ORIGINAL ARTICLE

ECG Risk Score Model to Predict SCD in HFrEF: Retrospective Review in a Tertiary Centre

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ABSTRACT

INTRODUCTION: Heart failure with reduced ejection fraction (HFrEF) patients need to be risk stratify as guidelines have shown that patients with left ventricular ejection fraction (LVEF) <35% could be prevented from sudden cardiac death (SCD) by insertion of prophylactic implantable cardioverter-defibrillator (ICD). Thus we conducted a retrospective single tertiary centre study to evaluate the used of electrocardiogram (ECG) risk score model in identifying the individuals who at higher risk of SCD. **MATERIALS AND METHODS:** A total of 356 heart failure with reduced ejection fraction (HFrEF) patients treated at University Malaya Medical Centre between January 2017 and December 2021 were enrolled into this study. The patients' demographics, types of heart failure, medications, and ECG parameters data were collected. The study outcomes were survivor or death in and the cause of death were subdivided into SCD or non-sudden cardiac death (non-SCD). **RESULTS:** A total of 156 study patients were survivor whereas another 120 had SCD and 70 had non-SCD. There were six ECG parameters that remained significant in the final model, namely the bundle branch block (BBB), abnormal P waves, QRS duration, QTc duration, TpTe interval and PR interval. The significant ECG parameters were combined into a risk score to enumerate prediction ability towards SCD. From our ECG risk score model, subject with ≥2 ECG abnormalities had more than 3-fold increased risk for SCD (HR 3.739, 95% CI 1.703-8.211, P 0.001) and the risk proportionately increased with increasing ECG abnormalities. **CONCLUSION:** Our findings suggested that the cumulative ECG risk score model was independently associated with SCD and particularly effective for LVEF <40% where risk stratification model remained scarce. So, we would like to propose for a prospective study to further evaluate our study outcome.

Keywords
Sudden Cardiac Death, Heart Failure, Electrocardiogram, Arrhythmia, Implantable Cardiac Device

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INTRODUCTION

Cardiovascular diseases (CVD) contributed approximately 17 millions of deaths per year in the world, of which 25% were sudden cardiac death (SCD).[1] Patients with heart failure (HF) have higher rate of SCD compared to the general population as they experience number of changes in the electrical function of the heart that predispose to potentially lethal cardiac arrhythmias. Studies have shown that most patients with left ventricular ejection fraction (LVEF) <35% could benefit from prophylactic implantable cardioverter-defibrillator (ICD) insertion. However, the local data shown that prevalence of SCD in heart failure with reduced ejection fraction (HFrEF) patients were as high as 42% which may be explained by the underutilization of implantable cardioverter-defibrillator (ICD) insertion.

Framingham study shown that incidence of SCD were 62% in men aged 45-54 years and 58% and 42% for men aged 55-64 years and 65-74 years respectively.[2] Incidence of SCD was lower in women than men mainly because they are protected against coronary artery disease (CAD) during premenopausal period. Study by Di Zhao *et al*, shown that Whites had a lower risk for SCD than Blacks.[3]

A study of sudden natural deaths in 545 medico legal autopsies cases conducted over 5-years period in

University Malaya Medical Centre (UMMC), Kuala Lumpur shown that a SCD accounted for 65% of all sudden natural death.[4] A study on SCD revealed that the most prevalence aged for SCD in Malaysian population were 41 to 50 years of age.[5]

Study shown that 90% who succumbed from SCD had warning signs such as shortness of breath, giddiness, chest pain and syncope prior to the event. Most of the deceased sustained previous medical illness including coronary artery disease, valvular heart disease, cardiomyopathies, congenital heart disease or been taking drugs that are capable of provoking ventricular tachyarrhythmias.

Despite advancement in heart failure treatment for the past decade, various studies have shown high rt mortality rates in these patients. An observational study conducted among acute heart failure patients treated in Sungai Buluh Hospital shown an exceptionally high 1-year mortality rate (49.7%).[6] Another local study in Sarawak General Hospital reported all-cause mortality of 16.8% at 90 days.[7]

An implantable cardioverter-defibrillator (ICD) is remarkably effective in prevention of sudden cardiac arrhythmia. The advent of the ICD has revolutionized prevention of SCD in high-risk patients with underlying cardiac diseases. However, several challenges remain. Identification of patients at risk who should receive an ICD is suboptimal, and the sole criterion applied in clinical practice is a severely reduced left ventricular ejection fraction (LVEF) despite the fact that SCD occurs mostly in patients with preserved or mildly reduced ejection fraction.

