ORIGINAL RESEARCH

T-Wave Abnormality as Electrocardiographic Signature of Myocardial Edema in Non-ST-Elevation Acute Coronary Syndromes

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***Background*—**T-wave abnormalities are common during the acute phase of non-ST-segment elevation acute coronary syndromes, but mechanisms underlying their occurrence are unclear. We hypothesized that T-wave abnormalities in the presentation of non-ST-segment elevation acute coronary syndromes correspond to the presence of myocardial edema.

***Methods and Results*—**Secondary analysis of a previously enrolled prospective cohort of patients presenting with non-ST-segment elevation acute coronary syndromes was conducted. Twelve-lead electrocardiography (ECG) and cardiac magnetic resonance with T2-weighted imaging were acquired before invasive coronary angiography. ECGs were classified dichotomously (ie, ischemic versus normal/nonischemic) and nominally according to patterns of presentation: no ST- or T-wave abnormalities, isolated T-wave abnormality, isolated ST depression, ST depression+T-wave abnormality. Myocardial edema was determined by expert review of T2-weighted images. Of 86 subjects (65% male, 59.4 years), 36 showed normal/nonischemic ECG, 25 isolated T-wave abnormalities, 11 isolated ST depression, and 14 ST depression+T-wave abnormality. Of 30 edema-negative subjects, 24 (80%) had normal/nonischemic ECGs. Isolated T-wave abnormality was significantly more prevalent in edema-positive versus edema-negative subjects (41.1% versus 6.7%, P=0.001). By multivariate analysis, an ischemic ECG showed a strong association with myocardial edema (odds ratio 12.23, 95% confidence interval 3.65-40.94, P<0.0001). Among individual ECG profiles, isolated T-wave abnormality was the single strongest predictor of myocardial edema (odds ratio 23.84, 95% confidence interval 4.30-132, P<0.0001). Isolated T-wave abnormality was highly specific (93%) but insensitive (43%) for detecting myocardial edema.

***Conclusions*—**T-wave abnormalities in the setting of non-ST-segment elevation acute coronary syndromes are related to the presence of myocardial edema. High specificity of this ECG alteration identifies a change in ischemic myocardium associated with worse outcomes that is potentially reversible. **(*J Am Heart Assoc*. 2018;7:e007118. DOI: 10.1161/JAHA.117.007118.)**

Key Words: acute coronary syndrome • electrocardiography • magnetic resonance imaging • myocardial edema • T-wave

Acute myocardial infarction is typically categorized as either ST-elevation or non-ST-elevation acute coronary syndrome (NSTE-ACS) based on the electrocardiographic (ECG) findings; importantly, NSTE-ACS comprises ≈70% of all acute myocardial infarctions.[1] NSTE-ACS presents with various ECG patterns including isolated ST-segment depression, isolated T-wave abnormality, transient ST-segment elevation, or normal/nonischemic abnormality.[2] Although invasive evaluation is commonly pursued, management of NSTE-ACS remains heterogeneous and not fully informed by myocardial substrate or ECG changes.[3]

A recent ECG substudy of GRACE (the Global Registry of Acute Coronary Events) and ACS Registry I (the Canadian Acute Coronary Syndromes ACS Registry I) involving more than 7000 patients with NSTE-ACS showed that the presence versus absence of T-wave abnormalities, at presentation ECG, portended significantly higher in-hospital and 6-month mortality risk.[4] Although that study highlights the clinical importance of abnormal T waves in the context of NSTE-ACS, it does not elucidate its pathophysiologic mechanism.

Ischemia leads to the formation of myocardial edema by inducing alterations in fluid balance,[5,6] and myocardial edema precedes the onset of irreversible injury in acute ischemia.[7] Cardiac magnetic resonance (CMR) can uniquely demonstrate myocardial edema with T2-weighted (T2W) imaging. In reperfused ST-elevation myocardial infarction, the region of

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An accompanying Table S1 is available at http://jaha.ahajournals.org/content/7/3/e007118/DC1/embed/inline-supplementary-material-1.pdf

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Clinical Perspective

What Is New?

- In patients presenting with non-ST-segment elevation acute coronary syndromes, the presence of an ischemic ECG was strongly associated with myocardial edema as evaluated by cardiac magnetic resonance.
- Specifically T-wave abnormalities, a common neglected entity in the context of non-ST-segment elevation acute coronary syndromes, can help in identifying with high specificity myocardial edema in the non-ST-segment elevation acute coronary syndrome population.

