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T-wave and its association with myocardial fibrosis on cardiovascular magnetic resonance examination

Karolina M. Zareba MD[1] | Vien T. Truong MD[2] | Wojciech Mazur MD[2] | Suzanne M. Smart BS[1] | Xiaojuan Xia MSC[3] | Jean-Philippe Couderc PhD[3] | Subha V. Raman MD, MSEE[4]

[1]Division of Cardiovascular Medicine, The Ohio State University Wexner Medical Center, Columbus, OH, USA

[2]Division of Cardiology, The Christ Hospital Health Network, Cincinnati, OH, USA

[3]Heart Research Follow-Up Program, University of Rochester Medical Center, Rochester, NY, USA

[4]Division of Cardiology, Indiana University School of Medicine, Indianapolis, IN, USA

Correspondence
Karolina M. Zareba, MD, OSU Division of Cardiovascular Medicine, 473 W 12th Ave, Suite 200, Columbus, OH 43210, USA.
Emails: Karolina.Zareba@osumc.edu, kzarebamd@gmail.com

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Abstract

Background: Risk stratification in non-ischemic myocardial disease poses a challenge. While cardiovascular magnetic resonance (CMR) is a comprehensive tool, the electrocardiogram (ECG) provides quick impactful clinical information. Studying the relationships between CMR and ECG can provide much-needed risk stratification. We evaluated the electrocardiographic signature of myocardial fibrosis defined as presence of late gadolinium enhancement (LGE) or extracellular volume fraction (ECV) ≥29%.

Methods: We evaluated 240 consecutive patients (51% female, 47.1 ± 16.6 years) referred for a clinical CMR who underwent 12-lead ECGs within 90 days. ECG parameters studied to determine association with myocardial fibrosis included heart rate, QRS amplitude/duration, T-wave amplitude, corrected QT and QT peak, and Tpeak-Tend. Abnormal T-wave was defined as low T-wave amplitude ≤200 μV or a negative T wave, both in leads II and V5.

Results: Of the 147 (61.3%) patients with myocardial fibrosis, 67 (28.2%) had ECV ≥ 29%, and 132 (54.6%) had non-ischemic LGE. An abnormal T-wave was more prevalent in patients with versus without myocardial fibrosis (66% versus 42%, $p < .001$). Multivariable analysis demonstrated that abnormal T-wave (OR 1.95, 95% CI 1.09–3.49, $p = .03$) was associated with myocardial fibrosis (ECV ≥ 29% or LGE) after adjustment for clinical covariates (age, gender, history of hypertension, and heart failure). Dynamic nomogram for predicting myocardial fibrosis using clinical parameters and the T-wave was developed: https://normogram.shinyapps.io/CMR_Fibrosis/.

Conclusion: Low T-wave amplitude ≤ 200 μV or negative T-waves are independently associated with myocardial fibrosis. Prospective evaluation of T-wave amplitude may identify patients with a high probability of myocardial fibrosis and guide further indication for CMR.

KEYWORDS
electrocardiography, late gadolinium enhancement, myocardial fibrosis, T1 mapping

1 | INTRODUCTION

Cardiovascular magnetic resonance (CMR) is highly impactful by providing comprehensive information on structure, function, and myocardial tissue characterization (Bruder et al., 2013). Late gadolinium enhancement imaging (LGE) identifies macroscopic replacement myocardial fibrosis, while T1 mapping via extracellular volume fraction (ECV) quantifies microscopic diffuse interstitial expansion. These measures of myocardial fibrosis are both diagnostic and highly prognostic across disease states (Di Marco et al., 2017; Messroghli et al., 2017). The global burden of cardiovascular disease is steadily increasing and accounts for over 17 million deaths annually, thus incurring tremendous healthcare costs (Benjamin et al., 2019). These staggering figures highlight the importance of earlier and more cost-effective diagnosis and treatment to improve outcomes. Appropriate selection of patients who would benefit from advanced cardiac imaging is thus crucial.