In Malaysia, primary prevention for ICD insertion in HFrEF is limited by cost and resources. This amplify an urgent need to develop an assessment tool to further risk stratify our patients that will benefit the most from ICD.

MATERIALS AND METHODS

Heart Failure (HF) Registry

The primary study population were heart failure patients registered under University Malaya Medical Centre (UMMC) Heart Failure Registry (HF Registry). Our study enrolled a total of 356 patients of heart failure with reduced ejection fraction (HFrEF) treated in UMMC between January 2017 and December 2021. HF patients who were on cardiac resynchronisation therapy, ICD and pacemaker were excluded from this study.

During the study, we had collected information related to demographics, types of heart failure, medications, and electrocardiogram (ECG) parameters. We had divided the study outcomes into survivor or death, whereby the mortality was further subdivided into sudden cardiac death (SCD) or non-sudden cardiac death.

For patients who were lost to follow up during the study period, the patients and/or their family members were contacted for further information. Patients' cause of death was traced from National Registration Department (NRD).

The criteria used for SCD as the cause of death were as below.

1) In-hospital: within 1 hour of symptoms (chest pain or shortness of breath) onset
2) Outside hospital: within 24 hours of symptoms (chest pain or shortness of breath) onset

Electrocardiographic (ECG) Measurement

The patients' latest resting ECG with a paper speed of 50mm/s were analysed for the presence of:

1) Heart rate >75 beats per minute
2) Bundle branch block (BBB): left bundle branch block or right bundle branch block
3) QRS duration >120 milliseconds (ms)
4) PR interval: short PR <120ms or prolonged PR >220ms

5) Abnormal P waves morphology: atrial fibrillation, atrial flutter, retrograde P wave
6) QTC interval: QTc >450ms
7) T-peak to T-end interval, TpTe >90ms
8) Left ventricular hypertrophy (LVH)

Follow-up

The follow-up duration was limited to 5 years, to clarify the role of ECG in assessing risk of sudden cardiac death since the cardiovascular profile could ultimately change on longer follow-up period.

The primary endpoint was to identify ECG parameters that predict SCD whereas the secondary endpoint was to identify ECG parameters that predict non-SCD.

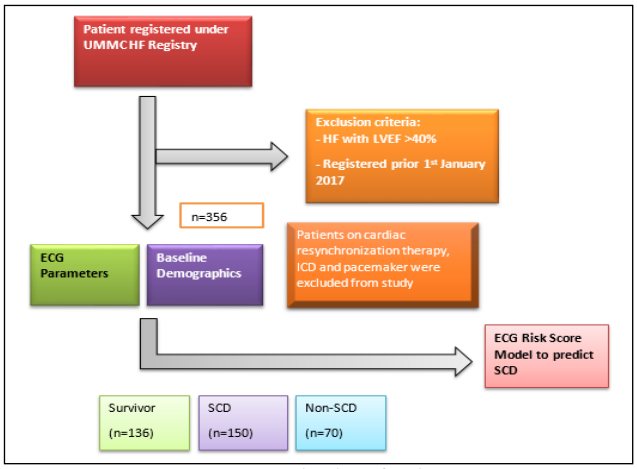

Figure 1. Flowchart of Study

Statistical Analysis

Initially one-way ANOVA and Pearson's Chi Square tests were used for bivariate case-control comparisons of continuous and categorical variables respectively. Secondly, a multivariate cox regression analysis was used to determine the independent predictors of sudden cardiac death and non-sudden cardiac death and the Crude Hazard Ratio (HR) with 95% confidence interval (95% CI) was obtained. Thirdly, the level of significance chosen was 2-tailed and considered at $P \leq 0.05$. Then, the significant ECG parameters and constructed an ECG risk score were identified. Next, the data were re-analysed with cox regression model to confirm the significance of newly postulated score. Finally, Kaplan-Meier survival analysis were used to compare the survival subjects with different ECG risk score. All statistical calculations were performed using SPSS version 26. For all analyses, value of $P \leq 0.05$ were considered statistically significant.

