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Predicting Persistent Left Ventricular Dysfunction Following Myocardial Infarction: PREDiction of ICd Treatment Study (PREDICTS)

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Abstract

BACKGROUND—Persistent severe left ventricular (LV) systolic dysfunction after myocardial infarction (MI) is associated with increased mortality and is a class I indication for implantation of a cardioverter-defibrillator.

OBJECTIVES—We developed models and assessed independent predictors of LV recovery to >35% and 50% after 90-day follow-up in patients presenting with acute MI and severe LV dysfunction..

METHODS—Our multicenter prospective observational study enrolled participants with ejection fraction (EF) of 35% at the time of MI (n = 231). Predictors for EF recovery to >35% and 50% were identified after multivariate modeling and validated in a separate cohort (n = 236).

RESULTS—In PREDICTS, 43% of patients had persistent EF 35%, 31% had an EF of 36% to 49%, and 26% had an EF 50%. The model that best predicted recovery of EF to >35%, included EF at presentation, length of stay, prior MI, lateral wall motion abnormality at presentation, and peak troponin. The model that best predicted recovery of EF to 50%, included EF at presentation,

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peak troponin, prior MI, and presentation with ventricular fibrillation or cardiac arrest. After predictors were transformed into point scores, the lowest point scores predicted a 9% and 4% probability of EF recovery to >35% and 50%, respectively, whereas profiles with the highest point scores predicted an 87% and 49% probability of EF recovery to >35% and 50%.

CONCLUSIONS—In patients with severe systolic dysfunction following acute MI with an EF 35%, 57% had EF recovery to >35%. A model using clinical variables present at the time of MI can help predict EF recovery.

Keywords

heart failure; remodeling; risk assessment; ventricular ejection fraction

Persistence of severe left ventricular (LV) dysfunction after acute myocardial infarction (MI) has important prognostic implications and is associated with increased morbidity and mortality from both congestive heart failure (HF) and sudden cardiac death. While implantable cardioverter-defibrillators (ICD) confer a survival benefit in patients with severe LV dysfunction, guidelines recommend implantation of an ICD after a 40-day waiting period (90 days if revascularization occurs) (1) for patients whose ejection fraction (EF) remains 35%. This waiting period is based on 2 studies showing no long-term mortality benefit from early implantation of an ICD (2,3). The proportion of patients and factors that predict which patients will continue to have an EF 35% 90 days after MI are unknown.

Creatine kinase (CK), troponin, Q waves, dyssynchrony, and wall motion abnormalities measured at the time of acute MI have all been shown to predict LV functional recovery (4–6). Cohorts in which these associations were made included heterogeneous acute MI patients, many of whom had EFs >35% (and often normal or near-normal EFs). Many of these studies occurred prior to the institution of modern HF therapies and rapid revascularization techniques, which may attenuate the inferences of these findings. Taken together, existing data provide limited utility to help us understand the unique risk profile of acute MI patients presenting with severe LV dysfunction. Therefore, it remains a clinical challenge to predict which acute MI patients with severe LV dysfunction will still meet the indications for an ICD at the end of 90 days. In the present study, we define the incidence, identify markers, and develop prediction models for LV recovery to >35% and 50% in patients with acute MI and EF 35% using data from the PREDiction of ICd Treatment Study (PREDICTS).

Methods

Study Samples

The model development study samples were drawn from PREDICTS, a 60-center international study conducted from July 2008 to May 2011 that followed participants previously randomized in VEST (Vest Prevention of Early Sudden Death Trial), a randomized, controlled clinical trial enrolling patients age 18 years or older, admitted with MI and LV systolic dysfunction (EF 35%) measured at least 8 hours after the MI or percutaneous coronary intervention (PCI). Upon discharge from the hospital, participants were randomized to a LifeVest® wearable defibrillator (ZOLL Medical Corporation,

Chelmsford, Massachusetts) and optimal medical therapy (OMT) or OMT alone with the primary endpoint of 90-day sudden death mortality.

At the conclusion of VEST participation, 90 days after discharge from hospitalization for an index MI, participants were enrolled in PREDICTS. In the PREDICTS study, patients were implanted with an ICD based on clinical indications or a Reveal® XT (Medtronic, Minneapolis, Minnesota) if the EF recovered to >35% for arrhythmia monitoring. The purpose of PREDICTS was to develop a risk stratification algorithm that predicted future ICD shock or sudden death over 5 years in patients who were admitted for an acute MI with an EF   35%. Of these 364 participants, 231 had follow-up echocardiograms at 90 days before the study was prematurely terminated. Inclusion criteria for PREDICTS was the same as noted above for VEST. Exclusion criteria for VEST and PREDICTS included significant valve disease, planned coronary artery bypass graft (CABG) surgery within 2 months, existing ICD, contraindication to eventual ICD, terminal condition, chronic renal failure, chest circumference >56 inches or <26 inches, pregnancy, and discharge to a skilled nursing facility. PREDICTS was stopped early due to slower than expected enrollment and termination of funding (from the National Institutes of Health and Medtronic).

After the termination of PREDICTS, VEST continued and the VEST Registry was created to follow those enrolled in VEST for 1 year. The VEST Registry has the same inclusion/exclusion criteria. Distinct from PREDICTS, a 90-day echocardiogram in the VEST study was not mandatory, but rather occurred at the discretion of the treating physician. Of the 509 participants in the VEST Registry available at the time of this analysis, 236 had echocardiograms at or near 90 days. This cohort was used for model validation (Online Figure 1).

Echocardiograms

Baseline echocardiograms were obtained at study sites using standard echocardiographic views and the PREDICTS Standard Operating Procedure (based on the American Society of Echocardiography guidelines) (7), more than 8 hours after MI or acute PCI. Ejection fraction was calculated by Simpson's Rule. PREDICTS sites underwent a certification process by the PREDICTS echocardiography core lab, during which the echocardiogram quality and EF calculation methods were verified. Sites were allowed to recruit only after they passed this certification process. The echocardiography core laboratory maintained quality assurance by randomly sampling 50% of the studies. Participants underwent follow-up echocardiograms 90 days after the initial MI systematically (PREDICTS) or as clinically indicated (VEST registry) as discussed earlier.

Risk Factors of Persistent LV Dysfunction

Patient demographics, clinical characteristics (including prior cardiovascular disease and pre-hospitalization medications), characteristics of the MI hospitalization (e.g., electrocardiographic parameters, biomarkers, length of hospital stay, and primary treatment of the MI), baseline echocardiographic parameters, and discharge medications were evaluated as potential predictors of persistent LV dysfunction.

Prolonged hospital stay was defined as a hospital stay >4 days, based on previously published studies demonstrating an association between hospital stays >4 days at the time of acute MI presentation and subsequent poor outcomes (8). Discharge medications were categorized as the following: beta-blockers (carvedilol specifically), angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), ACEI or ARBs, aldosterone receptor blockers, statins, aspirin, and diuretics.

