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JACC REVIEW TOPIC OF THE WEEK

The Hybrid Coronary Approach for Optimal Revascularization

JACC Review Topic of the Week

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ABSTRACT

Coronary revascularization is accomplished either by percutaneous coronary intervention (PCI), with low risk of immediate complications, or coronary artery bypass graft (CABG), with improved long-term, event-free survival attributable to use of the left internal mammary artery graft. Hybrid coronary revascularization (HCR) combines both. The left internal mammary artery graft is done by sternal-sparing approaches or by robotic-assisted, endoscopic surgery. HCR reduces bleeding, ventilator time, and length of stay compared with traditional CABG. Compared with PCI, HCR offers the durability and survival advantages of the left internal mammary artery. The large-scale National Heart, Lung, and Blood Institute–sponsored, randomized Hybrid Trial (Hybrid Coronary Revascularization Trial) was initiated to examine whether HCR is superior to multivessel PCI. However, enrollment was suboptimal, triggering premature study discontinuation. HCR integrates the positive features of both PCI and CABG, albeit requiring 2 procedures rather than 1. Adequately powered randomized trials are required to evaluate the outcomes and cost-effectiveness of HCR compared with CABG and multivessel PCI alone. (J Am Coll Cardiol 2020;76:321–33) © 2020 by the American College of Cardiology Foundation.

Cardiovascular disease continues to be the leading cause of death and accounts annually for 17.8 million deaths worldwide, corresponding to 330 million years of life lost, and another 35.6 million years lived with disability (1). Nonetheless, the current age-adjusted death rate per 100,000 population is 233, which represents a 10% reduction compared with 10 years ago (2). This achievement is largely attributable to improving medical therapy, prevention, and the promotion of cardiovascular health (3). Nevertheless, in addition to guidelines directed medical therapy, a significant number of patients with coronary artery disease (CAD) will benefit from percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) either for amelioration of symptoms in the case of PCI or to enhance longevity in the case of CABG. PCI offers very low risks of immediate complications and more rapid recovery, but long-term, event-free survival may be better with CABG in some patients (4).

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ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass graft

CAD = coronary artery disease

DAPT = dual antiplatelet therapy

DES = drug-eluting stent

HCR = hybrid coronary revascularization

LAD = left anterior descending artery

LIMA = left internal mammary artery

MACCE = major adverse cardiac and cerebrovascular events

MIDCAB = minimally invasive direct coronary artery bypass

OPCAB = off-pump coronary artery bypass

PCI = percutaneous coronary intervention

SVG = saphenous vein graft

Conversely, CABG may have increased immediate complications such as bleeding, stroke, atrial fibrillation, and prolonged hospitalization. Nevertheless, recurrent events with CABG are significantly reduced when compared with those with PCI, specifically in patients with complex disease and diabetes mellitus (4,5).

The risks and benefits of PCI and CABG are often independent from each other. Specifically, the risks of complications after CABG relates primarily to noncardiac patient comorbidities (i.e., frailty, peripheral vascular disease, renal and/or hepatic dysfunction), whereas the risk of complications after PCI relates primarily to the complexity of coronary artery disease (e.g., as assessed by the SYNTAX [Synergy Between PCI With Taxus and Cardiac Surgery] score). In this regard, the long-term benefits of CABG have been largely related to the durability of the left internal mammary artery (LIMA) graft to the left anterior descending (LAD) coronary artery (5). Conversely, drug-eluting stents (DESs) compared with saphenous vein grafts (SVGs) may offer longevity advantages. Thus, to optimize outcomes, coronary revascularization should offer minimal invasiveness to reduce risk and maximal durability to improve survival. As a result, a synergistic approach combining the best of both techniques may be considered in the treatment of patients with multivessel CAD.

HYBRID CORONARY REVASCULARIZATION

Coronary artery revascularization by CABG and PCI in the same patient is known as hybrid coronary revascularization (HCR) (**Figure 1**) and may offer the best of both procedures while minimizing the risks from each. Using off-pump, sternal-sparing incisions or robotic-assisted endoscopic techniques, the LIMA is anastomosed to the LAD. This approach has been shown to reduce neurological events, bleeding, infection, time of mechanical ventilation, and length of stay (6,7). The proven patency and survival benefits of LIMA-LAD revascularization will enhance long-term outcomes (5). For non-LAD vessels, DESs are used rather than SVGs, which despite recommendations for pan-arterial surgical revascularization remain the most common conduits used for non-LAD bypass grafts worldwide (8). The longevity of SVGs are relatively poor, with graft failure in ~20% in the first year and reaching 70% at 15 years (9). The PREVENT IV (Prevention of Autogenous Vein Graft Failure in Coronary Artery Bypass Procedures) trial reported an SVG failure of 45% at 12 to 18 months (10). Alternatively, contemporary DESs offer long-term patency rates of 96% to 98% (11,12).

HIGHLIGHTS

- HCR combines reduced invasiveness of PCI, with a LIMA to the LAD.
- The off-pump, minimally invasive CABG reduces cardiovascular accident, bleeding, infection, mechanical ventilation, and length of stay.
- The National Heart, Lung, and Blood Institute–sponsored Hybrid Trial, which randomized PCI versus HCR, was stopped prematurely for lack of enrollment.
- Powered randomized trials are needed to evaluate cost-effectiveness of HCR versus CABG or multivessel PCI.

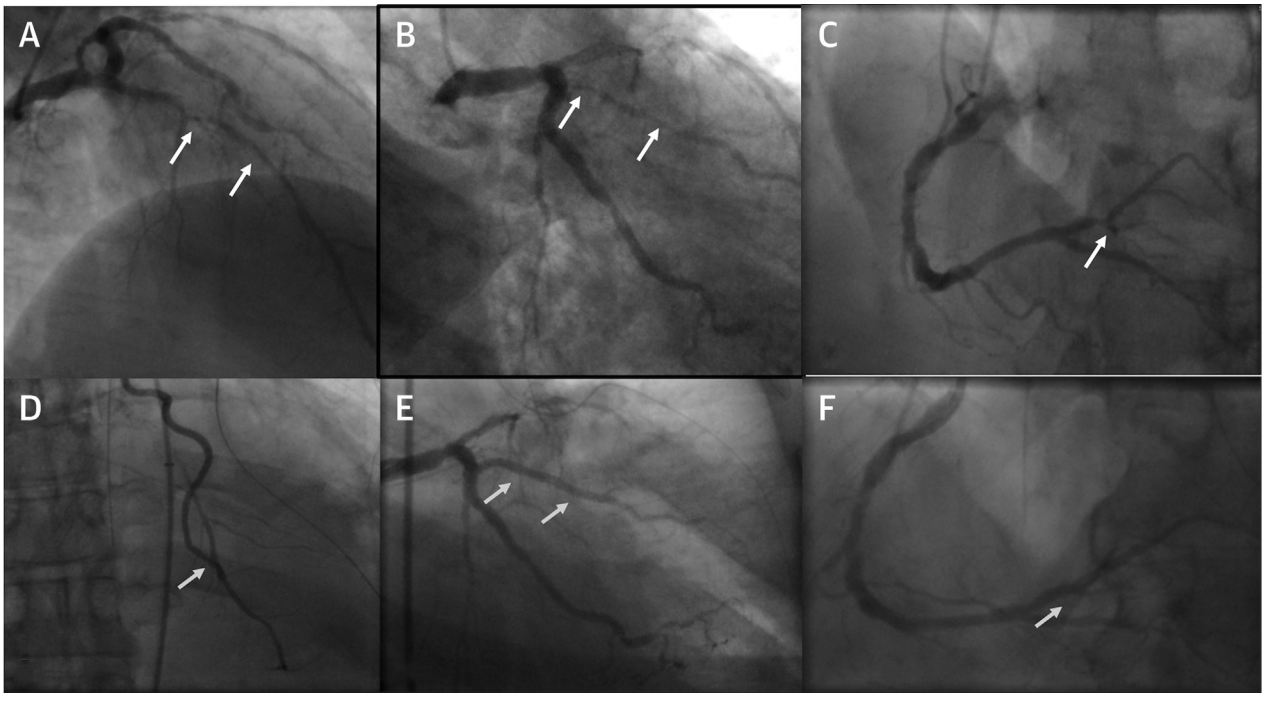
Thus, the synergistic application of LIMA to the LAD + DES to non-LAD vessels rather than a dichotomous approach of either multivessel CABG or PCI may provide the best of both worlds, minimizing risk and invasiveness, yet optimizing long-term outcomes (**Central Illustration**).

