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Status Quo of Hybrid Coronary Revascularization for Multi-Vessel Coronary Artery Disease

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Abstract

Hybrid coronary revascularization (HCR) combines bypass grafting of the left anterior descending (LAD) coronary artery with percutaneous coronary intervention (PCI) of non-LAD vessels. HCR has been performed as an alternative to CABG or multi-vessel PCI in thousands of patients since the late 1990s. In this review article, we provide an overview on patient selection, procedural sequence and timing, use of surgical techniques and anti-platelet agents. Additionally, patient recovery, satisfaction, costs and clinical outcomes of individual studies after HCR are evaluated. Future directions are also discussed, including the need for adequately powered randomized trials.

Coronary revascularization provides symptomatic relief and improves long-term outcomes in patients with multi-vessel coronary artery disease [1]. The optimal revascularization strategy remains controversial, and depends on the anatomic complexity of the lesions requiring revascularization, comorbidities, and the ability to use dual antiplatelet therapy [2, 3]. Although coronary artery bypass graft (CABG) surgery is a long-established revascularization approach and hence considered “gold standard,” rapid developments in percutaneous techniques and devices as well as advances in medical therapy continue to challenge the status quo [4]. The major therapeutic benefits of CABG surgery over percutaneous coronary intervention (PCI) is the use of the left internal mammary artery (LIMA) to bypass the left anterior descending (LAD) artery irrespective of its lesion complexity. The superior patency of LIMA-to-LAD graft provides prophylaxis against future proximal LAD lesions, which translates into better event-free survival and relief of angina [5]. The benefits of bypassing other non-LAD coronary vessels are much less clear [6]. Conduits for a non-LAD vessel may include other arterial grafts (“multi-arterial” or “complete arterial” revascularization) but the saphenous vein is by far the most commonly used. A major limitation of CABG with saphenous vein grafts (SVG) lies in the high graft failure rates with reports ranging from 13% to 29% at 1 year and up to 50% at 10 years after

surgery [7–9]. Although direct comparison data between SVG failure and PCI is not available, restenosis rates (<10%) and stent thrombosis rates (<1%) of drug-eluting stent (DES) in non-LAD lesions are markedly lower [10–12] (also see Fig 1). Additionally, subsequent revascularization for SVG failure is challenging and associated with much higher rates of periprocedural complications than native vessel PCI [8, 13, 14]. From a patient perspective, PCI also has the advantage of being minimally invasive with less patient discomfort, faster return to normal activities, and lower risk of complications such as stroke [15]. In order to combine the superior patency of the LIMA-to-LAD graft with the low restenosis rates of PCI to non-LAD regions, a hybrid approach was introduced to coronary revascularization. The present study provides an overview of evidence for the use of hybrid coronary revascularization (HCR) in the current DES era and explores strategies that may help improve the future role and implementation of HCR in patients with multi-vessel coronary artery disease.

Material and Methods

Two authors (R.E.H., R.D.L.) searched the MEDLINE database using the PubMed interface to identify published studies that examined hybrid coronary revascularization and were published from January 1, 1996 through May 1, 2013. The search was performed using the following terms: “hybrid coronary revascularization,” “integrated coronary revascularization,” and “hybrid myocardial revascularization.” Additionally, we reviewed references from these articles for studies not found through the initial search. Both original and review articles were included, and publications were restricted to studies published in the English literature. From the available literature we distilled information on patient selection, timing and sequence of procedures, surgical and interventional techniques, antiplatelet drugs, clinical outcomes, patient satisfaction, and costs.

