Hybrid Cardiovascular Procedures

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Hybrid procedures integrate and combine endovascular intervention with surgical therapy. The goal of such an approach is to offer a less invasive therapeutic modality while optimizing patient care and minimizing peri-operative morbidity and mortality.

This review will discuss the different forms of hybrid therapy that are currently available and focus on the role they play in the treatment of cardiac and vascular disease. It will also focus on the data, outcomes, and potential uses of hybrid therapy.

Hybrid Coronary Revascularization

The SYnergy Between PCI With TAXUS and Cardiac Surgery (SYNTAX) trial has demonstrated that in patients with multivessel coronary artery disease (CAD), coronary artery bypass grafting (CABG) surgery is superior to percutaneous coronary intervention (PCI), with a lower need for repeat revascularization.¹ PCI, however, offers a much less invasive revascularization modality with faster recovery and potentially a lower stroke rate compared with CABG alone.

Hybrid coronary revascularization (HCR) involves combining CABG surgery and PCI either in one setting or in a staged fashion. In this approach, the left internal mammary artery (LIMA) to left anterior descending (LAD) artery graft is combined with PCI of non-LAD coronary artery stenosis. The goal of HCR is to offer the patient the best of both techniques in a modality that is safe and less invasive than the standard surgical approach but does not compromise on long-term durability and survival. In HCR, saphenous vein grafts (SVGs) are substituted with coronary stents for the treatment of non-LAD coronary artery stenosis. The logic behind this is that SVGs have shown a high early failure rate of 6.2–30%, with an average of 20%,² while 12-month restenosis rates with drug-eluting stents (DES) have been reported to be between 0 and 16% with an average of 4.58%.³ For treatment of the LAD system, the LIMA graft has superior long-term patency rates to PCI and SVGs, which translates into superior event-free survival and relief of angina,⁴⁵ and contributes to the vast majority of the survival advantage observed in CABG surgery.⁴⁶–⁴⁸

Approximately 816 patients have undergone HCR to date.⁴⁹–⁵⁶ The published data come from small (15–70-patient), single-center experience with limited follow-up (from one to 41 months). Nonetheless, the data from these series suggest that HCR is safe, with mortality rates between 0 and 4.7% and with low morbidity. The rates of repeat revascularization following PCI range widely, from 0 to as high as 29.6%, depending on the strategy adopted (percutaneous coronary angioplasty alone (PTCA) or PTCA + PCI) and the stent technology used (bare-metal stents (BMS) or DES). Recent series of HCR using DES only have reported a restenosis rate of 0–6% at an average follow-up of six to 33 months, while the incidence of major adverse cardiac events is between 0 and 4.2%.⁵⁷–⁵⁹ Long-term outcome data for HCR are limited. Previous studies reported an event-free survival rate of 83–92%.⁶⁰ In one of the largest hybrid series (n=117 patients), the incidence of major adverse cardiac and cerebrovascular events at 12 months was 15%, which is comparable to that reported at one year in recent randomized CABG trials (7–12%).⁶¹

Techniques

The LIMA to LAD graft can be performed through a midline sternotomy or utilizing a minimally invasive approach. The benefits of using a
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Table 1: Advantages and Disadvantages of Different Hybrid Coronary Revascularization Strategies

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>One-stop</td>
<td>One procedure</td>
<td>Risk for bleeding due to clopidogrel loading</td>
</tr>
<tr>
<td></td>
<td>LIMA-LAD imaging</td>
<td>Longer OR times</td>
</tr>
<tr>
<td></td>
<td>Complications resolved in 1 setting</td>
<td>Need for hybrid OR</td>
</tr>
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<td></td>
<td></td>
<td>Need for team training</td>
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<tr>
<td>Two-stage</td>
<td>PCI followed by CABG</td>
<td>Risk for bleeding at CABG</td>
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<tr>
<td></td>
<td>Aggressive multivessel stenting</td>
<td>Due to clopidogrel loading</td>
</tr>
<tr>
<td></td>
<td>No risk for injury to newly placed grafts</td>
<td>No LIMA-LAD imaging</td>
</tr>
<tr>
<td></td>
<td>CABG back-up for suboptimal PCI results</td>
<td>Unless 3rd procedure carried out</td>
</tr>
<tr>
<td>CABG followed by PCI</td>
<td>LIMA-LAD protected in high-risk PCI</td>
<td>Incomplete revascularization at the time of CABG</td>
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<tr>
<td></td>
<td>Few bleeding complications due to clopidogrel</td>
<td>In the case of PCI</td>
</tr>
<tr>
<td></td>
<td>LIMA-LAD imaging completed</td>
<td>Complications a 3rd</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High-risk surgical procedure is required</td>
</tr>
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</table>

CABG = coronary artery bypass surgery; LAD = left anterior descending artery; LIMA = left internal mammary artery; OR = operating room; PCI = percutaneous coronary intervention.