PATIENT SELECTION

The ideal candidate for HCR has multivessel CAD involving the LAD and/or left main coronary arteries with at least 1 other coronary artery stenosis amenable to PCI (6,13). In patients with true distal left main bifurcation disease, HCR will provide a LIMA graft to LAD and a DES from the left main into the proximal left circumflex artery (13). All patients undergoing HCR should have the ability to tolerate dual antiplatelet therapy (DAPT) for at least 3 months and up to 12 months or longer according to the clinical presentation and relative risks of ischemia versus bleeding.

The robotic, off-pump approach is ideal for high-risk patients with multivessel CAD (14–16). Furthermore, in elderly patients with calcific aortas, HCR may reduce the risk of stroke (13,14). Patients with decreased left ventricular ejection fraction can undergo LIMA to LAD grafting totally off pump, reducing the chances of perioperative systolic failure (14). Patients with carotid disease, lack of vein conduits, and chronic kidney disease may also benefit from HCR (14,16). Finally, patients who are obese and/or diabetic will get the survival benefit of a LIMA

FIGURE 1 An Example of HCR



Coronary angiography shows a long severe lesion in the mid-left anterior descending **(A),** a long lesion in the first obtuse marginal branch of the left circumflex artery **(B),** and a focal severe stenosis in the posterolateral branch of the right coronary artery **(C).** Through a minimally invasive direct coronary artery bypass, the left anterior descending artery is bypassed with a left internal mammary artery. Angiography 3 days later shows widespread patency of the left internal mammary artery **(D).** The left circumflex artery and right coronary artery vessels are then treated successfully with drug-eluting stents **(E,F). (A to C) Arrows** indicate the lesions. **(D to F) Arrows** indicate the interventions. HCR = hybrid coronary revascularization.

graft without the risk of median sternotomy or sternal wound infection (17).

THE HYBRID PROCEDURE

SURGICAL CONSIDERATIONS. As previously mentioned, the LIMA-LAD graft may be performed using one of the following: a minimally invasive sternal-sparing approach; open sternotomy; or robotic-assisted, endoscopic surgery.

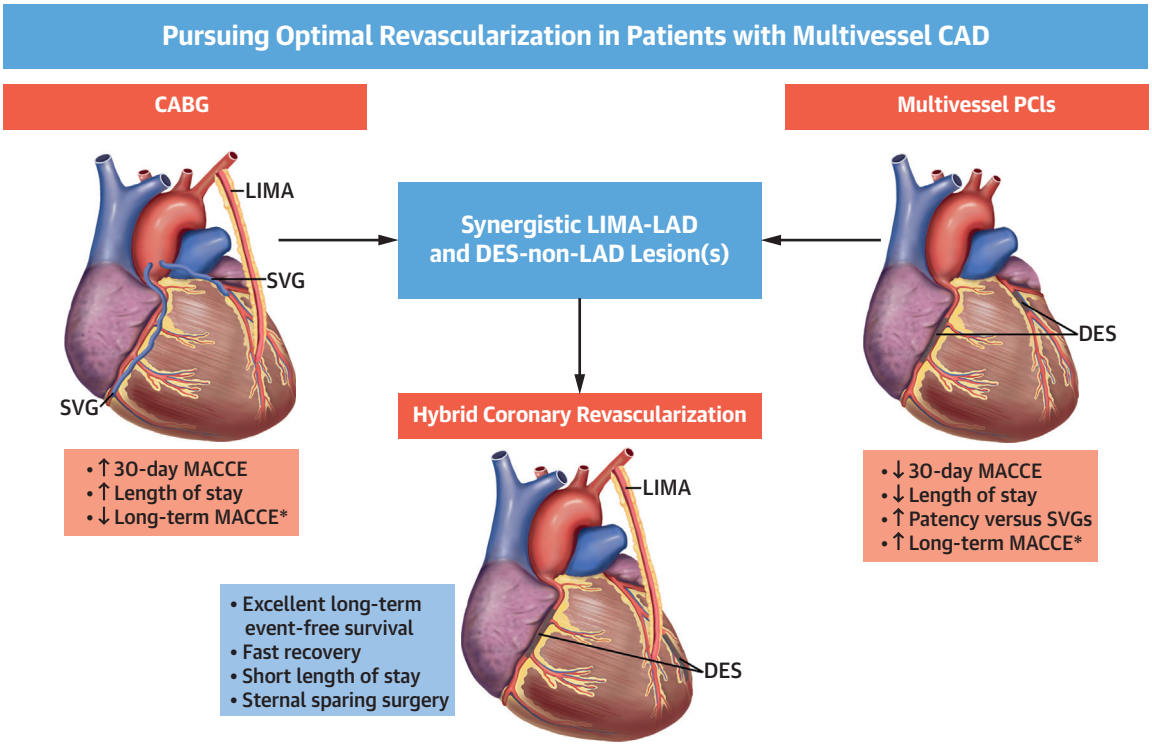
The sternal-sparing approach, also known as minimally invasive direct coronary artery bypass (MIDCAB), is defined as LIMA mobilization in an open fashion through a limited anterior or lateral thoracotomy incision. The anastomosis to the LAD is performed by hand, on the beating heart (18).

The open sternotomy off-pump approach, also known as off-pump coronary artery bypass (OPCAB) was developed to avoid the complications of cardiopulmonary bypass. It uses the same LIMA mobilization through a limited sternotomy (19).

The robotic-assisted endoscopic approach is performed through 3 port accesses introduced into the left chest. Using the Da Vinci surgical platform (Intuitive Surgical, Sunnyvale, California), the LIMA is harvested either in a skeletonized or pedicled fashion. Next, a micro-thoracotomy (3 to 5 cm) is made directly over the LAD, through which the anastomosis is carried out similar to the MIDCAB approach (20). The anastomosis is performed by hand, on the beating heart (19,20). An even less invasive approach is beating heart totally endoscopic coronary artery bypass, consisting of LIMA mobilization and LAD arteriotomy and anastomosis with the robot (21). Surgery performed with cardiopulmonary support is not part of modern HCR protocols.