The initial and most commonly obtained diagnostic tool in cardiovascular medicine is the electrocardiogram (ECG). Although it is one of the oldest and fastest cardiovascular tests, it continues to provide highly relevant and impactful clinical information. The association of ECG and CMR abnormalities has been widely studied. ECG measures of ventricular hypertrophy have been correlated with CMR-based myocardial mass (Rider et al., 2016). ECG and LGE-based detection and localization of myocardial scar have been studied (Bayes de Luna et al., 2006; Strauss et al., 2008; Wieslander et al., 2018). Conduction delay has been associated with LGE-evident fibrosis in several cohorts (Cheema et al., 2012; Raman et al., 2007). More recently, the impact of diffuse myocardial fibrosis on the ECG has been evaluated (Inoue et al., 2017; Rodrigues et al., 2017). These studies highlight the ongoing clinical impact of the ECG and the need for further investigation.

Driven by the potential of ECG-based risk stratification to guide need of advanced imaging and institution of timely therapy, the aim of our study was to identify the association of ECG parameters with myocardial fibrosis, defined as the presence of LGE or an elevated ECV ≥ 29%.

2 | METHODS

2.1 | Study population

We retrospectively evaluated 240 consecutive patients referred for a clinical CMR to the Ohio State University Ross Heart Hospital between March 2014 and June 2015. Criteria for inclusion consisted of a CMR examination with T1 mapping and LGE, and a routinely acquired, digitally stored 12-lead ECG within 90 days of the CMR. The goal of the study was to investigate the relationship between ECG and CMR parameters in patients with non-ischemic myocardial disease. As several disease states already have classic electrocardiographic signatures and specific imaging algorithms including cardiac amyloidosis, hypertrophic cardiomyopathy, and myocardial infarction, we elected to exclude these patients. Additionally, patients with bundle branch block (BBB) and ventricular paced rhythms were excluded. Clinical characteristics and comorbidities were established by review of the medical record. Heart failure was defined as prior admission for decompensated congestive heart failure as evidenced by physician documented signs and symptoms of heart failure, supporting clinical findings, and therapy for heart failure including diuretics (Kalogeropoulos et al., 2010). The Ohio State University Institutional Review Board approved this retrospective study and waived informed consent. The corresponding author has full access to all the data in the study and takes responsibility for its integrity and the data analysis.

2.2 | Electrocardiographic analysis

Electrocardiographic parameters were assessed from standard 12-lead surface ECGs. All ECGs were recorded digitally in a standard fashion at a 500 Hz sampling frequency with 4.88 μV/bit amplitude resolution and stored into the GE MUSE system (GE Healthcare). ECGs were evaluated for the following parameters: heart rate, QRS durations, Cornell voltage, QT and corrected QT intervals (Bazett formula), QT peak, Tpeak to Tend interval, and T-wave amplitude. Amplitude and duration measurements were performed in ECG leads II and V5. Lead II was chosen as the main lead of interest for amplitude and duration measurement given its vector relationship to the heart. All ECG measurements in Tables are presented for lead II. T-wave amplitude was measured from the apex of the T-wave to the isoelectric line following the T-wave. An abnormal T-wave was defined as low positive T-wave amplitude in leads II and V5 ≤ 200 μV or a negative T-wave regardless of amplitude. The following cutoff values were utilized from existing literature for key ECG parameters: HR > 70 bpm (Opdahl et al., 2014), QRS duration > 100 ms (Ilkhanoff et al., 2012), Cornell voltage > 2.0 mV (Rodrigues et al., 2008), corrected QT duration ≥ 450 ms (Moss & Robinson, 1992), and T-wave amplitude ≤ 200 μV (2 mm on a standard ECG; Gambill et al., 1995).

2.3 | Cardiovascular magnetic resonance

All patients underwent clinical CMR scans with a 1.5 Tesla scanner (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany). Steady-state free precession sequences were used for assessment of left ventricular (LV) volumes, ejection fraction (EF), and LV mass. LV volumes and EF were measured from contiguous short-axis cine

images using semi-automated software for endocardial segmentation using endocardial and epicardial contours at end-systole and end-diastole with Simpson's rule. LV mass was calculated from the total end-diastolic myocardial volume multiplied by the specific gravity of the myocardium (1.05 g/ml) (Reiter et al., 2004).

