ORIGINAL ARTICLE

Analysis of ECG Measures of Cardiac Repolarization in Relation to Arrhythmic Events in an Implantable Cardioverter Defibrillator Population

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Background: ECG-derived measures of cardiac repolarization may have utility in risk prediction of future ventricular arrhythmia, and a range of different measures have been proposed. We compared time-based, vectorcardiographic, and singular value decomposition (SVD) derived measures of repolarization to determine which was most predictive of appropriate therapy in an ICD population.

Methods: We examined the independent prognostic value of a range of repolarization measures derived from 60 second 12-lead ECG recordings in 150 patients receiving new ICD implants in relation to the occurrence of appropriate therapy during follow-up.

Results: Over an average follow-up of 2.15 ± 0.87 years, male gender, presence of premature ventricular complex (PVC), relative T wave residuum (TWR-rel, measures regional repolarization heterogeneity), and TCRT (the total cosine R-to-T, describes the global angle between repolarization and depolarization wavefronts) were the only independent predictors of appropriate therapy. With every 0.01% increase in TWR-rel, there was 2% increased risk of appropriate therapy (HR = 1.02, 95% CI 1.006–1.034, $P < 0.001$). With every 1° decrease in TCRT, there was an increase in arrhythmic risk of 0.9% (HR 1.009, 95% CI 1.003–1.015, $P = 0.003$).

Conclusions: The use of advanced analytic ECG techniques to derive measures of repolarization abnormality might have utility in risk stratification in an ICD population.

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noninvasive techniques – electrocardiography; implantable devices – ventricular tachycardia/fibrillation; cardiac repolarization

INTRODUCTION

Cardiac repolarization heterogeneity has been implicated to be a key predisposing factor to ventricular arrhythmia. Increased repolarization dispersion facilitates conduction block and leads to functional reentry resulting in sustained reentrant arrhythmia.^{1–3} Many ECG parameters have been proposed to capture such heterogeneity and shown to carry prognostic value of arrhythmia occurrence, thus may aid noninvasive risk stratification of patients at risk of ventricular arrhythmia.⁴

Acar et al.⁵ proposed a range of T wave descriptors based on the use of mathematical transformation of 12-lead ECG signals using singular

value decomposition (SVD). The parameters were proposed to characterize the spatial, temporal, and wavefront characteristics of repolarization, and have been found to predict adverse outcomes in clinical studies.^{6–9} However, these parameters have never been examined in an ICD population, and neither have they been examined alongside the other widely studied ECG measures of repolarization to assess their independent prognostic value, namely QT interval,¹⁰ QT dispersion,¹¹ the T peak to T end (TpTe) interval,^{12–14} and spatial QRS-T angle.^{15,16}

To assess the independent prognostic value of these proposed ECG measures of ventricular repolarization in relation to ventricular

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arrhythmia, we examined the conventional and novel cardiac repolarization measures derived from standard 12-lead ECG in a prospective cohort of ICD patients in relation to the delivery of appropriate device therapy.

METHODS

Study Population

All patients who received new ICD implants over the 3 years period from March 2010 to December 2012 at Wellington Regional Hospital were prospectively enrolled. Patient demographics and clinical characteristics were collected at the time of the ICD implantation, including demographics, clinical history, implant indication, comorbidities, and medication history. Implant indications were defined as secondary prevention if the patient has survived a cardiac arrest or experienced sustained ventricular tachyarrhythmia. Primary prevention was defined as the absence of cardiac arrest or sustained ventricular tachyarrhythmias. This study was reviewed by the Central Regional Ethics Committee and found to conform to the New Zealand standards for observational research.

All implants involved systems with transvenous leads. Programming was made at the discretion of implanting physician as well as guided by the NZ programming guideline,¹⁷ where programming of VF zone occurred in all cases, and programming of additional VT and monitoring zones was at the discretion of the implanting cardiologist. The average rate of VT1/VT2 zone (lowest rate) was 174 ± 18 bpm. Average VF zone rate was 216 ± 21 bpm.

