Hybrid Revascularization: A Review

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Keywords

Hybrid · Coronary artery · Coronary artery bypass graft · Revascularization · Multivessel disease · Coronary artery disease · Percutaneous coronary intervention

Abstract

Hybrid coronary revascularization (HCR) combines surgical bypass with percutaneous coronary intervention (PCI) performed either during the same procedure or in a staged approach within 60 days. Coronary artery bypass grafting using the left internal mammary artery (LIMA) has shown excellent long-term patency with improved patient survival. It remains the gold standard treatment for the majority of patients with multivessel coronary artery disease. However, saphenous vein grafts have poor long-term patency. Advances in stent technology have resulted in reduced rates of thrombosis and restenosis, making PCI a viable alternative to coronary surgery in selected patients. HCR is attractive as a less invasive method of coronary revascularization which preserves the benefits of the LIMA performed with less invasive surgical techniques with the efficacy of newer generation stents.

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Introduction

Hybrid coronary revascularization (HCR) combines surgical bypass with percutaneous coronary intervention (PCI) performed either during the same procedure or in a staged approach within 60 days [1].

There are several reasons HCR developed as a revascularization strategy for patients with multivessel coronary artery disease. Coronary artery bypass grafting (CABG) using the left internal mammary artery (LIMA) has excellent long-term patency with improved survival. However, saphenous vein grafts (SVG) have significantly worse long-term patency. As a result, surgeons have attempted all arterial revascularization utilizing several strategies including bilateral mammary, sequential mammary, and radial gastroepiploic arteries, but these approaches may be associated with increased complication rates [2].

Advances in stent technology have resulted in reduced rates of thrombosis and restenosis, making PCI a viable alternative to coronary surgery in selected patients. While multivessel PCI with newer-generation drug-eluting stents (DES) is an attractive strategy, use of the LIMA to the left anterior descending artery (LAD) provides the most predictable long-term results [2–4]. The hybrid approach takes advantage of the best features of percutaneous and surgical revascularization approaches. The volume of hybrid coronary revascularization in the US comprises only 0.5% of the volume of CABG operations [5].

However, because of the efficacy of newer generation stents, combined with more sophisticated simplified surgical techniques, the volume of hybrid procedures is expected to increase [1, 5, 6].

Evolution of Surgical Bypass Techniques

One of the major disadvantages of a standard CABG is the median sternotomy incision, with the attendant discomfort and temporary limitations on activity as well as the risks of complications including sternal instability and infection causing delayed recovery. Patients undergoing a standard CABG also often require cardiopulmonary bypass, and manipulation of the aorta increases the risk of stroke and reduced cognitive function [7–9]. Accordingly, surgical techniques have evolved with the goal of minimizing complications while attempting to achieve long-term patency of bypass grafts.

Off-Pump CABG

Off-pump CABG is a safe and effective approach to surgical revascularization. While this technique avoids the consequences of cardiopulmonary bypass, performing surgery on a beating heart can be complicated by hemodynamic compromise due to reduced venous return and cardiac output associated with manipulation of the heart. This type of operation is technically challenging and has been associated with decreased graft patency; however, the use of instruments to stabilize the myocardium and improve visualization of the distal anastomotic site has improved results. The use of an intracardiac shunt, which bypass coronary artery flow, allows for more precise sewing of the anastomosis, too [10]. However, a 5-year study comparing on-pump versus off-pump bypass surgery noted a slightly higher mortality (15.2 vs. 11.9%) in the off-pump group [11].

Minimally Invasive Techniques

CABGs can be performed via a left-sided thoracotomy between the 4th/5th interspace with special retractors suited for smaller incisions (4–5 cm). A smaller incision reduces postoperative discomfort and risk of infection as well as speeds recovery [12]. Although the LIMA is under direct visualization, doing this surgery through a smaller incision with a beating heart is technically challenging. Endoscopic atraumatic CABG can be performed via thoracoscopic incisions. This approach requires single lung ventilation and CO₂ insufflation but provides better visualization than a mini-left thoracotomy.

