Viability and Outcomes With Revascularization or Medical Therapy in Ischemic Ventricular Dysfunction

A Prespecified Secondary Analysis of the REVIVED BCIS2 Trial

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REVascularisation for Ischaemic VEntricular Dysfunction

(REVIVED-BCIS2)

trial REVIVED-BCIS2

In the Revascularization for Ischemic Ventricular Dysfunction (REVIVED-BCIS2) trial, percutaneous coronary intervention (PCI) did not improve outcomes for ischemic left ventricular dysfunction. patients with

Does myocardial viability testing identify patients with ischemic left ventricular dysfunction who benefit from percutaneous coronary intervention?

- ✓ Myocardial viability tests are thought to identify patients with ischemic cardiomyopathy who benefit from revascularization.

- These tests typically characterize myocardial tissue into 3 distinct states:

-Healthy myocardium contracting normally at rest

-viable or hibernating myocardium that contracts abnormally at rest where improvement in function is expected

-nonviable scarred myocardium

that contracts abnormally at rest but where improvement is not expected

Historically, viability has been regarded in a binary manner, and when classified in this way, observational, nonrandomized data suggest that patients with extensive myocardial viability might experience left ventricular recovery and improved survival after revascularization

However, when treatment was by random allocation in the Surgical Treatment for Ischemic Heart Failure (STICH) trial, no interaction was found between viability status and the effect of coronary artery bypass graft surgery.

We recently completed the Revascularization for Ischemic Ventricular Dysfunction (REVIVED-BCIS2) trial

a randomized comparison of

- ✓ percutaneous coronary intervention (PCI)
- ✓ optimal medical therapy (OMT) alone

patients with ischemic cardiomyopathy who had undergone mandatory viability testing.

Methods

REVIVED-BCIS2 was a prospective, multicenter, open-label randomized

clinical trial, the design and preliminary results of which have been published previously

Participants for this subgroup analysis were recruited from 40 sites in the United Kingdom between August 28, 2013, and March 19, 2020

Participants were eligible for enrollment

- a left ventricular ejection fraction less than or equal to 35%
- extensive coronary artery disease (British Cardiovascular Intervention Society jeopardy score ≥6)
- evidence of myocardial viability.

- The qualifying threshold for viability was defined as at least 4myocardial segments that were dysfunctional at rest,

Key exclusion criteria

- ✓ Myocardial infarction fewer than 4 weeks before randomization
- ✓ decompensated heart failure
- ✓ sustained ventricular tachycardia or ventricular fibrillation less than 72 hours before randomization.

Participants were randomized in a 1:1 ratio to a strategy of either PCI plus OMT(PCI group) or OMT alone(OMT group) via an online randomization system(Sealed Envelope).

Viability assessment

could be obtained by

- cardiovascular magnetic resonance (CMR) imaging
- dobutamine stress echocardiography
- single-photon emission computed tomography or positron emission tomo

graphy.

For this analysis, participants who had viability assessed with CMR imaging or

Do butamine stress echocardiography were included ,with CMR imaging data used when both were available. Given the small number of participants assessed only by single-photon emission computed tomography or positron emission tomography,

these participants were excluded

Table 1. Characterization of Myocardial Viability

Viability definition	Wall motion[a]	CMR-transmurality of enhancement	DSE-contractile reserve[b]
Segmental classification by CMR or DSE			
Normal	Normal	NA	NA
Viable	Dysfunctional	≤25%[c]	Present
Nonviable	Dysfunctional	>25%[c]	Absent
Participant-level classification by CMR[d]			
Scar burden (% LV)	Each segment was classified by transmural extent of LGE as 0%, 1%-25%, 26%-50%, 51%-75%, or 76%-100%.[10] LGE was summed across all segments and expressed as a proportion of the LV.[e]		

Abbreviations: CMR, cardiovascular magnetic resonance imaging; DSE, dobutamine stress echocardiography; LGE, late gadolinium enhancement; LV, left ventricular myocardial volume; NA, not applicable.

[a] Myocardial wall motion was graded on a 5-point scale as normal, hypokinetic, akinetic, dyskinetic, or aneurysmal.

[b] Contractile reserve was defined as an improvement in wall motion score greater than or equal to 1 or greater than or equal to 2 if the segment was dyskinetic at rest.

[c] Sensitivity analyses were performed for an LGE threshold of less than or equal to 50%.

[d] When calculating the extent of viable and nonviable myocardium at a participant level, segments with a nonischemic scar were excluded from the numerator; the denominator was all segments.

[e] Segmental LGE was calculated as the midpoint in each range (for instance, 13% for the range 1%-25%).

Results

Of the 700 participants randomized in the REVIVED-BCIS2 trial, 610 were included in this pre specified analysis,

295 assigned to the PCI group and 315 to the OMT group

The mean (SD) age of the participants was 69.3 (9.0) years. In the PCI group, 258 (87%) were male, and 37 (13%) were female; in the OMT group, 277 (88%) were male, and 38 (12%) were female

Participants were asked to select their ethnicity as Asian, Black, White,

other

The primary outcome

was a composite

- all-cause death
- hospitalization for heart failure

during a minimum follow-up period of 24 months.