Statistical Analysis

For model development, baseline characteristics of study participants were compared according to their EF at 90 days, categorized as ≤35%, 36% to 49%, and ≥50%, using Wilcoxon rank sum test and chi-square tests as appropriate, followed by pairwise tests between categories as well as tests for trend. We used student's t-tests to assess the association of baseline characteristics with change in EF.

We developed 2 logistic regression models: one to predict recovery of EF defined as 90-day values of >35% and one for the prediction of 90-day EF ≥50%. First we identified baseline characteristics associated with each recovery measure in single-predictor models at a significance level of $p < 0.1$. We determined which of the continuous predictors identified in the first step had nonlinear associations with each outcome variable in unadjusted models and used flexible 3-knot restricted cubic spline transformations to achieve a better fit. For each possible candidate logistic model, with 4 to 7 of the identified predictors, we estimated the c-statistic (to measure of discrimination) using 10 repetitions of 10-fold cross-validation to avoid optimism and overfitting. We estimated the Hosmer-Lemeshow goodness of fit statistic using the cross-validated predictions. Among the models with the highest cross-validated c-statistics, we selected the best performing model based on the following criteria: 1) competitive c-statistic; 2) Hosmer-Lemeshow $p > 0.1$; and 3) simplicity. When ranking the models, if there were other models within 0.03 of the model with the highest c-statistic, we selected the model with the best calibration as measured by the Hosmer-Lemeshow statistics. If more than 1 model was identified with equally high measures of discrimination and calibration, we chose the model that contained the most easily obtainable clinical variables. We then derived point scores based on the selected models for each outcome by categorizing continuous predictors, refitting the models, and rounding the logistic regression coefficients. We estimated the c-statistic and Hosmer-Lemeshow goodness of fit statistic for the point scores using 10 repetitions of 10-fold cross-validation.

For model validation, baseline characteristics of participants used in the derivation cohort were compared with those in the validation set and baseline characteristics of participants in the validation set without echocardiograms at 90 days were compared to those with echocardiograms at or near 90 days, using Wilcoxon rank sum and chi-square tests as appropriate. We then applied the models derived for the prediction of EF recovery to the data for registry participants' data. Predicted risk scores for sustained LV dysfunction were calculated using point scores derived from the PREDICTS derivation cohort and applied to the VEST registry cohort to estimate discriminative ability.

Results

Baseline Characteristics

Per the baseline characteristics of the 231 PREDICTS participants (Table 1), 40% were routinely taking aspirin prior to the index admission and 25% had a history of MI. Only 13% of participants had a prior history of congestive HF. The EF prior to the acute MI was not known for all patients and thus is not included in this analysis.

Characteristics of the index MI hospitalization are shown in Table 2. The mean EF was 28 ± 6.6%. Most participants (84%) had wall motion abnormalities noted at the time of presentation, with 78% and 73% of participants having apical and anterior wall motion abnormalities, respectively. The majority of the patients presented with ST-elevation MI (81%) and another 7% had elevated troponin with a new or presumed new left bundle branch block. Nearly 20% had cardiac arrest or ventricular fibrillation (VF) arrest at the time of presentation for their MI and an additional 7% had sustained ventricular tachycardia or ventricular tachycardia requiring cardioversion. PCI was performed in 84%, 13% of whom were first treated with lytic therapy. Forty percent of the patients required ventilator support and/or circulatory support with an intra-aortic balloon pump.

Follow-Up Characteristics

The mean time from discharge to followup echocardiogram was 81.3 ± 32.9 days. The mean EF increased by 12.2 ± 11.9% to a mean of 40.2 ± 11.5% at follow-up. Of the participants, 57% had an EF of greater than 35% and 26% had EF recovery to 50% or greater (Table 2). Only 18.6% had a worse EF at follow-up than at baseline. Univariate analysis demonstrated the following predictors of persistent severe systolic dysfunction: lower baseline EF, elevated baseline (nonfasting) glucose levels, prolonged hospital stay, a prior history of MI, troponin elevation, and a lateral wall motion abnormality (Online Table 1). A history of congestive HF was also associated with persistent EF <35% (Table 2). Analysis of the interaction between multiple wall motion abnormalities demonstrated that there were small multiplicative interactions between anterior or septal and apical wall motion abnormalities. No interaction was found between anterior, septal, or apical and lateral or inferior wall motion abnormalities.

In univariate analysis, EF at the time of MI was directly correlated with EF recovery to 50% (Online Table 2). Males had a lower chance of EF recovery to 50% (odds ratio [OR]: 0.37; p = 0.006). Notably, those who had VF or cardiac arrest at the time of presentation had higher odds of EF recovery to 50% (OR: 2.41; p = 0.03). Increasing level of peak troponin was associated with lower odds of EF recovery to 50%. A history of CABG or MI had a negative association with the recovery of EF to 50% (Table 1).

Most patients were discharged on guideline-directed medical therapy specific for post-MI (Table 3). Receipt of either beta-blockers or spironolactone was associated with persistent LV dysfunction (p = 0.013 and p 0.001, respectively). Receipt of a prescription of either furosemide or ACEI or ARBs was associated with a trend toward less EF recovery. Consistent with the concern that confounding by indication explained this apparent association; length of hospital stay was significantly associated with receipt of ACEI, ARBs,

diuretics, beta-blockers, and aldosterone inhibitors, and the receipt of diuretics was significantly associated with acute HF on presentation, history of HF, or lower EF at the time of presentation (Online Table 3).

Predictors of Systolic Recovery

The model with the highest discrimination and calibration for EF recovery to >35% included EF at the time of MI, prolonged hospital stay, history of MI, lateral wall motion abnormalities, and elevated troponin level. The overall c-statistic for this model was 0.72, increasing to 0.75 after transformation to a point score scale. The calibration of the model, as estimated by the Hosmer-Lemeshow goodness of fit, was 0.34 and improved to 0.99 after transformation into point score scale.

Ejection fraction on admission showed a strong and independent association with recovery to EF >35%. Compared to those with an admission EF of 25%, participants with EF of 26% to 30% and EF of 31% to 35% had increased chance of recovery to EF >35% (OR: 2.77; 95% confidence interval [CI]: 1.34 to 5.70; p < 0.01; and OR: 6.88; 95% CI: 3.26 to 14.5; p < 0.01, respectively). Predictors of hospital discharge within 4 days – lack of lateral wall motion on echocardiogram and no prior history of MI – all had a trend towards a higher odds ratio of EF recovery to >35% (OR: 1.58; 95% CI; 0.86 to2.89; p = 0.14; OR: 1.46; 95% CI: 0.79 to 2.72; p = 0.23; and OR: 1.52; 95% CI: 0.78 to 2.96; p = 0.22, respectively). A troponin peak of 50- and 51- to 500-fold above the upper limit of normal (ULN) had a trend towards higher odds of EF recovery to EF >35% compared to maximum troponin level >500-fold above the ULN (OR: 1.74; 95% CI: 0.82 to 3.69; p = 0.15; and OR: 1.81; 95% CI: 0.91 to 3.62; p = 0.09, respectively) (Online Table 1, top 5 models). After transforming model predictors into point scores, predictor profiles with the lowest score of 0 had a 9% (95% CI: 2.5% to 21.7%) probability of EF recovery to >35%, whereas predictor profiles with a score of 7 had an 87% (95% CI: 83.8% to 90.1%) probability of EF recovery to >35% (Table 4 and Figure 1; Online Table 4 for probability table).

