

Hybrid coronary revascularization in multivessel disease: Long-term clinical outcomes of a prospective randomized study

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INTRODUCTION

Conventional coronary artery bypass grafting (CABG) remains an evidence-based treatment option for patients with severe multivessel coronary artery disease (MVCAD) [1, 2].

The recently published guidelines also highlight hybrid coronary revascularization (HCR) as a promising management strategy [2].

In the POL-MIDES (HYBRID) (Safety and Efficacy Study of Hybrid Revascularization in Multivessel Coronary Artery Disease), we compared HCR with CABG in randomly assigned patients with MVCAD and demonstrated that HCR is feasible and safe, with similar 12-month and 5-year mortality and major adverse cardiac events rates [3, 4]. Similar findings were recently published, however with short-term follow-up [5]. Accordingly, this study aimed to evaluate long-term clinical outcomes for the patient population from the HYBRID study.

METHODS

The HYBRID study (ClinicalTrials.gov number NCT01035567) was a prospective, single-center, randomized, open-label, parallel, pilot study. The study protocol was approved by the local ethics committee and complied with the Declaration of Helsinki. Written informed consent was obtained from all study participants.

In summary, 200 consecutive patients with stable coronary disease and angiographically confirmed multivessel disease (MVD) involving the left anterior descending artery

and a critical (>70%) lesion in at least one (apart from the left anterior descending artery) major epicardial vessel referred for conventional surgical revascularization were randomly assigned to undergo CABG or HCR.

The primary endpoint of the study included the occurrence of all-cause long-term mortality. An occurrence of major adverse cardiac and cerebrovascular events such as all-cause death, myocardial infarction (MI), stroke, and repeat revascularization (percutaneous coronary intervention and/or coronary artery bypass graft) in 10 years after randomization was also assessed. The follow-up data for each deceased patient with exact dates of death, MI, stroke or repeat revascularization were obtained from the official National Health Fund records. The vital status was available for all of the patients enrolled in the HYBRID study. The follow-up status regarding the occurrence of MI, stroke, and repeat revascularization was available for 95.1% and 95.9% (for CABG and HCR, respectively) of all included patients. The rationale, and design of the HYBRID trial have been published previously [6].

Statistical analysis

The continuous variables are presented as the means, standard deviations, or medians and interquartile ranges. The categorical variables are presented as percentages. To test for differences between CABG and HCR groups, Student's t-test and the chi-square test were used, respectively. All-cause mortality events and combined follow-up endpoint were ana-