Secondary outcomes

were all cause death, cardiovascular death, hospitalization for heart failure, and improvement in left ventricular function at 6 months

A Cox proportional hazards model was used to assess the association between the extent of

viable myocardium,

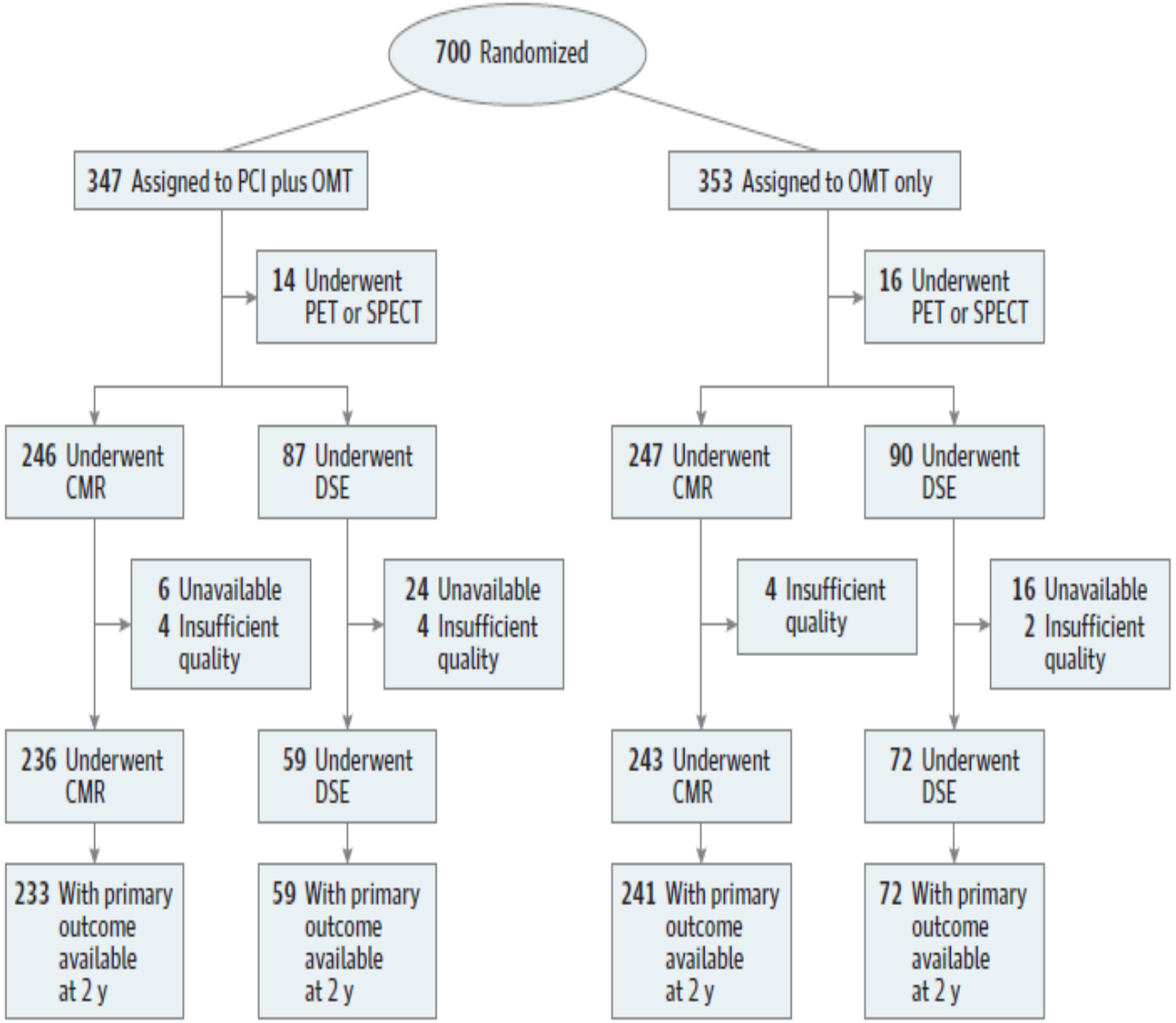
nonviable myocardium,

scar burden

the primary outcome across the whole population,

adjusted for baseline factors, including age, sex, previous heart failure hospitalization, presence of diabetes, chronic kidney failure, left ventricular ejection fraction, extent of coronary disease, and the modality of viability testing.

Figure 1. CONSORT Diagram Showing Flow of Participants Through the Study



CMR indicates cardiovascular magnetic resonance imaging; DSE, dobutamine stress echocardiography; OMT, optimal medical therapy; PCI, percutaneous coronary intervention; PET, positron emission tomography; and SPECT, single-photon emission computed tomography.

