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Impact of Anatomical and Viability-guided Completeness of Revascularization on Clinical Outcomes in Ischemic Cardiomyopathy

Brief Title: Impact of completeness of Revascularization in REVIVED-BCIS2

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Abstract

Background: Complete revascularization of coronary disease has been linked to improved outcomes in patients with preserved left ventricular (LV) function.

Objectives: To identify the impact of complete revascularization in patients with severe LV dysfunction.

Methods: Patients enrolled in the REVIVED-BCIS2 trial were eligible if baseline/procedural angiograms and viability studies were available for analysis by independent core laboratories. Anatomical and viability-guided completeness of revascularization were measured by the coronary and myocardial revascularization indices (RI_{coro} and RI_{myo}) respectively, where RI_{coro}=[change in BCIS Jeopardy Score (BCIS-JS)] / [baseline BCIS-JS] and RI_{myo}=[number of revascularized viable segments] / [number of viable segments supplied by diseased vessels]. The PCI group was classified as having complete or incomplete revascularization by median RI_{coro} and RI_{myo}. The primary outcome was death or hospitalization for heart failure.

Results: Of 700 randomized patients, 670 were included. The baseline BCIS-JS and SYNTAX scores were 8 (6 to 10) and 22 (15 to 29) respectively. In those assigned to PCI, median RI_{coro} and RI_{myo} values were 67% and 85%. Compared to the group assigned to optimal medical therapy alone, there was no difference in the likelihood of the primary outcome in those receiving complete anatomical or viability-guided revascularization (HR 0.90, 95% CI 0.62-1.32 and HR 0.95, 95% CI 0.66-1.35 respectively). A sensitivity analysis by residual SYNTAX score showed no association with outcome.

Conclusions: In patients with severe left ventricular dysfunction, neither complete anatomical nor viability-guided revascularization were associated with improved event-free survival compared to incomplete revascularization or treatment with medical therapy alone.

Condensed Abstract

Completeness of anatomical (RI_{coro}) and viability guided revascularization (RI_{myo}) in REVIVED-BCIS2 were assessed by core laboratory analysis. The median RI_{coro} and RI_{myo} achieved were 67% and 85% respectively. Complete revascularization with PCI, whether anatomical (HR 0.90, 95% CI 0.62-1.32) or viability guided (HR 0.95, 95%CI 0.66-1.35), were not associated with a reduction in the primary outcome of death or hospitalization for heart failure as compared with medical therapy. Our findings do not support pursuing complete revascularization in patients with ischemic cardiomyopathy and stable coronary disease.

Key words: Complete revascularization; heart failure; left ventricular dysfunction; percutaneous coronary intervention; stable coronary artery disease

Abbreviations:

BCIS-JS: British Cardiovascular Intervention Society Jeopardy Score

CABG: Coronary artery bypass grafting

CMR: Cardiovascular magnetic resonance imaging

DSE: Dobutamine stress echocardiography

PCI: Percutaneous coronary intervention

OMT: Optimal medical therapy

RI_{coro}: Coronary revascularization index

RI_{myo}: Myocardial revascularization index

Introduction

Treating as many diseased major coronary arteries as possible is a cornerstone of contemporary revascularization and the perceived ability to achieve this goal often affects the choice of revascularization method, namely percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) [1]. Incomplete revascularization has been associated with an increased incidence of death, myocardial infarction and need for repeat revascularization [2]. However, almost the entire evidence base for targeting complete revascularization has been derived from patients with good left ventricular function. Furthermore, whilst treatment of critical coronary disease can be directly translated to myocardial benefit in patients with preserved left ventricular function, a more nuanced approach needs to be used when evaluating completeness of revascularization in ischemic cardiomyopathy, one that integrates the viability of subtended myocardial territories as well as the severity of coronary disease.

The premise of PCI being beneficial in ischemic cardiomyopathy is based on two key underlying principles. Firstly, that hibernation is an (mal)adaptive state in response to repeated episodes of ischemia. This is designed to preserve myocyte integrity at the expense of contractile function, resulting in viable but dysfunctional myocardium. Secondly, that revascularization may reverse hibernation by relieving supply/demand mismatch, leading to angina relief, recovery in left ventricular function, and improved clinical outcomes [3]. Whether the premise of complete revascularization holds true in this context, remains unknown. This pre-specified analysis of REVIVED-BCIS2 therefore seeks to explore the relationship between the extent of core laboratory-adjudicated anatomical- and viability-guided revascularization and outcomes in ischemic cardiomyopathy.

Methods

The design and primary results of the REVIVED-BCIS2 (Revascularization for Ischemic Ventricular Dysfunction) trial (NCT01920048) have been previously published [4,5]. Briefly, eligible participants with ischemic left ventricular dysfunction (ejection fraction ≤35%), extensive coronary disease denoted by a British Cardiovascular Interventional Society jeopardy score (BCIS-JS) ≥6 and demonstrable viability in ≥4 myocardial segments amenable to revascularization, were randomized 1:1 to a strategy of either PCI + OMT (PCI group) or OMT alone (OMT group) at 40 centers in the UK. Whilst complete anatomical revascularization was not mandated in REVIVED-BCIS2, the protocol recommended revascularization of all major proximal coronary vessels and side branches ≥2.5mm subtending viable myocardium. This included vessels with chronic total occlusion (CTO), when specialist CTO operators anticipated a high likelihood of reopening these vessels successfully [5]. Clinical outcomes were adjudicated by a blinded clinical events committee and left ventricular ejection fraction was independently reported by a core laboratory with readers blinded to treatment assignment, outcome data and temporal sequence of the echocardiograms. The trial protocol was approved by the UK Health Research Authority and all participants provided written informed consent.

Pre-PCI BCIS-JS and SYNTAX scores were ascertained from all participants in whom an angiogram was available for analysis by an independent coronary angiography core laboratory (Golden Jubilee National Hospital, Glasgow). For participants assigned to the PCI group, post-PCI BCIS-JS and residual SYNTAX score (rSS) were also calculated following the final planned PCI procedure as reported by investigators. The core laboratory reported lesion severity by visual assessment, with significance defined at ≥70% luminal stenosis for non-left mainstem stenoses and ≥50% for left mainstem stenoses for calculation of the BCIS-JS [6,7]. Successful revascularization of a vessel was defined as a <30% diameter residual stenosis with normal (TIMI III) flow at the end of PCI. Anatomical completeness of

revascularization was described by the coronary revascularization index (RI_{coro}) calculated as [(Pre-PCI BCIS-JS) – (Post-PCI BCIS-JS)] / [Pre-PCI BCIS-JS] * 100 . A sensitivity analysis was preformed using rSS to define anatomical completeness of revascularization, with rSS dichotomized as less than or equal to 8 or greater than 8 [8]. RI_{coro} was 0 for all participants in the OMT group.

In patients who underwent viability assessment by cardiovascular magnetic resonance imaging (CMR) or dobutamine stress echocardiography (DSE), images were independently analyzed by dedicated core laboratories (CMR core laboratory at King's College London, UK and DSE core laboratory at King's Health Partners, UK) blinded to treatment assignment and outcome data. Myocardial viability was described using the American Heart Association 17 segment model [9]. For the current analysis, a segment was classified as viable if wall motion was normal at rest, or if dysfunctional at rest, when there was <50% transmural late gadolinium scar on CMR or the presence of contractile reserve on DSE. Segments which did not meet these criteria were classified as non-viable.

AHA myocardial segments were co-registered to a coronary artery based on the highest percentage chance of that segment being subtended by the relevant coronary artery [10] (Supplemental Figure 1). The status of each AHA myocardial segment was then classified as being supplied by an artery with significant disease and revascularized (REVASC), supplied by an artery with significant disease but not revascularized (NO REVASC) or not supplied by an artery with significant disease (NO DISEASE). The myocardial revascularization index (RI_{myo}) was calculated as (REVASC/(REVASC+NO REVASC)) * 100, limited to the number of viable myocardial segments (Supplemental Figure 2). Participants assigned to OMT were assumed to have an RI_{myo} of 0. Participants in the PCI group who did not have pre and post PCI angiography and a CMR or DSE viability test of sufficient quality for core lab analysis were excluded from this analysis.

The primary outcome was a composite of death from any cause or hospitalization for heart failure over all follow-up (minimum follow-up was 24 months). Secondary outcomes were all-cause death, cardiovascular death, hospitalization for heart failure and improvement in left ventricular function at six months (defined as a greater than the median absolute change in left ventricular ejection fraction on echocardiography).

Statistical Analysis

The statistical analysis plan was finalized prior to the lock and unblinding of angiographic core laboratory data. A formal power calculation was not performed for this secondary analysis. A Cox proportional hazards model was constructed to assess the relationship between each of RI_{coro}, RI_{myo} and the primary outcome, adjusted for age, sex, previous heart failure hospitalization, presence of diabetes, chronic renal failure, left ventricular ejection fraction, extent of coronary disease and presence of at least one chronic total occlusion; for RI_{coro} the model was also adjusted for the extent of non-viable myocardium. The proportionality assumption of Cox models was assessed by visual examination and, for the primary analyses, using Schoenfeld residuals. Results are reported as estimates with corresponding 95% confidence intervals, the widths of which have not been adjusted for multiplicity. Participants in the OMT group without baseline angiography available for core lab analysis were included in the Cox models for RI_{coro} and RI_{myo} as the RI in these cases was assumed to be 0. Missing values of left ventricular ejection fraction and the adjustment variables (Table S1) were imputed using a multiple imputation model with chained equations that included randomized treatment, age, sex, history of heart failure hospitalization, diabetes, estimated glomerular filtration rate, death during follow-up, hospitalization for heart failure during follow-up, and baseline, 6-month, and 12-month left ventricular ejection fractions. Twenty imputations were performed and effect estimates combined using Rubin's rules

RI_{coro} and RI_{myo} were considered as continuous variables and the median values of each also used to dichotomously define complete versus incomplete anatomical and viability-guided revascularization respectively; Kaplan Meier curves were created for each of the latter comparisons.

