The optimal revascularization strategy for multivessel coronary artery disease remains controversial, especially when there is diffuse disease involving the proximal segment of the left anterior descending artery (LAD). Coronary artery bypass graft surgery (CABG) remains the gold standard approach, although the evidence is increasingly being challenged by technological and procedural advances in percutaneous coronary intervention (PCI). The well-established survival benefit of surgery1–3 is conferred by the left internal mammary arterial (LIMA) graft to the LAD, which, through its resistance to thrombosis and atherosclerosis,4 has demonstrated patency rates of 95% to 98% at 10 years.5,6 Moreover, the LIMA has been shown to protect the proximal LAD territory against further ischemic injury from progressive disease.4 However, the incremental benefit of concomitant saphenous vein grafts (SVGs) supplying non-LAD territories is less clear.2,3 The longevity of vein grafts is relatively poor, with reported failure rates averaging 20% at 1 year and reaching up to 70% at 15 years.6–8 Interestingly, the Project of Ex-vivo Vein graft Engineering via Transfection IV (PREVENT IV) trial investigators reported an SVG failure rate of 45% at 12- to 18-month angiographic follow-up,7 a figure that, in the modern era, seems unacceptable.

So, is CABG a double-edged sword? It certainly seems plausible that the prognostic benefit conferred by the longevity of the LIMA-to-LAD graft might, in some way, be offset by the disappointing survival rates of SVG to non-LAD vessels. Although vein graft occlusion is certainly as frequent as stent thrombosis,9 stent thrombosis is characteristically associated with a higher incidence of major adverse cardiac events. Vein graft narrowing, in contrast, is at least 2 or 3 times more frequent than stent restenosis, although both tend to be associated with a recurrence of angina requiring reintervention. With newer stent technologies leading to a steady and progressive decline in restenosis and thrombosis and hence in the requirement for repeat revascularization,10–12 overall rates of stent occlusion, particularly in non-LAD vessels,13–15 are now lower than reported rates of SVG failure.

Despite the evidence supporting PCI as a superior strategy to SVG for non-LAD vessels, the LIMA-to-LAD graft continues to have unrivaled safety and efficacy, even in the drug-eluting stent (DES) era. There is evidence to suggest that a lesion in the proximal LAD is an independent predictor of in-stent restenosis, with rates between 19% and 44% reported with bare metal stents.16,17 In this context and with the knowledge that acute occlusion of the proximal LAD is likely to have catastrophic consequences, at best a large-territory infarction and at worst sudden death, treating complex proximal LAD disease percutaneously is not without risk and, some might argue, not ideal.

Combining the benefits of an LIMA-to-LAD graft with the benefits of percutaneous DES implantation in non-LAD...
vessels and, in doing so, providing a best of both worlds strategy to optimize long-term outcomes yet minimize risk is the fundamental rationale of hybrid coronary revascularization (HCR). It is certainly attractive that harvesting and grafting of this single arterial conduit to the LAD territory can be achieved through a minimally invasive approach, eliminating the need for open sternotomy and potentially for cardiopulmonary bypass (CPB).

Justification of a Surgical Procedure
Despite the perceived advantages of HCR in multivessel coronary artery disease, complete percutaneous revascularization has, in several trials, compared very favorably with CABG. Two recent meta-analyses of the randomized trials comparing CABG and PCI in almost 9000 patients showed similar survival out to 10 years, with inconsistent outcomes in the diabetic population. The small number of studies that report a survival benefit of CABG over PCI tend to be registry based with important differences among patients treated with surgery or DES and must therefore be interpreted with caution. The overriding message from all studies is that, regardless of stent technology, PCI is blighted by higher rates of repeat revascularization and less relief from angina. However, the short duration of follow-up comparing DES and SVG biases adverse outcomes against DES, and it might be that the reverse is seen in the longer term as vein grafts begin to fail. As things stand, the “real” advantage of HCR, like conventional CABG, lies in the reduction of repeat revascularization. Unlike conventional CABG, however, HCR provides a minimally invasive sternotomy and potentially CPB-sparing means of achieving this. The real question is whether a goal of reducing repeat revascularizations is enough to justify a surgical procedure of any kind.

The ability to harvest and graft the LIMA with a minimally invasive surgical approach certainly favors a hybrid strategy. A sternal-sparing incision with the avoidance of aortic manipulation and, when possible, CPB has been shown to reduce the incidence of adverse neurological events and pulmonary complications compared with conventional CABG. Although a mortality benefit has yet to be demonstrated, minimally invasive techniques have been associated with lower morbidity than conventional surgery, even in high-risk patients. The approach not only has resource-saving potential but has also been associated with shorter hospital stay, quicker recovery, less blood loss, and improved patient satisfaction compared with conventional techniques. The classic minimally invasive direct coronary artery bypass (MidCAB) technique, used in many of the earlier hybrid series, is performed through a left anterior minithoracotomy incision and involves the LIMA-to-LAD anastomosis being performed by hand on the beating heart. MidCAB is technically challenging, associated with longer operating times, and marred by postoperative pain arising from chest wall retraction, so it is easy to see why the technique is unappealing and, in some units, obsolete. Although this has, in the past, thwarted broader interest in the hybrid concept, some centers continue to boast excellent results with the classic MidCAB in their integrated approach to HCR.