Patient Selection for Hybrid Coronary Revascularization

Patients who would qualify for HCR are those with symptoms or signs of ischemia, due to multi-vessel disease with significant proximal LAD disease, along with lesions suitable for PCI in the left main, left circumflex or right coronary artery territories. As such, cases with chronic total occlusions, highly calcified segment, and diffusely diseased and bifurcation coronary lesions were usually deferred to conventional CABG. Patients with a lack of suitable conduits, prior sternotomy, severe ascending aortic disease, or coronary arteries not amenable for bypass, may also be suitable candidates. Those cases in which the decision to perform additional PCI based on intraoperative findings (poor conduits, ungraftable vessels, graft defects) and patients who underwent CABG after PCI, either for ongoing ischemia or complications, are considered unplanned HCR [16]. This also includes cases in the setting of acute coronary syndrome, where PCI of the culprit vessel is followed by CABG during the same hospitalization for grafting of the non-culprit coronary arteries. Table 1 summarizes clinical and angiographic characteristics that one should consider when opting for HCR. Decision making when opting for hybrid CABG, should involve close consultation between interventional cardiologist and cardiac surgeon, preferably in the setting of a “heart team.”

Timing and Sequence of Hybrid Revascularization

Planned HCR can be performed as either a concomitant procedure in a hybrid operating room in which CABG and PCI are performed in the same anesthesia setting, or performed in 2 stages in which PCI and CABG are performed separately within hours, days, or weeks. When HCR is performed staged, PCI can be performed first followed by CABG or vice versa. These approaches all have their merits and disadvantages, as displayed in Table 2. However, recommendations on the optimal choice of HCR are based on expert opinion and supported by very few data that actually support one HCR strategy over another. Table 3 summarizes available evidence on comparisons of various HCR strategies.

One-Stage HCR

The advent of hybrid operating suites allowed for complete revascularization at the same sitting, the ability to perform routine imaging of the LIMA-LAD, a safety net when PCI fails which also allows the performance of PCI in more challenging lesions such as bifurcation and left main lesions [17, 18]. Additionally, the simultaneous approach reduces waste and duplication of resources and is likely to result in a shorter length of stay compared with other approaches of HCR. However, some investigators do not favor the use of a 1-staged approach due to concerns about bleeding because of the use of dual anti-platelet therapy and incomplete heparin reversal, as well as the concern for acute stent thrombosis due to the proinflammatory milieu directly after surgery [19]. Other challenges that limit the applicability of 1-staged HCR in general practice are increased costs, need for a hybrid operating suite with trained personnel, inadequate hospital reimbursement, and the logistical difficulties of coordinating 2 different teams in the same operating room at different times.

Two-Stage: PCI Followed by CABG

Although performing PCI of non-LAD lesions prior to CABG has several advantages, it is currently reserved for patients with acute coronary syndrome with a non-LAD culprit. In cases where DES is used, this approach may complicate the surgical procedure because of bleeding risks associated with the need for continued use of dual antiplatelet therapy [20, 21]. Newer antiplatelet agents may lower bleeding rates compared with clopidogrel, but further study is required [22, 23]. Also, compared with other HCR approaches, PCI followed by CABG does not allow routine assessment of the patency of the LIMA-LAD graft.

Two-Stage: CABG Followed by PCI

The LIMA-LAD grafting and PCI-DES for non-LAD lesions is currently the most adopted HCR strategy. Unlike the other strategies, dual antiplatelet therapy can be freely given postoperatively without concern for intra-operative bleeding. Similar to 1-stage HCR, the patency of LIMA-LAD can be confirmed with angiography at the time of PCI. Although performing PCI after the CABG avoids operating on patients who have taken antiplatelet agents, in the rare scenario of a PCI complication or failure, an additional transfer to the operating room and emergent CABG would still be required. For the surgeon, this approach is also more challenging due to a higher risk for inducing ischemia during the hybrid surgical procedure, due to significant coronary disease in the non-LAD vessels.