Lastly, totally endoscopic CABG surgery (TECAB) is also available using the Da Vinci robotic system. The anastomosis can be made on a beating heart with a suture technique or without sutures utilizing an anastomotic connector device. However, TECAB is contraindicated in patients with severe pulmonary disease and hemodynamic instability, and for intramyocardial coronary arteries. TECAB is limited by a 10% conversion rate to standard CABG and the requirement of expensive technology and training [10].

Use of All Arterial Revascularization

One of the limitations of a standard CABG is poor SVG patency compared to PCI with newer generation DES. Although results vary widely, about 20% of vein grafts occlude in the 1st year, and by 10 years, vein graft patency is less than 50% due to an accelerated form of atherosclerosis [13, 14]. Despite these findings, SVG continue to be used in approximately 75% of patients even in experienced centers. Surgeons have sought to overcome the problem of poor SVG patency by performing all arterial revascularization. The most common approach is to use both mammary arteries. The Arterial Revascularization Trial (ART) did not show any significant difference between single (SIMA) and bilateral internal mammary artery (BIMA) mortality outcomes at the 5-year follow-up; however, sternal wound complications were more prevalent in the bilateral artery approach group [15]. Sternal reconstruction rates were 1.9% in the BIMA group versus 0.6% in the SIMA group [16]. However, the ART post hoc analysis showed that using an additional radial artery rather than SVG during a SIMA or BIMA is associated with a lower risk of major adverse cardiac events in patients undergoing CABG [17]. The outcomes of a 10-year follow up are still pending.

Evolution of DES and Percutaneous Techniques

First-generation DES (sirolimus and paclitaxel eluting) are associated with a 2% 1-year and up to 5% 10-year risk of stent thrombosis [18]. The development of second-generation stents with thinner struts, more compatible polymers, and effective cytostatic drugs resulted in reductions in mortality (0.4 vs. 3.1%) and major adverse cardiovascular and cerebral events (MACCE) in patients with multivessel disease [19, 20].

In patients with multivessel disease, target vessel revascularization rates were 14.6% in the DES PCI group and 6.8% in the CABG group ($p < 0.001$). This contributed to a higher MACCE in PCI (21.2 vs. 16.3%) [21]. PCI

Fig. 1. Drug-eluting stents can effectively treat the culprit lesion in a non-LAD vessel. However, these patients may require re-intervention due to stent thrombosis and restenosis (A) or disease progression distal to the stent (B). While saphenous vein grafts bypass the entire coronary vessel avoiding the problem (C) with disease progression, accelerated atherosclerosis within the venous conduit itself is associated with high rates of occlusion (D).

using newer everolimus stents in patients with low to intermediate angiographic risk scores is noninferior to CABG with similar rates of death, myocardial infarction (MI), and stroke at 3 years [22]. Although newer-generation DES have decreased risks of thrombosis and restenosis, the need for target vessel revascularization remains a concern for patients undergoing a hybrid procedure [3, 5]. Similarly, repeat revascularization was higher in HCR than standard CABG due to disease in non-LAD locations (3.8% HCR vs. 1.4% CABG after 1 year) [3]. MACCE rates in patients undergoing multivessel PCI were significantly higher than in patients undergoing HCR due to repeat revascularization of the LAD in the PCI group (22.7 vs. 6.4%, $p < 0.001$) (Fig. 1) [23].

Indications for Hybrid Revascularization

The 2012 ACC/AHA guidelines recommend HCR for patients with heavily calcified proximal aortas, poor bypass conduits and landing targets for non-LAD vessels that are otherwise amenable for PCI. Use of the LIMA as part of

a hybrid procedure is especially advantageous if there is complex LAD anatomy making that vessel relatively unsuitable for PCI. Specific features that make the LAD unsuitable include heavily calcified lesions, tortuosity, bifurcation lesions, and chronic total occlusions (class IIa, level B evidence). HCR should also be considered for patients in whom HCR would improve the risk-benefit ratio compared to CABG or PCI (class IIb, level C evidence) [24]. Patients with multiple comorbidities such as malignancies, diabetics with a high risk of wound infections, severe obesity, or frailty may also be considered for HCR (Table 1) [25].