Late gadolinium enhancement imaging was performed using a gradient-echo inversion recovery sequence with magnitude and phase-sensitive inversion recovery reconstructions 10 min after standard dose of gadolinium-based contrast agent (Kellman et al., 2002). The presence of LGE was assessed by 2 expert level 3 trained operators blinded to clinical and electrocardiographic data and had to be present in either two consecutive short-axis slices or in two orthogonal imaging planes.

MOdified Look-Locker Inversion Recovery (MOLLI) 5(3)3 acquisition schemes were used to acquire T1 maps produced using vendor software before and 15 min after administration of contrast. T1 values and extracellular volume fraction (ECV) were measured and calculated utilizing interventricular septal values from the mid-short-axis view. The region of interest was placed in the mid myocardium with manual tracing to avoid partial volume effects (Moon et al., 2013; Puntmann et al., 2016). Myocardial ECV was calculated as previously described (Messroghli et al., 2007). Reference values for the myocardium based on 44 healthy subjects at our institution (36 ± 15 years, 59% female) are as follows: native T1 999 ± 31 ms, post-contrast T1 453 ± 30 ms, and ECV 23.8 ± 2.6%. In line with previous literature, the abnormal value for ECV was 29%, corresponding to 2SD above the reference value (Kawel-Boehm et al., 2015), which indicates diffuse interstitial expansion (Messroghli et al., 2017). All T1 measurements were performed by a single operator blinded to clinical and electrocardiographic data.

2.4 | Statistical analysis

Categorical data are presented as frequency (percentage), and comparison between groups was performed using the chi-square test or Fisher exact test. Continuous variables are presented as mean ± standard deviation (*SD*) for normal distribution or expressed as median (interquartile range) for non-normal distribution. Differences in continuous variables between two groups were analyzed using Student's *t*-test for normally distributed continuous variables or the Mann–Whitney *U*-test for variables without a normal distribution. Multivariable logistic regression analysis was used to find independent electrocardiographic variables associated with myocardial fibrosis. A clinical model was developed which included age, gender, history of hypertension and heart failure. An initial multivariate analysis was performed by adding each ECG parameter one at a time to the clinical model. Subsequently, all dichotomized ECG parameters, which demonstrated statistical significance in the initial multivariate analysis, were then combined with the clinical model to generate the final model. To further investigate the incremental value of low T-wave amplitude to the clinical model to predict myocardial fibrosis, the likelihood ratio test was performed. The change in global chi-square values was reported. Statistical significance was set at two tailed $p < .05$. All statistical analyses were performed with R software, version 3.6.1 (The R Foundation). Lastly, we have developed a dynamic nomogram online clinical tool to estimate the likelihood of myocardial fibrosis based on clinical parameters and T-wave data (Jalali et al., 2019). The data that support the findings of this study are available from the corresponding author upon reasonable request.

3 | RESULTS

3.1 | Clinical and imaging characteristics

A total of 240 patients were included in the study, 51% female, mean age 47.1 ± 16.6 years. Clinical indications for CMR examination were as follows: cardiomyopathy/heart failure 52.1%, ventricular arrhythmias / premature ventricular contractions 30.8%, chest pain 5.4%, myocarditis 5.0%, atrial arrhythmias 3.3%, syncope 2.9%, and valvular disease 0.4%. Clinical and imaging characteristics for all 240 patients are presented in Table 1. There were 147 (61.3%) patients with myocardial fibrosis (LGE or ECV ≥ 29%). There were 67 (27.9%) patients with an ECV ≥ 29% and 132 (55%) patients with LGE. All patients with LGE exhibited a non-ischemic pattern (mid-myocardial or epicardial) with a median involvement of 1 segment. Two patients did not have adequate T1 maps for analysis and were excluded from the ECV portion of the analysis.