The development of thoracoscopic and robotic techniques for grafting the LIMA to the LAD is certainly more appealing and has led to renewed interest in HCR. These techniques range from endoscopic or robotic harvesting of the LIMA with manual construction of the LAD anastomosis to a completely endoscopic approach performed on a beating heart. Although considerable technical skill, acquired only through specific training and operator experience, is necessary for these techniques, the concept is exciting and has already generated some excellent results, with several series reporting 93% to 96% LIMA patency at the end of the procedure and 86% freedom from major adverse cardiac events at 1 year. Despite the perception that procedural times are longer than for conventional on-pump or off-pump CABG (OPCABG), published data are scanty and inconsistent. Hu et al recently demonstrated that simultaneous (1-stage) HCR performed with the classic MidCAB did not take significantly longer than conventional OPCABG (246±84 versus 204±42 minutes, respectively). Furthermore, Kiaii et al reported very impressive procedural times of 205±39 minutes for simultaneous HCR performed with robotically assisted LIMA harvesting in their series of 58 patients. These groups are clearly experienced with the techniques, and their outcomes and impressive procedural times demonstrate very well that with increased uptake and experience, robotic and endoscopic techniques can be learned and perfected. The advantages over conventional CABG are clear, and with patients’ increasing desire for less invasive strategies without sacrificing durability, and current guidelines continuing to recommend conventional surgery for high-risk patients with multivessel disease, a hybrid approach can certainly be justified. Not only might less invasive options prove superior to conventional surgery, but they could offer a lower-risk alternative for sicker patients deemed unsuitable for on-pump or conventional sternotomies. The tendency for this patient population to be associated with poorer surgical outcomes should not dampen enthusiasm for the use of minimally invasive hybrid strategies.

HCR: What Is the Evidence?
The concept of a planned integrated approach is not new, with early reports dating back to 1996 when Angelini and colleagues used a minimally invasive thoracotomy to harvest and graft the LIMA to the LAD, thereafter performing balloon angioplasty to suitable non-LAD vessels in 6 patients. Despite the lack of randomized trial data some 15 years later and hence no recommendation for HCR in current revascularization guidelines, the first observational trial aimed at defining the population eligible for HCR is currently underway. Sponsored by the National Heart, Lung, and Blood Institute, this observational trial aims to recruit 700 patients.
undergoing either HCR or PCI and will pave the way for a randomized trial.

Almost 1000 patients have undergone HCR since its introduction in 1996, and despite predominantly retrospective data from single-center experience (Table 1), the safety and technical feasibility of the procedure have repeatedly been demonstrated, with in-hospital mortality rates as low as 0% to 2%.32–40,42–51 Other advantages include lower morbidity related to the minimally invasive surgical component, which in turn translates into shorter intensive care, shorter overall hospital stay, and, important from a patient’s perspective, faster recovery with superior cosmetic results.26–40,42–51

In the few series comparing HCR and conventional CABG, clinical outcomes have been comparable, if not superior, at 30 days and out to at least 6 months.32,33,48–50 Most series reported shorter intubation times, shorter intensive care and hospital stays, and even reduced postprocedural bleeding and transfusion requirements in the HCR groups despite the need for additional antiplatelet therapy (Table 2). Although no mortality benefit has yet been demonstrated, HCR has been associated with lower morbidity than conventional surgery. In their hybrid series, Kon et al48 reported the incidence of major adverse cardiac events at 1 year to be one third that of conventional OPCABG. Perhaps even more striking are the clinical outcomes reported at 18 months by Hu et al,33 with a 99% freedom from major adverse cardiac and cerebrovascular events after simultaneous HCR compared with 90.4% in a similar group matched by propensity scoring and treated with OPCABG and ministernotomy (P=0.03).

Among the 25 predominantly single-center hybrid series summarized in Table 1, the event-free survival at 6 to 12 months is between 70% and 100%.26–40,42–51 Being a strong reflection of operator experience, results from single-center series can vary considerably. Katz et al acknowledged that although they achieved excellent perioperative results from a robotically mediated endoscopic approach in 27 patients, their reintervention rate exceeded that reported elsewhere. The exceptionally high restenotic rate of 26% (3 bare metal stents and 4 DES) likely reflects lesion complexity and operator experience and therefore must be interpreted with caution. Although the largest series of 117 patients reports a 1-year incidence of major adverse cardiac and cerebrovascular events of 15%, this figure additionally incorporates a recurrence or persistence of angina and must also be interpreted in context. In reality, although 23 patients underwent repeat angiography during the “208 patient-years” of follow-up, only 1 had an occluded LIMA graft, and 5 had in-stent restenosis. It is noteworthy that among these hybrid series, DES use was infrequent at only 25%. Therefore, although we have already seen event-free survival approximating 90% at 1 year with published experience thus far, with increased operator experience and uptake of newer stent technology, this figure could, without question, be improved.

