ORIGINAL RESEARCH

Estimating Myocardial Infarction Size With a Simple Electrocardiographic Marker Score

Daniel C. Lee, MD, MS; Christine M. Albert, MD, MPH; Dhiraj Narula, MD; Alan H. Kadish, MD; Gopi Krishna Panicker, BHMS, PGDCR; Edwin Wu, MD; Andi Schaechter, BSN; Julie Pester, BA; Neal A. Chatterjee, MD, MSc; Nancy R. Cook, ScD; Jeffrey J. Goldberger, MD, MBA

***Background*—**Myocardial infarction (MI) size is a key predictor of prognosis in post-MI patients. Cardiovascular magnetic resonance (CMR) is the gold standard test for MI quantification, but the ECG is less expensive and more widely available. We sought to quantify the relationship between ECG markers and cardiovascular magnetic resonance infarct size.

***Methods and Results*—**Patients with prior MI enrolled in the DETERMINE (Defibrillators to Reduce Risk by Magnetic Resonance Imaging Evaluation) and PRE-DETERMINE Trial and Registry were included. ECG leads were analyzed for markers of MI: Q waves, fragmented QRS, and T wave inversion. DETERMINE Score=number of leads with [Q waves×2]+[fragmented QRS]+[T wave inversion]. Left ventricular ejection fraction (LVEF) and infarct size as a percentage of left ventricular mass (MI%) were quantified by cardiovascular magnetic resonance. The Modified Selvester Score estimates MI size from 37 ECG criteria. In 551 patients (aged 62.1±10.9 years, 79% men, and LVEF=40.3±11.0%), MI% increased as the number of ECG markers increased ($P<0.001$). By univariable linear regression, the DETERMINE Score (range 0–26) estimated MI% ($R^2=0.18$, $P<0.001$) with an accuracy approaching that of LVEF ($R^2=0.22$, $P<0.001$) and higher than the Modified Selvester Score ($R^2=0.09$, $P<0.001$). By multivariable linear regression, addition of the DETERMINE Score improved estimation of MI% over LVEF alone ($P<0.001$) and over Modified Selvester Score alone ($P<0.001$).

***Conclusions*—**In patients with prior MI, a simple ECG score estimates infarct size and improves infarct size estimation over LVEF alone. Because infarct size is a powerful prognostic indicator, the DETERMINE Score holds promise as a simple and inexpensive risk assessment tool. **(*J Am Heart Assoc*. 2020;9:e014205. DOI: 10.1161/JAHA.119.014205.)**

Key Words: electrocardiography • magnetic resonance imaging • myocardial infarction • prognosis • sudden death

Myocardial infarction (MI) is a leading cause of death and disability worldwide. Cardiovascular magnetic resonance imaging (CMR) is now considered the gold standard for visualization and quantification of MI. The presence and extent of MI by CMR has been shown to predict a wide array of adverse cardiovascular outcomes[1,2] including death,[3] recurrent MI, arrhythmias, congestive heart failure, angina, and revascularization.[4]

In clinical practice, electrocardiography remains the first-line diagnostic test for the evaluation of patients with suspected ischemic heart disease because of its safety, low cost, and near universal availability. Several ECG abnormalities can be seen in patients with prior MI including Q waves (QW), fragmented QRS (FQRS),[5] and T wave inversions (TWI).[6] Presently, these abnormalities are considered as dichotomous markers for the presence or absence of infarction and their independent relationship to infarct size has not been studied.

The aim of this study was to evaluate whether abnormal ECG markers could be used to quantify infarct size measured by CMR in patients with prior MI. We hypothesized that the presence and extent of abnormal ECG markers would have independent and additive effects on estimation of infarct size. We sought to compare the accuracy for estimating infarct size of a simple ECG score based on the presence and extent of abnormal ECG markers (DETERMINE Score) to left ventricular ejection fraction (LVEF) and the Modified Selvester Score, a 37-criteria/29-point ECG scoring system that has been previously demonstrated to estimate infarct size and

From the Northwestern University Feinberg School of Medicine, Chicago, IL (D.C.L., E.W., A.S.); Brigham and Women's Hospital, Boston, MA (C.M.A., J.P., N.A.C., N.R.C.); Cedars Sinai Medical Center, Los Angeles, CA (C.M.A.); Quintiles Cardiac Safety Services, Mumbai, India (D.N., G.K.P.); Touro College and University System, New York, NY (A.H.K.); University of Washington Medical Center, Seattle, WA (N.A.C.); University of Miami Miller School of Medicine, Miami, FL (J.J.G.).

Accompanying Tables S1 and S2 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.014205

Correspondence to: Daniel C. Lee, MD, MS, 303 E. Chicago Ave, Tarry 14-725, Chicago, IL 60611. E-mail: dlee@northwestern.edu

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Clinical Perspective

What Is New?

- To our knowledge, this is the first study to simultaneously quantify the independent and additive contribution of Q waves, fragmented QRS, and inverted T waves on 12-lead ECG to estimation of infarct size measured by cardiovascular magnetic resonance imaging in patients with prior myocardial infarction in a large multicenter study.
- The DETERMINE (Defibrillators to Reduce Risk by Magnetic Resonance Imaging Evaluation) score equals the number of leads with Q waves (×2), plus the number of leads with fragmented QRS, plus the number of leads with T wave inversion.
- The DETERMINE Score estimated infarct size with an accuracy approaching that of left ventricular ejection fraction, and higher than the Modified Selvester Score or contiguous Q waves.

What Are the Clinical Implications?

- Combining the DETERMINE Score with left ventricular ejection fraction improved estimation of infarct size over left ventricular ejection fraction alone.
- An ECG screening tool that provides an estimate of infarct size could potentially be used to identify patients more likely to have a large infarct burden and benefit from more intensive diagnosis and treatment strategies.

prognosis in patients with prior MI. The ability to easily estimate infarct size from a 12-lead ECG would be extremely useful in the clinical evaluation of patients with prior MI.

