



ΔΗΜΟΚΡΙΤΕΙΟ
ΠΑΝΕΠΙΣΤΗΜΙΟ
ΘΡΑΚΗΣ

DEMOCRITUS
UNIVERSITY
OF THRACE

Percutaneous Revascularization for Ischemic Left Ventricular Dysfunction REVIVED-BCIS2 STUDY

Κουτρούλος Μάριος-Βασίλειος
Ειδικευόμενος Καρδιολογίας
Πανεπιστημιακή Καρδιολογική Κλινική
Π.Γ.Ν.Αλεξανδρούπολης
Διευθ. Καθ. Τζιακάς Δημήτριος



NO CONFLICT OF INTERESTS

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

OCTOBER 13, 2022

VOL. 387 NO. 15

Percutaneous Revascularization for Ischemic Left Ventricular
Dysfunction

Divaka Perera, M.D., Tim Clayton, M.Sc., Peter D. O'Kane, M.D., John P. Greenwood, Ph.D.,
Roshan Weerackody, Ph.D., Matthew Ryan, Ph.D., Holly P. Morgan, M.B., B.Ch., Matthew Dodd, M.Sc.,
Richard Evans, B.A., Ruth Canter, M.Sc., Sophie Arnold, M.Sc., Lana J. Dixon, Ph.D., Richard J. Edwards, Ph.D.,
Kalpa De Silva, Ph.D., James C. Spratt, M.D., Dwayne Conway, M.D., James Cotton, M.D.,
Margaret McEntegart, Ph.D., Amedeo Chiribiri, Ph.D., Pedro Saramago, Ph.D., Anthony Gershlick, M.D.,
Ajay M. Shah, M.D., Andrew L. Clark, M.D., and Mark C. Petrie, M.D., for the REVIVED-BCIS2 Investigators*

BACKGROUND

Randomized Control Trial	Population	Treatment Arms	Outcomes	Considerations
HEART (2011)	138 patients with persistent heart failure for >6 weeks, receiving diuretics, evidence of CAD on angiography or prior MI, with LVEF <25%, and at least 5 viable segments with reduced contractility	Invasive (angiography and revascularization with CABG or PCI) vs. conservative	After a median follow-up of 59 months, 37% in conservative strategy died and 38% in the invasive strategy died. No difference in quality of life at 6 months. Study was underpowered to detect differences due to early termination.	Study terminated as enrollment was low (only 138 of planned 800 patients)
PARR-2 (2007)	430 patients with EF ≤ 35% and suspected CAD	PET-guided care (revascularization if significant viability) vs standard care	At 1-year follow-up, no difference in composite primary endpoint of cardiac death/MI : 37% in PET arm vs. 36% in standard care.	After longer follow-up (5 years), PET group did not significantly reduce cardiac outcomes
COURAGE (2007)	2,287 patients with stable CAD and ≥70% stenosis in at least one coronary artery and evidence of myocardial ischemia	PCI with optimal medical therapy (OMT) vs OMT alone	After a median of 4.6 years, no difference in composite primary endpoint of cardiac death or non-fatal MI	Drug-eluting stents not approved until the final 6 months of the study
STICH (2011)	1,212 patients with EF ≤ 35% and CAD amenable to CABG. 85% pts were NYHA Class II or III	CABG vs. optimal medical therapy	At a median follow-up of 56 months: <ul style="list-style-type: none"> • No difference in rate of death (1° outcome) from any cause with CABG vs. medical therapy alone (HR 0.86; 95% CI 0.72-1.05; p = 0.12) • Rate of death from CV causes (2° outcome) was lower in patients assigned to CABG (HR 0.81; 95% CI 0.66-1.00, p = 0.05) • Rate of death from any cause or hospitalization for CV causes (2° outcome) was lower in CABG group (HR 0.74; 95% CI 0.64-0.85; p <0.001) 	
STICH Extension Study (2016)	1,212 patients with EF ≤ 35% and CAD amenable to CABG, evaluated over a 10-year period	CABG vs. optimal medical therapy	At a median follow-up of 9.8 years, there were lower rates of death from any cause (HR 0.85; 95%CI 0.73-0.97; p = 0.02), death from CV causes, and death from any cause or hospitalization in patients who underwent CABG in addition to medical therapy vs. medical therapy alone.	Younger population (mean age 60 years) - analysis showed that effect of CABG vs. medical therapy on all-cause mortality diminished with increasing age (p-interaction = 0.062)
ISCHEMIA (2020)	5,179 patients with stable CAD and stress testing showing moderate or severe reversible ischemia	Early revascularization (≤30 days; PCI or CABG) vs optimal medical therapy alone	After a median of 3.2 years, no difference in composite of CV death, MI, or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest	Did not meet target enrollment for original endpoint of CVD mortality or MI. Possible attenuation of effect from high crossover rate (21%)