In order to perform the hybrid procedure, patients should have a LIMA harvest possible using minimally invasive or endoscopic approaches. Patient characteristics such as deconditioning, difficult rehabilitation, and reluctance to undergo median sternotomy may also play a role in decision-making leaning towards HCR [26].

Conversely, if lesions in the right or left circumflex coronary arteries have a complex anatomy and require multiple stents, are highly calcific, or are chronically totally occluded, then HCR is not recommended [27, 28].

Table 1. Hybrid coronary revascularization

Indications	Contraindications
Inadequate or poor quality of venous conduits	Clinical characteristics
History of a prior CABG	Coagulopathies and contraindications to dual antiplatelet therapy
Poor graft insertion sites in non-LAD lesions	Severe chronic obstructive pulmonary disease
Non-LAD lesions amenable to PCI	Pulmonary hypertension
LAD lesion not amenable to PCI	Access limiting PVD
Severe aortic and mitral calcification	Need for additional procedures such as valve repairs
Previous chest radiation	Anatomy
	Complex non-LAD lesion requiring multiple stents or overlapping
	Poor LIMA graft quality or anastomosis site
	Logistic limitations
	Lack of hybrid OR (concurrent procedures)
	Paucity of experience and surgeon comfort level to harvest LIMA via a minimal incision or an endoscopic approach

CABG, coronary artery bypass grafting; LAD, left anterior descending artery; LIMA, left internal mammary artery; PCI, percutaneous coronary intervention; OR, operating room; PVD, peripheral vascular disease.

Concurrent versus Staged HCR

Current data suggests no differences in hospital death, MI, stroke, and repeat revascularization in staged versus concurrent procedures [3].

Concurrent Procedures

Concurrent procedures performed in a specially constructed hybrid suite provide the ability to switch to an open procedure if necessary [3]. This procedure also allows complications to be resolved immediately and avoids the need for 2 separate procedures. Real-time angiography may be performed after the completion of LIMA anastomosis to assure the quality of the anastomosis and permit revision if needed [14].

There was a discrete proximal right coronary artery lesion, easily treated with DES placement. The patient had dual antiplatelet therapy (DAPT) administered after the surgical portion of the procedure, thus minimizing the bleeding risk. He was discharged after 2 days and remained asymptomatic at the 6-month follow-up.

Undergoing multivessel revascularization in one setting in a concurrent approach also reduces contrast and anesthetic exposure and hence provides greater efficiency, shortens length of stay, and improves patient satisfaction (Fig. 2a, b) [3, 5, 13].

However, the bleeding risk is greater if DAPT is utilized [29]. Concurrent HCR could reduce the risk of bleeding with a “modified antiplatelet and anticoagulation protocol,” which includes continuous use of aspirin

perioperatively and a loading dose thienopyridines immediately before PCI [30]. The risk of stent thrombosis may also be greater due to the proinflammatory milieu during surgery [25, 31].

Staged – Surgery Followed by PCI

Surgery followed by PCI is the most frequently used approach. Bleeding risk is reduced when DAPT is administered after anastomosis completion. This approach is more challenging and time consuming for the surgeons depending on the learning curve especially while non-LAD regions still remain suboptimally perfused before PCI [26]. The advantages of surgical anastomosis followed by PCI provide a protected LAD and allows aggressive use of antiplatelet therapy to reduce the risk of stent thrombosis [24, 31]. Disadvantages include a higher cost [10]. Patients in this group may be at risk of a second surgery if PCI fails or complications occur following surgical anastomosis [1].

Staged – PCI Followed by Surgery

PCI followed by surgery is useful in patients with an emergent need for left circumflex or right coronary artery revascularization such as in an acute MI followed by surgical revascularization if there is also a nonurgent complex LAD lesion present on angiogram [25].