Hypertension (57.8% versus 31.2%, $p < .001$) and history of heart failure (41.5% versus 12.9%, $p < .001$) were significantly more prevalent in patients with versus without myocardial fibrosis (LGE or ECV ≥ 29%). There were no significant differences in the prevalence of diabetes among cohorts ($p = .15$). Men (65.3%) were more likely to have a LGE as compared to women (45.1%); however, there were no significant differences between genders in the prevalence of an ECV ≥ 29% ($p = .38$). The majority of patients (95.0%) exhibited normal sinus rhythm on their presenting ECG, while the remainder exhibited atrial fibrillation.

The mean LVEF of all patients was 52.9 ± 14.6%. All studied CMR parameters differed significantly between cohorts. Patients with myocardial fibrosis (LGE or ECV ≥ 29%) had larger indexed left ventricular volumes and mass, and lower ejection fraction.

3.2 | Electrocardiographic characteristics

3.2.1 | ECG parameters and ECV ≥ 29%

Patients with an elevated ECV exhibited higher heart rates (81 ± 20 versus 74 ± 17 bpm, $p = .005$) and Cornell voltage (1.6 ± 0.9 versus 1.3 ± 0.7 mV, $p = .02$) (Table 2). T-wave amplitude was lower (113 (−29–174) μV versus 216 (131–316) μV, $p < .0001$) in patients with an ECV ≥ 29% when compared to individuals with normal ECV values. We note a significant correlation between ECV and T-wave amplitude ($r = -.42$, $p < .001$) (Figure S1). Corrected QT ($p = .006$) and QT

TABLE 1 Baseline clinical and imaging characteristics

	Whole Cohort (*N* = 240)	ECV < 29% (*N* = 171)	ECV ≥ 29% (*N* = 67)	*p* value	No LGE (*N* = 108)	LGE (*N* = 132)	*p* value
Clinical Characteristics							
Age, years	47.1 ± 16.6	46.0 ± 16.8	49.1 ± 15.3	.19	43.7 ± 16.9	49.8 ± 16.0	.004
Female gender, *N* (%)	122 (50.8)	90 (52.6)	31 (46.3)	.38	67 (62.0)	55 (41.7)	.002
BMI, kg/m^2	28.6 ± 6.7	28.7 ± 6.5	28.4 ± 7.3	.78	27.4 ± 6.3	29.7 ± 6.8	.007
Diabetes, *N* (%)	33 (13.8)	19 (11.1)	13 (19.4)	.09	11 (10.2)	22 (16.7)	.15
Hypertension, *N* (%)	114 (47.5)	70 (40.9)	42 (62.7)	.002	36 (33.3)	78 (59.1)	<.001
Heart failure, *N* (%)	73 (30.4)	40 (23.4)	32 (47.8)	<.001	16 (14.8)	57 (43.2)	<.001
GFR, ml/min/1.73 m^2	58.1 ± 5.8	58.8 ± 4.5	56.1 ± 8.1	.001	58.5 ± 5.4	57.7 ± 6.2	.30
Hematocrit, %	38.9 ± 6.0	40.3 ± 4.4	35.2 ± 7.8	<.001	38.4 ± 5.9	39.3 ± 6.1	.28
CMR Characteristics							
Left ventricular EF, %	52.9 ± 14.6	55.8 ± 13.0	45.8 ± 16.1	<.001	60.1 ± 8.7	47.0 ± 15.8	<.001
EF ≥ 55%, *N* (%)	138 (57.5)	109 (63.7)	29 (43.3)	.004	85 (78.7)	53 (40.2)	<.001
LVEDVI, ml/m^2	86.7 ± 30.8	81.3 ± 23.1	101.9 ± 42.3	<.001	75.8 ± 16.0	95.3 ± 36.4	<.001
LVESVI, ml/m^2	44.1 ± 31.0	37.9 ± 22.4	61.0 ± 43.1	<.001	30.7 ± 10.7	54.6 ± 37.1	<.001
LVMI, mL/m^2	62.1 ± 21.3	57.4 ± 15.9	75.2 ± 28.4	<.001	51.7 ± 10.5	70.4 ± 24.0	<.001
Native myocardial T1, ms	1,019 ± 53	1,002 ± 42	1,065 ± 52	<.001	1,004 ± 50	1,031 ± 53	<.001
ECV, %	26.4 ± 4.9	23.9 ± 2.5	32.8 ± 3.9	<.001	25.2 ± 4.3	27.4 ± 5.2	.001
Presence of LGE, *N* (%)	132 (55.0)	79 (46.2)	52 (77.6)	<.001			
ECV ≥ 29%, *N* (%)	67 (27.9)				15 (14)	52 (39.7)	<.001

Note: Continuous variables are expressed as mean ± standard deviation or median (interquartile range).

