Midterm Outcomes of Simultaneous Hybrid Coronary Artery Revascularization for Left Main Coronary Artery Disease

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ABSTRACT

Background: The purpose of this study was to evaluate the feasibility, safety, and midterm outcomes of a simultaneous hybrid revascularization strategy for left main coronary artery disease (LMCAD), compared with conventional off-pump coronary artery bypass grafting (OPCAB).

Methods: We compared the in-hospital and midterm outcomes of a simultaneous hybrid revascularization strategy (minimally invasive direct coronary bypass grafting of the left anterior descending coronary artery [LAD] and percutaneous intervention to non-LAD lesions) in 20 patients with LMCAD in an enhanced operating room. These patients were matched by propensity score to a group of 20 control patients who underwent standard OPCAB between September 2007 and December 2009.

Results: All baseline clinical characteristics of the 2 groups were similar. All of the patients in the 2 groups underwent surgery uneventfully without conversion to on-pump coronary artery bypass grafting. Compared with OPCAB, the patients in the hybrid group had shorter lengths of stay in the intensive care unit (34.8 ± 37.6 hours versus 50.7 ± 34.5 hours, P = .01). Transfusion requirements were reduced in the hybrid patients compared with the OPCAB patients (5% versus 40%, P = .01). The 2 groups did not differ with respect to the occurrence of other important morbidities. During the mean (±SD) follow-up of 18.5 ± 9.8 months, the group of patients who underwent the simultaneous hybrid procedure experienced an incidence of major adverse cardiac or cerebrovascular events that was similar to that of the OPCAB control group (100% versus 90%, respectively; P = .31).

Conclusions: The midterm follow-up indicated that the simultaneous hybrid revascularization procedure for LMCAD is feasible, safe, and effective. These promising early findings warrant further prospective investigations.

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INTRODUCTION

Even in the era of drug-eluting stents (DESs), coronary artery bypass grafting (CABG), rather than percutaneous coronary intervention (PCI), remains the standard treatment for left main coronary artery disease (LMCAD) [Patel 2009]. Because the outcomes are similar to those obtained with conventional CABG, off-pump CABG (OPCAB), which avoids cardiopulmonary bypass–related morbidity, has gained worldwide acceptance for the treatment of LMCAD [Angelini 2002; Nathoe 2003; Puskas 2004]. More recently, the success of DES in reducing reintervention rates [Chieffo 2005; Byrne 2009; Rubartelli 2010] has raised the possibility that hybrid revascularization, which combines a minimally invasive approach of grafting the left internal mammary artery (LIMA) to the left anterior descending coronary artery (LAD) with DES placement in the non-LAD vessels, may now produce equal or even better results than the OPCAB procedure. The reports on this strategy for the treatment of LMCAD remain limited, however, except for a few case reports [Zimrin 2007]. Accordingly, we studied the feasibility, safety, and midterm outcomes of a simultaneous hybrid revascularization strategy in 20 patients with LMCAD carried out in an enhanced operating room. The in-hospital and follow-up clinical outcomes of these patients were compared with those for a group of 20 propensity score–matched control individuals who underwent the standard OPCAB procedure.

METHODS

Study Population

From September 2007 to December 2009, 20 patients with LMCAD underwent simultaneous hybrid coronary artery revascularization in an enhanced equipped operating room at Fu Wai Hospital. The decision was made on the basis of angiographic characteristics and the patient’s preference. Inclusion criteria were left main coronary artery stenosis (especially significant distal or bifurcated lesions) with severe stenosis or calcification, or total occlusion, of the LAD that was considered inappropriate for PCI but considered amenable to surgical revascularization. The non-LAD lesions, however, were considered suitable for PCI (as assessed by 2 cardiologists and 2 cardiac surgeons). Exclusion criteria...
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Patients who received the hybrid procedure, clopidogrel administration was discontinued at least 7 days preoperatively, and aspirin (100 mg/day) was continued until the operation. During MIDCAB, unfractionated heparin (100-120 IU/kg body weight) was administrated intravenously to obtain a kaolin-based ACT >300 seconds before the LIMA was harvested. After the grafting procedure was completed, heparin was antagonized with the recommended dose of protamine sulfate. A loading dose of clopidogrel (300 mg) administered through a nasogastric tube after intraoperative confirmation of LIMA graft patency was followed by 75 mg daily thereafter for at least 1 year. Aspirin was administered at a dosage of 300 mg/day for 1 month and then 100 mg/day thereafter. Glycoprotein IIb/IIIa antagonists were not used during the perioperative period.

