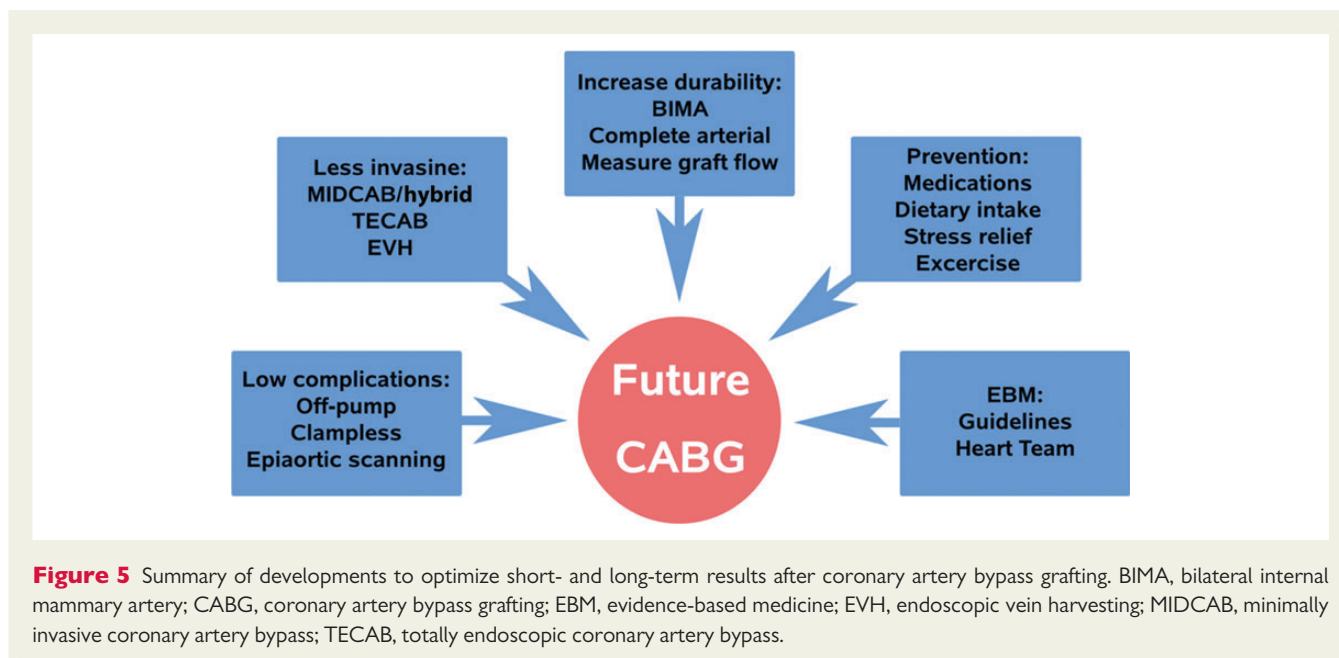
## Discussion

Broadening indications for and increasing use of PCI calls for more focus on the optimization of short- and long-term outcomes after CABG. Expanding the use of lesser invasive techniques may persuade patients to accept surgery as the preferable treatment option. Particularly studies comparing PCI with CABG require the most optimal surgical revascularization strategy to show superiority over PCI. Arterial revascularization with minimized aortic manipulation and intra-operative graft flow measurement is a relatively easy way to improve outcomes.

Adoption rates of new techniques have been low, despite all advances. This may be due to: (i) the familiarity that surgeons have with existing techniques, a reluctance to change and the willingness to go through the learning curve typical for a new technique, (ii) the more demanding nature of some technical advances, (iii) complications related to the use of a new technique and/or device, (iv) time-consuming steps that may have to be carried out during the procedure, and (v) logistic reasons with regard to the need for additional equipment, planning and sterility. Particularly when the presumed benefits with new techniques are not yet clearly proven, these factors play a major role in maintaining existing protocols. However, the benefit of advancements will often become evident when overcoming the learning curve. On the other hand, some techniques will always be time-consuming and reserved for highly specialized centres.

## Guidelines

One explanation for the underuse of new techniques and secondary prevention measures may be the lack of data supporting their benefit. This calls for large registries and randomized trials to provide additional rigorous evaluation of, in particular, MIDCAB, hybrid revascularization, epi-aortic scanning and graft flow measurement. Another reason for lack of widespread implementation and geographic variations may be the differing recommendations of the American and European guidelines concerning their use (Table 6). This is illustrated



by recommendations for epi-aortic scanning and graft flow assessment. The current European ESC/EACTS revascularization guidelines include a class 1C recommendation for intra-operative graft flow assessment<sup>3</sup> and the American guidelines state that ‘epi-aortic ultrasound is reasonable to evaluate...’, which translates to a class IIa B recommendation.<sup>148</sup> However, the American guidelines do not include a recommendation for graft flow assessment, while the European guidelines lack a recommendation for epi-aortic scanning.

### Patient, cost, and market considerations

Adoption of minimally invasive techniques that result in lower post-operative complications and reduced length of stay will significantly improve patient satisfaction, and raise patients’ willingness to undergo CABG as opposed to PCI. On the background of the issue of rising healthcare expenditures, these improvements may also help reduce overall costs.

Continued optimization of short- and long-term outcomes of CABG will reduce costs for health insurance providers who may therefore favour adoption of new techniques associated with shorter initial in-hospital stays, reduced complication rates and fewer repeat revascularizations. In addition, pay for performance is increasingly instated.<sup>156</sup> This system provides additional incentives to innovate and improve outcomes.

Containing costs to both health insurance providers and societies may in some healthcare systems require a reduction of the number of centres performing CABG. Innovation and integrating technological advances into everyday clinical practice may be rewarded by certification as a centre of excellence, by continued issuance of a practice licence and by more patient referrals. Implementation of the Heart Team decision-making process may furthermore strengthen the position of a centre. This approach highlights the centre’s collaborative environment between specialties, which is appreciated by patients.<sup>143</sup> There may also be major cost implications by eradicating suboptimal treatment: healthcare costs will be contained as rates of

adverse events requiring rehospitalization and additional procedures are reduced.

### Conclusion

Outcomes after surgical revascularization have the potential to improve beyond the level achieved during recent decades (Figure 5). However, to facilitate these improvements, surgeons need to be willing to adopt new techniques that increase procedural safety, patient satisfaction, and long-term survival. To achieve these goals, guidelines should be conclusive about recommending certain techniques and provide guidance for their use. Future trials will need to provide sufficient evidence for such recommendations by focussing on specific areas where optimal therapy has yet to be substantiated.