A major advantage of HCR is the ability to perform coronary graft angiography at the end of the procedure. Even with conventional CABG, early graft failure, usually resulting from technical error, occurs in as many as 5% to 20% of patients at discharge.52 Despite a LIMA patency of 100% being reported in the majority of hybrid series, it is our opinion that the added technical challenge of constructing a distal anastomosis under limited visualization mandates angiographic validation. Zhao et al50 performed completion angiography in 366 patients undergoing conventional CABG in a hybrid operating room, 67 of whom were scheduled for simultaneous PCI. Interestingly, they were able to demonstrate angiographic defects in as many as 12% of grafts. It is noteworthy that these figures are almost identical to those reported in the PREVENT IV study.7 They elected to intervene in all cases, making only minor adjustments in 2.8%, performing unplanned open-chest PCI in 6%, and carrying out surgical revision in the remaining 3.4%. Although it is surprising that angiographic defects were seen as frequently in LIMA as in SVG grafts (7% versus 8%, respectively), the clinical significance of such defects, which ranged from spasm or kinking to dissection, suture damage, and even the recognition of an incorrectly grafted target, remains unknown. It certainly seems plausible that spasm, kinks, and the majority of localized dissections will repair spontaneously in time, casting doubts on the need to intervene on all abnormalities. However, having the facility to check the patency of the LIMA graft and to recognize and ultimately deal with significant issues such as anastomotic defects or even technical mistakes such as an LIMA grafted to a non-LAD target has clear advantages. In hybrid practice, in which surgical access and hence visualization are limited, this should become the standard of care.

**Real-World Advantages: Quicker Recovery, Patient Satisfaction, and Cost Analysis**

It is reported in the literature that HCR, particularly when a 1-stop or even staged same-day approach is used, significantly reduces the length of intensive care and overall hospital stay (Table 2).32–48–50 In many studies, however, the length of stay depended on the timing of a second staged procedure rather than reflecting postoperative recovery per se. The most impressive reductions were reported by Kon et al48 and Reicher et al,49 from the same institution, who showed that compared with conventional OPCABG, simultaneous HCR with a MidCAB approach led to a 20-fold reduction in intubation times and cut hospital stay almost in half. Patients were discharged after a mean of only 3.7 days and were 7 times more likely to return to work within 1 month.48 The physical and psychological impact of this must not be underestimated and was reflected in much higher patient satisfaction scores (83% after HCR versus 42% after OPCABG).48 Although the MidCAB approach has been associated with greater pain in the early postoperative period, this is short-lasting compared with conventional approaches (10.3±10.0 versus 45.5±33.6 days; P=0.004) and, as indi-
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>n</th>
<th>Surgical Strategy (n)</th>
<th>PCI (%)</th>
<th>HCR Strategy (%)</th>
<th>IH Mortality, %</th>
<th>IH TLR, %</th>
<th>LIMA Patency (Early), %</th>
<th>TLR at 9 mo, %</th>
<th>Mean Follow-Up, mo</th>
<th>Event-Free Survival, %</th>
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<tbody>
<tr>
<td>Angelini et al</td>
<td>1996</td>
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<td>Simultaneous (33) MidCAB then PCI (67)</td>
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<td>Lloyd et al</td>
<td>1999</td>
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<td>PTCA (52), BMS (48)</td>
<td>Simultaneous (22) MidCAB then PCI (78)</td>
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<tr>
<td>Lewis et al</td>
<td>1999</td>
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<td>Open MidCAB</td>
<td>BMS (100)</td>
<td>PCI then MidCAB (4 h)</td>
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<td>Open MidCAB</td>
<td>PTCA (34), BMS (66)</td>
<td>Simultaneous (52) MidCAB then PCI (41), PCI then MidCAB (7)</td>
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<td>MidCAB then PCI (100)</td>
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<td>Wittwer et al</td>
<td>2000</td>
<td>35</td>
<td>Open MidCAB</td>
<td>PTCA (70), BMS (30)</td>
<td>MidCAB then PCI (100)</td>
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<td>De Caniere et al</td>
<td>2001</td>
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<td>Open MidCAB</td>
<td>PTCA (70), BMS (30)</td>
<td>PCI then MidCAB (45), MidCAB then PCI (55)</td>
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<td>Stahl et al</td>
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<td>Lee et al</td>
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<td>Davidovicus et al</td>
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<td>RE-MidCAB</td>
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<tr>
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<td>27</td>
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<td>BMS (30), DES (23.5)</td>
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<td>Us et al</td>
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<td>Bonatti et al</td>
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<td>Holzhey et al</td>
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<td>Open MidCAB (107), BH-TECAB (8), AH-TECAB (2)</td>
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<td>Kiali et al</td>
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<td>Gao et al</td>
<td>2009</td>
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<td>BMS (67), DES (23)</td>
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<td>On-pump CABG (80), OPCAB (22)</td>
<td>DES (84), BMS (8), DES/BMS (7)</td>
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<td>Delhaye et al</td>
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<td>18</td>
<td>On-pump CABG (13), OPCAB (5)</td>
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<td>CABG then PCI</td>
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<td>Hu et al</td>
<td>2011</td>
<td>104</td>
<td>Lower ministernotomy</td>
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<td>1.9</td>
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</table>