Methods

Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the DETERMINE Publications Committee by contacting the corresponding author. All participants provided written informed consent, and the study was approved by the institutional review boards at Northwestern University and Brigham and Women's Hospital.

Study Population

Patients with a clinical history of MI were identified from the Defibrillators to Reduce Risk by Magnetic Resonance Imaging Evaluation (DETERMINE) Trial and Registry and the PRE-DETERMINE study. The DETERMINE Trial (ClinicalTrials.gov ID NCT00487279) was a multicenter randomized trial which sought to test the hypothesis that implatable cardioverter defibrillator therapy would improve survival over optimal medical therapy in patients with coronary artery disease (CAD), LVEF >35% and infarct mass by CMR >10%.[7] Patients with a history of CAD and mild-to-moderate left ventricular dysfunction were eligible to be enrolled in the study and undergo CMR. Patients screened but ineligible (eg, LVEF <35%, infarct mass <10%) or unwilling to participate in the randomized arm of the trial were enrolled in either the PRE-DETERMINE Study (ClinicalTrials.gov ID NCT01114269) or the DETERMINE Registry. The PRE-DETERMINE Study is a prospective, multi-center study of patients with CAD and documentation of MI and/or mild-to-moderate left ventricular dysfunction (LVEF 35%–50%). Of the total 5993 patients enrolled in the above studies, late gadolinium enhanced (LGE) CMR images were collected in 920 patients from 66 field sites across the United States. The presence of an implatable cardioverter defibrillator at baseline was an exclusion criteria for enrollment in DETERMINE and PRE-DETERMINE, and none of the patients in this analysis had an implatable cardioverter defibrillator at the time of CMR scan. Patients were excluded because of insufficient image coverage/quality (n=100), patient withdrawal from the study (n=4), no prior history of MI (n=67), >1 year between ECG and CMR (n=44), left bundle branch block (n=41), and insufficient ECG data (n=116). Some exclusions overlapped. After exclusions, a total of 551 patients were included in this study.

Twelve-Lead ECG

Each patient ECG was analyzed by the ECG core laboratory (Quintiles Cardiac Safety Services Mumbai, India). Each lead of the patient ECG was analyzed for the presence or absence of abnormal ECG markers, excluding lead aVR (augmented Vector Right). ECG studies were excluded if >1 lead was not interpretable because of noise or artifact. Abnormal ECG markers were defined before examining the data based on accepted criteria in published literature. A pathologic Q wave (QW) was defined as any Q wave with (1) duration >40 ms and (2) Q/R amplitude ratio >0.25 or absence of an R wave. Fragmented QRS (FQRS) was defined on the patient ECG according to criteria described by Das et al[5]: QRS duration <120 ms and the RSR' pattern, defined by the presence of an additional R wave (R') or notching in the nadir of the S wave, or the presence of >1 R' (fragmentation). T wave inversion (TWI) was defined as the presence of an inverted T wave with the nadir deeper than 0.1 mV.

Each patient ECG was also coded for the presence of contiguous QWMI (cQWMI), contiguous fragmented QRS (cFQRS), and contiguous T wave inversion (cTWI). These contiguous ECG markers required involvement of ≥2 ECG leads corresponding to a major coronary artery territory (II-III-aVF, I-aVL, or V_{1-6}; aVF = augmented Vector Foot, aVL = augmented Vector Left). Figure 1 illustrates examples of ECG's with a range of contiguous ECG abnormalities, with corresponding CMR images.