Logistic regression models were created and adjusted for the same baseline co-variates as above to explore the relationship between RI_{coro}, RI_{myo} and improvement in left ventricular function. These analyses were restricted to participants who were alive at six months, with missing ejection fraction values imputed as previously described. Results are presented as mean (standard deviation (SD)) or median (inter-quartile range (IQR)). All analyses were conducted using Stata software, version 17·0 (StataCorp).

Results

Of the 700 participants in REVIVED, 670 were included were included in the anatomical completeness of revascularization analysis (317 assigned to PCI and 353 assigned to OMT) , and 619 were included in the viability guided completeness of revascularization analysis (266 PCI group and 353 OMT group) (Figure 1). Baseline clinical, demographic, anatomical and viability characteristics were well matched between the groups (Table 1). Prescription rates of guideline directed medical therapy were similar at baseline and follow up (Table S2).

Anatomical completeness of revascularization

658 participants had baseline coronary angiography available for core lab analysis. The median baseline BCIS-JS and SYNTAX scores were 8 (6-10) and 22 (15-29) respectively. 351 (53%) patients had at least one chronic total occlusion and 340 (52%) had at least one lesion with moderate-severe angiographic calcification. Of the 317 patients assigned to PCI (and included in this analysis), 62 (20%) had at least one CTO successfully treated. In the PCI group, the median post-PCI BCIS-JS was 2 (0-4) representing a median reduction of 6 (2-8) (Table S3) resulting in a RI_{coro} of 67% (IQR 50-100%) (Table S4). Core lab reported

RI_{coro} showed good agreement with site reported RI_{coro}, with only 6.7% of measurements lying outside the limits of agreement (Figure S4). Patients achieving complete anatomical revascularization tended to be younger, were less likely to have a history of myocardial infarction and had lower baseline BCIS-JS and SYNTAX scores as compared to those who received incomplete revascularization (Table S5).

Compared to OMT alone, complete anatomical revascularization did not reduce the primary outcome (adjusted HR 0.90, 95% CI 0.62 to 1.32, p=0.59) (Figure 2). A sensitivity analysis categorizing patients by rSS also found no difference in primary outcome between those who had a rSS≤8 compared to those assigned to OMT alone (HR 1.00, 95% CI 0.69 to 1.44, p>0.99) (Table S6). Similarly, there was no association between achieving complete anatomical revascularization and improvement in left ventricular function (OR 0.94, 95% CI 0.54 to 1.64, p=0.82) or occurrence of any of the other secondary outcomes (Central Illustration, Table S7). When treating RI_{coro} as a continuous variable in the PCI group only, there appeared to be a reduction in the incidence of the primary outcome with increasing degrees of revascularization (HR 0.92 per 10% increase in RI_{coro}, 95% CI 0.87 to 0.97, p=0.003) but this association was no longer apparent after adjustment for baseline risk (HR 0.94 per 10% increase in RI_{coro}, 95% CI 0.88 to 1.01, p=0.10) (Table S8).

Viability guided completeness of revascularization

Amongst the cohort included in this analysis, the median number of segments which were viable and subtended by significant coronary disease was 5 (IQR 3 to 7). In the PCI group 3 (IQR 1 to 6) segments were revascularized per participant yielding a median RI_{myo} of 85% (IQR 60-100%) (Table S4). Complete viability guided revascularization by PCI was not associated with a reduction in the occurrence of the primary outcome (HR 0.95, 95% CI 0.66 to 1.35, p=0.76) (Figure 3) or any of the secondary outcomes (Table S9). No difference was found in the rate of left ventricular improvement in those who achieved complete viability

guided revascularization (OR 1.00, 95% CI 0.58 to 1.73, p >0.99). Similarly to anatomically incomplete revascularization, those who received incomplete viability guided revascularization were older and had more extensive and complex baseline disease, including a higher incidence of left main stem disease (Table S10).

A sensitivity analysis using a late gadolinium transmurality cut-off of 25% to define viability similarly found no interaction with the primary outcome in the group whom achieved complete viability guided revascularization (HR 1.02, 95%CI 0.72 to 1.44, p=0.93) or with any of the secondary outcomes (Table S11). When considered as a continuous variable there was no evidence for an association with the primary outcome per 10% increase in RI_{myo} (unadjusted HR 0.98, 95% CI 0.91 to 1.04, p=0.47; adjusted HR 1.00, 95% CI 0.93 to 1.08, p=0.97) (Table S8).

Quality of life and completeness of revascularization

Baseline summary Kansas City Cardiomyopathy Questionnaire (KCCQ) was lowest amongst those achieving incomplete revascularization (Table S12). As compared with OMT alone, achieving complete anatomical revascularization was associated with a non-significant improvement (adjusted mean difference 4.6, 95% CI -0.2 to 9.5, p=0.06) in KCCQ score at 2 years (Table S12). A similar trend towards improvement was observed with those achieving complete viability-guided revascularization (adjusted mean difference 3.9, 95% CI -0.9 to 8.6, p=0.11).

Discussion

In this pre-specified analysis of REVIVED-BCIS2 utilizing core laboratory analyses of baseline and post-procedural angiograms as well as viability studies, we did not find an association between the extent of anatomical or viability-guided completeness of revascularization and the treatment effect of PCI with respect to the occurrence of death or hospitalization for heart failure, nor the likelihood of left ventricular recovery. Core

laboratory-adjudicated RI_{coro} was comparable to previously published site-reported RI_{coro} [4] and was lower than RI_{myo}, reflecting the large burden of non-viable myocardium, which is a key determinant of which diseased vessels are chosen as targets for revascularization. This also explains why increasing degrees of anatomical revascularization initially appeared to be associated with increased benefit, but this association was no longer evident when the extent of non-viable myocardium was taken into consideration.

The strongest evidence in support of complete revascularization comes from randomized studies of patients with multi-vessel disease presenting with acute coronary syndromes [11-13]. In the COMPLETE trial, the benefit was primarily driven by a reduction in subsequent myocardial infarction as opposed to cardiovascular death, suggesting that the risk relates to the likelihood of atherosclerotic plaque rupture which can in turn be modulated by revascularization [13]. On the other hand, in the CULPRIT-Shock trial which enrolled patients with acute left ventricular dysfunction following myocardial infarction, multi-vessel PCI was associated with worse outcomes as compared with culprit lesion only PCI, which may reflect the need to balance acute procedural risks against potential long-term benefits [14]. No prospective randomized studies of complete versus incomplete revascularization have been conducted to date in stable coronary artery disease. A post-hoc secondary analysis of the ISCHEMIA trial, reported an apparent reduction in the rate of cardiovascular death and myocardial infarction in those with complete anatomical revascularization, however these differences were no longer significant after adjustment for baseline characteristics [15]. In this sub-study, completeness of revascularization was not randomized but at the discretion of the attending clinicians; patients who received incomplete revascularization were found to be more co-morbid with more extensive and complex coronary disease. Similarly a post-hoc analysis of the patients assigned to the PCI arm of the SYNTAX trial found that patients with a rSS >8 (representing incomplete anatomical revascularization) was associated with an

increased risk of all cause death (35.3% vs 8.5% at 5 years, p<0.001) with a more pronounced effect in the subgroup with impaired LV function [16], although patients who had a rSS>8 were older, had higher rates of diabetes, peripheral vascular disease and chronic total occlusions resulting in higher baseline SYNTAX and EuroSCOREs. As the patient's baseline risk strongly influences (and is usually inversely related to) the degree of revascularization achieved, such non-randomized comparisons of complete versus incomplete revascularization are heavily confounded and are not fully accounted for by techniques such as propensity matching or modelling. We also found that patients receiving incomplete revascularization had lower baseline KCCQ scores, more comorbidities and more extensive and complex coronary disease. The finding of similar event rates in this cohort, despite having higher baseline risk, provides further indirect evidence that incomplete (anatomical or viability-guided) revascularization does not confer a prognostic penalty in patients with severe ischemic left ventricular dysfunction.

The distinction between anatomical and functional completeness of revascularization also merits further consideration. In stable coronary syndromes, in patients with preserved left ventricular function, these metrics may be discordant because it is well recognized that there is an imperfect correlation between the anatomical severity of a coronary lesion (most commonly visualized by angiography) and its ability to cause ischemia [17]. There is a growing body of evidence that better clinical outcomes can be achieved with a functional (ischemia-guided) revascularization strategy than one which is based on anatomical (angiographically apparent) coronary artery disease, even though the former usually results in fewer vessels and lesions being revascularized [18]. When treating patients with stable ischemic cardiomyopathy, the viability of subtended myocardium is a unique consideration. Only critically diseased vessels that subtend viable myocardium are usually considered for revascularization, as this is believed to be the primary substrate for regional ischemic ventricular dysfunction, whilst

there is no evidence that revascularization of scarred and non-viable regions is of benefit. In order to capture these specific goals, we have used a novel measure of viability-guided revascularization, the myocardial revascularization index (RI_{myo}), which expresses completeness of revascularization in relation to the extent of viable myocardium that is supplied by diseased coronary arteries. By this measure, the degree of viability-guided revascularization achieved in the PCI arm of REVIVED was high (approximately 85%) but, we found no evidence that complete viability-guided revascularization provided benefit above incomplete revascularization or OMT alone. These findings suggest that, in established ischemic cardiomyopathy, the risk of subsequent adverse events arises from the state of the myocardium rather than plaque rupture and also that reversal of advanced hibernation cannot be achieved by revascularization alone. These data corroborate the REVIVED viability analysis which demonstrated that the key determinant of clinical outcomes and ventricular recovery was the extent of non-viable myocardium [19].

