Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Panza JA, Ellis AM, Al-Khalidi HR, et al. Myocardial viability and long-term outcomes in ischemic cardiomyopathy. N Engl J Med 2019;381:739-48. DOI: 10.1056/NEJMoa1807365

Myocardial Viability and Long-Term Outcomes in Ischemic Cardiomyopathy

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Supplementary Appendix

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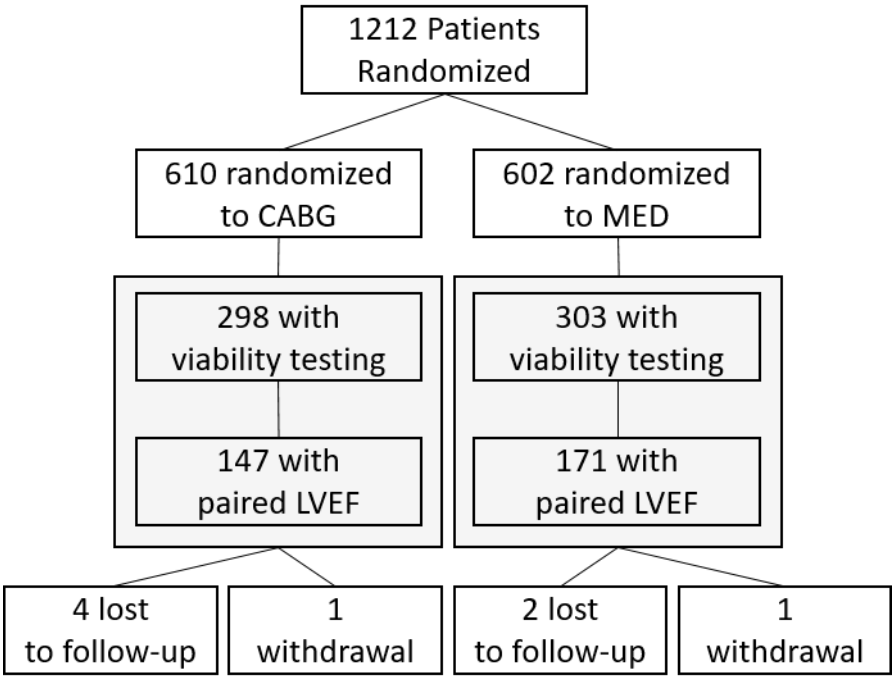
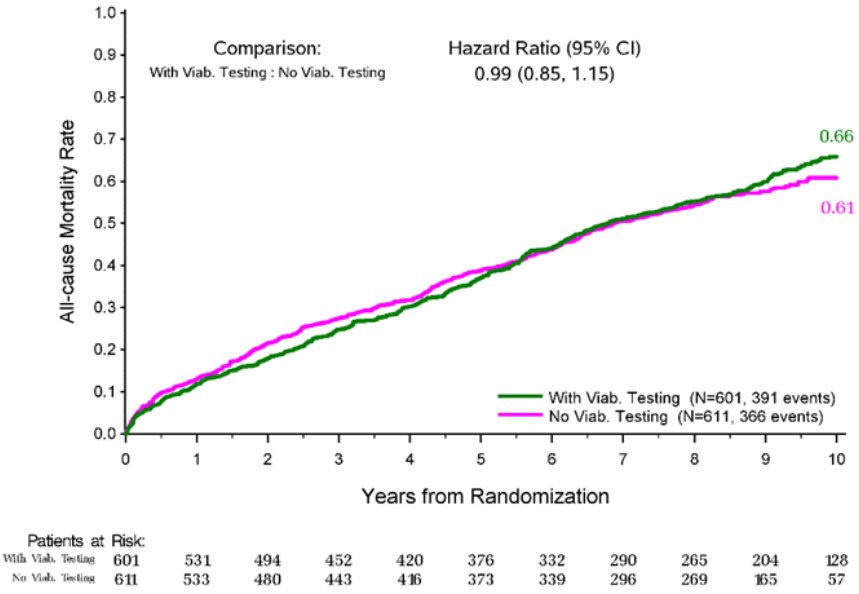
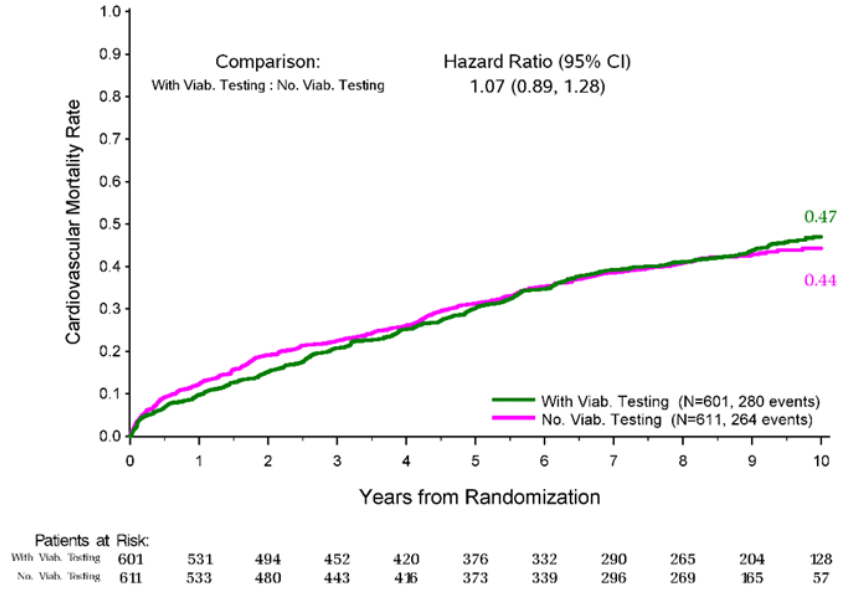
Figure S1



Consort diagram depicting the flow of patients included in this study.

