

Hybrid coronary revascularization: a mainstream revascularization strategy in the future?

Revascularization by coronary artery bypass grafting is superior to percutaneous coronary intervention in cases of complex multivessel coronary artery disease. The superiority is demonstrated by reduced rates of repeat revascularization, myocardial infarction and all-cause death. By contrast, stroke occurs more frequently after coronary artery bypass grafting. Hybrid coronary revascularization combines the survival benefits of left internal mammary artery-to-left anterior descending coronary artery grafting, fast recovery and minimized surgical trauma, reduced risk of stroke by avoidance of aortic manipulation and the long-term patency of drug-eluting stent treatment of left anterior descending coronary artery lesions. Accordingly, results from registry studies are compatible with the short- and long-term superiority of hybrid coronary revascularization as compared with conventional revascularization using percutaneous coronary intervention or coronary artery bypass grafting.

KEYWORDS: drug-eluting stent • Heart Team • hybrid coronary revascularization
 • hybrid revascularization • minimally invasive direct coronary artery bypass
 • minimally invasive surgery • off-pump coronary artery bypass surgery
 • percutaneous coronary intervention

In stable patients with multivessel coronary artery disease (CAD), coronary bypass operation (coronary artery bypass grafting [CABG]) has been found to be superior to percutaneous coronary intervention (PCI) using drug-eluting stents (DES) [1-3]. The finding is based on well-powered randomized studies [4,5] and large-scale registries [6,7]. The superiority of CABG is demonstrated by lower short- and long-term rates of repeat revascularization, myocardial infarction (MI) and death, which were pronounced in patients with complex coronary artery lesions. With equal consistency, short-term stroke rates have been found to be lower in PCI- than in CABG-treated patients [4,5,8].

Coronary revascularization is a moving target. Coronary stents are undergoing continuous improvements resulting in enhanced deliverability and long-term safety as compared with the first-generation sirolimus-eluting Cypher™ (Cordis, FL, USA) and paclitaxel-eluting Taxus™ (Boston Scientific, MA, USA) stents used in the SYNTAX [5] and the FREEDOM [4] trials, respectively. Similarly, up-to-date antithrombotic treatment is likely to improve the short-term outcome of catheter-based revascularization [3].

On the surgical side, the combination of off-pump techniques and total arterial grafting promises a strategy to improve long-term outcome and reduce neurologic complications by

avoidance of aortic manipulation [9-11]. In addition, minimally invasive techniques diminish the surgical trauma and bleeding [12,13]. These changes are not likely to change the overall results of the abovementioned landmark trials.

Substantial evidence indicates that left internal mammary artery (LIMA) grafting of the left anterior descending coronary artery (LAD) is the main determinant of the beneficial survival effect of CABG [14,15]. Therefore, current revascularization guidelines recommend CABG as the preferred treatment in patients with CAD with the exception of patients with one- or two-vessel disease without proximal LAD involvement [1-3]. The benefit of non-mammary artery conduits to non-LAD vessels is less clear, and the poor longevity, especially of saphenous vein grafts (SVG), may favor the use of PCI using DES in non-LAD territories [16,17]. The possible superiority of DES treatment as compared with grafting of non-LAD lesions using SVGs or arterial conduits remains to be addressed in randomized clinical trials.

The fundamental rationale of hybrid coronary revascularization (HCR) is to combine the prognostic benefits of the LIMA-to-LAD graft with minimal invasiveness and reduction of stroke risk. The concept of HCR has been assessed in a number of case reports and registry studies [18-30]. To date, HCR has mainly been used in patient subsets with a

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specific indication for a combined procedure, such as challenges including limited conduit availability and predicted reduced healing after sternotomy or following primary PCI of a non-LAD culprit lesion. Consecutive series with well-defined inclusion criteria are scarce, and randomized studies are nonexistent. This review (concurring with other recent scientific reports) advocates dedicated assessment of HCR procedures in prospective registries using predefined surgical and interventional techniques and in randomized controlled HCR versus traditional revascularization trials that are powered for clinical end points to prove the HCR concept [31–36].

The SYNTAX trial data & HCR

The SYNTAX trial is a unique comprehensive comparison of modern surgical and catheter-based revascularization using DES, incorporating coronary disease complexity into the evaluation of the clinical results [5,37]. The study offers a unique possibility to describe the characteristics and results of surgical and catheter-based revascularizations, and the likely results of combined procedures [38].

The SYNTAX trial demonstrated, for the first time, a dramatic negative effect of the complexity of CAD on PCI results using the SYNTAX score stratification [37]. After 5 years, compared with CABG, mortality was significantly increased in PCI patients with a high SYNTAX score [38]. Medium- and low-score patients had similar all-cause mortality in the PCI and CABG groups. PCI results were heavily dependent on the complexity of the CAD. In HCR, the LAD lesion can probably be omitted in the SYNTAX score calculation. In our own registry, including 100 consecutive patients treated with staged HCR, the SYNTAX score was reduced by half after omitting LAD lesions [33]. Therefore, even a highly complex general coronary pathology may be treated with a hybrid strategy with, in theory, low risk and favorable results. The surgical part of the revascularization, LIMA-to-LAD, is not influenced by lesion complexity and the stenting of non-LAD lesions may be performed in a low-SYNTAX score setting.

In the CABG treated patients, 5-year repeat revascularization rates were similar across the SYNTAX score groups, in contrast to the PCI group, where repeat revascularization increased from 23.0 in low to 30.9% in high SYNTAX score patients [38]. In the setting of HCR, the rate of repeat revascularization is likely to be acceptably low, owing to the lower SYNTAX

score of the PCI-treated lesions. Furthermore, repeat revascularization using modern DES in non-LAD vessels is likely to remain stable at a low rate, including beyond 5–10 years, when SVG failure results in new revascularizations and other cardiac events [39].

As compared with PCI, there was a higher risk of periprocedural stroke in patients undergoing CABG. At 1-year, 0.6% of PCI and 2.2% of CABG patients ($p = 0.003$) had suffered a stroke [5]. The risk converged over time and the difference was nonsignificant after 5 years (PCI 2.4 vs CABG 3.7%; $p = 0.09$) [38]. Of the patients who developed stroke, 68% in the CABG group and 47% in the PCI group had residual deficits [40]. Thus, stroke is a significant event often associated with severe disability. The increased risk of stroke after CABG is a major reason for considering surgical techniques that avoid any manipulation of the aorta [9].

