# Outcomes of coronary revascularization vs. optimal medical therapy alone for ischemic left ventricular dysfunction: A meta-analysis of randomized controlled trials

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## INTRODUCTION

Coronary artery disease (CAD) is the most frequent cause of heart failure with reduced ejection fraction worldwide. Observations that a large proportion of patients with ischemic heart failure have areas of dysfunctional-yet-viable myocardium have led to the hypothesis that coronary revascularization might improve left ventricular function and outcomes in this population [1].

Randomized controlled trials (RCTs) published in recent years did not demonstrate a significant superiority of routine coronary revascularization in patients with stable CAD over optimal medical therapy (OMT) [2]. However, patients with left ventricular systolic dysfunction (LVSD), who might potentially benefit the most from revascularization, were mainly excluded from these trials. Only a few RCTs compared coronary revascularization with OMT alone in patients with severe LVSD.

To the best of our knowledge, no meta-analysis has summarized the results of these trials. Therefore, we aimed to perform a meta-analysis comparing outcomes following coronary revascularization (both percutaneous and surgical) with OMT alone in patients with LVSD based on the latest available evidence from RCTs.

## METHODS

This systematic review was prospectively registered in the PROSPERO (International Prospective Register of Systematic Reviews) database (CRD42022379549) and conformed to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [3].

PubMed and Scopus were systematically searched for original articles published in English before December 8, 2022. The search strategy is presented in Supplementary material, *Table S1*. Articles were eligible for inclusion in this meta-analysis if they presented results of RCTs comparing coronary revascularization (coronary bypass surgery [CABG] or percutaneous coronary intervention [PCI]) with OMT alone in patients with severe LVSD (left ventricular ejection fraction of 35% or less). If multiple reports from the same RCTs were available, papers presenting the longest follow-up were included in the meta-analysis.

The following data were extracted from eligible reports: clinical trial name, publication year, sample size, inclusion and exclusion criteria, mode of revascularization, data on the baseline and angiographic characteristics, event rates, and hazard ratios (HRs) with corresponding 95% confidence intervals (CI).

Subsequently, the included studies were assessed for bias using the Cochrane risk-of-bias tool for randomized trials version 2 (RoB 2). Any discrepancies between the two co-authors who independently searched for eligible papers, extracted data, and assessed data for bias were resolved by consensus.

The primary outcome of interest was cardiovascular death. Secondary outcomes included death from any cause and death from any cause or hospitalization for heart failure. All analyzed endpoints were defined according to the study protocols.

### *Statistical analysis*

Random effects inverse variance meta-analysis was conducted based on estimates (i.e., log HR) and standard errors. Log HR and standard errors were calculated from HRs, and the corresponding 95% CI extracted from analyzed reports. If HRs and 95% CIs were unavailable, estimates and standard errors were calculated using reconstructed individual patient data from Kaplan-Meier survival curves using the freely available online tool: *IPDfromKM Shiny app* (https://www.trialdesign.org/one-page-shell.html#IPDfromKM). Heterogeneity was tested using Cochrane Q statistics. Publication bias was not assessed due to the small number of included studies. All statistical analyses were performed in *R* version 4.2.0 (R Core Team. R: A Language and Environment for Statistical Computing, https://www.r-project.org) with package *meta*. Relative treatment effects were presented as HR with 95% CI. A two-tailed *P*-value of <0.05 was considered significant.

## RESULTS AND DISCUSSION

An electronic search revealed 4 762 records, and after removing duplicates, the titles and abstracts of 3 499 records were screened for eligibility. Nineteen records were selected for full-text assessment, and 3 RCTs that enrolled 2 050 patients followed up for a weighted mean of 7.3 years fulfilled the inclusion criteria of this meta-analysis [4–6]. The PRISMA flowchart is presented in Supplementary material, *Figure S1*, and details on the included studies are presented in Supplementary material, *Table S2*. The risk of bias was low in all included studies. The baseline characteristics of patients included in these trials are summarized in Supplementary material, *Table S3*.

Two of the three included reports provided data on the primary endpoint of cardiovascular death. Coronary revascularization was associated with reduced risk of primary endpoint compared to OMT alone (HR, 0.81; 95% CI, 0.70–0.94; *P* <0.01); (Figure 1A). There was also a trend toward a lower risk of death from any cause in patients who underwent revascularization (HR, 0.88; 95% CI, 0.78–1.01; *P* = 0.06); (Figure 1B). However, there was no difference between treatment strategies regarding the composite endpoint of death from any cause or hospitalization for heart failure (Figure 1C). Event rates according to study groups are presented in Supplementary material, *Table S4*. No significant statistical heterogeneity was identified regarding any of the analyzed outcomes.

The main finding of our meta-analysis is that coronary revascularization might be associated with improved survival, mainly driven by reduced cardiovascular mortality in patients with severe LVSD. This finding is in line with the data from observational studies, which were summarized in the recent meta-analysis [1]. However, some important limitations should be acknowledged. First, the results of only three RCTs comparing revascularization with OMT have been published to date. The STICHES trial, an extended follow-up study of the STICH trial, which had the most significant impact on the pooled estimates for all analyzed endpoints in this meta-analysis, evaluated only surgical revascularization. This trial demonstrated a reduced mortality rate in revascularized patients at ten years of follow-up. The REVIVED-BCIS2 trial, which compared OMT to PCI, demonstrated similar efficacy in terms of the primary endpoint of death from any cause or hospitalization for heart failure. Only the HEART trial studied both modes of revascularization in the invasive strategy arm but enrolled only 138 of the planned 800 patients because of the withdrawal of funding.