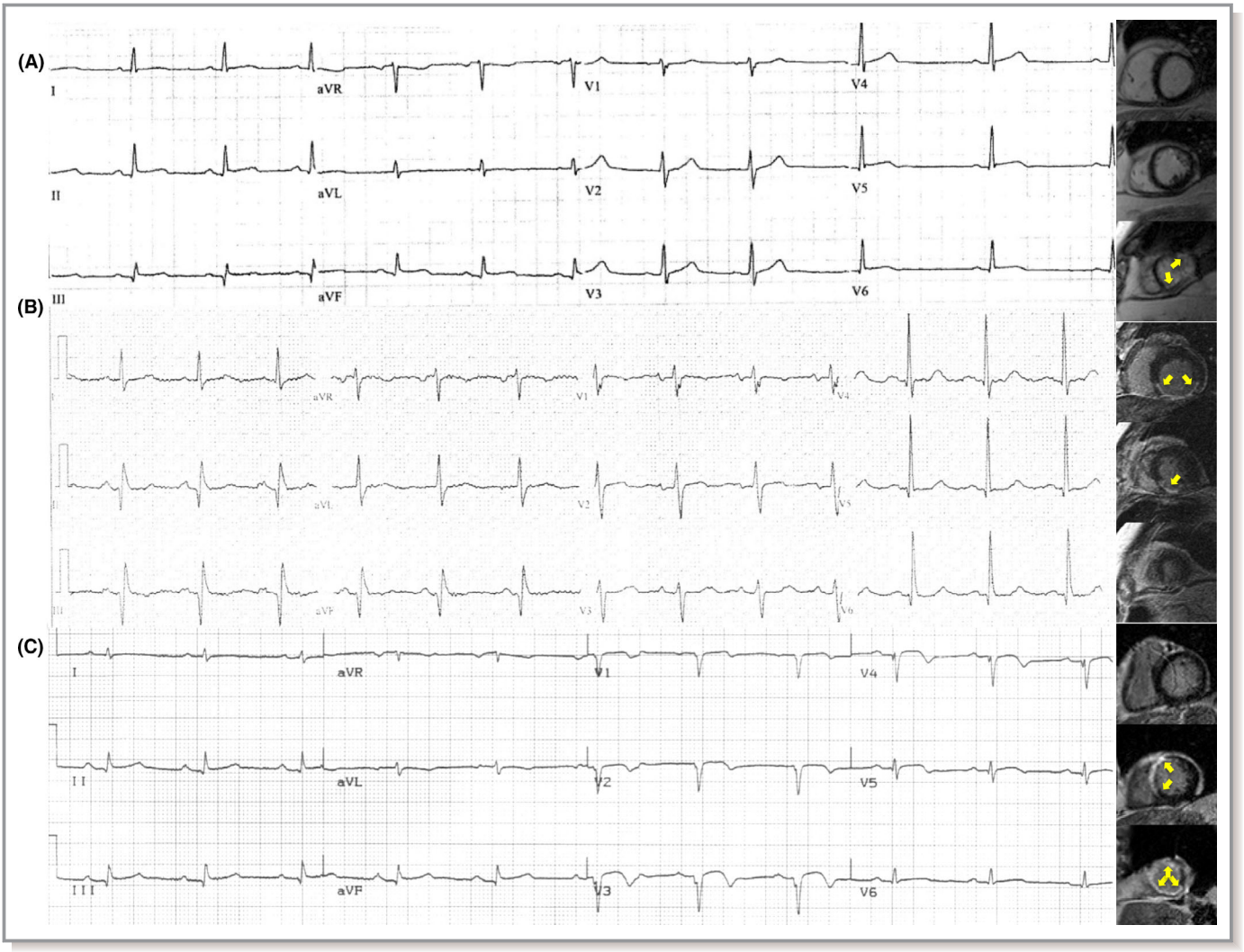

Figure 1. Patient examples. ECG and CMR in patients with (**A**) no abnormal ECG markers, DETERMINE Score 0, infarct size 4.3% in the left circumflex coronary artery territory, (**B**) pathological Q waves in leads III and aVF, one contiguous ECG marker (cQWMI), DETERMINE score 4, infarct size 13.8% in the right coronary artery territory, (**C**) pathological Q waves in leads $V_{1\text{-}3}$, fragmented QRS complexes in leads $V_{1\text{-}4}$, T wave inversion in leads $V_{2\text{-}4}$, 3 contiguous ECG markers (cQWMI, cFQRS, cTWI), DETERMINE Score 13, infarct size 24.8% in the left anterior descending coronary artery territory. Yellow arrows denote the location of myocardial infarction visualized by late gadolinium enhanced cardiovascular magnetic resonance imaging. CMR indicates cardiovascular magnetic resonance imaging; cFQRS, contiguous fragmented QRS; cQWMI, contiguous Q wave myocardial infarction; cTWI, contiguous T wave inversion; DETERMINE Score, simple ECG score for estimating infarct size based on the presence and extent of abnormal ECG markers.

DETERMINE Score and Selvester Score

The modified Selvester QRS scoring system was developed to estimate infarct size using 37 ECG criteria to calculate an overall score with a possible range of 0 to 29. We applied the criteria as previously defined.[8] We developed our own simplified scoring system to estimate infarct size based on the presence and extent of abnormal ECG markers. Multivariable linear regression was performed to assess the independent relationship between the number of leads affected by each ECG marker and MI% by CMR. In Model S3 of Table S1A the B coefficient relating the number of leads with QW to infarct size was approximately double the B coefficients relating the number of leads with FQRS and TWI to infarct size. Therefore, we defined: DETERMINE Score=[number of leads with QW (×2)]+[number of leads with FQRS]+[number of leads with TWI].

Magnetic Resonance Imaging

All CMR studies were analyzed centrally by the CMR core laboratory (Northwestern University Cardiovascular Imaging Core Laboratory—NUCICL, Chicago, USA). CMR studies were

composed of cine and LGE CMR performed in a short axis stack and multiple long axis views. Studies were excluded if the short axis stack did not include the entire LV from the mitral valve plane to the apex, or if image artifact precluded quantitative analysis. Quantitative analysis was performed using QMass MR 7.5 (Medis, Leiden, the Netherlands). Endo- and epicardial borders were manually planimetered on cine short axis images for calculation of LVEF. Infarct mass was defined by the full width half max technique[9] for the calculation of infarct size as a percentage of total LV myocardial mass (MI%) on LGE images.

Statistical Analysis

Study population

Patient demographics were reported as mean±SD, including MI% which was approximately normally distributed.

ECG markers and infarct size

One-way between subjects ANOVA was used to compare infarct size (MI%) in patients with 0, 1, and ≥2 ECG markers. If this was statistically significant ($P<0.05$), multiple comparisons were performed using independent sample *t*-tests with Bonferroni correction ($P<0.025$ was considered significant). Multivariable linear regression was performed to assess the independent relationship between the presence of contiguous ECG markers (independent variables: cQWMI, cFQRS, cTWI) and MI% by CMR. Multivariable linear regression was also performed to assess the independent relationship between the number of leads affected by each ECG marker and MI% by CMR. Parameter estimates±SE were reported, and $P<0.05$ was considered significant.

ECG markers, LVEF, and infarct size

We also evaluated whether ECG markers estimated MI% independent of LVEF. To assess the association between reduced LVEF and MI%, we considered LVEF ≥60% as normal, and the LVEF decrease (60% minus LVEF) was calculated for those with LVEF <60%. We performed multivariable linear regression analysis for the presence of contiguous markers, the extent of lead involvement, and LVEF decrease as an independent, continuous variable.

LVEF, DETERMINE Score, Modified Selvester Score, and infarct size

To evaluate the relationship between DETERMINE Score and infarct size, patients were grouped by DETERMINE Score into approximate quartiles (0–2, 3–5, 6–9, ≥10). One-way between subjects ANOVA was used to compare the groups. If this was statistically significant ($P<0.05$), multiple comparisons were performed using independent sample t tests with Bonferroni correction ($P<0.017$ was considered significant for 3 groups, and $P<0.008$ for 4 groups). To assess the relative accuracy for estimating MI%, we compared the relationship between LVEF decrease, the Modified Selvester Score, cQWMI, and the DETERMINE Score to MI% using univariable linear regression analysis with MI% as the dependent variable. Multivariable linear regression was then used to determine the independent associations between LVEF decrease, DETERMINE Score, Modified Selvester Score, and MI%. $P<0.05$ was considered significant. To graphically depict the relationship between the multivariable linear regression model including both LVEF plus DETERMINE Score and MI%, unstandardized predicted values based on the model were plotted against actual MI% for each patient.