The disadvantages include PCI with an unprotected LAD and increased risk of bleeding during subsequent CABG [26]. With PCI already performed, angiographic confirmation is also not readily available should any complications arise from the PCI or surgery [5]. Interruption of

Fig. 2. Angiograms of an 80-year-old man who presented with angina and was evaluated for a concurrent hybrid procedure. He received off-pump coronary artery bypass grafting with a left internal mammary artery (LIMA) to the left anterior descending artery (LAD) via left thoracotomy for a calcified bifurcation lesion. Black arrows indicate LAD/diagonal bifurcation lesion with a stenosis of the ostium.

DAPT prior to surgery is associated with an increased risk of stent thrombosis [25]. Regardless of which is performed first, the disadvantages of a staged procedure include having 2 teams, 2 handoffs, and a longer length of stay [5].

Outcomes of HCR

Standard CABG versus HCR

The majority of the head-to-head comparisons that are available currently are driven from compiled meta-analyses of smaller studies due to the lack of larger multicentered randomized studies (Table 2). In general, most of the meta-analyses conclude that HCR is noninferior to CABG in terms of cumulative MACCE; however, some

reports emphasized that repeat revascularization was more often required in the HCR group.

In terms of short-term outcomes, there is no difference in 30-day and 1-year outcomes including in-hospital MI, stroke, or death for HCR versus standard CABG [3]. Patients undergoing HCR required fewer transfusions and had reduced length of stay in the intensive care unit compared to patients undergoing standard CABG [3, 34]. In-hospital events, including reoperation, renal failure, ventilator duration, and infections, were significantly lower in the HCR (8.5%) than the CABG group (15.5%) ($p = 0.005$) [32]. The quality of life 6 weeks after discharge was better in the HCR group [3]. These attributes are secondary to the less invasive nature of a minimal incision compared to a cardiopulmonary bypass and sternotomy.

Table 2. Summary of major meta-analyses comparing hybrid coronary revascularization (HCR) to a standard coronary artery bypass grafting (CABG)

First author, year	Patients, n	Studies, n	HCR	CABG	Death	MI	Stroke	RR	MACCE	Conclusions
Zhu [8], 2015	6,176	10	623	5,553	1.76 vs. 1.67% <i>p</i> = 0.64	1.1 vs. 0.6% <i>p</i> = 0.54	1.1 vs. 1.1% <i>p</i> = 0.81	0 vs. 0.28% <i>p</i> = 0.68	2.5 vs. 3.5% <i>p</i> = 0.26	HCR noninferior to CABG inhospital and 1-year follow-ups
Hu [14], 2015	5,453	7	422	5,031	No diff. (in hospital) <i>p</i> = 0.47	Not discussed	Not discussed	Not discussed	No diff. (in hospital) <i>p</i> = 0.34	HCR did not improve survival compared to CABG but decreased secondary outcomes: blood transfusions, length of ICU stay and intubation; HCR also increased inhospital costs
Harskamp [3], 2014	1,190	6	366	824	3-year mortality: 4.5 vs. 7.3% <i>p</i> = 0.51	0.6 vs. 1.5% <i>p</i> = 0.39	At 1 year: 0 vs. 2.4% <i>p</i> = 0.31	3 years 8.3 vs. 3.4% <i>p</i> < 0.001	1 year 4.1 vs. 9.1% <i>p</i> = 0.13	HCR MACCE events are comparable to CABG outcomes during inhospital stay and at 1 year, but RR is more frequently seen in patients treated with HCR (especially greater need for LAD revascularization and nontarget lesion revascularization from native disease progression)
Harskamp [32], 2015	668	6	325	343	4.9 vs. 8.2% <i>p</i> = 0.24	2.2 vs. 4.4% <i>p</i> = 0.2	0.6 vs. 2.9% <i>p</i> = 0.039	6.9 vs. 2.1% <i>p</i> < 0.001	8.6 vs. 11.6% <i>p</i> = 0.24	HCR reduces risks of strokes compared to CABG but increases need for RR
Phan [33], 2014	1,664	8	505	1,159	30 days: 1 vs. 1.3% <i>p</i> = 0.8	5.7 vs. 4.9% <i>p</i> = 0.01	0.7 vs. 0.7% <i>p</i> = 0.96	11.3 vs. 3.2% <i>p</i> < 0.0001	1.7 vs. 3.4% <i>p</i> = 0.31	HCR is associated with fewer MI and shorter hospital stay but greater need for RR

All percentages are comparisons of HCR to CABG. diff., difference; MACCE, major adverse cardiovascular and cerebral events; MI, myocardial infarction; RR, repeat revascularization.