Categorical variables are presented as *n* (%).

Abbreviations: BMI, body mass index; ECV, extracellular volume fraction; EF, ejection fraction; GFR, glomerular filtration rate; LGE, late gadolinium enhancement; LVEDVI, left ventricular end-diastolic volume index; LVESVI, left ventricular end-systolic volume index; LVMI, left ventricular mass index.

TABLE 2 Electrocardiographic characteristics

ECG Characteristics	Whole Cohort	ECV < 29% (*N* = 171)	ECV ≥ 29% (*N* = 67)	*p* value	No LGE (*N* = 108)	LGE (*N* = 132)	*p* value
Heart rate, bpm	76 ± 18	74 ± 17	81 ± 20	.005	72 ± 15	80 ± 20	.002
QRS duration, ms	91 ± 12	91 ± 11	91 ± 14	.82	89 ± 11	92 ± 12	.03
Cornell voltage, mV	1.4 ± 0.7	1.3 ± 0.7	1.6 ± 0.9	.02	1.2 ± 0.5	1.6 ± 0.9	<.001
Cornell voltage ≥ 2.0 mV, *N* (%)	41 (17.1)	23 (13.5)	18 (26.9)	.01	9 (8.3)	32 (24.2)	.001
TW amplitude, μV	178 (100–291)	216 (131–316)	113 (–29–174)	<.001	219 (137–347)	152 (64–255)	<.001
TW amplitude ≤ 200 μV, *N* (%)	135 (56.3)	81 (47.4)	53 (80.3)	<.001	49 (45.4)	86 (65.6)	.002
QTc duration, ms	436 ± 47	429 ± 40	452 ± 59	.006	429 ± 41	441 ± 50	.05
QTc ≥ 450 ms, *N* (%)	76 (31.7)	45 (26.6)	30 (46.2)	.004	28 (25.9)	48 (37.5)	.06
QTpc duration, ms	345 ± 39	340 ± 35	359 ± 48	.004	341 ± 36	348 ± 41	.17
Tpeak-Tend, ms	83 ± 22	83 ± 19	82 ± 27	.80	81 ± 20	84 ± 23	.29

Note: Continuous variables are expressed as mean ± standard deviation or median (interquartile range).

Categorical variables are presented as *n* (%).

The measurements of T-wave amplitude, corrected QT and QT peak, and Tpeak-Tend are shown for lead II.

T-wave amplitude ≤ 200 μV includes low positive T-waves ≤200 μV and negative T-waves regardless of amplitude.

Abbreviations: ECG, electrocardiogram; ECV, extracellular volume fraction; LGE, late gadolinium enhancement; QTc, corrected QT; QTpc, corrected QT peak; TW amplitude, T-wave amplitude.

TABLE 3 Association of ECG parameters with myocardial fibrosis. ECG variables added one at a time to the clinical model in multivariate logistic regression analysis.

	Predicting Myocardial Fibrosis (ECV ≥ 29% or LGE)	
	OR (95% CI)	*p* value
Clinical Variables		
Age	1.00 (0.98–1.02)	.99
Hypertension	2.32 (1.20–4.49)	.01
Heart failure	3.76 (1.83–7.72)	<.001
Female gender	0.59 (0.33–1.03)	.06
ECG variables		
Heart rate > 70 bpm	1.48 (0.83–2.62)	.18
QRS duration (continuous)	0.99 (0.97–1.02)	.57
QRS duration > 100ms	1.05 (0.50–2.22)	.89
Cornell voltage (continuous)	1.04 (0.99–1.09)	.09
Cornell voltage > 2.0 mV	2.22 (0.93–5.30)	.07
QTc duration (continuous)	1.004 (0.99–1.01)	.23
QTc duration > 450 ms	1.26 (0.65–2.44)	.50
TW amplitude (continuous)	0.08 (0.01–0.48)	.006
TW amplitude ≤ 200μV	1.95 (1.09–3.49)	.03