Surgical Techniques Used for HCR

Single bypass graft of the LIMA to the LAD can be performed with a number of techniques, as summarized in Table 4. The rationale for the use of minimally invasive techniques is to perform isolated LIMA-LAD revascularization while avoiding thoracic access through median sternotomy, or aortic manipulation due to cross-clamping and cardiopulmonary bypass, which may reduce the incidence of adverse neurologic events, infection, bleeding, and pulmonary complications as seen in conventional CABG surgery [17, 24–27]. Choosing the right surgical approach for LIMA-LAD anastomosis depends on the individual patient characteristics as well as surgeon's familiarity with each of these techniques.

Use of (Novel) Antiplatelet Agents in Hybrid Procedures

Two major concerns with HCR in the DES era are bleeding complications and acute stent thrombosis related to perioperative anticoagulation and antiplatelet agents. Guidelines or consensus on the use of antiplatelet therapy specifically for HCR do not exist. A number of studies have reported their experiences with varying degrees of success in preventing acute stent thrombosis as well as perioperative bleeding. Part of the challenge lies in the order of staging (PCI followed by CABG or vice versa) as well as timing of initiation of therapy. In case series of simultaneous HCR (CABG directly followed by PCI), a loading dose of clopidogrel (300 or 600 mg) is given either directly before surgery in the holding area [17], after LIMA insertion [28, 29], or after PCI is completed [17, 30, 31]. Interestingly, although maximal inhibition of platelet aggregation occurs only after a couple of hours [32], meaning there is incomplete platelet inhibition at the time of procedure, the reported rates of acute stent thrombosis are low (0% to 7%). Some authors suggest that in procedures performed with cardiopulmonary bypass, the use of cardiopulmonary bypass may be protective against the risk of stent thrombosis [33]. Although most studies used heparin, 1 study used bivalirudin, claiming that the extended anticoagulation effect of bivalirudin will make up for the lack of adequate antiplatelet inhibition [30]. However, stent thrombosis in this series was higher (7%). As shown in Table 5, the available data do not suggest an increased risk of bleeding that requires reoperation. Some studies even suggest lower bleeding risk after HCR, as demonstrated by less requirements for transfusion, fewer units of red blood cells required, and a trend toward less chest tube output [17, 28, 31]. Newly developed P2Y₁₂ inhibitors such as prasugrel, ticagrelor, and cangrelor, are more potent and have a faster onset of action and reversal than clopidogrel, as shown in various registries and clinical trials among patients undergoing elective and acute PCI [32]. Because of these properties, such new agents may also play an important role in balancing the risk of acute stent thrombosis and perioperative bleeding. Currently, however, there is no experience or data to support the use of these agents in patients undergoing HCR.

Case Series Reporting on Clinical Outcomes After HCR

Many case series have been published on the procedural and mid-term outcomes after HCR. In a review study by DeRose [25], 492 cases were reviewed that were published in 13 case series from 1999 to 2009. These series show high LIMA patency rates (93% to 100%) as well as low 30-day mortality (0% to 1.4%). Among case series with mid-term clinical follow-up (6 to 33 months), event-free survival (70% to 100%), as well as target lesion

revascularization (0% to 29.6%) varied considerably at follow-up (6 to 33 months) [18, 18, 30, 34–44]. Recent case series in which HCR was performed with exclusively drug-eluting stents, event-free survivals were overall higher (89% to 100%) and target lesion revascularization rates were lower (0% to 7.6%) at follow-up (6 to 18 months) [17, 28, 30, 31, 43, 45–48]. A recently published 2-center experience ($n = 226$) on long-term outcomes simultaneous HCR with total endoscopic coronary artery bypass grafting (TECAB) and PCI (DES in 70%) on an intention-to-treat basis, showed 5-year survival of 92.9% and freedom from major adverse cardiac and cerebral events of 75.2% [49]. The data from these series suggest that HCR has a good safety profile among experienced operators but they do not provide insights on how HCR compares with conventional CABG.

