Supplementary Data

APPENDIX 1.

Detailed Statistical Analysis

Overview of Multivariable Modeling Approach

In order to identify and maximize the prognostic power of all measurements of global and regional LV structure and function, a four-step multivariable modeling plan was performed using all-cause death (N = 279) as the endpoint of interest to: Step 1) define the most prognostic clinical variables using the 1000 clinical site-reported LVEF values as the only LV function parameter; Step 2) In place of site-reported LVEF, substitute various combinations of core laboratory ESVI, EDVI, EF, and regional function total score in the central SVR-eligible zone (segments 17, 15, 14, 13, 9, 8); Step 3) For patients with more than one study source of global and regional function, identify the combination of ESVI source and image quality that produced the highest total model Chi square for the endpoint of death in the model developed in Steps 1 and 2; Step 4) Determine whether there is an interaction of ESVI and type of surgical treatment in the context of other prognostic clinical variables.

The initial multivariable Cox proportional hazards regression model for all-cause mortality was developed in the 978 SVR hypothesis patients without missing data for 42 candidate variables and site-reported LVEF as the only LV function variable. Variables chosen with some, but not all, of the forward, backward, and stepwise selection methods were included only if they improved the Akaike information criterion. Variables included in the multivariable Cox model

for mortality were tested for violations of the proportional hazards assumption and no violations were observed.

The 22 patients with at least one missing baseline clinical variable were imputed as follows. The mode was used to impute missing values of mitral regurgitation (mild or moderate, N=10) and hyperlipidemia (yes, N=3). Ability to walk was missing for 5 and it was imputed from the NYHA class (class II=yes, class III=no). Linear regression models containing the following variables were used to impute creatinine (N=2) and hemoglobin (N=2): age, sex, weight, diabetes, chronic renal insufficiency, hypertension, PVD, stroke, NYHA class, and MI. A non-linear regression model was developed to impute ESVI for those with missing values. Linear, quadratic, and cubic terms, linear splines, and a log transformation and were considered for LVEF. When a quadratic term was chosen, the following clinical characteristics were added to see if they improved the model: age, renal function, myocardial infarction, mitral regurgitation, age, NYHA class, and atrial fibrillation.

From this model with the clinical site LVEF as the only LV variable, the LVEF was sequentially supplemented with the best available core laboratory values for end-systolic volume index (ESVI), end-diastolic volume index (EDVI) and regional function score for left anterior descending coronary zones, and for remote myocardial zones to evaluate any additional independent contribution of all available LV function information.

This model, created to optimize prognosis from cardiac imaging studies, was used to identify the specific algorithm of alternate use of ESVI values from 13 different combinations of core

laboratory modality and quality scores that, in the context of clinical variables, maximized the total model Chi square. This approach would ensure optimization of the prognostic strength of the ESVI in these 1000 patients in the context of all other prognostic clinical information. The best definition of ESVI came from algorithm 8 which prioritizes CMR images over echo images and radionuclide images and has previously been published [16].

Categorizing Regional Function in the Case of Tied Ranks

In the case of tied ESVI scores at the deciles of increasing ESVI, groups were next classified by decreasing EF. If there were tied ranks at the tertiles of dyskinesia, deciles were further sorted by most normal function in least SVR-eligible segments (1, 5, 6, 11, 12) and increasing ESVI. Parameters of global dysfunction and survival were assessed for the 330, 330, and 340 patient cohorts to insure regrouping by regional dysfunction had not disrupted the desired independence of severity of global dysfunction and severity by regional dysfunction groupings.

APPENDIX 2

Patient Characteristics of the Least SVR Eligible Group by Whether Segmental Data Were Available

Characteristic	Least SVR eligible (N=152)	Missing regional data (N=188)	p*
Age at randomization	61.8 (54.5 - 68.4)	63.7 (55.4 - 69.0)	0.1828
Female	21 (13.8)	26 (13.8)	0.9970
White (non-hispanic)	139 (91.4)	152 (80.9)	0.0057
Myocardial infarction	131 (86.2)	156 (83.0)	0.4179
Diabetes	52 (34.2)	75 (39.9)	0.2815
Hyperlipidemia	105 (70.0)	129 (68.6)	0.7843
Hypertension	89 (58.6)	113 (60.1)	0.7718
Stroke	6 (3.9)	7 (3.7)	0.9147
Chronic renal insufficiency	10 (6.6)	17 (9.1)	0.3956
Hemoglobin (g/dL)	13.7 (12.5 - 14.6)	13.7 (12.3 - 14.8)	0.9303
Atrial flutter fibrillation	14 (9.2)	27 (14.4)	0.1470
MR= 0, 1-2, or 3			0.1428
None or trivial	64 (43.0)	65 (34.8)	
Mild or moderate	78 (52.3)	117 (62.6)	
Severe	7 (4.7)	5 (2.7)	
Current NYHA heart failure class			0.4910
1	16 (10.5)	16 (8.5)	
2	67 (44.1)	71 (37.8)	
3	61 (40.1)	88 (46.8)	
4	8 (5.3)	13 (6.9)	
EDVI (algorithm 8)	107 (78.3 - 140)	101 (81.3 - 132)	0.6791
ESVI (algorithm 8)	71.0 (56.5 - 107)	80.0 (60.0 - 98.0)	0.6635
EF (algorithm 8)	27.3 (22.1 - 33.6)	28.0 (23.6 - 32.2)	0.9199

* P-values come from chi-square and Wilcoxon rank sum tests

APPENDIX 3

Sensitivity Analysis that Excludes Patients with Missing Regional Function

Multivariable model for all-cause death in 812 SVR hypothesis patients with complete LV function data

Variable	HR	95% CI for HR	Chi- square	p
Creatinine, HR for 0.1 mg/dL increase between 1 and 1.6	1.19	1.12 - 1.26	33.3	<.0001
ESVI, HR for 10 unit increase*	1.08	1.05 - 1.12	20.4	<.0001
Age, HR for 10 year increase	1.35	1.16 - 1.57	14.8	<.0001
Current NYHA heart failure class				
1	1.00	-		
2	1.22	0.67 - 2.21	19.4	<0.0001
3	1.72	0.96 - 3.09		
4	3.14	1.58 - 6.26		
Atrial flutter or fibrillation	2.03	1.45 - 2.86	16.9	<.0001
Diabetes	1.49	1.12 - 1.97	7.7	0.0055
Hemoglobin, HR for 1 g/dL decrease below 14.3	1.13	1.02 - 1.25	5.5	0.0193
Mitral regurgitation				
None	1.00	-		
Mild/moderate	1.33	0.97 - 1.81	11.0	0.0041
Severe	2.63	1.48 - 4.68		
Myocardial infarction	1.65	1.06 - 2.57	4.9	0.0267
Hyperlipidemia	0.75	0.56 - 1.00	3.9	0.0489
Stroke	1.83	1.17 - 2.87	7.0	0.0083
White (non-hispanic)	1.56	0.93 - 2.60	2.9	0.0909
SVR eligibility category				
Least SVR eligible	1.00	-		
Intermediate eligibility	1.02	0.73 - 1.41	0.04	0.9805
Most SVR eligible	0.98	0.71 - 1.37		

* Three new SVR eligibility categories were assigned with 270 or 271 patients in each, and this variable replaces the one in Table 2 that assigns patients with missing regional function to the least eligible group.