2772-9931 293
https://doi.org/10.1016/j.atssr.2022.12.003

Coronary: Short Report

Staged Hybrid Coronary Revascularization in Acute Coronary Syndrome

Michele Rossi, MD, PhD,[1] Vincenzo Calabrese, MD,[2] Giovanni Tripepi, MD,[3] Gerlando Mallia, MD,[1] Frank Benedetto, MD,[4] and Pasquale Fratto, MD[1]

ABSTRACT

BACKGROUND In acute coronary syndrome (ACS) with non-ST elevation myocardial infarction, there is a subgroup of patients who are difficult to treat; these are patients with a complex left anterior descending artery (LAD) lesion or a non-LAD culprit lesion but who are not suitable for standard coronary artery bypass grafting (CABG). Staged hybrid coronary revascularization (HCR), combining primary percutaneous coronary intervention on the non-LAD culprit lesion with CABG, represents an attractive solution.

METHODS We conducted a retrospective observational study to compare effectiveness and safety of HCR vs CABG alone. From December 6, 2016, to December 21, 2021, at our institution, 339 patients underwent urgent CABG with or without previous primary percutaneous coronary intervention; 65 received HCR (study group) and 274 received CABG alone (control group). Primary outcomes were major adverse cardiac and cerebrovascular events at 30 days and at long-term follow-up. Secondary outcomes were in-hospital postoperative complications.

RESULTS Significant preoperative differences were detected in the mean EuroSCORE II: 3.4 (1.5-7.8) in HCR vs 2.5 (1.1-4.5) in CABG ($P < .05$). Patients in the CABG group needed more blood transfusions than patients in the HCR group ($P = .004$). Conversely, no other significant differences were detected for in-hospital postoperative complications. Survival analysis did not show significant differences between HCR and CABG, either to 30 days (hazard ratio, 0.51 [95% CI, 0.03-4.04]; $P = .52$) or to longer follow-up (maximum 5 years; hazard ratio, 0.40 [95% CI, 0.09-1.68]; $P = .21$).

CONCLUSIONS Our data support the safety and effectiveness of staged HCR in the scenario of ACS.

(Ann Thorac Surg Short Reports 2023;1:293-297)

In the setting of acute coronary syndrome (ACS) with non-ST elevation myocardial infarction (NSTEMI) and angiographic evidence of complex multivessel coronary disease, there is a subgroup of patients who are difficult to treat. In these patients, the indication for standard surgical coronary artery bypass grafting (CABG) is jeopardized by severe preexisting comorbidities, lack of suitable graft conduits, calcified aorta, tortuous vessels, or chronic total occlusion of the distal left main coronary artery. In these cases, if there is coexistence of a graftable left internal mammary artery (LIMA)-left anterior descending artery (LAD) with a

IN SHORT

- This retrospective observational study was conducted to compare staged hybrid coronary revascularization (HCR) with coronary artery bypass grafting alone in acute coronary syndrome.
- Survival analysis did not show significant differences between HCR and coronary artery bypass grafting, either to 30 days (hazard ratio, 0.51 [95% CI, 0.03-4.04]; $P = .52$) or to follow-up (maximum 5 years; hazard ratio, 0.40 [95% CI, 0.09-1.68]; $P = .21$).
- Our data support the safety and effectiveness of staged HCR in acute coronary syndrome.

Accepted for publication Dec 5, 2022.

[1]Department of Cardiac Surgery, Heart Center, Grande Ospedale Metropolitano "Bianchi-Melacrino-Morelli," Reggio Calabria, Italy; [2]Unit of Nephrology and Dialysis, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy; [3]Department of Medical Statistics, Centro Nazionale delle Ricerche (C.N.R), Reggio Calabria, Italy; and [4]Department of Cardiology, Heart Center, Grande Ospedale Metropolitano "Bianchi-Melacrino-Morelli," Reggio Calabria, Italy

Address correspondence to Dr Rossi, Department of Cardiac Surgery, Heart Center, Grande Ospedale Metropolitano "Bianchi-Melacrino-Morelli," Via Giuseppe Melacrino 21, 89124 Reggio Calabria, Italy; email: michele.r@libero.it.