Angiographic complete revascularization was achieved in 52.8% of the PCI patients and in 66.9% of patients treated with CABG [5]. Incomplete revascularization was associated with significantly increased 4-year mortality in both groups. In the PCI group, the presence of a total occlusion was the strongest predictor of incomplete revascularization. It is likely that incomplete revascularization is a marker of greater coronary complexity and comorbidity that may explain some of the poor outcomes in incompletely revascularized patients [6,41]. A HCR procedure encompassing the options of both surgical and PCI may reduce the rates of incomplete revascularization, compared with conventional CABG and PCI.

LIMA versus DES

Long-term outcome is closely related to patency of grafts and PCI-treated lesions. In this respect, the LIMA is a unique conduit. After 10 years, >85% of LIMA grafts are patent and only 1% have developed atherosclerotic lesions with significant stenosis [42,43]. The superior patency of the LIMA graft versus PCI using bare-metal stents in the treatment of proximal LAD lesions has been demonstrated in two small randomized trials with 1-year follow-up [44,45]. There are no well-powered randomized comparisons of LIMA versus DES-PCI in the treatment of proximal LAD lesions. However, it is unlikely that catheter-based treatment will be able to match the long-term LIMA-to-LAD results in the proximal LAD. Following DES treatment of LAD lesions, a 5-year rate of target vessel revascularization of 10–20% may be expected [46].

After the BARI trial comparing CABG and balloon angioplasty, it has been generally accepted that the survival advantage offered by CABG, compared with PCI was related to the presence of a patent LIMA-to-LAD graft [47]. Both the SYNTAX [5] and the FREEDOM [4] trials concur with these results, and the presence of a proximal LAD lesion in patients with multivessel disease strongly indicates a surgical revascularization. Accordingly, current revascularization guidelines recommend CABG as the primary treatment option in patients with CAD, with the exception of one- and two-vessel disease without proximal LAD involvement [1–3].

Non-LIMA grafting versus DES

The degeneration over time of the SVG is a major problem for the CABG patient. At 10 years, more than 50% of SVGs will be occluded [16]. Moreover, the revascularization of a SVG lesion or recanalization of its proximal coronary artery, which is often chronically occluded, may be challenging. Treatment of the degenerated SVG conveys a high risk of distal embolization and an increased risk of occlusion, restenosis and development of new lesions [41,48]. Aggressive statin treatment has been shown to reduce new revascularizations, and SVG disease progression can be assessed by angiography and intracoronary ultrasound [49,50]. The first-generation Cypher and Taxus stents have been used for almost 10 years, and the 5–10-year rates of target lesion revascularization seem to be approximately 10–20% [51,52]. Thus, it is likely that the long-term performance of the DES is superior to SVG. Ideally, this should be confirmed in a randomized study [30–39,46,53–55].

Bilateral internal mammary artery grafting

There are no long-term randomized comparisons of bilateral internal mammary artery (BIMA) versus CABG using SVG [56]. Large multivariate analyses and propensity score analyses document reduced mortality after BIMA, as compared with patients treated with LIMA and SVG grafting [56–58]. Despite the large number of patients in these studies and controlling for confounders, it must be taken into account that a large number of patients will never compensate for a stable, but unknown, selection bias. Using the BIMA, infection and instability have been of concern, especially in diabetic patients; the subgroup of patients that may need an arterial revascularization the most. The major reasons for not using BIMA grafts are the technical

difficulty, the concern of higher periprocedural morbidity, including sternal infection, and the lack of definitive evidence of benefits [59].

Other arterial conduits

Owing to the frequently occurring degeneration of SVGs, arterial conduits are increasingly being used to improve long-term surgical revascularization results [60–63]. Radial, gastroepiploic and inferior epigastric arteries have been used. The problems faced using these arterial grafts include spasm and atrophy in the grafting of lesions that are not highly stenotic. Thus, the long-term patency of noninternal mammary arterial conduits may not be better than those of SVGs.

HCV procedure

■ Surgical techniques

A number of minimally invasive techniques have been developed to anastomose the LIMA to the LAD. Minimally invasive direct CABG (MID-CAB) refers to LIMA harvest, with or without robotic assistance, and off-pump anastomosis under direct vision through a left-sided minithoracotomy [64,65]. In totally endoscopic coronary artery bypass surgery, both LIMA harvest and off-pump anastomosis are robotically assisted [66,67]. Finally, LIMA harvest and off-pump CABG (OPCAB) can be performed through an inferior left J-hemisternotomy under direct vision (a JOPCAB procedure) [25,33,68]. FIGURES 1–4 illustrate the minimally invasive character of the JOPCAB procedure. In a number of registries, with [12,69–77] or without [18–24,26–30] *ad hoc* control groups, these procedures have been demonstrated to be safe and efficient in dedicated centers.

■ Timing

Logistically, HCR may be performed in three ways. PCI can be performed prior to, or following,



Figure 1. Surgical suite during left internal mammary artery harvest.



Figure 2. Left internal mammary artery-to-left anterior descending coronary artery anastomosis.

surgical intervention in a two-staged approach. Moreover, surgery and PCI can be performed in a single setting using a hybrid surgical suite.

The advantages of surgery prior to a PCI strategy include fewer bleeding problems, as dual antiplatelet therapy may be instituted after the surgical procedure. Furthermore, the operative LIMA result can be assessed angiographically and complex non-LAD lesion stenting may be performed with the LAD protected by the LIMA conduit. It is a disadvantage that surgery is performed in a scenario of significant untreated non-LAD lesions that may result in preoperative ischemia. Most problematic is the fact that a failed PCI may result in an incomplete revascularization. In our series of 100 preplanned staged HCRs, 89% of the procedures were carried out 1–3 days after the JOPCAB. We experienced three cases with ischemia without biomarker release due to untreated non-LAD lesions, and their PCI was performed before scheduled [33].