**Conflict of interest:** none declared.

### References

1. Head SJ, Kieser TM, Valk F, Huysmans HA, Kappetein AP. Coronary artery bypass grafting: part 1—the evolution over the first 50 years. *Eur Heart J* 2013.
2. Gruntzig A. Transluminal dilatation of coronary-artery stenosis. *Lancet* 1978;**1**:263.
3. Kolh P, Wijns W, Danchin N, Di Mario C, Falk V, Folliguet T, Garg S, Huber K, James S, Knuuti J, Lopez-Sendon J, Marco J, Menicanti L, Ostojic M, Piepoli MF, Pirllet C, Pomar JL, Reifart N, Ribichini FL, Schalij MJ, Sergeant P, Serruys PW, Silber S, Sousa Uva M, Taggart D. Guidelines on myocardial revascularization. *Eur J Cardiothorac Surg* 2010;**38**(Suppl):S1–S52.
4. Stefanini GG, Kalesan B, Serruys PW, Heg D, Buszman P, Linke A, Ischinger T, Klaus V, Eberli F, Wijns W, Morice MC, Di Mario C, Corti R, Antoni D, Sohn HY, Eerdman P, van Es GA, Meier B, Windecker S, Juni P. Long-term clinical outcomes of biodegradable polymer biolimus-eluting stents vs. durable polymer sirolimus-eluting stents in patients with coronary artery disease (LEADERS): 4 year follow-up of a randomised non-inferiority trial. *Lancet* 2011;**378**:1940–1948.
5. Palmerini T, Biondi-Zoccai G, Della Riva D, Stettler C, Sangiorgi D, D’Ascenzo F, Kimura T, Briguori C, Sabate M, Kim HS, De Waha A, Kedhi E, Smits PC, Kaiser C, Sardella G, Marullo A, Kirtane AJ, Leon MB, Stone GW. Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *Lancet* 2012;**379**:1393–1402.