ECG Recording and Analysis

In all patients receiving new ICD implants, 60 second ECG recordings were obtained preimplant in the electrophysiology laboratory, with the patient in supine position after resting for a minimum of 5 minutes and prior to the administration of any sedative or anesthetic agents. Patients were on their regular medications. Recordings were made using the Philips Xper Information Management Physiomonitoring 5 system (Eindhoven, The Netherlands). The ECGs were exported and analyzed offline using custom written programs on LabVIEW 8.5 (National Instruments, Austin, TX, USA). Using a matched

filtering method the signal-averaged complex from each lead was derived from the 60 second ECG, and used as the representative waveform for analysis.^{18,19} QRS start, QRS end, and T end were determined in each signal-averaged complex using the differential threshold method, defined as the time instant of the differential to fall below the set threshold level. The threshold levels were determined empirically based on 20 patients ECG to achieve the best performance in accordance with visual inspection. The U wave was ignored by the algorithm and if the U wave followed close to the T wave, the T wave end was manually corrected to be the nadir between T and U wave. T wave peak was defined as the absolute maxima of the T wave regardless of polarity. ECG leads with T wave amplitude less than 0.1 mV were excluded due to unreliability of accurate determination of T wave end. Visual inspection was carried out in all complexes to judge the reliability of automatic detection and manually corrected if needed.

Repolarization Measures by Time Intervals

QRS, QT, and TpTe (T peak to T end) intervals were measured from each lead and averaged across the 12-leads. The QT interval was corrected using the Fridericia's formulae.²⁰ QT dispersion was defined as the difference between maximum and minimum QT interval across the 12 leads.

Repolarization Measures by Vectorcardiography

Spatial QRS-T angle was measured as described previously.²¹ The 12-lead ECG was transformed into vectorcardiography using Kors transformation.²² Integral QRS and T vectors were calculated from the integral area of the QRS and T loops. The spatial QRS-T angle was defined as the 3-D angle between the QRS and T vectors.

Repolarization Measures by Singular Value Decomposition

Acar et al.⁵ proposed a range of T wave morphology descriptors using singular value decomposition (SVD) to quantify the different characteristics of cardiac repolarization. This set

of parameters has never been applied in ICD patients before and was derived in this study as described by Acar et al.⁵ SVD is a mathematical technique of signal processing and analysis. It decomposes the eight independent ECG leads (I, II, V₁–V₆) into a minimal dimensional space consists of eight new orthogonal leads ranked from containing the greatest to the lowest energy. The first three orthogonal components represent the signal components that can be represented in 3-D space, the so-called dipolar components. The remaining 4th to 8th components represent signal components beyond that cannot be represented in a global 3D component, thus proposed to be reflection of regional repolarization heterogeneity.

Using this technique, several novel descriptors can be calculated to characterize the spatial, temporal, and wavefront characteristics of repolarization. T wave PCA ratio (T PCA) is defined as the ratio of the singular value of the second to the first component. It is a measure of the complexity of repolarization and higher value was proposed to represent inhomogeneous repolarization.^{5,7}

The absolute and relative T wave residuum are measures of regional repolarization heterogeneity. Absolute T wave residuum (TWR abs) is defined as the absolute sum of the squares of the 4th to 8th eigenvalues, representing the component reflecting regional repolarization heterogeneity. The relative T wave residuum (TWR rel) is the proportion of the absolute T wave residuum to the sum of squares of all the 1st to 8th eigenvalues, reported as %.⁵

T wave morphology dispersion (TMD) is a spatial heterogeneity measure of the T wave, measuring the difference between T wave shapes in individual leads. It is defined as the average angle between all possible pairs of reconstructed vectors of individual ECG leads created from the T wave loop.⁵ T wave loop dispersion (TWLD) was measure of temporal variation in the interlead relationship, derived as described previously.^{7,8} The descriptor total cosine R to T (TCRT) is a wavefront descriptor that measures the vector deviation between depolarization and repolarization by calculating the average cosine values between the three-dimensional QRS and T wave vector loops. For ease of interpretation, this parameter was reported in angle (degrees) in this study instead of the cosine value.

Follow-up and Clinical Events

Patients were followed up clinically with device interrogation at regular intervals of 3–6 months, as well as home monitoring which was enabled in 84% of patients. Home monitoring transmissions were reviewed as they arose. All antitachycardia pacing (ATP) or shock episodes were reviewed by specialized cardiac physiologists and classified as appropriate or inappropriate. If in doubt, they were reviewed independently by implanting cardiologists. The primary endpoint was defined as first occurrence of appropriate therapy (either ATP or shock) for VT/VF episodes.