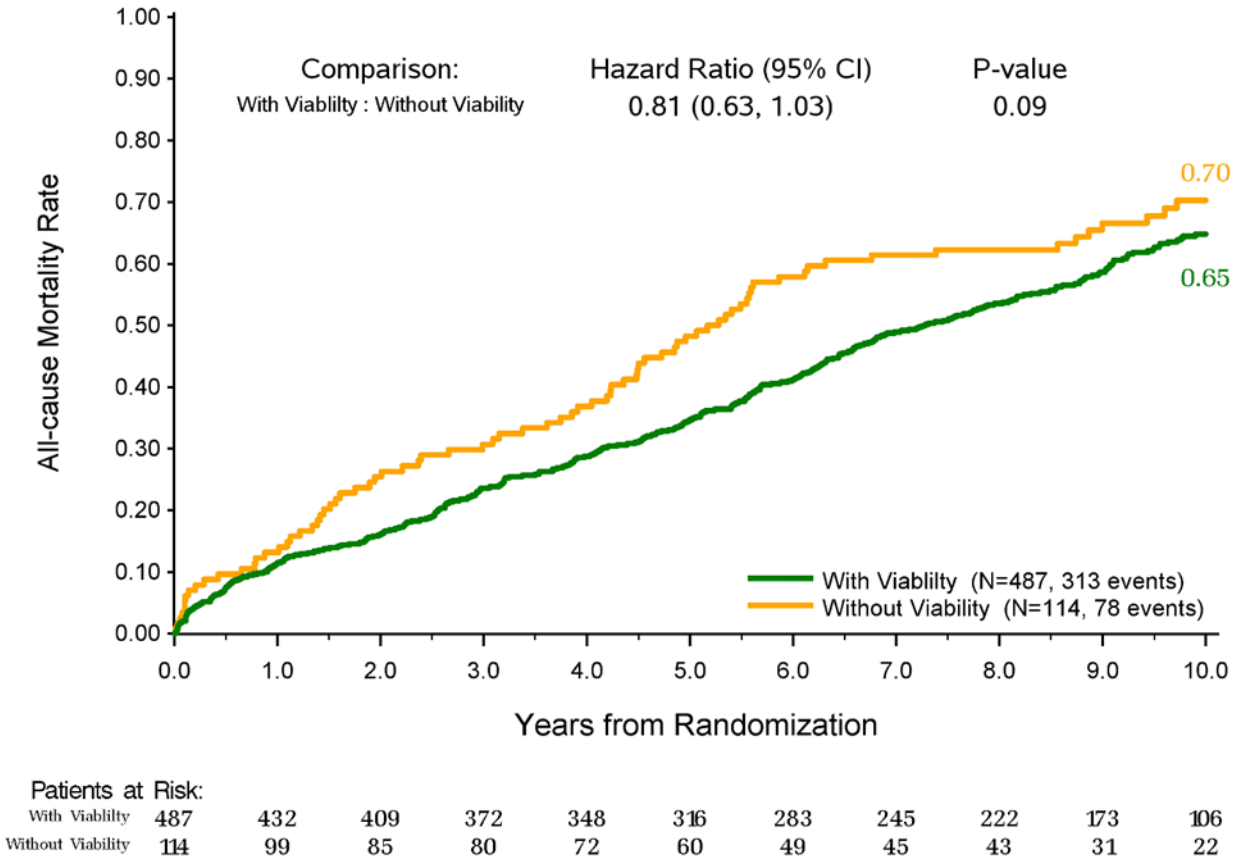
Figure S2





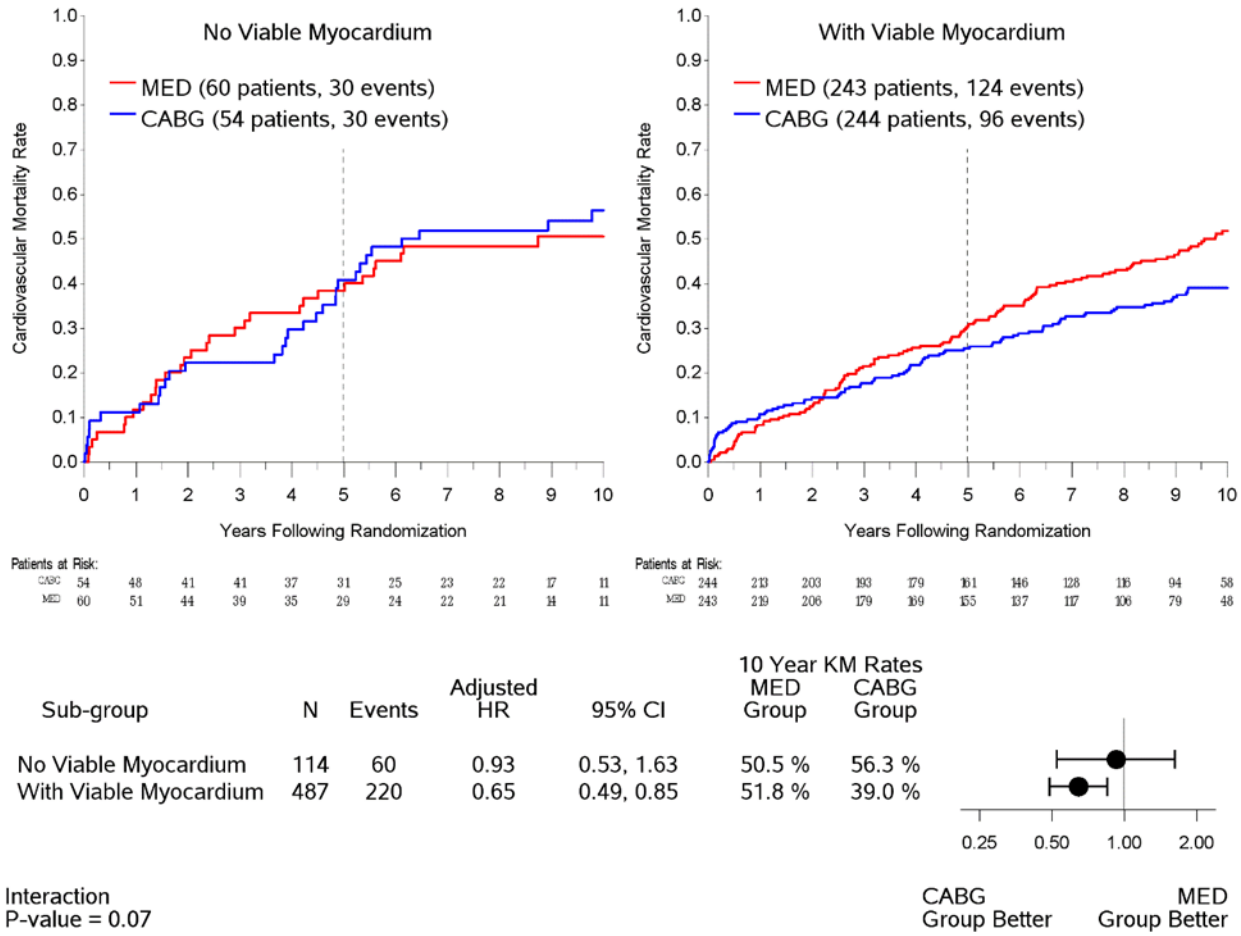
Kaplan Meier event rate curves for all-cause mortality (top panel) and cumulative incidence functions for cardiovascular mortality (bottom panel) with non-cardiovascular deaths as competing risks in patients with viability testing and without viability testing since randomization, with adjustment for baseline covariates (age, sex, race or ethnic group, New York Heart Association functional class at baseline, history of