

Published in final edited form as:

*Am Heart J.* 2008 April ; 155(4): 661–667. doi:10.1016/j.ahj.2007.12.032.

## Simultaneous “hybrid” percutaneous coronary intervention and minimally invasive surgical bypass grafting: Feasibility, safety, and clinical outcomes

Barry Reicher, MD<sup>a</sup>, Robert S. Poston, MD<sup>b</sup>, Mandeep R. Mehra, MD<sup>a</sup>, Ashish Joshi<sup>b</sup>, Patrick Odonkor<sup>b</sup>, Zachary Kon<sup>b</sup>, Peter A. Reyes, MD<sup>a</sup>, and David A. Zimrin, MD<sup>a</sup>

<sup>a</sup> *Division of Cardiology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD* and <sup>b</sup> *Division of Cardiothoracic Surgery, Department of Surgery, University of Maryland School of Medicine, Baltimore, MD*

### Abstract

Surgical and percutaneous coronary artery intervention revascularization are traditionally considered isolated options. A simultaneous hybrid approach may allow an opportunity to match the best strategy for a particular anatomic lesion. Concerns regarding safety and feasibility of such an approach exist. We examined the safety, feasibility, and early outcomes of a simultaneous hybrid revascularization strategy (minimally invasive direct coronary bypass grafting of the left anterior descending [LAD] artery and drug-eluting stent [DES] to non-LAD lesions) in 13 patients with multivessel coronary artery disease that underwent left internal mammary artery to LAD minimally invasive direct coronary bypass performed through a lateral thoracotomy, followed by stenting of non-LAD lesions, in a fluoroscopy-equipped operating room. Assessment of coagulation parameters was also undertaken. In-hospital and postdischarge outcomes of these patients were compared to a group of 26 propensity score matched parallel controls that underwent standard off-pump coronary artery bypass. Baseline characteristics were similar in both groups. All hybrid patients were successfully treated with DES and no in-hospital mortality occurred in either group. Hybrid patients had a shorter length of stay ( $3.6 \pm 1.5$  vs  $6.3 \pm 2.3$  days,  $P < .0001$ ) and intubation times ( $0.5 \pm 1.3$  vs  $11.7 \pm 9.6$  hours,  $P < .02$ ). Despite aggressive anticoagulation and confirmed platelet inhibition, hybrid patients had less blood loss ( $581 \pm 402$  vs  $1242 \pm 941$  mL,  $P < .05$ ) and decreased transfusions ( $0.33 \pm 0.49$  vs  $1.47 \pm 1.53$  U,  $P < .01$ ). Six-month angiographic vessel patency and major adverse cardiac events were similar in the hybrid and off-pump coronary artery bypass groups. A simultaneous hybrid approach consisting of minimally invasive coronary artery bypass grafting with left internal mammary artery to LAD combined with revascularization of the remaining coronary targets using percutaneous coronary artery intervention with DES is a feasible option accomplished with acceptable clinical outcomes without increased bleeding risk.

Traditionally, clinicians view percutaneous coronary intervention or surgical bypass as mutually exclusive options to be offered for revascularization of multivessel coronary artery disease (CAD). Each strategy is associated with advantages and disadvantages: Percutaneous coronary interventions using stenting techniques can be accomplished with minimal procedural risk, early facilitation of ambulatory discharge, and in the current era of drug-eluting stents, a lower target vessel failure rate.<sup>1</sup> In multivessel disease, however, coronary bypass surgery continues to offer long-term advantages over percutaneous coronary intervention, largely

attributable to the use of the left internal mammary artery (LIMA) graft as a durable conduit which provides protection against progression of disease proximal to the graft anastomosis.<sup>2,3</sup> On the other hand, saphenous vein graft (SVG) conduits have demonstrated inconsistent short-term patency rates and limited long-term durability.<sup>2</sup>

A “hybrid” approach has been undertaken that stages the surgical and percutaneous coronary intervention by separating them temporally.<sup>4</sup> More recently, a simultaneous “hybrid” procedure that combines the advantages of a minimally invasive LIMA conduit alongside with percutaneous revascularization using drug-eluting stents has been proposed, but safety and logistical concerns have been expressed.<sup>5</sup> These practical concerns include the need for close cooperation of surgical and interventional groups, logistical concerns of timing and sequencing of the procedures, and the use of aggressive antiplatelet therapy during percutaneous intervention that might complicate bleeding in the surgical patient.

The current study was designed to determine the safety, feasibility, and clinical outcomes of a simultaneous “hybrid” combining surgical and catheter-based intervention for treating multivessel coronary disease at the same operative setting. In this approach, we used a specially designed operating room with radiographic capability allowing the minimally invasive surgical (LIMA grafting to the left anterior descending [LAD]) and percutaneous coronary intervention (non-LAD targets revascularized with drug-eluting stent [DES]) to be accomplished concurrently along with intraoperative angiographic assessment of the LIMA graft. In particular, we also investigated the challenge inherent in effective platelet suppressive therapy and its impact on bleeding outcomes and vessel patency during the peri-operative and postdischarge period using this novel approach.