For the patients who were to undergo OPCAB, the current recommended antiplatelet therapy was applied. In brief, both clopidogrel and aspirin were discontinued at least 7 days preoperatively, and low molecular weight heparin was injected subcutaneously until the operation. During the operation, the ACT was kept at >400 seconds by heparin administration. Aspirin at a dosage of 100 mg daily was administered after the operation.

Clinical Definitions and Follow-up

Fu Wai Hospital records, including demographics, preoperative risk factors, and perioperative data, were reviewed. In-hospital outcome data for the 2 groups, including lengths of stay in the hospital and intensive care unit (ICU), intubation time, blood transfusion requirements, and complications, were compared. Major adverse cardiac or cerebrovascular events (MACCEs), including death, myocardial infarction, neurologic events (stroke or transient ischemic attack), and repeat revascularization of the target lesion or vessel, were recorded. Complete revascularization via interventional revascularization was defined as successful treatment of all lesions with stenosis 70% for segments >2.25 mm in diameter. Complete revascularization via surgical revascularization was defined as a graft bypassed to each of the 3 major vessel territories with 70% stenosis. Follow-up after discharge was completed for all patients by mail, by telephone, or by review of hospital records.

Statistical Analysis

Propensity score matching was constructed to control treatment-selection bias in this study. The propensity score represents the probability that a patient would undergo a simultaneous hybrid procedure. To develop a propensity score, we used a multivariate logistic regression model that used the variables known as risk factors for surgical revascularization or for potential bias for basic characteristics. These factors included male sex, age, smoking, diabetes, hypertension, hypercholesterolemia, renal dysfunction, previous cerebrovascular accident, chronic pulmonary occlusive disease, previous myocardial infarction, left ventricular ejection fraction, peripheral vascular disease, involvement of the LAD, involvement of the left circumflex artery, and involvement of the right coronary artery. Using nearest-neighbor propensity score matching, we subsequently used the score to match patients in the

Procedural Techniques

Surgical Bypass. Patients who received the hybrid procedure first underwent minimally invasive direct coronary bypass (MIDCAB) as previously described [Gao 2010]. In brief, after establishing general anesthesia, we performed a reversed-J inferior sternotomy up to the left second intercostal space in order to harvest the LIMA pedicle via direct vision. Unfractionated heparin (100-120 IU/kg body weight) was administrated intravenously to achieve an activated clotting time (ACT) of >300 seconds prior to LIMA harvesting. The anastomosis of the distal LIMA with the LAD was completed on the beating heart with the aid of a stabilizing device (Pilling Weck Surgical Company, Fort Washington, PA, USA) and use of a running 7-0 polypropylene suture. After completion of the anastomosis, protamine sulfate was used to antagonize the heparin. In the same operating room, which was equipped with a radiographic capability, we performed an angiography evaluation to confirm the patency of the LIMA graft and to treat the non-LAD lesions. Because a learning curve was involved in developing facility with this hybrid procedure, the operator completed the procedure with 10 patients with multivessel coronary disease before this study was commenced. All of the hybrid operations were accomplished by the same surgeon.