Advantages of a PCI prior to a surgery strategy include lower risks of ischemia during surgery and the possibility of performing grafting of non-LAD arteries in the case of suboptimal PCI results. In this strategy, bleeding complications

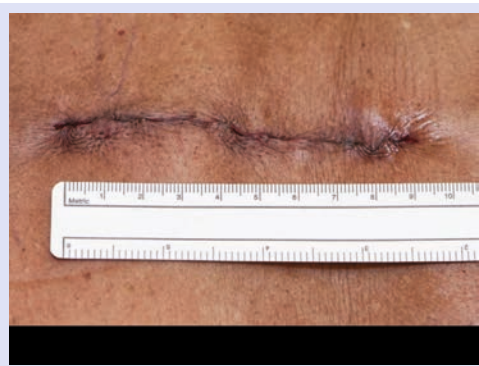


Figure 3. Completed wound closure.

constitute a significant problem, as the surgical part of the revascularization is performed during dual antiplatelet treatment. In addition, LIMA patency cannot be assessed routinely. The strategy may be used in lesions with a risk of PCI failure, in other words chronic total occlusions, and in partially revascularized patients after PCI for an acute coronary syndrome. In our series, 11% of patients were treated using this strategy and postoperative bleeding was found to be a concern [33].

Using a hybrid operation suite, surgery and subsequent PCI can be performed in the same setting. This simultaneous procedure is theoretically attractive as it is a single-step complete revascularization with immediate angiographic control of the LIMA-to-LAD revascularization and the option of surgical intervention in the case of PCI failure. The disadvantages include possible bleeding risk with dual antiplatelet therapy at the time of surgery and risk of stent thrombosis due to the general inflammatory response to surgery. Furthermore, there may be logistical issues and the need for a hybrid operation suite [12,69,73–76].

The Heart Team approach

In European and American guidelines for coronary revascularization, the multidisciplinary Heart Team approach has been considered a class I indication in coronary revascularization [1–3,78]. The SYNTAX trial documented the necessity for a preprocedure patient evaluation with participation of at least cardiac surgeons and interventional cardiologists to obtain a balanced and complementary approach to the treatment of the individual cardiac patient [5,37].

The Heart Team interaction is an essential element in the tailoring of a HCR procedure, and is mandatory for implementing a viable HCR program [33,79].

Clinical evaluation of HCR procedures

There have been numerous reports of successful HCR in patients with multivessel disease. The first procedures were described in the late 1990s, where the procedure was performed on special indications. For the surgeon, such scenarios include: patients without suitable conduits; a severely calcified aorta; conditions likely to prevent healing after sternotomy; or a nongraftable coronary vessel, where PCI remains an option. For the interventional cardiologist, severe tortuosity and calcification of the LAD or other complex lesion characteristics may call for a surgical

procedure. Furthermore, patients with comorbidities, old age, frailty, poor left ventricular function or renal dysfunction are likely to benefit from a minimally invasive revascularization technique [19,24,26,28]. In these clinical situations, the American and European guidelines classify hybrid revascularizations as a class IIa, level of evidence C indication [1,2].

In the bare-metal stents era, the high restenosis rate after PCI was discouraging for the general use of HCR procedures. At present, the interest in HCR seems to be increasing, possibly owing to the proven failure of DES in patients with multivessel disease, and a genuine and relevant interest in minimally invasive revascularization techniques.

There are no randomized clinical trials on HCR versus surgical revascularization or PCI. A number of case reports and registries seem to document the feasibility of the HCR procedure across different HCR strategies (timing of PCI and surgical techniques). A number of the studies included patients over a long time period and, frequently, the HCR procedure was performed in patients who were suboptimal surgical candidates [19,24,25,28]. A recent study by Repossini *et al.* documented excellent long-term outcome after HCR with an intention-to-treat strategy in 166 patients [80].

According to a PubMed search (6 May 2013), there are ten studies on HCR including a control group. These papers are mentioned in some detail in TABLE 1.

In 2001, de Cannière *et al.* assessed HCR using bare-metal stents in 20 patients with two-vessel coronary disease versus 20 matched (age, sex, comorbidities, coronary anatomy and ejection fraction) CABG patients [70]. The HCR was staged by 1–3 days. The HCR patients had a 2-year event-free survival rate of 85%, compared with 35% in the CABG group (events included episodes of atrial fibrillation, pericardial effusion, MI, blood transfusion requirement and leg wound dehiscence). Compared with conventional surgery, recovery was more rapid after HCR, and patients returned to work much sooner after HCR than after CABG (22 ± 8 vs 89 ± 22 days; $p < 0.005$).

Reicher *et al.* used the propensity scores to match 13 patients undergoing simultaneous HCR with 26 off-pump CABG patients [75]. Overall, the results were similar in the two groups, but the HCR patients had shorter hospital stays (3.6 ± 1.5 vs 6.3 ± 2.3 days; $p = 0.0001$) and a significantly lower need for blood transfusion.

In 2008, Kon *et al.* compared a simultaneous

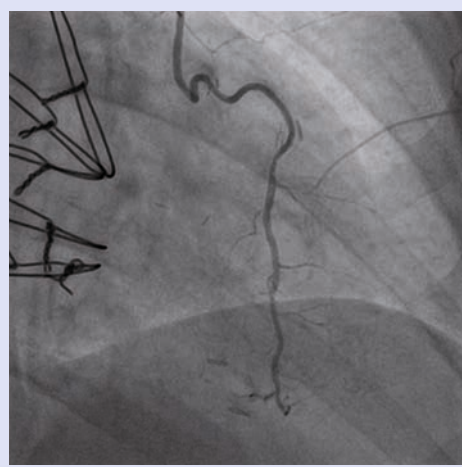


Figure 4. Postoperative angiogram of left internal mammary artery-to-left anterior descending coronary artery anastomosis.

approach HCR procedure including MIDCAB in 15 patients with 30 OPCAB controls [12]. The HCR patients received 325 mg of aspirin before the procedure, heparin during surgery and 300 mg of clopidogrel on returning to the intensive care unit. The results were much in favor of the HCR procedure. Thus, HCR patients had better preoperative hemodynamics, needed fewer blood cell transfusions, had shorter intubation times, less postoperative increase of serum creatinine values and reduced postoperative costs. Maximum pain scores were higher after MIDCAB, but the duration of time needed for pain to completely resolve was shorter for HCR. Overall satisfaction scores were significantly higher after the hybrid procedure. At 1 year, there was no mortality in either group. Major cardiac adverse events were noted in 7 of HCR and in 23% of OPCAB patients ($p = 0.05$). Patients returned to work or normal activities more quickly after HCR. Long-term graft patency was assessed using computed tomography angiography and demonstrated one stent failure in the hybrid group, compared with seven SVG failures in the OPCAB group ($p = 0.062$).