## Methods

### Study design

Thirteen consecutive patients underwent the simultaneous hybrid procedure at our institution, from January 2005 through September 2006. Using a prospective case-controlled study design, we also developed a propensity score matched parallel control group of 26 patients that underwent off-pump coronary artery bypass (OPCAB) via sternotomy matched by demographics, risk factors, comorbidities, coronary anatomy, and medical therapy (the same surgeon performed all cases in both groups). These matching criteria included known risk markers for outcomes with surgical revascularization (Table I).

Inclusion criteria for the hybrid procedure were presence of multivessel CAD that involved  $\geq 70\%$  LAD obstruction judged a suitable surgical target and  $\geq 70\%$  non-LAD coronary lesion (s) suitable for percutaneous coronary artery intervention (PCI; adjudicated by 2 interventionalists and 1 surgeon). Hemodynamic instability, acute coronary syndromes, or situations in which complete revascularization was not possible served as exclusion criteria.

Patients were followed daily until the end of their hospital stay. Demographics, preoperative risk factors and medications, and intra- and postoperative data were prospectively recorded onto Teleform case report forms (TELEform Elite; Cardiff Software Ltd, Vista, CA), electronically scanned, and imported into a relational database. All patients provided informed consent to be enrolled into this study (UMB IRB #25350).

### Procedural techniques

**Surgical bypass**—Patients underwent coronary artery bypass (LIMA to LAD) via a small thoracotomy, without use of cardiopulmonary bypass. “Hybrid” patients were intubated with a double lumen endotracheal tube to allow for collapse of the left lung. The surgical portion of the procedure was initiated first in all patients via an 8- to 10-cm anterior lateral thoracotomy

in the fourth intercostal space. The in situ LIMA was exposed using the LIMA lift retractor (Genzyme Cardiovascular, Cambridge, MA) and the conduit harvested under direct vision using a combination of electrocautery and vascular clips to secure the intercostal branches. Selective use of an intracoronary shunt was used during the LIMA-LAD anastomosis based on the findings of a 1-minute test occlusion of the LAD while monitoring for changes suggestive of anterior ischemia. The anastomosis was performed on the beating heart with the aid of a stabilizing device (Octopus 4.3, Medtronic, Inc, Minneapolis, MN) using 7-0 prolene. Using an operating room with cineangiographic equipment (Toshiba Infinix Digital Cinefluoroscopy Unit, Japan), we performed PCI and a follow-up angiogram to confirm patency of the LIMA graft at the same surgical setting. Anesthesia management was directed toward extubation in the operating room for the “hybrid” patients and a “fast-track” protocol for extubation of OPCAB patients within 6 hours of arrival to the intensive care unit.

The OPCAB control group was approached via median sternotomy. Conduits included the LIMA and saphenous vein, which was harvested endoscopically (VasoView 5, Guidant Systems, Inc, Minneapolis, MN). The proximal aortosaphenous anastomoses were performed first using a partial occluding aortic clamp, and distal anastomoses were performed using suction-based exposure and a stabilizing device (Octopus 4.3). Blood flow and flow waveform were measured in each graft using transit time ultrasound (Medistim, Inc). Those grafts with flow <10 mL/min and PI >5 (n = 1) or with a stenotic anastomotic appearance on intraoperative angiography (n = 1) underwent revision of the distal anastomosis.

**Percutaneous coronary artery intervention technique**—After completion of surgical grafting, PCI was accomplished via a femoral artery approach in 12 of the 13 patients. In 1 patient, severe peripheral vascular disease necessitated the use of brachial artery access. Guiding catheter, guidewire, and stent selection as well as pre- and postdilation were left to the discretion of the operator. Drug-eluting stents were implanted in all patients. Both the Cypher sirolimus-eluting stent (SES; Cordis Corporation, Miami Lakes, FL) and the Taxus paclitaxel-eluting stent (DES) (Boston Scientific Inc, Natick, MA) were used. Angiographic confirmation of vessel patency, including the surgical anastomosis, was performed in all patients.

### **Antithrombotic therapy**

For both hybrid and OPCAB patients, unfractionated heparin was given intraoperatively at a dose calculated to obtain a kaolin-based activated clotting time (ACT) >300 seconds and heparin level >2 IU/mL according to heparin-protamine titration assay (HMS heparin assay cartridges, Medtronic). At completion of OPCAB, heparin was reversed by half the dose of protamine calculated using the heparin-protamine titration assay. No protamine was used to reverse the heparin effect in hybrid patients. Aspirin (325 mg once a day) was given to all patients before and continuing through the date of surgery with the first postoperative dose immediately on arrival to the ICU. A clopidogrel loading dose of 300 mg was given to hybrid patients on arrival to the ICU via nasogastric tube followed by 75 mg daily thereafter. GPIIb/IIIa antagonists were not used.