Study limitations

The present analysis does have some limitations to consider. Firstly, we did not randomize to a strategy of complete versus incomplete revascularization and hence our results are prone to selection bias, that has affected other observational studies in this arena. However, the finding of similar event rates in those who had complete versus incomplete revascularization, despite a more adverse risk profile in the latter, adds further weight to our conclusion, that completeness of revascularization does not affect outcomes in this population. Secondly, co-registration of AHA segments to a coronary vessel territory was standardized based on coronary dominance. An approach customized to individual coronary anatomy may have allowed improved accuracy of co-registration, but would be prone to subjectivity and hence be less reproducible. Third, for simplicity of analysis and presentation, we used a binary classification of complete vs incomplete even though a spectrum of revascularization exists.

However, our findings were congruent even when RI_{coro} and RI_{myo} were analyzed as continuous variables. Fourth, we did not systematically capture intracoronary physiology and imaging data and hence the core laboratory analysis is purely based on visual assessment of angiograms, whereas these data will have been used by clinicians to inform the BCIS-JS calculation and to guide management of patients assigned to PCI, as recommended by the trial protocol. Finally, we only assessed revascularization with PCI. CABG represents a fundamentally different method of achieving revascularization which might be associated with different outcomes.

Conclusion

This study does not show a difference in event-free survival or frequency of improved left ventricular function in patients with stable coronary disease and severe impairment of left ventricular function, who were assigned to PCI and subsequently received complete revascularization, compared to those assigned to PCI but received incomplete revascularization or those assigned to OMT alone. This finding is consistent whether completeness of revascularization was classified by the overall angiographic burden of coronary disease, or the extent of revascularization of viable myocardium.

Perspectives

Competency in Medical Knowledge: In patients with severe ischemic left ventricular dysfunction, complete revascularization by PCI, compared to incomplete revascularization, did not reduce the incidence of death or heart failure hospitalization.

Translational Outlook: Randomized trials are needed to clarify the impact of complete revascularization compared to incomplete revascularization by PCI in patients with stable coronary artery disease.

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Figure Legends

Figure 1. Study consort diagram. 18 patients in the OMT arm had missing baseline angiography but were included in completeness of revascularization analyses as the revascularization index was assumed to be 0. CMR – cardiac magnetic resonance imaging, FDG-PET fluorodeoxyglucose positron emission tomography, OMT – optimal medical therapy, PCI – percutaneous coronary intervention

Figure 2. Anatomical completeness of revascularization vs OMT. Kaplan-Meier plot of the primary outcome (death or hospitalization for heart failure). The presented HR for comparisons are adjusted. Incomplete AR vs OMT: Unadjusted HR = 1.13 (95% CI 0.85 to 1.51), p=0.40. Complete AR vs OMT: Unadjusted HR = 0.75 (95% CI 0.54 to 1.06), p=0.10. AR – anatomical revascularization, CI – confidence interval, HR – hazard ratio, OMT – optimal medical therapy

Figure 3. Viability guided completeness of revascularization vs OMT. Kaplan-Meier plot of the primary outcome (death or hospitalization for heart failure). The presented HR for comparisons are adjusted. Incomplete VGR vs OMT: Unadjusted HR = 0.93 (95% CI 0.67 to 1.30), p=0.68. Complete VGR vs OMT: Unadjusted HR = 0.80 (95% CI 0.56 to 1.13), p=0.20. CI – confidence interval, HR – hazard ratio, OMT – optimal medical therapy, VGR – viability guided revascularization

Figure 4. Primary and secondary outcomes for complete revascularization

Forest plot presenting the treatment effect of complete anatomical and viability guided revascularization on primary and pre-specified secondary outcomes. AR – anatomical revascularization, CI – confidence interval, CV – cardiovascular, HHF – hospitalization for heart failure, LV – left ventricle, VGR – viability guided revascularization

Central Illustration. Completeness of Revascularization in REVIVED-BCIS2

Core lab analyzed coronary angiography and cardiac magnetic resonance imaging were used to define anatomical and viability guided completeness of revascularization. Primary and secondary outcomes are presented for those achieving complete revascularization vs OMT. CV- cardiovascular, HHF – hospitalization for heart failure, LV – left ventricle, OMT – optimal medical therapy, RI_{coro} – coronary revascularization index, RI_{myo} – myocardial revascularization index

Table 1. Baseline characteristics of participants in anatomical and viability guided completeness of revascularization analyses

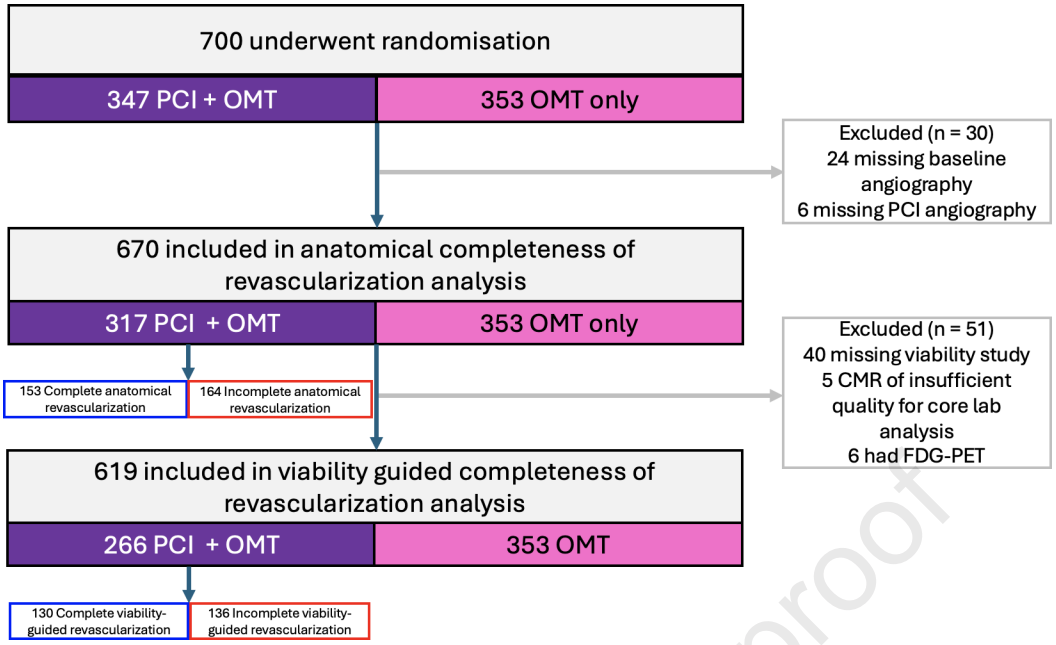
	REVIVED trial (N=700)	Anatomical CoR analysis (N= 670)	Viability-guided CoR analysis (N=619)
Ag, mean (SD), years	69.4 ± 9.1	69.2 ± 9.1	69.1 ± 9.0
Male sex (%)	614 (87.7)	587 (87.6)	544 (87.9)
Body-mass index (IQR)	28.0 (24.7 to 31.7)	28.1 (24.9 to 31.9)	28.1 (24.9 to 32.0)
Diabetes (%)	289 (41.3)	277 (41.3)	260 (42.0)
Hypertension (%)	391 (55.9)	378 (56.5)	348 (56.3)
Current or previous smoker (%)	510 (72.9)	490 (73.1)	454 (73.3)
Cerebrovascular disease (%)	84 (12.0)	81 (12.1)	70 (11.3)
Peripheral vascular disease (%)	94 (13.4)	90 (13.4)	85 (13.7)
Race (%)[a]			
Asian	49 (7.0)	47 (7.0)	40 (6.5)
Black	6 (0.9)	6 (0.9)	6 (1.0)
Mixed, other or not reported	11 (1.6)	11 (1.6)	10 (1.6)
White	634 (90.6)	606 (90.4)	563 (91.0)
History of myocardial infarction (%)	372 (53.1)	356 (53.1)	327 (52.8)
Hospitalization for heart failure in prior 2 years (%)	233 (33.3)	221 (33.0)	213 (34.4)
Previous PCI (%)	142 (20.3)	136 (20.3)	121 (19.5)
Previous CABG (%)	34 (4.9)	33 (4.9)	31 (5.0)
CCS Angina Class			
0	464 (66.6)	448 (67.2)	418 (67.9)
1	143 (20.5)	137 (20.5)	126 (20.5)
2	75 (10.8)	70 (10.5)	61 (9.9)
3	14 (2.0)	12 (1.8)	11 (1.8)
4	1 (0.1)	0 (0.0)	0 (0.0)
NYHA Class			
I	126 (18.1)	121 (18.2)	115 (18.7)
II	387 (55.7)	373 (56.1)	347 (56.5)
III	172 (24.7)	163 (24.5)	145 (23.6)
IV	10 (1.4)	8 (1.2)	7 (1.1)
Cardiac medication (%)			
RAAS inhibitor	584 (83.5)	557 (83.3)	511 (82.7)
Beta blocker	634 (90.6)	608 (90.7)	561 (90.6)
Mineralocorticoid receptor antagonist	364 (49.4)	332 (49.6)	308 (49.8)
Baseline BCIS jeopardy score, median (IQR)[b]	8 (6 to 10)	8 (6 to 10)	8 (6 to 10)
Post-PCI BCIS jeopardy score, median (IQR)	2 (0 to 4)	2 (0 to 4)	2 (0 to 4)
Baseline syntax score, median (IQR)	22.0 (15.0 to 28.5)	22.0 (15.0 to 28.5)	22.0 (15.0 to 29.0)
Residual syntax score, median (IQR)	8.0 (2.0 to 14.0)	8.0 (2.0 to 14.0)	8.0 (2.0 to 14.0)
ICD +/- CRT at randomization (%)	148 (21.1)	140 (20.9)	129 (20.8)
Left main coronary artery disease (%)	95 (13.6)	88 (13.2)	85 (13.8)
Left ventricular ejection fraction, mean (SD), %[c]	31.9 ± 9.9	31.9 ± 9.8	32.1 ± 9.8
Viability test (%)			
CMR	479 (78.5)	458 (78.2)	453 (78.0)
DSE	131 (21.5)	128 (21.8)	128 (22.0)
Number of viable segments (IQR)	7 (4 to 10)	7 (4 to 10)	7 (4 to 10)