6. Onuma Y, Serruys PW, Ormiston JA, Regar E, Webster M, Thuesen L, Dudek D, Veldhof S, Rapoza R. Three-year results of clinical follow-up after a bioresorbable everolimus-eluting scaffold in patients with de novo coronary artery disease: the ABSORB trial. *EuroIntervention* 2010;**6**:447–453.
7. Serruys PW, Garcia-Garcia HM, Onuma Y. From metallic cages to transient bioresorbable scaffolds: change in paradigm of coronary revascularization in the upcoming decade? *Eur Heart J* 2012;**33**:16–25b.
8. Epstein AJ, Polsky D, Yang F, Yang L, Groeneveld PW. Coronary revascularization trends in the United States, 2001–2008. *JAMA* 2011;**305**:1769–1776.
9. Mohr FW, Morice MC, Kappetein AP, Feldman TE, Stahle E, Colombo A, Mack MJ, Holmes DR Jr, Morel MA, Van Dyck N, Houle VM, Dawkins KD, Serruys PW. Coronary artery bypass graft surgery vs. 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**:629–638.
10. Weintraub WS, Grau-Sepulveda MV, Weiss JM, O'Brien SM, Peterson ED, Kolm P, Zhang Z, Klein LW, Shaw RE, McKay C, Ritzenthaler LL, Popma JJ, Messenger JC, Shahian DM, Grover FL, Mayer JE, Shewan CM, Garratt KN, Moussa ID, Dargas GD, Edwards FH. Comparative effectiveness of revascularization strategies. *N Engl J Med* 2012;**366**:1467–1476.
11. Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dargas G, Mack M, Yang M, Cohen DJ, Rosenberg Y, Solomon SD, Desai AS, Gersh BJ, Magnuson EA, Lansky A, Boineau R, Weinberger J, Ramanathan K, Sousa JE, Rankin J, Bhargava B, Buse J, Hueb J, Smith CR, Muratov V, Bansilal S, King S III, Bertrand M, Fuster V. Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med* 2012;**367**:2375–2384.
12. Kappetein AP, Head SJ, Morice MC, Banning AP, Serruys PW, Mohr FW, Dawkins KD, Mack MJ, SYNTAX Investigators. Treatment of complex coronary artery disease in patients with diabetes: 5-year results comparing outcomes of bypass surgery and percutaneous coronary intervention in the SYNTAX trial. *Eur J Cardiothorac Surg* 2013;**45**:1006–1013.
13. Afilalo J, Rasti M, Ohayon SM, Shimony A, Eisenberg MJ. Off-pump vs. on-pump coronary artery bypass surgery: an updated meta-analysis and meta-regression of randomized trials. *Eur Heart J* 2012;**33**:1257–1267.
14. Abu-Omar Y, Taggart DP. The present status of off-pump coronary artery bypass grafting. *Eur J Cardiothorac Surg* 2009;**36**:312–321.
15. Van Dijk D, Jansen EW, Hijman R, Nierich AP, Diephuis JC, Moons KG, Lahpor JR, Borst C, Keizer AM, Nathoe HM, Grobbee DE, De Jaegere PP, Kalkman CJ, Octopus Study G. Cognitive outcome after off-pump and on-pump coronary artery bypass graft surgery: a randomized trial. *JAMA* 2002;**287**:1405–1412.
16. Mack MJ, Pfister A, Bachand D, Emery R, Magee MJ, Connolly M, Subramanian V. Comparison of coronary bypass surgery with and without cardiopulmonary bypass in patients with multivessel disease. *J Thorac Cardiovasc Surg* 2004;**127**:167–173.
17. Racz MJ, Hannan EL, Isom OW, Subramanian VA, Jones RH, Gold JP, Ryan TJ, Hartman A, Culliford AT, Bennett E, Lancey RA, Rose EA. A comparison of short- and long-term outcomes after off-pump and on-pump coronary artery bypass graft surgery with sternotomy. *J Am Coll Cardiol* 2004;**43**:557–564.
18. Kuss O, von Salviati B, Borgegmann J. Off-pump versus on-pump coronary artery bypass grafting: a systematic review and meta-analysis of propensity score analyses. *J Thorac Cardiovasc Surg* 2010;**140**:829–835.
19. Williams ML, Muhlbaier LH, Schroder JN, Hata JA, Peterson ED, Smith PK, Landolfo KP, Messier RH, Davis RD, Milano CA. Risk-adjusted short- and long-term outcomes for on-pump vs. off-pump coronary artery bypass surgery. *Circulation* 2005;**112**:I366–I370.
20. Filardo G, Grayburn PA, Hamilton C, Hebel RF Jr, Cooksey WB, Hamman B. Comparing long-term survival between patients undergoing off-pump and on-pump coronary artery bypass graft operations. *Ann Thorac Surg* 2011;**92**:571–577. discussion 577–578.
21. Hattler B, Messenger JC, Shroyer AL, Collins JF, Haugen SJ, Garcia JA, Baltz JH, Cleveland JC Jr, Novitzky D, Grover FL, Veterans Affairs Randomized On/Off Bypass Study Group. Off-Pump coronary artery bypass surgery is associated with worse arterial and saphenous vein graft patency and less effective revascularization: results from the Veterans Affairs Randomized On/Off Bypass (ROOBY) trial. *Circulation* 2012;**125**:2827–2835.
22. Widimsky P, Straka Z, Stros P, Jirasek K, Dvorak J, Votava J, Lisa L, Budesinsky T, Kolesar M, Vanek T, Brucek P. One-year coronary bypass graft patency: a randomized comparison between off-pump and on-pump surgery angiographic results of the PRAGUE-4 trial. *Circulation* 2004;**110**:3418–3423.
23. Puskas JD, Williams WH, Mahoney EM, Huber PR, Block PC, Duke PG, Staples JR, Glas KE, Marshall JJ, Leimbach ME, McCall SA, Petersen RJ, Bailey DE, Weintraub WS, Guyton RA. Off-pump vs. conventional coronary artery bypass grafting: early and 1-year graft patency, cost, and quality-of-life outcomes: a randomized trial. *JAMA* 2004;**291**:1841–1849.
24. Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, Lucke JC, Baltz JH, Novitzky D, Veterans Affairs Randomized On/Off Bypass Study Group. On-pump versus off-pump coronary-artery bypass surgery. *N Engl J Med* 2009;**361**:1827–1837.
25. Puskas JD, Mack MJ, Smith CR. On-pump versus off-pump CABG. *N Engl J Med* 2010;**362**:851. author reply 853–854.
26. Sousa Uva M, Cavaco S, Oliveira AG, Matias F, Silva C, Mesquita A, Aguiar P, Bau J, Pedro A, Magalhaes MP. Early graft patency after off-pump and on-pump coronary bypass surgery: a prospective randomized study. *Eur Heart J* 2010;**31**:2492–2499.
27. Takagi H, Matsui M, Umamoto T. Lower graft patency after off-pump than on-pump coronary artery bypass grafting: an updated meta-analysis of randomized trials. *J Thorac Cardiovasc Surg* 2010;**140**:e45–e47.
28. Synnnergren MJ, Ekroth R, Oden A, Rexius H, Wiklund L. Incomplete revascularization reduces survival benefit of coronary artery bypass grafting: role of off-pump surgery. *J Thorac Cardiovasc Surg* 2008;**136**:29–36.
29. Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E, Straka Z, Piegas LS, Akar AR, Jain AR, Noiseux N, Padmanabhan C, Bahamondes JC, Novick RJ, Vaiyanath P, Reddy S, Tao L, Olavegeascoechea PA, Airan B, Sulling TA, Whitlock RP, Ou Y, Ng J, Chrolavicius S, Yusuf S, CORONARY Investigators. Off-pump or on-pump coronary-artery bypass grafting at 30 days. *N Engl J Med* 2012;**366**:1489–1497.
30. Lamy A, Devereaux PJ, Dorairaj P, Taggart DP, Hu S, Paolasso E, Straka Z, Piegas LS, Akar AR, Jain AR, Noiseux N, Padmanabhan C, Bahamondes JC, Novick RJ, Vaiyanath P, Reddy SK, Tao L, Olavegeascoechea PA, Airan B, Sulling TA, Whitlock RP, Ou Y, Pogue J, Chrolavicius S, Yusuf S, CORONARY Investigators. Effects of off-pump and on-pump coronary-artery bypass grafting at 1 year. *N Engl J Med* 2013;**368**:1179–1188.
31. Puskas JD, Thourani VH, Kilgo P, Cooper W, Vassiliades T, Vega JD, Morris C, Chen E, Schmotzter BJ, Guyton RA, Lattouf OM. Off-pump coronary artery bypass disproportionately benefits high-risk patients. *Ann Thorac Surg* 2009;**88**:1142–1147.
32. Sharony R, Bizakis CS, Kanchuger M, Galloway AC, Saunders PC, Applebaum R, Schwartz CF, Ribakove GH, Culliford AT, Baumann FG, Kronzon I, Colvin SB, Grossi EA. Off-pump coronary artery bypass grafting reduces mortality and stroke in patients with atherosclerotic aortas: a case control study. *Circulation* 2003;**108**(Suppl 1):II15–II20.
33. Head SJ, Kappetein AP. Off-pump or on-pump coronary-artery bypass grafting. *N Engl J Med* 2012;**367**:577–578.
34. Magee MJ, Coombs LP, Peterson ED, Mack MJ. Patient selection and current practice strategy for off-pump coronary artery bypass surgery. *Circulation* 2003;**108**(Suppl. 1):II9–II14.
35. Diegeler A, Borgegmann J, Kappert U, Breuer M, Boning A, Ursulescu A, Rastan A, Holzhey D, Treede H, Riess FC, Veeckmann P, Asfoor A, Reents W, Zacher M, Hilker M, The GOPCABE Study Group. Off-pump versus on-pump coronary-artery bypass grafting in elderly patients. *N Engl J Med* 2013;**368**:1189–1198.
36. Puskas JD, Edwards FH, Pappas PA, O'Brien S, Peterson ED, Kilgo P, Ferguson TB Jr. Off-pump techniques benefit men and women and narrow the disparity in mortality after coronary bypass grafting. *Ann Thorac Surg* 2007;**84**:1447–1454. discussion 1454–1456.
37. Guerrieri Wolf L, Abu-Omar Y, Choudhary BP, Pigott D, Taggart DP. Gaseous and solid cerebral microembolization during proximal aortic anastomoses in off-pump coronary surgery: the effect of an aortic side-biting clamp and two clampless devices. *J Thorac Cardiovasc Surg* 2007;**133**:485–493.
38. Borgegmann J, Hakim K, Renner A, Parsa A, Aboud A, Becker T, Masshoff M, Zittermann A, Gummert JF, Kuss O. Clampless off-pump versus conventional coronary artery revascularization: a propensity score analysis of 788 patients. *Circulation* 2012;**126**:S176–S182.
39. Emmert MY, Seifert B, Wilhelm M, Grunenfelder J, Falk V, Salzberg SP. Aortic no-touch technique makes the difference in off-pump coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2011;**142**:1499–1506.
40. Misfeld M, Brereton RJ, Sweetman EA, Doig GS. Neurologic complications after off-pump coronary artery bypass grafting with and without aortic manipulation: meta-analysis of 11,398 cases from 8 studies. *J Thorac Cardiovasc Surg* 2011;**142**:e11–e17.
41. Cohen DJ, Van Hout B, Serruys PW, Mohr FW, Macaya C, den Heijer P, Vrakking MM, Wang K, Mahoney EM, Audi S, Leadley K, Dawkins KD, Kappetein AP, SYNTAX Investigators. Quality of life after PCI with drug-eluting stents or coronary-artery bypass surgery. *N Engl J Med* 2011;**364**:1016–1026.
42. Serruys P, Morice M, Kappetein A, Colombo A, Holmes DR, Mack MJ, Stähle E, Feldman TE, van den Brand MJ, Bass E, van Dyck N, Leadley K, Dawkins KD, Mohr FW, SYNTAX Investigators. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med* 2009;**360**:961–972.
43. Hlatky MA, Boothroyd DB, Bravata DM, Boersma E, Booth J, Brooks MM, Carrie D, Clayton TC, Danchin N, Flather M, Hamm CW, Hueb WA, Kahler J, Kelsey SF, King SB, Kosinski AS, Lopes N, McDonald KM, Rodriguez A, Serruys P,