Statistical Analysis

Categorical variables are expressed as absolute numbers and percentages. Continuous variables are expressed as mean $\pm$ standard deviation or median (interquartile range) as appropriate. A normality test for each variable was carried out using D'Agostino & Pearson omnibus normality test. Univariate Cox proportional hazard modeling was used to examine the predictive value of clinical and ECG variables in association with the occurrence of appropriate therapy. Multivariate analysis was carried out using stepwise backward selection of the Cox proportional hazard model ($P < 0.1$ for entry, $P > 0.05$ for removal) to assess any independent variables correlated with the occurrence of appropriate therapy. Hazard ratio was reported with 95% CI. A P value of <0.05 was considered statistical significant for all tests. All statistical analysis was performed using SPSS 19 (IBM, New York, NY, USA).

RESULTS

There were 159 patients who received new ICD implants over the study period. Patients were excluded if they were ventricular paced (3 patients), the ECG quality was inadequate for analysis (4 patients), no ECG was recorded preimplant (1 patient) and in 1 patient where anesthetic medication was inadvertently given before the ECG was recorded. After exclusion, 150 patients remained for analysis.

Over an average follow-up of 2.15 ± 0.87 years (785 ± 318 days) with minimum follow-up of 1.1 years, appropriate therapy occurred in 47/150 (31%) patients. The Kaplan–Meier curve for the

occurrence of appropriate therapy is shown in Figure 1. The 1, 2, and 3 year cumulative appropriate therapy rates were 21.6%, 31.2%, and 38.9%, respectively. Inappropriate therapy was delivered in 12 (8%) patients, in seven patients this was delivered when the underlying rhythm was AF and in five due to other SVT. There were 13 patients (8.6%) who died during the follow-up period.

Clinical Characteristics

Demographics and clinical characteristics of all patients and patients with and without appropriate therapy are shown in Table 1. The study population was predominantly males (81%) with an average age of 59 ± 14 years. Ischemic heart disease was the underlying pathology in the majority of patients (51%), followed by nonischemic dilated cardiomyopathy (DCM) (29%), and other cardiac diseases. The mean LVEF was $36.9 \pm 17.2\%$, 53% had heart failure and 27% had history of atrial arrhythmias including atrial fibrillation and flutter. More than half of patients were implanted for secondary prevention (57%).

On univariate analysis, male gender was the only clinical characteristic significantly predictive of appropriate therapy, where male patients had a higher therapy rates than females (36.9% vs 7.1%), with males being 6.49 times as likely to receive appropriate therapy (95% CI 1.57–26.8, $P = 0.01$) than female patients.

Patients with secondary prevention tended to be more likely to receive appropriate therapy, however, this was not statistically significant

($P = 0.086$). None of the any other clinical variables were associated with appropriate device therapy.

ECG Variables

There were 17 patients in AF at the time of implantation, one patient was atrially paced and the rest of patients were in sinus rhythm. Bundle branch block was present in 67 (45%) patients with the majority being LBBB. There were 71 patients who had one or more PVC during the 60 second ECG recording. Details of ECG variables are shown in Table 2.

On univariate analysis, presence of PVC, TMD, TWR rel, and TCRT were significant ECG predictors of appropriate therapy, as shown in Table 3. In detail, patients with one or more PVCs were 1.79 times likely to receive appropriate therapy than those without PVC (95% CI 1.0–3.20, $P = 0.05$). Each decrease of 1 degree in TMD was associated with slight increase in risk (HR = 1.009, 95% CI 1.00–1.019, $P = 0.044$). Each increase of 0.01% TWR rel raised the risk of receiving appropriate therapy by 2.6% (HR 1.026, 95% CI 1.013–1.039, $P < 0.001$). Each decrease of 1 degree angle of TCRT was associated with 1% increase in risk (HR = 1.01 95% CI 1.004–1.016, $P = 0.001$).

Multivariate Model

In the multivariate model, potential risk markers that had univariate significance value of $P < 0.1$ were entered into the model as specified in the statistics section. These were as follows: male gender, secondary prevention, presence of PVC, spatial QRS-T angle, TMD, TWR rel, and TCRT. The result of multivariate analysis is shown in Table 4. It was found that male gender, PVC, TWR rel, and TCRT were the only independent predictors of appropriate therapy. Male patients were 5.01 times likely to receive appropriate therapy (95% CI 1.20–20.9, $P = 0.027$). The presence of one or more PVC indicated increased risk (HR 1.94, 95% CI 1.07–3.51, $P = 0.028$). The novel ECG measures TWR rel and TCRT were the only two other independent ECG parameters that were predictive of arrhythmic events. With every 0.01% increase in TWR rel, there was 2% increased risk of appropriate therapy (HR = 1.02, 95% CI 1.006–1.034, $P < 0.001$). For TCRT with

Figure 1. Kaplan-Meier curve for overall appropriate therapy in the study population over the follow-up period.