Studies Comparing Outcomes After HCR Versus CABG and Multi-Vessel PCI

Table 5 summarizes available studies that have compared the outcomes of HCR with CABG or multi-vessel PCI in the era of drug-eluting stents. All studies used a non-randomized design, and involved unmatched, matched, or consecutive cohorts. Overall, in-hospital mortality, stroke, and reoperation for bleeding rates were comparable among reported studies, with the exception of 1 small subset of high-risk patients where favorable outcomes were seen in patients after conventional CABG [50]. In studies reporting long-term follow-up, survival ranges from 86.8% to 100% after HCR and 83.4% to 100% after conventional CABG. These studies suggest that in patients with non-LAD lesions amenable for PCI, the outcomes for HCR and conventional CABG surgery may be similar. However, as none of the studies used random treatment allocation and were individually too small to detect meaningful clinical differences, definite conclusions cannot be drawn.

Patient Satisfaction, Recovery, and Costs After HCR

Studies on patient satisfaction found that although 30-day satisfaction was similar, 1-year patients' satisfaction was remarkably better in patients after HCR compared with off pump coronary artery bypass (OPCAB) [17, 51]. Quality of life assessment was also found to be better in the HCR group (physical score: 32.8 ± 10.4 vs 41.6 ± 10.3 , $p = 0.009$, using SF-12) [51]. A number of reasons may contribute to this difference in quality of life and patient satisfaction. Postoperative pain management is of importance for patient satisfaction. Although pain experienced after minimally invasive direct coronary artery bypass is higher compared with other minimally invasive surgical techniques and with sternotomy, the duration for pain to subside is shorter after HCR (10.3 ± 10.9 vs 45.5 ± 33.6 days, $p = 0.004$) [17, 51]. Additionally, the length of intensive care and hospital stay is significantly shorter after HCR compared with CABG or OPCAB, particularly in those who underwent simultaneous or same-day staged HCR (Table 5). After discharge home, patients who underwent HCR returned to work and normal activities much quicker. A study led by Kon and colleagues [17] reported that the odds of returning to work at less than 1 month were significantly better for HCR versus OPCAB after adjusting for potential confounders (odds ratio, 7.60; 95% confidence interval, 1.61 to 35.91; $p = 0.01$). The average time to return to work in patients after HCR was 1.75 ± 1.0 months versus 4.4 ± 3.1 months after patients who underwent OPCAB. A recent study by Bachinsky and colleagues [51] confirmed these findings in a case series of patients undergoing 1-stage HCR with Endo-ACAB, with average time to return to work of 5.3 ± 3.0 weeks versus 8.2 ± 4.6 weeks ($p = 0.01$).

Apart from greater patient satisfaction and shorter length of hospital stay, some studies have also specified costs related to HCR in comparison with complete revascularization with CABG. Some reports suggest that HCR is more costly than OPCAB, the most cost-effective surgical form of complete revascularization [9], while others suggest equal in-hospital costs. We summarized in-hospital cost-specific data for studies using simultaneous HCR with the use of DES versus OPCAB in Figure 2. Hidden cost data include the financial resources spent on the construction of a cardiac hybrid operating room as well as training of personnel. An operational cardiac hybrid room requires a radiolucent operating table suitable for CABG and PCI, X-ray source and imaging camera equipment, surgical and interventional equipment, echocardiography machine, equipment for continuous arterial monitoring and digital imaging, cardiac anesthesia monitoring equipment, and a cardiopulmonary bypass pump. Construction of these rooms usually requires the conversion of at least 2 standard operating rooms [52].