- Sigwart U, Stables RH, Owens DK, Pocock SJ. Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials. *Lancet* 2009;**373**:1190–1197.
44. Hannan EL, Wu C, Walford G, Culliford AT, Gold JP, Smith CR, Higgins RS, Carlson RE, Jones RH. Drug-eluting stents vs. coronary-artery bypass grafting in multivessel coronary disease. *N Engl J Med* 2008;**358**:331–341.
  45. Acuff TE, Landreneau RJ, Griffith BP, Mack MJ. Minimally invasive coronary artery bypass grafting. *Ann Thorac Surg* 1996;**61**:135–137.
  46. Groh MA, Sutherland SE, Burton HG III, Johnson AM, Ely SW. Port-access coronary artery bypass grafting: technique and comparative results. *Ann Thorac Surg* 1999;**68**:1506–1508.
  47. Diegeler A, Walther T, Metz S, Falk V, Krakor R, Autschbach R, Mohr FW. Comparison of MIDCAP vs. conventional CABG surgery regarding pain and quality of life. *Heart Surg Forum* 1999;**2**:290–295. discussion 295–296.
  48. Martens TP, Argenziano M, Oz MC. New technology for surgical coronary revascularization. *Circulation* 2006;**114**:606–614.
  49. Lapierre H, Chan V, Sohmer B, Mesana TG, Ruel M. Minimally invasive coronary artery bypass grafting via a small thoracotomy versus off-pump: a case-matched study. *Eur J Cardiothorac Surg* 2011;**40**:804–810.
  50. Holzhey DM, Cornely JP, Rastan AJ, Davierwala P, Mohr FW. Review of a 13-year single-center experience with minimally invasive direct coronary artery bypass as the primary surgical treatment of coronary artery disease. *Heart Surg Forum* 2012;**15**:E61–E68.
  51. Taggart DP, D'Amico R, Altman DG. Effect of arterial revascularisation on survival: a systematic review of studies comparing bilateral and single internal mammary arteries. *Lancet* 2001;**358**:870–875.
  52. Kieser TM, Lewin AM, Graham MM, Martin BJ, Galbraith PD, Rabi DM, Norris CM, Faris PD, Knudtson ML, Ghali WA, Approach Investigators. Outcomes associated with bilateral internal thoracic artery grafting: the importance of age. *Ann Thorac Surg* 2011;**92**:1269–1275. discussion 1275–1276.
  53. Alexander JH, Hafley G, Harrington RA, Peterson ED, Ferguson TB Jr, Lorenz TJ, Goyal A, Gibson M, Mack MJ, Gennevois D, Califf RM, Kouchoyos NT, Prevent IV Investigators. Efficacy and safety of edfoligide, an E2F transcription factor decoy, for prevention of vein graft failure following coronary artery bypass graft surgery: PREVENT IV: a randomized controlled trial. *JAMA* 2005;**294**:2446–2454.
  54. Friedrich GJ, Bonatti J, Dapunt OE. Preliminary experience with minimally invasive coronary-artery bypass surgery combined with coronary angioplasty. *N Engl J Med* 1997;**336**:1454–1455.
  55. Kon ZN, Brown EN, Tran R, Joshi A, Reicher B, Grant MC, Kallam S, Burris N, Connerney I, Zimrin D, Poston RS. Simultaneous hybrid coronary revascularization reduces postoperative morbidity compared with results from conventional off-pump coronary artery bypass. *J Thorac Cardiovasc Surg* 2008;**135**:367–375.
  56. Halkos ME, Rab ST, Vassiliades TA, Morris DC, Douglas JS, Kilgo PD, Liberman HA, Guyton RA, Thourani VH, Puskas JD. Hybrid coronary revascularization versus off-pump coronary artery bypass for the treatment of left main coronary stenosis. *Ann Thorac Surg* 2011;**92**:2155–2160.
  57. Halkos ME, Vassiliades TA, Douglas JS, Morris DC, Rab ST, Liberman HA, Samady H, Kilgo PD, Guyton RA, Puskas JD. Hybrid coronary revascularization versus off-pump coronary artery bypass grafting for the treatment of multivessel coronary artery disease. *Ann Thorac Surg* 2011;**92**:1695–1701. discussion 1701–1702.
  58. Bonaros N, Schachner T, Lehr E, Kofler M, Wiedemann D, Hong P, Wehman B, Zimrin D, Vesely MK, Friedrich G, Bonatti J. Five hundred cases of robotic totally endoscopic coronary artery bypass grafting: predictors of success and safety. *Ann Thorac Surg* 2013;**95**:803–812.
  59. 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**:S78–S84.
  60. Bonatti JO, Zimrin D, Lehr EJ, Vesely M, Kon ZN, Wehman B, de Biasi AR, Hofauer B, Weidinger F, Schachner T, Bonaros N, Friedrich G. Hybrid coronary revascularization using robotic totally endoscopic surgery: perioperative outcomes and 5-year results. *Ann Thorac Surg* 2012;**94**:1920–1926. discussion 1926.
  61. Holzhey DM, Jacobs S, Mochalski M, Merk D, Walther T, Mohr FW, Falk V. Minimally invasive hybrid coronary artery revascularization. *Ann Thorac Surg* 2008;**86**:1856–1860.
  62. Bonatti J, Schachner T, Bonaros N, Lehr EJ, Zimrin D, Griffith B. Robotically assisted totally endoscopic coronary bypass surgery. *Circulation* 2011;**124**:236–244.
  63. Thiele H, Neumann-Schriedewind P, Jacobs S, Boudriot E, Walther T, Mohr FW, Schuler G, Falk V. Randomized comparison of minimally invasive direct coronary artery bypass surgery versus sirolimus-eluting stenting in isolated proximal left anterior descending coronary artery stenosis. *J Am Coll Cardiol* 2009;**53**:2324–2331.
  64. D'Ancona G, Vassiliades TA, Boyd WD, Donias HW, Stahl KD, Karamanoukian H. Is hybrid coronary revascularization favored by cardiologists or cardiac surgeons? *Heart Surg Forum* 2002;**5**:393–395.
  65. Goldman S, Zadina K, Moritz T, Ovitt T, Sethi G, Copeland JG, Thottapurathu L, Krasnicka B, Ellis N, Anderson RJ, Henderson W, V. A. Cooperative Study Group. Long-term patency of saphenous vein and left internal mammary artery grafts after coronary artery bypass surgery: results from a Department of Veterans Affairs Cooperative Study. *J Am Coll Cardiol* 2004;**44**:2149–2156.
  66. Hayward PA, Buxton BF. Contemporary coronary graft patency: 5-year observational data from a randomized trial of conduits. *Ann Thorac Surg* 2007;**84**:795–799.
  67. Kim KB, Kim JS, Kang HJ, Koo BK, Kim HS, Oh BH, Park YB. Ten-year experience with off-pump coronary artery bypass grafting: lessons learned from early post-operative angiography. *J Thorac Cardiovasc Surg* 2010;**139**:256–262.
  68. FitzGibbon GM, Burton JR, Leach AJ. Coronary bypass graft fate: angiographic grading of 1400 consecutive grafts early after operation and of 1132 after one year. *Circulation* 1978;**57**:1070–1074.
  69. Lytle BW, Blackstone EH, Loop FD, Houghtaling PL, Arnold JH, Akhrass R, McCarthy PM, Cosgrove DM. Two internal thoracic artery grafts are better than one. *J Thorac Cardiovasc Surg* 1999;**117**:855–872.
  70. Taggart DP, Altman DG, Gray AM, Lees B, Nugara F, Yu LM, Campbell H, Flather M, ART Investigators. Randomized trial to compare bilateral vs. single internal mammary coronary artery bypass grafting: 1-year results of the Arterial Revascularisation Trial (ART). *Eur Heart J* 2010;**31**:2470–2481.
  71. Kappetein AP. Bilateral mammary artery vs. single mammary artery grafting: promising early results: but will the match finish with enough players?. *Eur Heart J* 2010;**31**:2444–2446.
  72. Tabata M, Grab JD, Khalpey Z, Edwards FH, O'Brien SM, Cohn LH, Bolman RM III. Prevalence and variability of internal mammary artery graft use in contemporary multivessel coronary artery bypass graft surgery: analysis of the Society of Thoracic Surgeons National Cardiac Database. *Circulation* 2009;**120**:935–940.
  73. Kinoshita T, Asai T. Bilateral internal thoracic artery grafting: current state of the art. *Innovations (Phila)* 2011;**6**:77–83.
  74. Collins P, Webb CM, Chong CF, Moat NE, Radial Artery Versus Saphenous Vein Patency Trial Investigators. Radial artery versus saphenous vein patency randomized trial: five-year angiographic follow-up. *Circulation* 2008;**117**:2859–2864.
  75. Deb S, Cohen EA, Singh SK, Une D, Laupacis A, Fremes SE, RAPS Investigators. Radial artery and saphenous vein patency more than 5 years after coronary artery bypass surgery: results from RAPS (Radial Artery Patency Study). *J Am Coll Cardiol* 2012;**60**:28–35.
  76. Tranbaugh RF, Dimitrova KR, Friedmann P, Geller CM, Harris LJ, Stelzer P, Cohen BM, Ko W, DeCastro H, Lucido D, Hoffman DM. Coronary artery bypass grafting using the radial artery: clinical outcomes, patency, and need for re-intervention. *Circulation* 2012;**126**:S170–S175.
  77. Achouh P, Isselmou KO, Boutekadjirt R, D'Alessandro C, Pagny JY, Fouquet R, Fabiani JN, Acar C. Reappraisal of a 20-year experience with the radial artery as a conduit for coronary bypass grafting. *Eur J Cardiothorac Surg* 2012;**41**:87–92.
  78. Schwann TA, Al-Shaar L, Engoren M, Habib RH. Late effects of radial artery vs. saphenous vein grafting for multivessel coronary bypass surgery in diabetics: a propensity-matched analysis. *Eur J Cardiothorac Surg*; doi: 10.1093/ejcts/ezt061. Published online ahead of print 21 February 2013.
  79. Zacharias A, Habib RH, Schwann TA, Riordan CJ, Durham SJ, Shah A. Improved survival with radial artery versus vein conduits in coronary bypass surgery with left internal thoracic artery to left anterior descending artery grafting. *Circulation* 2004;**109**:1489–1496.
  80. Locker C, Schaff HV, Dearani JA, Joyce LD, Park SJ, Burkhart HM, Suri RM, Greason KL, Stulak JM, Li Z, Daly RC. Multiple arterial grafts improve late survival of patients undergoing coronary artery bypass graft surgery: analysis of 8622 patients with multivessel disease. *Circulation* 2012;**126**:1023–1030.
  81. Goldman S, Sethi GK, Holman W, Thai H, McFalls E, Ward HB, Kelly RF, Rhenman B, Tobler GH, Bakaeen FG, Huh J, Soltero E, Moursi M, Haime M, Crittenden M, Kasirajan V, Ratliff M, Pett S, Irimpen A, Gunnar W, Thomas D, Fremes S, Moritz T, Reda D, Harrison L, Wagner TH, Wang Y, Planting L, Miller M, Rodriguez Y, Juneman E, Morrison D, Pierce MK, Kreamer S, Shih MC, Lee K. Radial artery grafts vs. saphenous vein grafts in coronary artery bypass surgery: a randomized trial. *JAMA* 2011;**305**:167–174.
  82. Khot UN, Friedman DT, Pettersson G, Smedira NG, Li J, Ellis SG. Radial artery bypass grafts have an increased occurrence of angiographically severe stenosis and occlusion compared with left internal mammary arteries and saphenous vein grafts. *Circulation* 2004;**109**:2086–2091.
  83. Ruttman E, Fischler N, Sakic A, Chevtchik O, Alber H, Schistek R, Ulmer H, Grimm M. Second internal thoracic artery versus radial artery in coronary artery bypass grafting: a long-term, propensity score-matched follow-up study. *Circulation* 2011;**124**:1321–1329.
  84. Desai ND, Cohen EA, Naylor CD, Fremes SE, Radial Artery Patency Study Investigators. A randomized comparison of radial-artery and saphenous-vein coronary bypass grafts. *N Engl J Med* 2004;**351**:2302–2309.