RESULTS

Baseline Characteristics

A total of 356 heart failure patients were included in this study. The enrolled patients were stratified into survivor (n=136), SCD (n=150) and non-SCD (n=70). The demographics and clinical characteristics of enrolled patients were summarized in Table I.

Our data shown no difference in age and race between cases. The survivor group (control) had a mean follow-up of 2.88±1.22 years whereas death cases had lower follow-up duration due to early mortality (SCD 1.83± 1.12 years vs non-SCD 1.74±1.11 years, P<0.001). SCD patients were predominantly male (P=0.028) and exhibited ischemic type of heart failure (P=0.017). Among patients with death end-point, smoking history was observed more in SCD group (P=0.004), while dyslipidaemia and chronic coronary syndrome were prevalent in non-SCD group (P=0.010 and P=0.017, respectively). Heart failure medications such as angiotensin receptor neprilysin inhibitor (ARNI), angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB), beta blocker, sodium/glucose-cotransporter-inhibitor (SGLT2i) and mineralocorticoid receptor antagonist (MRA) were extensively used among survivor groups compared to SCD and non-SCD (P<0.001).

There were eight ECG parameters assessed across the group. An abnormal P wave morphology, bundle branch block, LVH pattern, short PR interval, long QTc and long TpTe, were all significantly prevalent in SCD group compared to control (P ranging 0<0.001 to 0.005). A similar pattern seen in non-SCD group (P ranging <0.001 to 0.002) except that PR interval and long QTc were not significantly different. The heart rate and QRS duration were similar across all three groups.

Table I: Baseline characteristics of heart failure patients according to survival outcomes

Demographics	Survivor n = 136	SCD n = 150	Non-SCD n = 70	P-value
Age (years)	62 ± 13	62 ± 11	65 ± 12	0.170
Follow up (years)	2.88 ± 1.22	1.83 ± 1.12	1.74 ± 1.11	<0.001
Races:				
Malay	69 (50.0)	73 (48.7)	39 (55.7)	0.192
Indian	40 (29.4)	53 (35.3)	14 (20.0)	
Chinese	28 (20.6)	24 (16.0)	17 (24.3)	
Gender:				
Male	94 (69.1)	122(82.0)	56(80.0)	0.028
Female	42 (30.9)	27 (18.0)	14 (20.0)	
LV Ejection Fraction (LVEF)	27.3 ± 7.6	27.0 ± 7.9	28.2 ± 7.3	0.538
HF Aetiology:				
Ischemic	99 (72.8)	104 (69.3)	61 (87.1)	0.017
Non-ischemic	37 (27.2)	46 (30.7)	9 (12.9)	
Risk factors:				
Smoking status	47 (34.6)	37 (24.7)	13 (18.6)	0.033
Hypertension	98 (72.1)	122 (81.3)	49 (70.0)	0.092
Diabetes Mellitus	92 (67.6)	103 (68.7)	57 (81.4)	0.090
Dyslipidaemia	113 (83.1)	125 (83.3)	67 (95.7)	0.028
History of CAD	102 (75.0)	101 (67.3)	58 (82.9)	0.045
Revascularization	86 (63.2)	81 (54.0)	45 (64.3)	0.189
LDL	2.19 ± 1.08	2.53 ± 1.31	2.17 ± 1.17	0.029
Medications:				
ARNI	57 (41.9)	34 (23.4)	4 (5.7)	<0.001
ACE-I / ARB	55 (40.4)	51 (34.0)	33 (47.1)	0.162
B-Blocker	125 (91.9)	103 (68.7)	40 (57.1)	<0.001
SGLT2i	95 (69.9)	52 (34.7)	3 (4.3)	< 0.001
MRA	97 (71.3)	66 (44.0)	16 (22.9)	<0.001
ECG Variables:				
Heart Rate > 75bpm	99 (72.8)	102 (68.0)	45 (64.3)	0.520
Abnormal P morphology	8 (5.9)	19 (12.7)	14 (20.0)	0.009
Bundle Branch Block	23 (16.9)	54 (36.0)	30 (42.9)	<0.001
LVH Pattern	38 (27.9)	68 (45.3)	39 (55.7)	<0.001
PR Interval (ms)	164.79 ±	148.06 ±	147.77 ±	0.030
- PR < 120ms	51.28	58.55	68.61	0.011
- PR > 220ms#	13 (10.2)	30 (23.6)	7 (12.5)	0.793
	1 (0.8)	2 (1.6)	1 (1.8)	
QRS duration (ms)	107.40 ±	111.36 ±	113.33 ±	0.179
- QRS > 120ms	21.66	25.20	24.61	0.058
	38 (27.9)	58 (38.7)	30 (42.9)	
QTc duration (ms)	464.74 ±	482.55 ±	484.57 ±	0.001
- QTc > 450ms*	44.22	44.76	49.32	0.004
	89 (65.4)	124 (82.7)	52 (74.3)	
TpTe Interval (ms)	76.91 ±	95.80 ±	89.86 ±	<0.001
- TpTe > 90ms	17.44	18.51	14.39	<0.001
	28 (20.6)	87 (58.0)	31 (44.3)	