### **Hemostatic monitoring**

Platelet function was assessed on citrated blood samples obtained preoperatively and on postoperative hour 1 and days 1 and 3 in all patients using 3 assays: (1) thrombelastography (TEG, Haemoscope, Niles, IL): the maximum amplitude (MA) parameter derived from the TEG was used to determine overall platelet activity; (2) whole blood aggregometry (Chronolog, Havertown, PA): the response to clopidogrel was documented by monitoring the perioperative platelet response to adenosine-diphosphate (ADP; 5 µg/mL); and (3) serum 11-dehydro-TXB2 levels (for aspirin response) using an ELISA kit (Assay Designs Inc, Ann

Arbor, MI); platelet poor plasma was analyzed to assess aspirin resistance as described previously.<sup>6</sup> Standard tests of coagulation (international normalized ratio, partial thromboplastin time, fibrinogen levels, and quantitative d-dimer levels) were also obtained at the same time points from citrated blood samples.

### Clinical and economic end points

The primary end points of this study were the comparison of hospital outcomes including lengths of stay and intubation, blood transfusion requirements, and costs in the hybrid versus OPCAB groups and postdischarge outcomes. The secondary end points were to establish the safety of performing the hybrid in a simultaneous manner by documenting successful early suppression of platelet ADP responsiveness without significantly increasing the risks of bleeding (ie, chest tube output, transfusion requirement) and thrombosis (ie, early LIMA and stent patency confirmed by predischarge computed tomography [CT] angiography).

**Graft patency**—Predischarge LIMA graft patency was determined by blinded review of a 16-detector row, CT angiography scan (420-millisecond rotation, 100–150 mL contrast agent IV at 5 mL/s) using retrospective electrocardiogram gating. Patency was defined as any flow through the entire graft regardless of the presence of stenosis. The graft was classified as nonpatent if a stump was seen or if there was no contrast in an area known by operative report to contain a graft, a recently validated definition of postoperative bypass graft failure.<sup>7</sup>

**Inhospital outcomes**—Hospital length of stay, duration of critical care, inhospital complications (particularly major bleeding complications and renal function), and discharge disposition were analyzed for all patients.

**Cost analysis**—Variable costs were used to define postoperative hospitalization costs for each patient, including supplies, drugs, transfusions, and the salary of staff that provided direct care during the index hospitalization. Readmissions ( $n = 3$ ) and preoperative costs were excluded from analysis. The mean total costs were calculated and compared between groups.

**Postdischarge outcomes**—We undertook angiographic follow-up (invasive coronary angiography to assess vessel and graft patency for clinically indicated situations or CT angiography at 6 months in both groups). Six-month major adverse cardiac events were evaluated, defined as cardiac readmissions, acute coronary syndrome, chest pain requiring angiography, or death.

### Statistical analysis

Baseline characteristics listed in Table I were independent variables in the multivariate logistic regression model to create the propensity score. Thirteen patients undergoing simultaneous hybrid procedure were matched on nearest propensity score (range 0.15–0.87) using greedy matching techniques with 26 OPCAB-treated patients. Control patients with missing variables necessary for calculation of the propensity score were excluded from this analysis. No interaction terms were used. The C-statistics for the propensity model was 0.68. All results were analyzed with SAS 8.2 software (SAS Institute, Cary, NC). Tests that were obtained serially in each group were compared by calculating the area under the concentration/volume-time curve using the trapezoidal method. Differences in the area under the curve were compared by Student *t* test. A *P* value  $\leq 0.05$  was considered statistically significant. Statistical analysis was performed using the InStat statistical package (InStat) with the assistance of a statistician.

## Results

### Baseline characteristics and coronary anatomy

The group of 13 consecutive patients that underwent the simultaneous hybrid procedure and the matched control group of 26 OPCAB patients were similar in all baseline characteristics (Table I). In addition to LIMA grafting, hybrid patients underwent DES placement either in the left main involving the ostium of the left circumflex (62%), within the circumflex proper and its branches (38%), and/or the right coronary artery (15%) distributions. Seventy-seven percent of the lesions treated met the American College of Cardiology/American Heart Association criterion for high-risk type C lesion morphology. The mean number of stents placed was 1.7 (range 1–3). Identical number of PES (11/22) or SES (11/22) was used (Table II). One patient required intraoperative revision of the LIMA anastomosis as angiography demonstrated a suboptimal result. On follow-up, this graft was found to remain patent.