What Are the Clinical Implications?

- Prompt identification of myocardium edema could have important clinical implications, especially when the presence of myocardial edema is considered as a diagnostic, therapeutic, or prognostic target.

increased T2 after revascularization delineates the previously underperfused area that remains viable and helps quantify myocardial salvage.[8] The ability to interrogate the myocardium with T2W CMR before angiography in NSTE-ACS affords the delineation of at-risk myocardium before revascularization.

We previously showed in a cohort of patients with NSTE-ACS that presence of edema strongly predicted a cardiovascular event or death at 6 months regardless of initial revascularization.[9] We subsequently showed that myocardial edema by T2 CMR delineates at-risk but salvageable myocardium in a large-animal model of NSTE-ACS.[10] Thus, T2 CMR before angiography can delineate at-risk but salvageable myocardium in NSTE-ACS.[11] However, deployment of such a strategy may be limited by timely CMR availability and underscores the need for readily available bedside biomarkers of myocardium at risk.

Both T-wave abnormalities and myocardial edema in the context of NSTE-ACS carry significant prognostic value for adverse cardiovascular events; however, no studies have explored the possible interrelation between these 2 phenomena. In the present work we hypothesized that T-wave abnormalities by standard 12-lead ECG may be associated with the presence of myocardial edema in NSTE-ACS.

Methods

In accordance with AHA Journals' policy, we declare that the data, analytic methods, and study materials will be made available to other researchers in accordance with institutional regulations for data sharing for purposes of reproducing the results or replicating the procedure.[12]

Study Population

Leveraging a previous prospectively enrolled cohort of patients presenting with NSTE-ACS[9] between 2006 and 2008, we conducted secondary analyses of ECG and CMR findings. Consecutive patients hospitalized with NSTE-ACS awaiting coronary angiography were enrolled. Diagnosis required either suspected cardiac chest pain (or anginal equivalent) or ischemic ECG abnormality, and an abnormal serum troponin-I (Tn-I) level.[13] Excluded from enrollment were those with magnetic resonance–incompatible implants, severe claustrophobia, allergy to gadolinium-based contrast, hemodynamic instability, urgent or emergent need for invasive angiography, or evidence of illicit drug ingestion. Patients under age 30 years were also excluded to minimize coronary events mediated by nonatherosclerotic processes. Medical history, clinical and ECG findings, serological markers, GRACE and TIMI (Thrombolysis in Myocardial Infarction) risk scores, were recorded at entry, as were results of clinically acquired invasive angiography and postcatheterization management. Time intervals from symptom onset to admission ECG and from ECG to CMR were recorded. All patients provided written informed consent to participate in this Institutional Review Board–approved protocol. Clinical decision making was performed by providers blinded to CMR results. For this study, only subjects with adequate baseline 12-lead ECG and T2W images were included. All CMR exams were performed after clinical decision to perform coronary angiography had been confirmed, and all CMR exams were completed before invasive angiography.

ECG Definitions

Definitions for T-wave abnormality and ST depression were in accordance with "Recommendations for the Standardization and Interpretation of the Electrocardiogram" by the American Heart Association, American College of Cardiology, and Heart Rhythm Association consensus statement.[14] Isolated T-wave abnormality was considered present if the T wave was inverted (at least 0.1 mV), isoelectric, or biphasic in leads V3 to V6, aVL, I, and II. In leads V1, aVR and III, T-wave abnormalities were not evaluated, as those can be found as normal variants.[14] Isolated ST-depression was defined as the presence of at least 0.1 mV depression from the J point in at least 2 contiguous leads.[14] ST depression and T-wave abnormality were considered to be simultaneously present when the T wave extended from the J point+60 ms until complete ventricular repolarization. Presence of ST-segment and/or T-wave abnormality constituted an "ischemic ECG." A "nonischemic ECG" was defined as absence of any ST-segment and/or T-wave abnormality. ECG profiles were classified either as a dichotomous variable (ie, ischemic versus normal/nonischemic ECG) or a nominal variable

according to individual pattern of presentation: isolated T-wave abnormality, isolated ST depression, ST depression+T-wave abnormality (when simultaneously present), or normal/nonischemic ECG. When T-wave abnormality was present, the number of leads with abnormal T waves was also recorded. Data on PR, QRS, QTc intervals, and QRS angle were also collected.