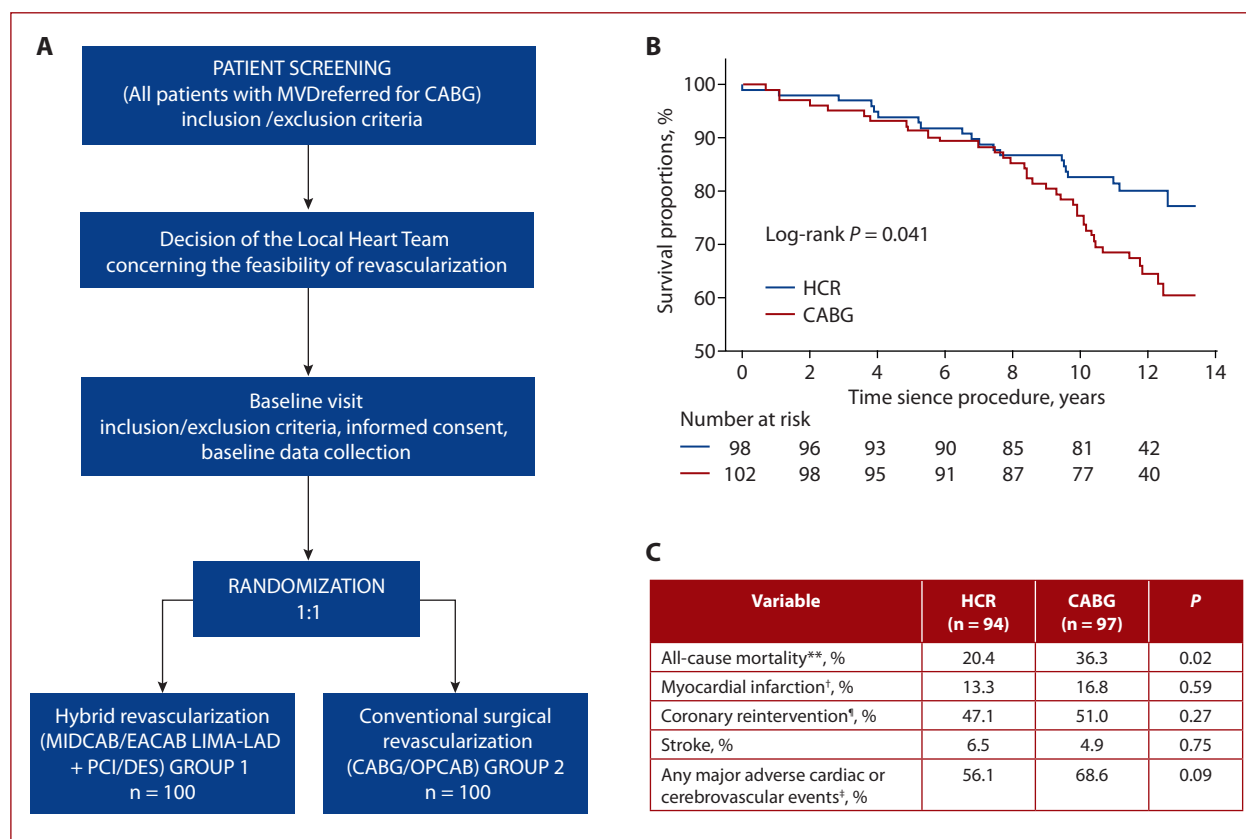


Figure 1. A. Study flowchart. B. Kaplan–Meier estimates for all-cause mortality. C. Long-term major adverse cardiac and cerebrovascular events in the studied groups. Graphical presentation of the major findings of our study

lyzed with the Kaplan–Meier method and log-rank test. All analyses were based on the intention-to-treat principle. A 2-sided P -value of less than 0.05 was considered statistically significant. Statistical tests were performed with STATISTICA 10PL software (StatSoft, Inc.).

RESULTS AND DISCUSSION

From November 2009 to July 2012 200 patients with confirmed MVD and referred for conventional CABG were randomized to HCR ($n = 98$) or CABG ($n = 102$) groups. The median follow-up was 12.21 years (range 10.72–13.42 years) (Figure 1A). Nine patients (4 in HCR and 5 in CABG group) were lost to the follow-up. Finally, 191 patients (94 in the HCR group and 97 in the CABG group) were included in the analysis. No sex-based differences were present.

All-cause mortality available for the entire cohort at long-term follow-up was significantly lower in patients after hybrid revascularization as compared to patients after CABG (20.4% vs. 36.3%; $P = 0.02$, respectively) (Figure 1B). No significant differences in the rates of myocardial infarction (13.3% vs. 16.7%; $P = 0.63$), repeat revascularization (45.9% vs. 51.0%; $P = 0.57$), stroke (5.9% vs. 7.1%; $P = 0.72$), and major adverse cardiac and cerebrovascular events (56.1% vs. 68.6%; $P = 0.09$), for the HCR and CABG group, respectively, were observed (Figure 1C–F).

This study is the first and only RCT reporting long-term survival after HCR as compared to CABG. In this trial, we

showed significantly lower all-cause mortality in selected patients with MVCAD after HCR. Accordingly, this study provides unique long-term insights into survival after HCR versus CABG by extending follow-up to a median of 12.2 years, which could provide an important insight into the decision-making process to determine the optimal revascularization strategy for MVCAD patients. Moreover, the primary endpoint of all-cause death focused on the most robust endpoint that is clinically relevant for both patients and physicians. Last but not least, the follow-up was complete for all randomly assigned patients in the HYBRID study.

RCT, if correctly carried out, provide unique data and evidence and remain the gold standard, confirming the efficacy and feasibility of clinical interventions. However, the follow-up periods may be limited due to economic and logistical issues. The main reason for extending randomized trials is to estimate the potential long-term benefits of an intervention. Following a scoping review of RCTs performed by Fitzpatrick et al. [7], in nearly 20% of RCTs, statistically significant long-term benefits regarding hard-point events were seen only in the trial extension phase.

This study is a follow-up to a previously published feasibility study. The HYBRID study was not powered to detect differences in all-cause mortality between compared CABG and hybrid coronary revascularization treatment options. Because of the limited number of patients at risk

at maximum followup, these results should be interpreted as hypothesis-generating and could be used for sample size calculation in randomized controlled trials comparing HCR with CABG. Therefore, the discussion about the statistically insignificant difference that favors a hybrid approach may be speculative and misleading and should be interpreted with caution. However, one of the strengths of the present study is that all-cause mortality assessment was performed *via* a central, national database, which allowed a robust and complete capture of all deaths.

Our study showed a high proportion of patients with repeated coronary interventions. This can be explained by the fact that we have only general data on recurrent coronary interventions (any PCI and/or any CABG), without related details, such as target lesion, target vessel, or *de novo* lesion reintervention. However, the definition of endpoints in different studies, such as coronary reintervention, varied to some degree, which may have weakened the results of our analysis.

Our study shows that HCR, as compared to conventional CABG, was associated with higher long-term survival. This warrants further validation in multi-center, adequately powered randomized studies to definitively assess the absolute benefits and risks of HCR. But even so, before the outcomes of such trials are widely available, our results might already provide an important indication for Heart Team evaluating MVDCAD patients and consider HCR a potential course of treatment.

Article information

Conflict of interest: None declared.

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