Vassiliades *et al.* compared 91 HCR and 4175 OPCAB procedures, adjusting for confounding background variables [77]. Surgery in HCR involved MIDCAB with thoracoscopic LIMA harvest. The authors used a staged treatment strategy; 93.4% had surgery first and PCI on average 2.2 days later. The remaining patients had PCI first and LIMA grafting 2 months later, while still on clopidogrel. The major cardiac and cerebral adverse events (MACCE; death, MI, stroke and need for repeat intervention) rates were similar between the two study groups (1.1

Table 1. Registry studies comparing hybrid coronary revascularization with conventional coronary artery bypass grafting and percutaneous coronary intervention.

Study (year)	Patients/ controls (n)	HCR procedure	Surgical procedure	Timing	Follow-up	Authors' conclusions	Ref.
Shen <i>et al.</i> (2013)	141/141	MIDCAB	CABG or PCI	Simultaneous	3 years	Similar MACCE in HCR vs CABG, but increased vs PCI. HCR higher MACCE than CABG in high SYNTAX score and euroSCORE patients	[76]
Leacche <i>et al.</i> (2013)	80/301	OPCAB or CABG	OPCAB or CABG	Simultaneous	1 month	HCR a safe alternative to CABG Increased repeat revascularization in HCR >33 SYNTAX score	[74]
Bachinsky <i>et al.</i> (2012)	25/27	Robotic MIDCAB	OPCAB	Simultaneous	1 month	HCR feasible and safe	[69]
Hu <i>et al.</i> (2011)	104/104	MIDCAB	OPCAB	Simultaneous	1.5 years	HCR better 18-month clinical outcome (MACCE)	[73]
Halkos <i>et al.</i> (2011)	147/588	MIDCAB	OPCAB	Staged	3.2 years	Similar rate of death and MACCE, revascularization increased in HCR	[71]
Halkos <i>et al.</i> (2011)	27/81	MIDCAB	OPCAB	Staged	3.2 years	HCR is a safe and feasible in left main disease	[72]
Vassiliades <i>et al.</i> (2009)	91/4175	MIDCAB	Endo-ACAB	Staged	3 years	HCR noninferior in 30-day MACCE and 3-year survival	[77]
Kon <i>et al.</i> (2006)	15/30	MIDCAB	OPCAB	Simultaneous	1 year	Similar clinical results High patient satisfaction with HCR	[12]
Reicher <i>et al.</i> (2008)	13/26	MIDCAB	OPCAB	Simultaneous	6 months	Similar safety and efficacy Shorter hospital stay after HCR	[75]
de Cannière <i>et al.</i> (2001)	20/20	MIDCAB	CABG	Mixed	2 years	Similar clinical results Less perioperative morbidity	[70]

CABG: Coronary artery bypass grafting; Endo-ACAB: Endoscopic atraumatic coronary artery bypass; HCR: Hybrid coronary revascularization; MACCE: Major cardiac and cerebral adverse event; MIDCAB: Minimally invasive direct coronary artery bypass grafting; OPCAB: Off-pump coronary artery bypass grafting; PCI: Percutaneous coronary intervention.

in hybrid vs 3.0% in OPCAB; $p = 0.48$), and the 3-year Kaplan–Meier survival estimates at 3 years were also similar.

Halkos *et al.* assessed a HCR procedure using a robotic technique in 147 patients that were compared with 588 OPCAB controls [71]. The prevailing surgical technique was MIDCAB with thoracoscopic LIMA harvest and, since 2009, totally endoscopic coronary artery bypass surgery. This is, so far, the largest HCR series published. Patients with non-LAD lesions unfavorable for PCI were excluded (long lesions, small vessels, bifurcations and chronic total occlusions). The vast majority of patients were treated with surgery first and stenting after 2–3 days. The few PCI-first patients underwent surgery on clopidogrel treatment. The in-hospital MACCE rate (death, stroke and MI) were similar in the two groups. After a median 3.2-year follow-up period, the need for repeat revascularization was increased in HCR patients (12.2 vs 3.7%; $p < 0.001$). Interestingly, this was primarily due to LIMA and LIMA/LAD problems. The estimated 5-year survival rates were similar in the two groups (HCR: 86.8% and OPCAB: 84.3%; $p = 0.61$).

In 2011, the same group published results on HCR versus OPCAB revascularization of

patients with left main stenosis [72]. A total of 27 HCR patients were matched with 81 OPCAB controls. Again, after 3.2 years, rates of MACCE were similar between groups, and there were more repeat revascularizations in HCR patients (7.4 vs 1.2%; $p = 0.09$). In all HCR cases, the LIMA-to-LAD anastomosis was performed first and the left main coronary artery stenting was performed 2–3 days later after angiographical documentation of a patent LIMA-to-LAD.

In a study from 2011, Hu *et al.* performed simultaneous HCR in 104 patients and compared 18-month clinical results with a 1:1 matched OPCAB group [73]. HCR procedure implied a JOPCAB procedure in patients pretreated with low-dose aspirin. Unfractionated heparin was given at the beginning of the operation and was reversed after the graft procedure. Clopidogrel was administered via a nasogastric tube before stenting and the patient was re-heparinized. The total HCR procedure required longer operation time compared with OPCAB, but the need for blood transfusion was reduced. After 18 months, MACCE-free survival in HCR-treated patients compared favorably with OPCAB (99.0 vs 90.4%; $p = 0.03$).

Bachinsky *et al.* prospectively evaluated a same-sitting robotic-assisted HCR in 25 patients and compared the results to 27 consecutive low-to-moderate risk OPCAB patients [69]. The anticoagulation and antithrombotic regimen was similar to that mentioned above. In this short-term study, overall major cardiac adverse event rates were similar between both groups. The postoperative need for blood transfusions was reduced and the length of hospital stay was shorter in the HCR group. However, owing to higher procedural costs, the HCR treatment was more expensive than conventional OPCAB. Importantly, the HCR patients had a faster return to work (5.3 vs 8.2 weeks; $p = 0.01$).