PERCUTANEOUS CORONARY INTERVENTION. PCI is done following appropriateness criteria for revascularization (22). Second- or third-generation DES should always be used (23). Radial intervention is preferred to minimize vascular and bleeding complications. DAPT should be continued as per current guidelines with duration dictated by individual patient risk (24,25).

CENTRAL ILLUSTRATION **Pursuing Optimal Revascularization in Patients With Multivessel Coronary Artery Disease**



Moreno, P.R. et al. J Am Coll Cardiol. 2020;76(3):321–33.

Traditionally, multivessel coronary artery disease (CAD) requiring revascularization is treated with coronary artery bypass graft (CABG) or multivessel percutaneous coronary intervention (PCI). The benefits and complications of each technique are summarized in the figure. The synergistic approach of left internal mammary artery (LIMA) to left anterior descending (LAD) and drug-eluting stent (DES) to non-LAD lesions is known as hybrid coronary revascularization. This approach combines the advantages of both techniques while reducing complications, as summarized in the **lower center** of the figure. *In patients with high SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) scores or diabetes. MACCE = major adverse cardiac and cerebrovascular events; SVG = saphenous vein graft.

TIMING OF THE HCR PROCEDURES. Three possible timing strategies can be used: CABG and PCI performed simultaneously; CABG first followed by PCI; or CABG following PCI (as shown in **Table 1**).

One-step HCR is performed in a hybrid suite, starting with surgery first, followed by PCI. A significant advantage is the immediate assessment of the LIMA-LAD anastomosis by angiography. Any major issue with the graft can be addressed (26–28). Also, the non-LAD PCI is performed with LAD territory already protected and with a surgical team at the bedside for any possible complication or unsuccessful PCI (26). This approach reduces hospital stay, readmission, and improves patient satisfaction (19). However, hybrid suites are costly and not universally available (26). In addition, minimizing bleeding while preventing stent thrombosis can be challenging. Numerous approaches have been suggested for DAPT use in this setting (27,29). The 1-step HCR approach counts for approximately 20% of all HCR procedures in the United States (30).

The 2-step HCR approach may include CABG first follow by PCI or vice versa. CABG first is more common, followed by PCI the next day, weeks, or sometimes 1 to 2 months afterward (31). The LIMA-LAD anastomosis is rapidly assessed by angiography prior to PCI (ideally from the left radial approach). Severe anastomotic problems can be immediately addressed via PCI. It should be recognized, however, that peri-anastomotic edema may lead to the appearance of a pseudo-stenosis at the distal anastomotic sites for days or weeks post-procedure (32). Thus, PCI

TABLE 1 Hybrid Procedure: Concurrent Versus Staged Procedures

1-Step HCR	2-Step HCR	
	Standard HCR	Reverse HCR
MIDCAB followed by PCI as 1 procedure	MIDCAB first followed by PCI on another day	PCI first followed by MIDCAB on another day
Complete revascularization achieved in a single procedure; CABG of non-LAD lesions can be performed in PCI that is unsuccessful or complicated	Prior LIMA-LAD graft can be angiographically assessed and treated if required during the second stage of the procedure	Most common approach for patients presenting with ACS of non-LAD lesions, or if non-LAD lesion severity is much greater than LAD lesion severity
Allows immediate assessment of the LIMA-LAD anastomosis	Allows use of dual antiplatelet therapy without increasing the risk of surgical-related bleeding	If unsuccessful PCI, CABG can be performed during the second stage of the procedure
Short hospital stay and possibly better patient satisfaction	Less myocardium at ischemic risk during the PCI	Complex antiplatelet therapy management; potentially higher risk of stent thrombosis and/or bleeding
Requires a hybrid room	During the waiting period, the patient may require urgent revascularization of the non-LAD lesions	Unable to angiographically assess the LIMA-LAD graft
Potential increase in bleeding, AKI and stent thrombosis		

ACS = acute coronary syndrome; AKI = acute kidney injury; CABG = coronary artery bypass graft; HCR = hybrid coronary revascularization; LAD = left anterior descending artery; LIMA = left internal mammary artery; MIDCAB = minimally invasive direct coronary artery bypass; PCI = percutaneous coronary intervention.

of the distal LIMA-LAD anastomosis should generally be avoided unless there is TIMI (Thrombolysis In Myocardial Infarction) flow grade 0 to 2 or ongoing ischemia, regardless of the severity of the stenosis. If PCI is required, it should be performed with an undersized, low-pressure balloon, with the goal of restoring patency only.

After the LIMA graft is assessed, stent implantation of the remaining diseased segments is performed. DAPT may be given without the risk of mediastinal bleeding (20). Potentially, lesion instability in the waiting period between the CABG and PCI may require earlier, nonplanned hospitalization (33).

The final approach includes the performance of PCI first, followed by CABG. Also known as reverse HCR, this approach is usually preferred in the setting of acute coronary syndromes when the culprit lesion is located in a non-LAD vessel (or occasionally in stable CAD when the severity of the non-LAD stenoses are significantly greater than that of the LAD). Stenting of the non-LAD artery (arteries) is performed first and the LIMA to LAD is scheduled after 30 days, when oral $P2Y_{12}$ blockers can be withheld. However, all surgical procedures activate platelets and invoke a systemic inflammatory response, increasing the risk of stent thrombosis, especially after early interruption of DAPT (34). In patients with high risk for stent thrombosis an alternative may include in-hospital admission 3 to 5 days before surgery, stopping oral $P2Y_{12}$ inhibitors, and bridging treatment with intravenous cangrelor (35).

EVIDENCE SUPPORTING HCR

The evidence supporting HCR is shown in Table 2.

HCR VERSUS CONVENTIONAL MULTIVESSEL CABG.

In a prospective nonrandomized study, Bachinsky et al. (26) reported significant reductions in blood transfusions and hospital length of stay favoring HCR ($p < 0.01$). In the HCR versus CABG arm of the Shen et al. (27) observational study, HCR was associated with improved outcomes at 3-year follow-up. Freedom from major adverse cardiac and cerebrovascular events (MACCE) were 93.6% after HCR, 86.5% after CABG, and 77.3% after PCI ($p = 0.003$). The POL-MIDES (Safety and Efficacy Study of Hybrid Revascularization in Multivessel Coronary Artery Disease) trial was a prospective, single-center, randomized, pilot trial of 200 patients comparing HCR with conventional CABG (36). The 5-year respective rates of death (6.4% vs. 9.2%), myocardial infarction (4.3% vs. 7.2%), repeat revascularization (37.2% vs. 45.4%), and stroke (2.1% vs. 4.1%) were numerically in favor of HCR, but comparisons were not statistically significant (17). Despite the modest sample size, this trial suggested that HCR is safe and feasible in patients with multivessel disease referred for surgical revascularization. A small randomized pilot study done by Esteves et al. (37) showed no differences in mortality or MACCE at 2 years, but there was a tendency for increased revascularization and MACCE in the HCR arm compared with in the CABG arm in patients with complex multivessel disease and high