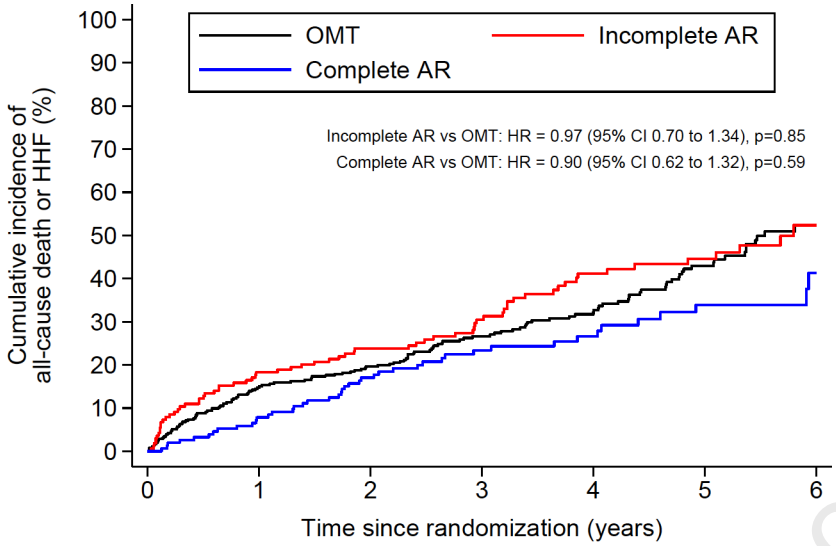
BCIS denotes British Cardiovascular Intervention Society, CABG coronary artery bypass grafting, CCS Canadian Cardiovascular Society, CMR cardiovascular magnetic resonance imaging, CoR completeness of revascularization, CRT cardiac resynchronization therapy, CTO chronic total occlusion, DSE dobutamine stress echocardiography, ICD implantable cardioverter defibrillator, IQR interquartile range, NYHA New York Heart Association, PCI percutaneous coronary intervention, RAAS renin angiotensin aldosterone system.

[a] Race as self-reported by participants using options defined by the investigators.

[b] The British Cardiovascular Intervention Society (BCIS) jeopardy score is a quantification of the extent of myocardial jeopardy relating to clinically significant coronary artery stenoses. The score ranges from 0 (no significant coronary disease) to 12 (disease jeopardizing the whole left ventricular myocardium). The score presented is as calculated by angiography core laboratory.

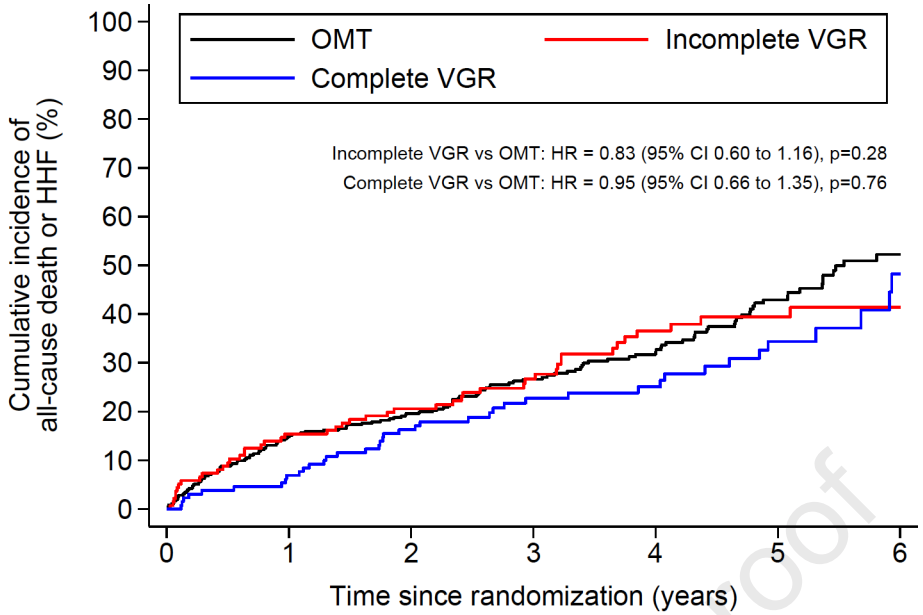
[c] Baseline left ventricular ejection fraction measured by the blinded echocardiography core laboratory.



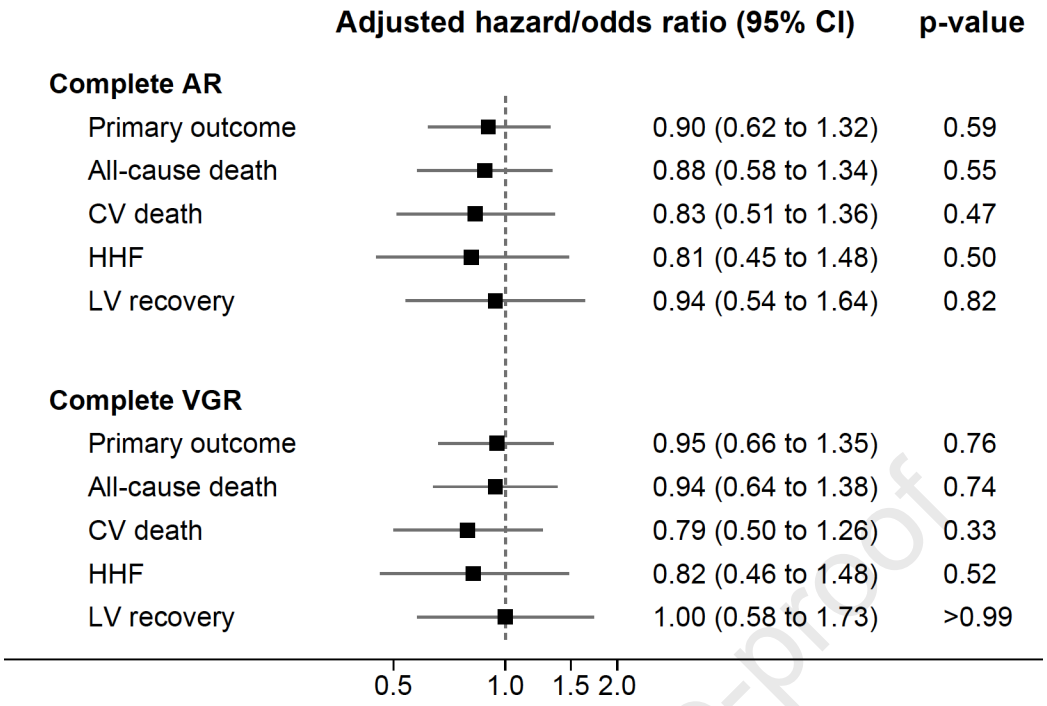


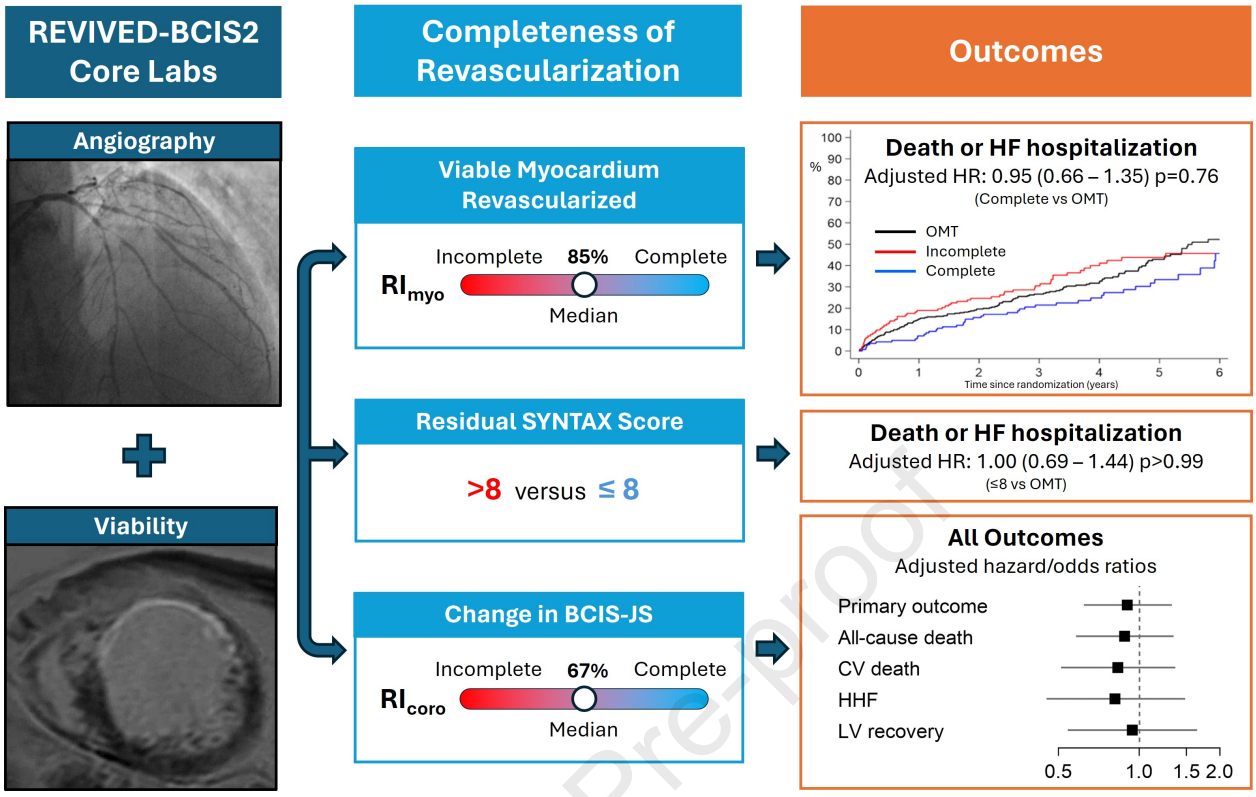
Number at risk

OMT	353	299	276	191	142	82	33
Incomplete AR	164	134	121	86	60	41	16
Complete AR	153	141	124	83	62	35	16