Recommendations on revascularizations in patients with chronic heart failure and systolic left ventricular dysfunction (ejection fraction $\leq 35\%$)

Recommendations	Class ^a	Level ^b
In patients with severe LV systolic dysfunction and coronary artery disease suitable for intervention, myocardial revascularization is recommended. ^{81,250}	I	B
CABG is recommended as the first revascularization strategy choice in patients with multivessel disease and acceptable surgical risk. ^{68,81,248,255}	I	B
In patients with one- or two-vessel disease, PCI should be considered as an alternative to CABG when complete revascularization can be achieved.	IIa	C
In patients with three-vessel disease, PCI should be considered based on the evaluation by the Heart Team of the patient's coronary anatomy, the expected completeness of revascularization, diabetes status, and comorbidities.	IIa	C
LV aneurysmectomy during CABG should be considered in patients with NYHA class III/IV, large LV aneurysm, large thrombus formation, or if the aneurysm is the origin of arrhythmias.	IIa	C
Surgical ventricular restoration during CABG may be considered in selected patients treated in centres with expertise. ^{252–254,256,257}	IIb	B

CABG = coronary artery bypass grafting; LV = left ventricular; NYHA = New York Heart Association; PCI = percutaneous coronary intervention.
^aClass of recommendation.
^bLevel of evidence.

7. Revascularization in SIHD

7.1. Revascularization to Improve Survival in SIHD Compared With Medical Therapy

Recommendations for Revascularization to Improve Survival in SIHD Compared With Medical Therapy
 Referenced studies that support the recommendations are summarized in [Online Data Supplement 10](#).

COR	LOE	Recommendations
Left ventricular dysfunction and multivessel CAD		
1	B-R	1. In patients with SIHD and multivessel CAD appropriate for CABG with severe left ventricular systolic dysfunction (left ventricular ejection fraction $<35\%$), CABG is recommended to improve survival. ^{1,2}
2a	B-NR	2. In selected patients with SIHD and multivessel CAD appropriate for CABG and mild-to-moderate left ventricular systolic dysfunction (ejection fraction $35\%–50\%$), CABG (to include a left internal mammary artery [LIMA] graft to the LAD) is reasonable to improve survival. ³⁻⁸

REVIVED-BCIS2 Trial

was a prospective, multicenter, randomized, open label trial. Although the trial was open label, researchers in charge of adjudication and analyses were blinded. Randomization was stratified by center in a 1:1 fashion.

- A presumed mechanism for the benefit of revascularization is the reversal of myocardial hibernation. **Myocardial hibernation** is an adaptive response that favors cardiomyocyte survival over contractile function.
- Whether revascularization by **PCI** can improve event-free survival and left ventricular function in patients with severe ischemic left ventricular systolic dysfunction, as compared with **optimal medical therapy** alone.

Enrollment Criteria

INCLUSION CRITERIA	<ul style="list-style-type: none">- LVEF \leq 35% by echo or cMRI- Extensive CAD as defined by BCIS jeopardy score \geq 6*- Viability in at least four dysfunctional myocardial segments that can be revascularised by PCI	<ul style="list-style-type: none">- Acute MI within 4 weeks- Acute decompensated heart failure requiring inotropes, ventilatory support, or circulatory support- Ventricular arrhythmia or appropriate defibrillator shock within 72 hours of randomization- Valve disease requiring immediate intervention- Age $<$ 18 years	EXCLUSION CRITERIA
--------------------	--	---	--------------------

* In patients without prior coronary artery bypass grafts, a score of \geq 6 requires the presence of left main coronary artery disease, proximal left anterior descending coronary artery disease, proximal disease in a dominant circumflex artery or multivessel coronary disease. A score of 12 indicates proximal disease in all three major epicardial coronary arteries.