Table 1. Patient Demographics and Clinical Characteristics

	All (n = 150)	No Therapy (n = 103)	Therapy (n = 47)	P Value
Male	122 (81%)	77 (75%)	45 (96%)	0.01
Age	59 ± 14	58 ± 14	60 ± 15	0.34
Underlying pathology				
Ischemic heart disease	76 (51%)	49 (48%)	27 (57%)	0.35
Nonischemic DCM	43 (29%)	32 (31%)	11 (23%)	ns
HCM	4 (2%)	3 (3%)	1 (2%)	ns
ARVC	1 (1%)	0 (0%)	1 (2%)	ns
Channelopathy ^a	2 (1%)	1 (1%)	1 (2%)	ns
Idiopathic VT/VF	15 (10%)	12 (12%)	3 (6%)	ns
Other ^b	9 (6%)	6 (6%)	3 (6%)	ns
Clinical history				
Heart failure	79 (53%)	55 (53%)	24 (51%)	0.64
Hx of atrial arrhythmias	40 (27%)	29 (28%)	11 (23%)	0.70
LVEF %	36.9 ± 17.2	36.9 ± 16.6	36.7 ± 18.7	0.98
Medication				
β-blocker	132 (88%)	89 (86%)	43 (91%)	0.23
Class III antiarrhythmic	28 (19%)	18 (17%)	10 (21%)	0.34
ACEI/ARBs	113 (75%)	78 (76%)	35 (74%)	0.93
Diuretics	70 (47%)	47 (46%)	23 (22%)	0.60
Spironolactone	32 (21%)	20 (19%)	12 (26%)	0.35
Implant information				
Secondary prevention	86 (57%)	55 (53%)	31 (66%)	0.09
Single chamber	73 (49%)	48 (47%)	25 (53%)	0.34
Dual chamber	53 (35%)	37 (36%)	16 (34%)	0.80
CRT-D	25 (17%)	18 (17%)	6 (13%)	0.34

^aChannelopathy include Brugada syndrome and LQTS. ^bOther includes myocarditis, cardiac sarcoidosis, congenital heart disease, and mitral valve prolapse. Class III antiarrhythmic defined as amiodarone, sotalol, and ibutilide. ns = nonsignificant.

each 1° decrease, there was an increase in arrhythmic risk of 0.9% (HR 1.009, 95% CI 1.003–1.015, *P* = 0.003).

DISCUSSION

In this study, we examined the prognostic value of clinical variables and a range of ECG based parameters of repolarization heterogeneity in relation to arrhythmic risk in an ICD population. The variables that were found to carry independent prognostic value were male gender, presence of PVC, increased TWR rel, and reduced TCRT angle, whereas many other traditional measures such as LVEF and QT interval were not significant predictors of appropriate device therapy.

Cardiac repolarization heterogeneity has long been implicated in the development of ventricular arrhythmia. A range of different ECG

measurements derived from 12-lead ECGs have been proposed on the basis that they will reflect repolarization heterogeneity. The SVD-based repolarization descriptors proposed by Acar et al., have been examined in various populations and have shown to be associated with adverse outcome,^{6–9,23–27} however, this group of descriptors have not been previously examined in an ICD population. In addition, these measures have not been examined alongside other measures that theoretically also capture aspects of repolarization heterogeneity.

A novel finding of this study was that the relative T wave nondipolar component (TWR rel) and the wavefront measure TCRT were both independent predictor of appropriate therapy. Increased TWR rel, where each 0.01% increase was associated with 2% increased risk of appropriate therapy (HR = 1.02, 95% CI 1.006–1.034, *P* < 0.001).

Table 2. ECG Parameters in All ICD Patients, and Those with and without Therapy, Statistical Analysis Carried out by Cox Proportional Hazard Model. ECG Values are Expressed as Median (Interquartile Range) or Mean $\pm$ Standard Deviation

