Percutaneous Revascularization for Ischemic Ventricular Dysfunction: Rationale and Design of the REVIVED-BCIS2 Trial

Percutaneous Coronary Intervention for Ischemic Cardiomyopathy

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ABSTRACT

OBJECTIVES Evaluate whether PCI in combination with optimal medical therapy (OMT) will reduce all-cause death and hospitalization for HF compared to a strategy of OMT alone.

BACKGROUND Ischemic cardiomyopathy (ICM) is the most common cause of heart failure (HF) and is associated with significant mortality and morbidity. Surgical revascularization has been shown to improve long-term outcomes in some patients, but surgery itself carries a major early hazard. Percutaneous coronary intervention (PCI) may allow a better balance between risk and benefit.

METHODS REVIVED-BCIS2 is a prospective, multi-center, open-label, randomized controlled trial, funded by the National Institute for Health Research in the United Kingdom. Follow-up will be for at least 2 years from randomization. Secondary outcomes include left ventricular ejection fraction (LVEF), quality of life scores, appropriate implantable cardioverter defibrillator therapy and acute myocardial infarction. Patients with LVEF <35%, extensive coronary disease and demonstrable myocardial viability are eligible for inclusion and those with a myocardial infarction within 4 weeks, decompensated HF or sustained ventricular arrhythmias within 72 h are excluded. A trial of 700 patients has more than 85% power to detect a 30% relative reduction in hazard.

RESULTS A total of 400 patients have been enrolled to date.

CONCLUSIONS International guidelines do not provide firm recommendations on the role of PCI in managing severe ICM, because of a lack of robust evidence. REVIVED-BCIS2 will provide the first randomized data on the efficacy and safety of PCI in ICM and has the potential to inform guidelines pertaining to both revascularization and HF. (Study of Efficacy and Safety of Percutaneous Coronary Intervention to Improve Survival in Heart Failure [REVIVED-BCIS2]; NCT01920048) (REVascularisation for Ischaemic VEntricular Dysfunction; ISRCTN45979711) (J Am Coll Cardiol HF 2018;6:517–26) © 2018 Published by Elsevier on behalf of the American College of Cardiology Foundation.
The prevalence of heart failure (HF) due to left ventricular (LV) systolic dysfunction is increasing (1), and ischemic cardiomyopathy (ICM) accounts for approximately 60% of all cases of HF (2,3). Pathophysiological, ICM encompasses a spectrum of sequelae of coronary disease including myocardial infarction (MI), which leads to irreversible fibrosis, and hibernation, a potentially reversible adaptation to repetitive ischemia, which often co-exist in a given patient and can both lead to adverse remodeling and LV dysfunction. “Hibernation” was a word coined nearly 40 years ago to describe the reversal of remodeling and augmentation of systolic function following surgical coronary artery bypass grafting (CABG), noted in patients with chronic stable angina and severe LV dysfunction (4). Although subsequent observational studies of surgical revascularization appeared to confirm the existence of hibernation (5,6), until recently, this had not been adequately assessed in a randomized study.

The seminal STICH (Surgical Treatment for Ischemic Heart Failure) trial—the only randomized evaluation of CABG for ICM to date—enrolled patients with left ventricular ejection fraction (LVEF) \( \leq 35\% \). At a median of 4.6 years, the primary outcome all-cause mortality was not significantly different between patients treated with optimal medical therapy (OMT) alone compared with those assigned to CABG surgery (41% vs. 36%; hazard ratio [HR]: 0.86; 95% confidence interval [CI]: 0.72 to 1.04; \( p = 0.12 \)) (7). Mortality in the first 30 days was significantly higher in the surgical group (4% vs. 1%; HR: 3.12; 95% CI 1.33 to 7.32; \( p = 0.009 \)). This finding is in keeping with the known association between mortality and LV dysfunction following CABG surgery (8). The early hazard of CABG may have negated the benefits of revascularization, which become gradually manifest in those who survive the complications of surgery. The STICHES (Surgical Treatment for Ischemic Heart Failure Extension Study) reported longer-term mortality data from the STICH trial. At median follow-up of approximately 10 years, 59% of patients assigned to CABG died versus 66% in the medical therapy group (HR: 0.84; 95% CI: 0.73 to 0.97; \( p = 0.02 \)) (9). Death from cardiovascular causes and several pre-specified composite secondary endpoints also occurred less often in the CABG group. The critical balance between safety and efficacy is also borne out when examining the impact of age on treatment effect in STICH. Long-term survival benefit was most apparent in the youngest patients enrolled in the trial (in whom the risks of peri-procedural mortality and morbidity are lowest), and this benefit diminished with increasing age (10).

Given the lower procedural risks associated with percutaneous coronary intervention (PCI), it has the potential to allow the benefits of revascularization to be realized with fewer complications than CABG surgery, but this assertion is yet to be tested in a randomized trial. Table 1 summarizes randomized and observational studies of revascularization versus medical therapy published in the past 15 years and includes the proportion of patients treated with PCI. It should be noted that the risk of longer-term complications, such as restenosis and late stent thrombosis, in this population who tend to have complex coronary disease and multiple comorbidities, is largely unknown. Although numerous comparisons have been made between PCI and CABG in patients with symptomatic coronary disease, most of the large randomized trials excluded patients with impaired LV function. Less than 2% of all patients included in the largest randomized controlled trial comparing PCI with CABG—SYNTAX—had significant LV impairment (EF <30%) at baseline (11). We reported outcomes of PCI in 301 patients with severe ICM (mean EF 24%), showing 30-day, 6-month, and 4-year mortality rates of 1.3%, 6%, and 33%, respectively (12,13). These results appear to compare favorably with the surgical data, but, as these are not matched cohorts, further comparison is not possible. On the other hand, the degree of LV impairment is a known determinant of adverse outcome even in patients undergoing PCI (14); whether this modality of revascularization would offer incremental prognostic benefit—over and above contemporary HF medication and device...