For EF recovery to 50%, the model with the highest discrimination and calibration included EF at the time of MI, history of MI, troponin elevation, and VF and/or cardiac arrest at presentation. The overall c-statistic for this model was 0.79 with a calibration of 0.34, as estimated by the Hosmer-Lemeshow goodness of fit calibration statistic. Neither the discrimination nor calibration changed after transformation into a point score scale. Ejection fraction on admission, VF or cardiac arrest on presentation, and troponin elevation all showed strong and independent associations with recovery to EF 50%. Compared to those with an admission EF of 25%, participants with EF of 26% to 30% or EF of 31% to 35% had an increased chance of recovery to EF 50% (OR: 3.08; 95% CI: 0.93 to 10.24; p = 0.07; and OR: 7.61; 95% CI: 2.48 to 23.33; p < 0.01, respectively). VF or cardiac arrest on presentation was associated with 5.53-fold higher odds of EF recovery to EF 50% (95% CI: 2.04 to 14.99; p < 0.01). A troponin peak of 50- or 51- to 500-fold above the ULN increased odds of EF recovery to 50% (OR: 12.02; 95% CI: 3.53 to 40.9; p < 0.01; and OR: 9.02; 95% CI: 2.82 to 28.83; p < 0.01, respectively) compared to a troponin peak of >500-fold above the ULN. The lack of prior history of MI approached significance for predicting EF recovery to 50% (odds ratio of 2.40; 95% CI: 0.85 to 6.78; p = 0.10) (Online Appendix,

top 5 models). After transforming model predictors into point scores, predictor profiles with the lowest score of 0 to 2 had a 4% (95% CI: 3% to 7%) probability of EF recovery to 50%, whereas predictor profiles with a score of 9 to 11 had a 49% (95% CI: 44 to 54%) probability of EF recovery to 50% (Table 5 and Figure 2; Online Table 3 for probability table).

Validation in the vest registry cohort

Characteristics of VEST registry participants, as well as differences between VEST registry and PREDICTs participants, are depicted in Tables 3 and 6. Echocardiograms were performed 20 days later in VEST registry compared to the PREDICTS patients (101 ± 36.9 vs. 81.3 ± 32.9 days; $p < 0.01$). VEST registry participants had a lower mean EF on follow-up (37.2% vs. 40.2%), and more patients in the VEST registry had a decrease in EF at follow-up (30.1% vs. 18.6%). VEST registry participants were less likely to have a prior history of PCI (22.9 vs. 36.1%; $p = 0.02$) and there was a trend toward lower prevalence of prior MI, HF, or prior CABG. Registry participants were less likely to have apical wall motion abnormalities (74.7 vs. 78.4%; $p = 0.03$). VEST registry participants also had higher B-type natriuretic peptide (BNP) values (3,231 vs. 1,054; $p = 0.05$), but lower peak troponin (1,061- vs. 1,592-fold increase above the ULN; $p < 0.01$) and lower low-density lipoprotein cholesterol on presentation (98 mg/dl vs. 109 mg/dl; $p = 0.04$).

When applied to the VEST registry patients, the prediction models remained significantly predictive, though they performed less well. The c-statistic for the model that predicts partial recovery to EF of 35% was 0.66 with a Hosmer-Lemeshow goodness of fit p value of 0.25. The model predicting EF recovery to 50% remained robust with a c-statistic of 0.72 with excellent calibration (Hosmer-Lemeshow goodness of fit p value of 0.85).

Discussion

The incidence of EF recovery in patients presenting with severe LV dysfunction at the time of acute MI has not been well described. In this study of patients with EF 35% at the time of MI, 57% of patients had recovered to an EF >35% by 90 days, and 26% had an EF that returned to normal or near normal (50%). Systolic function at the time of MI was an independent predictor of EF recovery to >35%. A history of MI, prolonged hospital stay, serum troponin level, and presence of lateral wall motion abnormalities demonstrated large associations with EF recovery to >35% that approached statistical significance (Central Illustration). A model incorporating these variables had fair discrimination and good calibration for predicting EF recovery to >35%.

Independent predictors of EF recovery to 50% included systolic function at the time of MI, troponin elevation, and VF and/or cardiac arrest at presentation. A history of MI approached significance for EF recovery to 50%. A model incorporating these variables had good discrimination and good calibration for predicting EF recovery to 50%.

In a large study involving more than 10,000 registry participants with EF 35% at the time of MI, Pokorney et al. demonstrated that only 8% of patients received an ICD within 1 year. Those who received an ICD had 36% lower risk of death within 2 years of their MI

compared to those who did not receive an ICD, after adjusting for age, sex, prior MI, prior stroke, and other covariates (9). A crucial limitation of this study was that measures of EF used to define ICD eligibility were available only at the time of hospitalization for MI. We found that 43% of our participants would continue to be eligible to receive an ICD at 90 days. An 8% ICD implantation rate for primary sudden cardiac death prevention, as was seen in the Pokorney study, suggested a marked underutilization of proven therapy and may explain the higher mortality rate in those without ICD implantation.

Risk scores derived from our prediction models demonstrated that those with the highest risk profile had a 9% and 4% probability of EF recovery to >35% and 50%, respectively, whereas those with the lowest risk profile had a 90% and 50% probability of EF recovery to >35% and 50%. Randomized studies have shown that alerts to physicians to consider ICDs in post-MI patients can increase appropriate primary prevention ICD implantation rates by 12-fold (10); however, these alerts are rarely used in practice. A risk score predicting those most likely to have a persistently low EF may focus attention on those at highest risk and frame the ICD discussion with the patient at the time of discharge to ensure follow-up. It is unlikely that this risk score will replace a follow-up echocardiogram; however, it is clear from previous studies that follow-up echocardiograms and ICD implantation are underused (9). Regardless of a patient's risk of persistent severe LV dysfunction, we recommend following current guideline recommendations to delay ICD implantation until an EF of 35% is demonstrated 40-days post AMI (90 days if revascularization occurs).