Abbreviations: ECG, electrocardiogram; ECV, extracellular volume fraction; LGE, late gadolinium enhancement; QTc, corrected QT; TW amplitude, T-wave amplitude.

peak ($p = .004$) were both significantly longer in patients with an elevated ECV. There were no differences in QRS durations or Tpeak-Tend between cohorts.

3.2.2 | ECG parameters and the presence of LGE

Patients with non-ischemic LGE exhibited higher heart rates (80 ± 20 versus 72 ± 15 bpm, $p = 0.002$) and Cornell voltage (1.6 ± 0.9 versus 1.2 ± 0.5 mV, $p < .001$) as compared to those without LGE. QRS duration was mildly longer in patients with LGE. T-wave amplitude was significantly lower (152 (64–255) μV versus 219 (137–347) μV, $p < .001$) in patients with versus without LGE. There were no differences in corrected QT ($p = .05$) and QT peak, and Tpeak-Tend in patients with versus without LGE.

3.3 | Association of ECG parameters with myocardial fibrosis

Multivariate analysis was performed to evaluate the association of ECG parameters with myocardial fibrosis. The clinical model included age, gender, history of hypertension, and heart failure. The initial multivariate analysis by adding each ECG parameter one at a time to the clinical model is presented in Table 3. Dichotomized ECG variables, which demonstrated statistical significance in the initial multivariate analysis, were then combined with the clinical model to generate the final model (Table 4). We demonstrate that an abnormal T-wave (amplitude ≤ 200μV or negative T wave) is significantly associated with myocardial fibrosis after controlling for clinical covariates. Upon addition of an abnormal T-wave to the clinical model, the area under the curve (AUC) for predicting myocardial fibrosis was 72.8% (95% CI: 67–79, $p < .001$) (Figure 1). Sequential addition of an abnormal T-wave to the clinical model did show a significant increase in chi-square value (chi-square

TABLE 4 Final models for association of ECG parameters with myocardial fibrosis

	Predicting Myocardial Fibrosis (ECV ≥ 29% or LGE)	
	OR (95% CI)	*p* value
Clinical Variables		
Age	0.99 (0.98–1.02)	.78
Hypertension	2.11 (1.08–4.15)	.03
Heart failure	3.57 (1.72–7.39)	.001
Female gender	0.59 (0.33–1.04)	.069
ECG variables		
TW amplitude ≤ 200 μV	1.95 (1.09–3.49)	.03

Abbreviations: ECG, electrocardiogram; ECV, extracellular volume fraction; LGE, late gadolinium enhancement; TW amplitude, T-wave amplitude.