Ann Thorac Surg Short Reports
2023;1:293-297

Abbreviations and Acronyms

ACS = acute coronary syndrome
CABG = coronary artery bypass grafting
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
NSTEMI = non-ST elevation myocardial infarction
PCI = percutaneous coronary intervention

non-LAD culprit lesion, staged hybrid coronary revascularization (HCR) is an attractive method to achieve optimal myocardial revascularization.[1] Staged HCR, in our practice, consists of primary percutaneous coronary intervention (PCI) with a drug-eluting stent (DES) on the non-LAD culprit lesion, followed by delayed surgical CABG at a set time interval (10-14 days after) but during the same hospital admission because of the severity of the LAD disease that precludes patients from discharge. This strategy attains immediate clinical stability by primary PCI together with the mortality benefit and higher patency rates of having the LIMA grafted onto the LAD.[2] Although this practice is not new,[3-6] little is known about its safety and efficacy for use in ACS, particularly regarding the risk of early coronary stent thrombosis because of early surgical procedure (10- to 14-day time gap) or excessive postoperative bleeding due to dual antiplatelet therapy. We conducted a retrospective observational study to evaluate safety and efficacy of staged HCR at the Heart Center of Grande Ospedale Metropolitano "Bianchi-Melacrino-Morelli" di Reggio Calabria, Italy.

PATIENTS AND METHODS

From December 6, 2016, to December 21, 2021, there were 339 patients presenting with NSTEMI and multivessel disease with an indication for urgent revascularization who underwent CABG with or without previous PCI with DES at our center. The 65 patients treated with staged HCR represented the study group; 274 patients underwent CABG alone and represented the control group. In the HCR group, patients with multivessel critical coronary disease received PCI with DES only on the non-LAD culprit lesion; every other coronary target was revascularized by CABG.

HCR SELECTION CRITERIA. For the HCR group (n = 65), the selection criteria were as follows: angiography demonstrating at least 2-vessel coronary disease involving the LAD; treatment with primary PCI with DES on the culprit non-LAD vessel; and surgical CABG performed 10 to 14 days after PCI, always during the same hospital admission. Patients underwent urgent CABG if primary PCI on the non-LAD culprit lesion failed as well as if PCI was not technically feasible owing to complex anatomy or chronic total occlusion; these patients fall in the control group.

PATIENT SELECTION ALGORITHM FOR STAGED HCR. Patients were scheduled for staged HCR when the indication for standard CABG was mainly jeopardized by the presence of at least 1 of the following conditions at the heart team's discretion (n = number of times that condition was identified in a patient; a single patient could have >1 condition met):

- Lack of suitable conduits for surgical graft (n = 37)
- Severely calcified aorta (n = 13)
- Complex LAD lesion or LAD tortuosity that made PCI complex (n = 42)
- Non-LAD lesion amenable to PCI (n = 9)
- Critical LAD lesion that made patients unsuitable for discharge after primary PCI on non-LAD culprit (n = 65)
- Prior sternotomy (n = 4)
- Poor left ventricle function (n = 3)
- Significant noncardiac disease or complex medical history (n = 9)
- Severe extracardiac arteriopathy (n = 11)

DUAL ANTIPLATELET MANAGEMENT

In the Control Group. All 274 CABG patients were taking aspirin; 74 of them received dual antiplatelet therapy, that is, with the addition of a second antiplatelet drug (clopidogrel or ticagrelor). Aspirin was restarted 6 hours after surgery if bleeding was <100 mL/h in the last 2 consecutive hours.

In the Study Group. All 65 HCR patients were taking oral aspirin. A second oral antiplatelet drug (clopidogrel or ticagrelor) was exchanged through a specific protocol approved by the hospital board and ethical committee to intravenous tirofiban infusion as a bridge to cover major surgical procedure. Patients signed an ad hoc informed consent form. Five days before scheduled CABG operation, oral clopidogrel or ticagrelor was stopped and aspirin alone was continued. Forty-eight hours later, intravenous tirofiban infusion was started, with a fast loading dose and a maintenance one, as in the ACS protocol, according to the patient's body weight and serum creatinine concentration. On the day of surgery, the infusion was stopped 4 hours (or 6 hours if creatinine concentration was >2.0 mg/dL) before. Tirofiban infusion was restarted in the intensive care unit 6 hours after arrival together with aspirin if the bleeding was <100 mL/h in the last 2 consecutive hours. Tirofiban infusion was stopped, usually, on the morning of the first postoperative day, when the patient was extubated and a second antiplatelet was restarted at normal dose.