Risk factors for persistent LV dysfunction identified in our study largely agree with various findings from prior work. Systolic function and troponin levels at the time of MI have been shown to have strong associations with subsequent functional recovery (4,6,11). Prior studies have reported an association between BNP elevation and adverse remodeling at 4 months (increase in LV end-diastolic volume by 20%), a finding not repeated in our study (12,13). In these prior studies, the mean EF at the time of MI was higher (55% to 46% vs. 28.8% in our study), and mean BNP was lower (195 ± 109 pg/ml and 137 ± 118 pg/ml vs. $1,054 \pm 1,735$ pg/ml here). These reports may describe a fundamentally different population of patients than our cohort.

In our study, VF or cardiac arrest at presentation predicted near normal functional recovery. This may appear paradoxical given the association of VF/arrest with higher levels of troponin in both the PREDICTS and VEST cohorts ($p < 0.01$ and $p = 0.04$, respectively). Patients who had experienced VF or cardiac arrest may have had myocardial stunning, leading to a low EF assessment at enrollment (though this does not explain higher troponin elevations in these participants). Alternatively, VF may be a marker for ischemia with spontaneous reperfusion (troponin release kinetics differ under conditions of spontaneous reperfusion, non-reperfusion, or when intervention is performed) (14). Animal models demonstrate that spontaneous VF is more likely in ischemia-reperfusion than under ischemia alone (15). One could also speculate that those who suffer VF with spontaneous reperfusion are more likely to survive long enough to present to the hospital compared to those who had VF with no reperfusion (making resuscitation less likely). Finally, it should be noted that VF occurred in 20% of the participants in our study, higher than the 11% incidence of VF at the

time of MI reported in other studies (16). Our study specifically enrolled MI patients with EF 35%, in which one would expect a higher occurrence of VF.

Study Limitations

Strengths of this study included the prospective collection of a broad range of clinical data, the multicenter design, data collected soon after an acute MI, a validation cohort with identical inclusion criteria, and baseline data collection to the derivation cohort. An important weakness of the validation cohort (VEST Registry) was that follow-up echocardiograms were performed at the discretion of the clinician, rather than as part of a pre-defined study protocol (as was done in the derivation cohort, PREDICTS); this could be an important source of selection bias. There may be measured and unmeasured confounders that influenced the clinicians' decision to order the follow-up echocardiogram. Likely confounders that were measured include significant lower peak troponin, less frequent PCI, higher levels of BNP, and fewer apical wall motion abnormalities in the registry. Because the inclusion and exclusion criteria are identical for PREDICTS and VEST Registry, the presence of significant differences in covariates may indicate informative censoring. Validation in an external cohort is needed to better estimate the models predictive capacity. Variables and alternative models identified during model selection may have significant predictive power in this and other cohorts.

An important covariate that was not available to us was time to revascularization. All sites in the study were major cardiovascular care centers with on-call interventionalists. In the era of reporting door-to-balloon time measures of quality, it can be assumed that most PCIs were performed within a few hours of presentation. We did not have information regarding LV function prior to the index MI, or the occurrence of staged revascularization after initial hospitalization. These variables, if known, could act as powerful predictors of left ventricular recovery.

Conclusions

Recovery of systolic function to an EF >35% occurs in the majority of patients who present with severe systolic dysfunction at the time of MI. Clinical variables at the time of acute myocardial infarction can predict the probability of EF recovery to greater than 35% as well as the probability of recovery to near normal systolic function.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

ABBREVIATIONS

ACEI	angiotensin-converting enzyme inhibitor
ARB	angiotensin receptor blocker
CK	creatine kinase
EF	ejection fraction
ICD	implantable cardioverter-defibrillator
VF	ventricular fibrillation

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Appendix

PREDICTS and VEST Registry Site PI's

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Perspectives

COMPETENCY IN MEDICAL KNOWLEDGE

Most patients with severe left ventricular dysfunction in the acute phase of myocardial infarction exhibit improvement in LV function 90 days later. Prior MI, early ventricular fibrillation or cardiac arrest, peak serum troponin, and ejection fraction early after presentation are predictors of later myocardial recovery.