RE  **IVED**

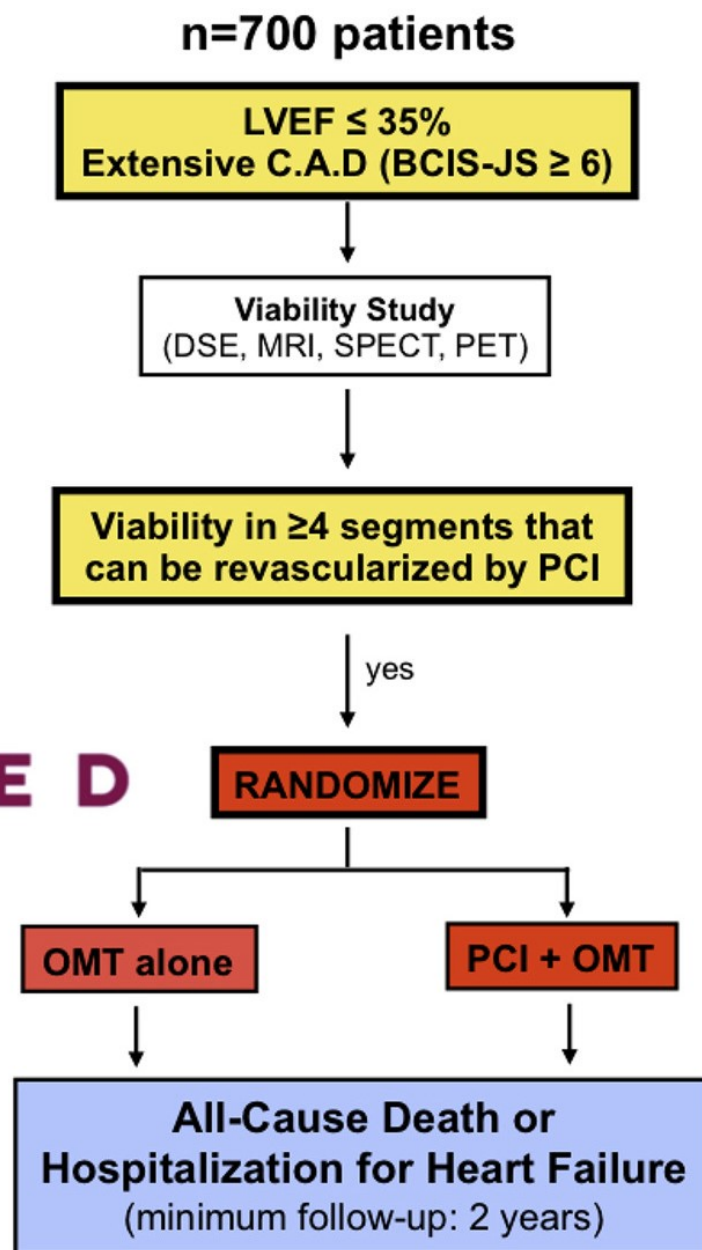


Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	PCI (N=347)	Optimal Medical Therapy (N=353)
Age — yr	70.0±9.0	68.8±9.1
Male sex — no. (%)	302 (87)	312 (88)
Race — no. (%)†		
White	306 (88)	328 (93)
Asian	32 (9)	17 (5)
Black	3 (1)	3 (1)
Mixed, other, or not reported	6 (2)	5 (1)
Body-mass index‡	28.4±5.5	28.7±5.4
Hypertension — no./total no. (%)	184/347 (53)	207/352 (59)
Diabetes — no. (%)	136 (39)	153 (43)
Current or previous smoker — no. (%)	243 (70)	267 (76)
Previous myocardial infarction — no. (%)	175 (50)	197 (56)
Previous PCI — no. (%)	66 (19)	76 (22)
Previous CABG — no. (%)	12 (3)	22 (6)
NYHA functional class — no./total no. (%)§		
I or II	265/345 (77)	248/350 (71)
III or IV	80/345 (23)	102/350 (29)
CCS angina class — no./total no. (%)¶		
No angina	228/346 (66)	236/351 (67)
I or II	111/346 (32)	107/351 (30)
III	7/346 (2)	8/351 (2)
Left ventricular ejection fraction — %	27.0±6.6	27.0±6.9
Coronary artery disease characteristic		
Median BCIS jeopardy score (IQR)**	10 (8–12)	10 (8–12)
Left main coronary artery disease — no./total no. (%)	50/346 (14)	45/352 (13)
Three-vessel coronary artery disease — no./total no. (%)	133/346 (38)	148/352 (42)
Two-vessel coronary artery disease — no. (%)	178 (51)	166 (47)
Median NT-proBNP — pg/ml (IQR)	1376 (697–3426)	1461 (712–3365)

* Plus-minus values are means ±SD. Percentages may not total 100 because of rounding. CABG denotes coronary-artery bypass grafting, IQR interquartile range, NT-proBNP N-terminal pro-B-type natriuretic peptide, and PCI percutaneous coronary intervention.