PCI indicates percutaneous coronary intervention; HCR, hybrid coronary revascularization; IH, in-hospital; TLR, target lesion revascularization; LIMA, left internal mammary artery; MidCAB, minimally invasive direct coronary artery bypass grafting; PTCA, percutaneous transluminal coronary angioplasty; BMS, bare metal stent; DES, drug-eluting stent; RE-MidCAB, robotically enhanced minimally invasive direct coronary artery bypass grafting; AH-TECAB, arrested heart totally endoscopic coronary artery bypass; CABG, coronary artery bypass graft surgery; BH-TECAB, beating heart totally endoscopic coronary artery bypass; and OPCAB, off-pump coronary artery bypass.
contrast, Kon et al.48 performed a detailed cost analysis and Zhao et al.50 2009 Simultaneous PCI remains weak and for whom the merits of LIMA-to-LAD grafting are unparalleled. As with any revascularization strategy, it is essential that a proximal LAD lesion is amenable to stenting or the vessel is nondominant. Complex distal left main stem stenosis could also be managed by a hybrid approach if the circumflex coronary occlusion involving the LAD, particularly when reopening the non-LAD vessel appears straightforward, although the LAD itself may prove too complex for a successful percutaneous approach (Figure 1). Additional scenarios include diffuse disease of the proximal LAD in which a long stent (>30 mm) would otherwise be necessary, a proximal LAD occlusion with unfavorable anatomy, a chronic occlusion of the LAD for which PCI has previously been unsuccessful, and diffuse disease of the proximal LAD involving a major bifurcation. Complex distal left main stem stenosis with multiple lesions involving all major epicardial vessels could also be managed by a hybrid approach if the circumflex lesion is amenable to stenting or the vessel is nondominant (Figure 2). Arguably, however, most complex distal left main bifurcations requiring a 2-stent strategy should be considered for bilateral mammary grafting in the first place. HCR or full percutaneous revascularization should be considered a second option for patients unsuitable for conventional surgery. We hope that the results of the ongoing Evaluation of Xience Prime or Xience V Versus CABG for Effectiveness of Left Main Revascularization (EXCEL) study will clarify this issue. Finally, the development of aggressive restenosis of DES involving the left main stem and/or proximal LAD should prompt consideration of a surgical strategy. Again, a hybrid approach may be a viable alternative in selected cases.

To qualify for any hybrid procedure, regardless of the indication, 2 essential anatomic criteria must be fulfilled: The angiographically clear-cut critical before a hybrid procedure is considered. Any uncertainty requires additional evaluation by intravascular ultrasound and/or fractional flow reserve, with a cross-sectional area <4.0 mm² or a fractional flow reserve <0.75 indicating anatomic and functional significance. A hybrid approach may be of value for a double coronary occlusion involving the LAD, particularly when reopening the non-LAD vessel appears straightforward, although the LAD itself may prove too complex for a successful percutaneous approach (Figure 1). Additional scenarios include diffuse disease of the proximal LAD in which a long stent (>30 mm) would otherwise be necessary, a proximal LAD occlusion with unfavorable anatomy, a chronic occlusion of the LAD for which PCI has previously been unsuccessful, and diffuse disease of the proximal LAD involving a major bifurcation. Complex distal left main stem stenosis with multiple lesions involving all major epicardial vessels could also be managed by a hybrid approach if the circumflex lesion is amenable to stenting or the vessel is nondominant (Figure 2). Arguably, however, most complex distal left main bifurcations requiring a 2-stent strategy should be considered for bilateral mammary grafting in the first place. HCR or full percutaneous revascularization should be considered a second option for patients unsuitable for conventional surgery. We hope that the results of the ongoing Evaluation of Xience Prime or Xience V Versus CABG for Effectiveness of Left Main Revascularization (EXCEL) study will clarify this issue. Finally, the development of aggressive restenosis of DES involving the left main stem and/or proximal LAD should prompt consideration of a surgical strategy. Again, a hybrid approach may be a viable alternative in selected cases.

To qualify for any hybrid procedure, regardless of the indication, 2 essential anatomic criteria must be fulfilled: The

cated by satisfaction scores, appears to have little lasting impact.

The construction of a designated hybrid suite incurs significant costs in the early stages. Beyond that, however, routine HCR might prove to be a cost-saving strategy. The literature is inconsistent, primarily because of the large variation in hybrid strategies from the stents used to the coronary artery bypass. percutaneous transluminal coronary angioplasty; MidCAB, minimally invasive direct coronary artery bypass grafting; DES, drug-eluting stent; and OPCAB, off-pump coronary artery bypass.