ECG exclusion criteria were left bundle branch block, atrial flutter, paced rhythm, low voltage, poor ECG quality, and ventricular tachycardia. The presence of a left ventricular hypertrophy strain pattern was also excluded from the analysis. Left ventricular hypertrophy strain was defined as the presence of a downsloping convex ST segment concomitantly with an inverted asymmetrical T-wave in leads V5 and V6.[15] Further, whenever possible, we compared the ECG with previous records to ensure that abnormalities represented dynamic ischemic changes.

Two expert physicians (S.F.S. and A.C.) blinded to patient clinical and imaging data independently interpreted the ECGs, and disagreements were resolved by consensus.

CMR Protocol

All images as previously described[9] were acquired on a single 1.5-Tesla magnetic resonance scanner with a 12-element phased array chest coil (MAGNETOM Avanto, Siemens Medical Solutions, Inc, Erlangen, Germany). The CMR protocol included multiplane cine and T2W imaging, the latter using the short-τ inversion recovery segmented turbo spin echo technique; resting first-pass perfusion imaging, and late gadolinium enhancement (LGE) images in multiple planes were also obtained. Two experts blinded to clinical information read CMR exams (S.V.R. and O.P.S.) and rated by consensus, after independent review, each patient's CMR images by recording 17-segment[16] scores for each of the following: left ventricular myocardial T2 signal intensity, wall motion, perfusion, and LGE. Each variable was scored: T2, 0=normal, 1=intramyocardial hyperintensity; wall motion, 0=normal, 1=hypokinetic, 2=akinetic, 3=dyskinetic; perfusion, 0=normal, 1=abnormal; and LGE, 0=none, 1=hyperenhancement. T2 score was calculated as the sum of each left ventricular segment rated as having increased signal intensity on T2W images.

Statistical Analyses

The mean values of continuous, normally distributed variables were compared with the 2-sample t test. Comparison of median values or proportions was done with the 2-sample Wilcoxon rank-sum test and Fisher exact test, respectively. The strength of the relation between nonnormal variables was assessed with Spearman correlation. Univariate logistic regression analysis was used to find individual clinical predictors of edema positivity at CMR. Multivariate stepwise backward logistic regression analysis was used to find independent predictors of myocardial edema starting with all variables that were significant as univariate predictors (10% tolerance was adopted). For multivariate analysis 2 different models were used, either considering the ECG as a dichotomous variable (ie, ischemic versus normal/nonischemic abnormality) (model 1), or considering individual ECG profiles (model 2). Specificity, sensitivity, and diagnostic accuracy were calculated for independent predictors of myocardial edema. Statistical significance was set at 2-tailed $P<0.05$. IBM SPSS Statistic 21.0 (Chicago, IL) was used for all statistical analyses.

Results

Patient Characteristics

From the original cohort, 86 patients, 65% male, age 59.4±12.1 years, had adequate T2W imaging quality and an interpretable ECG (Table 1). Fifty-six (65%) demonstrated myocardial edema at CMR (median T2 score=2, range=1-8). Comorbidities did not differ between patients presenting with versus without myocardial edema. Peak Tn-I was higher in the edema-positive group ($P<0.0001$). Subsequent need for coronary revascularization was also significantly higher in the edema-positive group ($P<0.0001$). Median time from admission ECG to CMR was 22 hours (interquartile range 16-45 hours). Time intervals between symptoms onset and admission ECG, and from admission ECG to CMR exam, did not differ between edema-positive and edema-negative groups, nor were clinical risk prediction models (GRACE and TIMI risk scores). Patients with myocardial edema had a significantly lower ejection fraction, higher wall motion score index, and higher LGE score when compared to those without myocardial edema (Table 2).

ECG Findings

Data on ECG characteristics are reported in Table 3. Of the study cohort, 84 patients were in sinus rhythm, and 2 in atrial fibrillation, at the time of ECG and CMR examination. Of 86 subjects, 36 (42%) ECGs showed normal/nonischemic abnormality, 25 (29%) had isolated T-wave abnormality, 11 (13%) had isolated ST depression, and 14 (16%) had ST depression+T-wave abnormality.