TRANSLATIONAL OUTLOOK

Prospective studies are needed to assess whether earlier implantation of automatic defibrillators in patients with a low likelihood of myocardial recovery improves survival post-MI.
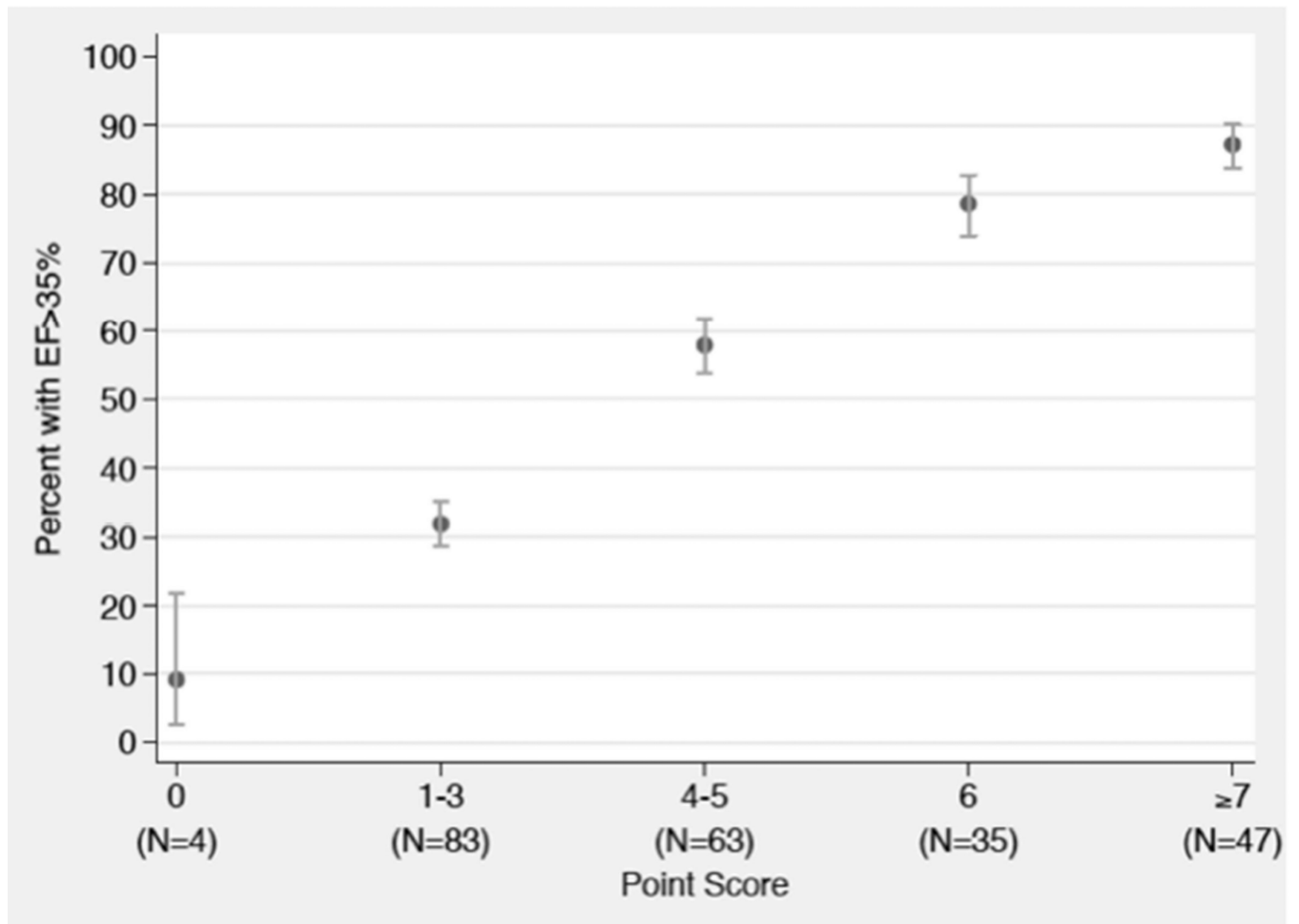
Figure 1. Frequency of EF Recovery   35%
The observed left ventricular functional recovery to an ejection fraction (EF) >35% 90 days after the index myocardial infarction improved as point score increased (n = number of participants in the derivation set).
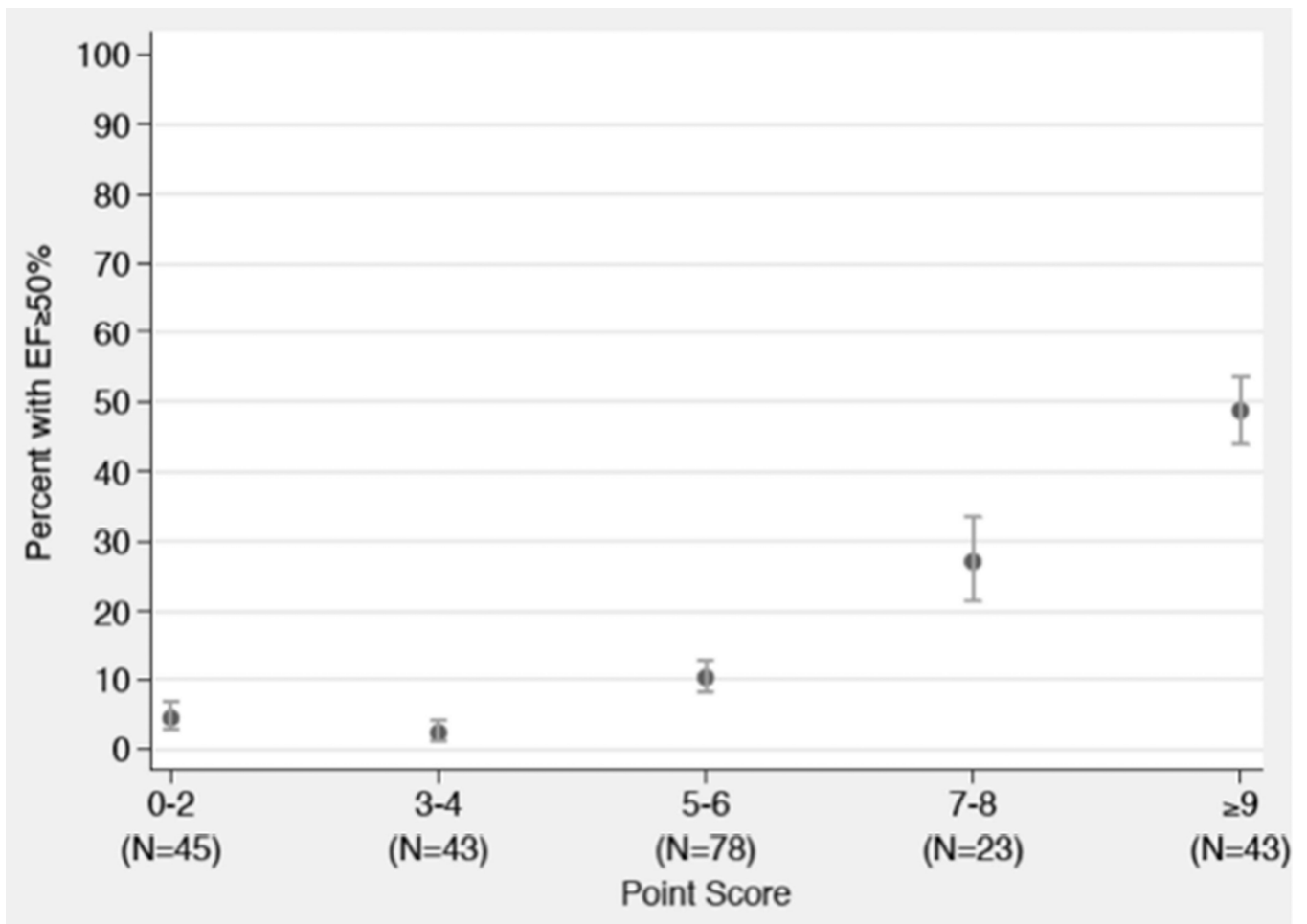
Figure 2. Frequency of EF Recovery   50%
The observed left ventricular functional recovery to an EF   50% 90 days after the index myocardial infarction also improved as point score rose (n = number of participants in the derivation set). Abbreviations as in Figure 1.

Near Normal (EF ≥ 50%)
Predictors:
•Higher EF at Presentation
•Female
•Lower Peak Troponin
•No Prior MI
•VF or Arrest at Presentation

Partial Recovery (EF 36-49%)
Predictors:
•Higher EF at Presentation
•Length of Stay ≤ 4 Days
•No Prior MI
•No Lateral WMA
•Glucose < 100 at Presentation
•Lower Peak Troponin

Persistent Severe (EF ≤ 35%)