### Coagulation parameters and platelet function

As the result of different protocols for heparin reversal, there was a significant difference in the ACT measured immediately at the completion of the case for hybrid patients compared to the OPCAB group (ACT  $235 \pm 56$  vs.  $132 \pm 23$  seconds,  $P < .001$ ). With the exception of platelet ADP response, there were no significant differences noted for any of the standard coagulation or platelet function tests between groups at any of the measured time points, including day 3 when differences in coagulation status between groups are most likely to be present (Table III).<sup>7</sup> As a result of the postoperative administration of clopidogrel solely to hybrid patients, there was a significant reduction in platelet responsiveness to ADP in whole blood aggregometry assays obtained on days 1 and 3 (Figure 1).

### Inhospital outcomes

No in-hospital mortality occurred in either group. One patient in the OPCAB control group was found to have an asymptomatic failure of an SVG detected on pre-discharge CT angiography. All LIMA grafts were found to be patent in both groups at the time of discharge, as previously confirmed intraoperatively by angiography. Compared to OPCAB, the hybrid group demonstrated significantly shorter lengths of hospital stay and intubation. The hybrid group also had a shorter ICU length of stay and less perioperative blood loss, although these differences did not reach statistical significance (Table IV). Despite more aggressive antithrombotic therapy, hybrid patients demonstrated significantly less requirement for transfusion (21% vs 59% transfused,  $P < .05$ ), fewer units of RBC required, and a trend toward less chest tube output over the initial 24 hours (Table IV). However, in part due to the costs of DES for the hybrid patients, there was a nonsignificant increase in total hospital costs versus the OPCAB group ( $\$34980 \pm \$13460$  vs  $\$30843 \pm \$12221$ ,  $P = \text{NS}$ ).

### Postdischarge clinical outcomes

Of the 13 patients included in the hybrid group, we performed CT angiography at 6 months in 6 (mean 14 months from initial surgery). In addition, 4 patients underwent conventional angiography: 2 for atypical symptoms that proved to have patent stents/graft, 1 for failed LIMA with patent stent, and 1 for failed stent with patent LIMA. The single stent thrombosis case occurred in a patient with adequate responsiveness to antiplatelet therapy and was deemed technical (occurred in a bifurcation lesion). The remaining 3 patients did not undergo angiography but had no major adverse cardiac events on 6-month follow-up. A comparison of vessel patency with 18 of 26 patients in the OPCAB group that underwent CT angiography demonstrated no significant difference in outcome (Figure 2).

## Discussion

The principal findings of this investigation support the perioperative safety and feasibility of a simultaneous “hybrid” strategy of combining minimally invasive coronary artery bypass grafting (CABG) and catheter-based coronary intervention as an alternative to conventional open-sternum OPCAB. In this prospectively case-controlled, parallel cohort study, we also established that use of a specially designed operating room that allows coronary artery stenting and bypass grafting in a single setting results in better inhospital outcomes compared to OPCAB. Interestingly, concerns that a simultaneous hybrid approach that requires clopidogrel therapy to preserve stenting outcomes would result in increased bleeding were unfounded. An analysis of vascular patency and mid-term clinical outcomes (6 months) revealed no significant differences in the hybrid and OPCAB strategy.

Prior studies have alluded to the presence of clopidogrel hypo-responsiveness in the early postoperative period after conventional coronary artery bypass surgery.<sup>8</sup> We documented significant blockade of platelet ADP receptors in response to clopidogrel use on the first morning after the hybrid procedure.<sup>9</sup> Our findings that blood loss and transfusion requirements were reduced in hybrid patients compared to OPCAB corroborate other studies suggesting that clopidogrel has minimal impact on hemostasis when introduced immediately after<sup>10</sup> as compared to before<sup>11</sup> the surgical procedure. Importantly, the lower bleeding risk in the presence of clopidogrel demonstrated in our study was likely due to the less invasive nature of the minimally invasive direct coronary bypass (MIDCAB) compared to OPCAB. Data suggest that P2Y<sub>12</sub> inhibition is most effective when introduced before PCI.<sup>12</sup> If bleeding risk is in fact reduced by this approach, clopidogrel pretreatment would likely be safe and potentially beneficial. The therapeutic window of clopidogrel pretreatment as well as use of higher doses than those used in our study in patients undergoing hybrid revascularization has not been established and will require further study.