TABLE 2 Major Hybrid Revascularization Studies

First Author, Year (Ref. #)	Type of Study	N	30-Day Mortality	Blood Transfusion (%)	Stroke (%)
HCR vs. CABG					
Esteves et al., 2020 (37)	Prospective randomized	HCR = 40	12.5	NA	0
		CABG = 20	0	NA	0
Tajstra et al., 2018 (17)	Prospective randomized	HCR = 94	0	19 (p = 0.23)	2.1 (p = 0.35)
		CABG = 97	0	26	4.1
Bachinsky et al., 2012 (26)	Prospective cohort	HCR = 25	0 (p = 0.99)	12 (p < 0.001)	0 (p = 0.999)
		CABG = 27	3.7	67	0
HCR vs. OPCAB					
Hage et al., 2019 (42)	Retrospective propensity matching	HCR = 147	0 (p = 0.15)	15 (p = 0.6)	2.1
		OPCAB = 216	1	28	1
Song et al., 2016 (40)	Prospective propensity matching	HCR = 573	NA	29.2% (p = 0.076)	0 (p = 0.046)
		OPCAB = 700	NA	39.6	3.6
Halkos et al., 2011 (39)	Retrospective propensity matching	HCR = 147	0.7 (p = 0.84)	35.4% (p < 0.001)	0.7 (p = 0.8)
		OPCAB = 588	0.9	56%	0.7
Vassiliades et al., 2009 (48)	Prospective propensity matching	HCR = 91	0 (p = 0.20)	NA	0 (p = 0.31)
		OPCAB = 4,175	1.7	NA	1.1
HCR vs. CABG vs. PCI					
Ganyukov et al., 2020 (43)	Prospective randomized	HCR = 49	1.9	9.6	3.2
		PCI = 49	0	0	0
		CABG = 51	0	20	0
Qiu et al., 2019 (49)	Retrospective propensity matched cohort	HCR = 47	0	NA	4.5
		PCI = 47	0	NA	6.8
		OPCAB = 47	2	NA	6.8
Shen et al., 2013 (27)	Retrospective propensity matched cohort	HCR = 141	NA	21.3	2 (p = 0.083)
		PCI = 141		NA	3
		CABG = 141		31.9	9
HCR vs. PCI					
Puskas et al., 2016 (6)	Prospective propensity matched cohort	HCR = 200	0.5	NA	2.5 (p = 0.021)
		PCI = 98	0		0
Meta-analysis HCR vs. CABG/OPCAB†					
Nolan et al., 2018 (33)	9 studies, CABG and OPCAB included	HCR = 306	4.9	48	1.6
		CABG = 918	2.1 OR: 1.35 (0.72–2.52)	67 OR: 0.43 (0.27–0.68)	2.5 OR: 0.76 (0.34–1.73)
Reynolds et al., 2018 (50)	14 studies, conventional CABG only	HCR = 1,350	NA	22.8	0.9
		CABG = 2,910	NA	46.1 OR: 0.38 (0.31–0.46)	1.4 OR: 0.72 (0.31–1.69)
Sardar et al., 2018 (51)	9 studies, CABG and OPCAB included	HCR = 735	1.2	19	0.9
		CABG = 1,510	0.9 OR: 1.72 (0.38–7.82)	44 OR: 0.29 (0.14–0.56)	1.9 OR: 0.53 (0.23–1.20)
Harskamp et al., 2014 (38)	6 studies, CABG and OPCAB included	HCR = 366	0.6	NA	0.3
		CABG = 824	0.8 OR: 0.85 (0.24–2.99)		0.6 OR: 0.93 (0.24–3.59)

*Values are mean or mean ± SD. †ORs are reported with (95% CI).
CI = confidence interval; MACCE = major adverse cardiac and cerebrovascular events; NA = not available; OPCAB = off-pump coronary artery bypass; OR = odds ratio; other abbreviations as in Table 1.

SYNTAX scores. This increase in repeat revascularization after HCR compared with CABG was also observed in a 9-study meta-analysis by Nolan et al. (33). However, HCR was associated with shorter ICU and hospital stays and fewer infections compared with CABG, with non-significant differences in mortality and MACCE (33). Finally, a meta-analysis by Harskamp et al. (38) reported nonsignificant differences in the rates of death, myocardial infarction, stroke, or repeat revascularization between HCR and CABG at 1 year (HR: 0.49; 95% confidence interval: 0.20 to 1.24; p = 0.13). Importantly, all randomized comparisons of HCR versus CABG published to date have suffered from inadequate sample size.

TABLE 2 Continued

Patent LIMA-LAD (%)	Hospital Length of Stay (Days)*	Follow-Up Time	Any MACCE (%)	Revascularization (%)	Death (%)
HCR vs. CABG					
NA	NA	2 yrs	19.3	14.5	12.5
NA	NA		5.9	5.9	0.0
NA					
96	8.6 ± 4.1 (p = 0.86)	5 yrs	45.4 (p = 0.39)	NA	6.4 (p = 0.69)
NA	8.5 ± 5.2		53.4		9.2
NA	5.1 ± 2.8 (p = 0.008)	30 days	0 (p = 0.999)	NA	0 (p = 0.999)
	9.1 ± 5.4		0		3.7
HCR vs. OPCAB					
NA	4.5 (p = 0.10)	8 yrs	NA	9 (p = 0.8)	4 (p = 0.054)
NA	8.1		NA	8	15
NA	7 (p = 0.627)	3 yrs	7.4 (p = 0.612)	4.7 (p = 0.488)	2.7% (p = 1.00)
NA	7		8	2.3	2.8
95.2 (p < 0.001)	6.6 ± 6.7 (p = 0.48)	5 yrs	2 (p = 1)	12.2 (p < 0.001)	13.2 (p = 0.61)
99	6.1 ± 4.7		2	3.7	15.7
NA	NA	3 yrs	10	NA	6 (p = 0.14)
NA	NA		NA	NA	11
HCR vs. CABG vs. PCI					
NA	13.5	1 yr	13.4 (p = 0.83)	13.5 (p = 0.095)	5.8 (p = 0.78)
NA	13.8		13.2	17	3.8
	4.5		12	4	2
NA	15.3 ± 4.5 (p = 0.027)	4.9 yrs	11 (p = 0.007)	4.5 (p = 0.002)	1 (p = 0.811)
NA	NA		35	2.2	2
NA	17.6 ± 5.4		13	22	2
98	8.19 ± 2.54	3 yrs	9 (p = 0.003)	6 (p < 0.001)	0.7 (p = 0.034)
NA	NA		19	18	3.5
98	8.49 ± 2.54		32	3	2.8
HCR vs. PCI					
NA	NA	2 yrs	11.5 (p = 0.103)	7 (p = 0.061)	1.5 (p = 0.012)
			12.2 (p = 0.103)	10.2 (p = 0.084)	2 (p = 0.016)
Meta-analysis HCR vs. CABG/OPCAB†					
NA	NA	≥1 yr	8	6.3	2.4
			12 OR: 0.71 (0.31–1.62)	1.8 OR: 3.1 (1.39–6.90)	3.9 OR: 0.64 (0.28–1.47)
NA	Mean difference: −1.48	≥1 yr	NA	NA	1.7
					1.8 OR: 1.15 (0.69–1.92)
NA	NA	≥1 yr	3.6	3.8	1.3
			5.4 OR: 0.53 (0.24–1.16)	4.5 OR: 1.28 (0.50–2.83)	1.5 OR: 0.85 (0.38–1.88)
NA	NA	≥1 yr	4.1	8.3	4.5
			9.1 OR: 0.49 (0.20–1.24)	3.4 OR: 3.25 (1.80–5.87)	7.3 OR: 0.73 (0.29–1.85)