43%

26%

31%
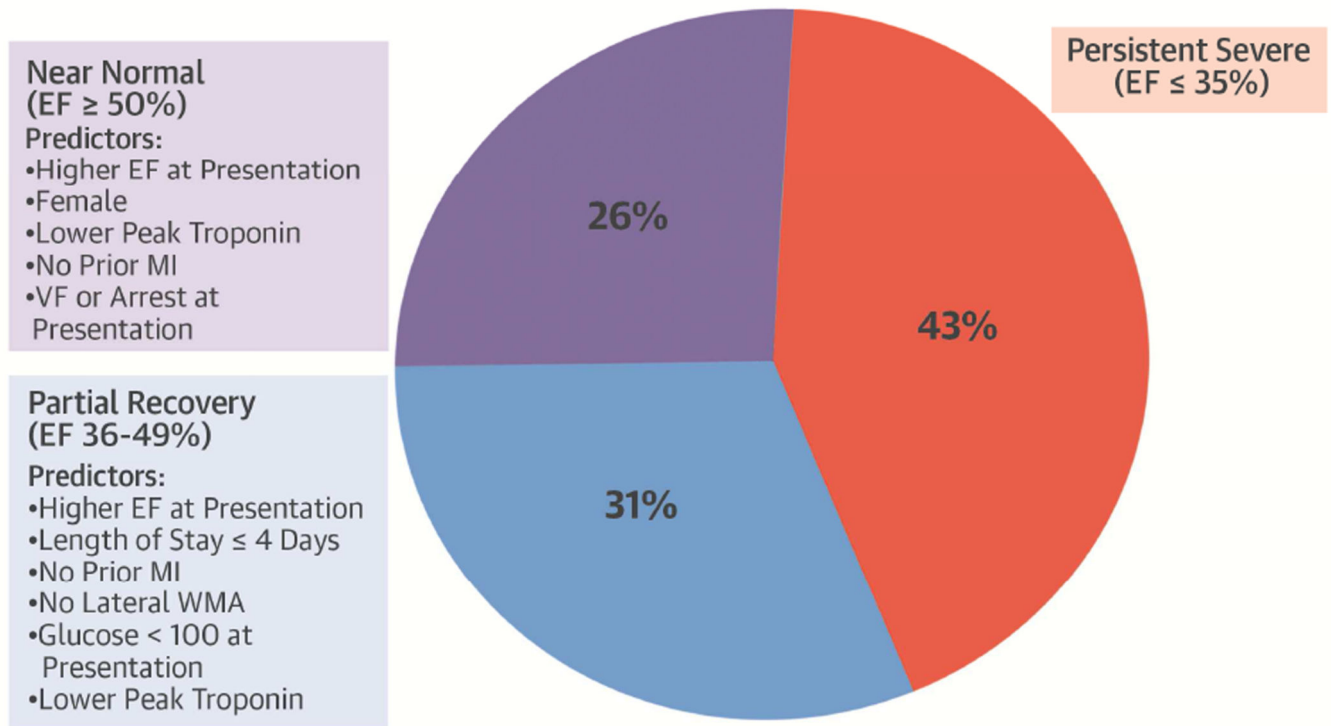
Central Illustration. Left Ventricular Dysfunction after Acute MI: Ejection Fraction 90 Days Acute Myocardial with Severe Systolic Dysfunction (EF   35%)
Severe left ventricular (LV) systolic dysfunction after myocardial infarction (MI) is associated with increased mortality. To better determine which patients with an ejection fraction (EF)   35% at time of acute MI may be more likely to improve systolic function, models assessing variables that predict LV recovery to an EF >35% and   50% 90 days after the event were developed. Although more patients continue to experience severe dysfunction, several variables predict partial or near normal recovery in these patients. VF = ventricular fibrillation.

Table 1

Baseline Characteristics at Time of Index MI

Characteristics at Presentation	Total (n = 231)	35 (n = 100)	90-day EF (%) 36–49 (n = 72)	50 (n = 59)	p Value
Age, yrs	60.4 ± 11.8	60 ± 12	59 ± 11	62 ± 12	0.5029
Male	165	76 (46.1)	53 (32.1)	36 (21.8) **	0.0455
BMI, kg/m²	28.6 ± 4.9	29.1 (4.8)	28.2 (4.9)	28.3 (5.0)	0.3116
Diabetes Mellitus	80	34 (42.5)	27 (33.8)	19 (32.2)	0.8164
History of congestive HF	31	17 (54.8)	9 (29.0) *	5 (16.1)	0.1326
History of MI	66	37 (56.1)	18 (28.8) *	10 (15.2)	0.0074
History of PCI	84	39 (46.4)	27 (32.1)	18 (21.4)	0.2808
History of CABG	26	14 (53.8)	10 (38.5)	2 (8.7) **	0.0317
History of CVA	12	7 (58.3)	3 (25.0)	2 (16.7)	0.3413
History of AF	21	12 (57.1)	4 (19.1)	5 (23.8)	0.2140
History of ASA	90	46 (51.1)	26 (28.9)	18 (20.0)	0.1303
Tobacco use					0.8269
Never	86	36 (41.9)	26 (30.2)	24 (28.6)	
Former	80	36 (45.0)	25 (31.2)	19 (23.7)	
Current	65	28 (43.1)	21 (32.3)	16 (24.6)	

Values are mean ± SD or n (%).

*
p < 0.05 for EF 35% vs. EF >35%

**
p < 0.05 for EF <50% vs. 50%

AF = atrial fibrillation; ASA = aspirin; BMI = body mass index; CABG = coronary artery bypass graft; CVA = cerebrovascular accident; EF = ejection fraction; HF = heart failure; MI = myocardial infarction; PCI = percutaneous coronary intervention.

TABLE 2

Clinical Characteristics at Time of Index MI

Characteristics at Presentation	Total (n = 231)	35 (n = 100)	90-day EF 36–49 (n = 72)	50 (n = 59)	p Value
EF at index MI	28.1 ± 6.6	25 ± 6.9	30 ± 5.6	31 ± 5.0	< 0.0001
EF 25 %	88	60 (68.2)	17 (19.3)	11 (12.5)	< 0.0001
EF 26%–30 %	64	24 (37.5)	24 (37.5)	16 (25.0)	
EF >30 %	79	16 (20.3)	31 (39.2)	32 (40.5)	
Mitral Regurgitation					0.2124
None-Mild	176	76 (43.2)	53 (30.1)	47 (26.7)	
Mild-Moderate	25	10 (40.0)	10 (20.0)	5 (20.0)	
Moderate- Severe	6	5 (83.3)	1 (16.7)	0	
WMA					
Any	204	89 (43.6)	64 (31.4)	51 (25.0)	0.6727
Anterior	177	80 (45.2)	52 (29.4)	45 (25.4)	0.8124
Inferior/posterior	111	54 (48.7)	33 (29.7)	24 (21.7)	0.1355
Septal	166	76 (45.8)	50 (30.1)	40 (24.1)	0.3669
Lateral	93	49 (52.7)	26 (28.0)	18 (19.4)	0.293
Apical	181	81 (44.8)	53 (29.4)	47 (26.0)	0.8590
STEMI	186	79 (42.5)	62 (33.3)	45 (24.2)	0.6883
New LBBB	18	10 (55.6)	5 (27.8)	3 (16.7)	0.2745
New Q waves	59	26 (44.1)	19 (32.2)	14 (23.7)	0.7498
AF on presentation	27	15 (55.6)	7 (25.9)	5 (18.5)	0.2306
Acute HF	35	14 (40.0)	11 (31.4)	10 (28.6)	0.6158
Cardiogenic shock	40	20 (50.0)	12 (30.0)	8 (20.0)	0.3030
Revascularization					