85. Tranbaugh RF, Dimitrova KR, Friedmann P, Geller CM, Harris LJ, Stelzer P, Cohen B, Hoffman DM. Radial artery conduits improve long-term survival after coronary artery bypass grafting. *Ann Thorac Surg* 2010;**90**:1165–1172.
86. Rupperecht HJ, Hamm C, Ischinger T, Dietz U, Reimers J, Meyer J. Angiographic follow-up results of a randomized study on angioplasty versus bypass surgery (GABI trial). *GABI Study Group. Eur Heart J* 1996;**17**:1192–1198.
87. Alfieri O, Maisano F, Benussi S, Toracca L, Castiglioni A. Drug-eluting stents or drug-eluting conduits for multivessel disease?. *J Cardiovasc Med (Hagerstown)* 2007;**8**:359–361.
88. Dimitrova KR, Hoffman DM, Geller CM, Dincheva G, Ko W, Tranbaugh RF. Arterial grafts protect the native coronary vessels from atherosclerotic disease progression. *Ann Thorac Surg* 2012;**94**:475–481.
89. Lumsden AB, Eaves FF III, Ofenloch JC, Jordan WD. Subcutaneous, video-assisted saphenous vein harvest: report of the first 30 cases. *Cardiovasc Surg* 1996;**4**:771–776.
90. Dacey LJ. Endoscopic vein-graft harvest is safe for CABG surgery. *JAMA* 2012;**308**:512–513.
91. Cadwallader RA, Walsh SR, Cooper DG, Tang TY, Sadat U, Boyle JR. Great saphenous vein harvesting: a systematic review and meta-analysis of open versus endoscopic techniques. *Vasc Endovascular Surg* 2009;**43**:561–566.
92. Lopes RD, Hafley GE, Allen KB, Ferguson TB, Peterson ED, Harrington RA, Mehta RH, Gibson CM, Mack MJ, Kouchoukos NT, Califf RM, Alexander JH. Endoscopic versus open vein-graft harvesting in coronary-artery bypass surgery. *N Engl J Med* 2009;**361**:235–244.
93. Zenati MA, Shroyer AL, Collins JF, Hattler B, Ota T, Almassi GH, Amidi M, Novitzky D, Grover FL, Sonel AF. Impact of endoscopic versus open saphenous vein harvest technique on late coronary artery bypass grafting patient outcomes in the ROOBY (Randomized On/Off Bypass) Trial. *J Thorac Cardiovasc Surg* 2011;**141**:338–344.
94. Dacey LJ, Braxton JH Jr, Kramer RS, Schmoker JD, Charlesworth DC, Helm RE, Frumiento C, Sardella GL, Clough RA, Jones SR, Malenka DJ, Olmstead EM, Ross CS, O'Connor GT, Likosky DS, Northern New England Cardiovascular Disease Study Group. Long-term outcomes of endoscopic vein harvesting after coronary artery bypass grafting. *Circulation* 2011;**123**:147–153.
95. Williams JB, Peterson ED, Brennan JM, Sedrakyan A, Tavis D, Alexander JH, Lopes RD, Dokholyan RS, Zhao Y, O'Brien SM, Michler RE, Thourani VH, Edwards FH, Duggirala H, Gross T, Marinac-Dabic D, Smith PK. Association between endoscopic vs. open vein-graft harvesting and mortality, wound complications, and cardiovascular events in patients undergoing CABG surgery. *JAMA* 2012;**308**:475–484.
96. Desai P, Kiani S, Thiruvanthan N, Henkin S, Kurian D, Ziu P, Brown A, Patel N, Poston R. Impact of the learning curve for endoscopic vein harvest on conduit quality and early graft patency. *Ann Thorac Surg* 2011;**91**:1385–1391. discussion 1391–1392.
97. Allen K, Cheng D, Cohn W, Connolly M, Edgerton J, Falk V, Martin J, Ohtsuka T, Vitali R. Endoscopic vascular harvest in coronary artery bypass grafting surgery: a consensus statement of the International Society of Minimally Invasive Cardiothoracic Surgery (ISMICS) 2005. *Innovations (Phila)* 2005;**1**:51–60.
98. Grant SW, Grayson AD, Zacharias J, Dalrymple-Hay MJ, Waterworth PD, Bridgewater B. What is the impact of endoscopic vein harvesting on clinical outcomes following coronary artery bypass graft surgery? *Heart* 2012;**98**:60–64.
99. Whitley WS, Glas KE. An argument for routine ultrasound screening of the thoracic aorta in the cardiac surgery population. *Semin Cardiothorac Vasc Anesth* 2008;**12**:290–297.
100. Davila-Roman VG, Barzilai B, Wareing TH, Murphy SF, Schechtman KB, Kouchoukos NT. Atherosclerosis of the ascending aorta. Prevalence and role as an independent predictor of cerebrovascular events in cardiac patients. *Stroke* 1994;**25**:2010–2016.
101. Davila-Roman VG, Kouchoukos NT, Schechtman KB, Barzilai B. Atherosclerosis of the ascending aorta is a predictor of renal dysfunction after cardiac operations. *J Thorac Cardiovasc Surg* 1999;**117**:111–116.
102. Van Zaane B, Zuithoff NP, Reitsma JB, Bax L, Nierich AP, Moons KG. Meta-analysis of the diagnostic accuracy of transesophageal echocardiography for assessment of atherosclerosis in the ascending aorta in patients undergoing cardiac surgery. *Acta Anaesthesiol Scand* 2008;**52**:1179–1187.
103. Davila-Roman VG, Barzilai B, Wareing TH, Murphy SF, Kouchoukos NT. Intraoperative ultrasonographic evaluation of the ascending aorta in 100 consecutive patients undergoing cardiac surgery. *Circulation* 1991;**84**:III47–III53.
104. Royse C, Royse A, Blake D, Grigg L. Screening the thoracic aorta for atheroma: a comparison of manual palpation, transesophageal and epiaortic ultrasonography. *Ann Thorac Cardiovasc Surg* 1998;**4**:347–350.
105. Djaiani G, Ali M, Borger MA, Woo A, Carroll J, Feindel C, Fedorko L, Karski J, Rakowski H. Epiaortic scanning modifies planned intraoperative surgical management but not cerebral embolic load during coronary artery bypass surgery. *Anesth Analg* 2008;**106**:1611–1618.