Relationship Between ECG and CMR Findings

Prevalence of individual ECG profiles according to the presence or absence of myocardial edema is summarized in

Table 1. Characteristics of NSTE-ACS Patients (N=86)

	Myocardial Edema		
	Positive (N=56)	Negative (N=30)	*P* Value
Age, y*	59.8±13.1	58.6±10.2	0.619
Male, N (%)†	38 (67.9)	18 (60)	0.486
Body mass index, kg/m^2*	29.4 (5.9)	29.5 (8.7)	0.924
Diabetes mellitus, N (%)†	25 (44.6)	11 (36.7)	0.501
Smoking, N (%)†	27 (48.2)	9 (30)	0.115
Hypertension, N (%)†	41 (73.2)	25 (83.3)	0.423
Hyperlipidemia, N (%)†	43 (76.8)	21 (70)	0.605
History of CAD, N (%)†	29 (51.8)	17 (56.7)	0.821
HR, bpm*	81.2±17.4	73.1±16.3	0.039§
SBP, mm Hg*	143.9±31.4	143.5±30.5	0.952
DBP, mm Hg*	80.1±15.9	79.9±18.0	0.820
TIMI Risk Score‡	4 (1-6)	4 (1-6)	0.374
GRACE in-hospital mortality (%)‡	3 (1-15)	2 (1-8)	0.614
GRACE 6-month mortality (%)‡	12 (5-30)	10.5 (4-21)	0.169
Peak Tn-I, mg/dL‡	4.74 (12.96)	0.42 (1.23)	<0.0001§
Symptom onset to admission ECG, h‡	2.0 (1-24)	2.5 (1-24)	0.672
Admission ECG to CMR, h‡	21 (2-135)	36 (2-77)	0.761
No. of coronary arteries with >70% stenosis‡			0.301
0	1 (2)	9 (30)	
1	14 (25)	3 (10)	
2	23 (41)	7 (23)	
3	18 (32)	11 (37)	
Need for coronary revascularization‡	49 (87.5)	8 (26.7)	<0.0001§

Data are presented as mean±SD, N (%), or median (range). CAD indicates coronary artery disease; CMR, cardiac magnetic resonance; DBP, diastolic blood pressure; ECG, electrocardiogram; GRACE, Global Registry of Acute Coronary Events; HR, heart rate; NSTE-ACS, non-ST-elevation acute coronary syndrome; SBP, systolic blood pressure; TIMI, Thrombolysis in Myocardial Infarction; Tn-I, troponin-I.
Differences between groups were assessed with 2-sample t test,* Fisher exact test,† or Wilcoxon rank-sum test.‡
§*P*<0.05 considered significant.

Figure 1. The great majority of patients without myocardial edema presented with normal/nonischemic ECG (80% versus 21.4%, *P*<0.0001). Patients with myocardial edema had a markedly higher prevalence of isolated T-wave abnormality as compared to those without edema (41.1% versus 6.7%, *P*=0.001). Isolated ST depression and ST depression+T-wave abnormality patterns tended to be more prevalent in patients with myocardial edema: number of edema-positive versus edema-negative patients were 10 versus 1 for isolated ST depression and 11 versus 3 for ST depression+T-wave abnormality (*P*=0.088, and 0.361, respectively). There was a significant positive association between number of leads with abnormal T waves and number of left ventricular segments showing myocardial edema (*r*=0.268, *P*=0.013).

Table 2. CMR Findings

	Myocardial Edema		
	Positive (56)	Negative (30)	*P* Value
Ejection fraction on admission*	45±14	56±14	0.013‡
WMSI†	5 (0-22)	1 (0-21)	0.001‡
LGE Score†	2 (0-12)	0 (0-4)	0.004‡

Data are presented as mean±SD or median (range). CMR indicates cardiac magnetic resonance; LGE, late gadolinium enhancement; WMSI, wall motion score index.
Differences between groups were assessed with 2-sample t test* or Wilcoxon rank-sum test.†
‡*P*<0.05 considered significant.