Table 2. Demographic and Clinical Characteristics of the Participants at Baseline[a]

Characteristic	PCI (n = 295)	OMT (n = 315)
Age, mean (SD), y	69.8 (9.1)	68.8 (8.9)
Sex, No. (%)		
Male	258 (87)	277 (88)
Female	37 (13)	38 (12)
Diabetes, No. (%)	116 (39)	134 (43)
Race and ethnicity, No. (%)[b]		
Asian	26 (9)	13 (4)
Black	3 (1)	3 (1)
White	261 (88)	296 (94)
Other or not reported	5 (2)	3 (1)
History of myocardial infarction, No. (%)	146 (49)	175 (56)
Hospitalization for heart failure in prior 2 y, No. (%)	104 (36)	102 (32)
Cardiac medication, No. (%)		
RAAS inhibitor	258 (87)	282 (90)
β-Blocker	266 (90)	285 (90)
Mineralocorticoid receptor antagonist	153 (52)	151 (48)
BCIS jeopardy score, median (IQR)[c]	10 (8-12)	10 (8-12)
ICD ± CRT at randomization, No. (%)	65 (22)	58 (18)
Left main coronary artery disease, No. (%)	46 (16)	40 (13)
Left ventricular ejection fraction, mean (SD), %[d]	32 (10)	32 (10)
Viability test, No. (%)[e]		
CMR	236 (80)	243 (77)
DSE	59 (20)	72 (23)
Extent of viable myocardium, median (IQR), %	29 (18-53)	29 (12-47)
Extent of nonviable myocardium, median (IQR), %	29 (12-41)	29 (12-41)
Scar burden, median (IQR), %	19 (9-28)	18 (9-28)

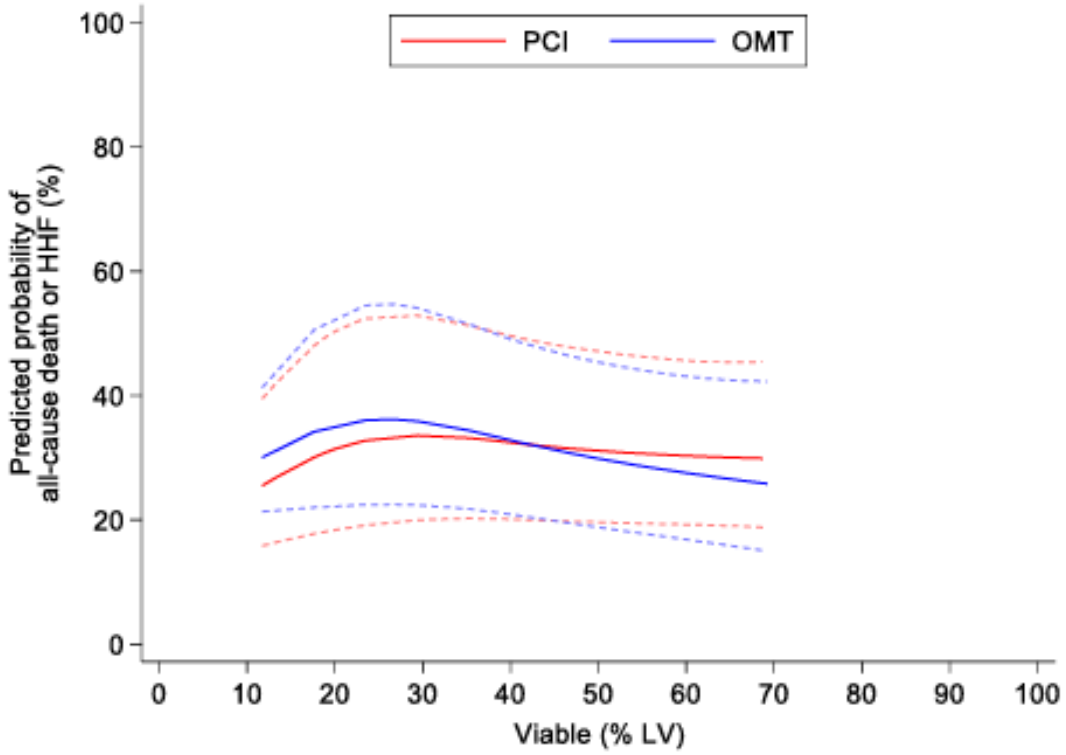
Abbreviations: BCIS, British Cardiovascular Intervention Society; CMR, cardiovascular magnetic resonance imaging; CRT, cardiac resynchronization therapy; DSE, dobutamine stress echocardiography; ICD, implantable cardioverter-defibrillator; OMT, optimal medical therapy; PCI, percutaneous

eTable 2. Primary and clinical secondary outcomes*

	PCI group (n=295)	OMT group (n=315)	Hazard ratio (95% CI)	p-value
All-cause death or hospitalisation for heart failure	107 (36.3)	114 (36.2)	0.99 (0.76 to 1.29)	0.93
All-cause death	91 (30.9)	98 (31.1)	0.96 (0.72 to 1.28)	0.79
Cardiovascular death	64 (21.7)	75 (23.8)	0.88 (0.63 to 1.23)	0.47
Hospitalisation for heart failure	37 (12.5)	47 (14.9)	0.84 (0.54 to 1.29)	0.42
Acute myocardial infarction Periprocedural Spontaneous Sudden death	31 (10.5) 14 (45.2) 15 (48.4) 2 (6.5)	34 (10.8) 0 (0) 30 (88.2) 4 (11.8)	0.99 (0.61 to 1.61)	0.96
Unplanned revascularization PCI CABG	10 (3.4) 9 (90.0) 1 (10.0)	34 (10.8) 26 (76.5) 8 (23.5)	0.30 (0.15 to 0.61)	0.0003