An open question remains whether the benefit of both modes of revascularization in patients with LVSD is similar. Contemporary RCTs have shown the superiority of CABG over PCI in patients with higher disease burden and lesion complexity, which is often the case in patients with ischemic heart failure [7]. However, patients with severe LVSD were underrepresented or excluded from these trials. Because severe LVSD and high comorbidity burden accompanying heart failure strongly increase perioperative risks, the results of these trials should not be translated to patients with severely impaired ventricular function. Unfortunately, no RCTs compared PCI against CABG in this population to date. The only available evidence comes from observational studies, which showed similar all-cause mortality in patients treated with PCI using drug-eluting stents in comparison to CABG [1].

Second, most of the analyzed patients in this meta-analysis were enrolled in the RCTs over a decade ago. Meanwhile, substantial progress in OMT was made. This might diminish the potential benefits from a revascularization strategy. On the other hand, the outcomes of patients treated invasively, mainly with PCI, improved as well, owing to broader utilization of newer generation stents and physiology- and imaging-guided revascularization [8].

Finally, considering the small number of included RCTs, statistical tools used in meta-analysis might be underpowered to assess between-study heterogeneity. For the same reason, we were unable to perform any meta-regression or subgroup analyses to identify the groups of patients who benefit the most from revascularization.

In conclusion, coronary revascularization in addition to OMT seems to be associated with reduced cardiovascular mortality in patients with severely impaired left ventricular

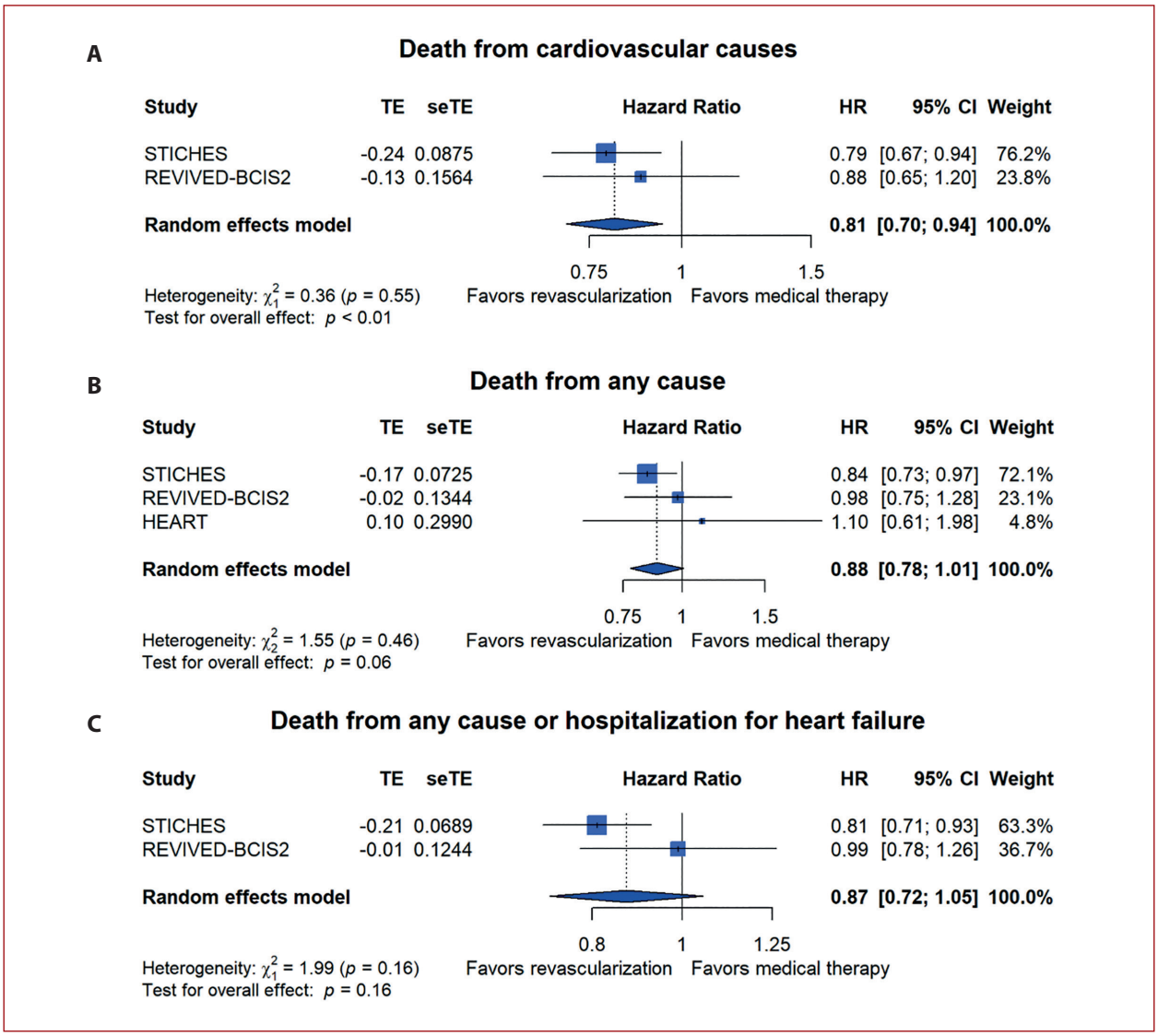


**Figure 1.** Forest plots presenting the meta-analysis results for primary (**A**) and secondary outcomes (**B, C**)

Abbreviations: CI, confidence interval; HEART, Heart Failure Revascularisation Trial; HR, hazard ratio; REVIVED-BCIS2, Revascularization for Ischemic Ventricular Dysfunction Trial; seTE, standard error of treatment estimate; STICHES, Surgical Treatment for Ischemic Heart Failure Extension Study; TE, estimate of treatment effect

function. However, whether this effect is independent of the mode of revascularization remains unclear.

## *Supplementary material*

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

## *Article information*

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