PRIMARY OUTCOMES. The primary outcomes were major adverse cardiac and cerebrovascular events (MACCE) at

TABLE 1 Demographic Characteristics of Patients

Characteristic	HCR (n = 65)	CABG (n = 274)	*P* Value
Age, y	67 ± 9	65 ± 9	.18
Male	54	222	.70
Body mass index, kg/m^2	27.5 ± 3.8	27.3 ± 4.1	.67
EuroSCORE II, mean value	3.4	2.5	**.02**
NYHA class			.32
0	2	7	
I	3	31	
II	35	118	
III	24	107	
IV	1	11	
CCS class			.41
0	3	6	
I	1	8	
II	12	42	
III	39	151	
IV	10	67	
Creatinine mean baseline value, mg/dL	0.90	0.90	.78
Creatinine level >2.0 mg/dL	1	9	.69
Dialysis	0	10	.22
Previous stroke	3	27	.18
Diabetes on insulin	31	136	.78
Hypertension	60	259	.56
PVD	11	64	.26
Preoperative IABP	18	94	.31
Previous PCI	65	69	**<.001**
EF, %, mean	55	50	.15
EF <30%	3	12	1.00

Boldface *P* values represent statistical significance. CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; EF, ejection fraction; EuroSCORE, European System for Cardiac Operative Risk Evaluation; HCR, hybrid coronary revascularization; IABP, intra-aortic balloon pump; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease.

TABLE 2 Surgical Data

Variable	HCR (n = 65)	CABG (n = 274)	*P* Value
No. of grafts			
1	11	15	**.006**
2	27	102	
3/+	27	157	
Graft type			
LIMA to LAD	65	274	1.00
SVG to non-LAD	52	256	**.001**
Cardiopulmonary bypass	80% (52)	96.4% (264)	**.005**
Off pump	20% (13)	3.6% (10)	**.005**

Boldface *P* values represent statistical significance. CABG, coronary artery bypass grafting; HCR, hybrid coronary revascularization; LAD, left anterior descending artery; LIMA, left internal mammary artery; SVG, saphenous vein graft.

30 days and at long-term follow-up (minimum, 6 months; maximum, 5 years; last follow-up, April 2022). All patients received a first visit in person at 4 weeks after the operation, followed by telephone interview with an ad hoc prefilled form.

SECONDARY OUTCOMES. Secondary outcomes measured during the in-hospital stay included blood transfusion, acute renal injury, dialysis or continuous venovenous hemofiltration, deep sternal wound infection, prolonged mechanical ventilation (>72 hours), and intensive care unit length of stay.

STATISTICAL ANALYSIS. The data set was collected prospectively and extracted by the local cardiac surgery database. Categorical variables were expressed as frequencies and percentages; continuous variables were reported as medians and interquartile ranges because they were not normally distributed (Kolmogorov-Smirnov test for normal distribution). Student *t*-test and Pearson χ^2 test were performed to analyze the differences between the 2 groups for continuous or categorical variables, respectively. Cox regression analysis was performed to evaluate mortality incidence.

RESULTS

Baseline features are summarized in Table 1. Significant preoperative differences were detected in the mean EuroSCORE II (3.4 [1.5-7.8] in HCR vs 2.5 [1.1- 4.5] in CABG; $P < .05$). Creatinine value and prevalence of creatinine concentration >2 mg/dL were analyzed in patients who did not undergo dialysis. Previous PCI was significantly higher in the CABG group; in fact, in the HCR group, no patient underwent PCI before the hybrid revascularization (staged PCI-CABG). However, even including all HCR patients as previous PCI before surgery (even though it was a part of the same hybrid treatment), the previous PCI rate remains higher in the CABG group ($P < .001$). Table 2 summarizes differences in surgical data between the 2 groups. In detail, the CABG group showed a significantly higher number of grafts performed on the non-LAD target. As expected, surgical procedure was performed more with cardiopulmonary bypass in the CABG group, whereas off-pump surgery prevailed in the HCR group ($P < .005$). In-hospital postoperative complications and MACCE at 30 days are summarized in Table 3. Patients in the CABG group needed more blood transfusion than HCR patients (235 vs 46, respectively; $P = .004$). Length of stay in the intensive care unit did not show any difference. Conversely, no other significant differences were detected for in-hospital postoperative complications or in MACCE at 30 days (Table 3). Survival analysis was performed with the univariate Cox analysis, which did not show significant differences between the 2 groups either to 30 days (hazard ratio, 0.51 [95% CI, 0.03-4.04]; $P = .52$) or to longer follow-up (6 months minimum-maximum 5 years; hazard ratio, 0.40 [95% CI, 0.09-1.68]; $P = .21$; Figure).