Number at risk							
OMT	353	299	276	191	142	82	33
Incomplete VGR	136	115	106	74	51	35	14
Complete VGR	130	121	105	77	59	32	14





Supplementary Material

Contents

1. REVIVED Sites and Investigators

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Mrs Paula Young, Patient, Carer and Public representative

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3. Figures

Figure S1 – Co-registration of coronary lesions to American Heart Association myocardial segments

Figure S1A – Right dominant circulation

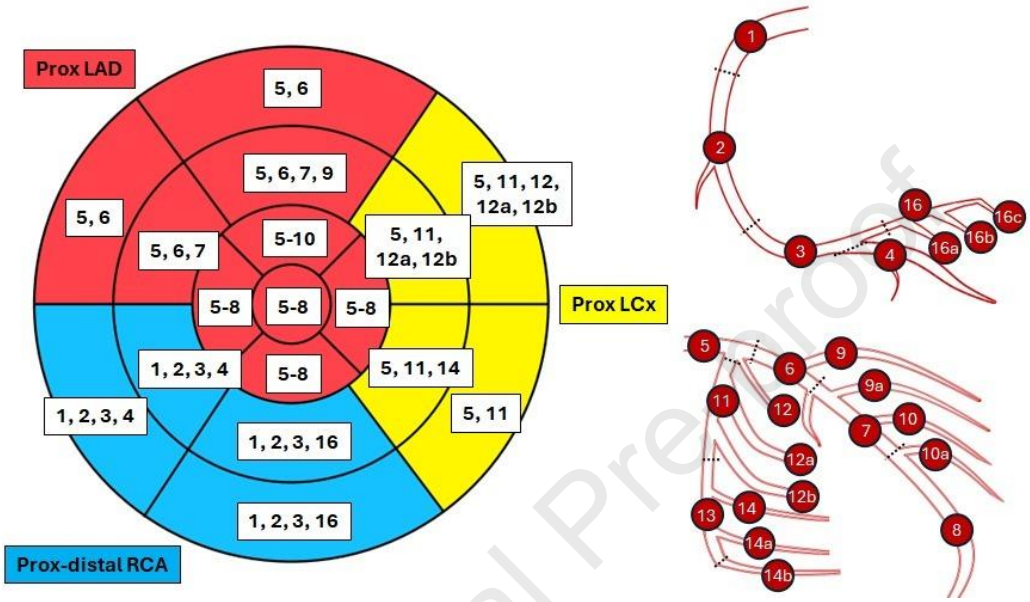
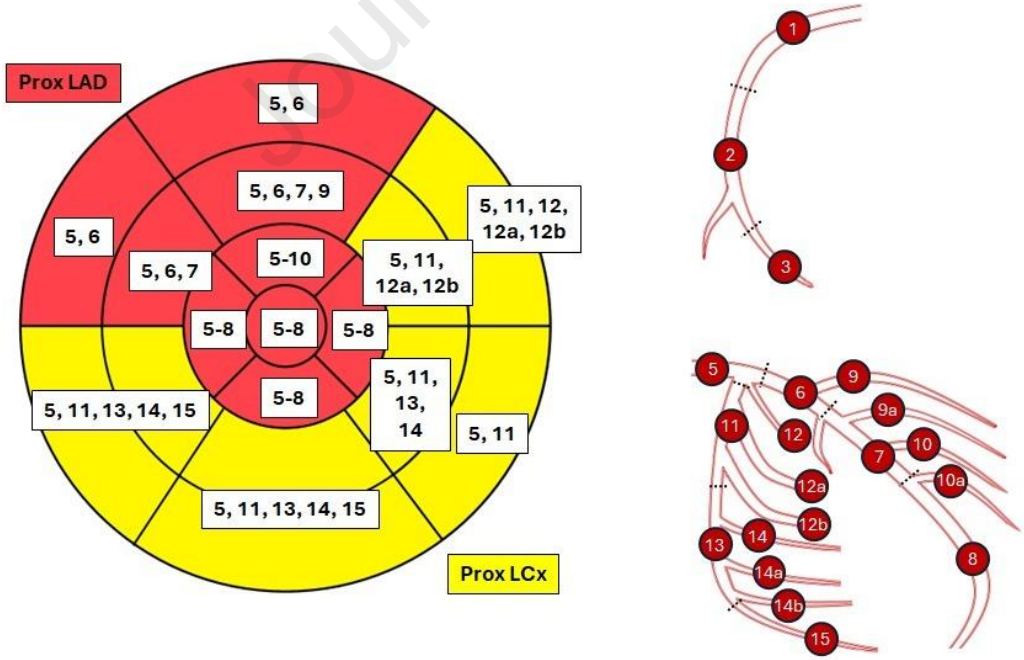
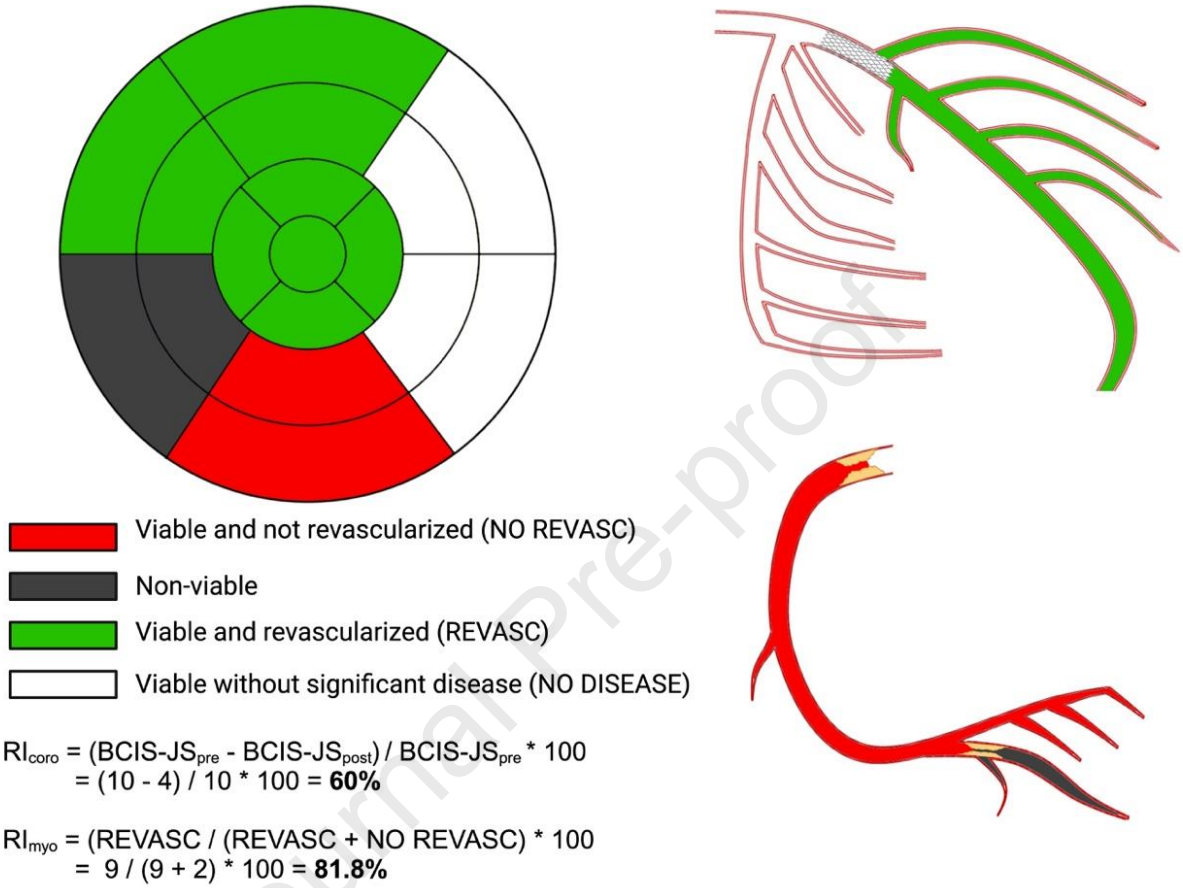