myocardial infarction, previous revascularization, baseline EF, number of diseased vessels, chronic renal insufficiency, mitral regurgitation, history of stroke, and history of atrial fibrillation).

Figure S3



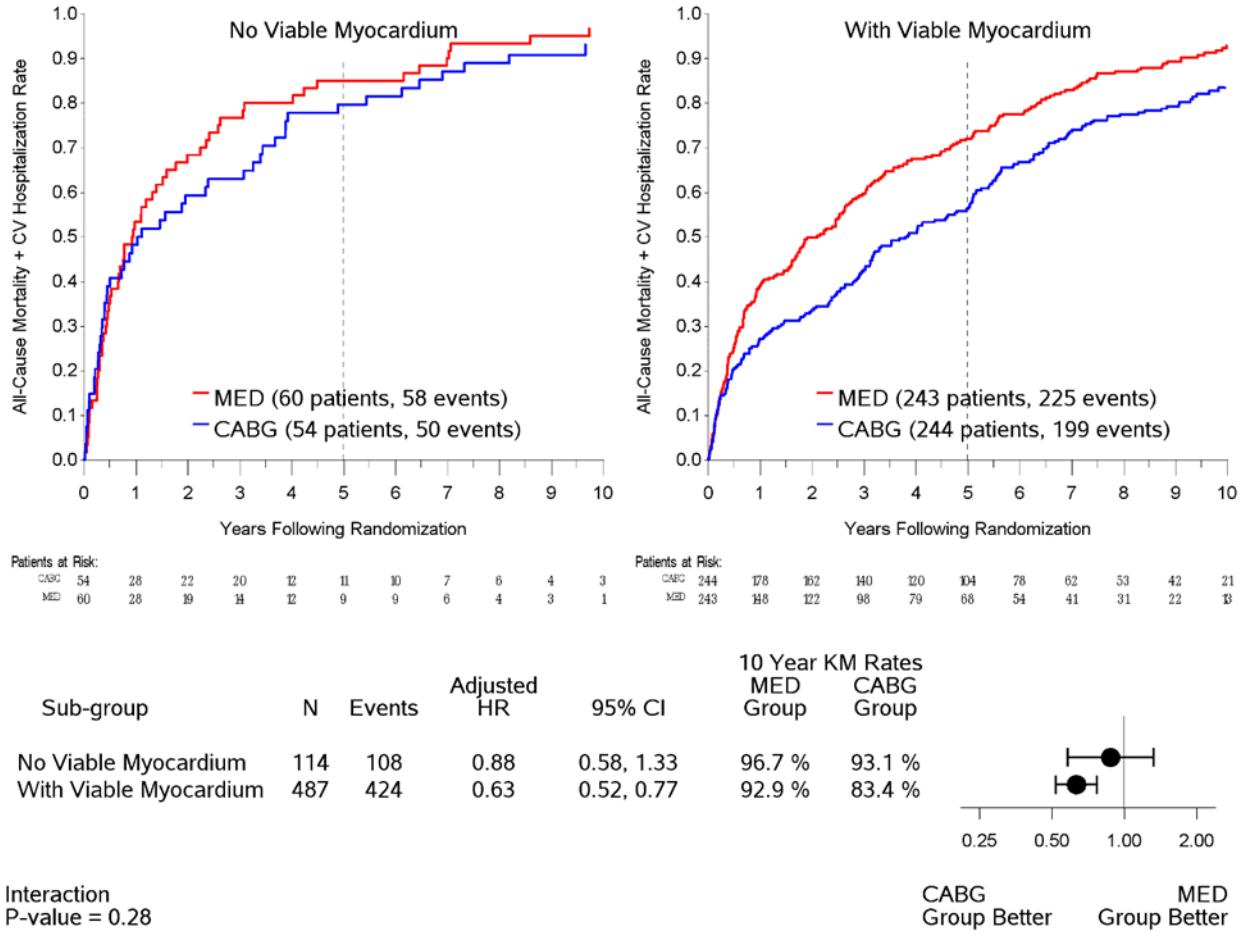
Kaplan Meier event rate curves for rates of all-cause mortality in patients with and without viable myocardium and results of Cox proportional hazards model. After adjustment for baseline covariates, the between-group difference was also not significant (P=0.64).