Ann Thorac Surg Short Reports
2023;1:293-297

TABLE 3 In-Hospital Postoperative Complications and MACCE at 30 Days

Complications	HCR (n = 65), % (No.)	CABG (n = 274), % (No.)	*P* Value
Atrial fibrillation	30.7 (20)	29.6 (81)	.85
Prolonged ventilation (>72 h)	9.2 (6)	11.7 (32)	.57
Acute renal injury (creatinine level >2 mg/dL)	9.2 (6)	13.1 (36)	.35
Continuous venovenous hemofiltration	4.6 (3)	9.1 (25)	.24
Deep sternal wound infection	3 (2)	5.1 (14)	.75
Blood transfusion	70.7 (46)	85.7 (235)	**.004**
ICU LOS, d, mean	3	3	.22
Death	1.53 (1)	3.64 (10)	.7
Stroke	1.53 (1)	2.91 (8)	.53
Repeated PCI	0	2.55 (7)	.35

Boldface *P* values represent statistical significance. CABG, coronary artery bypass grafting; HCR, hybrid coronary revascularization; ICU, intensive care unit; LOS, length of stay; MACCE, major adverse cardiac and cerebrovascular events; PCI, percutaneous coronary intervention.

COMMENT

Hybrid revascularization has been used as an alternative strategy of coronary revascularization since 1996.[3] Meta-analyses, small randomized controlled trials, and observational studies have found similar rates of death, myocardial infarction, stroke, and repeated revascularization compared with standard CABG.[1-6] When PCI is done first, as in our study, it has the advantage of being able to address any stent complications with CABG in addition to managing ACS with primary PCI on non-LAD lesions. The disadvantages are the risk of stent thrombosis due to the hypercoagulative state after major surgical procedure; the risk of excessive postoperative bleeding due to dual antiplatelet therapy; and that the LIMA graft cannot be routinely imaged to assess its patency by an interventional cardiologist at the time of the PCI, even though this last disadvantage might be mitigated by intraoperative graft flow assessment, such as by transit-time flow measurement, as routinely done at our institution. HCR, because of logistic and training time, is not usually considered in ACS. There is solid evidence that PCI with DES cannot be compared with the excellent long-term graft patency rate of the LIMA-LAD graft,[7] and the "gold standard" for multivessel coronary disease remains multiarterial coronary grafts.[2] Nevertheless, in several countries, including the United States, only 10% of CABG procedures are done with >2 arterial grafts and <1% with 3 grafts.[8] We found similar rates of multiarterial graft use in our center. Comparison against venous graft PCI with DES has shown lower rates of failure and restenosis.[9] In this context, the HCR strategy appears suitable for both surgeons and interventional cardiologists. In our center, we support the hybrid revascularization strategy in elective cases, thinking