Characteristics at Presentation	Total (n = 231)	90-day EF 35 (n = 100)	90-day EF 36–49 (n = 72)	90-day EF 50 (n = 59)	p Value
None	37	16 (43.2)	14 (37.8)	7 (18.9)	0.4302
Lytics	1	1 (100)	0	0	
PCI	166	72 (43.3)	48 (29.1)	46 (27.7)	
Both	27	11 (40.7)	10 (37.0)	6 (22.2)	
Intubation	34	16 (47.1)	7 (20.6)	11 (32.4)	0.6679
Balloon pump	53	28 (52.8)	14 (26.4)	11 (20.8)	0.1853
Arrest or VF	43	16 (37.2)	13 (30.2)	14 (32.6)[**]	0.2289
VT	18	10 (55.6)	5 (27.8)	3 (16.7)	0.2745
LOS, days	6.1 ± 4.6	7.1 ± 5.4	5.5 ± 3.8[*]	5.3 ± 3.5	0.0089
Prolonged HS (>4 days)	118	62 (52.5)	31 (26.3)	25 (21.2)	0.0163
Laboratory analysis					
Maximum Cr, mg/dl	1.2 ± 0.5	1.2 ± 0.5	1.2 ± 0.4	1.2 ± 0.7	0.4409
Baseline glucose, mg/dl	207 ± 467	158 ± 203	324 ± 782	145 ± 118	0.4094
Fasting glucose, mg/dl	185 ± 373	152 ± 234	265 ± 584	140 ± 140	0.2015
LDL–C, mg/dl	109 ± 40	114 ± 40.4	102 ± 41	107 ± 39	0.3159
HDL–C, mg/dl	39.7 ± 12.2	40 ± 12	39 ± 14	40 ± 11	0.9987
Triglyceride, mg/dl	129 ± 64	132 ± 75	120 ± 48	135 ± 65	0.5728
Troponin max, x ULN	$1,592 \pm 3,180$	$2,347 \pm 4,408$	$1,238 \pm 1,560$	$743 \pm 1,455$[**]	0.0067
BNP max, pg/ml	$1,054 \pm 1,735$	$987 \pm 1,506$	$936 \pm 1,208$	$1,381 \pm 2,681$	0.1363
Medications on discharge					
ACEI or ARB	175	81 (46.3)	55 (31.4)	39 (22.3)[**]	0.0349

Characteristics at Presentation	Total (n = 231)	35 (n = 100)	90-day EF 36–49 (n = 72)	50 (n = 59)	p Value
Aspirin	202	89 (44.1)	62 (30.7)	51 (25.2)	0.6308
Beta-blocker	207	94 (45.4)	65 (31.4)	48 (23.2)	0.0127
Statin	196	86 (43.9)	57 (29.1)	53 (27.0)	0.4816
Furosemide	75	38 (50.7)	24 (32.0)	13 (17.3)	0.0372
Spironolactone	57	34 (59.6)	17 (29.8) *	6 (10.5) **	0.0008
Any diuretic	110	57 (51.8)	36 (32.7)	17 (15.5) **	0.0006

Values are mean ± SD or n (%).

*
p < 0.05 for EF <35% vs. EF   35%

**
p < 0.05 for EF<50% vs.   50%

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BNP = B-type natriuretic peptide; Cr = creatinine; HDL-C = high-density lipoprotein cholesterol; HS = hospital stay; LBBB = left bundle branch block; LDL-C = low-density lipoprotein cholesterol; LOS = length of stay; STEMI = ST-elevation myocardial infarction; ULN = fold increase above upper limit of normal; VF = ventricular fibrillation; VT = ventricular tachycardia; WMA = wall motion abnormalities; other abbreviations as in Table 1.

Table 3

Clinical Characteristics at Time of Index MI: Derivation and Validation Cohorts

Characteristics at Presentation	PREDICTS (Derivation)	VEST Registry Overall Cohort	VEST Registry without 90-day Echocardiogram	VEST Registry with 90-day Echocardiograpm (Validation)	p Value[*]
	(n = 231)	(n = 509)	(n = 273)	(n = 236)	
EF at index MI	28.1 ± 6.6	28.2 ± 5.9	28.2 ± 6.0	28.2 ± 5.7	(0.54,0.87)
EF <25 %	88 (38.1)	188 (36.9)	95 (34.8)	93 (39.4)	
EF 26%–30 %	64 (27.7)	171 (33.6)	98 (35.9)	73 (30.9)	
EF >30 %	79 (34.2)	150 (29.5)	80 (29.3)	70 (29.7)	
Mitral regurgitation					(0.94,0.85)
None-Mild	176 (76.2)	398 (84.1)	212 (84.1)	186 (84.2)	
Mild-Moderate	25 (10.8)	60 (12.7)	31 (12.3)	29 (13.1)	
Moderate- Severe	6 (2.6)	15 (3.2)	9 (3.6)	6 (2.7)	
WMA					
Any	204 (88.3)	395 (90.4)	198 (88.0)	197 (92.9)	**(0.20,0.08)**
Anterior	177 (76.6)	341 (74.0)	166 (69.2)	175 (79.2)	(0.60,0.01)
Inferior/Posterior	111 (48.1)	247 (53.6)	125 (52.1)	122 (55.2)	(0.37,0.50)
Septal	166 (71.9)	318 (69.0)	161 (67.1)	157 (71.0)	(0.23,0.36)
Lateral	93 (40.3)	205 (44.5)	103 (42.9)	102 (46.2)	(0.46,0.49)
Apical	181 (78.4)	338 (73.3)	173 (72.1)	165 (74.7)	**(0.03,0.53)**
STEMI	186 (80.5)	357 (70.3)	188 (68.9)	169 (71.9)	(0.03,0.45)
New LBBB	18 (7.8)	30 (5.9)	17 (6.3)	13 (5.5)	(0.32,0.72)
New Q waves	59 (25.5)	108 (21.3)	57 (21.0)	51 (21.6)	(0.32,0.86)
AF on presentation	27 (11.7)	53 (10.5)	28 (10.3)	25 (10.6)	(0.71,0.92)
Acute HF	35 (15.2)	69 (13.6)	36 (13.3)	33 (14.0)	(0.72,0.82)
Cardiogenic shock	40 (17.3)	62 (12.2)	25 (9.2)	37 (15.7)	**(0.63,0.03)**