Predictors of Myocardial Edema

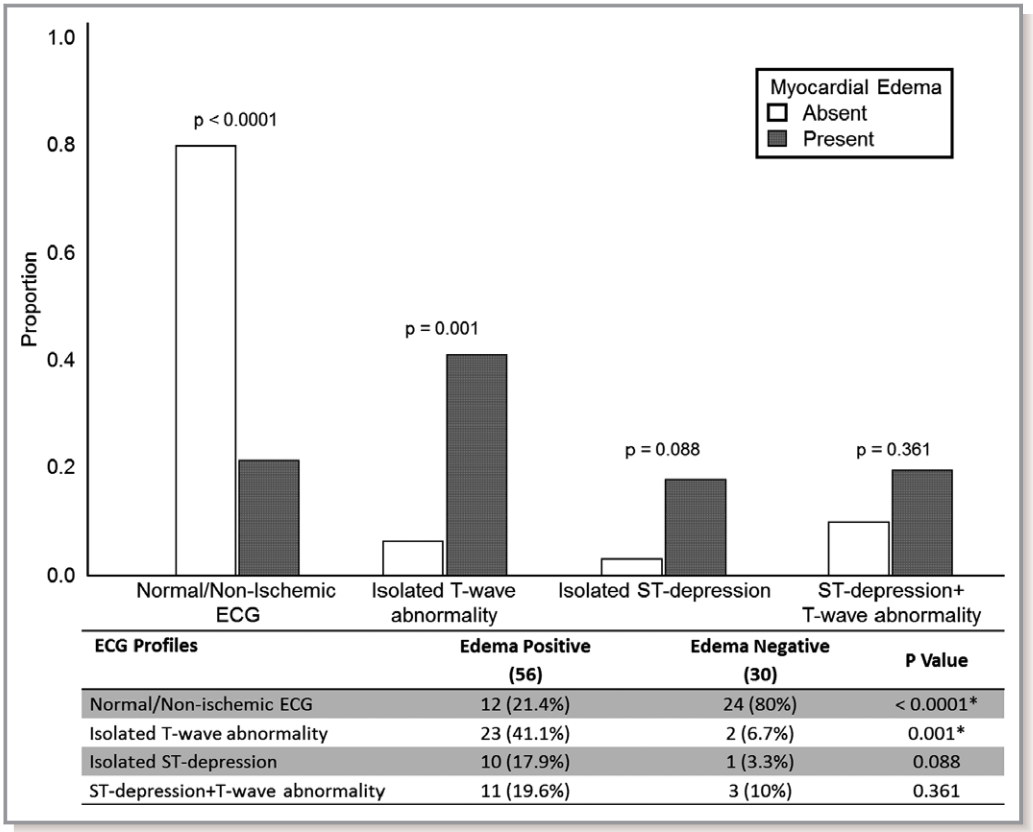
Univariate Analysis

By univariate logistic regression analysis, presence of an ischemic ECG (ie, ischemic versus normal/nonischemic ECG), isolated T-wave abnormality, heart rate, peak Tn-I, and its natural logarithmic transformation (peak Ln-Tn-I), wall motion score index, and LGE score were significant predictors of myocardial edema (Table 4). Isolated ST depression and ST depression+T-wave abnormality profiles did not reach significance (full regression analysis is shown in Table S1).

Table 3. Electrocardiographic Characteristics

	Myocardial Edema		
	Positive (N=56)	Negative (N=30)	*P* Value
PR interval, ms*	166±32	156±26	0.141
QRS interval, ms*	93±14	90±15	0.382
QTc interval, ms*	433±26	432±22	0.793
QRS axis*	24.7±39.5	29.7±35.2	0.555
Normal/nonischemic ECG†	12 (21.4%)	24 (80%)	<0.001‡
Isolated T-wave abnormality†	23 (41.1%)	2 (6.7%)	0.001‡
Isolated ST depression†	10 (17.9%)	1 (3.3%)	0.088
ST depression+T-wave abnormality†	11 (19.6%)	3 (10%)	0.361

Data are presented as mean±SD or N (%). ECG indicates electrocardiogram.
Differences between groups were assessed with 2-sample t test* or Fisher exact test.†
‡*P*<0.05 considered significant.



ECG Profiles	Edema Positive (56)	Edema Negative (30)	P Value
Normal/Non-ischemic ECG	12 (21.4%)	24 (80%)	< 0.0001*
Isolated T-wave abnormality	23 (41.1%)	2 (6.7%)	0.001*
Isolated ST-depression	10 (17.9%)	1 (3.3%)	0.088
ST-depression+T-wave abnormality	11 (19.6%)	3 (10%)	0.361

Figure 1. ECG profiles in NSTE-ACS and prevalence of myocardial edema. Prevalence of individual ECG profiles varied significantly according to the presence of myocardial edema by T2W imaging at NSTE-ACS presentation. The vast majority of patients with a normal/nonischemic ECG did not have myocardial edema. Isolated T-wave abnormality was significantly more common in edema-positive vs edema-negative patients. ECG indicates electrocardiogram; NSTE-ACS, non-ST-segment elevation acute coronary syndromes; T2W, T2-weighted.