Results

Study Population

Patient demographics for the 551 patients (mean age 62.1±10.9 years, 79% men, and mean LVEF=40.3±11.0%) included in this analysis are shown in Table 1. The distribution of contiguous ECG markers is illustrated in Figure 2: 208 (38%) had cQWMI, 85 (15%) had cFQRS, 234 (42%) had cTWI, and 188 (34%) had none of these contiguous ECG markers. Multiple ECG markers were present in 142 (26%) patients. MI date was available for 497 patients, 447 of whom had ECG performed >7 days after the index MI. The average time between MI and ECG was 5.4±7.6 years.

Table 1. Patient Characteristics

Patient Characteristics (N=551)	
Age, y	62.1±10.9
Male sex (%male)	433 (79%)
BMI	29.7±7.7
Prior CABG (%)	217 (39%)
Prior PCI (%)	398 (72%)
Diabetes mellitus (%)	176 (32%)
Hypertension (%)	401 (73%)
Current smoking (%)	74 (13%)
Peripheral vascular disease (%)	53 (10%)
Stroke (%)	36 (7%)
LVEF by CMR (%)	40.3±11.0%
Infarct size by CMR (%)	15.7±9.2%
Time from MI to ECG, y*	5.4±7.6

Values are mean±SD or n (%). BMI indicates body mass index; CABG, coronary artery bypass graft surgery; CMR, cardiovascular magnetic resonance imaging; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention.
*MI date was available for 497/551 patients.

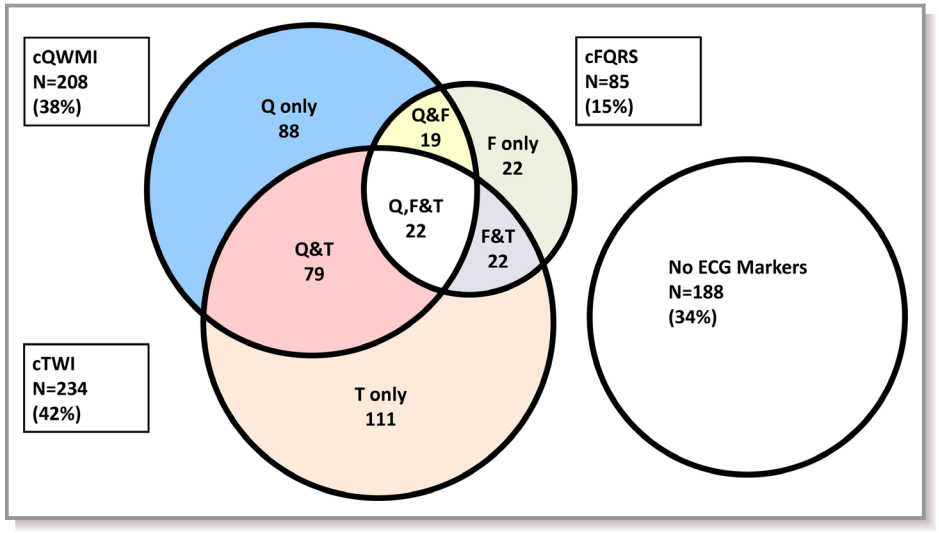

Figure 2. Distribution of contiguous ECG markers of myocardial infarction in 551 patients. Most patients (66%) had at least 1 ECG marker, and many (26%) had multiple ECG markers.. cFQRS indicates contiguous fragmented QRS; cQWMI, contiguous Q wave myocardial infarction; cTWI, contiguous T wave inversion. F indicates cFQRS; Q, cQWMI; T, cTWI. For example: Q only=patients with cQWMI, but without cFQRS or cTWI. Q&F=patients with cQWMI and cFQRS, but without cTWI.

ECG Markers and Myocardial Infarction Size

Patients without any contiguous ECG markers (cQWMI, cFQRS, cTWI) had a mean infarct size of 10.8±6.9%. Infarct size was significantly higher (16.6±8.1%, $P<0.001$) in patients with 1 ECG marker, and higher still (20.9±10.1%, $P<0.001$) in those with ≥2 ECG markers (Figure 3).

In multivariable linear regression models, the presence of cQWMI, cFQRS, and cTWI were each independently associated with an increase in MI% by 5.65±0.74% ($P<0.001$), 2.69±1.00% ($P=0.007$), and 4.12±0.73% ($P<0.001$), respectively (Table S2). We further investigated the association between the number of leads with abnormal ECG markers and MI size (Table S1). In this analysis, involvement of contiguous leads was not required. Multivariable linear regression demonstrated a significant continuous relationship between infarct size and the number of leads affected by QW, FQRS, and TWI: MI% increased by 1.78±0.22% ($P<0.001$), 0.74±0.23% ($P=0.001$), and 0.81±0.18% ($P<0.001$) for each lead affected by QW, FQRS, and TWI, respectively.

ECG Markers, LVEF, and Myocardial Infarction Size

The addition of contiguous ECG markers to LVEF in the multivariable linear regression model improved the overall accuracy of the model (R^2 increased from 0.22 to 0.29, $P<0.001$; Table S2C). Adding the extent of lead involvement improved overall accuracy of the model over LVEF alone (R^2 increased from 0.22 to 0.30, $P<0.001$; Table S1C).