Figure S4



Cumulative incidence functions for rates of cardiovascular mortality with non-cardiovascular deaths as competing risks in patients without viable myocardium (left panel) and with viable myocardium (right panel) by treatment at randomization and results of cumulative incidence function for interaction between viability and treatment with adjustment for baseline covariates. The vertical dash lines indicate the 5-year follow-up time point.

Figure S5



Sub-group	N	Events	Adjusted HR	95% CI	10 Year KM Rates MED Group	10 Year KM Rates CABG Group
No Viable Myocardium	114	108	0.88	0.58, 1.33	96.7 %	93.1 %
With Viable Myocardium	487	424	0.63	0.52, 0.77	92.9 %	83.4 %

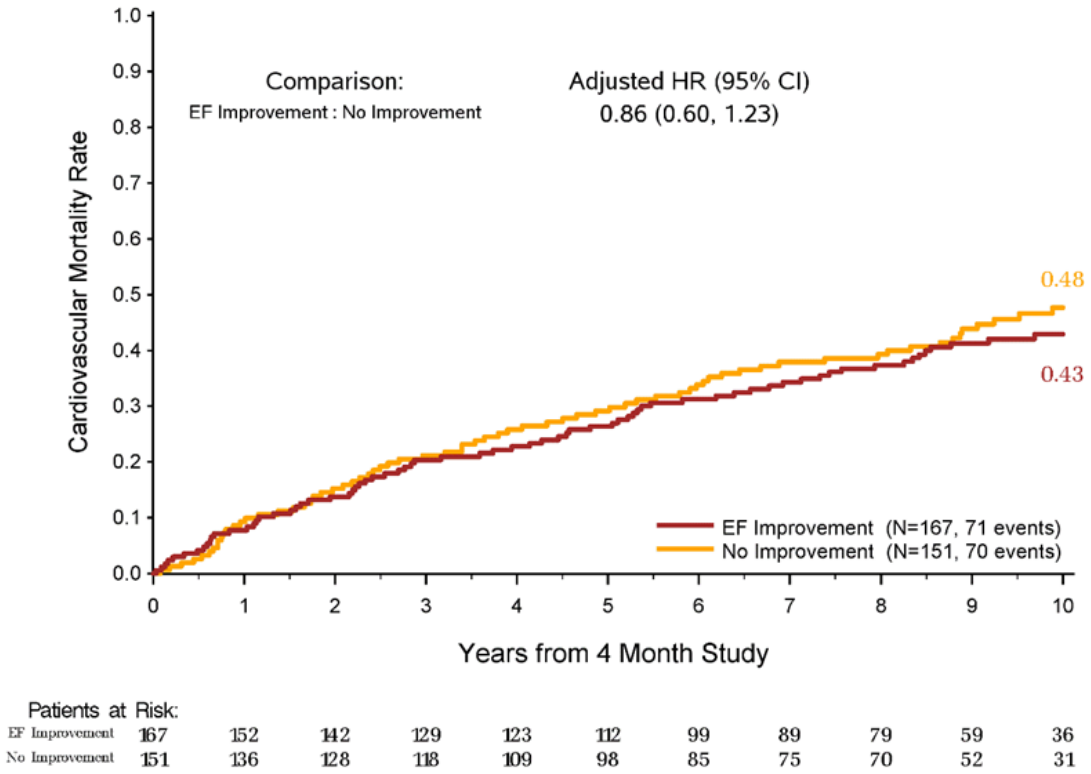
Interaction
P-value = 0.28

CABG Group Better

MED Group Better

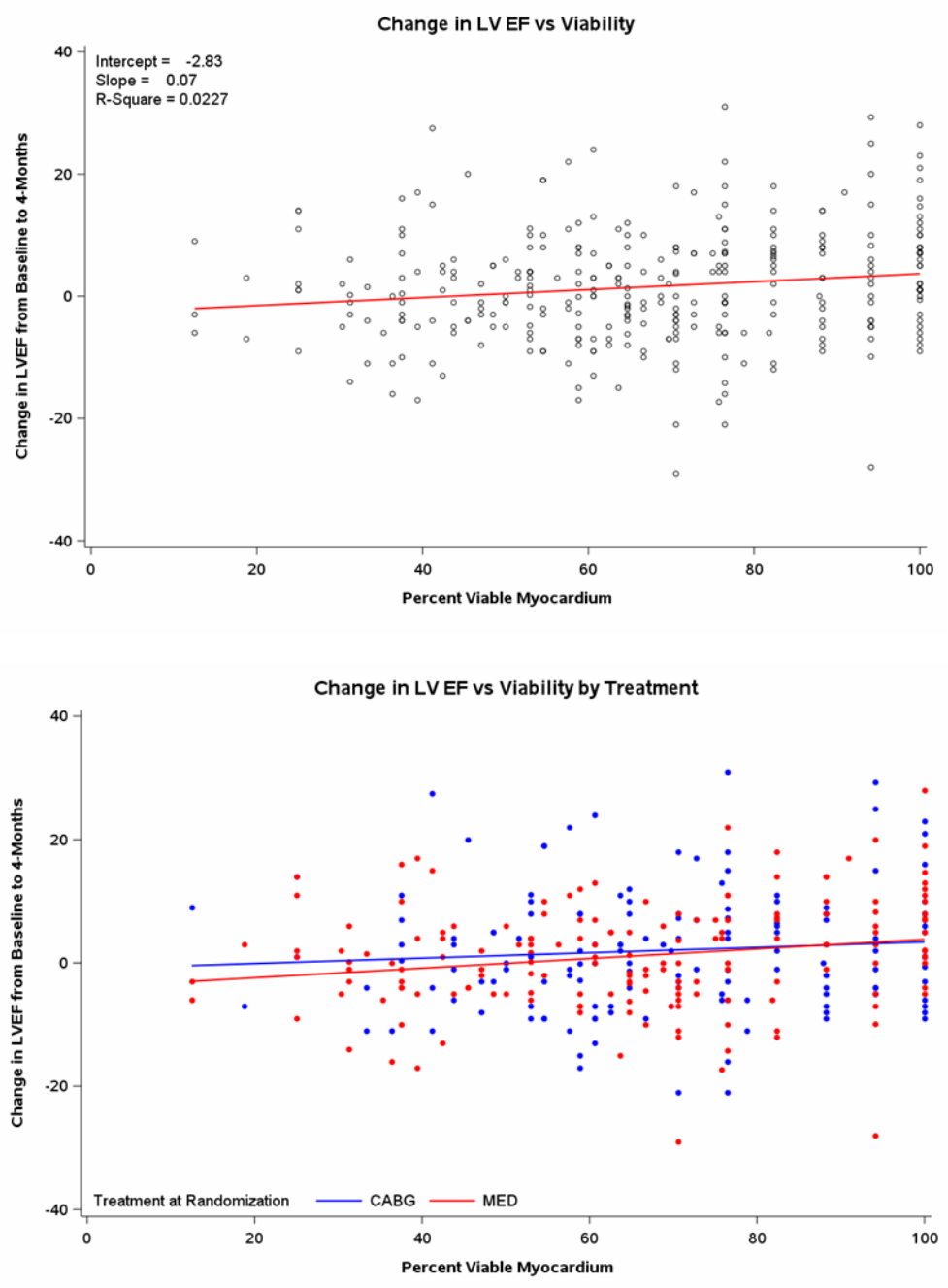
Kaplan Meier event rate curves for rates of all-cause mortality + CV hospitalization in patients without viable myocardium (left panel) and with viable myocardium (right panel) by treatment at randomization, and results of Cox proportional hazards model for interaction between viability and treatment with adjustment for baseline covariates and with imputation for missing values. The vertical dash lines indicate the 5-year follow-up time point.