**Table 2. Published Series Comparing Hybrid Coronary Revascularization With Coronary Artery Bypass Graft Surgery**

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>HCR Strategy (n)</th>
<th>CABG Strategy (n)</th>
<th>Postoperative MACE, %</th>
<th>Intubation Time, h</th>
<th>Hospital LOS, d</th>
<th>Transfusion, U</th>
<th>Mortality at 1 y, %</th>
<th>MAZE at 6- to 18-mo Follow-up, %</th>
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<tbody>
<tr>
<td>De Canniere et al46</td>
<td>2001</td>
<td>PTCA first (45%)/MidCAB first (55%) (29)</td>
<td>On-pump CABG (20)</td>
<td>0 10 NA NA</td>
<td>6.7±0.7</td>
<td>9.0±1.2</td>
<td>NA NA</td>
<td>0 0 5 0</td>
<td></td>
</tr>
<tr>
<td>Kon et al48</td>
<td>2008</td>
<td>Simultaneous MidCAB/DES (15)</td>
<td>OPCAB with stenotomy (30)</td>
<td>0 23.3 1.3±3.4 20.8±25.7</td>
<td>3.7±1.4</td>
<td>6.4±2.2</td>
<td>0.2±0.4</td>
<td>1.4±1.4</td>
<td>0 0 7 23</td>
</tr>
<tr>
<td>Reicher et al49</td>
<td>2008</td>
<td>Simultaneous MidCAB/DES (13)</td>
<td>OPCAB with thoracotomy (26)</td>
<td>0 0 0.5±1.3 11.7±9.6</td>
<td>3.6±1.5</td>
<td>6.3±2.3</td>
<td>0.3±0.5</td>
<td>1.5±1.5</td>
<td>0 0 0.15 0.15</td>
</tr>
<tr>
<td>Zhao et al50</td>
<td>2009</td>
<td>Simultaneous MidCAB/DES (84%) (112)</td>
<td>On-pump CABG (93%) OPCAB (7%) (254)</td>
<td>1.8 NA NA NA</td>
<td>6 (1–97)</td>
<td>5 (1–33)</td>
<td>1.0 (0–10)</td>
<td>1.0 (0–20)</td>
<td>NA NA NA NA</td>
</tr>
<tr>
<td>Hu et al51</td>
<td>2011</td>
<td>Simultaneous MidCAB/DES (104)</td>
<td>OPCAB with ministernotomy (13)</td>
<td>0 0 11.6±6.3 13.8±6.8</td>
<td>8.2±2.6</td>
<td>9.5±4.5</td>
<td>28.8%</td>
<td>51.9%</td>
<td>0 1.0 1 9.6</td>
</tr>
</tbody>
</table>

HCR indicates hybrid coronary revascularization; CABG, coronary artery bypass graft surgery; MACE, major adverse clinical events; LOS, length of stay; PTCA, percutaneous transluminal coronary angioplasty; MidCAB, minimally invasive direct coronary artery bypass grafting; DES, drug-eluting stent; and OPCAB, off-pump coronary artery bypass.
distal LAD must be of adequate caliber to enable LIMA insertion, and the non-LAD vessels must be amenable to stent implantation. Furthermore, there should be no contraindication to dual antiplatelet therapy because, in our opinion, the use of DES for any high-risk multivessel PCI is mandatory.

Interestingly, some preliminary data presented by Dr Zhao at the American Heart Association 2010 showed inferior results with HCR compared with conventional CABG for patients with high Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery (SYNTAX) scores (D.X. Zhao, MD, unpublished data, 2010). It must be remembered, however, that the SYNTAX score is disproportionately weighted toward LAD lesions compared with lesions located in other vessels. Certainly, if the major contribution to the SYNTAX score is complex disease of the right coronary or circumflex artery, percutaneous treatment of these vessels might compromise the overall outcome from a hybrid approach. However, if a high SYNTAX score is generated predominantly by complex LAD disease and the non-LAD vessels are amenable to PCI, the benefit of the LIMA-to-LAD graft should be similar, regardless of whether a hybrid or conventional surgical approach is used. In reality, one would assume that HCR should be considered only when a high SYNTAX score is generated by LAD disease.

Where Should Hybrid Procedures Be Performed?
Although not essential for HCR, access to a designated suite facilitates complete revascularization in a single setting or at least completion angiography after CABG. The concept merges 2 or 3 major functions, traditionally housed in separate rooms, into a combined theater with enhanced capability, thereby providing the necessary imaging equipment to perform coronary and structural heart disease interventions, in addition to all the standard support for open cardiovascular surgery54 (Figure 3). The design and implementation of hybrid operating rooms is a complex multidisciplinary process requiring input from surgeons, interventional cardiologists, anesthesiologists, nursing, perfusion, and technical support staff. Essential equipment, including a fixed floor- or ceiling-mounted usually single-plane angiography unit, an operating table with full rotation capability, an anesthesia unit, a perfusion machine, and monitor, and control room must all be strategically positioned to facilitate safe yet dynamic transition between procedural modalities. For effective functioning, a floor space of 1000 to 1200 sq ft is recommended, making the simple “upgrading” of existing standard 600- to 700-sq ft operating rooms impossible. For this reason, hybrid suites require a significant investment and are justifiable only if productive and efficient use from a number of specialties is likely.