Leacche *et al.* retrospectively analyzed the 30-day outcome of 381 consecutive CABG patients versus 80 HCR patients (simultaneous PCI and OPCAB/CABG) [74]. The procedure was not preplanned in 25% of the HCR patients. The authors stratified the patients in a 2×2 matrix according to low/high SYNTAX score and low/high euroSCORE. The main challenging finding of the study was that the composite end point (death from any cause, stroke, MI and low cardiac output syndrome) was marked as increased in the HCR group with high SYNTAX score and high euroSCORE owing to high mortality in the HCR patients.

Recently, Shen *et al.* published the most comprehensive evaluation of HCR to date [76]. The authors performed simultaneous HCR using the JOPCAB technique with an inferior partial sternotomy in 141 patients. The outcome was compared with 141 matched PCI and 141 CABG controls. The three patient groups were stratified by euroSCORE and SYNTAX score. The algorithm for anticoagulation and antithrombotic treatment was similar to that described by Hu *et al.* [73]. At 3-year follow-up, actuarial survival in the HCR, CABG and PCI groups was 99.3, 97.2 and 96.5%, respectively ($p = 0.344$). Six patients in the HCR group, three patients in the CABG group and 18 patients in the PCI group underwent repeat revascularization ($p = 0.001$). There were two, nine and three neurologic events in the HCR, CABG and PCI patients, respectively ($p = 0.083$). The cumulative MACCE rate in the hybrid group (6.4%) was significantly lower than in the PCI group (22.7%; $p < 0.001$), but similar to the CABG group. In patients with a high euroSCORE, HCR was associated with a lower MACCE rate than CABG ($p = 0.030$) and PCI ($p = 0.006$). High SYNTAX score was

associated with improved results in HCR versus PCI ($p = 0.002$), while the results were similar in the HCR and CABG groups ($p = 0.362$).

■ Comments on the existing clinical evaluation of HCR

There are considerable scientific weaknesses in the abovementioned registries, and the results should be considered hypothesis-generating. Even the studies with the highest numbers of patients are likely to be grossly underpowered to detect differences in clinical events. In addition, the patient selection cannot always be considered consecutive and the inclusion criteria were not always well defined. Furthermore, the matched controls are unlikely to be sufficiently adjusted for selection bias. In short, HCR seems to be less traumatic than conventional CABG and the MACCE results are as good as CABG, at least at medium-term follow-up.

A number of questions need to be assessed in prospective registries with well-defined inclusion criteria. The long-term safety and efficacy issues of HCR versus CABG/PCI need to be addressed in larger scale randomized clinical trials, as already proposed by other groups [31,32, 35,36,81]. In this context, the design and conduct of the trials will be difficult owing to the complex nature of the problem and the multitude of techniques used. Another practical problem is the need for long-term follow-up; 5–10 years to obtain a definitive evaluation.

Finally, HCR necessitates an extensive synergy between interventional cardiologists and cardiac surgeons and a general acceptance of MIDCAB/JOPCAB procedures in the surgical environment. Such cultural changes may be challenging.

Conclusion & future perspective

HCR is a promising treatment strategy that combines the survival benefits of a LIMA conduit to the LAD with DES treatment of non-LAD lesions in a minimally invasive procedure. Today, HCR is a treatment option in patient and lesion subsets not suitable for CABG and PCI [1,2].

Well-defined prospective registry studies and randomized clinical trials will be necessary to complement our understanding on the role of HCR coronary revascularization. HCR is likely to become an important element in a revascularization scenario encompassing PCI, conventional surgery and HCR procedures, taking coronary revascularization and the Heart Team approach to another level.

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Executive summary

Background for hybrid coronary revascularization

- There are prognostic benefits of left internal mammary artery (LIMA)-to-anterior descending coronary artery (LAD):
 - The risk of stroke will be reduce.
 - The surgical treatments are minimally invasive procedures.

The SYNTAX trial data & hybrid coronary revascularization

- In hybrid coronary revascularization (HCR), LIMA-to-LAD is not influenced by lesion complexity.
- Stenting of non-LAD lesions may be performed in a low-SYNTAX score setting.

LIMA vs drug-eluting stents

- The long-term LIMA-to-LAD grafting results are probably superior to drug-eluting stent treatment.

Non-LIMA grafting versus DES

- The long-term performance of drug-eluting stent is probably superior to saphenous vein grafts.

The Heart Team approach

- The Heart Team interaction is an essential element in the tailoring of a HCR procedure, and is mandatory for implementing a viable HCR program.

Clinical evaluation of HCR procedures

- In registry studies, the procedure has been associated with faster recovery and clinical results that are comparable to conventional revascularization.

Future perspective

- HCR is a treatment option in patient and lesion subsets that are not suitable for coronary artery bypass grafting and percutaneous coronary intervention.
- Well-defined prospective registry studies and randomized clinical trials will be necessary to define the role of HCR coronary revascularization.
- HCR is likely to become an important option in coronary revascularization.

References

Papers of special note have been highlighted as:

- of interest
- of considerable interest

- 1 Hillis LD, Smith PK, Anderson JL *et al.* 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery. A report of the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons. *J. Am. Coll. Cardiol.* 58(24), e123–e210 (2011).
- 2 Kolh P, Wijns W, Danchin N *et al.* Guidelines on myocardial revascularization. *Eur. J. Cardiothorac. Surg.* 38(Suppl.), S1–S52 (2010).
- 3 Wijns W, Kolh P, Danchin N *et al.* Guidelines on myocardial revascularization. *Eur. Heart J.* 31(20), 2501–2555 (2010).
- 4 Farkouh ME, Domanski M, Sleeper LA *et al.* Strategies for multivessel revascularization in patients with diabetes. *N. Engl. J. Med.* 367(25), 2375–2384 (2012).
- 5 Serruys PW, Morice MC, Kappetein AP *et al.* Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N. Engl. J. Med.* 360(10), 961–972 (2009).
- 6 Hannan EL, Wu C, Walford G *et al.* Drug-eluting stents vs. coronary-artery bypass grafting in multivessel coronary disease. *N. Engl. J. Med.* 358(4), 331–341 (2008).
- 7 Weintraub WS, Grau-Sepulveda MV, Weiss JM *et al.* Comparative effectiveness of revascularization strategies. *N. Engl. J. Med.* 366(16), 1467–1476 (2012).
- 8 Lee MS, Bokhoor P, Park SJ *et al.* Unprotected left main coronary disease and ST-segment elevation myocardial infarction: a contemporary review and argument for percutaneous coronary intervention. *JACC Cardiovasc. Interv.* 3(8), 791–795 (2010).
- 9 Emmert MY, Seifert B, Wilhelm M, Grunenfelder J, Falk V, Salzberg SP. Aortic no-touch technique makes the difference in off-pump coronary artery bypass grafting. *J. Thorac. Cardiovasc. Surg.* 142(6), 1499–1506 (2011).
- 10 Lattouf OM, Thourani VH, Kilgo PD *et al.* Influence of on-pump versus off-pump techniques and completeness of revascularization on long-term survival after coronary artery bypass. *Ann. Thorac. Surg.* 86(3), 797–805 (2008).
- 11 Puskas JD, Kilgo PD, Lattouf OM *et al.* Off-pump coronary bypass provides reduced mortality and morbidity and equivalent 10-year survival. *Ann. Thorac. Surg.* 86(4), 1139–1146 (2008).
- 12 Kon ZN, Kwon MH, Collins MJ *et al.* Off-Pump coronary artery bypass leads to a regional hypercoagulable state not detectable using systemic markers. *Innovations (Phila.)* 1(5), 232–238 (2006).
- 13 Valley MP, Bannon PG, Bayfield MS, Hughes CF, Kritharides L. Quantitative and temporal differences in coagulation, fibrinolysis and platelet activation after on-pump and off-pump coronary artery bypass surgery. *Heart Lung Circ.* 18(2), 123–130 (2009).
- 14 Cameron A, Davis KB, Green G, Schaff HV. Coronary bypass surgery with internal-thoracic-artery grafts – effects on survival over a 15-year period. *N. Engl. J. Med.* 334(4), 216–219 (1996).

- 15 Loop FD, Lytle BW, Cosgrove DM *et al.* Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. *N. Engl. J. Med.* 314(1), 1–6 (1986).
- 16 Goldman S, Zadina K, Moritz T *et al.* Long-term patency of saphenous vein and left internal mammary artery grafts after coronary artery bypass surgery: results from a Department of Veterans Affairs Cooperative Study. *J. Am. Coll. Cardiol.* 44(11), 2149–2156 (2004).
- 17 Nwasokwa ON. Coronary artery bypass graft disease. *Ann. Intern. Med.* 123(7), 528–545 (1995).
- 18 Davidavicius G, Van Praet F, Mansour S *et al.* Hybrid revascularization strategy: a pilot study on the association of robotically enhanced minimally invasive direct coronary artery bypass surgery and fractional-flow-reserve-guided percutaneous coronary intervention. *Circulation* 112(9 Suppl.), I317–I322 (2005).
- 19 Fedakar A, Tasar M, Rabus MB, Alsalehi S, Tokar ME, Balkanay M. Hybrid coronary revascularization for the treatment of left main coronary artery disease in high-risk patients. *Heart Surg. Forum* 15(1), E51–E55 (2012).
- 20 Gilard M, Bezon E, Cornily JC *et al.* Same-day combined percutaneous coronary intervention and coronary artery surgery. *Cardiology* 108(4), 363–367 (2007).
- 21 Katz MR, Van Praet F, de Cannière D *et al.* Integrated coronary revascularization: percutaneous coronary intervention plus robotic totally endoscopic coronary artery bypass. *Circulation* 114(1 Suppl.), I473–I476 (2006).
- 22 Kiaii B, McClure RS, Kostuk WJ *et al.* Concurrent robotic hybrid revascularization using an enhanced operative suite. *Chest* 128(6), 4046–4048 (2005).
- 23 Lewis BS, Porat E, Halon DA *et al.* Same-day combined coronary angioplasty and minimally invasive coronary surgery. *Am. J. Cardiol.* 84(10), 1246–1247 (1999).
- 24 Presbitero P, Nicolini F, Maiello L *et al.* ‘Hybrid’ percutaneous and surgical coronary revascularization: selection criteria from a single-center experience. *Ital. Heart J.* 2(5), 363–368 (2001).
- 25 Riess FC, Schofer J, Kremer P *et al.* Beating heart operations including hybrid revascularization: initial experiences. *Ann. Thorac. Surg.* 66(3), 1076–1081 (1998).