Renewed interest in the hybrid concept, first introduced in the mid-1990s,<sup>13</sup> is due to the abundant evidence of the long-term benefits of the LIMA graft<sup>3,14</sup> and the reduced restenosis rates using DES.<sup>15–17</sup> In addition, recent improvements in enabling technology for performing beating heart surgery such as suction-based vessel stabilization have improved the efficacy of the MIDCAB procedure.<sup>18</sup> In the hybrid, the advantage of the most durable graft (LIMA) placed to the most important vessel (LAD) is gained without a stenotomy, thereby decreasing surgical morbidity. The use of the LIMA graft reduces the number of stents required, which may reduce the risk of thrombosis and improve long-term outcomes when compared to the use of multivessel stenting for full revascularization or may facilitate performance of high-risk revascularization in a single setting.<sup>19</sup>

Performing MIDCAB and PCI simultaneously in a single setting (as described in this report) has advantages compared to a “staged” procedure in which MIDCAB and PCI are performed at separate locations and/or different days.<sup>5</sup> First, performing these procedures in a single setting is more convenient to the patient and may reduce costs. In addition, technical concerns with each part of the procedure are more easily addressed: The adequacy of the LIMA-LAD anastomosis performed via the mini-thoracotomy is assessed by intraoperative angiography. This enables immediate revision of the LIMA graft, as was done in one of our patients. Inability to place stents or complications of PCI can be dealt with by surgical intervention immediately, although this did not occur in our series. As compared to PCI before surgery, the simultaneous strategy makes it possible to delay the initiation of clopidogrel until after internal mammary artery harvest. Although recent reports have considered this hybrid approach, they were either not compared to a control group, had inconsistent standardization of the procedure (whether PCI was performed before or after the surgery), or did not assess antithrombotic therapy to ensure platelet hypo-responsiveness.<sup>20,21</sup>

All-arterial CABG is often considered to be the surgical treatment of choice for multivessel CAD.<sup>22</sup> Many of the hybrid patients in this report might have been candidates for this treatment. However, despite the theoretical potential for long-term benefit, multiarterial grafting is used infrequently by most cardiac surgeons because, other than the LIMA, the best choices for arterial conduits remain controversial. For example, the right internal mammary artery is used in a minority of cases due to concerns about poor healing of the sternal wound after harvest,<sup>23</sup> and the radial artery has shown inconsistent early patency results.<sup>24</sup> As a result, a recent survey of the Society of Thoracic Surgeons database indicates that 95% of CABG cases nationwide involve the grafting of multiple saphenous vein segments. The hybrid procedure may be a more practical solution for avoiding the well-known limitations of the SVG than all-arterial grafting. In clinical follow-up, our hybrid patients demonstrated excellent graft patency with a single case of LIMA failure (de novo disease close to the anastomosis, not in the graft itself, possibly due to plaque disruption) and one case of stent thrombosis (overlapping stents in the circumflex).

Current data suggest that lesion and procedural complexity increase the risk of both early and late stent thromboses.<sup>25,26</sup> The specter of late stent thrombosis is particularly relevant when drug-eluting stent platforms are used.<sup>27,28</sup> We have found that this new approach minimizes the number of stents and complex lesion stenting.<sup>19</sup>

There are several limitations to this study. Although we accounted for most variables that ascertain peri-operative risk, it is conceivable that use of matched controls could allow confounding covariates to enter that were unaccounted for in the analysis, a potential limitation that randomization could have avoided. The patient population enrolled for the hybrid procedure initially consisted of those patients with few traditional options. Such patients were poor candidates for multi-vessel PCI (eg, left main trifurcation disease, long chronic LAD occlusions) and had been turned down for conventional bypass surgery (eg, no available additional arterial grafts, pulmonary problems, or other comorbidities). This is reflected in the longer than usual hospital stays of patients in the control group. Although this limitation decreases generalizability, it may also offer an advantage for consideration of those patients considered poor candidates for either PCI or surgical procedures. The control group did not undergo intraoperative angiography as in the treatment group. However, all grafts were analyzed by intraoperative flow readings, a validated technique for confirming anastomotic quality. Given the close correlation between abnormalities in flow readings compared to angiographic findings in prior studies, we do not feel that adding intraoperative angiography to the OPCAB group would have altered our study's conclusions. Conversely, immediate intraoperative angiography may result in false-positive findings that do not correlate with long-term patency and are simply a result of edema and operative handling.

In conclusion, we report that a simultaneous hybrid approach consisting of minimally invasive CABG with LIMA to LAD combined with revascularization of the remaining coronary targets using PCI with DES is a feasible option for the treatment of selected patients with multivessel CAD. In particular, concerns that bleeding risk could be heightened by the presence of clopidogrel in the peri-operative setting and that clopidogrel might be ineffective postoperatively were dispelled by this study. Importantly, vascular patency and 6-month clinical outcomes were well preserved with this strategy. Further study will be necessary both to help identify those patients who would most benefit from this approach and to assess the long-term outcomes of this novel strategy.