Bypass time >100 min is a risk factor for major infection [35]. LIMA harvest can be time consuming as it still depends on the learning curve through smaller left thoracotomy incision. Angiography during the hybrid procedure provides confirmation of graft patency when PCI is followed by surgery [7]. The conversion from HCR to a standard CABG occurred in 6.1% of cases [10]. In HCR, long-term survival rate is 92.5–100% at 1 year and 93% at 5 years [10]. In the HCR group, the LIMA patency over 3–5 years ranged from 93–100%, and re-intervention on the LAD anastomosis was low at 1–4% [10]. Non-LAD revascularization was most frequently required in patients with diabetes [25].

Compared to standard CABG, heart teams opted for HCR due to poor grafts and conduits 43.4% of the time and to minimize surgical risk 47.8% of the time [4]. A useful tool to assess disease severity based on angiographic findings, the SYNTAX score, allows stratification of patients according to lesion complexity and the amount of myocardium at risk. In patients with increased disease complexity, triple vessel disease, and high-to-intermediate SYNTAX score, a standard CABG is preferred [4, 5].

PCI versus HCR

In HCR, stent restenosis ranged from 9 to 13%, and thrombosis ranged from 2.2 to 3.7% [10, 36, 37]. One of the causes of non-LAD revascularization was stent thrombosis (in bare-metal stents and DES), which was as high as 6% in a small study including 100 patients followed for a mean of 5 years [25]. The risk of stent thrombosis is highest if PCI is performed before a surgery secondary to DAPT interruption beforehand [10]. These rates are similar to DES thrombosis rates noted in the SYNTAX trial, which utilized older-generation stents (3.3% at 12 months) [38, 39]. Guidelines established following the SYNTAX trial for patients with left main disease recommend that patients with low to intermediate syntax score (0–32) may undergo PCI as a class 2a or 2b indication [40]. Of note, a head-to-head comparison between SVG performance against newer-generation DES is lacking.

HCR versus BIMA

Five percent of coronary artery bypass surgery utilizes BIMA [1]. Although there is no difference in 5-year mortality rates, sternal wound infections and reconstruction rates were greater in patients undergoing BIMA than SIMA CABG [2]. Based on the Society of Thoracic Sur-

geons database, the predicted mortality risk in HCR is 1.6 versus 1.1% in BIMA conduits [34]. A direct comparison of BIMA revascularization with HCR is still lacking.

HCR versus On-Pump and Off-Pump CABG

HCR avoids the consequences of a cardiopulmonary bypass, aortic cross clamping, and sternotomy [3]. Coronary occlusion time is significantly shorter in HCR (single graft placement and 30-second intervals for stent placements) than off-pump CABG (8–12 min per anastomosis). Troponin leaks are lower, and recovery is quicker in HCR patients [14, 41]. The all-cause mortality was similar (1.2% on pump vs. 1.1% off pump at 1 month and 2.5% on pump vs. 2% off pump at 1 year) [42]. However, graft patency is better with on-pump revascularization [6].

HCR Outcomes in High-Risk Groups

Patients in the high-risk group (SYNTAX score >32) performed better with a standard CABG than HCR (mortality risk of 7.5 vs. 23%) [10, 43, 44]. The MACCE and target vessel revascularization rates were higher in the HCR group in patients with a SYNTAX score of ≥ 22 [25]. Repeat revascularization in patients with higher SYNTAX scores makes HCR less desirable than CABG.

Stroke

Stroke rates are lower in off-pump CABG (0.14%) and on-pump beating-heart CABG (0%) but higher in cardioplegic CABG (0.5%) [35]. There is an increased risk of stroke in patients undergoing CABG due to cardiopulmonary bypass and surgery on the ascending aorta [8]. The risk of stroke increases in elderly patients. In a study comparing HCR to CABG in patients over 65 years old, stroke rates were approximately 1.4% in both groups [27].