Future Directions

Despite the promising early and mid-term results, recovery parameters and patient satisfaction, HCR still remains relatively limited in its use. A number of factors are accountable. First, there have been no randomized clinical trials that have compared HCR with CABG or multi-vessel PCI to establish an accepted standard of use. In order to demonstrate that HCR is non-inferior or even superior to conventional revascularization strategies in terms of long-term death, myocardial infarction, stroke, and additional revascularization, adequately sized randomized controlled clinical trials are warranted. Apart from studies on clinical outcomes, additional studies are needed to study the optimal timing and sequence of procedures as well as the use, timing and dosage of (novel) antiplatelet agents to lower the risks of bleeding and acute stent thrombosis. Particular interest should be given to women, older adults, individuals with diabetes mellitus, or chronic kidney disease because research on those vulnerable patient populations is currently lacking. Apart from clinical trial data, the construction of national registries with detailed in-hospital data and longitudinal follow-up are warranted as single-center registries are currently too small to address these questions. Second, there remain numerous logistical challenges, particularly for centers that want to perform 1-stage HCR, as many institutions do not have the resources for successful implementation of a hybrid revascularization program, which includes the costs associated with planning, hybrid operating room, and training of personnel. Lastly, seamless collaboration of interventional cardiologists and cardiac surgeons, and their respective nursing, technical, and planning teams is required to implement a successful HCR program.

Hybrid coronary revascularization is a promising technique that combines the advantages of the LIMA-to-LAD graft with the superior patency of DES compared with SVGs on non-LAD vessels. As such, HCR provides a minimally invasive alternative to conventional CABG and may provide a more durable alternative to multi-vessel PCI. Despite the rapid advances in stent technology and surgical techniques, experience with HCR is currently limited to a little over a thousand cases in a dozen centers around the globe. In order to find a larger and more permanent role for HCR as a mainstream revascularization strategy in the management of patients with multi-vessel disease, further study into the comparative

effectiveness of HCR to both conventional and off-pump CABG and multi-vessel PCI is warranted.

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Fig 1.

Rates of vein graft failure with 1-year angiography and restenosis and stent thrombosis rates in drug-eluting stents [7–12, 66].

Fig 2.

In-hospital cost-specific data of the average patient after 1-stage hybrid coronary revascularization (HCR) versus complete revascularization with off-pump coronary artery bypass graft surgery (OPCAB).

Table 1

Recommendations for Suitable Candidates for Hybrid Coronary Revascularization Versus Conventional Coronary Revascularization

Characteristic	PCI	HCR	CABG
Angiographic characteristics			
ULMD	-	+	+
Intramyocardial LAD	+	-	-
Complex LAD lesion [53, 54, 55]	-	+	+
Complex non-LAD lesion [53, 54]	-	-	+
Comorbidities			
Advanced age	+	+	-
Frailty [53, 54]	+	+	-
LVEF <30%	-	+	+
Diabetes mellitus	-	+	+
Renal insufficiency	-	+	+
Severe chronic lung disease	+	-	-
Prior left thoracotomy	+	-	+
Prior sternotomy [55]	+	+	-
Limited vascular access	-	-	+
Lack of available conduits [53, 54]	+	+	-
Severe aortic calcification [53, 54]	+	+	-
Contraindication for DAPT	-	-	+

+ = recommended; - = not recommended.

CABG = coronary artery bypass graft; DAPT = dual antiplatelet therapy; HCR = hybrid coronary revascularization; LAD = left anterior descending artery; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; ULMD = unprotected left main disease.

Table 2

Advantages and Limitations of Use of Various HCR Approaches

Factor	One-Setting	CABG Followed by PCI	PCI Followed by CABG
LIMA-LAD patency	Assessment directly after completing anastomosis	Assessment during follow-up PCI	Not routinely assessed
Suitable in non-elective setting	No	No	Yes
PCI of complex lesions	Possible	Possible	Possible, but more risky with non-revascularized LAD
Arterial access for PCI	Obtain before anticoagulation administered for surgery	Obtain at the time of PCI	Obtain at the time of PCI
Anticoagulation	Administered once	Administered twice	Administered twice
Discontinue DAPT	No	No	Yes/No
Risk for intraoperative bleeding	High	Low	High (if DAPT continued)
Risk of acute stent thrombosis	Intermediate	Low	High
DES use	Suitable	Suitable	Not suitable
LOS	Likely to be shorter	Likely to be longer ^a	Likely to be longer ^a
Degree of coordination between teams	High degree of coordination	Lesser degree of coordination	Lesser degree of coordination
Costs	Hybrid room	Two procedures	Two procedures
	Training of personnel	Reimbursement	Reimbursement
	Reimbursement		