How Should HCR be Performed? The 1-Stage Versus 2-Stage Controversy
The optimal timing of each hybrid component has been heavily debated. All hybrid procedures are in reality staged, the only distinction being the duration of the staging. A
2-stage approach refers to CABG and PCI performed in 2 different operative suites, with the procedures separated by hours, days, or occasionally weeks but usually performed during the same hospital stay. In contrast, a 1-stage or simultaneous procedure refers to hybrid CABG and PCI performed in the same setting, usually in a custom-built operating room with a digital C arm to facilitate angioplasty. In most 1-stage procedures, the surgical arm is performed first, enabling the interventionalist to check the patency of the LIMA graft and anastomosis before embarking on DES implantation. This has the advantage of achieving complete revascularization in a single setting, thereby avoiding the risk of lesion destabilization between procedures separated by days or weeks. Not only is patient satisfaction higher with a single-procedure concept, but the overall cost is lower. The major disadvantage, however, is the need to balance the risk of perioperative bleeding related to dual antiplatelet therapy with achieving sufficient platelet inhibition to mitigate stent thrombosis. Moreover, the response of DES to heparin reversal with protamine at the end of surgical grafting has yet to be fully established.55 Other disadvantages include the risk of nephrotoxicity from the double insult of surgery and contrast injection and the possible time constraint when PCI is complex.

In the event of a 2-stage procedure, the issue of whether CABG should precede PCI or vice versa has been heavily debated. In our opinion, there is no right or wrong answer; rather, cases should be considered on individual merit and in the context of the clinical presentation. For example, in the setting of acute coronary syndrome with a non-LAD culprit, we believe that a 1-stage procedure is preferable, with PCI performed at the same time as CABG. However, when non-LAD lesions are stable, we recommend protecting the anterior wall with an LIMA-to-LAD graft before embarking on DES implantation in the forthcoming days when platelet inhibition is optimal. Although this approach provides an excellent opportunity to validate early graft patency, significant anastomotic problems might necessitate a second and, by all accounts, higher-risk surgical procedure. On the other hand, performing PCI first allows aggressive multivessel...
stenting in the knowledge that, should a complication arise or stenting be unsuccessful, further grafting can easily be performed. The main disadvantage is that subsequent CABG must be performed with high doses of antiplatelet therapy on board. In addition, the risks of performing PCI in an unprotected environment without the benefit of the LIMA-LAD graft are not insignificant, particularly in the setting of left ventricular dysfunction. On balance, therefore, this approach seems less favorable. The advantages and disadvantages of each strategy are summarized in Table 3.

Although the availability of a hybrid operating room is preferable for the successful implementation of an HCR program, most centers lack this dedicated facility. As a result, 2-stage procedures are more commonplace and in any case have the advantage of minimizing the bleeding risk when CABG precedes the initiation of antiplatelet therapy. This approach is certainly acceptable, provided that there is a consensus that should LIMA-related defects become apparent during angiographic validation, they should be corrected with a percutaneous approach. However, the psychological impact of a dual procedure separated by days or weeks with the potential for 2 hospital admissions is often a major boundary to implementation. Moreover, the 2-stage approach subjects patients to the additional risk of an adverse event during the interim period while incurring the cost of 2 procedures.

Despite the clear advantages of a 1-stage approach, it is our opinion that certain patients/anatomies are in fact more suited to a staged procedure and that the decision should be made on an individual basis. For example, in patients with SYNTAX scores in the third tertile, indicating the presence of complex and extensive disease, a 2-stage approach may be superior.

### The Antiplatelet Controversy

Balancing the risk of perioperative bleeding with the risk of stent thrombosis is a major challenge in HCR. Ensuring adequate platelet inhibition during and after stent implantation is critical to mitigating the risk of acute thrombosis, particularly with DES use. So far, there is no consensual agreement on optimal antiplatelet therapy, with practice varying widely across the literature. Most series reporting simultaneous HCR with DES have used a strategy of continuous aspirin with a single loading dose of 300 mg clopidogrel either after LIMA insertion or after PCI is completed. Despite a lack of platelet inhibition during the periprocedural period, a very low incidence of stent thrombosis has been reported (0%–7%; mean, 1.8%). Kiapi et al used bivalirudin instead of heparin and justified the periprocedural lack of antiplatelet cover by the extended anticoagulatory effect of bivalirudin. Stent thrombosis was higher in this series (7%) with 3.3% requiring resternotomy for bleeding. Zhao et al

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**Table 3. Advantages and Disadvantages of Hybrid Coronary Revascularization Strategies**