Figure S1B – Left dominant circulation



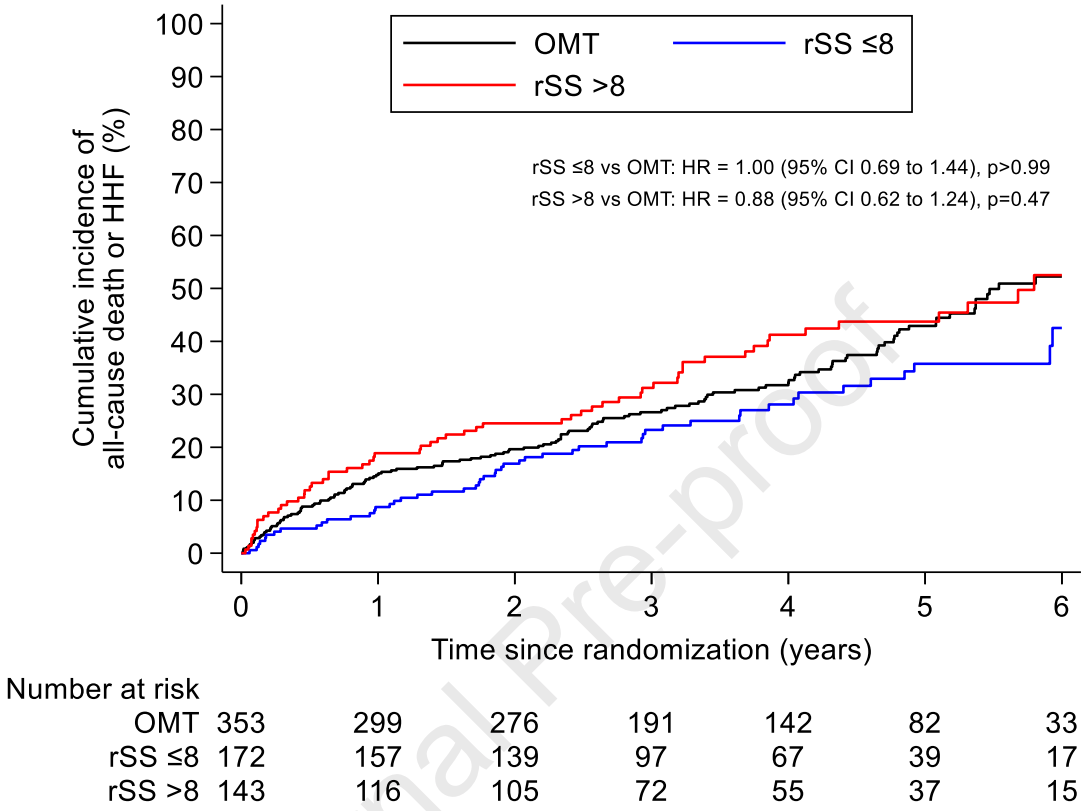
Each coronary lesion with a visual diameter stenosis of >70% was assigned to a SYNTAX segment by core lab readers. SYNTAX segments were then linked to American Heart Association segments as demonstrated in these polar maps depending on coronary dominance.

Figure S2 – Example of coronary and myocardial revascularization index calculation



BCIS-JS - British Cardiovascular Interventional Society jeopardy score, RI_{coro} – Coronary revascularization index, RI_{myo} – Myocardial revascularization index

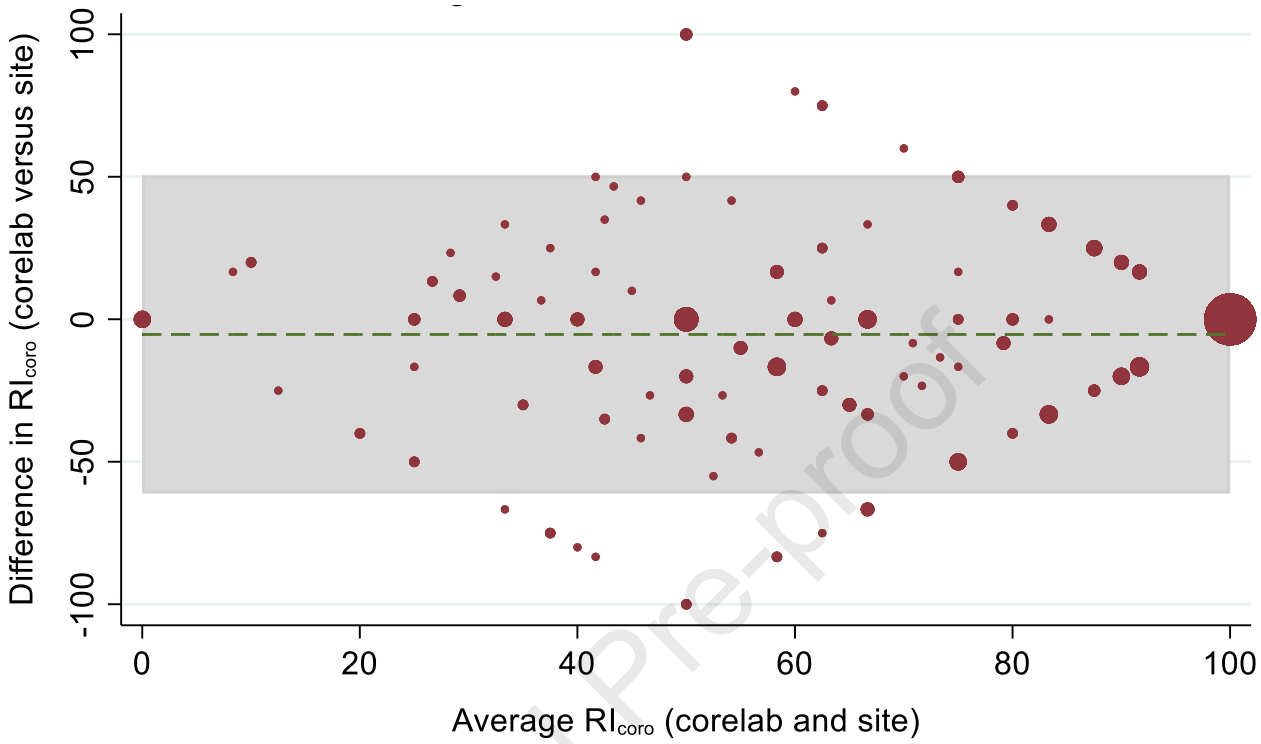
Figure S3 – Impact of anatomical completeness of revascularization by residual SYNTAX score on the primary outcome



The Kaplan-Meir plot presents the adjusted HR for comparisons. rSS ≤ 8 vs OMT: Unadjusted HR = 0.79 (95% CI 0.57 to 1.08), p=0.14. rSS >8 vs OMT: Unadjusted HR = 1.13 (95% CI 0.84 to 1.53), p=0.42

CI – confidence interval, HR – hazard ratio, OMT – optimal medical therapy, rSS – residual SYNTAX score

Figure S4 – Comparison of core lab vs site reported anatomical completeness of revascularization (PCI Group)



Bland-Altman plot comparing core lab and site reported RI_{coro}. Mean difference observed was -5.3%.
RI_{coro} – Coronary revascularization index

4. Tables

Table S1 – Imputed missing data

Anatomical completeness of revascularization analysis (n=670)	
Variable	Number of missing values
eGFR	9
LVEF at baseline	153
LVEF at 6 monyhd	154
LVEF at 12 months	164
Viability guided completeness of revascularization analysis (n=619)	
Variable	Number of missing values
eGFR	9
LVEF at baseline	137
LVEF at 6 months	146
LVEF 12 months	150

eGFR – estimated glomerular filtration rate, LVEF – left ventricular ejection fraction

Table S2 – Utilization of guideline directed medical therapy

	REVIVED trial (n=700)	Anatomical CoR analysis (n=670)	Viability-guided CoR analysis (n=619)
6 months			
RAAS inhibitor	493/647 (76.2)	475/625 (76.0)	438/579 (75.7)
Beta blocker	604/647 (93.4)	584/625 (93.4)	542/579 (93.6)
Mineralocorticoid receptor antagonist	343/647 (53.1)	333/624 (53.4)	312/578 (54.0)
1 year			
RAAS inhibitor	466/625 (74.6)	451/606 (74.4)	414/561 (73.8)
Beta blocker	585/625 (93.6)	566/606 (93.4)	527/561 (93.9)
Mineralocorticoid receptor antagonist	340/624 (54.5)	332/605 (54.9)	310/560 (55.4)
2 years			
RAAS inhibitor	369/567 (65.1)	356/550 (64.7)	326/509 (64.1)
Beta blocker	529/569 (93.0)	512/552 (92.8)	477/511 (93.4)
Mineralocorticoid receptor antagonist	315/567 (55.6)	310/550 (56.4)	288/510 (56.5)

CoR completeness of revascularization, RAAS renin angiotensin aldosterone system.

Table S3 – Core-lab adjudicated BCIS-JS

	OMT arm	PCI arm only	
Baseline BCIS-JS†	**Baseline**	**Baseline**	**Post-PCI**
0	2/335 (0.6)	4/317 (1.3)	122/317 (38.5)
2	10/335 (3.0)	13/317 (4.1)	56/317 (17.7)
4	27/335 (8.1)	26/317 (8.2)	68/317 (21.5)
6	84/335 (25.1)	72/317 (22.7)	49/317 (15.5)
8	67/335 (20.0)	68/317 (21.5)	12/317 (3.8)
10	68/335 (20.3)	56/317 (17.7)	5/317 (1.6)
12	77/335 (23.0)	78/317 (24.6)	5/317 (1.6)
Median (IQR)	8 (6 to 10)	8 (6 to 10)	2 (0 to 4)

† The British Cardiovascular Intervention Society jeopardy score (BCIS-JS) is a quantification of the extent of myocardial jeopardy relating to clinically significant coronary artery stenoses. The score ranges from 0 (no significant coronary disease) to 12 (disease jeopardizing the whole left ventricular myocardium).