OPCAB was performed via a median sternotomy. Conduits included the LIMA and saphenous veins, which were obtained by conventional open techniques. The distal anastomosis was first performed on the beating heart with an Octopus stabilizer (Medtronic, Minneapolis, MN, USA) for stabilization of the target coronary artery. The proximal anastomosis was then completed by partially clamping and occlusion of the aorta. Blood flow and flow curves were measured for each graft by means of a transit-time ultrasound device (MediStim BF 2004; MediStim, Oslo, Norway). Grafts with a flow rate of <10 mL/min and a pulsatility index >5 required revision of the distal anastomosis.

PCI Technique. PCI was accomplished via femoral artery access. The guiding catheter, guidewire, and choice of stent, as well as pre- and postdilation, were determined by the operator. Stent patency was confirmed for all patients.

Antithrombotic Protocol. The detailed antiplatelet protocol of the 1-stop hybrid approach has previously been documented [Gao 2010]. For patients undergoing the hybrid procedure, clopidogrel administration was discontinued at least
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Table 1. Baseline Characteristics*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hybrid Procedure (n = 20)</th>
<th>OPCAB Procedure (n = 20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>61 ± 14</td>
<td>59 ± 15</td>
<td>.66</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>18 (90)</td>
<td>19 (95)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cardiac comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>8 (40)</td>
<td>9 (45)</td>
<td>.75</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>5 (25)</td>
<td>4 (20)</td>
<td>1.00</td>
</tr>
<tr>
<td>Noncardiac comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 (15)</td>
<td>4 (20)</td>
<td>.68</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>10 (50)</td>
<td>14 (70)</td>
<td>.20</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>4 (20)</td>
<td>3 (15)</td>
<td>1.00</td>
</tr>
<tr>
<td>Previous cerebrovascular accident</td>
<td>1 (5)</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>History of smoking</td>
<td>14 (70)</td>
<td>13 (65)</td>
<td>.74</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>6 (30)</td>
<td>4 (20)</td>
<td>.47</td>
</tr>
<tr>
<td>LVEF overall, %</td>
<td>60.5 ± 7.6</td>
<td>62.6 ± 6.3</td>
<td>.36</td>
</tr>
<tr>
<td>No. of diseased vessels</td>
<td>2.4 ± 0.6</td>
<td>2.5 ± 0.6</td>
<td>.79</td>
</tr>
<tr>
<td>Distal bifurcation, n (%)</td>
<td>15 (75)</td>
<td>15 (75)</td>
<td>1.00</td>
</tr>
<tr>
<td>LM + 1-vessel disease, n (%)</td>
<td>1 (5)</td>
<td>4 (20)</td>
<td>.34</td>
</tr>
<tr>
<td>LM + 2-vessel disease, n (%)</td>
<td>10 (50)</td>
<td>7 (35)</td>
<td>0.34</td>
</tr>
<tr>
<td>LM + 3-vessel disease, n (%)</td>
<td>9 (45)</td>
<td>9 (45)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

*Data are presented as the mean ± SD unless otherwise indicated. OPCAB indicates conventional off-pump coronary artery bypass grafting; LVEF, left ventricular ejection fraction; LM, left main coronary artery.

simultaneous hybrid group and the OPCAB group. The C statistic for the propensity model was 0.72.

Continuous data were expressed as the mean ± SD; categorical variables were expressed as a percentage. Mean values of continuous variables were compared by means of the Student t test for variables with a normal distribution and by Wilcoxon rank sum tests for variables not normally distributed. Categorical variables for the 2 groups were compared with the chi-square statistic. The Fisher exact test and the Mann-Whitney test were used when appropriate. MACCE-free survival curves were constructed and compared with log-rank tests. A P value <.05 was considered statistically significant. All statistical analyses were performed retrospectively with the SPSS software package for Windows (version 15.0; SPSS, Chicago, IL, USA).