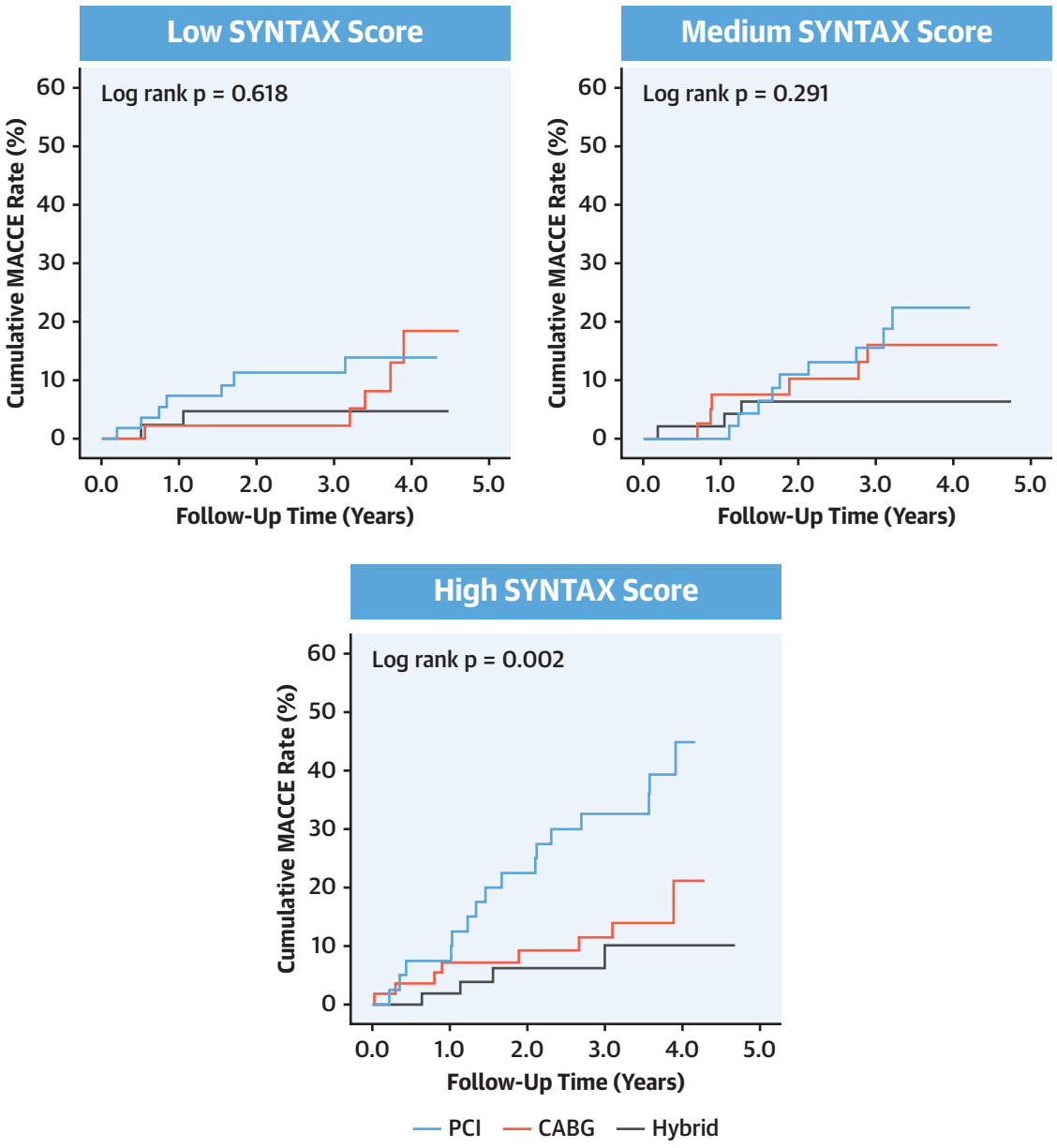
HCR VERSUS OPCAB

Halkos et al. (39) compared HCR versus OPCAB in patients with left main disease. HCR was associated with reduced blood transfusions and mechanical ventilation. MACCE rates were similar in both groups. Song et al. (40) noted reductions in chest tube drainage, mechanical ventilation, and intensive care unit stay in propensity-matched patients having 1-step HCR compared with OPCAB. Again, MACCE rates were similar in both groups. Harskamp et al. (41) reported a 46% reduction of troponin I release after HCR compared with after OPCAB, suggesting reduced myocardial injury with HCR. Finally, Hage et al. (42) demonstrated a trend toward reduced mortality over a long period of follow-up in patients that underwent single-stage HCR compared with OPCAB.

HCR VERSUS CABG VERSUS PCI

Shen et al. (27) from Beijing reported an underpowered, 3-way comparison of propensity-matched

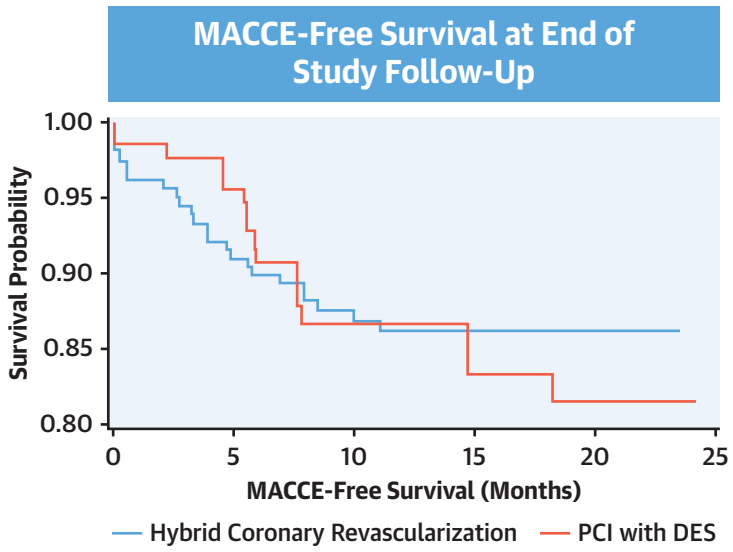
FIGURE 2 Cumulative MACCE Rate in HCR, CABG, and PCI Groups in Patients With Low, Medium, and High SYNTAX Score Tertiles