- 26 Riess FC, Bader R, Kremer P *et al.* Coronary hybrid revascularization from January 1997 to January 2001: a clinical follow-up. *Ann. Thorac. Surg.* 73(6), 1849–1855 (2002).
- 27 Stahl KD, Boyd WD, Vassiliades TA, Karamanoukian HL. Hybrid robotic coronary artery surgery and angioplasty in multivessel coronary artery disease. *Ann. Thorac. Surg.* 74(4), S1358–S1362 (2002).
- 28 Wittwer T, Cremer J, Klima U, Wahlers T, Haverich A. Myocardial ‘hybrid’ revascularization: intermediate results of an alternative approach to multivessel coronary artery disease. *J. Thorac. Cardiovasc. Surg.* 118(4), 766–767 (1999).
- 29 Zenati M, Cohen HA, Griffith BP. Alternative approach to multivessel coronary disease with integrated coronary revascularization. *J. Thorac. Cardiovasc. Surg.* 117(3), 439–444 (1999).
- 30 Zhao DX, Leacche M, Balaguer JM *et al.* Routine intraoperative completion angiography after coronary artery bypass grafting and 1-stop hybrid revascularization results from a fully integrated hybrid catheterization laboratory/operating room. *J. Am. Coll. Cardiol.* 53(3), 232–241 (2009).
- 31 Friedrich GJ, Bonatti J. Hybrid coronary artery revascularization – review and update 2007. *Heart Surg. Forum* 10(4), E292–E296 (2007).
- 32 Green KD, Lynch DR Jr, Chen TP, Zhao D. Combining PCI and CABG: the role of hybrid revascularization. *Curr. Cardiol. Rep.* 15(4), 351 (2013).
- 33 Modrau IS, Nielsen PH, Bøtker HE *et al.* Procedural feasibility and early safety of hybrid coronary revascularization combining off-pump coronary surgery through J-hemisternotomy with percutaneous coronary intervention. *EuroIntervention* (2013) (In Press).
- 34 Murphy GJ, Bryan AJ, Angelini GD. Hybrid coronary revascularization in the era of drug-eluting stents. *Ann. Thorac. Surg.* 78(5), 1861–1867 (2004).
- 35 Umakanthan R, Leacche M, Gallion AH, Byrne JG. A comparison of hybrid coronary revascularization and off-pump coronary revascularization. *Expert Rev. Cardiovasc. Ther.* 11(4), 395–397 (2013).
- 36 Wrigley BJ, Dubey G, Spyt T, Gershlick AH. Hybrid revascularisation in multivessel coronary artery disease: could a combination of CABG and PCI be the best option in selected patients? *EuroIntervention* 8(11), 1335–1341 (2013).
- 37 Sianos G, Morel MA, Kappetein AP *et al.* The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention* 1(2), 219–227 (2005).
- **Description of the SYNTAX score.**
- 38 Mohr FW, Morice MC, Kappetein AP *et al.* Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. *Lancet* 381(9867), 629–638 (2013).
- 39 Sarno G, Lagerqvist B, Frobert O *et al.* Lower risk of stent thrombosis and restenosis with unrestricted use of ‘new-generation’ drug-eluting stents: a report from the nationwide Swedish Coronary Angiography and Angioplasty Registry (SCAAR). *Eur. Heart J.* 33(5), 606–613 (2012).
- 40 Mack MJ, Head SJ, Holmes DR Jr *et al.* Analysis of stroke occurring in the SYNTAX Trial comparing coronary arterybypass surgery and percutaneous coronary intervention in the treatment of complex coronary artery disease. *JACC Cardiovasc. Interv.* 6(4), 344–354 (2013).
- 41 Bell MR, Gersh BJ, Schaff HV *et al.* Effect of completeness of revascularization on long-term outcome of patients with three-vessel disease undergoing coronary artery bypass surgery. A report from the Coronary Artery Surgery Study (CASS) Registry. *Circulation* 86(2), 446–457 (1992).
- 42 Fitzgibbon GM, Kafka HP, Leach AJ, Keon WJ, Hooper GD, Burton JR. Coronary bypass graft fate and patient outcome: angiographic follow-up of 5,065 grafts related to survival and reoperation in 1,388 patients during 25 years. *J. Am. Coll. Cardiol.* 28(3), 616–626 (1996).
- 43 Sabik JF 3rd, Lytle BW, Blackstone EH, Houghtaling PL, Cosgrove DM. Comparison of saphenous vein and internal thoracic artery graft patency by coronary system. *Ann. Thorac. Surg.* 79(2), 544–551 (2005).
- 44 Diegeler A, Thiele H, Falk V *et al.* Comparison of stenting with minimally invasive bypass surgery for stenosis of the left anterior descending coronary artery. *N. Engl. J. Med.* 347(8), 561–566 (2002).
- 45 Drenth DJ, Winter JB, Veeger NJ *et al.* Minimally invasive coronary artery bypass grafting versus percutaneous transluminal coronary angioplasty with stenting in isolated high-grade stenosis of the proximal left anterior descending coronary artery: six months’ angiographic and clinical follow-up of a prospective randomized study. *J. Thorac. Cardiovasc. Surg.* 124(1), 130–135 (2002).
- 46 Stefanini GG, Kalesan B, Serruys PW *et al.* Long-term clinical outcomes of biodegradable polymer biolimus-eluting stents versus durable polymer sirolimus-eluting stents in patients with coronary artery disease (LEADERS): 4 year follow-up of a randomised non-inferiority trial. *Lancet* 378(9807), 1940–1948 (2011).