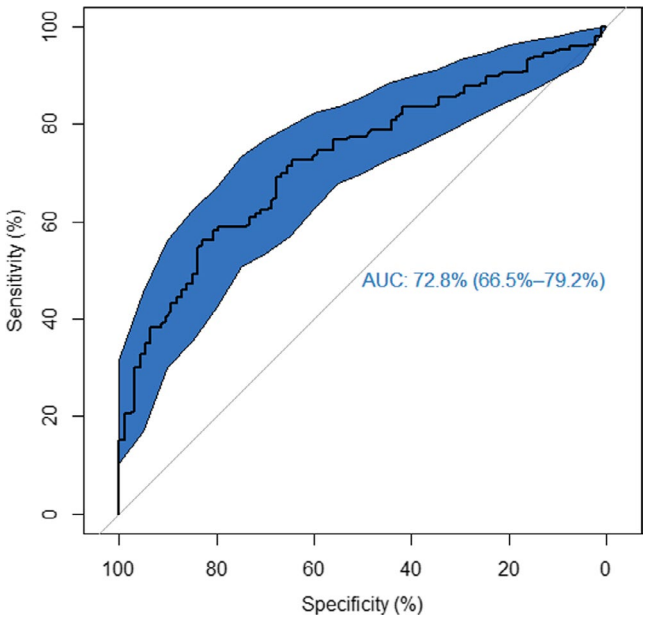

FIGURE 1 Predicting myocardial fibrosis. The area under the curve (AUC) as a measure of model performance for the prediction of myocardial fibrosis defined as the presence of late gadolinium enhancement, or extracellular volume fraction ≥29%. Upon addition of an abnormal T-wave to the clinical model (age, hypertension, heart failure, and gender), the AUC for predicting myocardial fibrosis was 72.8% (95% CI: 67–79, $p < .001$)

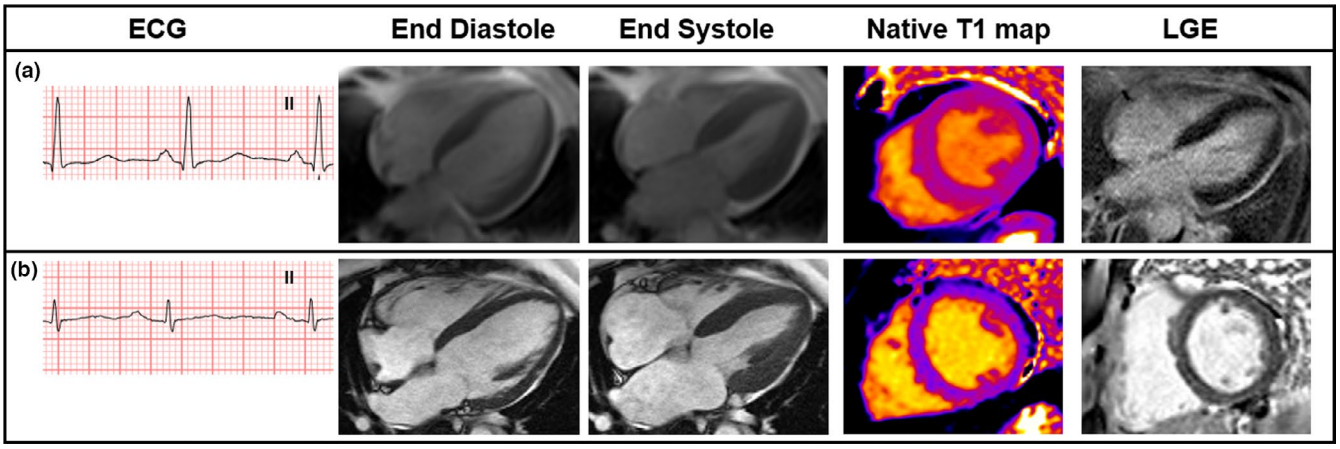

FIGURE 2 ECG and CMR manifestations in two patients. Patient A: 55-year-old female with premature ventricular contractions. ECG demonstrates T-wave amplitude of 113 μV, left ventricular EF 60%, ECV 31%, and no evidence of LGE. Patient B: 64-year-old female with dyspnea. ECG demonstrates T-wave amplitude of 88 μV, EF 62%, ECV 25%, midwall LGE. CMR: cardiovascular magnetic resonance; ECG: electrocardiogram; ECV: extracellular volume fraction; EF: ejection fraction; LGE: late gadolinium enhancement

difference = 5.03, $p = .025$), demonstrating the incremental predictive value of an abnormal T-wave. The dynamic nomogram for likelihood of myocardial fibrosis defined as an ECV ≥ 29% or LGE using clinical parameters and T-wave data was developed and can be accessed online at https://normogram.shinyapps.io/CMR_Fibrosis/. Of note, univariate and multivariate analyses were also conducted in ECG lead V5 and demonstrated consistent findings as in lead II. Figure 2 demonstrates examples of ECG and CMR manifestations in two patients.

A subanalysis of the 167 patients without a history of heart failure (mean EF 58.6 ± 9.5%) was also performed. An abnormal T-wave (OR 1.98, CI: 1.07–3.67, $p = .03$) remained independently associated with myocardial fibrosis.