Among patients in the low and medium SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) score tertiles, the long-term major adverse cardiac and cerebrovascular events (MACCE) rate in the hybrid coronary revascularization (HCR) group was similar to those in the coronary artery bypass graft (CABG) ($p = 0.70$ and $p = 0.25$, respectively) and percutaneous coronary intervention (PCI) groups ($p = 0.22$ and $p = 0.11$, respectively). Among patients in the high SYNTAX score tertile, 1-step HCR had lower long-term MACCE rates than that with PCI ($p = 0.002$), but similar to that with CABG ($p = 0.36$). Reprinted with permission from Shen et al. (27).

patients who had 1-step HCR (LIMA-LAD via mini-sternotomy plus DES to non-LAD lesions) versus isolated CABG via sternotomy versus multivessel PCI. At 3-year follow-up, the cumulative MACCE rate in the hybrid group (6.4%) was significantly lower than that in the PCI group (22.7%; $p < 0.001$), but it was nonsignificantly different than that in the CABG group (13.5%; $p = 0.14$). HCR had numerically lower cumulative MACCE than either CABG or PCI across all 3 tertiles of the SYNTAX score; in particular, the MACCE rate for patients in the high SYNTAX score tertile was significantly lower after HCR than after PCI

FIGURE 3 MACCE-Free Survival at End of Study Follow-Up in the Hybrid Pilot Study



In a multicenter observational study of HCR (n = 200) and multivessel PCI (n = 98) in patients with hybrid-eligible coronary anatomy, the risk-adjusted MACCE rates were similar between groups through 12 months of follow-up. During longer follow-up, the event-free survival curves for HCR versus PCI began to diverge, with increasing MACCE in the multivessel PCI group, although the differences remained nonsignificant. Reprinted with permission from Puskas et al. (6). DES = drug-eluting stent; other abbreviations as in Figures 1 and 2.

(p = 0.002) but similar to that for CABG (p = 0.36) (Figure 2). A recent small, prospective randomized study done by Ganyukov et al. (43), did not find significant differences in MACCE or residual myocardial ischemia at short-term follow-up (12 months) between HCR and PCI. However, significant reductions in hospital stay and major bleeding were observed in the PCI arm.

TABLE 3 MACCE Rates From the Multicenter Hybrid Pilot Study

	HCR (n = 200)		PCI With DES (n = 98)		
	n	Incidence Rate Per Person-Year	n	Incidence Rate Per Person-Year	HR (95% CI)
MACCE incidence at 30 days					
Any MACCE	6	0.393	2	0.264	2.658 (0.839–8.421)
Death	1	0.064	0	0.000	
Myocardial infarction	3	0.195	1	0.131	
Stroke	0	0.000	0	0.000	
Revascularization	4	0.260	1	0.131	
MACCE incidence at 12 months					
Any MACCE	23	0.143	10	0.119	1.063 (0.666–1.697)
Death	3	0.017	1	0.011	
Myocardial infarction	4	0.024	3	0.034	
Stroke	5	0.030	0	0.000	
Revascularization	14	0.085	8	0.094	
MACCE incidence through end of study					
Any MACCE	23	0.103	12	0.103	0.868 (0.556–1.355)
Death	3	0.012	2	0.016	
Myocardial infarction	4	0.017	3	0.024	
Stroke	5	0.021	0	0.000	
Revascularization	14	0.061	10	0.084	

DES = drug-eluting stent; HR = hazard ratio; other abbreviations as in Tables 1 and 2.

TABLE 4 Potential Advantages and Disadvantages of Hybrid Revascularization

Advantages	Disadvantages
Faster recovery time compared with traditional CABG	Not suitable for emergency operations
Reduced neurological events, bleeding, infection, time of mechanical ventilation, and length of stay compared with traditional CABG	Longer recovery time compared with PCI alone
Sternal-sparing incisions, no aortic manipulation, and no use of cardiopulmonary bypass compared with traditional CABG	Patients without LM or LAD disease are not candidates
Higher patency rate of LAD lesions treated with a LIMA than DES, and of non-LAD lesions treated with contemporary DES compared with SVGs	Technically more challenging than conventional CABG or multivessel PCI
Theoretically better long-term event-free survival compared with multivessel PCI of conventional CABG	Special and costly equipment is needed (hybrid rooms, robotic surgical systems); in-hospital costs of 2 procedures likely greater than PCI or CABG alone

LM = left main artery; SVG = saphenous vein graft; other abbreviations as in Tables 1 to 3.

HCR VERSUS PCI

The prospective, observational Hybrid pilot study sponsored by the National Heart, Lung, and Blood Institute explored the feasibility and practices of HCR in patients with hybrid-eligible coronary anatomy (defined as a proximal and/or mid LAD lesion plus at least 1 other non-LAD lesion) at 11 clinical centers in North America (6). Two hundred and ninety-eight patients were enrolled, including 200 treated with HCR and 98 treated with multivessel PCI with DES at the discretion of local cardiologists and surgeons. The HCR approach included robotic (n = 108), robotic totally endoscopic (n = 42), MIDCAB (n = 38), and planned sternotomy (n = 12) approaches. Event-free survival was similar between the 2 groups at 12 months (hazard ratio: 1.06; 95% confidence interval: 0.66 to 1.69) and at 18 months (hazard ratio: 0.86; 95% confidence interval: 0.56 to 1.36) (**Figure 3, Table 3**). This effort provided the data necessary to design a prospective randomized comparative effectiveness trial, the Hybrid Trial (Hybrid Coronary Revascularization Trial) (44).

THE HYBRID TRIAL

The Hybrid Trial (NCT03089398) was a National Heart, Lung, and Blood Institute-sponsored multicenter randomized controlled trial of HCR versus PCI designed to enroll 2,354 patients with multivessel CAD involving the LAD distribution at 70 sites in North America. The protocol included follow-up at 30 days, 6 months, and every 6 months through 5 years. The trial was powered to detect superiority of HCR compared with PCI for MACCE (all-cause death, myocardial infarction, stroke or unplanned repeat revascularization). A total of 200 patients were enrolled. Unfortunately, slow enrollment in North America, combined with delayed recruitment of clinical sites outside North America, triggered premature discontinuation of the trial by the National Heart, Lung, and Blood Institute. The analysis of the 200 randomized patients is ongoing and the 2-year outcomes will be presented in the near future.

DEVELOPMENT OF A HYBRID HEART TEAM

The performance of HCR depends on the development and maintenance of a cooperative (coronary) heart team. While the contemporary heart team is devoted to structural heart cases in many institutions, the original concept of a heart team developed during the early days of PCI. The necessary elements of such a coronary heart team depend on multiple factors that we believe must be common among all centers seeking to provide optimal care for patients with coronary artery disease. These are:

1. A shared recognition by interventional cardiologists and coronary surgery specialists that medical management, PCI, and surgical revascularization all must play important roles in the care of coronary patients with multivessel CAD, and that a collaborative coronary heart team is the sine qua non of genuinely patient-centered comprehensive coronary care.
2. A shared recognition that "'can' does not equal 'should.'" In other words, the evident feasibility of either multivessel PCI or surgical revascularization in an individual patient is not an indication to perform that procedure. Rather, only a collaborative discussion of the relative short- and long-term benefits of guidelines directed medical therapy, PCI, traditional CABG, and HCR can optimize the assignment of patients to each of these alternative therapies.

