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

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**Background**—Robotically enhanced minimally invasive direct coronary artery bypass (RE-MIDCAB) graft of the left internal mammary artery to the left anterior descending coronary artery (LAD) and/or the first diagonal branch might be the least traumatic surgical revascularization approach available so far. When combined with fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI) in the non-LAD vessels, this “hybrid” strategy takes advantage of the survival benefit conferred by the internal mammary artery graft to the LAD while providing the patients with a truly minimally invasive, functionally complete revascularization.

**Methods and Results**—Twenty patients with multivessel disease were selected to undergo combined PCI and RE-MIDCAB because they had a lesion amenable to PCI in the right and/or the left circumflex coronary artery and a lesion in the LAD and/or the first diagonal branch that was considered less than ideal for PCI. PCI was actually performed only when FFR was <0.80 (“provisional PCI”). In 7 stenoses, FFR was >0.80 and the planned PCI was not performed. Surgery was performed before provisional PCI in 6 cases. An angiogram was obtained in all patients before discharge, and a complete clinical follow-up including a stress test was obtained in all patients after a mean of 12 months. There were no significant intraoperative complications, conversions to cardiopulmonary bypass, or reinterventions for bleeding. At early control angiogram, 2 moderate stenoses just proximal to anastomosis were observed, both with normal run-off. After 12 months there were no objective signs of ischemia at stress testing. After an average follow-up of 19±10 months there were no deaths, myocardial infarctions, or repeat revascularizations.

**Conclusion**—A hybrid strategy combining FFR-guided PCI and RE-MIDCAB seems safe and provides selected patients with a functionally complete revascularization with minimal surgical trauma and excellent clinical outcomes.

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**Key Words:** revascularization ■ bypass ■ artery

Hybrid revascularization is defined as the intentional combination of percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) to treat patients with multivessel coronary artery disease. Despite the enormous progress in percutaneous revascularization techniques, CABG is still considered the gold standard to achieve complete revascularization in patients with multivessel coronary artery disease. Disadvantages of CABG include its invasiveness, the use of cardiopulmonary bypass, and the occlusion rate of bypasses when they are placed on hemodynamically nonsignificant stenosis. The major limitations of PCI in patients with multivessel disease have been restenosis and the need for repeat procedures. In addition, some subsets of lesions are still beyond the reach of PCI (chronic total occlusions and long calcified lesions) or remain associated with high restenosis rates even with the use of drug-eluting stents. Several groups have proposed the combined use of PCI and minimally invasive direct coronary artery bypass (MIDCAB). This approach takes advantage of the survival benefit conferred by the internal mammary artery graft to the left anterior descending coronary artery (LAD) while minimizing the invasiveness of the revascularization strategy. Robotically enhanced (RE)-MIDCAB might be the least traumatic and safest approach available thus far. In addition, revascularizing hemodynamically nonsignificant stenoses is useless.

Accordingly, we proposed to apply a hybrid strategy in patients with multivessel disease that combined left internal...
mammary artery (LIMA) grafting on the LAD by RE-MIDCAB and PCI of the lesions located in the right coronary artery (RCA) and left circumflex coronary artery (LCx), provided the latter were hemodynamically significant as assessed by fractional flow reserve (FFR) measurements (“provisional PCI”). Such a strategy should provide these patients with the best of both worlds. The present study examines the 1-year follow-up of patients with multivessel disease by angiography in whom such a hybrid strategy was applied.

**Methods**

**Study Population**

Between January, 2001 and November, 2003, 20 patients (14 men, mean age was 65±9 years, range 49 to 81 years) with multivessel disease shown by coronary angiography were selected to undergo combined PCI and RE-MIDCAB because they had a lesion amenable to PCI in the RCA and/or the LCx and a lesion in the LAD and/or the first diagonal branch that was considered less than ideal for PCI (total chronic occlusion, n=4; calcified type C stenosis, n=7; ostial stenosis, n=5; involvement of the left main stem, n=1; proliferative in-stent restenosis, n=2; failed attempt, n=1). All values are given as mean standard deviations.