Figure S6



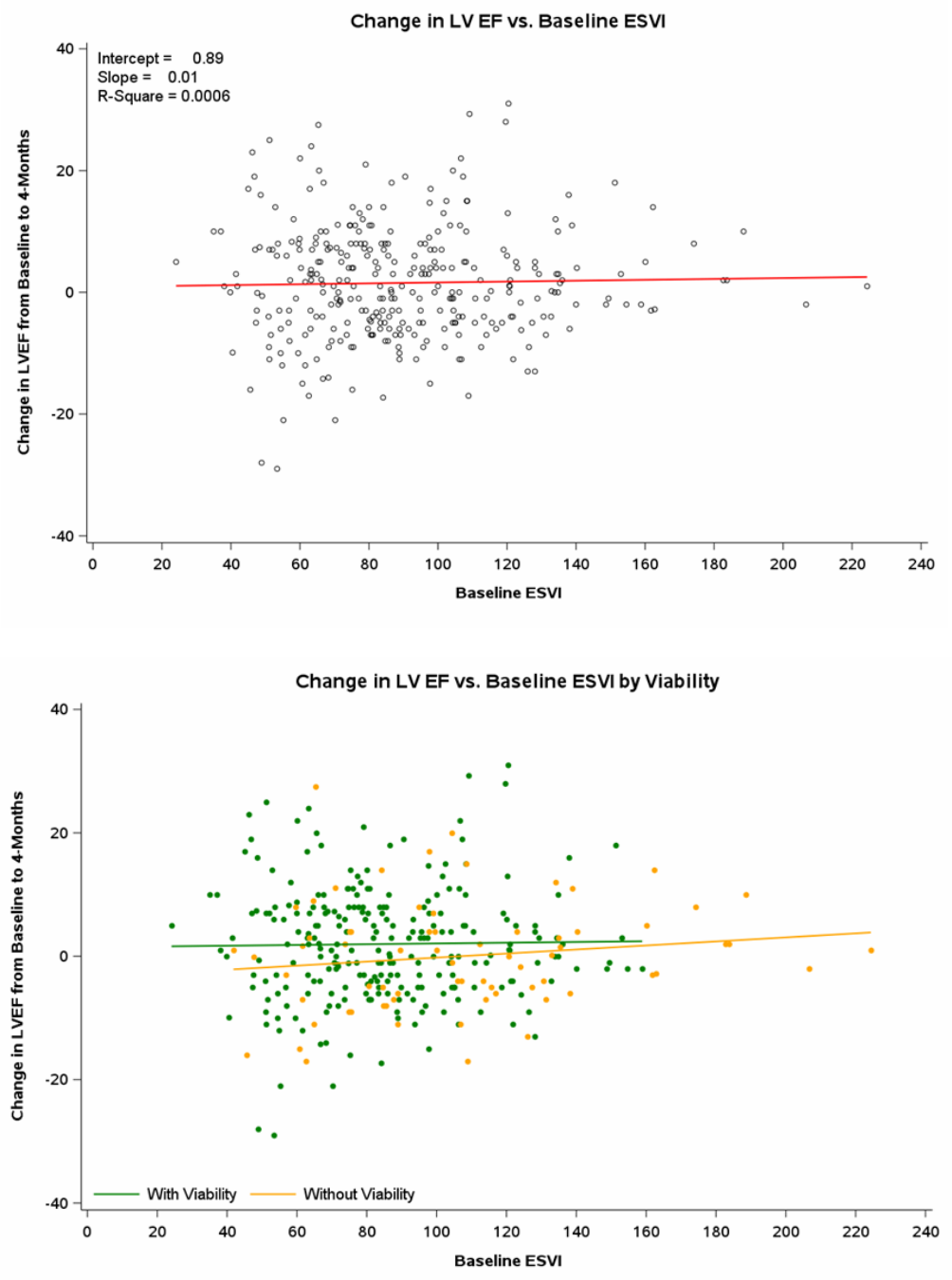
Landmark analysis for the 318 patients with viability testing and paired EF's showing cumulative incidence function for cardiovascular mortality with non-cardiovascular deaths as competing risks in patients with and without LV EF improvement and results of Cox proportional hazards models with adjustment for baseline covariates.