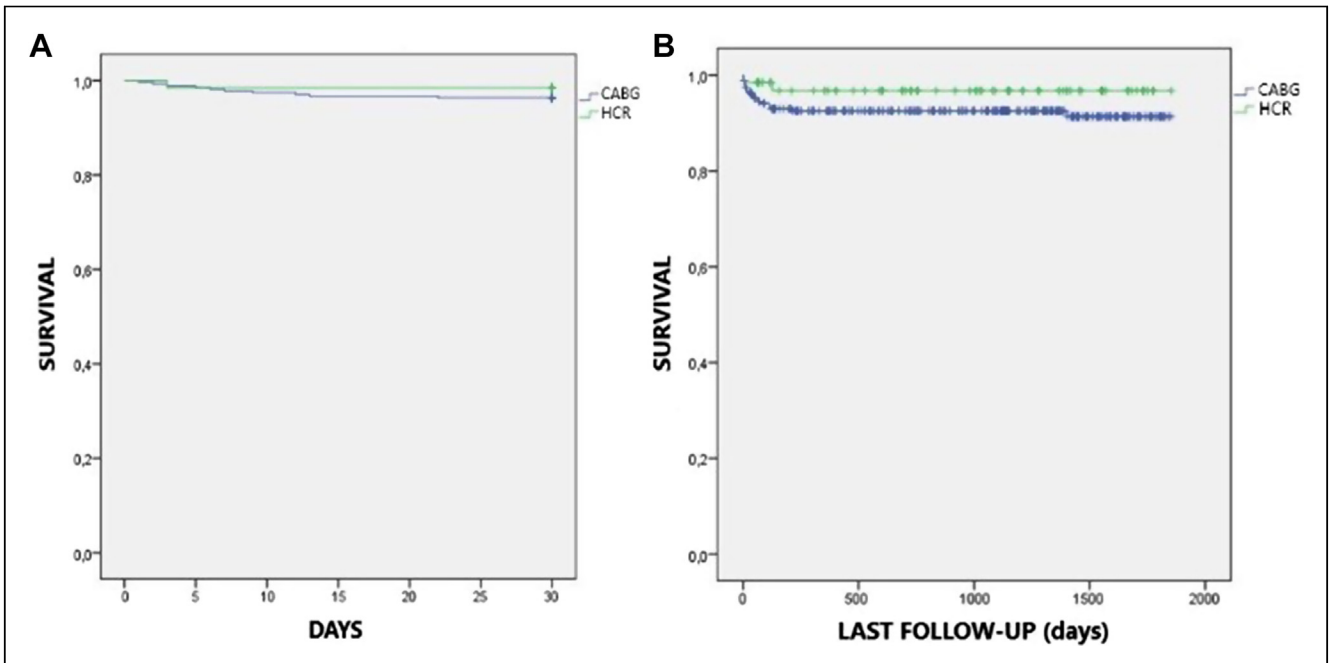

FIGURE Kaplan-Meier curve showing postoperative survival. (A) At 30 days. (B) At follow-up (minimum, 6 months; maximum, 5 years). (CABG, coronary artery bypass grafting [blue line]; HCR, hybrid coronary revascularization [green line].)

that given the long-term benefit of grafting the LIMA onto the LAD combined with the less invasiveness of PCI, DES on the non-LAD target is the perfect marriage between safety, efficacy, and patient demand for less invasive treatment. Supported by our cardiologist, we started to apply the hybrid approach, with bedside multidisciplinary discussion, also in difficult ACS/NSTEMI cases. In our HCR group, patients had a critical LAD lesion that precluded their discharge before treatment was completed. Our data showed that HCR, in the specific subset of patients described, is feasible and safe with no difference in reopening, excessive bleeding, or acute stent thrombosis. Actually, the similar rates of mortality or MACCE at 30 days or long-term follow-up support the benefit of the staged HCR approach, given that the HCR group started with higher mean EuroSCORE II (3.4 vs 2.5 in CABG; $P = .02$). Interestingly, despite the continuous infusion of tirofiban intravenously in HCR, it was the CABG group that had the higher number of blood transfusions ($P = .004$).

This is a retrospective single-center observational study with the limitations of this kind of analysis. Given the specific subgroup analyzed, we believe that more statistically powerful studies are difficult to run. A clear cost analysis between the 2 strategies is missing. However, despite the small sample size of the study, we believe that our results encourage the use of HCR in ACS.

FUNDING SOURCES

The authors have no funding sources to disclose.

DISCLOSURES

The authors have no conflicts of interest to disclose.

REFERENCES

1. Lowenstern A, Wu J, Bradley SM, et al. Current landscape of hybrid revascularization: a report from the NCDR CathPCI registry. *Am Heart J*. 2019;215:167-177.

2. Royse AG, Brennan AP, Ou-Young J, et al. 21-year survival of left internal mammary artery–radial artery–Y graft. *J Am Coll Cardiol*. 2018;72:1332-1340.

3. Angelini GD, Wilde P, Salerno TA, et al. Integrated left small thoracotomy and angioplasty for multivessel coronary artery revascularisation. *Lancet*. 1996;347:757-758.

4. Zhu P, Zhou P, Sun Y, et al. Hybrid coronary revascularization versus coronary artery bypass grafting for multivessel coronary artery disease: systematic review and meta-analysis. *Cardiothorac Surg*. 2015;10:63.

5. 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*. Published online January 3, 2020. https://doi.org/10.1155/2020/5458064

6. 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.

7. Kitahara H, Nisivaco S, Balkhy HH. Graft patency after robotically assisted coronary artery bypass surgery. *Innovations (Phila)*. 2019;14:117-123.

8. Schwann TA, Tatoulis J, Puskas J, et al. Worldwide trends in multiarterial coronary artery bypass grafting surgery 2004-2014: a tale of 2 continents. *Semin Thorac Cardiovasc Surg*. 2017;29:273-280.

9. 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*. 2009;360:961-972.