† Race was reported by the patient.

‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.

§ The New York Heart Association (NYHA) functional class ranges from I (no symptoms) to IV (symptoms at rest or on minimal activity).

¶ In the Canadian Cardiovascular Society (CCS) grading of angina pectoris, grade I denotes symptoms only with strenuous or prolonged exertion; grade II, slight limitation of ordinary activity; and grade III, marked limitation of ordinary physical activity.

|| The baseline left ventricular ejection fraction was assessed by echocardiography or cardiovascular magnetic resonance imaging; the values were reported by the recruiting center.

** 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).

OUTCOMES

Primary Outcome:

- Composite of death from any cause or heart failure hospitalization

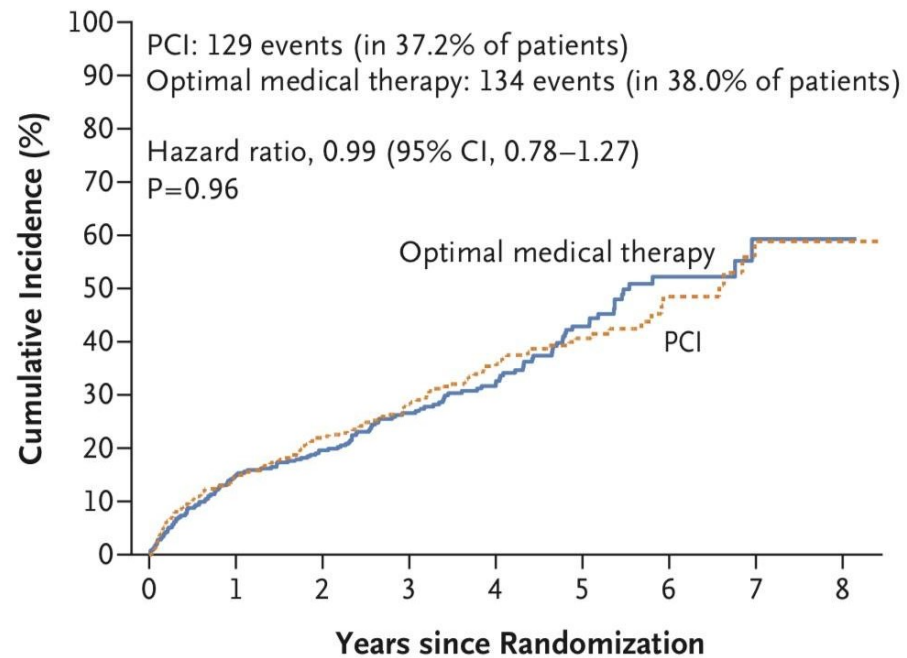
Secondary Outcomes:

Major

- LVEF at 6 and 12 months as measured by echocardiography
- Kansas City Cardiomyopathy Questionnaire (KCCQ) score
- EuroQol Group 5-Dimensions 5-Level Questionnaire score
- NYHA functional class

Other

- All-cause mortality
- HF hospitalization
- Cardiovascular mortality
- Acute MI



No. at Risk

PCI	347	295	262	179	130	80	32	14	3
Optimal medical therapy	353	299	276	191	142	82	33	10	1

Figure 1. Primary Outcome of Death from Any Cause or Hospitalization for Heart Failure.