106. Lyons JM, Thourani VH, Puskas JD, Kilgo PD, Baio KT, Guyton RA, Lattouf OM. Intraoperative epiaortic ultrasound scanning guides operative strategies and identifies patients at high risk during coronary artery bypass grafting. *Innovations (Phila)* 2009;**4**:99–105.
107. Zingone B, Rauber E, Gatti G, Pappalardo A, Benussi B, Dreas L, Lattuada L. The impact of epiaortic ultrasonographic scanning on the risk of perioperative stroke. *Eur J Cardiothorac Surg* 2006;**29**:720–728.
108. Rosenberger P, Shernan SK, Loffler M, Shekar PS, Fox JA, Tuli JK, Nowak M, Eltzschig HK. The influence of epiaortic ultrasonography on intraoperative surgical management in 6051 cardiac surgical patients. *Ann Thorac Surg* 2008;**85**:548–553.
109. Hangler HB, Nagele G, Danzmayr M, Mueller L, Ruttman E, Lauffer G, Bonatti J. Modification of surgical technique for ascending aortic atherosclerosis: impact on stroke reduction in coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2003;**126**:391–400.
110. Wareing TH, Davila-Roman VG, Barzilai B, Murphy SF, Kouchoukos NT. Management of the severely atherosclerotic ascending aorta during cardiac operations. A strategy for detection and treatment. *J Thorac Cardiovasc Surg* 1992;**103**:453–462.
111. Daniel WT III, Kilgo P, Puskas JD, Thourani VH, Lattouf OM, Guyton RA, Halkos ME. Trends in aortic clamp use during coronary artery bypass surgery: effect of aortic clamping strategies on neurologic outcomes. *J Thorac Cardiovasc Surg*; doi: 10.1016/j.jtcvs.2013.02.021. Published online ahead of print 8 March 2013.
112. Magee MJ, Alexander JH, Hafley G, Ferguson TB Jr, Gibson CM, Harrington RA, Peterson ED, Califf RM, Kouchoukos NT, Herbert MA, Mack MJ, Prevent IV Investigators. Coronary artery bypass graft failure after on-pump and off-pump coronary artery bypass: findings from PREVENT IV. *Ann Thorac Surg* 2008;**85**:494–499. discussion 499–500.
113. Balacumaraswami L, Taggart DP. Intraoperative imaging techniques to assess coronary artery bypass graft patency. *Ann Thorac Surg* 2007;**83**:2251–2257.
114. Balacumaraswami L, Abu-Omar Y, Choudhary B, Pigott D, Taggart DP. A comparison of transit-time flowmetry and intraoperative fluorescence imaging for assessing coronary artery bypass graft patency. *J Thorac Cardiovasc Surg* 2005;**130**:315–320.
115. Mack MJ. Intraoperative coronary graft assessment. *Curr Opin Cardiol* 2008;**23**:568–572.
116. Desai ND, Miwa S, Kodama D, Koyama T, Cohen G, Pelletier MP, Cohen EA, Christakis GT, Goldman BS, Fremes SE. A randomized comparison of intraoperative indocyanine green angiography and transit-time flow measurement to detect technical errors in coronary bypass grafts. *J Thorac Cardiovasc Surg* 2006;**132**:585–594.
117. Waseda K, Ako J, Hasegawa T, Shimada Y, Ikeno F, Ishikawa T, Demura Y, Hatada K, Yock PG, Honda Y, Fitzgerald PJ, Takahashi M. Intraoperative fluorescence imaging system for on-site assessment of off-pump coronary artery bypass graft. *JACC Cardiovasc Imaging* 2009;**2**:604–612.
118. Jokinen JJ, Werkkala K, Vainikka T, Perakyla T, Simpanen J, Ihlberg L. Clinical value of intra-operative transit-time flow measurement for coronary artery bypass grafting: a prospective angiography-controlled study. *Eur J Cardiothorac Surg* 2011;**39**:918–923.
119. Di Giammarco G, Pano M, Cirmeni S, Pelini P, Vitolla G, Di Mauro M. Predictive value of intraoperative transit-time flow measurement for short-term graft patency in coronary surgery. *J Thorac Cardiovasc Surg* 2006;**132**:468–474.
120. Tokuda Y, Song MH, Ueda Y, Usui A, Akita T. Predicting early coronary artery bypass graft failure by intraoperative transit time flow measurement. *Ann Thorac Surg* 2007;**84**:1928–1933.
121. Kieser TM, Rose S, Kowalewski R, Belenkie I. Transit-time flow predicts outcomes in coronary artery bypass graft patients: a series of 1000 consecutive arterial grafts. *Eur J Cardiothorac Surg* 2010;**38**:155–162.
122. Mangano DT, Multicenter Study of Perioperative Ischemia Research Group. Aspirin and mortality from coronary bypass surgery. *N Engl J Med* 2002;**347**:1309–1317.
123. Chan AY, McAlister FA, Norris CM, Johnstone D, Bakal JA, Ross DB, Alberta Provincial Program for Outcome Assessment in Coronary Heart Disease Investigators. Effect of beta-blocker use on outcomes after discharge in patients who underwent cardiac surgery. *J Thorac Cardiovasc Surg* 2010;**140**:182–187.
124. Kjoller-Hansen L, Steffensen R, Grande P. The Angiotensin-converting Enzyme Inhibition Post Revascularization Study (APRES). *J Am Coll Cardiol* 2000;**35**:881–888.
125. The effect of aggressive lowering of low-density lipoprotein cholesterol levels and low-dose anticoagulation on obstructive changes in saphenous-vein coronary-artery bypass grafts. The Post Coronary Artery Bypass Graft Trial Investigators. *N Engl J Med* 1997;**336**:153–162.
126. Shah SJ, Waters DD, Barter P, Kastelein JJ, Shepherd J, Wenger NK, DeMicco DA, Breazna A, LaRosa JC. Intensive lipid-lowering with atorvastatin for secondary prevention in patients after coronary artery bypass surgery. *J Am Coll Cardiol* 2008;**51**:1938–1943.
127. Benedetto U, Melina G, di Bartolomeo R, Angeloni E, Sansone D, Falaschi G, Capuano F, Comito C, Roscitano A, Sinatra R. n-3 polyunsaturated fatty acids after coronary artery bypass grafting. *Ann Thorac Surg* 2011;**91**:1169–1175.