Figure S7



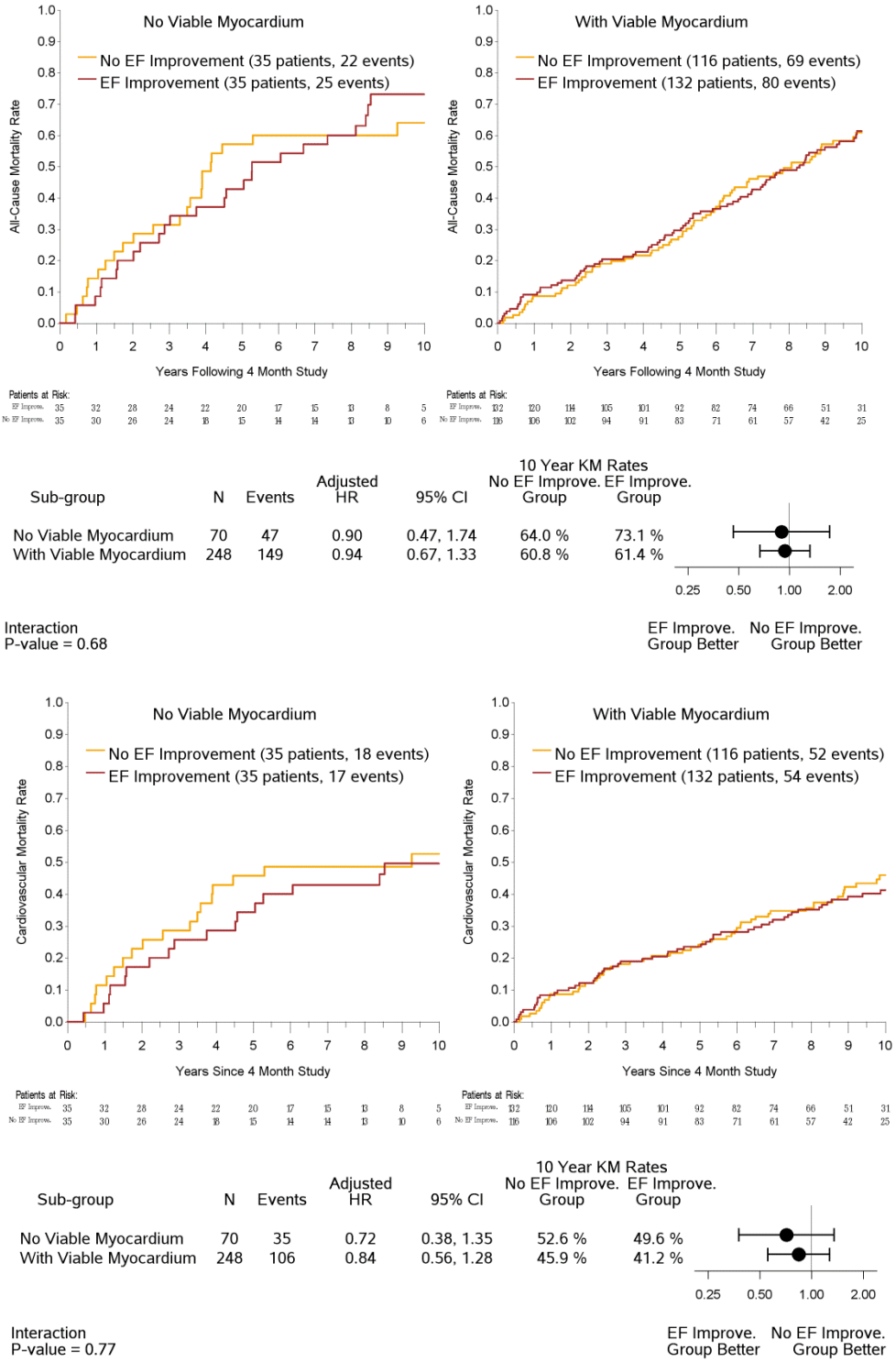
Scatter plot and regression lines for change in LV EF from baseline to 4-month study versus percent viable myocardium for all patients with a viability test (top panel) and separately dividing patients by treatment assignment (CABG or MED) (bottom panel) .