**Provisional PCI Procedure**

The PCI procedure was planned before RE-MIDCAB (range, 2 to 83 days) in 14 patients and after surgery (range, 2 to 180 days) in 6. The timing of the procedures was discussed on a case-by-case basis and was guided by the clinical context and anatomical considerations. PCI was performed via the femoral artery through 6F guiding catheters. Unfractionated heparin (100 U/kg of body weight) was given intravenously at the beginning of the procedure. In all RCAs or LCxs, quantitative coronary angiography was performed. Using the catheter as a scaling device, the reference diameter, the minimal luminal diameter, and the percentage of the diameter stenosed were determined. In addition, in all RCA and LCx lesions, pressure-derived FFR measurements were obtained before the planned PCI. When FFR was >0.80 (n=7), the PressureWire (Radi Medical Systems) was removed and the planned PCI was actually deferred. When FFR was ≥0.80, PCI was performed (“provisional PCI”). All patients in whom PCI was performed received at least 1 stent. Only 1 patient received a drug-eluting stent. Patients were all given clopidogrel (75 mg/d) and aspirin (80 mg/d) for at least 4 days before the procedure. When provisional PCI was performed shortly after RE-MIDCAB, a loading dose of 300 mg of clopidogrel and 160 mg of aspirin were given the day of the PCI.

**Surgical Procedure**

The goal of the surgical procedure was to obtain an arterial revascularization by connecting the LIMA graft to the LAD and/or diagonal artery on the beating heart through a keyhole approach without spreading the ribs. The patient was placed on the operating table in supine position and was anesthetized with the use of a left main bronchus blocker, which allowed for single lung ventilation. An inflatable bag was placed under the left hemithorax to create some elevation. The first part of the procedure consisted of the takedown of the LIMA in a completely closed chest using a robotic telemanipulation system (da Vinci Surgical System). A camera port was entered in the fourth intercostal space, and a left and right robotic arm were placed on the anterior axillary line through the seventh and second intercostal space, respectively. The full length of the semi-skeletonized LIMA (no fascia) was harvested. Side branches were controlled by the use of electrocautery or hemoclips. Pericardial fat on the anterior aspect of the pericardium was removed using the same robot system, allowing for more working space between the heart and the overlying ribs. The robotic system was then removed. During the second part of the procedure, an antero-

lateral mini-thoracotomy (4 to 6 cm) was performed starting from the camera port. No rib retractor was used so as to avoid postoperative pain. A thoroscope was placed in the port of the former right robotic arm that also served as an internal light source. The keyhole was kept open with a soft-tissue retractor (Cardiovations). The LIMA was exteriorized and checked for sufficient length and good flow. After pericardial incision, the LAD (or diagonal artery) was identified. If a diagonal artery had to be bypassed, the Starfish NS (Medtronic, Inc) was used to rotate the heart and bring the target vessel in the surgical field. The coronary artery was encircled only proximally using a 4/0 Gore-Tex (DuPont) suture. A stabilizer was placed on the target area to create a motionless anastomosis area. After incision of the coronary artery, the anastomosis was hand-sewn using 1 running 8/0 polypropylene suture. After completion, protamine was administered. A left thoracic drain was placed through the former left robotic arm port. The mini-thoracotomy was closed in multiple layers without the use of rib-encircling sutures. All patients remained ventilated in the intensive care unit for ≈4 to 6 hours postoperatively.

**Follow-Up**

Before discharge, all patients underwent an angiographic control of the LIMA graft whether or not provisional PCI had yet to be performed. Special care was taken in analyzing the anastomotic site. No systematic control angiogram was performed thereafter unless clinically indicated. Clinical follow-up including a maximal bicycle stress test was obtained in all patients at least 12 months after the last revascularization procedure.

**Results**

**Baseline Characteristics**

The Table shows the patients’ clinical characteristics, risk factors, clinical presentations, comorbidities, and left ventricular function.