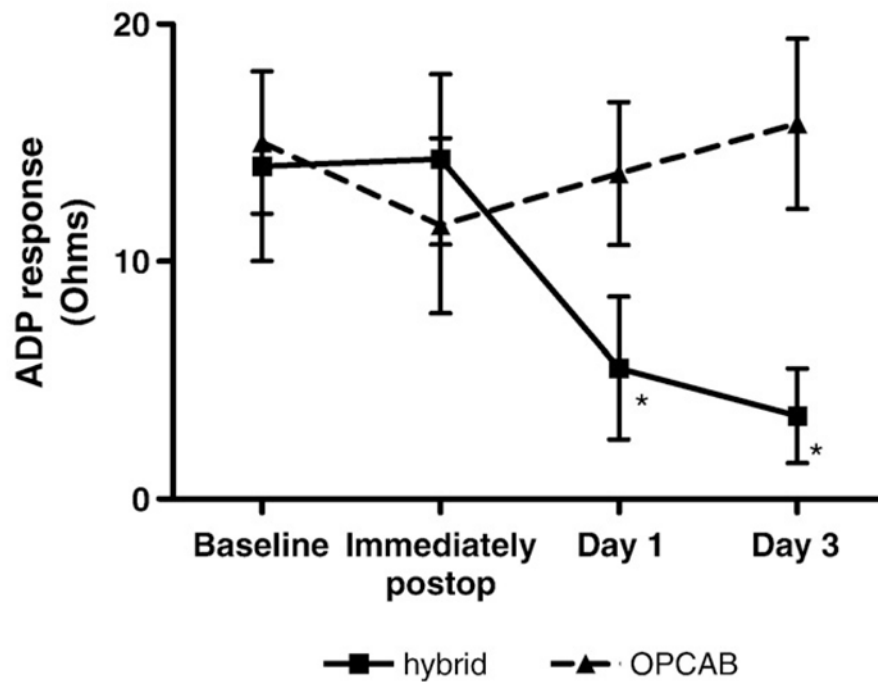
## References

1. Salam AM, Al Suwaidi J, Holmes DR Jr. Drug-eluting coronary stents. *Curr Probl Cardiol* 2006;31:8-119. [PubMed: 16389102]

2. Guyton RA. Coronary artery bypass is superior to drug-eluting stents in multivessel coronary artery disease. *Ann Thorac Surg* 2006;81:1949–57. [PubMed: 16731112]
3. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal mammary artery graft on 10-year survival and other cardiac events. *N Engl J Med* 1986;314:1–6. [PubMed: 3484393]
4. Amodeo VJ, Donias HW, Dancona G, et al. The hybrid approach to coronary artery revascularization: minimally invasive direct coronary artery bypass with percutaneous coronary intervention. *Angiology* 2002;53:665–9. [PubMed: 12463619]
5. Kiaii B, McClure RS, Kostuk WJ, et al. Concurrent robotic hybrid revascularization using an enhanced operative suite. *Chest* 2005;128:4046–8. [PubMed: 16354880]
6. Poston RS, White C, Gu J, et al. Endothelial injury and acquired aspirin resistance promote regional thrombin formation and early vein graft failure after coronary artery bypass. *J Thorac Cardiovasc Surg* 2006;131:122–30. [PubMed: 16399303]
7. Frazier A, Qureshi F, White C, et al. Coronary artery bypass grafts: MDCT assessment in the early and late post-operative setting. *Radiographics* 2005;25:881–96. [PubMed: 16009813]
8. Lim E, Cornelissen J, Routledge T, et al. Clopidogrel did not inhibit platelet function early after coronary bypass surgery: a prospective randomized trial. *J Thorac Cardiovasc Surg* 2004;128:432–5. [PubMed: 15354104]
9. Ivandic BT, Schlick P, Staritz P, et al. Determination of clopidogrel resistance by whole blood platelet aggregometry and inhibitors of the P2Y12 receptor. *Clin Chem* 2006;52:383–8. [PubMed: 16423907]
10. Halkos ME, Cooper WA, Petersen R, et al. Early administration of clopidogrel is safe after off-pump coronary artery bypass surgery. *Ann Thorac Surg* 2006;81:815–9. [PubMed: 16488678]
11. Ascione R, Ghosh A, Rogers CA, et al. In-hospital patients exposed to clopidogrel before coronary artery bypass graft surgery: a word of caution. *Ann Thorac Surg* 2005;79:1210–6. [PubMed: 15797051]
12. Claeys MJ. Antiplatelet therapy for elective coronary stenting: a moving target. *Semin Vasc Med* 2003;3:415–8. [PubMed: 15199448]
13. Angelini GD, Wilde P, Salerno TA, et al. Integrated left small thoracotomy and angioplasty for multivessel coronary artery revascularisation. *Lancet* 1996;347:757–8. [PubMed: 8602013]
14. Diegeler A, Thiele H, Falk V, et al. Comparison of stenting with minimally invasive bypass surgery for stenosis of the left anterior descending coronary artery. *N Engl J Med* 2002;347:61–6.
15. Morice M, Serruys PW, Sousa JE, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med* 2002;346:1773–80. [PubMed: 12050336]
16. Moses JW, Leon MB, Popma JJ, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003;349:1315–23. [PubMed: 14523139]
17. Stone GW, Ellis SG, Cox DA, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med* 2004;350:221–31. [PubMed: 14724301]
18. D'Ancona G, Vassiliades TA, Boyd WD, et al. Is hybrid coronary revascularization favored by cardiologists or cardiac surgeons? *Heart Surg Forum* 2002;5:393–5. [PubMed: 12538124]
19. Zimrin D, Reyes PA, Reicher B, et al. A hybrid alternative for high risk left main disease. *Catheter Cardiovasc Interv* 2006;69:123–7. [PubMed: 17139676]
20. Davidavicius G, Van Praet F, Mansour S, et al. Hybrid revascularization strategy: a pilot study on the association of robotically enhanced minimally invasive direct coronary artery bypass surgery and fractional-flow-reserve-guided percutaneous coronary intervention. *Circulation* 2005;112(9 Suppl):I317–22. [PubMed: 16159838]
21. Katz MR, Van Praet F, de Canniere D, et al. Integrated coronary revascularization: percutaneous coronary intervention plus robotic totally endoscopic coronary artery bypass. *Circulation* 2006;114(1 Suppl):I473–6. [PubMed: 16820621]
22. Herz I, Moshkovitz Y, Loberman D, et al. Drug-eluting stents versus bilateral internal thoracic grafting for multivessel coronary disease. *Ann Thorac Surg* 2005;80:2086–90. [PubMed: 16305850]
23. Sofer D, Gurevitch J, Shapira I, et al. Sternal wound infections in patients after coronary artery bypass grafting using bilateral skeletonized internal mammary arteries. *Ann Surg* 1999;229:585–90. [PubMed: 10203094]