Stroke prevention methods should include epiaortic ultrasound to assess aortic calcifications and the burden of atherosclerosis [45]. DAPT after concurrent HCR may help reduce stroke rates [13]. Whether DAPT after concurrent HCR prevents postoperative strokes needs to be further evaluated to formulate guidelines on therapy depending on the type of HCR performed (concurrent, PCI first vs. LIMA to LAD first) [46].

Limitations of the HCR Procedure

The limitations of HCR include a potentially longer operative time as a result of inexperience and working through small incisions [26]. Successful HCR heavily relies on the quality of anastomosis. LIMA failure can have severe long-

term implications [3]. While patency is still >95%, 2 studies that assessed long-term outcomes of LIMA failure showed a higher prevalence in HCR compared to standard CABG. This may in part be due to increased detection when completion angiography is performed [47, 48]. Seven percent of LIMA grafts in standard CABG have angiographic evidence of defects, and angiographic confirmation may be helpful in revising the anastomosis in HCR [49].

Revascularization may be less complete in HCR, and long-term effects of underrevascularization are yet to be determined. Long-term data on MACCE are lacking for emergent conversion of off-pump bypass [50]. Patients who were converted from an off-pump to on-pump CABG had a higher mortality rate [35]. Other limitations of HCR also include limited guidelines for patient selection [34, 51]. While the initial hospitalization is relatively shorter and more cost effective, the uncertainty of long-term outcomes especially with newer stents, subsequent hospitalization for restenosis, and further angiograms must also be evaluated (Fig. 3) [5].

Future Direction

Long-term outcomes of HCR relative to the type of coronary anatomy and comorbidities need further evaluation. Furthermore, development of an optimal antiplatelet regimen requires refinement. Currently, thienopyridines are administered either after CABG or after PCI but without definite guidelines [26]. The use of agents which reduce the bleeding risk (tranexamic acid) may make surgery safer in patients who require DAPT in staged and concurrent procedures [52]. The role of HCR is expected to grow with the aging patient population with multiple comorbid conditions and complex diseases.

Heart team discussions should weigh the benefits of a minimally invasive procedure in a poor surgical candidate against the complications such as repeat revascularization in those with greater disease burden or higher SYNTAX scores. The data are limited mainly because of selection bias, lack of direct comparison to other modes of treatment (PCI/CABG), lack of randomization, the retrospective nature of published studies, and small sample sizes. The strikingly reduced thrombosis rates with newer antiplatelets such as prasugrel and ticagrelor and restenosis rates with newer generation stents will promote a greater use of HCR [23].

Clopidogrel and prasugrel are 2 commonly used antiplatelets for DAPT purposes. While prasugrel is superior to clopidogrel with respect to potency, they irreversibly bind to the P2Y₁₂ receptor, which creates a bleeding risk

Fig. 3. Flowchart of current treatment of multivessel disease. CABG, coronary artery bypass grafting; DAPT, dual antiplatelet therapy; LAD, left anterior descending artery; OR, operating room; PCI, percutaneous coronary intervention; SVG, saphenous vein graft.

when used around the time of surgery. Due to a faster onset, ticagrelor may be more useful in concurrent procedures immediately following surgery or even prior to surgery due to reversible mechanism of action [53]. Cangrelor is another novel rapid-acting intravenous medication that has shown to reduce acute stent thrombosis and MI rates without increasing bleeding risk compared to clopidogrel [54]. The implications of these findings in HCR have not been evaluated.

Given the absence of randomized trials, a major study will be undertaken: the HCR Pivotal trial. This will compare outcomes of a standard HCR to drug-eluting metallic stent PCI (including the LAD) in patients with multivessel disease [55].

Coronary bypass surgery has remained the gold standard for revascularization in patients with multivessel disease. However, improvements in PCI technology, coupled with advances in minimally invasive surgical tech-

niques, now make it possible to consider a hybrid approach in carefully selected patients. To this end, a heart team approach with a careful review of patients' clinical and anatomic characteristics should be utilized.

Conflict of Interest

The authors have no conflict of interest to disclose.

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