A minimally invasive approach is faster patient recovery, less utilization of blood products, superior cosmetic results, and a decrease in the magnitude of the surgery. However, there is a steep learning curve and, due to the surgical technique being more difficult, the quality of the anastomosis and the harvested LIMA may be somewhat lower than when utilizing the conventional approach.

Below are some of the minimally invasive operations used for HCR:

- A minimally invasive direct coronary artery bypass (MIDCAB) is an operation in which the LIMA harvesting is undertaken in an open fashion through a limited anterior or lateral thoracotomy incision. The anastomosis is then performed by hand on the beating heart.
- A thoracoscopic endoscopic atraumatic coronary artery bypass (endo-ACAB) is a procedure in which the LIMA is mobilized through a thoracoscopic port access approach. Both directed non-rib-spread and small rib-spread thoracotomies can be used for surgical access to the LAD. The anastomosis is performed by hand on the beating heart.
- A robotically assisted CABG consists of robotic LIMA harvesting followed by a hand-sewn beating heart anastomosis as used in the MIDCAB approach.
- In the beating heart totally endoscopic CABG (TECAB), both the LIMA take-down and the anastomosis are performed with the assistance of a robot. The anastomosis can be performed endoscopically on the beating heart or on the arrested heart with the adjuvant of cardiopulmonary bypass instituted peripherally.

Timing

HCR can be performed in one setting (‘one-stop’) or in a delayed (‘two-stage’) fashion separated by hours or days, but typically within the same hospitalization. In order to perform one-stop HCR, a specially designed operating room (OR) suite (hybrid OR) that combines a fully functional catheterization laboratory with a fully functional and fully equipped OR is necessary. As the majority of hospitals do not have a hybrid OR, the most common form of HCR is two-stage. In this approach, CABG can be performed first followed by PCI, or vice versa. Table 1 summarizes the benefits and potential drawbacks of one-stop and two-stage HCR. In our view, if a two-stage hybrid procedure is performed, the optimal sequence is CABG first followed by PCI.

Antiplatelet Strategy

The antiplatelet strategies adopted for HCR vary from center to center. For one-stop HCR, different strategies have been used in order to balance the risk for bleeding and acute stent thrombosis with protamine reversal of heparin. In our center we have adopted a strategy of 300mg of clopidogrel to be given in the holding area for planned hybrid procedures, while for unplanned hybrid procedures (those procedures determined at the time of the surgery and dictated by incomplete revascularization, poor conduits, or a significant angiographic defect found at the time of completion angiogram) we give 300mg of clopidogrel though the nasogastric tube in the OR. The rate of stent thrombosis observed in our series was less than 1%, with no differences in the rate of re-exploration for bleeding between patients undergoing hybrid procedures and those undergoing standard CABG surgery only.\(^{26}\)

Other investigators have adopted a strategy of non-reversing heparin with protamine at the end of HCR and loading the patient with clopidogrel (300mg) on arrival at the intensive care unit.\(^{27}\) Satisfactory results have been reported with this strategy, with no re-exploration for bleeding or acute stent thrombosis.

A third strategy, used by Bonatti et al.,\(^{28}\) is to load the patient with 300mg of clopidogrel and 100mg of aspirin 12 hours prior to surgery.

Alternative antiplatelets have also been considered, such as ticlopidine, which, compared with clopidogrel, has a delayed onset of antiplatelet effects. Gilard et al.\(^{26}\) have used 250mg of ticlopidine after the initial PCI procedure and 500mg more after the MIDCAB procedure (one-stop HCR completed within 16 hours).

All of the above-mentioned strategies seem reasonable and have reported good results; however, there are currently no guidelines or indications on which strategy might be preferable, and this is certainly an area for future research. A tailored approach to the antiplatelet strategy according to the patient’s drug response based on point-of-care platelet activity may be the next step to determine which drug to use and the correct dosing.