LVEF, DETERMINE Score, and Modified Selvester Score

The mean±SD and range were: LVEF (40.3±11.0%, 9.5–69.1%), Modified Selvester Score (6.6±4.4, 0–26), and DETERMINE Score (6.0±4.6, 0–26). As seen in Figure 4, when patients were grouped by DETERMINE Score into approximate quartiles (0–2, 3–5, 6–9, ≥10) mean infarct size increased linearly (10.5±6.6, 14.6±8.1, 17.6±8.8, 21.7±9.8) and differences between groups were statistically significant ($P\leq0.002$ for all comparisons).

Comparison of LVEF, DETERMINE Score, cQWMI, and Modified Selvester Score for the Estimation of Infarct Size

By univariable linear regression analysis (Table 2), the DETERMINE Score estimated MI% (0.84% MI per point, $R^2=0.18$, $P<0.001$) with an accuracy approaching that of LVEF (0.40% MI per LVEF%, $R^2=0.22$, $P<0.001$) and higher than the Modified Selvester Score (0.65% MI per point, $R^2=0.09$, $P<0.001$) and the presence of cQWMI.

By multivariable linear regression (Table 3), addition of the DETERMINE Score significantly improved estimation of MI% over LVEF alone (R^2 increased from 0.22 to 0.30, $P<0.001$) and over the Modified Selvester Score alone (R^2 increased

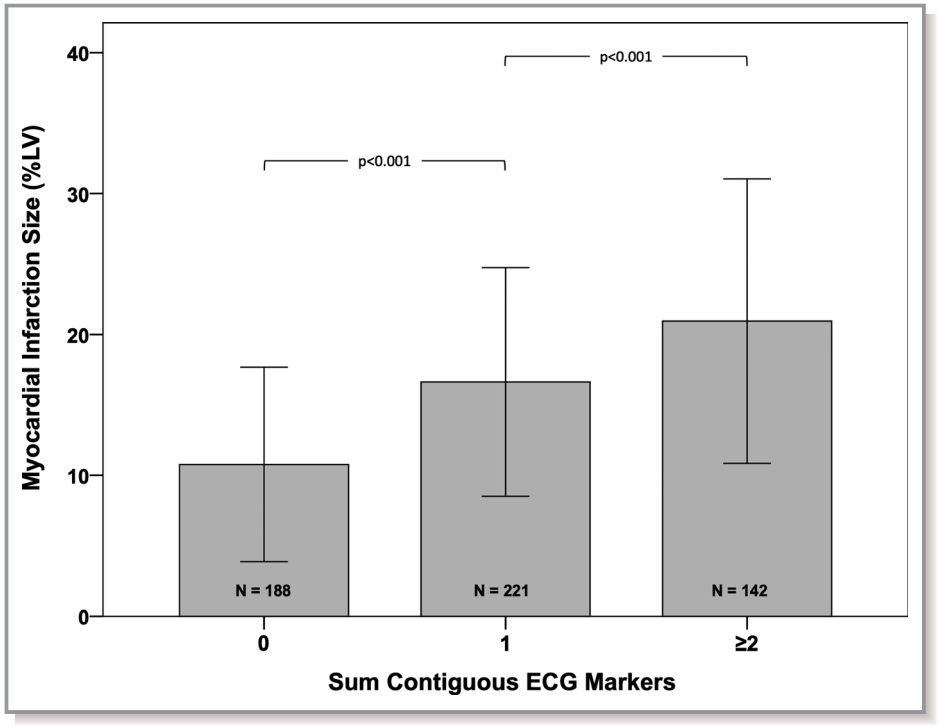

Figure 3. Number of contiguous ECG markers and myocardial infarction size by cardiovascular magnetic resonance. Myocardial infarction size increased as the number of ECG markers increased (P<0.001). Bar graphs denote mean and error bars denote standard deviation. cFQRS indicates contiguous fragmented QRS; cQWMI, contiguous Q wave myocardial infarction; cTWI, contiguous T wave inversion; LV, left ventricle.

from 0.09 to 0.18, P<0.001). In the combined multivariable model, DETERMINE Score remained significantly associated with MI size (P<0.001) while the Modified Selvester Score was not (P=0.198). An increase of the DETERMINE Score by 2.6 points was associated with a similar increase in MI size as a 5% drop in LVEF. Figure 5 graphically illustrates the relationship to MI size of (A) Modified Selvester Score, (B) DETERMINE Score, (C) LVEF, and (D) Model 2 from Table 3 (LVEF and DETERMINE Score).

Discussion

This study is the first to our knowledge to simultaneously quantify the independent and additive contribution of Q waves, fragmented QRS, and inverted T waves seen by 12-lead ECG to estimation of infarct size measured by CMR in patients with prior MI in a large multicenter study. Not only did infarct size increase with the presence of each contiguous ECG marker, but there was an independent and continuous relationship between infarct size and the number of leads exhibiting these ECG markers. Furthermore, the presence and extent of these ECG markers remained associated with infarct size even after accounting for a patient's LVEF. We also introduce the DETERMINE Score, a simple ECG score based on the number of leads with each of these ECG markers (QW, FQRS, and TWI). We demonstrated that the DETERMINE Score is at least as good, and potentially better, at estimating infarct size than the presence of contiguous Q wave MI and the Modified Selvester Score—a validated ECG scoring system that has been shown to estimate infarct size and predict prognosis in patients with prior MI, but is more complex to implement. We demonstrated that the DETERMINE Score estimated infarct size nearly as well as LVEF measured by CMR. Most importantly, combining the DETERMINE score with LVEF improved estimation of infarct size over LVEF alone. As the ECG is the most basic diagnostic test in the clinician's toolbox, these data provide an important new context for the clinician that may help guide further evaluation in the patient with a history of MI.