128. Goyal A, Alexander JH, Hafley GE, Graham SH, Mehta RH, Mack MJ, Wolf RK, Cohn LH, Kouchoukos NT, Harrington RA, Gennevois D, Gibson CM, Califf RM, Ferguson TB Jr, Peterson ED, Prevent IV Investigators. Outcomes associated with the use of secondary prevention medications after coronary artery bypass graft surgery. *Ann Thorac Surg* 2007;**83**:993–1001.
129. Kulik A, Voisine P, Mathieu P, Masters RG, Mesana TG, Le May MR, Ruel M. Statin therapy and saphenous vein graft disease after coronary bypass surgery: analysis from the CASCADE randomized trial. *Ann Thorac Surg* 2011;**92**:1284–1290. discussion 1290–1291.
130. Eritsland J, Arnesen H, Gronseth K, Fjeld NB, Abdelnoor M. Effect of dietary supplementation with n-3 fatty acids on coronary artery bypass graft patency. *Am J Cardiol* 1996;**77**:31–36.
131. de Leon N, Jacevicius CA. Use of aspirin and clopidogrel after coronary artery bypass graft surgery. *Ann Pharmacother* 2012;**46**:678–687.
132. Martin TN, Irving RJ, Sutherland M, Sutherland K, Bloomfield P. Improving secondary prevention in coronary bypass patients: closing the audit loop. *Heart* 2005;**91**:456–459.
133. Kotseva K, Wood D, De Backer G, De Bacquer D, Pyorala K, Keil U, Group ES. Cardiovascular prevention guidelines in daily practice: a comparison of EUROASPIRE I, II, and III surveys in eight European countries. *Lancet* 2009;**373**:929–940.
134. Hiratzka LF, Eagle KA, Liang L, Fonarow GC, LaBresh KA, Peterson ED, Get With the Guidelines Steering Committee. Atherosclerosis secondary prevention performance measures after coronary bypass graft surgery compared with percutaneous catheter intervention and nonintervention patients in the Get With the Guidelines database. *Circulation* 2007;**116**:1207–1212.
135. Kappetein AP, Feldman TE, Mack MJ, Morice MC, Holmes DR, Stahle E, Dawkins KD, Mohr FW, Serruys PW, Colombo A. Comparison of coronary bypass surgery with drug-eluting stenting for the treatment of left main and/or three-vessel disease: 3-year follow-up of the SYNTAX trial. *Eur Heart J* 2011;**32**:2125–2134.
136. Turley AJ, Roberts AP, Morley R, Thornley AR, Owens WA, de Belder MA. Secondary prevention following coronary artery bypass grafting has improved but remains sub-optimal: the need for targeted follow-up. *Interact Cardiovasc Thorac Surg* 2008;**7**:231–234.
137. van Domburg RT, op Reimer WS, Hoeks SE, Kappetein AP, Bogers AJ. Three life-years gained from smoking cessation after coronary artery bypass surgery: a 30-year follow-up study. *Am Heart J* 2008;**156**:473–476.
138. Opie LH, Commerford PJ, Gersh BJ. Controversies in stable coronary artery disease. *Lancet* 2006;**367**:69–78.
139. Clark AM, Hartling L, Vandermeer B, McAlister FA. Meta-analysis: secondary prevention programs for patients with coronary artery disease. *Ann Intern Med* 2005;**143**:659–672.
140. Griffo R, Ambrosetti M, Tamarin R, Fattorioli F, Temporelli PL, Vestri AR, De Feo S, Tavazzi L, ICAROS Investigators. Effective secondary prevention through cardiac rehabilitation after coronary revascularization and predictors of poor adherence to lifestyle modification and medication. Results of the ICAROS Survey. *Int J Cardiol*. doi:10.1016/j.ijcard.2012.04.069. Published online 10 May 2012.
141. Kotseva K, Wood D, De Backer G, De Bacquer D, Pyorala K, Keil U, EUROASPIRE Study Group. Cardiovascular prevention guidelines in daily practice: a comparison of EUROASPIRE I, II, and III surveys in eight European countries. *Lancet* 2009;**373**:929–940.
142. Clark AM, Haykowsky M, Kryworuchko J, MacClure T, Scott J, DesMeules M, Luo W, Liang Y, McAlister FA. A meta-analysis of randomized control trials of home-based secondary prevention programs for coronary artery disease. *Eur J Cardiovasc Prev Rehabil* 2010;**17**:261–270.
143. Head SJ, Kaul S, Mack MJ, Serruys PW, Taggart DP, Holmes Jr DR, Leon MB, Marco J, Bogers AJ, Kappetein AP. The rationale for Heart Team decision-making for patients with stable complex coronary artery disease. *Eur Heart J*; doi:10.1093/eurheartj/eh059. Published online ahead of print 26 February 2013.
144. Marso SP, Teirstein PS, Kereiakes DJ, Moses J, Lasala J, Grantham JA. Percutaneous coronary intervention use in the United States: defining measures of appropriateness. *JACC Cardiovasc Interv* 2012;**5**:229–235.
145. Chandrasekharan DP, Taggart DP. Informed consent for interventions in stable coronary artery disease: problems, etiologies, and solutions. *Eur J Cardiothorac Surg* 2011;**39**:912–917.
146. Head SJ, Bogers AJ, Serruys PW, Takkenberg JJ, Kappetein AP. A crucial factor in shared decision making: the team approach. *Lancet* 2011;**377**:1836.
147. Head SJ, Holmes Jr DR, Mack MJ, Serruys PW, Mohr FW, Morice M, Colombo A, Kappetein AP. Risk profile and 3-year outcomes from the SYNTAX percutaneous coronary intervention and coronary artery bypass grafting nested registries. *JACC Cardiovasc Interv* 2012;**5**:618–625.
148. Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, Cigarroa JE, Disesa V, Hiratzka LF, Hutter AM Jr, Jessen ME, Keeley EC, Lahey SJ, Lange RA, London MJ, Mack MJ, Patel MR, Puskas JD, Sabik JF, Selnes O, Shahian DM, Trost JC, Winniford MD, American College of Cardiology Foundation, American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, Society of Thoracic Surgeons. 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2011;**58**:e123–e210.
149. Tonino PA, De Bruyne B, Pijls NH, Siebert U, Ikeno F, van't Veer M, Klauss V, Manoharan G, Engstrom T, Oldroyd KG, Ver Lee PN, MacCarthy PA, Fearon WF. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *N Engl J Med* 2009;**360**:213–224.
150. De Bruyne B, Pijls NH, Kalesan B, Barbato E, Tonino PA, Piroth Z, Jagic N, Mobius-Winckler S, Rioufol G, Witt N, Kala P, MacCarthy P, Engstrom T, Oldroyd KG, Mavromatis K, Manoharan G, Verlee P, Frobert O, Curzen N, Johnson JB, Juni P, Fearon WF. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N Engl J Med* 2012;**367**:991–1001.
151. Botman CJ, Schonberger J, Koolen S, Penn O, Botman H, Dib N, Eeckhout E, Pijls N. Does stenosis severity of native vessels influence bypass graft patency? A prospective fractional flow reserve-guided study. *Ann Thorac Surg* 2007;**83**:2093–2097.
152. Kim YH, Ahn JM, Park DW, Song HG, Lee JY, Kim WJ, Yun SC, Kang SJ, Lee SW, Lee CW, Moon DH, Chung CH, Lee JW, Park SW, Park SJ. Impact of ischemia-guided revascularization with myocardial perfusion imaging for patients with multi-vessel coronary disease. *J Am Coll Cardiol* 2012;**60**:181–190.
153. de Boer SP, Lenzen MJ, Oemrawsingh RM, Simsek C, Duckers HJ, van der Giessen WJ, Serruys PW, Boersma E. Evaluating the 'all-comers' design: a comparison of participants in two 'all-comers' PCI trials with non-participants. *Eur Heart J* 2011;**32**:2161–2167.
154. Head SJ, Farooq V, Serruys PW, Kappetein AP. The SYNTAX Score and its clinical implications. *Heart*; doi:10.1136/heartjnl-2012-302482. Published online ahead of print 28 March 2013.
155. Farooq V, van Klaveren D, Steyerberg EW, Meliga E, Vergouwe Y, Chieffo A, Kappetein AP, Colombo A, Holmes DR Jr, Mack M, Feldman T, Morice MC, Stahle E, Onuma Y, Morel MA, Garcia-Garcia HM, van Es GA, Dawkins KD, Mohr FW, Serruys PW. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. *Lancet* 2013;**381**:639–650.
156. Sutton M, Nikolova S, Boaden R, Lester H, McDonald R, Roland M. Reduced mortality with hospital pay for performance in England. *N Engl J Med* 2012;**367**:1821–1828.