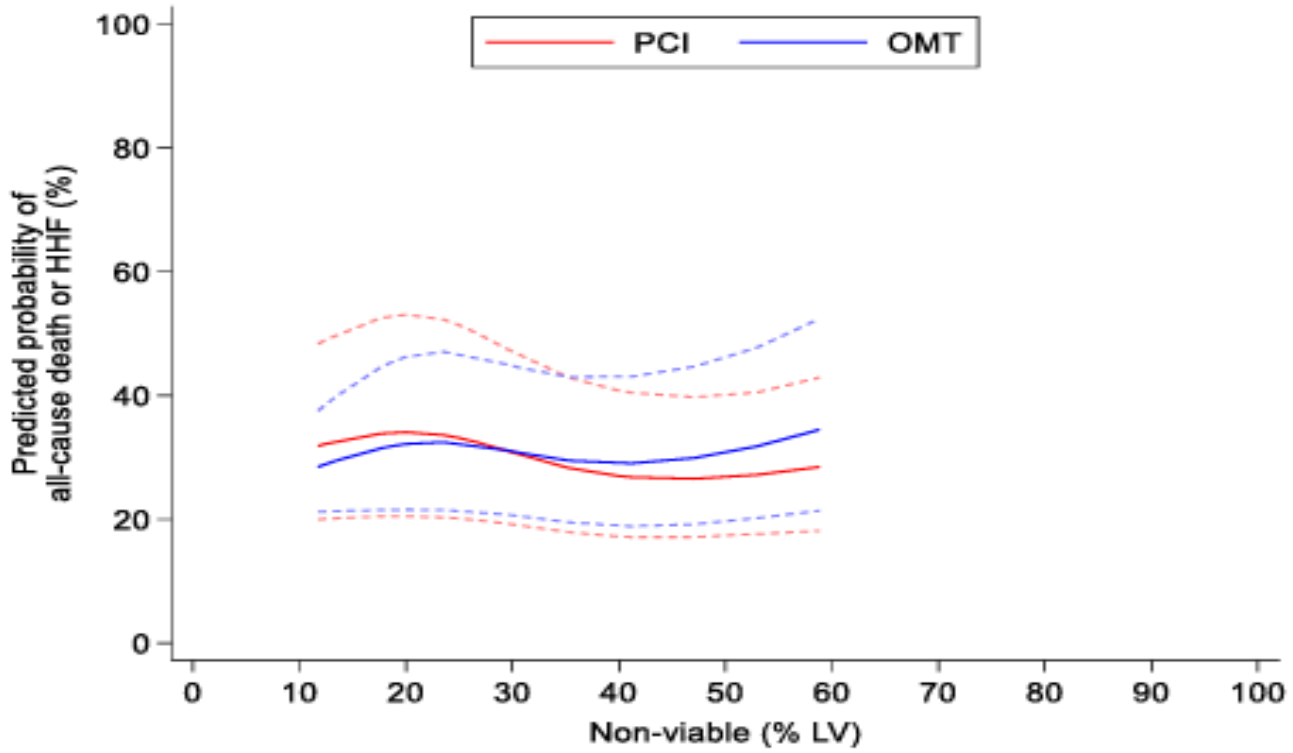
eFigure 1. Relationship between viability characteristics and the primary outcome by treatment assignment

Figure e1A – The extent of viable myocardium (continuous)