Figure S8



Scatter plot and regression lines for change in LV EF from baseline to 4-month study versus baseline end-systolic volume index (ESVI) for all patients with a viability test (top panel) and separately dividing patients by viability (with vs. without viable myocardium [green dots and orange dots, respectively]) (bottom panel) .

Figure S9



Landmark analysis for the 318 patients with viability testing and paired EF's showing Kaplan Meier event rate curves for all-cause mortality (top panels) and cumulative incidence functions for cardiovascular mortality (bottom panels) in patients without viable myocardium (left panels) and in those with viable myocardium (right panels) according to improvement or no improvement in LV EF between baseline and 4 months, and results of Cox proportional hazards models with adjustment for baseline covariates.

Table S1. STICH trial entry criteria

Inclusion criteria*
• Men
• Women not of childbearing potential
• Age ≥18 years
• LVEF ≤0.35 measured by contrast magnetic resonance ventriculogram, gated SPECT ventriculogram, echo, or contrast ventriculogram within 3 months of trial entry
• CAD suitable for revascularization
Exclusion criteria†
• Failure to provide informed consent
• Aortic valvular heart disease indicating need for aortic valve repair or replacement
• Cardiogenic shock (within 72 hrs of randomization); defined by need for IABP support or requirement of IV inotropic support
• Plan for PCI of CAD
• Recent acute MI judged to be an important cause of LV dysfunction
• History of more than 1 prior CABG
• Non-cardiac illness with a life expectancy of <3 yrs
• Non-cardiac illness imposing substantial operative mortality
• Conditions/circumstances likely to lead to poor treatment adherence (e.g., history of poor compliance, alcohol or drug dependency, psychiatric illness, no fixed abode)
• Prior heart, kidney, liver, or lung transplant
• Current participation in another clinical trial in which patient is taking an investigational drug or receiving an investigational medical device
MED therapy eligibility criteria
• Absence of left main CAD defined by intraluminal stenosis ≥50%
• Absence of Canadian Class III angina or great (angina markedly limiting ordinary activity)

*Patients may qualify for inclusion in the study. †None of these may exist at randomization. LV = left ventricular; EF = ejection fraction; SPECT = single photon emission computed tomography; CAD = coronary artery disease; IV = intravenous; IABP = intraaortic balloon pump; PCI = percutaneous coronary intervention; MI = myocardial infarction; CABG = coronary artery bypass grafting; MED = medical therapy; SVR = surgical ventricular reconstruction.

Table S2. Baseline characteristics of patients with and without testing of myocardial viability