4 | DISCUSSION

In our study of consecutive patients referred for CMR without prior myocardial infarctions, we demonstrate a significant association of an abnormal T-wave (T-wave amplitude ≤ 200μV or negative T-wave both in leads II or V5) with myocardial fibrosis defined as the presence of LGE or an elevated ECV ≥ 29%. Prospective evaluation of the T-wave may identify patients with a high probability of myocardial fibrosis and thus at increased risk of adverse events.

T-wave amplitude is a signature of ventricular repolarization and carries significant clinical value (Shi et al., 2013). Decades ago it was demonstrated that T-wave amplitude varies with alterations in LV chamber size (Feldman et al., 1985). T-wave amplitude is lower in hypertensive patients with versus without hypertrophy and may be an early marker of repolarization abnormality (Dilaveris et al., 2000). Animal studies have demonstrated that T-wave flattening in diabetes relates to redistribution of ventricular repolarization patterns (Sedova et al., 2017). Concurrently, CMR studies have demonstrated diffuse interstitial fibrosis by T1 mapping both in hypertensive (Wang et al., 2017) and diabetic (Wong et al., 2014) patients. In our study, we note significantly decreased T-wave amplitude in patients with an elevated ECV and with focal LGE, suggesting that replacement and interstitial fibrosis may play a role in abnormal ventricular repolarization. Our study also demonstrates incremental predictive value of low T-wave amplitude over standard clinical variables, thus increasing its utility.

4.1 | Clinical implications

The results of our study support an ECG-based approach in evaluating patients at risk of adverse events due to myocardial fibrosis. The T-wave could be evaluated during a clinical visit to identify patients with a high probability of myocardial fibrosis, and guide choice of and need for advanced imaging. Importantly, our data not only demonstrate T-wave myocardial fibrosis associations in patients with heart failure, but also in those without heart failure—a cohort in which risk stratification is key to guide need for advanced imaging. In the era of artificial intelligence and rising healthcare costs, it is important to remember that clinically impactful information can be obtained from a fast, easy, and inexpensive ECG (Attia et al., 2019).

5 | LIMITATIONS

This is a retrospective study of patients referred for a clinical CMR; our findings should be confirmed prospectively in a large validation cohort. The goal of our study was to demonstrate associations of ECG parameters with myocardial fibrosis. This is a derivation study which hopes to identify a simple clinical risk stratification tool to be validated in a separate cohort. We utilized single cutoff values for each studied ECG variable rather than specifying gender-based cutoffs. All values were taken from previous literature and applied in our predictive model. Information on electrolyte values as well as concomitant medication use, which may affect ECG parameters, was

not available for this cohort. Lastly, given the retrospective nature of this study, we had access to only mid-ventricular short-axis T1 maps; hence, our ECV is a mid-septal ECV rather than a whole-heart ECV.

6 | CONCLUSION

We demonstrate an independent and significant association of an abnormal T-wave (low T-wave amplitude ≤ 200 μV or negative T-wave in leads II and V5), with myocardial fibrosis defined as the presence of LGE or an ECV ≥ 29%, even after adjustment for key clinical parameters including heart failure. Prospective evaluation of the T-wave may help identify patients with a high probability of replacement or interstitial myocardial fibrosis and guide further indication for CMR.

CONFLICT OF INTEREST

All authors report no conflict of interest.

FUNDING INFORMATION

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AUTHOR CONTRIBUTION

Contributed to study design, data extraction, EKG and CMR data analysis, statistical analysis, manuscript drafting and critical revisions: KMZ. Contributed to statistical analysis and critical manuscript revisions: VTT, WM. Contributed to CMR data analysis and critical manuscript revisions: SMS. Contributed to EKG data analysis and critical manuscript revisions: XX, JPC. Contributed to study design, CMR data analysis, and critical manuscript revisions: SVR.

ETHICAL APPROVAL

The Ohio State University Institutional Review Board approved this retrospective study and waived informed consent.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Karolina M. Zareba https://orcid.org/0000-0002-4891-4106

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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