Hybrid Valve Procedures

Hybrid valve/PCI procedures can be used to treat concomitant valve disease and multivessel CAD.\(^{29,30}\) In patients with poor conduit quality, poor coronary target vessel quality, and low ejection fraction, and in patients undergoing re-operative cardiac surgery, the risks of a conventional surgical approach (CABG and valve surgery) may outweigh the benefits.\(^{29,30}\) Hybrid valve/PCI procedures may lower the magnitude of the surgery by addressing the CAD with PCI and the valve disease
with a minimally invasive surgical approach. This approach is especially useful for re-operative surgery in which an aortic valve prosthesis is in position and/or patent bypasses are present. In such high-risk patients we have adopted a strategy of PCI to treat the CAD and minimally invasive mitral valve surgery through a right-antero-lateral thoracotomy in 32 patients.42 Forty-three percent of the patients were in congestive heart failure, 43% underwent urgent or emergent surgery, and 38% had prior heart surgery. The operative mortality rate was only 3%, which was substantially lower than the Society of Thoracic Surgeons (STS) mean predicted mortality of 8.7±6.9% for combined CABG and valve surgery.

Another category of patients potentially best treated by this approach are those who present with acute coronary syndrome in the setting of significant CAD and valve disease.43 In this approach, PCI is used first to treat the culprit coronary lesions and stabilize the patient, followed during the same hospitalization by valve surgery.43 In 2005 we reported our results in this high-risk group of patients; the predicted STS mortality rate was 22% for combined CABG and valve surgery, while the observed mortality rate was 3.8%.43 Other authors44 have adopted such a strategy in patients with combined aortic valve and CAD, combining PCI and minimally invasive aortic valve replacement, with low (5%) operative mortality and morbidity.

Hybrid Therapy for Combined Coronary Artery and Carotid Artery Disease
Carotid artery disease is often associated with CAD and carries a higher risk for post-CABG surgery stroke if severe and left untreated.45 The optimal timing for correcting concomitant carotid disease and CAD is still debated. In the past, both staged carotid endarterectomy (CEA) + CABG or combined CEA + CABG have been used; however, the combined approach has a higher rate of morbidity and mortality compared with CABG surgery alone.46 Carotid angioplasty with or without stent placement (CAS) has emerged as an alternative to CEA.

Few data exist on CEA and CAS in the setting of CABG surgery. From a nationwide outcomes registry of 27,084 patients discharged after CEA + CABG surgery between 2000 and 2004, only 3.3% of patients underwent CAS followed by CABS.47 In the group of patients who underwent CAS followed by CABG, the incidence of post-operative stroke (2.4 versus 3.9%; p<0.001) and that of combined stroke and death (6.9 versus 8.6%; p<0.001) were lower than in the CEA + CABG group, while in-hospital mortality was similar (5.2 versus 5.4%; p=NS). After risk stratification, the CEA + CABG patients had a 62% increased risk for post-operative stroke compared with those undergoing CAS + CABG.

In a recent systematic review of published reports on 760 patients who underwent CAS + CABG surgery, the 30-day risk for death/stroke was 9%, comparable to data from systematic reviews evaluating CEA + CABG (staged or one-stop).48 In another study comparing combined CEA + CABG surgery versus staged CAS + CABG surgery, the latter had comparable adverse events (death, stroke, or myocardial infarction), despite the patient population being at higher risk at baseline.49

In a recent large series, Versaci et al.46 used a one-stop hybrid approach (CAS + CABG surgery) in 101 consecutive patients with severe carotid disease and concomitant severe CAD. The operative mortality rate was 2% and the adverse neurologic event rate was 2%. Combining CAS and CABG avoids the risks of peri-procedural myocardial infarction while awaiting the CABG procedure and the need for the patient to undergo two separate procedures. However, in the event of an adverse neurologic outcome, the surgery needs to be delayed until clinical recovery; moreover, because of the dye load there is concern that the nephrotoxic effects of the dye may combine with the adverse effects of the cardiopulmonary bypass, resulting in renal injury.

In summary, carotid artery stenting followed by CABG has shown comparable short- and long-term outcome rates to CEA, but could offer a less invasive (and safer) approach in CABG surgery patients.

Hybrid Atrial Fibrillation Procedures
Atrial fibrillation (AF) is the most common cardiac arrhythmia. It is projected that by 2050 five million people will be affected by this arrhythmia, which significantly increases the risk for cardiovascular mortality.48,49 Catheter ablation is an emerging and important new therapeutic option to treat patients with AF. The goal of this approach is to achieve permanent electrical isolation of the pulmonary veins. In patients with long-standing persistent AF, however, the mechanisms of maintaining AF lie beyond the pulmonary veins. Thus, the success rate for catheter ablation alone is much lower than in those with paroxysmal AF. A "hybrid maze" combines minimally invasive endoscopic surgical therapy with catheter-based therapy to produce epicardial and endocardial lesions.49 The hypothesis is that epicardial and endocardial ablation is more likely to address several of the etiologic factors that result in persistent or recurrent AF. In this technique, a bilateral thoracoscopic approach allows the left atrial appendage to be manipulated and legated (off-pump) and radiofrequency ablation to be used on the epicardium, while endocardial ablation utilizes a percutaneous vascular access.