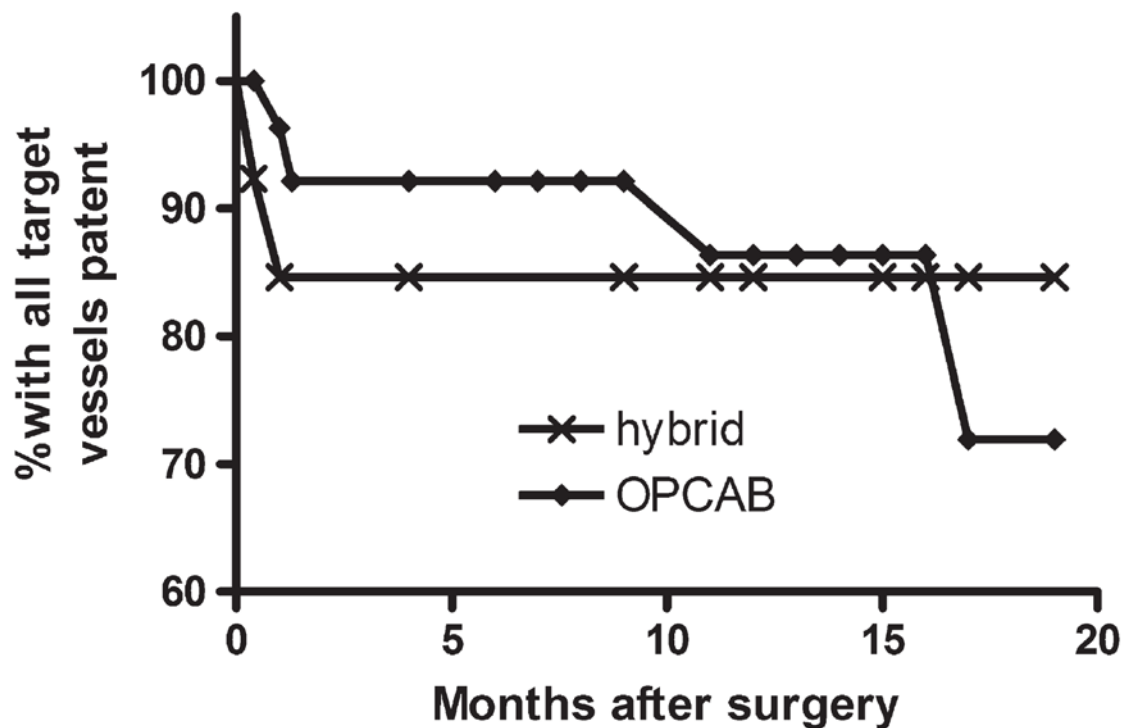
24. Khot UN, Friedman DT, Pettersson G, et al. Radial artery bypass grafts have an increased occurrence of angiographically severe stenosis and occlusion compared with left internal mammary arteries and saphenous vein grafts. *Circulation* 2004;109:2086–91. [PubMed: 15123539]
25. Iakovou I, Ge L, Colombo A. Contemporary stent treatment of coronary bifurcations. *J Am Coll Cardiol* 2005;46:1446–54. [PubMed: 16226167]
26. Hoye A, Iakovou I, Ge L, et al. Long term outcomes after stenting of bifurcation lesions with the “crush” technique. *J Am Coll Cardiol* 2006;47:1949–58. [PubMed: 16697310]
27. Iakovou I, Schmidt T, Bonizzi E, et al. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. *JAMA* 2005;293:2126–30. [PubMed: 15870416]
28. Kuchulakanti PK, Chu WW, Torguson R, et al. Correlates and long-term outcomes of angiographically proven stent thrombosis with sirolimus- and paclitaxel-eluting stents. *Circulation* 2006;113:1108–13. [PubMed: 16490815]