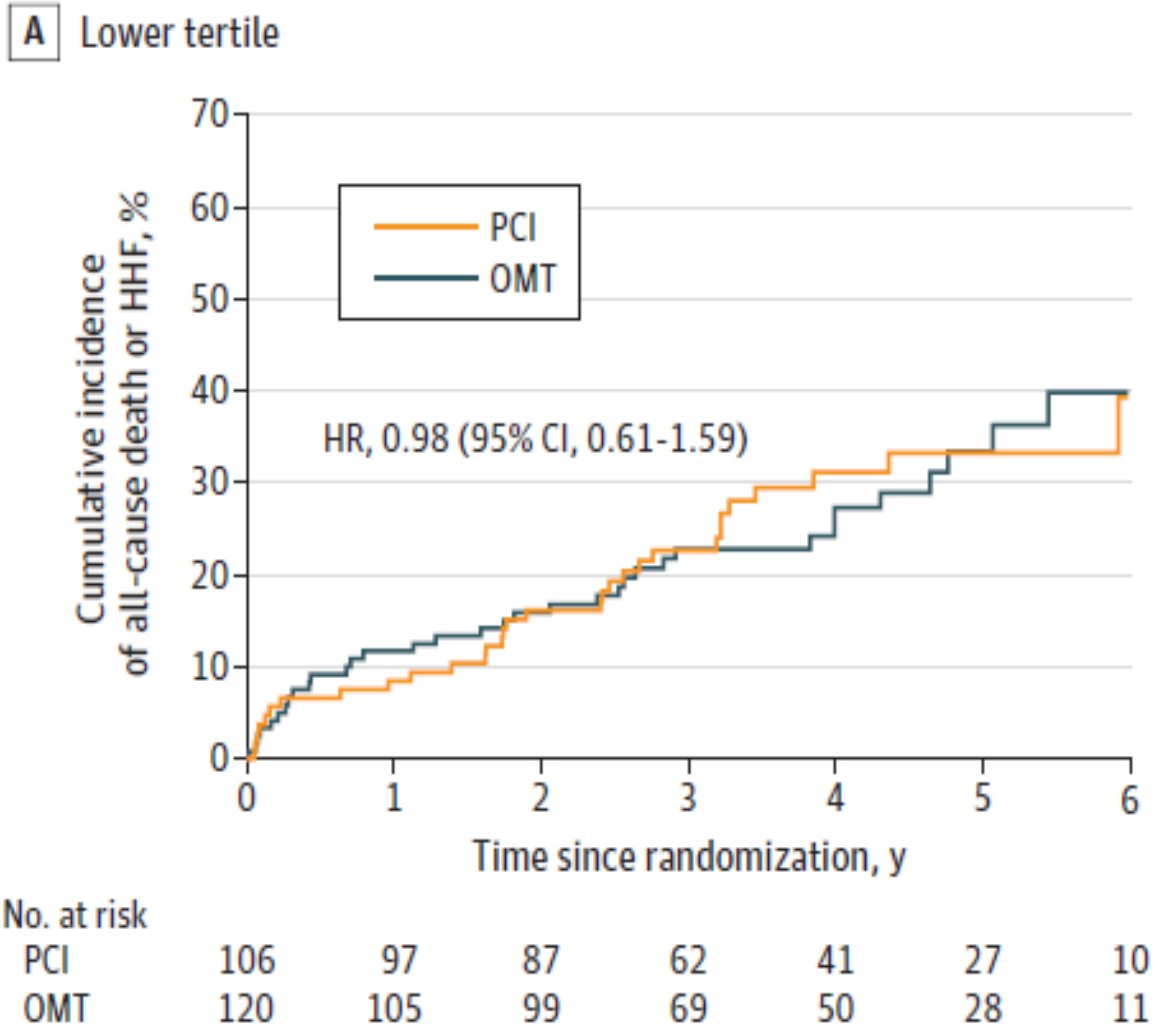
OMT – optimal medical therapy. PCI – percutaneous coronary intervention. Data are presented as cubic splines – these were not specified in the statistical analysis plan but are presented for clarity of visualisation of the data. Dotted lines represent 95% confidence intervals.

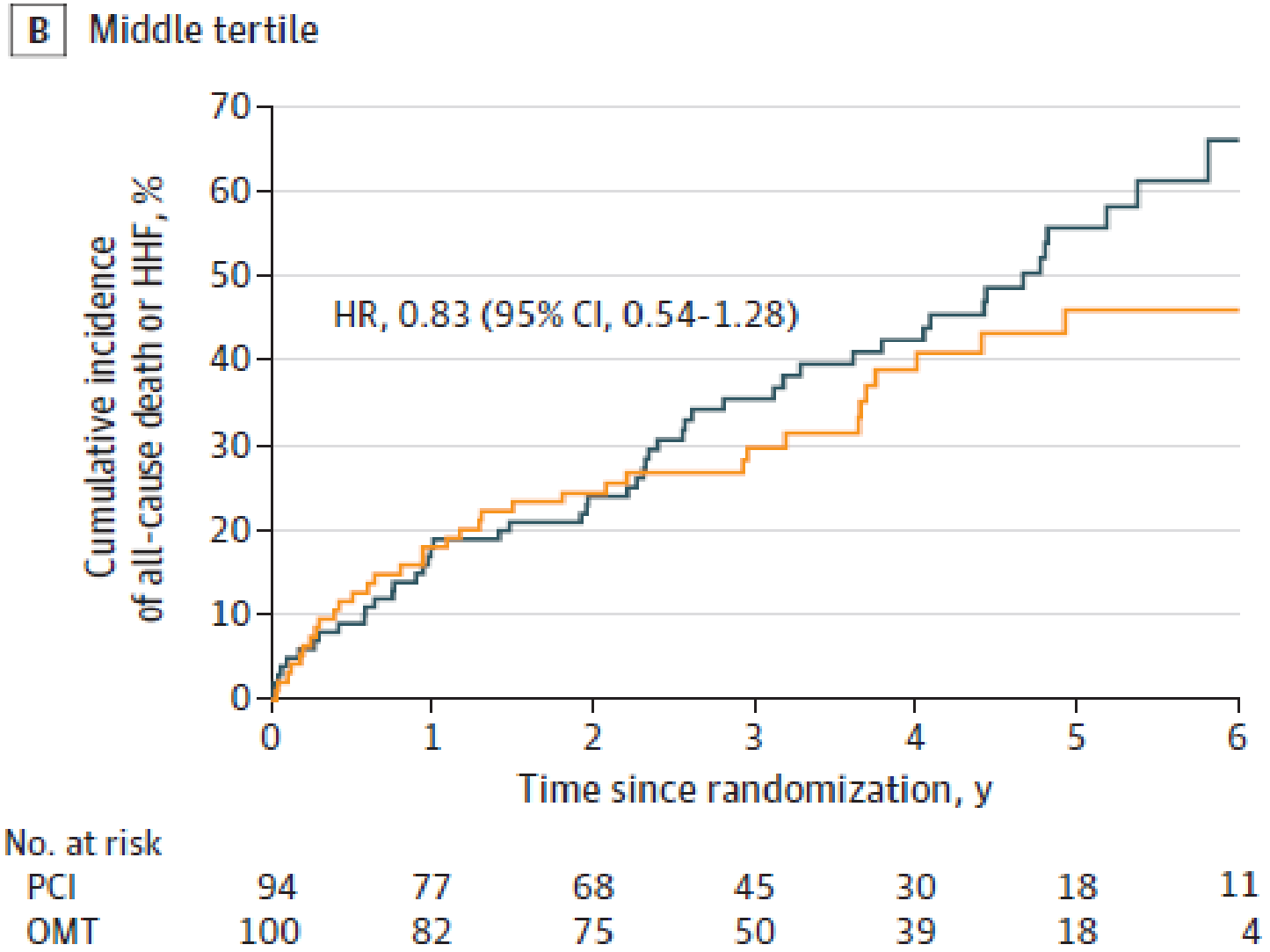
Figure e1B – The extent of non-viable myocardium (continuous)