Table S4 – Core-lab adjudicated anatomical and viability-guided completeness of revascularization

Revascularization index	**RI_{coro} n (%)**	**RI_{myo} n (%)**
≤20%	28/317 (8.8)	22/266 (8.3)
21 to 40%	47/317 (14.8)	18/266 (6.8)
41 to 60%	62/317 (19.6)	29/266 (10.9)
61 to 80%	50/317 (15.8)	54/266 (20.3)
81 to 99%	12/317 (3.8)	32/266 (12.0)
100%	118/317 (37.2)	111/266 (41.7)
Median (IQR)	66.7 (50.0 to 100.0)	84.6 (60.0 to 100.0)

RI_{coro} – Coronary revascularization index. RI_{myo} – Myocardial revascularization index.

Table S5 – Comparison of baseline characteristics in those achieving complete vs incomplete anatomical revascularization

	Optimal medical therapy (N=353)	Incomplete anatomical revascularization (RI_{coro} ≤66.7) (N=164)	Complete anatomical revascularization (RI_{coro} >66.7) (N=153)	P-value[d]
Age, mean (SD), years	68.8 (9.1)	70.8 ± 8.4	68.7 ± 9.6	0.03
Male sex (%)	312 (88.4)	143 (87.2)	132 (86.3)	0.81
Body-mass index (IQR)	27.9 (24.9 to 32.0)	27.7 (24.4 to 31.6)	28.7 (25.0 to 32.0)	0.50
Diabetes (%)	153 (43.3)	61 (37.2)	63 (41.2)	0.47
Hypertension (%)	207 (58.8)	91 (55.5)	80 (52.3)	0.57
Current or previous smoker (%)	267 (75.6)	117 (71.3)	106 (69.3)	0.69
Cerebrovascular disease (%)	46 (13.0)	21 (12.8)	14 (9.2)	0.29
Peripheral vascular disease (%)	46 (13.0)	26 (15.9)	18 (11.8)	0.29
Race (%)[a]				0.17
Asian	17 (4.8)	19 (11.6)	11 (7.2)	
Black	3 (0.8)	2 (1.2)	1 (0.7)	
Mixed, other or not reported	5 (1.4)	1 (0.6)	5 (3.3)	
White	328 (92.9)	142 (86.6)	136 (88.9)	
History of myocardial infarction (%)	197 (55.8)	94 (57.3)	65 (42.5)	0.01
Hospitalization for heart failure in prior 2 years (%)	121 (34.3)	48 (29.3)	52 (34.0)	0.37
Previous PCI (%)	76 (21.5)	28 (17.1)	32 (20.9)	0.38
Previous CABG (%)	22 (6.2)	9 (5.5)	2 (1.3)	0.06
CCS Angina Class				0.32
0	236 (67.2)	102 (62.6)	110 (71.9)	
1	75 (21.4)	35 (21.5)	27 (17.6)	
2	32 (9.1)	23 (14.1)	15 (9.8)	
3	8 (2.3)	3 (1.8)	1 (0.7)	
4	0 (0.0)	0 (0.0)	0 (0.0	
NYHA Class				0.09
I	57 (16.3)	27 (16.6)	37 (24.3)	
II	191 (54.6)	93 (57.1)	89 (58.6)	
III	96 (27.4)	42 (25.8)	25 (16.4)	
IV	6 (1.7)	1 (0.6)	1 (0.7)	
ICD +/- CRT at randomization (%)	71 (20.1)	42 (25.6)	27 (17.6)	0.09
Baseline BCIS jeopardy score, median (IQR)[b]	8 (6 to 10)	10 (6 to 12)	8 (6 to 10)	0.0008
Post-PCI BCIS jeopardy score, median (IQR)	-	4 (4 to 6)	0 (0 to 0)	<0.0001
Baseline SYNTAX score, median (IQR)	22 (15 to 29)	23.5 (19.0 to 30.8)	18.0 (13.0 to 24.5)	<0.0001
Residual SYNTAX score, median (IQR)	-	13.0 (8.3 to 20.0)	1.0 (0.0 to 5.0)	<0.0001
Left main coronary artery disease (%)	45 (12.8)	25 (15.2)	18 (11.8)	0.37
Left ventricular ejection fraction, mean (SD), %[c]	31.9 ± 9.6	31.1 ± 9.1	32.8 ± 11.0	0.19
Viability test (%)				
CMR	243 (77.1)	116 (81.1)	99 (77.3)	-
DSE	72 (22.9)	27 (18.9)	29 (22.7)	
Number of viable segments (IQR)	7 (4-10)	6 (4-10)	7 (5-11)	0.21

[a] Race as self-reported by participants using options defined by the investigators.

[b] British Cardiovascular Intervention Society jeopardy score (BCIS-JS) as reported by angiography core laboratory.

[c] Baseline left ventricular ejection fraction measured by the blinded echocardiography core laboratory

[d] P-value denotes comparison between Incomplete vs complete anatomical revascularization groups

BCIS denotes British Cardiovascular Intervention Society, CABG coronary artery bypass grafting, CCS Canadian Cardiovascular Society, CMR cardiovascular magnetic resonance imaging, CRT cardiac resynchronization therapy, CTO chronic total occlusion, DSE dobutamine stress echocardiography, ICD implantable cardioverter defibrillator, IQR interquartile range, NYHA New York Heart Association, PCI percutaneous coronary intervention, RI_{coro} Coronary revascularization index.

Table S6 – Primary and clinical secondary outcomes by residual SYNTAX score

	Optimal medical therapy group§ (Reference)	rSS >8§	Hazard / Odds ratio* (95% CI)	p-value	rSS ≤8§	Hazard / Odds ratio* (95% CI)	p-value
All-cause death or hospitalization for heart failure	134 (38.0)	61(42.7)	0.88 (0.62 to 1.24)	0.47	53 (30.8)	1.00 (0.69 to 1.44)	>0.99
All-cause death	115 (32.6)	52(36.4)	0.81 (0.55 to 1.18)	0.27	44 (25.6)	0.99 (0.66 to 1.47)	0.95
Cardiovascular death	88 (24.9)	36 (25.2)	0.68 (0.43 to 1.07)	0.10	29 (16.9)	0.90 (0.56 to 1.45)	0.67
Hospitalization for heart failure	54 (15.3)	23 (16.1)	0.77 (0.44 to 1.37)	0.37	24 (14.0)	0.85 (0.48 to 1.52)	0.58
Improvement in left ventricular ejection fraction	101 (50.2)	44 (51.8)	1.05 (0.57 to 1.94)	0.87	48 (45.7)	0.78 (0.45 to 1.35)	0.37

CI – confidence interval; HR-hazard ratio; rSS – residual SYNTAX score
* Adjusted Hazard ratios calculated with OMT group as reference
§ Event rate - n(%)

Table S7 – Primary and clinical secondary outcomes by anatomical completeness of revascularization

	Optimal medical therapy§ (Reference)	Complete anatomical revascularization§ (RI_{coro} >66.7)	Hazard / Odds ratio* (95% CI)	p-value	Incomplete anatomical revascularization§ (RI_{coro} ≤66.7)	Hazard / Odds ratio* (95% CI)	p-value
All-cause death or hospitalization for heart failure	134 (38.0)	45 (29.4)	0.90 (0.62 to 1.32)	0.59	70 (42.7)	0.97 (0.70 to 1.34)	0.85
All-cause death	115 (32.6)	36 (23.5)	0.88 (0.58 to 1.34)	0.55	60 (36.6)	0.88 (0.62 to 1.25)	0.48
Cardiovascular death	88 (24.9)	24 (15.7)	0.83 (0.51 to 1.36)	0.47	41 (25.0)	0.73 (0.48 to 1.12)	0.15
Hospitalization for heart failure	54 (15.3)	21 (13.7)	0.81 (0.45 to 1.48)	0.50	27 (16.5)	0.84 (0.49 to 1.44)	0.53
Improvement in left ventricular ejection fraction	101 (50.2)	44 (46.8)	0.94 (0.54 to 1.64)	0.82	48 (49)	0.85 (0.48 to 1.51)	0.58

CI – confidence interval; HR-hazard ratio; RI_{coro} – Coronary revascularization index
* Adjusted Hazard/Odds ratios calculated with OMT group as reference
§ Event rate - n(%)

Table S8 – Relationship between completeness of revascularization and outcomes (with RI_{coro} and RI_{myo} as continuous variables)

Revascularization index	Outcome measure	Association Unadjusted HR/OR; 95% CI	Association Adjusted HR/OR; 95% CI
RI_{coro} *per 10% increase (PCI arm only)*	Death or HHF	0.92 (0.87 to 0.97)	0.94 (0.88 to 1.01)
	All-cause death	0.92 (0.86 to 0.97)	0.93 (0.86 to 1.01)
	CV death	0.91 (0.84 to 0.98)	0.94 (0.86 to 1.04)
	HHF	0.96 (0.88 to 1.05)	0.98 (0.87 to 1.10)
	LV improvement	1.05 (0.97 to 1.14)	1.06 (0.95 to 1.18)
RI_{myo} *per 10% increase (PCI arm only)*	Death or HHF	0.98 (0.91 to 1.04)	1.00 (0.93 to 1.08)
	All-cause death	0.98 (0.91 to 1.06)	1.00 (0.92 to 1.09)
	CV death	0.98 (0.90 to 1.07)	1.01 (0.91 to 1.11)
	HHF	0.93 (0.84 to 1.03)	0.97 (0.86 to 1.08)
	LV improvement	1.04 (0.95 to 1.14)	1.03 (0.91 to 1.15)

CI – confidence interval; CV- cardiovascular; HHF- hospitalization for heart failure; HR-hazard ratio; LV – left ventricle; OR - odds ratio; PCI – percutaneous coronary intervention; RI_{coro} – Coronary revascularization index; RI_{myo} – Myocardial revascularization index.