RESULTS

Characteristics of the Patients

The group of 20 patients who underwent the simultaneous hybrid procedure and the matched control group of 20 OPCAB patients were similar with respect to all baseline characteristics (Table 1). The mean age was approximately 60 years, and the majority of patients (90%) were male. Seventy-five percent of the patients in the 2 groups had distal bifurcation lesions, which are not suitable for PCI. The mean number of diseased vessels per patient was approximately 2.5, and 45% of the patients had 3-vessel disease.

In-Hospital Outcomes

All 40 patients underwent either the simultaneous hybrid procedure or the OPCAB procedure uneventfully. No conversion to conventional on-pump CABG was needed. LIMA grafts were used in all patients who underwent the simultaneous hybrid procedure, and graft patency was confirmed by coronary angiography in the operating suite for all patients. Thirty-four non-LAD lesions were treated by PCI, 36 DESs were implanted in 31 lesions (91.2%), and balloon angioplasty alone was performed in the remaining 3 lesions (8.8%). The mean number of stents implanted per patient in the hybrid group was 1.8 ± 1.0. In the OPCAB group, a mean of 2.0 ± 0.9 vessels were grafted per patient.

No deaths and no readmissions occurred in either group during the postoperative period. Postoperative renal dysfunction developed in 4 patients (20%) after OPCAB but developed in none of the patients who underwent the simultaneous procedure. Compared with the OPCAB group, the patients in the hybrid group experienced significantly shorter lengths of stay in the ICU (34.8 ± 37.6 hours versus 50.7 ± 34.5 hours, P = .01). Reoperation was needed in 1 patient (5%) in the OPCAB group for severe bleeding and tamponade after the operation. Despite the use of dural antiplatelet therapy in the hybrid patients, transfusion requirements were reduced in the patients who underwent the hybrid procedure, compared with those who underwent OPCAB (5% versus 40%, P = .01). In addition, blood loss in the hybrid group was not greater than in the OPCAB group (hybrid group, 1310 ± 905 mL; OPCAB group, 1760 ± 510 mL; P = .06). Fewer distal anastomoses were needed per patient in the patients who underwent the simultaneous hybrid procedure than in the OPCAB group (1.0 ± 0.0 versus 3.0 ± 0.9, P < .001) (Table 2). There were no statistically significant differences between the 2 groups

Table 2. Operative Outcomes*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hybrid Procedure (n = 20)</th>
<th>OPCAB Procedure (n = 20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure success, n (%)</td>
<td>20 (100)</td>
<td>20 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>No. of distal anastomoses per patient</td>
<td>1.0 ± 0.0</td>
<td>3.0 ± 0.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No. of stents implanted per patient</td>
<td>1.8 ± 1.0</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>No. of vessels grafted per patient</td>
<td>—</td>
<td>2.0 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>Complete revascularization, n (%)</td>
<td>20 (100)</td>
<td>20 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>Blood loss, mL</td>
<td>1310 ± 905</td>
<td>1760 ± 510</td>
<td>.06</td>
</tr>
</tbody>
</table>

*Data are presented as the mean ± SD unless otherwise indicated. OPCAB indicates conventional off-pump coronary artery bypass grafting.
with respect to the length of stay in the hospital, intubation
time, or major in-hospital complications; however, owing
to the costs of DESs for the patients who underwent the simul-
taneous hybrid procedure, hospital costs were significantly
higher in this group than in the OPCAB group (¥89,847.4 ±
¥25,302.0 versus ¥64,430.7 ± ¥17,671.9, 

Follow-up Outcomes

All patients completed follow-up. During the mean follow-
up of 18.5 ± 9.8 months, no myocardial infarctions, deaths, or
revascularization procedures occurred in either group. Stroke
was noted in 2 patients (10%) after OPCAB, but stroke was
not seen during follow-up in any of the patients who under-
went the hybrid procedure. The MACCE-free survival rate
in the hybrid group was comparable to that in the OPCAB
group (100% versus 90%, respectively; 

**DISCUSSION**

The principal findings of this study demonstrate the feasi-
bility, safety, and midterm efficacy of the simultaneous hybrid
revascularization procedure of combining minimally invasive
CABG and PCI in patients with LMCAD as an alternative to
conventional OPCAB.