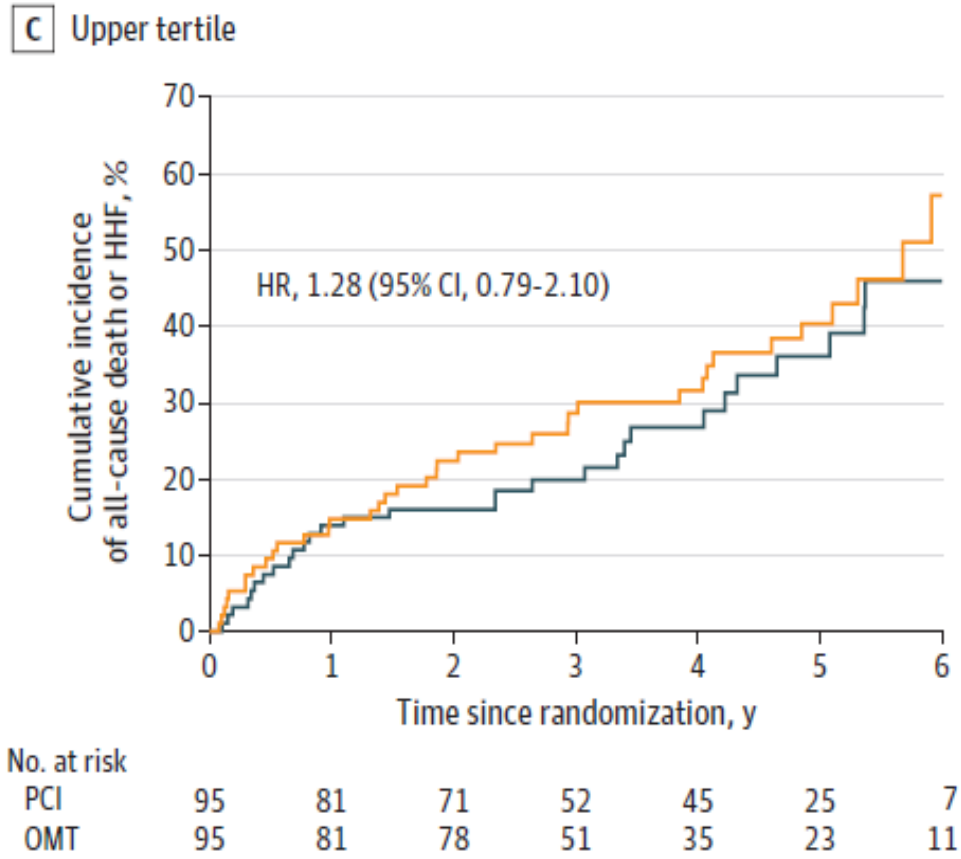


OMT – optimal medical therapy. PCI – percutaneous coronary intervention. Data are presented as cubic splines – these were not specified in the statistical analysis plan but are presented for clarity of visualisation of the data. Dotted lines represent 95% confidence intervals.