The hybrid maze has been adopted by several groups, and the results have been encouraging. There are, however, scarce clinical data, most of which come from isolated single-center experiences or case reports. In one of the largest series published comparing three different strategies to treat permanent AF, Elayi et al. randomly assigned 144 patients with long-standing permanent AF to circumferential pulmonary vein ablation (n=47), pulmonary vein antrum isolation (n=48), or a hybrid maze combining ablation of complex fractionated or rapid atrial electrograms in both atria followed by a pulmonary vein antrum isolation (n=49). The hybrid strategy had the highest likelihood of freedom from recurrent AF.50

With advances in our knowledge and better understanding of the patterns and pathophysiology of AF, new therapeutic interventions combining surgical and catheter approaches may play a significant role in the treatment of long-standing AF.

Aortic Debranching Procedures
Endovascular stenting has emerged as an alternative to open repair for the treatment of chronic aneurysmal disease of the descending thoracic aorta and in some complex aortic arch aneurysms and complex thoraco-abdominal aneurysms. Endovascular repair can be limited by inadequate proximal and distal landing zones. A debranching procedure expands landing zones and facilitates endovascular repair.
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The most common clinical scenario is a patient with a thoraco-abdominal aortic aneurysm (TAAA) who is not a candidate for open surgical repair because of significant comorbidities, but who is not a candidate for endovascular repair either because of anatomic extension of the aneurysm. In a TAAA debranching procedure, visceral aortic debranching with retrograde revascularization of the splanchic and renal arteries is performed along with aneurysm exclusion using stent grafts. This enables distal extension into the visceral portion of the abdominal aorta. Results to date suggest that this technique is a safe alternative to conventional repair for TAAA, with high peri-procedural success (90%) and acceptable operative mortality rates (13%). Less often, debranching procedures are used to treat aortic arch aneurysms. In a recent systematic review of aortic arch debranching procedures, 18 studies comprising 195 patients were analyzed. The overall technical success rate was 86% and the operative mortality rate was 9%. The overall peri-operative morbidity rate was 21%, with the two most common complications being endovascular leaks (9%) and peri-procedural stroke (7%).

Hybrid Therapy for Congenital Heart Disease

An integrated hybrid approach combining surgical and interventional techniques is appealing in the treatment of various congenital heart conditions in order to overcome the limitations of each stand-alone procedure. There are scarce data on hybrid congenital approaches, and they mostly come from single-center experiences in a small number of patients.

Clinical scenarios in which a hybrid approach is useful include conditions in which an interventional approach is the preferred therapeutic approach but is limited by several factors, such as patient weight, limited vascular access, and the need for surgical repair of concomitant congenital lesions. To overcome such limitations, in a hybrid approach the devices are placed under direct vision with or without cardioplegic myocardial arrest through a standard surgical or minimally invasive approach. Examples of a hybrid approach are intraoperative device closure of muscular ventricular septal defects that are difficult to visualize and close surgically, treatment of critical aortic stenosis in neonates and infants with intraoperative balloon dilatation or stenting, balloon occlusion of Blalock-Taussig shunts and patent ductus arteriosus, and intraoperative implantation of self-expandable mounted pulmonary valves.

While the hybrid approach to congenital cardiac surgery has been shown to be feasible and safe, it is not a standardized approach, long-term follow-up is not available, and the decision to use a hybrid approach depends mostly on the surgeon’s experience.

Conclusions

Integrated hybrid therapies can be used as treatment options for a variety of cardiovascular conditions. This strategy has the potential to decrease the magnitude of the surgery, being less invasive while not compromising the quality of care. The absolute requirement for success is not the availability of the technology but rather the need for co-operation, trust, a culture of teamwork, and a shared vision and purpose among cardiologists and cardiac surgeons.

As the patients referred for surgery and interventions become ever higher-risk and more complex, hybrid therapies, by combining all the tools available to surgeons and interventionalists, have the potential to deliver new treatment modalities for various cardiovascular diseases. In addition, hybrid therapy provides a vehicle to narrow the current division between cardiologists and cardiac surgeons. Collaboration rather than competition between cardiologists and cardiac surgeons will ultimately benefit patients, hospitals, and healthcare providers and enable optimal utilization of healthcare resources.