**Figure 1.**

Platelet responsiveness to ADP, determined using whole blood aggregometry, was equivalent between groups when assessed at the baseline and immediate postoperative time points. A loading dose of clopidogrel (300 mg postoperatively) was given within 2 hours of completing the surgical procedure for the hybrid but not OPCAB group. As a result, the platelet's ADP responsiveness was significantly reduced ( $*P < .05$ ) in the hybrid group on days 1 and 3 after surgery.

## Midterm Efficacy of Revascularization: Hybrid vs. OPCAB



**Figure 2.** Kaplan-Meier plot for a comparison of angiographic follow-up for 10 hybrid and 18 OPCAB patients. There were 4 vein grafts that failed in the OPCAB group (2 early, 2 late) and 2 targets that failed (1 LIMA, 1 stent) in the hybrids (both early, none late).  $\chi^2$  *P* value is .79 and the hazard ratio for assignment to hybrid 1.25 (95% CI 0.21–7.54).

**Table I**

## Baseline characteristics

	Hybrid (n = 13)	OPCAB (n = 26)	P value
Age (y)	62 ± 10	64 ± 10	NS
BMI	29 ± 6	31 ± 8	NS
COPD	22%	18%	NS
Current smoker	36%	36%	NS
Diabetes	29%	41%	NS
Sex (male)	80%	83%	NS
History of carotid artery disease	20%	13%	NS
Hypercholesterolemia	73%	83%	NS
Hypertension (>90 and/or >140)	87%	75%	NS
No. of diseased territories	2.7 ± 0.3	2.9 ± 0.7	NS
Peripheral vascular disease	14%	25%	NS
Previous heart surgery	7%	3%	NS
Previous myocardial infarction	47%	50%	NS
Previous stroke	0%	0%	NS
Previous TIA	3%	0%	NS
Ejection fraction <40%	31%	27%	NS
Baseline medications			
ACE inhibitor	33%	53%	NS
Aspirin	100%	97%	NS
β Blocker	90%	83%	NS
Intravenous heparin	27%	50%	NS
Intravenous nitrates	7%	17%	NS

*BMI*, Body mass index; *COPD*, chronic obstructive pulmonary disease; *TIA*, transient ischemic attack; *ACE*, angiotensin-converting enzyme.

**Table II**

## Baseline PCI data

---

Average stent number	1.7 (range 1–3)
Average stent diameter	3.0 mm
Average total stent length per patient	38.8 mm (range 18–68 mm)
Average number of vessels treated	1.5
Number of SESs	11 (50%)
Number of paclitaxel-eluting stents	11 (50%)

---

**Table III**

## Coagulation and platelet function

Coagulation/platelet function assay	Hybrid (n = 13)	OPCAB (n = 26)	P value
TEG-MA (mm)	71.4 ± 5.6	70.6 ± 4.1	NS
Aggregometry (Ω6 min)			
Collagen	13.5 ± 3.2	14.4 ± 3.7	NS
ADP	3.3 ± 1.4	15.2 ± 4.2	<.01
Fibrinogen (mg/dL)	615 ± 211	695 ± 129	NS
International normalized ratio	1.0 ± 0.3	1.1 ± 0.3	NS
D-dimer (ng/mL)	1788 ± 267	1944 ± 243	NS

**Table IV**

## Postoperative outcomes

	Hybrid (n = 13)	OPCAB (n = 26)	P value
Hospital LOS (day)	3.6 ± 1.5	6.3 ± 2.3	.0001
ICU LOS (h)	20 ± 2.4	44.5 ± 36.4	.1211
Intubation time (h)	0.5 ± 1.3	11.7 ± 9.6	.0190
Blood loss (mL)	581 ± 402	1242 ± 941	.0563
PRBC Transfusion (U)	0.33 ± 0.49	1.47 ± 1.53	.0133

LOS, Length of stay; PRBC, packed red blood cell.