Figure 2. All-Cause Death or Hospitalization for Heart Failure (HHF) in Participants Assigned to Percutaneous Coronary Intervention (PCI) or Optimal Medical Therapy (OMT), Stratified by Viability Tertile

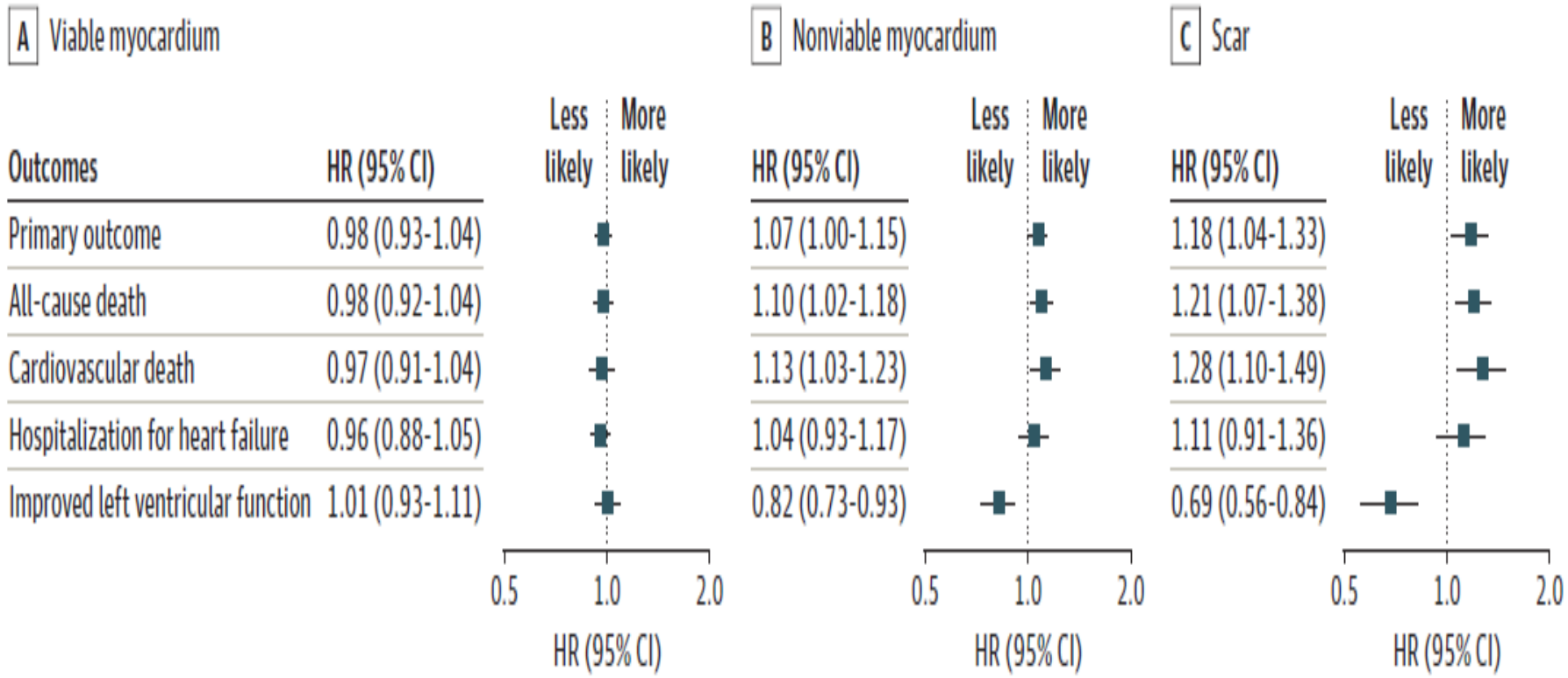



B
Middle tertile
Cumulative incidence of all-cause death or HHF, %
70
60
50
40
30
20
10
0
HR, 0.83 (95% CI, 0.54-1.28)
0
1
2
3
4
5
6
Time since randomization, y
No. at risk
PCI 94 77 68 45 30 18 11
OMT 100 82 75 50 39 18 4



Kaplan-Meier estimates of the cumulative incidence of death from any cause of HHF in a time-to-first-event analysis, stratified by tertiles of the extent of myocardial viability. A, For the lower tertile, the extent of viability was less than or equal to 18%. B, For the middle tertile, the extent of viability was greater than 18% to less than or equal to 41%. C, For the upper tertile, the extent of viability was greater than 41%. HR indicates hazard ratio.

Figure 3. Association Between Viability Characteristics and Trial Outcomes



Forest plot of the hazard ratio (HR) (for clinical outcomes) or odds ratio (for improvement in left ventricular function) for the primary and secondary outcomes according to the extent of viable myocardium, extent of nonviable myocardium, and scar burden. Data relate to the whole trial population. Ratios are expressed per 10% absolute increase in the characteristic relative to overall left ventricular mass. The values relating to this graph are reported in eTable 5 in Supplement 2. HR indicates hazard ratio.

eTable 4. Relationship between viability characteristics (continuous) and outcomes