Current guidelines recommend CABG as the standard
treatment for patients with LMCAD. OPCAB, which has pro-
duced equivalent midterm outcomes at a reduced cost com-
pared with conventional CABG, has been a primary option
for these patients. More recently, the success with DESs
in reducing reintervention rates has supported the wider
application of the hybrid strategy, which was introduced in
1996 [Angelini 1996]. Despite the superior long-term patency
of arterial grafts, vein grafts are still used in most OPCAB
procedures for non-LAD lesions, mainly owing to the ready
availability of vein grafts and the multivessel nature of the
disease. Several studies have suggested that approximately
10% of venous grafts are occluded at the time of discharge
[Grondin 1989], and 19% to 27% are occluded by the 1-year
follow-up [Campeau 1983]. Less than 50% of venous grafts
remain patent by 5 years after discharge [Fitzgibbon 1996].
Therefore, PCI with DESs may be an alternative option for
non-LAD lesions because of the relatively low occlusion rate
with this approach.

No conversion to conventional CAGB was needed during
the hybrid procedure, and all patients in the hybrid group
achieved complete revascularization, as did the patients who
underwent the traditional surgical approach. No major com-
lications occurred after the hybrid procedure. No patient
in the hybrid group experienced stroke, whereas 2 patients
in the OPCAB group developed stroke (P = .48). The inci-
dence of stroke after OPCAB in the present study was much
higher than described in other publications [Mehta 2008;
Møller 2008]. This result may be due to chance because of
our small sample size. Compared with the OPCAB patients,
the patients in the hybrid group had shorter lengths of stay
in the ICU (34.8 ± 37.6 hours versus 50.7 ± 34.5 hours,
P = .01), a finding similar to the results of previous stud-
ies [Kon 2008; Reicher 2008]. Although shorter stays in
the ICU and reduced transfusion requirements tended to
lower postoperative costs for our patients who underwent a
hybrid procedure, the longer operative times and the costs
of coated stents increased the total in-hospital costs for
these patients.
Although none of the patients in our study underwent coronary artery angiography during follow-up, no MACCEs (including death, myocardial infarction, and revascularization) occurred in the hybrid group. This result implies that the grafts and stents remained functional until at least the midterm follow-up (18.5 ± 9.8 months).

In this study, we applied a simultaneous hybrid revascularization procedure instead of a “staged” procedure because of several advantages of the former. First, a simultaneous procedure avoids the need to transfer patients between the operating room and the catheterization laboratory and thus minimizes both inconvenience and anesthetic exposure. In addition, the adequacy of the LIMA-LAD anastomosis can be assessed by intraoperative angiography, and the possible complications of PCI can be dealt with by immediate surgical intervention, although such complications did not occur in our patients [Reicher 2008]. However, the aggressive antiplatelet therapy, which is mandatory for the prevention of stent thrombosis, could increase perioperative bleeding and transfusion requirements. In this study, we applied a modified antiplatelet protocol that had been verified in our previous study [Gao 2010]. Interestingly, our findings showed that blood loss and transfusion requirements were reduced in the hybrid patients compared with the OPCAB patients. The lower degree of bleeding in the hybrid group was likely due to the less-invasive manipulation inherent in the MIDCAB approach, compared with conventional OPCAB.

This pilot retrospective study has several limitations that need to be considered when interpreting the data. First, the sample size is very small. Second, the assignment of patients to the 2 groups was not randomized; however, propensity score matching balanced the bias. Third, we did not perform angiographic evaluations of the patients to investigate the patencies of the grafts and stents.

In summary, the midterm follow-up indicated that the simultaneous hybrid revascularization for LMCAD is feasible, safe, and effective. These promising early findings warrant further prospective clinical trials for the simultaneous hybrid revascularization strategy for LMCAD.

REFERENCES