<table>
<thead>
<tr>
<th>HCR Strategy</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI followed by MICABG</td>
<td>Minimized risk of ischemia during MICABG</td>
<td>Risk of stent thrombosis unless adequate platelet inhibition during MICABG</td>
</tr>
<tr>
<td></td>
<td>Conventional CABG possible if PCI unsuccessful</td>
<td>Increased perioperative bleeding risk with dual antiplatelet therapy</td>
</tr>
<tr>
<td></td>
<td>Reduced surgical risk by treating non-LAD culprit in ACS</td>
<td>Angiographic validation of LIMA-to-LAD graft not possible</td>
</tr>
<tr>
<td>MICABG followed by PCI</td>
<td>Allows optimal platelet inhibition following PCI without perioperative bleeding risk</td>
<td>Potential need for higher-risk redo CABG if PCI unsuccessful</td>
</tr>
<tr>
<td></td>
<td>Angiographic validation of LIMA-to-LAD graft</td>
<td>Psychological impact of 2 procedures</td>
</tr>
<tr>
<td></td>
<td>Protection of anterior wall during high risk PCI of non-LAD vessels</td>
<td>Additional cost of 2 procedures</td>
</tr>
<tr>
<td>Simultaneous MICABG/PCI</td>
<td>Immediate angiographic validation of LIMA-to-LAD graft</td>
<td>Increased perioperative bleeding risk with dual antiplatelet therapy</td>
</tr>
<tr>
<td></td>
<td>Aggressive PCI of high-risk lesions with anterior wall protection</td>
<td>Risk of stent thrombosis associated with inadequate platelet inhibition during PCI if not loaded preoperatively, inflammatory response of surgery, and heparin reversal at end of procedure</td>
</tr>
<tr>
<td></td>
<td>Complete revascularization in single procedure; patient satisfaction</td>
<td>Risk of nephrotoxicity related to long procedure times, surgical insult, and contrast</td>
</tr>
<tr>
<td></td>
<td>Conventional CABG possible if PCI unsuccessful</td>
<td>Possible time constraint, particularly with learning curve</td>
</tr>
<tr>
<td></td>
<td>Avoids risk of lesion destabilization between staged procedures</td>
<td>Logistical and economic issues associated with construction of hybrid room</td>
</tr>
</tbody>
</table>

HCR indicates hybrid coronary revascularization; PCI, percutaneous coronary intervention; MICABG, minimally invasive coronary artery bypass grafting; CABG, coronary artery bypass graft surgery; LAD, left anterior descending artery; ACS, acute coronary syndrome; and LIMA, left internal mammary artery.
Hybrid Valve Replacement/PCI

The concept of hybrid surgery is not unique to coronary revascularization and has been successfully applied to valvular disease when coexisting with coronary artery disease, carotid disease, and complex thoracic aortic pathology, and even to the management of complex arrhythmias. Although discussion of these is beyond the scope of this article, the rapid growth of transcatheter techniques is such that hybrid valve procedures cannot be overlooked. The rationale is to substitute PCI for conventional CABG, thereby converting a sternotomy-requiring procedure into an isolated valve procedure that can be performed with minimally invasive techniques. The requirement for concomitant coronary revascularization immediately doubles the mortality of isolated valve surgery. Moreover, in selected patients with acute coronary syndrome, poor conduit or target vessel quality, significant left ventricular dysfunction, or previous sternotomy, the risk of a conventional “double procedure” can be prohibitively high, with mortality approaching 20%. A hybrid approach simplifies the operation into 2 lower-risk procedures, with initial PCI performed selectively, usually to a culprit vessel, and serves to stabilize a patient before minimally invasive valve surgery. In this way, hybrid approaches have been shown to improve outcomes and to lower mortality in high-risk patients.

Again, there have been no randomized trials for hybrid valve surgery, with only a small number of isolated single-center series published in the literature. In a small series of 18 elderly patients who underwent PCI with DES followed within 24 hours by minimally invasive aortic valve replacement, Brinster et al reported a lower-than-predicted 5.5% in-hospital mortality and an impressive 95% survival at the 19-month follow-up. In another series of 26 very-high-risk patients with aortic valve disease, Byrne et al reported an operative mortality of only 3.8%, dramatically lower than the 22% predicted by the Society of Thoracic Surgery. Given that 92% of the PCI and staged valve procedures were in the setting of acute coronary syndrome, 15% in cardiogenic shock, and that almost 50% of patients underwent redo valve surgery, these results are certainly impressive. The same group recently reported 39 patients undergoing 1- and 2-stage PCI and minimally invasive mitral valve replacement in a similarly high-risk patient cohort, with an operative mortality again significantly lower than predicted by the Society of Thoracic Surgery (2.6% versus 14%).

In our opinion, the 2 most important scenarios for a hybrid valve approach are the requirement for valve surgery in the setting of acute coronary syndrome and reoperative valve surgery in the presence of concomitant coronary artery disease. The facility to avoid redo sternotomy and, most important, the potential disruption of a patent LIMA graft cannot be overemphasized. Indeed, it has been reported that in valvular patients, sternal reentry has a 4% risk of complication, attributed mainly to the proximity of the often enlarged heart to the posterior sternum. Furthermore, pericardial adhesions make exposure of the mitral valve particularly difficult by redo sternotomy, with significantly better visualization achieved with a minimally invasive right thoracotomy approach. With the increased risk of mortality, morbidity, sternal dehiscence, and bleeding, sternal reentry should, when a viable alternative exists, be avoided.