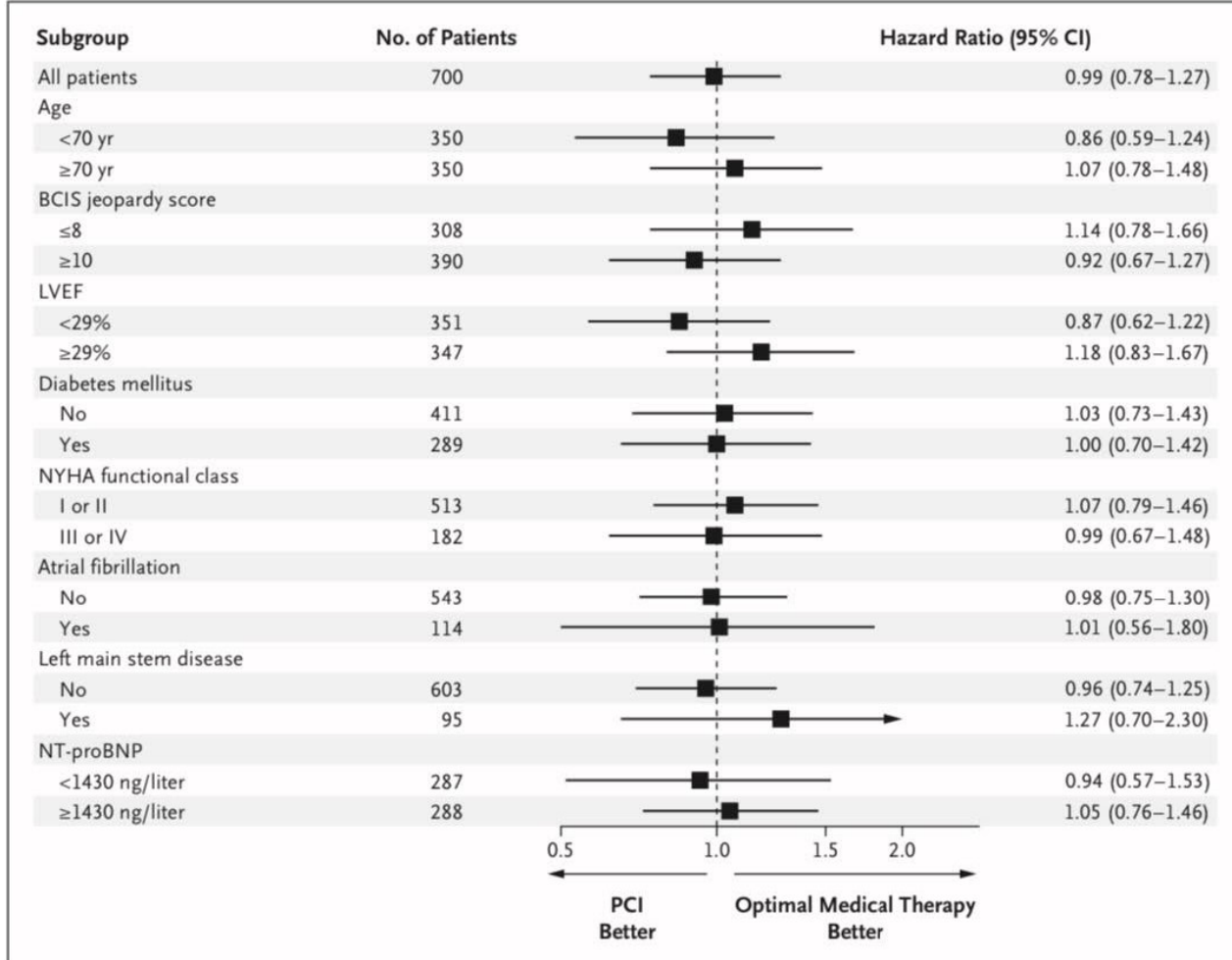
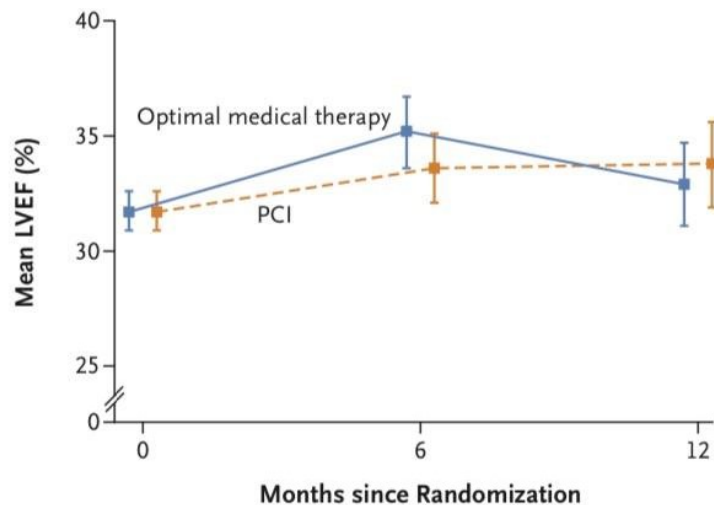


Figure 2. Subgroup Analyses of the Primary Outcome.

Shown is a forest plot of hazard ratios for a primary-outcome event according to prespecified subgroups. The British Cardiovascular Intervention Society (BCIS) jeopardy score ranges from 0 to 12, with higher scores indicating greater extent of disease. The dashed vertical line represents the null hypothesis of no treatment effect. LVEF denotes left ventricular ejection fraction, NT-proBNP N-terminal pro-B-type natriuretic peptide, and NYHA New York Heart Association.