3. A collective skill set that allows the institutional coronary heart team to offer state-of-the-art care in guidelines directed medical therapy (with close follow-up and high level of compliance), multivessel PCI (with contemporary DESs, technical excellence, and routine use of fractional flow reserve), CABG (with multiple or all-arterial conduits, minimizing or avoiding aortic manipulation) and HCR (with minimally invasive sternal-sparing techniques, applied with a high level of success and minimal morbidity and mortality).
4. When items 1 to 3 are achieved, then the coronary heart team will collaboratively decide which therapy to recommend to each individual patient, based not on a zero-sum competition but on an assurance that all members of our heart team will collectively benefit by fulfilling our ethical obligation to provide the best care to every patient. For instance, in our institution, this has led us to recommend PCI for many elderly frail patients whose coronary anatomy might traditionally be referred for CABG, whereas many younger patients (especially diabetic patients) whose multivessel CAD is commonly treated with multivessel PCI at other centers are referred for CABG with multiple arterial conduits. Patients who might have PCI are typically offered HCR, as are many patients with CABG-like coronary artery disease who are referred from inside or outside our institution for surgery.

It is our strong impression that the collaborative culture of the coronary heart team at our institution has been an important driver of programmatic excellence and growth.

COST ANALYSIS

The impact of HCR on hospital costs and reimbursement was elegantly calculated by Halkos et al. (45). Medicare patients undergoing HCR versus CABG were compared. Despite a higher total cost for HCR when compared with OPCAB, Medicare reimbursements were significantly higher for HCR than for OPCAB. In addition, there was a reduction in blood transfusion, ventilator time, and post-operative length of stay in favor of HCR. As a result, the total contribution margin (+$8,771; $p < 0.0001$) was greater for HCR than for OPCAB.

CONCLUSIONS AND FUTURE DIRECTIONS

The benefits of traditional CABG principally arise from the LIMA anastomosis to the LAD, because a single arterial conduit continues to be used in the large majority of cases (8). Moreover, conventional CABG is a highly invasive procedure with increased risk of stroke and short-term morbidity compared with less invasive options such as PCI (4). HCR retains the benefits of the LIMA anastomosis to the LAD without the comorbidities associated with traditional CABG. Furthermore, contemporary DESs may provide superior long-term results compared with SVGs in the treatment of non-LAD lesions in many patients. HCR thus integrates the positive features of both PCI and CABG (**Table 4**).

The evidence that HCR may reduce in-hospital complications and length of stay and improve patient satisfaction compared with conventional CABG while preserving the benefits of the LIMA and replacing SVGs with DES suggests the potential utility of HCR. Ongoing technical refinements of advanced hybrid revascularization offering multiple internal mammary arterial grafts done totally endoscopically hold great promise (46). However, minimally invasive surgical techniques also have a distinct learning curve (47). The success of HCR (and indeed optimizing revascularization in all patients with complex CAD) depends on close collaboration among general cardiologists, interventional cardiologists, and cardiac surgeons in a formal heart team setting. Finally, despite the intuitive advantages of the HCR approach in combining the best that both CABG and PCI have to offer, the safety, efficacy and cost-effectiveness of this approach must be proven in appropriately powered randomized trials, especially given the upfront costs of performing 2 procedures (in most HCR strategies) as opposed to a single multivessel PCI or CABG.

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REFERENCES

1. Mensah GA, Roth GA, Fuster V. The global burden of cardiovascular diseases and risk factors: 2020 and beyond. J Am Coll Cardiol 2019;74:2529–32.

2. Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statistics—2020 update: a report from the American Heart Association. Circulation 2020;41:e139–596.

3. Turco JV, Inal-Veith A, Fuster V. Cardiovascular health promotion: an issue that can no longer wait. J Am Coll Cardiol 2018;72:908–13.

4. Stone GW, Pieter Kappetein A, Sabik JF, et al., for the EXCEL Trial Investigators. Five-year outcomes after PCI or CABG for left main coronary disease. N Engl J Med 2019;381:1820–30.

5. Farkouh ME, Domanski M, Sleeper LA, et al., for the FREEDOM Trial Investigators. Strategies for multivessel revascularization in patients with diabetes. N Engl J Med 2012;367:2375–84.

6. Puskas JD, Halkos ME, Derose JJ, et al. Hybrid coronary revascularization for the treatment of multivessel coronary artery disease: a multicenter observational study. J Am Coll Cardiol 2016;68:356–65.

7. Lamy A, Devereaux PJ, Prabhakaran D, et al. Off-pump or on-pump coronary-artery bypass grafting at 30 days. N Engl J Med 2012;366:1489–97.

8. Head SJ, Milojevic M, Taggart DP, Puskas JD. Current practice of state-of-the-art surgical coronary revascularization. Circulation 2017;136:1331–45.

9. Parang P, Arora R. Coronary vein graft disease: pathogenesis and prevention. Can J Cardiol 2009;25:e57–62.

10. Alexander JH, Hafley G, Harrington RA, et al. Efficacy and safety of edifoligide, an E2F transcription factor decoy, for prevention of vein graft failure following coronary artery bypass graft surgery PREVENT IV: a randomized controlled trial. JAMA 2005;294:2446–54.

11. Stone G, Rizvi A, Newman W, et al., for the SPIRIT IV Investigators. Everolimus-eluting versus paclitaxel-eluting stents in coronary artery disease. N Engl J Med 2010;362:1663–74.

12. Bangalore S, Toklu B, Patel N, Feit F, Stone GW. Newer-generation ultrathin strut drug-eluting stents versus older second-generation thicker strut drug-eluting stents for coronary artery disease. Circulation 2018;138:2216–26.

13. Halkos ME, Rab ST, Vassiliades TA, et al. Hybrid coronary revascularization versus off-pump coronary artery bypass for the treatment of left main coronary stenosis. Ann Thorac Surg 2011;92:2155–60.

14. Davierwala PM. Current outcomes of off-pump coronary artery bypass grafting: evidence from real world practice. J Thorac Dis 2016;8:S772–86.

15. Hannan EL, Wu C, Smith CR, et al. Off-pump versus on-pump coronary artery bypass graft surgery: differences in short-term outcomes and in long-term mortality and need for subsequent revascularization. Circulation 2007;116:1145–52.

16. Puskas JD, Thourani VH, Kilgo P, et al. Off-pump coronary artery bypass disproportionately benefits high-risk patients. Ann Thorac Surg 2009;88:1142–7.

17. Tajstra M, Hrapkowicz T, Hawranek M, et al., for the POL-MIDES Study Investigators. Hybrid coronary revascularization in selected patients with multivessel disease: 5-year clinical outcomes of the prospective randomized pilot study. J Am Coll Cardiol Intv 2018;11:847–52.

18. Mack MJ, Acuff TE, Casimir-Ahn H, Lönn UJ, Jansen EWL. Video-assisted coronary bypass grafting on the beating heart. Ann Thorac Surg 1997;63 Suppl 6:S100–3.

19. Kon ZN, Brown EN, Tran R, et al. Simultaneous hybrid coronary revascularization reduces postoperative morbidity compared with results from conventional off-pump coronary artery bypass. J Thorac Cardiovasc Surg 2008;135:367–75.