Comparing ECG Markers and CMR Infarct Size

The ECG remains the first line diagnostic test for the evaluation of patients with prior MI. According to the European Society of Cardiology, American College of Cardiology Foundation, American Heart Association, and the World Heart Federation Third Universal Definition of MI,[6] Q waves in the absence of QRS confounders are considered pathognomonic for prior MI, and inverted T waves increase the likelihood of MI. Fragmented QRS alone or in combination

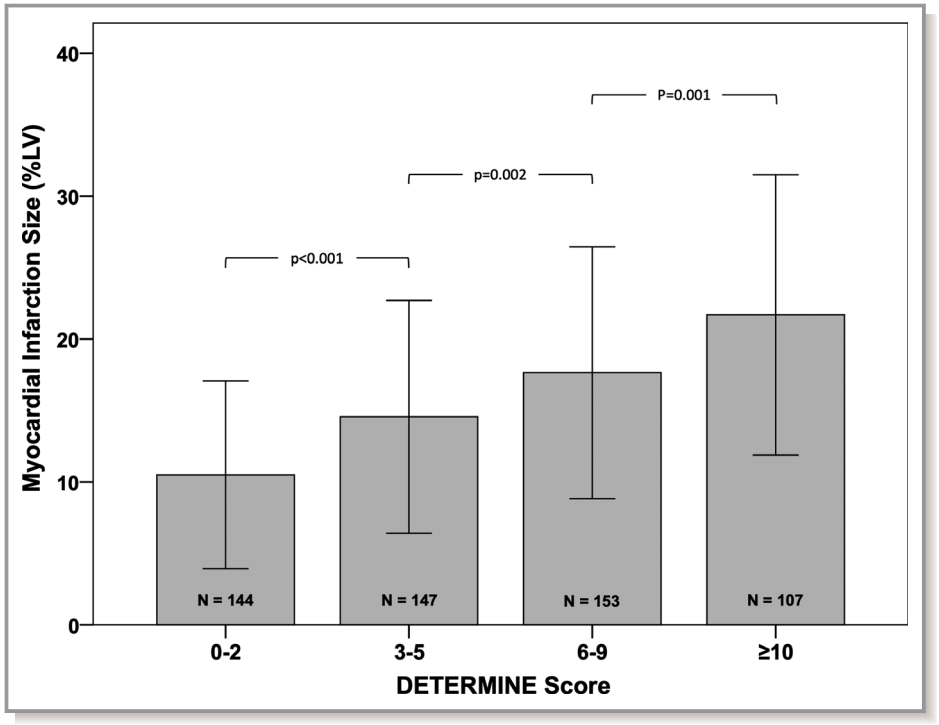

Figure 4. Myocardial infarction size according to DETERMINE Score. Myocardial infarction size increased as the DETERMINE Score increased (P<0.001). The DETERMINE Score is calculated by summing the number of leads with Q waves (× 2), fragmented QRS, and T wave inversion. Bar graphs denote mean, and error bars denote standard deviation. DETERMINE Score indicates simple ECG score for estimating infarct size based on the presence and extent of abnormal ECG markers; LV, left ventricle.

with Q waves improve the detection of myocardial scar on single photon emission computed tomography.[5] These definitions are useful for the dichotomous determination of the presence or absence of MI by ECG criteria, but have not provided any correlate to the extent of infarction.

CMR has enabled MI to be characterized with high precision in vivo and compared with abnormalities seen on ECG. Most studies have been single center studies focused on defining the diagnostic accuracy of the ECG, rather than the ability to estimate infarct size.[10] Sensitivity, specificity, and area under the receiver operating characteristics curve for the detection of MI seen by CMR in 180 patients were reported for Q wave MI (60.6%, 90.0%, 0.75) and fragmented QRS (67.8%, 30.0%, 0.51).[11] The probability of having Q wave MI on ECG increased with increasing MI size in a study of 100 patients with ECG and CMR.[12] In patients scanned following acute MI, infarct size was a significant predictor of FQRS even when controlling for LVEF.[13] Although previous studies have evaluated Q waves and FQRS in isolation, ours is the largest study comparing ECG markers to infarct size by CMR, and the

Table 2. Univariable Linear Regression Analysis Evaluating Relationship to Infarct Size (MI%) of CMR LVEF, Modified Selvester Score, Presence of Contiguous Q Wave Myocardial Infarction, and DETERMINE Score

Univariable Analysis				
	ß±SE	Constant±SE	R^2	P Value
CMR LVEF	0.40±0.03%	7.96±0.73%	0.22	<0.001
DETERMINE Score	0.84±0.08%	10.67±0.59%	0.18	<0.001
Modified Selvester Score	0.65±0.09%	11.51±0.68%	0.09	<0.001
Contiguous Q wave MI	6.24±0.76%	13.39±0.47%	0.11	<0.001

CMR LVEF indicates left ventricular ejection fraction measured by cardiovascular magnetic resonance imaging; DETERMINE Score, Defibrillators to Reduce Risk by Magnetic Resonance Imaging Evaluation (simple ECG score for estimating infarct size based on the presence and extent of abnormal ECG markers); MI, myocardial infarction.

Table 3. Multivariable Linear Regression Analysis Demonstrates the Independent and Additive Value of DETERMINE Score Over the Modified Selvester Score (Model 1) and CMR LVEF (Model 2) for the Estimation of Infarct Size

Multivariable Analysis			
	ß	SE	*P* Value
Model 1: Selvester score plus DETERMINE score (R^2=0.18, P<0.001)			
Modified Selvester Score	0.14%	0.11%	0.198
DETERMINE Score	0.76%	0.10%	<0.001
Constant	10.27%	0.66%	<0.001
Model 2: LVEF plus DETERMINE score (R^2=0.30, P<0.001)			
CMR LVEF	0.31%	0.03%	<0.001
DETERMINE Score	0.60%	0.08%	<0.001
Constant	6.10%	0.73%	<0.001

CMR LVEF indicates left ventricular ejection fraction measured by cardiovascular magnetic resonance imaging; DETERMINE Score, Defibrillators to Reduce Risk by Magnetic Resonance Imaging Evaluation (simple ECG score for estimating infarct size based on the presence and extent of abnormal ECG markers).

first to evaluate QW, FQRS, and TWI in each lead simultaneously by multivariable analysis—allowing quantification of the independent and additive impact of the presence and extent of each marker on infarct size.