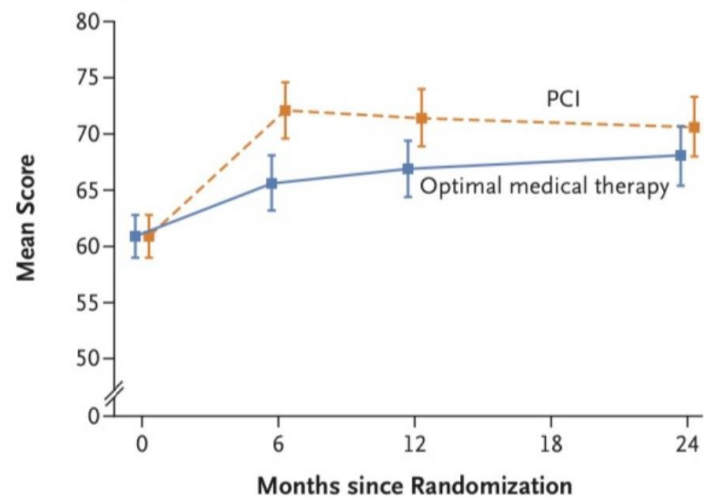
A Echocardiographic Estimates of LVEF



No. of Patients

PCI	264	276	262
Optimal medical therapy	276	264	267

B KCCQ Overall Summary Score



No. of Patients

PCI	319	270	268	228
Optimal medical therapy	318	285	268	228

Table 2. Primary and Secondary Outcomes.

Outcome	PCI (N=347)	Optimal Medical Therapy (N=353)	Treatment Effect (95% CI)*
Primary outcome			
Death from any cause or hospitalization for heart failure — no. (%)†	129 (37.2)	134 (38.0)	0.99 (0.78–1.27)
Secondary outcomes‡			
Components of the primary outcome			
Death from any cause	110 (31.7)	115 (32.6)	0.98 (0.75–1.27)
Hospitalization for heart failure§	51 (14.7)	54 (15.3)	0.97 (0.66–1.43)
Death from cardiovascular causes — no. (%)¶	76 (21.9)	88 (24.9)	0.88 (0.65–1.20)
Acute myocardial infarction — no. (%)	37 (10.7)	38 (10.8)	1.01 (0.64–1.60)
Periprocedural — no. (%)**	14 (37.8)	0	
Spontaneous — no. (%)**	18 (48.7)	33 (86.8)	
Sudden death — no. (%)**††	5 (13.5)	5 (13.2)	
Unplanned revascularization — no. (%)‡‡	10 (2.9)	37 (10.5)	0.27 (0.13–0.53)
PCI — no. (%)§§	9 (90.0)	29 (78.4)	
CABG — no. (%)§§	1 (10.0)	8 (21.6)	
Major bleeding — no. (%)			
At 1 yr	10/319 (3.1)	2/316 (0.6)	4.95 (1.09–22.43)
At 2 yr	10/292 (3.4)	7/290 (2.4)	1.42 (0.55–3.68)



CONCLUSIONS

- *The addition of revascularization by PCI to optimal medical therapy in patients with severe LV dysfunction and coronary artery disease but with viable myocardium did not significantly improve overall mortality or rates of heart failure hospitalization.*
- *PCI with OMT was not superior to OMT alone in improving LV systolic function, NYHA functional class, or quality of life.*

LIMITATIONS

- Few patients with anginal symptoms (66% with no angina and 32% with CCS angina class I/II)
- Concordance between coronary arteries revascularized by PCI and viable myocardial segments has not been determined yet.
- The extent of CAD, in terms of anatomical location, stenosis severity, degree of ischemia, and functional significance, in the trial is not known.
- Longer-term follow-up data is needed

REVIVED VS STITCH

- REVIVED had higher rate of MRA and ARNIs use
- REVIVED had higher proportion of patients with cardiac devices
- Mean age differs about 10 years
- MR at 28% in intervention groups at both studies, OMT at REVIVED better than STITCH
- Time since diagnosis of Reduced LVEF not mentioned

A close-up photograph of a computer keyboard. The central focus is a large, rectangular blue key with the words "Thank You!" printed in white, sans-serif font. The key is slightly raised and has rounded corners. Surrounding it are several other white keys with black text: a key with a hyphen and curly brace, a key with a tilde and curly brace, a key with a vertical bar, and a key with the word "alt". The keyboard is set against a light-colored, textured background.

Thank You!