Multivariate Analysis

Initial predictors included in the multivariate logistic regression model were heart rate, wall motion score index, LGE score, peak Ln-Tn-I, and the presence of an ischemic ECG. After backward selection process, the presence of an ischemic ECG and peak Ln-Tn-I were the only independent predictors of myocardial edema. Presence of an ischemic ECG showed a strong association with myocardial edema (odds ratio [OR] 12.23, 95% confidence interval [CI] 3.65-40.94, $P<0.0001$). Peak Ln-Tn-I was also a significant predictor of edema (OR 3.41, 95% CI 1.80-6.47, $P<0.0001$) (model 1).

Among individual ECG profiles, isolated T-wave abnormality was the strongest predictor of myocardial edema (OR 23.84, 95% CI 4.30-132, $P<0.0001$), followed by isolated ST-depression pattern (OR 14.12, 95% CI 1.38-144, $P=0.026$). ST depression+T-wave abnormality was not an independent predictor of edema ($P=0.191$). Peak Ln-Tn-I was also a significant predictor of edema (OR 3.44, 95% CI 1.51-7.81, $P=0.003$) (model 2).

Isolated T-wave abnormality pattern revealed high specificity (93%; 95% CI 79% to 98%), whereas sensitivity was low (41%; 95% CI 29% to 54%) for detecting myocardial edema. Based on our prevalence, isolated T-wave abnormality carried a high positive predictive value for detecting myocardial edema (92%; 95% CI 75% to 98%), but negative predictive value was low (46%; 95% CI 34% to 58%) (Figure 2).

Discussion

In this analysis of ECGs and myocardial edema imaging with CMR in patients presenting with NSTE-ACS, the presence of an ischemic ECG was strongly associated with myocardial edema as evaluated by CMR. Further, among different ECG profiles, the presence of isolated T-wave abnormalities was the strongest independent predictor of myocardial edema.

Among different ECG patterns that can be encountered in ACS patients, isolated T-wave abnormality is relatively common: its prevalence in NSTE-ACS varies from 14% to 27%.[17-19] Although evidence supports T-wave abnormality's adverse prognostic significance,[4,20,21] our data for the first time indicate that myocardial edema may be the substrate for T-wave abnormality.

Table 4. Predictors of Myocardial Edema in Patients With NSTE-ACS

	OR	95% CI	*P* Value
Univariate logistic regression analysis			
Predictors			
HR, bpm	1.030	1.00 to 1.060	0.046
Peak Tn-I, mg/dL	1.11	1.01 to 1.21	0.030
Peak Ln-Tn-I, mg/dL	3.41	1.80 to 6.47	<0.0001
Ischemic ECG vs normal/nonischemic ECG	14.67	4.89 to 44.02	<0.0001
ECG profiles*			
Isolated T-wave abnormality	9.76	2.11 to 45.07	0.004
Isolated ST depression	6.30	0.77 to 51.87	0.087
ST depression+T-wave abnormality	2.20	0.56 to 8.60	0.257
WMSI	1.10	1.01 to 1.21	0.036
LGE score	1.45	1.09 to 1.93	0.010
Multivariate logistic regression analysis			
Model 1			
Ischemic ECG vs normal/nonischemic ECG	12.23	3.65 to 40.94	<0.0001
Peak Ln-Tn-I, mg/dL	3.05	1.52 to 6.14	0.002
Model 2			
ECG Profiles†			
Isolated T-wave abnormality	23.84	4.30 to 132	<0.0001
Isolated ST depression	14.12	1.38 to 144	0.026
ST depression+T-wave abnormality	3.03	0.57 to 16.04	0.191
Peak Ln-Tn-I, mg/dL	3.44	1.51 to 7.81	0.003

CI indicates confidence interval; ECG, electrocardiogram; HR, heart rate; LGE, late gadolinium enhancement; Ln, natural logarithm; NSTE-ACS, non-ST-elevation acute coronary syndrome; OR, odds ratio; Tn-I, Troponin-I; WMSI, wall motion score index.
*The entire cohort was used as the control group.
†Normal/nonischemic ECG was used as the control group. OR is computed for unit change for continuous and ordinal predictors.

Recently, an association between T-wave abnormalities and myocardial edema evaluated with T2W imaging has been reported in patients with conditions other than ACS, namely myocarditis and takotsubo cardiomyopathy.[22,23] The pathophysiological links between myocardial edema and T-wave abnormality remain to be fully elucidated, although we could speculate that edematous myocardium is marked by dispersion of repolarization potentials to produce this specific ECG finding.