Estimating Infarct Size From the ECG

The Original Selvester Score consists of 57 ECG criteria used to assign up to 32 points, with each point corresponding to infarction of ≈3% of the LV.[14] The Original Selvester Score better estimates infarct size by positron emission tomography than the number of leads with QW or FQRS,[15] and correlates with CMR infarct size (r=0.40–0.43) in chronic MI patients.[16,17] Estimation of infarct size by PET and CMR correlate well,[18] but discrepancies can be seen possibly because of differences in spatial resolution and the mechanism for evaluating myocardial viability using gadolinium based contrast agents versus positron emission tomography tracers. The Modified Selvester Score was developed as a simplified alternative and is composed of 37 ECG criteria used to assign up to 29 points.[19] The Modified Selvester Score correlates well against infarct size measured at autopsy,[20,21] and predicts worsened 3-year survival in patients with CAD.[8]

Our study suggests that the DETERMINE Score—calculated from a simple tally of the number of ECG leads with QW, FQRS, and TWI—estimates infarct size as well as, and potentially better than the Modified Selvester Score. Unlike the Modified Selvester Score, which uses different cutoff values for minimum Q wave duration (20–60 ms), R wave duration (20–60 ms), maximum R/Q ratio (0.5–2), and maximum R/S ratio (0.5–2) depending on the particular ECG lead, we selected criteria which are widely recognized and applied them uniformly across all leads. Prior studies have found that ECG markers and the Selvester score do not perform well at predicting infarct size when the ECG is acquired in the acute setting before discharge after reperfused MI.[22,23] The vast majority of patients in our study had ECG performed >7 days after MI. For both the Selvester score and the DETERMINE score, the correlation with infarct size was similar whether all 551 patients were included or if only the 447 patients known to have ECG >7 days after MI were analyzed. The DETERMINE Score also performed better than the presence or absence of contiguous Q wave MI, the standard method used clinically to assess for myocardial scar.

Prognostic Importance of Infarct Size by CMR

The presence of MI by CMR has consistently been shown to be a powerful predictor of adverse cardiovascular events, independent of LVEF,[24–26] with hazard ratios for hard events ranging between 2.82 and 9.43.[1] The extent of MI provides further prognostic information over its presence alone. Infarct size by CMR has consistently been shown to predict mortality independently of LVEF,[27] performing better than LVEF in multiple large cohorts.[25,28,29]

One likely explanation for the increased mortality associated with LGE in post-MI patients is its identification of substrate for ventricular arrhythmias and sudden cardiac death. Infarct size by CMR has been shown to predict inducible ventricular arrhythmias during electrophysiologic study,[30] appropriate device therapies, and sudden cardiac death in patients receiving clinically indicated implantable cardioverter defibrillators,[31–34]—all independent of LVEF. And in patients presenting with sudden cardiac death, the presence and extent of LGE on CMR were the strongest independent predictors of recurrent events.[35]

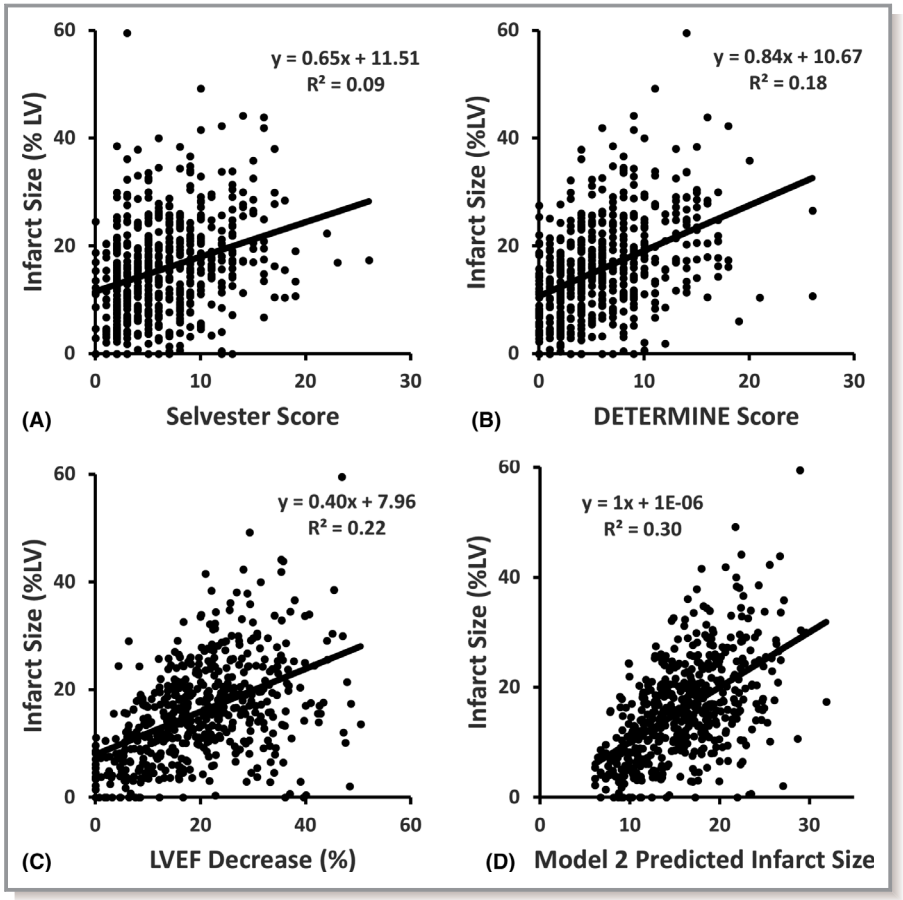

Figure 5. Relationship to infarct size of (**A**) Modified Selvester Score, (**B**) DETERMINE Score, (**C**) left ventricular ejection fraction, and (**D**) infarct size predicted by Model 2 from Table 3 (left ventricular ejection fraction plus DETERMINE Score). DETERMINE score indicates simple ECG score for estimating infarct size based on the presence and extent of abnormal ECG markers; LV, left ventricle; LVEF, left ventricular ejection fraction.