	All 9n = 1500	No Therapy 9n = 1030	Therapy 9n = 470	P Value
Atrial fibrillation	17 (11%)	11 (10.7%)	6 (13%)	0.60
PVC	71 (47%)	43 (42%)	28 (60%)	0.05
BBB	67 (45%)	44 (43%)	23 (49%)	0.57
LBBB	50 (33%)	36 (35%)	14 (30%)	0.32
Avg QRS (ms)	115 (102–150)	115 (102–151)	116 (102–145)	0.68
Avg QTc (ms)	451 $\pm$ 38	452 $\pm$ 39	447 $\pm$ 36	0.50
Avg TpTe (ms)	103 $\pm$ 18	104 $\pm$ 18	102 $\pm$ 17	0.51
QTd (ms)	48 (32–72)	48 (32–72)	40 (32–64)	0.18
Spatial QRS-T angle	148 (111–166)	149 (120–166)	138 (95–166)	0.06
T PCA	0.141 (0.112–0.256)	0.153 (0.113–0.248)	0.134 (0.112–0.287)	0.13
TMD (°)	70.6 (33.0–86.1)	71.3 (40.5–86.1)	57.8 (21.8–86.1)	0.04
TWR abs (mV ²)	0.0212 (0.00988–0.0512)	0.0214 (0.00895–0.0542)	0.0210 (0.0102–0.0491)	0.20
TWR rel (%)	0.0258 (0.0111–0.0647)	0.0241 (0.0116–0.0585)	0.0282 (0.0096–0.0978)	<0.001
TWLD	35 (35–36)	35 (35–36)	35 (35–36)	0.24
TCRT (°)	153 (109–166)	154 (130–167)	131 (59–166)	0.001

Table 3. Significant Univariate Clinical and ECG Predictors in Relation to Appropriate Therapy

	Hazard Ratio (95% CI)	P Value
Male	6.49 (1.57–26.8)	0.01
PVC	1.79 (1.00–3.20)	0.05
TWR rel (per 0.01% increase)	1.026 (1.013–1.039)	<0.001
TMD° (per 1 degree decrease)	1.009 (1.00–1.019)	0.044
TCRT° (per 1 degree decrease)	1.01 (1.004–1.016)	0.001

TWR rel is theoretically a measure of regional repolarization heterogeneity. Its calculation is based on mathematical elaboration of the ECG signal, using SVD as described in the methods section. The concept is to extract information from eight of the 12 ECG leads, and present them as eight components in descending order of containing the most important to least important energy. The first three components contain the most energy representing the dipolar components of the T wave vector in 3D space, which tracks

Table 4. Statistically Significant Independent Predictors of Appropriate Therapy Using Multivariate Cox Regression Model

	Hazard Ratio (95% CI)	P Value
Male	5.01 (1.20–20.91)	0.027
PVC	1.94 (1.07–3.51)	0.028
TWR rel (per 0.01% increase)	1.02 (1.006–1.034)	0.005
TCRT° (per 1 degree decrease)	1.009 (1.003–1.015)	0.003

the global voltage change during the repolarization phase contributed by synchronous signals from different regions of the myocardium. The remaining components are signals that cannot be represented by the 3D dipole, and are called the nondipolar component, and it has been argued that these correspond to discrepancy and asynchrony between different myocardial regions.²⁸ Thus increased TWR rel represents increased regional repolarization heterogeneity. A simulation study has shown that the nondipolar component of T wave is increased with increased

repolarization heterogeneity.²⁹ It is recognized that TWR can also be influenced by signal noise, and better understanding of the true electrophysiological meaning of such repolarization measures are needed before their clinical use.

Absolute T wave nondipolar component (TWR abs) on the other hand was not a significant predictor in our study, which suggested that it was the increase in relative proportion of the nondipolar component adjusted for the overall global T wave energy (TWR rel = TWR abs/overall energy) that contained predictive value. Previous study that has examined these parameters in a cohort of patients with cardiovascular disease found both absolute and relative TWR to be independent predictors of total mortality.⁸ As previously discussed it is proposed that TWR rel is measure of regional repolarization heterogeneity. As such, the independent association of TWR rel with appropriate therapy in this study is consistent with the view that repolarization heterogeneity is important in arrhythmogenesis.

Reduced TCRT was also found to be an independent predictor of appropriate therapy in this study, where each 1 degree reduction in TCRT was associated with 0.9% increase in risk (95% CI 1.003–1.015, $P = 0.003$). TCRT was the wavefront direction descriptor that measures the angle between the QRS and T loop in the three-dimensional space spanned by the first 3 principal components. This is similar to the measure of spatial QRS-T angle. Spatial QRS-T angle is based on vectorcardiography and the X, Y, Z axes represent true spatial orientation. The first three components of SVD represent the first major independent components of the ECG and while these can be presented in a 3D space, this space does not represent true geometrical meaning. In this study, there was a strong correlation between QRS-T angle and TCRT ($r = 0.797$, $P < 0.001$).