**Provisional PCI, Angiographic, and Functional Results**

The arteries in which PCI was contemplated were large (reference diameter: 3.3±0.09 mm) (Figure). Lesion length was 12±5 mm. In 13 patients, the lesions in the RCA and/or the LCx had a FFR <0.80. These lesions underwent PCI. In 7 stenoses, FFR was >0.80. In those lesions, PCI was deferred. The percentage of the diameter stenosed was 63±10% (range 48% to 78%) and FFR was 0.65±0.09 (range 0.39 to 0.75) for lesions in which stenting was performed. The corresponding values were 47±7% (range 38% to 58%) and 0.86±0.05 (range 0.82 to 0.97) in stenoses in which stenting was not performed. After PCI, the percentage of the diameter stenosed was reduced to 12±10% (range 3% to 37%). There were no complications related to PCI. Among the 14 patients in whom provisional PCI (stenting or FFR measurements) was performed before surgery, 8 were discharged the day after the procedure, 4 were discharged the same day, and 2 were transferred to the department of surgery. All were free of restenosis at early repeat angiogram performed after RE-MIDCAB. Among the 6 provisional PCIIs performed after surgery, 5 were done during the hospital stay as required by the surgical procedure and 1 was done electively 160 days later as an outpatient procedure.

**Surgical Procedure and In-Hospital Phase**

RE-MIDCAB off-pump surgery was successfully performed in all 20 patients. Fifteen patients received a LIMA graft to...
Clinical Characteristics of the Patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No. of Patients</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>65±9 (49 to 81)</td>
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<tr>
<td>Male gender</td>
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<tr>
<td>Cardiovascular risk factors</td>
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<td>Current smoking</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Hyperlipidemia</td>
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<tr>
<td>Family history of CHD</td>
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<td>Clinical presentation</td>
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<td>Stable angina</td>
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</tr>
<tr>
<td>Unstable angina</td>
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<tr>
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<td>5</td>
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<td>Peripheral vascular disease</td>
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<tr>
<td>Previous myocardial infarction</td>
<td>4</td>
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<tr>
<td>Previous cerebrovascular disease</td>
<td>2</td>
</tr>
<tr>
<td>History of prior PCI</td>
<td>5</td>
</tr>
<tr>
<td>Left ventricular function</td>
<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>76±11 (55 to 89)</td>
</tr>
<tr>
<td>End-diastolic volume index, mL/m</td>
<td>77±31 (55 to 85)</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD (range) or n as indicated.

CHD indicates congenital heart disease; COPD, chronic obstructive pulmonary disease.

the LAD and 5 patients received a sequential anastomosis to the diagonal artery and LAD. In 2 patients, because of insufficient length, the LIMA was extended by a short saphenous vein graft fragment. The mean total length of hospital stay required by the surgical procedure was 8.1±1.6 (range 6 to 11) days. There were no significant intraoperative complications or conversions to cardiopulmonary bypass. The postoperative blood drainage averaged 966±373 mL, and an average of 1.6 U of packed cells was necessary in 5 patients. These values of blood loss and hospital stay are similar to those observed in the last 286 patients undergoing CABG via median sternotomy. There were no reinterventions for bleeding. There were no new Q-wave appearances on postoperative ECG. Postoperative coronary angiography was performed 5±5 days (range 0 to 24 days) after surgery. Left ventricular global function was well preserved in all patients without any deterioration after surgery (left ventricular ejection fraction 75±11 versus 76±8%, NS; \(P>0.05\)). The arterial bypass grafts were patent in all 20 cases, with good TIMI-3 flow. In 18 patients, no stenosis could be detected. In 2 patients who had a sequential graft connecting the LIMA with the diagonal artery and LAD, a moderate stenosis of 44% in one patient and 65% in second was present at or just proximal to the site of anastomosis of the sequential graft diagonal to the LAD with TIMI-3 flow.

During the in-hospital phase, there were no deaths, myocardial infarctions, or urgent revascularizations. All patients remained free of angina pectoris during hospital stay. In 1 patient, a moderate pericardial effusion was noticed on the fifth postoperative day and was treated medically.