The Prognostic Significance of Clinical and ECG Parameters in SCD: Primary Outcome

Cox regression model was created to determine association of clinical and EGG parameters that predict SCD. By using the univariate analysis, male gender, HF medications (beta blocker, SGLT2i, MRA) alongside with all ECG parameters were found to have association with SCD. In a multivariable analysis, all significant parameters from individual analysis were included in clinical and ECG models separately. For clinical parameters, beta blocker (HR 0.58; 95% CI 0.40-0.84; P=0.04), SGLT2i (HR 0.44; 95% CI 0.31-0.62; P<0.001) was associated with reduced risk of SCD. However, other clinical risk factors were not associated with SCD.

For ECG parameters, there were six variables which remained significantly associated with SCD, namely abnormal P morphology (HR 1.69; 95% CI 1.03-2.78; P=0.039), bundle branch block (HR 2.18; 95% CI 1.53-3.10; P<0.001), QRS duration (HR 1.01; 95% CI 1.003-1.02; P=0.018), QTc interval (HR 1.007; 95% CI 1.004-1.01; P<0.001), TpTe interval (HR 1.03; 95% CI 1.02-1.03; P<0.001) and PR interval (HR 0.995; 95% CI 0.993-0.998; P<0.001). The latter exhibited bidirectional increase risk of SCD, explaining paradoxical effect of risk reduction when analysing continuous variable of PR interval. All continuous ECG parameters were subcategorized into PR interval <120m (HR 1.87; 95% CI 1.23-2.86; P 0.004), PR interval >220ms (HR 7.27; 95% 1.67-31.62; P 0.008), QRS >120ms (HR 1.84; 95% CI 1.26 -2.77; P=0.002), QTc >450ms (>460ms for female) (HR 2.04; 95% CO 1.18-3.55; P=0.005), TpTe >90ms (HR 2.27; 95% CI 1.51-3.41; P<0.001; which all demonstrated association of increased SCD. Further details were summarized in Table II.

The Prognostic Significance of Clinical and ECG Parameters in Non-SCD: Secondary Outcome

The multivariable model of clinical characteristic was not significant in predicting non-SCD except for ARNI (HR 0.25, 95% CI 0.091-0.71; P=0.009) and SGLT2i (HR 0.057; CI 0.017-0.19; P<0.001) which both reduced risk of non-SCD. The multivariable cox of ECG parameters demonstrated bundle branch block (HR 2.89; 95% CI 1.64-5.086; P<0.001), LVH pattern (HR 2.54; 95% CI 1.48-4.35; P=0.001), QRS duration (HR 1.01; 95% CI 1.002-1.023; P=0.023) along with QRS > 120ms (HR 1.86; 95% CI 1.056-3.26; P=0.032), TpTe interval (HR 1.02; 95% CI; P=0.002-1.014P=0.007) particularly TpTe > 90ms (P=0.004) predicted higher risk of SCD. As opposed to SCD group, abnormal P morphology, PR interval and QTc interval were not associated with non-SCD occurrence, whereas the LVH pattern was distinctive predictor for non-SCD. The result details were summarized in Table III.