Characteristics at Presentation	PREDICTS (Derivation) (n = 231)	VEST Registry Overall Cohort (n = 509)	VEST Registry without 90-day Echocardiogram (n = 273)	VEST Registry with 90-day Echocardiogram (Validation) (n = 236)	p Value*
Revascularization					(0.57,0.06)
None	37 (16.0)	98 (19.3)	52 (19.2)	46 (19.5)	
Lytics	1 (0.4)	7 (1.4)	7 (2.6)	0 (0.0)	
PCI	166 (71.9)	357 (70.4)	192 (70.9)	165 (69.9)	
Both	27 (11.7)	45 (8.9)	20 (7.4)	25 (10.6)	
Intubation	34 (14.7)	54 (10.7)	28 (10.3)	26 (11.0)	(0.23,0.08)
Balloon pump	53 (22.9)	73 (14.4)	36 (13.3)	37 (15.7)	**(0.05,0.44)**
Arrest or VF	43 (18.6)	51 (10.1)	20 (7.4)	31 (13.1)	**(0.11,0.03)**
VT	18 (7.8)	27 (5.3)	12 (4.4)	15 (6.4)	(0.55,0.33)
LOS, days	6.1 ± 4.6	6.2 ± 4.9	6.3 ± 5.1	6.2 ± 4.7	(0.84,0.88)
Prolonged HS (>4 days)	119 (51.5)	268 (52.9)	146 (53.9)	122 (51.7)	(0.89,0.62)
Laboratory analysis	34 (14.7)	54 (10.7)	28 (10.3)	26 (11.0)	(0.23,0.08)
Maximum Cr, mg/dl	1.2 ± 0.5	1.3 ± 0.6	1.3 ± 0.7	1.2 ± 0.76	(0.90,0.42)
Baseline glucose, mg/dl	207 ± 466	170 ± 311	174 ± 388	164 ± 194	(0.24,0.81)
Fasting glucose, mg/dl	185 ± 373	165 ± 341	177 ± 452	152 ± 147	(0.05,0.37)
LDL-C, mg/dl	109 ± 40	95 ± 44	92 ± 45	98 ± 42	**(0.04,0.20)**
HDL-C, mg/dl	39.7 ± 12.2	42 ± 17	42 ± 19	42 ± 16	(0.13,0.75)
Triglyceride, mg/dl	129 ± 64	128 ± 98	125 ± 84	132 ± 111	(0.21,0.99)
Troponin max, x ULN	1,592 ± 3,180	1,069 ± 3,124	1,061 ± 2,655	1,076 ± 3,583	**(0.01,0.73)**
BNP max, pg/ml	1,054 ± 1735	3,180 ± 5,812	3,231 ± 5,609	3,119 ± 6,073	**(0.05,0.48)**
Medications on discharge					
ACEI or ARB	175 (75.8)	383 (75.3)	206 (75.5)	177 (75.0)	(0.89,0.91)
Aspirin	202 (87.4)	447 (87.8)	233 (85.4)	214 (90.7)	(0.26,0.07)
Beta-blocker	207 (89.6)	441 (86.6)	231 (84.6)	210 (89.0)	(0.83,0.15)

Characteristics at Presentation	PREDICTS (Derivation)	VEST Registry Overall Cohort	VEST Registry without 90-day Echocardiogram	VEST Registry with 90-day Echocardiograpm (Validation)	p Value*
	(n = 231)	(n = 509)	(n = 273)	(n = 236)	
Statin	196 (84.8)	435 (85.5)	239 (87.6)	196 (83.1)	(0.60,0.15)
Furosemide	75 (32.5)	146 (28.7)	77 (28.2)	69 (29.2)	(0.62,0.80)
Spironolactone	57 (24.7)	129 (25.3)	74 (27.1)	55 (23.3)	(0.73,0.33)
Any diuretic	110 (47.6)	231 (45.4)	124 (45.4)	107 (45.3)	(--,0.99)

Values are mean ± SD or n (%).

*
The first p value is shows denotes the significance of the difference between the Predicts Derivation cohort and those in the VEST Registry without 90 day echocardiograms, the second p value demonstrates the significance of the difference between the cohort in the VEST registry that had a 90 day echocardiograms and those without a 90-day echo cardiograms.

Abbreviations as in Tables 1 and 2.

Table 4

EF Recovery to >35% 90 Days After MI

Characteristic		Points
EF at MI presentation	31%–35%	4
	26%–30%	2
Length of stay	4 days	1
No history of MI		1
No lateral WMA		1
Troponin max fold increase	< 500	1
Total Possible Points		**8**

Abbreviations as in Tables 1 and 2.

Table 5

EF Recovery to ≥50% 90 Days After MI

Characteristic		Points
EF at MI presentation	31%–35%	4
	26%–30 %	1
No history of MI		1
Troponin max fold increase	< 500	4
Present with VF or arrest		3
Total Possible Points		**11**

Abbreviations as in Tables 1 and 2.

Table 6

Baseline Characteristics at Time of Index MI: Derivation and Validation Cohorts

Characteristics at Presentation	PREDICTS (Derivation) (n = 231)	VEST Registry Overall Cohort (n = 509)	VEST Registry without 90-day Echocardiogram (n = 273)	VEST Registry with 90-day Echocardiogram (Validation) (n = 236)	p Value*
Age, yrs	60.4 ± 11.8	61 ± 11.7	61.7 ±11.9	60.4 ±11.5	(0.81, 0.32)
Male	165 (71.4)	385 (75.8)	213 (78.3)	172 (72.9)	(0.73,0.15)
BMI, kg/m²	28.6 ± 4.9	28.2± 5.8	28.0 ± 6.2	28.5 ± 5.4	(0.63, 0.24)
Diabetes mellitus	80 (34.6)	159 (31.2)	87 (31.8)	72 (30.5)	(0.34,0.74)
History of congestive HF	31 (13.4)	77 (15.1)	50 (18.3)	27 (11.4)	**(0.52,0.03)**
History of MI	66 (28.6)	129 (25.3)	76 (27.8)	53 (22.5)	(0.13,0.16)
History of PCI	84 (36.4)	128(25.2)	74 (27.1)	54 (22.9)	**(0.02,0.27)**
History of CABG	26 (11.3)	48 (9.4)	30 (11.0)	18 (7.6)	(0.18,0.20)
History of CVA	12 (5.2)	46 (9.0)	29 (10.6)	17 (7.2)	(0.37,0.18)
History of AF	21 (9.1)	45 (8.8)	27 (9.9)	18 (7.6)	(0.57,0.37)
History of ASA	90 (39.0)	210 (42.7)	111 (42.4)	99 (43.0)	(0.25,0.88)
Tobacco use					(0.10,0.89)
Never	86 (37.3)	140 (27.5)	73 (26.7)	67 (28.4)	
Former	80 (34.6)	190 (37.4)	103 (37.9)	87 (36.9)	
Current	65 (28.1)	179 (35.2)	97 (35.7)	82 (34.8)	

Values are mean ± SD or n (%).

*
The first p value is shows denotes the significance of the difference between the Predicts Derivation cohort and those in the VEST Registry without 90 day echocardiograms, the second p value demonstrates the significance of the difference between the cohort in the VEST registry that had a 90-day echocardiograms and those without a 90 day echocardiograms

Abbreviations as in Table 1.