Our findings suggest that in NSTE-ACS, T-wave abnormalities may be a marker of myocardial edema that ensues and persists after severe ischemia, whereas acute ST depression represents active ischemia. In fact, it is well established that in the early phase of myocardial ischemia (such as what can occur with exercise stress testing) only ST-segment abnormalities develop, and T-wave abnormalities are virtually unseen.[24,25] On the other hand, T-wave abnormalities are to be seen after resolution of prolonged ischemia.

The ability to detect with high specificity the presence of myocardial edema with an early and simple means using the standard 12-lead ECG may have important clinical implications. In NSTE-ACS, edema indicates regions of myocardium that remain potentially viable but at risk of irreversible injury after 1 or more acute ischemic episodes. In such patients the presence of myocardial edema strongly predicts 6-month cardiovascular event or death, regardless of initial revascularization.[9] Importantly, CMR was performed over a narrow time window: times from symptom onset to admission ECG and from admission ECG to CMR did not differ between edema-positive and edema-negative patients. Because CMR offers high accuracy in delineating myocardial edema in NSTE-ACS, further studies with serial ECG and CMR with edema imaging are needed to improve understanding of the association between dynamic T-wave abnormalities and myocardial edema, particularly with contemporary revascularization and medical therapies. Such data will also help to determine (1) which patients warrant further assessment with CMR and (2) how changes in management based on edema detection can improve NSTE-ACS outcomes.

Limitations

Myocardial T2 mapping was not available at the time CMR data were acquired in this cohort.[26,27] Further studies that incorporate CMR-based myocardial relaxometry toward quantitation of both presence and severity of myocardial edema are warranted. We did not quantify the extent of myocardial edema from T2W images, nor did we quantify infarct size beyond LGE score. However, this approach is usually based on qualitative or semiquantitative analyses that rely on signal intensity relative to another tissue such as skeletal muscle that, too, may be abnormal.[28,29]

It is known that dynamic ECG changes occur during the acute phase of ACS[25,30]; our finding that isolated T-wave abnormality has low sensitivity should prompt caution in relying on a single-time-point 12-lead ECG to rule out myocardial edema because T-wave abnormalities may become evident at a different time.

Ten subjects (12%) in our cohort had nonobstructive coronary artery disease at angiography, raising the possibility of acute myocarditis as an alternative diagnosis to NSTE-ACS. However, 4 of these patients had subendocardial scar consistent with ischemic injury (eg, plaque disruption, vasospasm, or thromboembolism) but no epicardial damage