Current guidelines recommend assessment of LVEF in all patients following MI, as LVEF remains one of the strongest prognostic markers and guides therapeutic decisions such as the initiation of guideline directed medical therapy and candidacy for implantable cardioverter defibrillators. We found the DETERMINE Score was nearly as accurate as LVEF for estimating infarct size, and it provided independent and additive value over LVEF alone. These results signal the potential of the DETERMINE Score as a screening tool in patients with prior MI.

Potential Clinical Applications

Prevention of sudden cardiac death remains challenging. Although prior myocardial infarction and reduced ejection fraction identify patients at high risk for sudden cardiac death, the majority of patients who suffer sudden cardiac death do not meet current guidelines for implatable cardioverter defibrillator implantation. CMR studies have demonstrated a high prevalence of unrecognized MI in a variety of patient cohorts, and that the presence of unrecognized MI is associated with higher rate of cardiovascular death. An ECG screening tool that provides an estimate of infarct size could potentially be used to identify patients more likely to have a large infarct burden and benefit from more intensive diagnosis and treatment strategies.

Our study does have important limitations. Only patients with prior MI were included, so the estimation of infarct size from ECG markers in patients without prior MI may differ significantly. These findings may be limited to the study population, which was a fairly broad population of patients with CAD and documentation of MI and/or mild-to-moderate left ventricular dysfunction (LVEF 35%–50%). These findings will need to be validated in other populations. Overall, the R^2 for the association between the DETERMINE score and CMR infarct size is low. It is worth noting that the correlation between the DETERMINE Score and infarct size (r=0.42) was similar to that of LVEF (r=0.47), one of the most powerful

predictors of prognosis following MI. The moderate correlation may in part be because of inherent limitations in the predictive value of ECG. Additionally, in this multicenter study CMR imaging was performed at 66 different sites on systems from several major CMR vendors using different vendor-specific pulse sequences. Although a potential limitation, the multicenter nature of this study improves generalizability of the findings. All CMR studies conformed to the parameters set forth by the DETERMINE Study and were inspected for image quality before analysis by the CMR core laboratory.

Conclusions

To our knowledge, this is the first study to demonstrate that the presence and extent of Q waves, fragmented QRS, and T wave inversions on ECG are independently associated with an increase in infarct size, and that the DETERMINE Score calculated from the number of leads with these markers can be used to estimate infarct size measured by CMR in patients with a history of MI. The DETERMINE Score estimated infarct size nearly as well as LVEF measured by CMR, and the addition of the DETERMINE score to LVEF improved infarct size estimation over LVEF alone. Because infarct size is a powerful predictor of adverse cardiovascular events, the DETERMINE Score holds promise as a screening tool for risk assessment in patients following MI.

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SUPPLEMENTAL MATERIAL

Table S1. Association between the number of ECG leads with abnormal markers (QW, FQRS, TWI) and infarct size by multivariable linear regression.

(A) Model S3: ΔMI%, per ECG lead				(B) Model S4: ΔMI%, per ECG lead and LVEF%			
	ß	Std. Err.	p value		ß	Std. Err.	p value
QW	1.78%	0.22%	< 0.001	**QWMI**	1.28%	0.21%	< 0.001
FQRS	0.74%	0.23%	0.001	**FQRS**	0.44%	0.22%	0.042
TWI	0.81%	0.18%	< 0.001	**TWI**	0.60%	0.17%	< 0.001
				LVEF	0.31%	0.03%	< 0.001
Constant	10.70%	0.59%	< 0.001	**Constant**	6.09%	0.74%	< 0.001

(C)	LVEF alone	Model S3: ECG leads	Model S4: LVEF plus ECG leads
R Square	0.22	0.18	0.30
Sig.	<0.001	<0.001	<0.001

(A) Independent relationship between the number of leads with ECG markers on infarct size (ΔMI%), (B) Independent relationship between LVEF, the number of leads with ECG markers, and infarct size, (C) R square and p values for the different models.

FQRS = fragmented QRS; LVEF = left ventricular ejection fraction; QW = Q wave; TWI = T wave inversion

Table S2. Association between contiguous ECG markers (QW, FQRS, TWI) and infarct size (MI%) by multivariable linear regression.

(A) Model S1: ΔMI%, per cECG marker				(B) Model S2: ΔMI%, per cECG marker and LVEF%			
	ß	Std. Err.	p value		ß	Std. Err.	p value
cQWMI	5.65%	0.74%	< 0.001	**cQWMI**	4.13%	0.71%	< 0.001
cFQRS	2.69%	1.00%	0.007	**cFQRS**	1.82%	0.94%	0.055
cTWI	4.12%	0.73%	< 0.001	**cTWI**	2.80%	0.70%	< 0.001
				LVEF	0.31%	0.03%	< 0.001
Constant	11.44%	0.54%	< 0.001	**Constant**	6.73%	0.72%	< 0.001

(C)	LVEF alone	Model S1: cECG markers	Model S2: LVEF plus cECG markers
R Square	0.22	0.17	0.29
Sig.	<0.001	<0.001	<0.001

(A) Independent relationship between contiguous ECG (cECG) markers and infarct size (ΔMI%), (B) Independent relationship between LVEF, contiguous ECG markers, and infarct size, (C) R square and p values for the different models.

cECG markers = contiguous ECG markers; cFQRS = contiguous fragmented QRS; cQWMI = contiguous Q wave myocardial infarction; cTWI = contiguous T wave inversion; LVEF = left ventricular ejection fraction