CABG = coronary artery bypass graft; DAPT = dual antiplatelet therapy; DES = drug-eluting stent; LAD = left anterior descending artery; LIMA = left internal mammary artery; LOS = length-of-stay; PCI = percutaneous coronary intervention.

^aThe difference between LOS in 1-setting and staged settings depends primarily on the time interval between the 2 staged procedures.

Table 3

Available Data on Outcomes After Simultaneous and Staged HCR Strategies

Author, Year (Ref)	No.	PCI Strategy	CABG Strategy	In-Hospital Mortality	In-Hospital Stroke	Reoperation For Bleeding	In-Hospital LIMA Patency	Hospital Stay (Days)	F/U Period	Survival	Freedom From MACCE ^a	TLR
Simultaneous HCR												
Kon, 2008 [17]	15	DES (100)	MIDCAB	0	0	0	100	3.7 ± 1.4	12 mo	100	93	6.7
Bonatti, 2008 [45]	5	DES (100)	TECAB	0	0	0	100	6 (5-7)	6 mo	100	100	0
Kiaii, 2008 [30]	58	DES (90), BMS (10)	Endo-ACAB	0	1.7	5.2	93	4.3 ± 1.4	20 mo	100	100	2.3
Reicher, 2008 [31]	13	DES (100)	MIDCAB	0	0	0	100	3.6 ± 1.5	14	100	92	7.6
Zhao, 2009 [16]	112	DES (84), BMS (8)	On-pump CABG (90), OPCAB (22)	2.7	1.8	2.7	93	6 (1-97)	—	—	—	—
Hu, 2011 [28]	104	DES (98), BMS (2)	MIDCAB	0	0	3.8%	96	8.2 ± 2.6	18	100	99	1.9
Staged HCR: PCI followed by CAB												
Lewis, 1999 [56]	14	BMS (100)	MIDCAB	0	0	0	100	3.4 ± 2.1 ^a	1-14 mo	100	90	9.6
Lee, 2004 [57]	6	BMS (100)	MIDCAB	0	0	0	—	6 (4-7)	12 mo	100	—	16
Gilard, 2007 [44]	70	BMS (100)	On-pump CABG	1.4	0	0	100	—	33 mo	98.6	96	2.3
Staged HCR: CAB followed by PCI												
Isomura, 2000 [58]	37	PTCA (100)	MIDCAB	0	0	—	100	—	0-24 mo	97.3	92	8.1
Wittwer, 2000 [59]	35	PTCA (70), BMS (30)	MIDCAB	0	0	0	100	7.5 ± 4.1	—	—	—	—
Cisowski, 2002 [41]	50	PTCA (22), BMS (78)	Endo-ACAB	0	0	2.8	100	4.4 ± 1.7	12 mo	100	88	10
Riess, 2002 [39]	57	PTCA (7), BMS (93)	MIDCAB	0	0	0	98	5.7 ± 1.8	24 mo	98.2	98	14
Gao, 2009 [35]	10	BMS (67), DES (33)	Endo-ACAB (6), TECAB (4)	0	0	0	100	—	5 mo	100	100	0
Delhaye, 2010 [46]	18	DES (100)	OPCAB (5), On-pump CABG (13)	0	0	0	100	10 (10-11.2)	12 mo	100	89	12

BMS = bare-metal stents; CABG = coronary artery bypass grafting; CAD = coronary artery disease; DES = drug-eluting stent; Endo-ACAB = endoscopic atraumatic coronary artery bypass; F/U = follow-up; HCR = hybrid coronary revascularization; LIMA = left internal mammary artery; MACCE = major adverse cardiac and cerebrovascular events; MIDCAB = minimally invasive direct coronary artery bypass; mo = months; OPCAB = off pump coronary artery bypass; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty; TLR = target lesion revascularization.