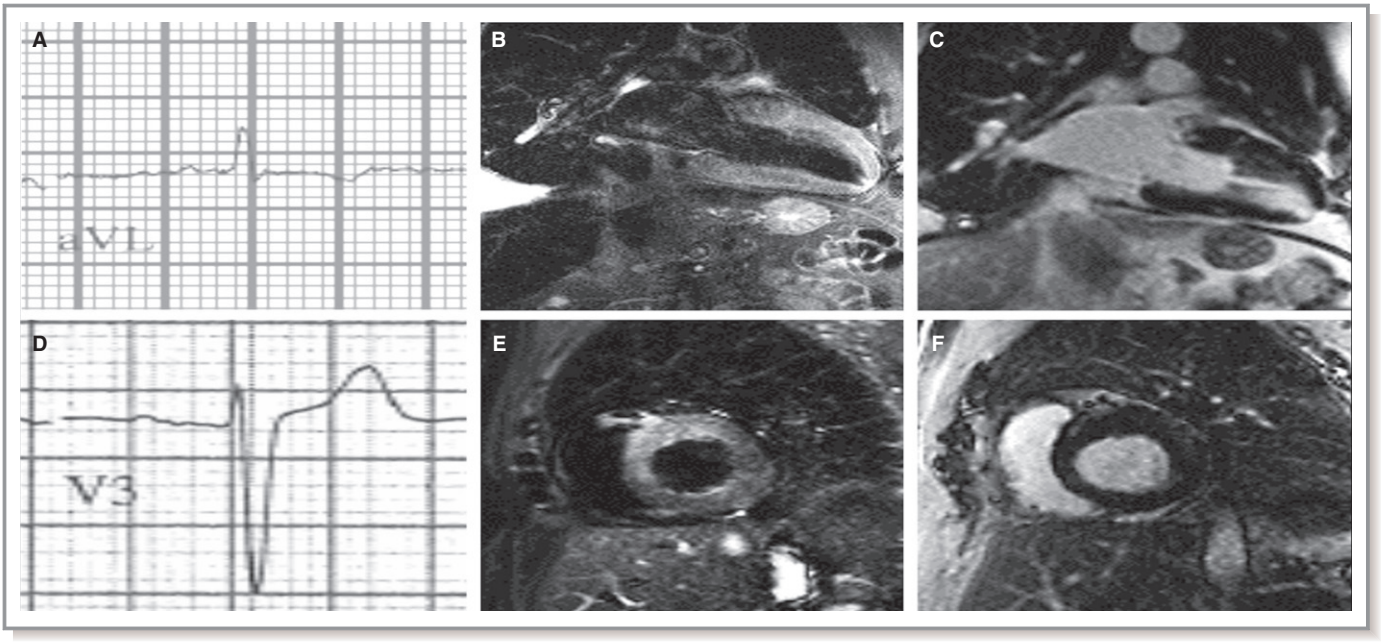


Figure 2. High specificity vs low sensitivity of T-wave abnormality for myocardial edema. High specificity of T-wave abnormality is shown in the ECG (A) of a 50-year-old man with increasing frequency of chest discomfort for 1 month before presentation with severe resting symptoms. T2W imaging showed myocardial edema in the anterior wall and apex (B) with minimal myocardial damage by LGE (C); invasive coronary angiography showing significant multivessel disease prompting hybrid coronary revascularization. Low sensitivity of T-wave abnormality in detecting myocardial edema is evident by ECG (D) from a 57-year-old man admitted with persistent chest pain; T2W imaging showed prominent anteroseptal myocardial edema (E) with no significant damage by LGE (F). Cardiac catheterization demonstrated epicardial coronary disease with aortic valve stenosis prompting valve replacement with revascularization. ECG indicates electrocardiogram; LGE, late gadolinium enhancement imaging; T2W, T2-weighted.

by LGE as typically seen in myocarditis. The other 6 patients had negative T2W imaging, making acute myocarditis less likely. Further, even though acute myocarditis cannot be entirely excluded among this entity's own challenges in diagnosis,[31,32] the mean age of these subjects (53.5 years), who had multiple atherosclerosis risk factors, strongly supports acute myocardial ischemia as the causative mechanism of myocardial injury.

This work correlated individual ECG patterns and CMR findings in the specific context of ongoing myocardial ischemia (ie, NSTE-ACS at presentation). In the early phase of NSTE-ACS, T-wave abnormality and ST depression reflect changes in myocardial cellular electrophysiology related to temporary myocardial ischemia without permanent cell damage.[33] Furthermore, T-wave abnormality can occur in conditions other than acute myocardial ischemia, and each may have a different underlying pathophysiological mechanism.[34]

Conclusion

In conclusion, this is the first demonstration that standard 12-lead ECG T-wave abnormalities seen during the acute phase of NSTE-ACS are related to the presence of myocardial edema. T-wave abnormality is a simple, highly specific but less sensitive marker of myocardial edema. The electrophysiological mechanisms and prognostic implications of this underlying pathophysiology warrant further investigation.

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Disclosures

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SUPPLEMENTAL MATERIAL

Table S1. Full Univariate Logistic Regression Analysis of Individual Predictors of Myocardial Edema.

Single Predictors of Myocardial Edema			
Predictors	**OR**	**95% CI**	**P value**
Age	1.00	0.97-1.05	0.640
Male	1.41	0.56-3.53	0.467
Body mass index, kg/m2	0.97	0.93-1.07	0.912
Diabetes	1.39	0.56-3.46	0.476
Smoking	2.17	0.85-5.56	0.106
Hypertension	0.55	0.18-1.69	0.547
Hyperlipidemia	1.42	0.52-3.84	0.493
History of CAD	0.82	0.34-2.00	0.666
SBP, mmHg	1.00	0.99-1.01	0.952
DBP, mmHg	1.00	0.98-1.03	0.810
TIMI Risk Score	1.15	0.81-1.64	0.430
GRACE in hospital mortality	1.07	0.88-1.30	0.500
GRACE 6 Moths mortality	1.07	0.97-1.18	0.163
No. Of Vessels with CAD	1.45	0.92-2.27	0.106
Symptoms onset to admission, hrs	1.00	0.95-1.07	0.783
ECG to CMR, hrs	1.00	0.98-1.02	0.915
Ejection Fraction on admission	0.97	0.93-1.00	0.073

CAD: coronary artery disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; ECG: electrocardiogram; CMR: cardiac magnetic resonance.