ECG Risk Score for SCD Prediction

All significant ECG parameters for SCD derived from Cox Proportional Hazard multivariable model were combined to enumerate SCD prediction ability based on cumulative ECG parameters. ECG risk score which

Table II: Univariable and Multivariable Predictors of Sudden Cardiac Death (SCD) in Cox Proportional Hazards Model

Variables	Univariable		Multivariable	
	Hazard ratio (95% CI)	**P-value**	**Hazard ratio (95% CI)**	**P-Value**
Clinical Variables				
Age	1.002 (0.989-1.102)	0.773		
Male	1.580 (1.040-2.401)	0.032	1.380 (0.906-2.103)	0.134
LVEF	0.991 (0.971-1.012)	0.093		
Ischaemic HF	0.840 (0.594-1.189)	0.326		
Smoking status	0.727 (0.502-1.054)	0.093		
Hypertension	1.378 (0.913-2.079)	1.378		
Diabetes Mellitus	0.877 (0.620-1.240)	0.456		
Dyslipidaemia	0.893 (0.581-1.372)	0.604		
History of CAD	0.729 0.518-1.026)	0.069		
Revascularization	0.781 (0.567-1.077)	0.132		
LDL	1.108 (0.974-1.261)	0.118		
ARNI	0.692 (0.474-1.011)	0.057		
ACE-I / ARB	0.724 (0.516-1.017)	0.063		
B-Blocker	0.513 (0.363-0.725)	<0.001	0.577 (0.398-0.837)	0.004
SGLT2i	0.405 (0.289-0.568)	<0.001	0.437 (0.309-0.620)	<0.001
MRA	0.519 (0.376-0.717)	<0.001	0.730 (0.513-1.039)	0.080
ECG Variables				
Heart Rate > 75bpm	0.677 (0.479-0.957)	0.027	0.929 (0.691-1.511)	0.913
Abnormal P morphology	2.008 (1.238-3.256)	0.005	1.690 (1.026-2.782)	0.039
Bundle Branch Block	2.490 (1.770-3.504)	<0.001	2.177 (1.531-3.096)	<0.001
LVH Pattern	1.809 (1.308-2.502)	<0.001	1.152 (0.815-1.628)	0.422
PR Interval (1-SD increase)	0.995 (0.993-0.998)	<0.001	0.997 (0.995-0.999)	0.017
PR Interval < 120ms	1.813 (1.203-2.734)	0.004	1.871 (1.225-2.856)	0.004
PR Interval > 220ms	4.273 (1.045-17.468)	0.043	7.272 (1.673-31.618)	0.008
QRS duration (1SD increase)	1.008 (1.001-1.016)	0.018	1.010 (1.003-1.017)	0.007
QRS > 120ms	1.616 (1.161-2.249)	0.004	1.837 (1.261-2.676)	0.002
QTc Interval (1-SD increase)	1.007 (1.004-1.010)	<0.001	1.005 (1.001-1.009)	0.011
QTc > 450ms*	2.057 (1.346-3.145)	0.001	2.044 (1.178-3.548)	0.005
TpTe Interval (1-SD increase)	1.025 (1.018-1.033)	<0.001	1.023 (1.015-1.031)	<0.001
TpTe > 90ms	2.429 (1.756-3.362)	<0.001	2.271 (1.512-3.410)	<0.001

Table III: Univariable and Multivariable Predictors of Non-Sudden Cardiac Death (Non-SCD) in Cox Proportional Hazards Model