Mid-Term Follow-Up

The average length of follow-up after the last revascularization procedure was 19±10 months (range 12 to 33 months). During this period, there were no deaths, myocardial infarctions, or repeat revascularizations. A complete clinical follow-up was obtained in all patients at least 12 months after the last revascularization procedure. A symptom-limited bicycle exercise stress test was performed in all but 2 patients (one 79-year-old woman who was unable to exercise and one 68-year-old man who declined the invitation for the repeat stress test). Six patients reported atypical chest discomfort. In all 6, a stress test revealed nonspecific changes for ischemia. One patient had a typical episode of angina 10 months after surgery. Because the exercise test remained normal, no control angiogram was performed. In 1 other patient, a coronary angiogram performed 2 months after surgery because of recurrent chest pain showed a good LIMA-LAD graft patency, and a focal 29% stenosis in 1 of 3 stents deployed in the RCA (FFR=0.89). Subsequent stress tests performed 1 and 10 months later ruled out any sign of ischemia. Percardial effusion was identified in 2 patients 30 and 45 days after surgery, respectively. In 3 patients, episodes of recurrent atrial fibrillation were recorded at follow-up. One patient had a transient ischemic attack 124 days after surgery.

In total, 4 hospitalizations were needed at follow-up in 3 patients because of coronary angiography (n=1), pericardial effusion with subsequent right heart catheterization (n=1), and pacemaker implantation with repeated readmission 60 days later because of a transient ischemic attack.

Discussion

The present pilot study suggests that a hybrid revascularization strategy consisting of a LIMA connected by RE-MIDCAB to the LAD and/or a diagonal branch combined with FFR-guided PCI of 1 or 2 lesions located in the RCA and the LCx is safe and provides the patients with an excellent functional status after 12 months. This approach has the following advantages: (1) a truly minimally invasive approach without sternotomy, rib retraction, or cardiopulmonary bypass; (2) the survival benefit provided by the LIMA graft on the LAD without need for venous bypass grafts, which have a high attrition rate; and (3) a functionally complete revascularization without unnecessary stenting of lesions that are hemodynamically nonsignificant.

Previous Reports

The intentional combination of surgical revascularization of the LAD and percutaneous treatment of the non-LAD arteries was first proposed by Renkin et al.\(^{21}\) The idea was to provide the patients with “all-arterial” revascularization by substituting the use of saphenous venous grafts to non-LAD vessels with PCI (at that time plain balloon angioplasty) while still conferring the life-long benefits of the LIMA graft to the LAD. At that time, however, CABG included extracorporeal circulation and median sternotomy, so a hybrid approach exposed the patient to the cumulative risk of both invasive
Since 1996, several groups have reported their experiences of combining MIDCAB with PCI. In particular, Stahl et al proposed a combination similar to that in the present study. The number of patients in each of these studies is limited and no randomized study exists. Yet, taken together, the data suggest that, in selected patients, this approach is effective and safe, with early and mid-term results that are at least as good as either classical CABG or multivessel PCI. Moreover, Riess et al also showed that the patency rates early after operation and at 6 months were almost identical. The present study confirms these previous reports. During the follow-up period there were no deaths, myocardial infarctions, nor emergency revascularization procedures. Only 1 patient had to undergo a repeat angiogram, which ruled out an ischemic origin of the recurrent chest pains. The duration of the hospital stay was not prolonged. After 1 year, the patient’s clinical status was excellent, as indicated by normal stress testing.

**Timing of the Procedures**

In some series, PCI was always performed after surgery. As in other studies, the sequence of the revascularization procedures in the present study was determined on a case-by-case basis as a function of anatomical and clinical factors. Patients admitted with unstable angina attributable to a critical stenosis in the RCA or LCx were first treated by PCI. When the LAD lesion was considered the culprit the order was reversed. Some authors have advocated a same-day combined surgical and PCI procedure performed in the operating suite. Even though our experience with PCI performed in the operating room is limited, it is our conviction that the specificities of a modern operating theater and a modern catheterization laboratory are such that performing both RE-MIDCAB and PCI in a single “revascularization suite” is suboptimal. Rather, an outstanding and ongoing cooperation and communication between interventional cardiologists and cardiac surgeons is paramount. With increasing experience, the PCI can be performed ad hoc, immediately after the diagnostic catheterization, while the RE-MIDCAB is delayed by a few days, or even weeks, depending on the clinical needs. One potential advantage of having surgery before PCI is that the patients have not yet taken clopidogrel, which is mandatory in preventing stent thrombosis. Stahl et al reported a higher than expected rate of bleeding. In our series, 10 patients underwent RE-MIDCAB while taking clopidogrel and aspirin because of the recent stent implantation. We did not find that this antiplatelet drug altered perioperative management.