Characteristic	All patients (n=1212)	Patients with a viability test (n=601)	Patients without a viability test (n=611)	P value
Age, mean ± SD	60.3 ± 9.3	60.7 ± 9.4	59.9 ± 9.2	0.113
Male, no. (%)	1064 (87.7)	521 (86.7)	543 (88.9)	0.246
Race, no. (%)				<0.001
White	827 (68.2)	496 (82.5)	331 (54.2)	
Black	31 (2.6)	18 (3.0)	13 (2.1)	
Asian	209 (17.2)	29 (4.8)	180 (29.5)	
Other	141 (11.6)	54 (9.0)	87 (14.2)	
Multiracial	4 (0.3)	4 (0.7)	0 (0.0)	
Prior myocardial infarction, no. (%)	934 (77.1)	481 (80.0)	453 (74.1)	0.015
Diabetes, no. (%)	478 (39.4)	224 (37.3)	254 (41.6)	0.126
Stroke, no. (%)	92 (7.6)	53 (8.8)	39 (6.4)	0.109
Hypertension, no. (%)	738 (60.1)	363 (60.4)	365 (59.7)	0.814
Hyperlipidemia, no. (%)	730 (60.3)	403 (67.3)	327 (53.5)	<0.001
Current smoker, no. (%)	252 (20.8)	126 (21.0)	126 (20.7)	0.894
Chronic renal insufficiency, no. (%)	94 (7.8)	43 (7.2)	51 (8.3)	0.443
Atrial flutter/fibrillation, no. (%)	153 (12.6)	90 (15.0)	63 (10.3)	0.015
Peripheral vascular disease,no. (%)	184 (15.2)	91 (15.1)	93 (15.2)	0.969
RAR score, mean ± SD	12.7 ± 8.8	12.5 ± 8.8	12.9 ± 8.8	0.311
Previous CABG, no. (%)	36 (3.0)	16 (2.7)	20 (3.3)	0.531
Bypass graft status, no. (%)				
≥1 stenosed or occluded	35 (97.2)	15 (93.8)	20 (100)	0.444
≥1 occluded	29 (80.6)	14 (87.5)	15 (75.0)	0.426
Previous PCI, no. (%)	156 (12.9)	104 (17.3)	52 (8.5)	<0.001
Previous ICD, no. (%)	29 (2.4)	16 (2.7)	13 (2.1)	0.543
CAD distribution, no. (%)				
No. of diseased vessels ≥75%				0.416
None*	25 (2.1)	12 (2.0)	13 (2.1)	
One-vessel	282 (23.2)	152 (25.3)	130 (21.3)	
Two-vessel	462 (38.2)	221 (36.8)	241 (39.4)	
Three-vessel	442 (36.5)	215 (35.8)	227 (37.2)	
Proximal LAD stenosis ≥75%	826 (68.2)	389 (64.8)	437 (71.5)	0.012
Left main stenosis (≥50%)	32 (2.6)	14 (2.3)	18 (2.9))	0.506
Current CCS angina class, no. (%)				0.023
No angina	442 (36.5)	236 (39.3)	206 (33.7)	
I	187 (15.4)	94 (15.6)	93 (15.2)	
II	525 (43.3)	253 (42.1)	272 (44.5)	
III	48 (4.0)	14 (2.3)	34 (5.6)	
IV	10 (0.8)	4 (0.7))	6 (1.0)	
Highest NYHA functional class within 3 months, no. (%)				0.231
I	69 (5.7)	27 (4.5)	42 (6.9)	
II	438 (36.1)	212 (35.3)	226 (37.0)	
III	540 (44.6)	275 (45.8)	265 (43.4)	
IV	165 (13.6)	87 (14.5)	78 (12.8)	
Medications at baseline, no. (%)				
Beta blocker	1036 (85.5)	534 (88.9)	502 (82.2)	<0.001
ACE inhibitor	996 (82.2)	514 (85.5)	482 (78.9)	0.002
Angiotensin receptor blocker	115 (9.5)	46 (7.7)	69 (11.3)	0.031
ACE inhibitor or ARB	1085 (89.5)	554 (92.2)	531 (86.9)	0.003

Statin	983 (81.1)	508 (84.5)	475 (77.7)	0.003
Aspirin	1002 (82.7)	513 (85.4)	487 (80.0)	0.014
Digoxin	245 (20.2)	109 (18.1)	136 (22.3)	0.074
Blood pressure, mean ± SD				
Systolic (mmHg)	121.2 ± 17.5	119.8 ± 17.3	122.5 ± 17.7	0.003
Diastolic (mmHg)	75.5 ± 11.0	74.7 ± 10.7	76.3 ± 11.3	0.022
Heart rate, mean ± SD	74.9 ± 14.7	73.3 ± 12.9	76.4 ± 16.1	<0.001
LV ejection fraction, mean ± SD	0.282 ± 0.086	0.273 ± 0.086	0.292 ± 0.086	<0.001
LVEDVI (ml/m2), mean ± SD	117.6 ± 39.2	122.8 ± 41.9	110.4 ± 33.9	<0.001
LVESVI (ml/m2), mean ± SD	85.5 ± 36.2	91.7 ± 38.9	78.6 ± 31.6	<0.001
Hemoglobin (g/dL), mean ± SD	13.8 ± 1.7	13.9 ± 1.7	13.6 ± 1.8	0.005
Creatinine (mg/dL), mean ± SD	1.2 ± 0.6	1.2 ± 0.7	1.2 ± 0.5	0.004
BUN (mg/dL), mean ± SD	29.3 ± 21.2	29.2 ± 19.7	29.5 ± 22.3	0.980

*Although some patients had no coronary artery stenosis ≥75%, all patients had a coronary artery with stenosis ≥50%.

ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker; BUN = blood urea nitrogen; CABG = coronary artery bypass graft surgery; CAD = coronary artery disease; EDVI = end-diastolic volume index; ESVI = end-systolic volume index; ICD = implantable cardioverter defibrillator; LV= left ventricular; NYHA = New York Heart Association; RAR = risk at randomization

Table S3. Summary of baseline and 4-month functional data for subjects in the paired functional analysis presented as mean ± standard deviation.

Characteristic	Patients with Myocardial Viability and Paired Data (N=248)				Patients without Myocardial Viability and with Paired Data (N=70)			
	Medical Therapy (N=127)		CABG (N=121)		Medical Therapy (N=44)		CABG (N=26)	
	Baseline	4 Months	Baseline	4 Months	Baseline	4 Months	Baseline	4 Months
Left ventricular ejection fraction — %	28.6±8.3	30.5±9.5	27.8±7.5	30.3±10.8	24.1±8.8	24.5±8.8	24.8±8.5	25.1±11.2
Left ventricular end-diastolic volume index — ml/m2 of body-surface area	115.5±30.3	114.1±32.9	118.6±27.1	114.6±30.8	142.4±36.8	146.8±41.7	134.3±48.3	127.0±53.7
Left ventricular end-systolic volume index — ml/m2 of body-surface area	83.6±27.6	80.9±30.4	86.3±24.3	81.7±29.3	110.3±36.6	112.7±39.8	102.9±45.5	97.3±50.0