Myocardial Characteristic	Outcome measure	Association HR/OR; 95% CI
Viable *per 10% absolute increase by LV myocardial volume*	Death or HHF	0.98 (0.93 to 1.04)
	All-cause death	0.98 (0.92 to 1.04)
	CV death	0.97 (0.91 to 1.04)
	HHF	0.96 (0.88 to 1.05)
	LV improvement	1.01 (0.93 to 1.11)
Non-viable *per 10% absolute increase by LV myocardial volume*	Death or HHF	1.07 (1.00 to 1.15)
	All-cause death	1.10 (1.02 to 1.18)
	CV death	1.13 (1.03 to 1.23)
	HHF	1.04 (0.93 to 1.17)
	LV improvement	0.82 (0.73 to 0.93)
Scar burden *per 10% absolute increase by LV myocardial volume*	Death or HHF	1.18 (1.04 to 1.33)
	All-cause death	1.21 (1.07 to 1.38)
	CV death	1.28 (1.10 to 1.49)
	HHF	1.11 (0.91 to 1.36)
	LV improvement	0.69 (0.56 to 0.84)

CI – confidence interval; CV- cardiovascular; HHF- hospitalization for heart failure; HR- hazard ratio; LV – left ventricle; OMT – optimal medical therapy; OR - odds ratio; PCI – percutaneous coronary intervention

eTable 5. Sensitivity analysis (incorporating 50% LGE transmurality threshold) of interaction between treatment assignment, viability characteristics (continuous) and primary outcome

	Adjusted hazard ratio (95% CI)	Interaction p-value
Viable (per 10% LV increase)	1.01 (0.95 to 1.06)	-
PCI group	1.03 (0.95 to 1.11)	0.52
OMT group	0.99 (0.92 to 1.07)	
Non-viable (per 10% LV increase)	1.04 (0.96 to 1.13)	-
PCI group	0.99 (0.89 to 1.11)	0.21
OMT group	1.08 (0.98 to 1.20)	

CI – confidence interval. LV – left ventricle. OMT – optimal medical therapy. PCI – percutaneous coronary intervention

eTable 7. Determinants of binary improvement in left ventricular ejection fraction at 6- and 12-months

Table e7A – Interaction between treatment assignment, viability characteristics (continuous) and likelihood of left ventricular improvement at 6-months

	Adjusted odds ratio (95% CI)	Interaction p-value
Viable (per 10% LV increase)	1.01 (0.93 to 1.11)	-
PCI group	1.01 (0.89 to 1.14)	0.92
OMT group	1.02 (0.90 to 1.16)	
Non-viable (per 10% LV increase)	0.82 (0.73 to 0.93)	-
PCI group	0.88 (0.75 to 1.04)	0.24
OMT group	0.77 (0.65 to 0.91)	
Scar (per 10% LV increase)	0.69 (0.56 to 0.84)	
PCI group	0.72 (0.54 to 0.96)	0.68
OMT group	0.66 (0.50 to 0.88)	

CI – confidence interval. LV – left ventricle. OMT – optimal medical therapy. PCI – percutaneous coronary intervention

- A event occurred for 107 of 295 participants in the PCI group and 114 of 315 participants in the OMT group (36.3%vs 36.2%.)at a median of 3.4 years

There was no evidence of an interaction between the extent of viable myocardium and the effect of assignment to PCI vs OMT on occurrence of the primary outcome or any of the secondary outcomes

there was no evidence of an interaction between the extent of nonviable myocardium and the effect of assignment to PCI vs OMT on occurrence of the primary outcome or any of the secondary outcomes

no association was observed between the extent of viable myocardium and occurrence of the primary outcome or any of the secondary outcomes

an increasing volume of nonviable myocardium was associated with a greater likelihood of the primary outcome

- Scar burden did not interact with the effect of assignment to PCI vs OMT on the risk of the primary outcome or any secondary outcomes

- A greater scar burden was associated with an increased incidence

of the primary outcome

- None of the viability characteristics interacted with the effect of assignment to PCI vs OMT on the likelihood of improvement in left ventricular function

- the extent of viable myocardium was not associated with improvement in left ventricular function at 6 months but increasing volumes of nonviable myocardium and scar were associated with a lower likelihood of improvement in left ventricular function

Conclusions

In conclusion, in this subgroup analysis of a randomized clinical trial of PCI vs OMT alone, viability testing did not identify participants for whom PCI would confer a prognostic benefit or improve left ventricular function.

In this population with ischemic left ventricular dysfunction, the extent of viable myocardium as estimated by CMR imaging or do butamine stress echocardiography did not correlate with event-free survival or the likelihood of improvement in left ventricular function of 5% or greater, although the extent of nonviable myocardium (by CMR imaging or dobutamine stress echocardiography) And the total left ventricular scar burden(by CMR imaging) were associated with both outcomes

نتیجه

- میزان vaiability مزایای پیش آگهی و اثر گذاری در بهبود عملکرد بطنی را در بیمارانی که از pciدر مقابل OMTاستفاده کردند را نتوانست شناسایی کند

- در بیماران با اختلال عملکرد بطن چپ ایسکمیک ,مقدار میوکارد زنده در گروه PCI+OMT نسبت به گروه Only OMT با بقا و بهبود فانکشن بطن چپ ارتباطی نداشت اما در صورت وجود میوکارد غیر زنده یا اسکار احتمال عوارض افزایش می یافت در هر دو گروه.