^aIn the case series of Lewis et al [56], PCI and MIDCAB occurred within 1 day, but took place in 2 stages.

Table 4**Surgical Techniques Used for LAD Revascularization During Hybrid Coronary Revascularization**

Abbreviation	Description of Surgical Procedure
MIDCAB	<u>Minimally invasive direct coronary artery bypass grafting</u> Thoracic access: left-sided thoracotomy or lower partial mini-sternotomy LIMA harvest: direct vision Anastomosis: direct vision Single lung ventilation: improves exposure, not required CPB: not required, but can be performed by cannulation of femoral vein and artery (avoids aorta cross clamping and arresting the heart)
Endo-ACAB	<u>Endoscopic atraumatic coronary artery bypass graft surgery</u> Thoracic access: non/limited rib-spreading left-sided thoracotomy LIMA harvest: robotic or thoracoscopically Anastomosis: hand-sutured Single lung ventilation: required when robot is used CPB: not required
TECAB	<u>Totally endoscopic coronary artery bypass graft surgery</u> Thoracic access: thoracoscopic access LIMA harvest: robotic Anastomosis: thoracoscopically (or robotic → robotic-assisted CAB) Single lung ventilation: required CPB: not required
OPCAB	<u>Off-pump CABG</u> Thoracic access: midline sternotomy LIMA harvest: direct vision Anastomosis: direct vision with stabilizers Single lung ventilation: improves exposure CPB: no

CAB = coronary artery bypass; CABG = coronary artery bypass grafting; CPB = cardiopulmonary bypass; Endo-ACAB = endoscopic atraumatic coronary artery bypass; LIMA = left internal mammary artery; MIDCAB = minimally invasive direct coronary artery bypass; OPCAB = off pump coronary artery bypass; TECAB = totally endoscopic coronary artery bypass.

Table 5

Studies Comparing Outcomes After HCR Versus CABG or PCI in the Drug-Eluting Stent Era