In the literature, increased QRS-T angle and TCRT angle have been associated with adverse outcome including mortality and arrhythmic risk,^{7–9,15,16} and increased spatial angle was believed to reflect repolarization heterogeneity. In this study, however, decreased instead of increased TCRT angle was associated with appropriate therapy. This discrepancy may be influenced by the composition of the study population. In the literature, abnormal QRS-T angle was defined between >90 – 135° , and studies of ICD patients of primary prevention or the general population have shown

abnormal QRS-T angle to be associated with adverse outcome.^{16,30} There was less literature data on TCRT angles. Acar et al. reported the average value in a group of normal subjects being 58° . In other studies that examined TCRT in groups of post-MI patients or males with cardiovascular disease, the mean TCRT values were 96 to 110° , and increased TCRT angle was associated with adverse clinical outcome.^{7,8} In our study, both QRS-T and TCRT angles were significantly larger than those previously reported in the literature suggesting our study population differs from those previously studied. Given these conflicting findings relating to the TCRT angle further study is required to clarify its role.

In this study, the presence of one or more PVC over the 60 second ECG recording was found in 46% of patients and was independently predictive of arrhythmic events where it was associated with a hazard ratio of 1.94 (95% CI 1.07–3.51, $P = 0.028$). The presence of ventricular arrhythmia in the form of PVCs or NSVT on Holter recordings have long been recognized as a risk factor for adverse outcome. MADIT-I and MUSTT used NSVT as inclusion criteria.³¹ Frequent PVCs over 10 min ($>3/10$ min) were associated with increased risk of appropriate ICD therapy in MADIT-II patients over mean follow-up of 20 months.³² Mechanistically, PVCs have been found to be responsible for the initiation of majority of VT and VF episodes in ischemic patients and initiation of VT in nonischemic patients,^{33–35} therefore, it is not unexpected that they carry prognostic values. The best method to quantify PVCs with the greatest predictive value remains unknown. Longer ECG recordings such as Holter monitoring may provide better prognostic value than shorter recordings, as they can quantify PVC burden in terms of number per hour as well as catchment of NSVT. However, it appeared that PVC occurrence over shorter recordings may be a simple way of reflecting high ectopic burden, and acts as a tool to prompt more investigations or a risk factor to be incorporated into a composite risk model for ventricular arrhythmia.

In addition to the ECG variables, gender was the only independent clinical predictor of appropriate therapy, where males were 5.01 (95% CI 1.20–20.91, $P = 0.027$) times likely to receive appropriate therapy. There has been ongoing controversy about the use of ICDs in females. A number of studies have shown women to have

lower therapy rate, and either similar or lower rate of all-cause mortality.^{36–39} Women appeared not to derive the same mortality benefit from primary prevention ICDs as males in two different meta-analyses.^{39,40} However, another study did not conclude such a finding.⁴¹ The reason for the apparent lack of benefit of ICDs in females is uncertain. Studies have suggested women tended to have lower arrhythmic risk but similar all-cause mortality possibly due to difference in myocardial remodeling in response to different insults.⁴² The gender issue is controversial, however, it may be that combination with additional risk markers can give us a better picture to risk assess female patients.

LIMITATIONS

The relatively small sample size and heterogeneity of the study population constrained our ability to detect risk markers due to a lack of statistical power. Despite this, three ECG-derived parameters were found useful in a multivariate model of risk. The patient population for this study is heterogeneous in etiology. All ICD implants were included with no exclusion criteria. While the majority of the patient group consists of IHD and DCM, other pathologies such as HCM, ARVC, channelopathy, and idiopathic VT/VF can potentially have different drivers of arrhythmic risk. Further investigations with larger sample size and more homogeneous populations such as primary prevention only, and single etiology are warranted to confirm and validate the use of ECG parameters as potential risk stratifiers. TWR rel is a repolarization measure derived from SVD, and to be noted that it contains information on repolarization heterogeneity as well as can be influenced by signal noise. We would assume that signal noise would be random across the patient group, and thus would not have introduced a significant bias within the study. However, further studies are needed to clarify the true electrophysiological meaning of such ECG based repolarization measures.

CONCLUSIONS

Novel ECG repolarization measures (TWR rel, TCRT), presence of PVC and male gender were identified to be independent risk predictors of arrhythmic events in a group of ICD patients. Our findings suggested that the use of advanced

analytic ECG techniques might provide additional risk stratification beyond the use of LVEF and other clinical variables. Further investigations are required to confirm and validate our findings in larger cohort with more homogenous population. It is likely that a combined approach to risk stratification for ventricular arrhythmia including multiple risk factors would be a better approach to enable use to predict these events in a more robust way in the future.

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