20. Halkos ME, Liberman HA, Devireddy C, et al. Early clinical and angiographic outcomes after robotic-assisted coronary artery bypass surgery. J Thorac Cardiovasc Surg 2014;147:179–85.

21. Bonatti J, Schachner T, Bonaros N, Lehr EJ, Zimrin D, Griffith B. Robotically assisted totally endoscopic coronary bypass surgery. Circulation 2011;124:236–44.

22. Patel MR, Calhoon JH, Dehmer GJ, et al. ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Thoracic Surgeons. J Am Coll Cardiol 2017;69:2212–41.

23. Puri R, Reed GW. Refining coronary stent platforms in the modern DES era: thinning, eluting, inhibiting, and absorbing. J Am Coll Cardiol 2018;72:3298–300.

24. Valgimigli M, Bueno H, Byrne RA, et al., for the ESC Scientific Document Group. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS. Eur J Cardiothorac Surg 2018;53:34–78.

25. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2016;68:1082–115.

26. Bachinsky WB, Abdelsalam M, Boga G, Kiljanek L, Mumtaz M, McCarty C. Comparative study of same sitting hybrid coronary artery revascularization versus off-pump coronary artery bypass in multivessel coronary artery disease. J Interv Cardiol 2012;25:460–8.

27. Shen L, Hu S, Wang H, et al. One-stop hybrid coronary revascularization versus coronary artery bypass grafting and percutaneous coronary intervention for the treatment of multivessel coronary artery disease: 3-year follow-up results from a single institution. J Am Coll Cardiol 2013;61:2525–33.

28. Adams C, Burns DJP, Chu MWA, et al. Single-stage hybrid coronary revascularization with long-term follow-up. Eur J Cardiothorac Surg 2014;45:438–43.

29. Reicher B, Poston RS, Mehra MR, et al. Simultaneous "hybrid" percutaneous coronary intervention and minimally invasive surgical bypass grafting: feasibility, safety, and clinical outcomes. Am Heart J 2008;155:661–7.

30. Harskamp RE, Brennan JM, Xian Y, et al. Practice patterns and clinical outcomes after hybrid coronary revascularization in the United States: an analysis from the Society of Thoracic Surgeons Adult Cardiac Database. Circulation 2014;130:872–9.

31. Lowenstern A, Wu J, Bradley SM, Fanaroff AC, Tcheng JE, Wang TY. Current landscape of hybrid revascularization: a report from the NCDR CathPCI Registry. Am Heart J 2019;215:167–77.

32. Chen JP, Srivastava S. A vanishing lesion. J Am Coll Cardiol Intv 2010;3:360–1.

33. Nolan S, Filion KB, Atallah R, Moss E, Reynier P, Eisenberg MJ. Hybrid coronary revascularization vs complete coronary artery bypass grafting for multivessel coronary artery disease: a systematic review and meta-analysis. J Invasive Cardiol 2018;30:E131–49.

34. Panoulas VF, Colombo A, Margonato A, Maisano F. Hybrid coronary revascularization: promising, but yet to take off. J Am Coll Cardiol 2015;65:85–97.

35. Khan AA, Helton T, Forrest T, Ratkovec R. Use of intravenous cangrelor/DAPT bridge therapy for post-PCI patients undergoing gastrointestinal surgery. J Am Coll Cardiol 2019;73 Suppl 1:2670.

36. Gasior M, Zembala MO, Tajstra M, et al., for the POL-MIDES (HYBRID) Study Investigators. Hybrid revascularization for multivessel coronary artery disease. J Am Coll Cardiol Intv 2014;7:1277–83.

37. Esteves V, Oliveira MAP, Feitosa FS, et al. Late clinical outcomes of myocardial hybrid revascularization versus coronary artery bypass grafting for complex triple- vessel disease: long-term follow-up of the randomized MERGING clinical trial. Catheter Cardiovasc Interv 2020 Jan 10 [E-pub ahead of print].

38. Harskamp RE, Bagai A, Halkos ME, et al. Clinical outcomes after hybrid coronary revascularization versus coronary artery bypass surgery: a meta-analysis of 1,190 patients. Am Heart J 2014;167:585–92.

39. Halkos ME, Vassiliades TA, Douglas JS, et al. Hybrid coronary revascularization versus off-pump coronary artery bypass grafting for the treatment of multivessel coronary artery disease. Ann Thorac Surg 2011;92:1695–702.

40. Song Z, Shen L, Zheng Z, et al. One-stop hybrid coronary revascularization versus off-pump coronary artery bypass in patients with diabetes mellitus. J Thorac Cardiovasc Surg 2016;151:1695–701.

41. Harskamp RE, Abdelsalam M, Lopes RD, et al. Cardiac troponin release following hybrid coronary revascularization versus off-pump coronary artery bypass surgery. Interact Cardiovasc Thorac Surg 2014;19:1008–12.

42. Hage A, Giambruno V, Jones P, et al. Hybrid coronary revascularization versus off-pump coronary artery bypass grafting: comparative effectiveness analysis with long-term follow-up. J Am Heart Assoc 2019;8:e014204.

43. Ganyukov V, Kochergin N, Shilov A, et al. Randomized clinical trial of surgical vs. percutaneous vs. hybrid revascularization in multivessel coronary artery disease: residual myocardial ischemia and clinical outcomes at one year—Hybrid Coronary Revascularization Versus Stenting or Surgery (HREVS). J Interv Cardiol 2020;2020:5458064.

44. ClinicalTrials.gov. Hybrid Coronary Revascularization Trial. NCT03089398. Available at: https://clinicaltrials.gov/ct2/show/NCT03089398. Accessed February 6, 2019.

45. Halkos ME, Ford L, Peterson D, et al. The impact of hybrid coronary revascularization on hospital costs and reimbursements. Ann Thorac Surg 2014;97:1610–6.

46. Balkhy HH, Kitahara H, Hirai T, Matsukage H, Nathan S. Residual SYNTAX score after advanced hybrid robotic totally endoscopic coronary revascularization. Ann Thorac Surg 2020;109:1826–32.

47. Cheng N, Gao C, Yang M, Wu Y, Wang G, Xiao C. Analysis of the learning curve for beating heart, totally endoscopic, coronary artery bypass grafting. J Thorac Cardiovasc Surg 2014;148:1832–6.

48. Vassiliades TA, Kilgo PD, Douglas JS, et al. Clinical outcomes after hybrid coronary revascularization versus off-pump coronary artery bypass: a prospective evaluation. Innovations (Phila) 2009;4:299–306.

49. Qiu J, Zhu P, Liu Z, Xu H, Liu J, Zhao Q. Hybrid coronary revascularization versus off-pump coronary artery bypass grafting and percutaneous coronary intervention for the treatment of two-vessel coronary artery disease with proximal left anterior descending artery stenosis. J Thorac Dis 2019;11:2402–9.

50. Reynolds AC, King N. Hybrid coronary revascularization versus conventional coronary artery bypass grafting: systematic review and meta-analysis. Medicine (Baltimore) 2018;97:e11941.

51. Sardar P, Kundu A, Bischoff M, et al. Hybrid coronary revascularization versus coronary artery bypass grafting in patients with multivessel coronary artery disease: a meta-analysis. Catheter Cardiovasc Interv 2018;91:203–12.

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