- 47 BARI Investigators. The final 10-year follow-up results from the BARI randomized trial. *J. Am. Coll. Cardiol.* 49(15), 1600–1606 (2007).
- 48 Keeley EC, Velez CA, O’Neill WW, Safian RD. Long-term clinical outcome and predictors of major adverse cardiac events after percutaneous interventions on saphenous vein grafts. *J. Am. Coll. Cardiol.* 38(3), 659–665 (2001).
- 49 The effect of aggressive lowering of low-density lipoprotein cholesterol levels and low-dose anticoagulation on obstructive changes in saphenous coronary-artery bypass grafts. The Post Coronary Artery Bypass Graft Trial Investigators. *N. Engl. J. Med.* 336, 153–162 (1997).
- 50 Jensen LO, Thayssen P, Pedersen KE *et al.* Regression of coronary atherosclerosis by simvastatin: a serial intravascular ultrasound study. *Circulation.* 110(3), 265–270 (2004).
- 51 Kimura T, Morimoto T, Nakagawa Y *et al.* Very late stent thrombosis and late target lesion revascularization after sirolimus-eluting stent implantation: five-year outcome of the j-Cypher Registry. *Circulation* 125(4), 584–591 (2012).
- 52 Sousa JE, Costa JR Jr, Abizaid A. 10-year follow-up of the first Cypher stent implanted in human: an invasive evaluation with angiography, intravascular ultrasound, and optical coherence tomography. *JACC Cardiovasc. Interv.* 3(5), 556–558 (2010).
- 53 Jensen LO, Thayssen P, Hansen HS *et al.* Randomized comparison of everolimus-eluting and sirolimus-eluting stents in patients treated with percutaneous coronary intervention: the Scandinavian Organization for Randomized Trials with Clinical Outcome IV (SORT OUT IV). *Circulation* 125(10), 1246–1255 (2012).
- 54 Capodanno D, Tamburino C. Unraveling the EXCEL: promises and challenges of the next trial of left main percutaneous coronary intervention. *Int. J. Cardiol.* 156(1), 1–3 (2012).
- 55 Lagerqvist B, James SK, Stenestrand U, Lindback J, Nilsson T, Wallentin L. Long-term outcomes with drug-eluting stents versus bare-metal stents in Sweden. *N. Engl. J. Med.* 356(10), 1009–1019 (2007).
- 56 Taggart DP, Altman DG, Gray AM *et al.* Randomized trial to compare bilateral vs. single internal mammary coronary artery bypass grafting: 1-year results of the Arterial Revascularisation Trial (ART). *Eur. Heart J.* 31(20), 2470–2481 (2010).
- 57 Buxton BF, Ruengsakulrach P, Fuller J, Rosalion A, Reid CM, Tatoulis J. The right internal thoracic artery graft – benefits of grafting the left coronary system and native vessels with a high grade stenosis. *Eur. J. Cardiothorac. Surg.* 18(3), 255–261 (2000).
- 58 Ioannidis JP, Galanos O, Katritsis D *et al.* Early mortality and morbidity of bilateral versus single internal thoracic artery revascularization: propensity and risk modeling. *J. Am. Coll. Cardiol.* 37(2), 521–528 (2001).
- 59 Catarino PA, Black E, Taggart DP. Why do UK cardiac surgeons not perform their first choice operation for coronary artery bypass graft? *Heart* 88(6), 643–644 (2002).
- 60 Acar C, Ramsheyi A, Pagny JY *et al.* The radial artery for coronary artery bypass grafting: clinical and angiographic results at five years. *J. Thorac. Cardiovasc. Surg.* 116(6), 981–989 (1998).
- 61 Glineur D, D’hoore W, El Khoury G *et al.* Angiographic predictors of 6-month patency of bypass grafts implanted to the right coronary artery a prospective randomized comparison of gastroepiploic artery and saphenous vein grafts. *J. Am. Coll. Cardiol.* 51(2), 120–125 (2008).
- 62 Moran SV, Baeza R, Guarda E *et al.* Predictors of radial artery patency for coronary bypass operations. *Ann. Thorac. Surg.* 72(5), 1552–1556 (2001).
- 63 Suma H, Isomura T, Horii T, Sato T. Late angiographic result of using the right gastroepiploic artery as a graft. *J. Thorac. Cardiovasc. Surg.* 120(3), 496–498 (2000).
- 64 Angelini GD, Wilde P, Salerno TA, Bosco G, Calafiore AM. Integrated left small thoracotomy and angioplasty for multivessel coronary artery revascularisation. *Lancet* 347(9003), 757–758 (1996).
- 65 Repossini A, Moriggia S, Cianci V *et al.* The LAST operation is safe and effective: MIDCABG clinical and angiographic evaluation. *Ann. Thorac. Surg.* 70(1), 74–78 (2000).
- 66 Bonaros N, Schachner T, Lehr E *et al.* Five hundred cases of robotic totally endoscopic coronary artery bypass grafting: predictors of success and safety. *Ann. Thorac. Surg.* 95(3), 803–812 (2013).
- 67 Lee JD, Bonaros N, Hong PT *et al.* Factors influencing hospital length of stay after robotic totally endoscopic coronary artery bypass grafting. *Ann. Thorac. Surg.* 95(3), 813–818 (2013).
- 68 Trehan N, Malhotra R, Mishra Y, Shrivastava S, Kohli V, Mehta Y. Comparison of ministernotomy with minithoracotomy regarding postoperative pain and internal mammary artery characteristics. *Heart Surg. Forum* 3(4), 300–306 (2000).
- 69 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.* 25(5), 460–468 (2012).
- 70 de Cannière D, Jansens JL, Goldschmidt-Clermont P, Barvais L, Decroly P, Stoupe E. Combination of minimally invasive coronary bypass and percutaneous transluminal coronary angioplasty in the treatment of double-vessel coronary disease: two-year follow-up of a new hybrid procedure compared with ‘on-pump’ double bypass grafting. *Am. Heart J.* 142(4), 563–570 (2001).
- 71 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.* 92(5), 1695–1701 (2011).
- 72 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.* 92(6), 2155–2160 (2011).
- 73 Hu S, Li Q, Gao P *et al.* Simultaneous hybrid revascularization versus off-pump coronary artery bypass for multivessel coronary artery disease. *Ann. Thorac. Surg.* 91(2), 432–438 (2011).
- 74 Leacche M, Byrne JG, Solenkova NS *et al.* Comparison of 30-day outcomes of coronary artery bypass grafting surgery versus hybrid coronary revascularization stratified by SYNTAX and euroSCORE. *J. Thorac. Cardiovasc. Surg.* 145(4), 1004–1012 (2013).
- 75 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.* 155(4), 661–667 (2008).
- 76 Shen L, Hu S, Wang H *et al.* One-Stop Hybrid coronary revascularization versus coronary artery bypass graft and percutaneous coronary intervention for the treatment of multivessel coronary artery disease: three-year follow-up results from a single institution. *J. Am. Coll. Cardiol.* 61(25), 2525–2533 (2013).
- ■ **Nonrandomized comparison of hybrid coronary revascularization, coronary bypass operation and percutaneous coronary intervention.**
- 77 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)* 4(6), 299–306 (2009).
- 78 Patel MR, Dehmer GJ, Hirshfeld JW *et al.* ACCF/SCAI/STS/AATS/AHA/ASNC/

HFSA/SCCT 2012 appropriate use criteria for coronary revascularization focused update: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, American Society of Nuclear Cardiology, and the Society of Cardiovascular Computed

Tomography. *J. Thorac. Cardiovasc. Surg.* 143(4), 780–803 (2012).

- 79 Holmes DR Jr, Rich JB, Zoghbi WA, Mack MJ. The heart team of cardiovascular care. *J. Am. Coll. Cardiol.* 61(9), 903–907 (2013).
- **Description of the Heart Team approach.**
- 80 Repossini A, Tespili M, Saino A *et al.* Hybrid revascularization in multivessel coronary artery disease. *Eur. J. Cardiothorac. Surg.*

doi:10.1093/ejcts/ezt016 (2013) (Epub ahead of print).

- **Registry of 166 patients treated with an intention-to-treat hybrid coronary revascularization strategy.**
- 81 Popma JJ, Nathan S, Hagberg RC, Khabbaz KR. Hybrid myocardial revascularization: an integrated approach to coronary revascularization. *Catheter Cardiovasc. Interv.* 1(75 Suppl. 1), S28–S34 (2010).