Author, Year (Ref)	No.	CAD	Group(s)	One-Stop	Hospital Stay (Days)	In-Hospital Stroke	Reoperation for Bleeding	In-Hospital Mortality	LIMA Patency	F/U Period	Survival
Studies comparing HCR with CABG											
Bachinsky, 2012 [51]	52	MVD	Robotic HCR (n=25) vs. OPCAB (n=27)	Yes	5.1±2.8 vs 8.2±5.4	0% vs 0%	0% vs 0%	0% vs 4%	96%	30 days	100% vs 96%
Hu, 2012 [29]	40	LMD	MIDCAB HCR (n=20) vs. OPCAB (n=20)	Yes	7.5 (6-14) vs 9 (7-24)	0% vs 0%	0% vs 5%	0% vs 0%	100%	18.5 +/- 9.8 months	100% vs 100%
Leacche, 2013 [50]	381	MVD	SYNTAX 33 + EuroSCORE>5 HCR (n=9), CABG (n=27)	Yes	6(1-25) vs 6(4-63)	11% vs 0%	0% vs 0%	22% vs 0%	—	—	—
		MVD	SYNTAX 33 + EuroSCORE 5 HCR (n=5), CABG (n=48)	Yes	6.5 (5-32) vs 5 (3-33)	0% vs 2%	0% vs 0%	25% vs 0%	—	—	—
		MVD	SYNTAX<33 + EuroSCORE>5 HCR (n=25), CABG (n=81)	Yes	6(3-19) vs 6(1-32)	4% vs 4%	0% vs 4%	0% vs 5%	—	—	—
		MVD	SYNTAX<33 + EuroSCORE<5 HCR (n=42), CABG (n=145)	Yes	5(3-97) vs 5 (3-28)	0% vs 0%	7% vs 3%	2% vs 1%	—	—	—
Halkos, 2011 [60]	108	LMD	Endo-ACAB HCR ± robot (n=27) vs OPCAB (n=81)	No	6.6±5.6 vs 5.6±2.0	0.0% vs 0.0%	0% vs 0%	0.0% vs 3.7%	100%	3.2 years	5-year: 88.6% vs 83.4%
Hu, 2011 [28]	208	MVD	MIDCAB HCR (n=104) vs. OPCAB (n=104)	Yes	8.2±2.6 vs 9.5±4.5	0% vs 0%	3.8% vs 1.9%	0% vs 0%	100%	18 (±7.9) months	100% vs 99%
Halkos, 2011 [61]	735	MVD	Endo-ACAB HCR ± robot (n=147) vs. OPCAB (n=588)	No (yes <10)	6.6±6.7 vs 6.1±4.7	0.7% vs 0.7%	—	0.7% vs 0.9%	99.3%	3.2 years	5-year survival 86.8% vs 84.3%
Delhaye, 2010 [46]	36	MVD	HCR (18) vs CABG (18)	No	10 (10-11.2) vs 10.5 (10.0-12.5)	0% vs 0%	0% vs 0%	0% vs 0%	100%	12 mo	100% vs 94.4%
Vassiliades, 2009 [62]	4,266	MVD	HCR (n=91) vs OPCAB (n=4,175)	No	4.2±2.5 (no data OPCAB)	0.0% vs 1.1%	0%	0% vs 1.8%	96%	3 years	3-year 94.0% vs 89.2%
Zhao, 2009 [16]	366	MVD	HCR (n=112, unplanned: 45) or CABG (n=254)	Yes	6 (1-97) vs 5 (1-33)	1.7% vs 1.1%	3% vs 3%	2.6% vs 1.5%	92%	—	—
Kon, 2008 [17]	45	MVD	MIDCAB HCR (n=15) vs OPCAB (n=30)	Yes	3.7 ± 1.4 vs 6.4 ± 2.2	0% vs 3.3%	—	0% vs 0%	100% vs 94% (CTA)	12 mo	100% vs 100%
Reicher, 2008 [31]	39	MVD	HCR (n=13) vs OPCAB (n=26)	Yes	3.6±1.5 vs 6.3±2.3	0% vs 0%	0% vs 0%	0% vs 0%	100% vs 100% (CTA)	6 mo	100% vs 100%
Studies Comparing HCR With PCI (Or CABG)											
Puskas, 2013 [63]	298	MVD	MIDCABG HCR (n=200) vs MV-PCI (n=98)	No (Yes= 24)	—	—	—	—	—	17.6 (± 6.5) mo	1.5% vs 1.0%
Shen, 2013 [64]	423	MVD	MIDCAB HCR (n=141) vs CABG (n=141) vs MV-PCI (n=141)	Yes	—	—	—	—	100%	3 yrs	0.7% vs 2.8% vs 3.5%
Gao, 2010 [65]	43	MVD	MICAB HCR (n=23) vs PCI (n=20)	Yes	—	0% vs 0%	0% vs 0%	0% vs 0%	100%	30 days	0% vs 0%

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CTA = computed tomography angiography; DES = drug-eluting stent; Endo-ACAB = endoscopic atraumatic coronary artery bypass; EuroSCORE = European System for Cardiac Operative Risk Evaluation; F/U = follow-up; HCR = hybrid coronary revascularization; LIMA = left internal mammary artery; LMD = left main disease; MACCE = major adverse cardiac and cerebrovascular events; MICAB = minimally invasive coronary artery bypass; MIDCAB = minimally invasive direct coronary artery bypass; mo = months; MVD = multivessel disease; OPCAB = off pump coronary artery bypass; PCI = percutaneous coronary intervention.