**FFR-Guided Revascularization**

Pressure-derived FFR values accurately predict the hemodynamic significance of a stenosis detected by angiography. FFR values >0.80 are uniformly associated with normal stress testing, whereas stenoses with an FFR value <0.75 can
be responsible for stress-induced ischemia. FFR is therefore considered a surrogate for a stress test. The results are obtained on the spot and thus enable immediate clinical decision making. It has been shown in patients with single-vessel disease that deferring scheduled PCI is at least as effective and safe as performing the intervention. Recent data obtained in patients with multivessel disease extend the value of FFR measurement in determining the need for revascularization in patients with multivessel disease. In the present study, FFR was measured in all lesions in which stent implantation was considered. In 7 of 21 stenoses, FFR appeared to be >0.80 and the planned PCI was not performed. Even though the number of patients is limited, the absence of any symptoms or objective signs of ischemia at 1-year follow-up confirm that the need for revascularization can be guided by simple wire-based intracoronary pressure measurements. More generally, these findings illustrate the difference between anatomical and functional multivessel disease and the therapeutic implications of this difference.

Limitations
Before extrapolating these conclusions to a broader patient population, several limitations should be considered. Firstly, the present report is a pilot study with a small number of patients with low comorbidity and normal left ventricular function. In addition, the non-LAD stenoses were selected for PCI because of their a priori very low risk of restenosis; complex lesions were most often excluded, the stented arteries were large and the lesion length short so that only one stent was placed in the majority of lesions. All these factors combine to explain the absence of clinical restenosis despite the use of bare metal stents in the majority of patients. The present study does not provide any comparative data with more classical surgical techniques. Secondly, robotic technology is extremely expensive. Although a cost-efficiency analysis is beyond the scope of this pilot trial, it is almost certain that the present approach is more expensive than classical CABG. This might limit the widespread application of this hybrid strategy to patients in whom a median sternotomy should be avoided. Finally, postoperative pain levels and patient comfort were not assessed, and it is often argued that postoperative pain levels and patient comfort were not assessed, and it is often argued that the present approach is more expensive than classical CABG. This might limit the widespread application of this hybrid strategy to patients in whom a median sternotomy should be avoided. Finally, postoperative pain levels and patient comfort were not assessed, and it is often argued that the present approach is more expensive than classical CABG. This might limit the widespread application of this hybrid strategy to patients in whom a median sternotomy should be avoided. Finally, postoperative pain levels and patient comfort were not assessed, and it is often argued that the present approach is more expensive than classical CABG. 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Conclusions
This study suggests that in selected patients with multivessel coronary artery disease, and provided optimal communication between surgeons and interventional cardiologists exist, a hybrid strategy combining FFR-guided PCI and RE-MIDCAB (with LIMA to the LAD and/or the diagonal branch) is a reasonable strategy. It provides these patients with a functionally complete revascularization with minimal surgical trauma and good clinical outcome. Patients with diabetes, major obesity, depressed pulmonary function, or a combination of these conditions are the most likely to benefit from this approach. Because the restenosis rate after drug-eluting stent placement in long lesions and small vessels is very low, it is likely that the more widespread availability of drug-eluting stents will increase the number of patients in whom a hybrid strategy can be proposed. Preliminary results of complete revascularization by multivessel stenting are very encouraging. If these results are confirmed, patients in whom all lesions are amenable for PCI will probably be treated only by PCI. However, a sizable proportion of these patients have LAD lesions, which are not well-suited for PCI (bifurcations, calcifications, tortuosity). The present data suggest that this hybrid strategy is a reasonable alternative that offers the best of both the surgical and the interventional worlds.

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