Table S9 – Primary and secondary outcomes by viability-guided completeness of revascularization (50% late gadolinium enhancement threshold)

	Optimal medical therapy§ (Reference)	Complete viability guided revascularization§ (RI_{myo} >84.6)	Hazard / Odds ratio* (95% CI)	p-value	Incomplete viability guided revascularization§ (RI_{myo} ≤84.6)	Hazard / Odds ratio* (95% CI)	p-value
All-cause death or hospitalization for heart failure	134 (38.0)	42 (32.3)	0.95 (0.66 to 1.35)	0.76	49 (36.0)	0.83 (0.60 to 1.16)	0.28
All-cause death	115 (32.6)	36 (27.7)	0.94 (0.64 to 1.38)	0.74	40 (29.4)	0.77 (0.53 to 1.11)	0.16
Cardiovascular death	88 (24.9)	24 (18.5)	0.79 (0.50 to 1.26)	0.33	29 (21.3)	0.71 (0.47 to 1.10)	0.13
Hospitalization for heart failure	54 (15.3)	15 (11.5)	0.82 (0.46 to 1.48)	0.52	18 (13.2)	0.74 (0.43 to 1.27)	0.27
Improvement in left ventricular ejection fraction	101 (50.2)	40 (50.6)	1.00 (0.58 to 1.73)	>0.99	44 (53.0)	0.95 (0.54 to 1.67)	0.86

CI – confidence interval; HR-hazard ratio; RI_{myo} – Myocardial revascularization index
* Adjusted Hazard ratios calculated with OMT group as reference
§ Event rate - n(%)

Table S10 - Comparison of baseline characteristics in those achieving complete vs incomplete viability-guided revascularization

	Optimal medical therapy (N=353)	Incomplete viability guided revascularization (RI_{myo} ≤86.7) (N=136)	Complete viability guided revascularization (RI_{myo} >86.7) (N=130)	P-value[d]
Age, mean (SD), years	68.8 (9.1)	70.5 ± 8.3	68.3 ± 9.6	0.04
Male sex (%)	312 (88.4)	122 (89.7)	110 (84.6)	0.21
Body-mass index (IQR)	27.9 (24.9 to 32.0)	27.7 (24.2 to 30.9)	28.7 (25.1 to 32.4)	0.24
Diabetes (%)	153 (43.3)	56 (41.2)	51 (39.2)	0.75
Hypertension (%)	207 (58.8)	78 (57.4)	63 (48.5)	0.14
Current or previous smoker (%)	267 (75.6)	95 (69.9)	92 (70.8)	0.87
Cerebrovascular disease (%)	46 (13.0)	14 (10.3)	10 (7.7)	0.46
Peripheral vascular disease (%)	46 (13.0)	23 (16.9)	16 (12.3)	0.29
Race (%)[a]				0.71
Asian	17 (4.8)	14 (10.3)	9 (6.9)	
Black	3 (0.8)	1 (0.7)	2 (1.5)	
Mixed, other or not reported	5 (1.4)	3 (2.2)	2 (1.5)	
White	328 (92.9)	118 (86.8)	117 (90.0)	
History of myocardial infarction (%)	197 (55.8)	79 (58.1)	51 (39.2)	0.002
Hospitalization for heart failure in prior 2 years (%)	121 (34.3)	46 (33.8)	46 (35.4)	0.79
Previous PCI (%)	76 (21.5)	24 (17.6)	21 (16.2)	0.75
Previous CABG (%)	22 (6.2)	7 (5.1)	2 (1.5)	0.17
CCS Angina Class				0.31
0	236 (67.2)	92 (68.1)	90 (69.2)	
1	75 (21.4)	30 (22.2)	21 (16.2)	
2	32 (9.1)	11 (8.1)	18 (13.8)	
3	8 (2.3)	2 (1.5)	1 (0.8)	
4	0 (0.0)	0 (0.0)	0 (0.0	
NYHA Class				0.43
I	57 (16.3)	28 (20.69)	30 (23.1)	
II	191 (54.6)	77 (57.5)	79 (60.8)	
III	96 (27.4)	29 (21.6)	20 (15.4)	
IV	6 (1.7)	0 (0.0)	0 (0.0)	
ICD +/- CRT at randomization (%)	71 (20.1)	32 (23.5)	26 (20.0)	0.49
Baseline BCIS jeopardy score, median (IQR)[b]	8 (6 to 10)	10 (6 to 12)	8 (6 to 10)	0.0004
Post-PCI BCIS jeopardy score, median (IQR)	-	4 (2 to 6)	0 (0 to 2)	<0.0001
Baseline SYNTAX score, median (IQR)	22 (15 to 29)	26.0 (20.0 to 32.5)	18.0 (12.0 to 23.0)	<0.0001
Residual SYNTAX score, median (IQR)	-	26.0 (20.0 to 32.5)	18.0 (12.0 to 23.0)	<0.0001
Total number of lesions, median (IQR)	45 (12.8)	3 (3 to 4)	2 (2 to 3)	<0.0001
Left main coronary artery disease (%)	31.9 ± 9.6	28 (20.6)	12 (9.2)	0.009
Left ventricular ejection fraction, mean (SD), %[c]	243 (77.1) 72 (22.9)	31.1 ± 9.5	33.5 ± 10.4	0.07
Viability test (%)	7 (4-10)			
CMR		109 (80.1)	101 (77.7)	-
DSE		27 (19.9)	29 (22.3)	
Number of viable segments (IQR)		6 (4-10)	7 (5-11)	0.29

[a] Race as self-reported by participants using options defined by the investigators.

[b] British Cardiovascular Intervention Society jeopardy score (BCIS-JS) as reported by angiography core laboratory.

[c] Baseline left ventricular ejection fraction measured by the blinded echocardiography core laboratory

[d] P-value denotes comparison between Incomplete vs complete anatomical revascularization groups

BCIS denotes British Cardiovascular Intervention Society, CABG coronary artery bypass grafting, CCS Canadian Cardiovascular Society, CMR cardiovascular magnetic resonance imaging, CRT cardiac resynchronization therapy, CTO chronic total occlusion, DSE dobutamine stress echocardiography, ICD implantable cardioverter defibrillator, IQR interquartile range, NYHA New York Heart Association, PCI percutaneous coronary intervention, RI_{myo} Myocardial revascularization index.

Table S11 – Primary and secondary outcomes by viability guided completeness of revascularization (25% late gadolinium enhancement threshold)

	Optimal medical therapy§ (Reference)	Complete viability guided revascularization§ (RI_{myo} >86.7)	Hazard / Odds ratio* (95% CI)	p-value	Incomplete viability guided revascularization§ (RI_{myo} ≤86.7)	Hazard / Odds ratio* (95% CI)	p-value
All-cause death or hospitalization for heart failure	134 (38.0)	46 (34.8)	1.02 (0.72 to 1.44)	0.93	45 (33.8)	0.79 (0.56 to 1.11)	0.17
All-cause death	115 (32.6)	40 (30.3)	1.03 (0.71 to 1.50)	0.88	36 (27.0)	0.71 (0.48 to 1.04)	0.08
Cardiovascular death	88 (24.9)	27 (20.5)	0.88 (0.56 to 1.37)	0.56	26 (19.5)	0.66 (0.42 to 1.03)	0.07
Hospitalization for heart failure	54 (15.3)	15 (11.4)	0.80 (0.45 to 1.44)	0.46	18 (13.5)	0.76 (0.44 to 1.31)	0.33
Improvement in left ventricular ejection fraction	101 (50.2)	38 (48.1)	0.94 (0.54 to 1.65)	0.83	46 (55.4)	1.02 (0.58 to 1.77)	0.96

CI – confidence interval; HR-hazard ratio; RI_{myo} – Myocardial revascularization index
* Adjusted Hazard ratios calculated with OMT group as reference
§ Event rate - n(%)

Table S12 – Change in 2-year summary KCCQ score by anatomical and viability-guided completeness of revascularization

	KCCQ* at baseline	KCCQ* at 2 years	Adjusted** difference in means at 2 years (95% CI)	P-value
Anatomical completeness of revascularization (RI_{coro})				
OMT	63.0 (24.9)	70.5 (24.7)	Reference	
Incomplete anatomical revascularization (RI_{coro} ≤66.7%)	57.8 (26.0)	65.8 (26.2)	-1.1 (-6.1 to 3.9)	0.66
Complete anatomical revascularization (RI_{coro} >66.7%)	65.8 (22.6)	78.1 (22.9)	4.6 (-0.2 to 9.5)	0.06
Viability guided completeness of revascularization (RI_{myo})				
OMT	63.0 (24.9)	70.5 (24.7)	Reference	
Incomplete viability guided revascularization (RI_{myo} ≤86.7%)	60.6 (26.7)	69.8 (26.3)	0.1 (-4.8 to 5.0)	0.97
Complete viability guided revascularization (RI_{myo} >86.7%)	63.2 (22.1)	75.0 (24.0)	3.9 (-0.9 to 8.6)	0.11

CI – confidence interval; KCCQ – Kansas City Cardiomyopathy Questionnaire; OMT – optimal medical therapy; RI_{coro} – Coronary revascularization index; RI_{myo} – Myocardial revascularization index

Data are reported as mean (standard deviation); * KCCQ overall summary score; ** Adjusted for pre-specified adjustment variables and baseline KCCQ overall summary score.