As with HCR, concerns exist regarding the impact of antiplatelet therapy on perioperative bleeding. Although most published series have undertaken a 2-stage, early PCI approach with the valvular component performed within hours or days and under full platelet inhibition, reports of perioperative bleeding have been variable. Certainly, Byrne et al reported higher-than-expected rates of reoperation for bleeding (8%) and transfusion requirements, yet in their series, Brinster et al reported lower use of blood products with no cases of reoperation. Even with the small numbers involved, it is likely that the timing of surgery is strongly predictive of bleeding complications, with patients in the latter series undergoing minimally invasive aortic valve replacement within hours of PCI when platelet inhibition may have been submaximal. Again, with newer-generation thienopyridine and nonthienopyridine agents, which can quickly be switched on and off, this risk may be reduced significantly. Furthermore, the availability of a hybrid operating room or at least the facility for shorter staging between procedures would
enable minimally invasive aortic valve replacement to be performed before the full platelet-inhibitory effect of clopidogrel is reached.

Aside from the antiplatelet controversy, there are several limitations of hybrid valve surgery as things stand. First, unlike HCR, there is no option to perform minimally invasive valve surgery off pump; therefore, the advantages of avoiding CPB cannot be extrapolated. This, combined with longer operating times and the technical challenge associated with limited visualization, has been a major barrier to widespread implementation. However, it is our opinion that with the growth of transcatheter aortic valve implantation, particularly in the context of the Placement of Aortic Transcatheter Valve Trial (PARTNER) trial, which has demonstrated a survival advantage over medical therapy at 1 year, and, more recently, noninferiority compared with conventional AVR surgery at 1 year, hybrid transcatheter aortic valve implantation/PCI will be a huge step forward in the treatment of high-risk patients with concomitant valvular and coronary disease. Furthermore, we believe that this concept will, before too long, be extended to lower-risk groups of patients who would otherwise be suitable for a completely surgical strategy.

**Conclusion**

Rapid advances in stent technology along with improvements in operator skill have enabled most patients with complex coronary artery disease to be managed percutaneously. The concept of HCR stems from the fact that despite these advances, the LIMA-to-LAD graft provides an unrivalled prognostic advantage over DES, yet DES have superior longevity compared with SVGs on non-LAD vessels. Arguably, HCR is the most evidence-based approach to complete revascularization in multivessel disease. It provides the best of both worlds.

HCR provides an excellent option for selected patients with complex proximal LAD or left main stem disease, which is poorly amenable to successful PCI. Although 1-stage HCR has clear advantages in terms of logistics, control of platelet inhibition, patient satisfaction, and reduced long-term costs, it is justifiable only in centers with a demanding hybrid practice. We believe that widespread initiation of a successful hybrid program hinges on the adoption of a multidisciplinary approach to hybrid thinking, with good collaboration between interventional cardiologists and cardiac surgeons. Furthermore, it is critical that the expertise of both parties is comparable because implementing hybrid practice in a center more experienced in 1 revascularization modality than the other could be detrimental. Ultimately, we believe that the incorporation of HCR into global revascularization guidelines, along with the development of standardized guidelines for antiplatelet therapy, is crucial to expanding interest in an integrated approach. Indeed, we envisage that the emergence of newer antiplatelet agents with rapid onset and reversibility will enable the practice of HCR to be safer and more controlled in the future.

Hybrid valve surgery is a viable option for high-risk patients, particularly in the acute setting or when redo sternotomy is necessary. It is our opinion, however, that the transcatheter approach to valve implantation, combined with PCI, provides the most evidence-based approach to hybrid valve surgery and that indications will, before long, be expanded to include patients at much lower overall risk.

**Disclosures**

None.

**References**


Response to Shannon et al

Marzia Leacche, MD; David X. Zhao, MD; Ramanan Umakanthan, MD; John G. Byrne, MD

Hybrid coronary revascularization (HCR) combines the benefits of coronary artery bypass graft surgery (long-lasting patency of the left internal mammary artery–left anterior descending artery graft) with the benefits of percutaneous coronary intervention with drug-eluting stents of non–left anterior descending artery vessels. In this approach, saphenous vein graft conduits are substituted by drug-eluting stents. Patency rates of drug-eluting stents compare favorably to patency rates of saphenous vein graft. Moreover, the left internal mammary artery–left anterior descending artery graft can be performed through a minimally invasive approach. Thus, is HCR an ideal substitute for coronary artery bypass surgery? Despite the encouraging results from several experienced centers, HCR remains a surgical approach for few patients and rarely adopted. We read with great interest the review of HCR by Dr Shannon et al. As outlined by the authors, the Task Force on the Use of Antiplatelet Agents in Patients With Atherosclerotic Cardiovascular Disease of the European Society of Cardiology. Eur Heart J. 2003;107:2908–2913.

Hybrid Procedures Have Proven Clinical Utility and Are the Wave of the Future
Joanne Shannon, Antonio Colombo and Ottavio Alfieri

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