Variables	Univariable		Multivariable	
	Hazard ratio (95% CI)	**P-value**	**Hazard ratio (95% CI)**	**P-Value**
Clinical Variables				
Age	1.014 (0.995-1.034)	0.145		
Male	1.520 (0.845-2.733)	0.162		
LVEF	1.011 (0.979-1.044)	0.518		
Ischaemic HF	1.896 (0.941-3.819)	0.073		
Smoking status	0.534 (0.292-0.976)	0.042	0.614 (0.330-1.140)	0.122
Hypertension	1.011 (0.605-1.688)	0.968		
Diabetes Mellitus	1.578 (0.863-2.887)	0.139		
Dyslipidaemia	3.043 (0.957-9.678)	0.059		
History of CAD	1.312 (0.704-2.443)	0.392		
Revascularization	1.046 (0.641-1.706)	0.857		
LDL	1.014 (0.814-1.263)	0.901		
ARNI	0.137 (0.050-0.375)	<0.001	0.253 (0.091-0.707)	0.009
ACE-I / ARB	1.173 (0.733-1.876)	0.507		
B-Blocker	0.305 (0.190-0.490)	<0.001	0.927 (0.534-1.611)	0.789
SGLT2i	0.035 (0.011-0.112)	<0.001	0.057 (0.017-0.187)	<0.001
MRA	0.203 (0.116-0.356)	<0.001	0.574 (0.301-1.092)	0.091
ECG Variables				
Heart Rate > 75bpm	0.729 (0.446-1.191)	0.207	0.696 (0.393-1.231)	0.213
Abnormal P morphology	2.830 (1.567-5.111)	0.001	1.293 (0.622-2.688)	0.492
Bundle Branch Block	3.865 (2.383-6.269)	<0.001	2.889 (1.637-5.086)	<0.001
LVH Pattern	2.770 (1.722-4.457)	<0.001	2.537 (1.480-4.349)	0.001
PR Interval (1-SD increase)	0.994 (0.991-0.998)	<0.001	0.999 (0.994-1.003)	0.500
PR Interval < 120ms	1.482 (0.334-1.482)	0.334	1.237 (0.550-2.784)	0.607
PR Interval > 220ms	4.168 (0.568-30.60)	0.160	4.405 (0.590-32.899)	0.148
QRS duration (1-SD increase)	1.014 (1.004-1.025)	0.007	1.012 (1.002-1.023)	0.023
QRS > 120ms	2.048 (1.273-3.294)	0.003	1.857 (1.056-3.263)	0.032
QTc duration (1-SD increase)	1.011 (1.005-1.016)	<0.001	1.008 (1.002-1.014)	0.013
QTc > 450ms*	1.613 (0.942-2.762)	0.082		
TpTe Interval (1-SD increase)	1.031 (1.019-1.044)	<0.001	1.024 (1.010-1.038)	0.007
TpTe > 90ms	2.641 (1.643-4.246)	<0.001	2.000 (1.118-3.579)	0.020

represented number of abnormal ECG parameters was used to demonstrate this effect and was independent of HR magnitude of individual parameters. Table IV provided HR and 95% CI for SCD according to ECG risk score. Our findings demonstrated that every additional ECG abnormalities were associated with increasing risk for SCD, and patients with ECG score ≥4 exhibited moderate risk of developing SCD (HR 5.99; 95% CI 2.65-13.59; P<0.001).

Kaplan-Meier Survival Plot for SCD According to ECG Score

Survival analysis using Kaplan Meier (Figure 1) was performed to investigate event-free survival following ECG abnormalities. The association between ECG risk score and SCD shown sustained effect throughout follow-up duration up until 5 years (mean survival 3.3 ± 0.14 years for SCD; 4.1 ± 0.2 years for non-SCD). Post hoc analysis using pairwise comparison demonstrated

a significant difference in SCD event-free between the two groups; no ECG abnormalities group and group with two or more ECG abnormalities (P<0.001).

Table IV: Risk of SCD Associated with ECG Risk Score Among Patients with HFrEF

ECG risk score	Survivor	Sudden Cardiac Death		
	N (%)	N (%)	HR (95% CI)	P-value
0	19 (14.0)	7 (4.7)	Ref	
1	68 (50.0)	19 (12.7)	0.842 (0.353-2.005)	0.697
2	25 (18.4)	59 (39.3)	3.739 (1.703-8.211)	0.001
3	14 (10.3)	30 (20.0)	4.070 (1.782-9.297)	0.001
≥4	10 (7.4)	35 (23.3)	5.994 (2.645-13.586)	<0.001

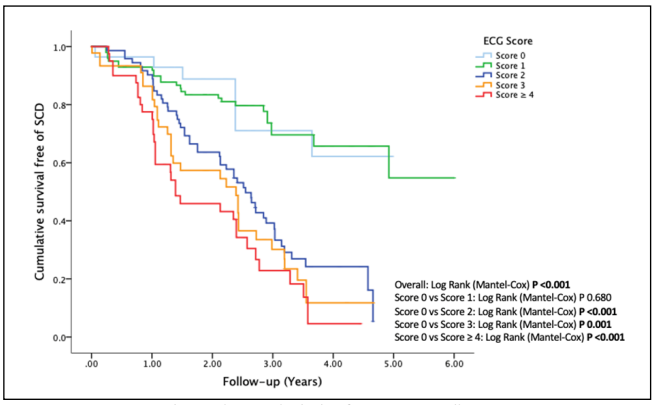

Figure 2. Kaplan-Meier Survival Plot for SCD according to ECG Score

DISCUSSION

Although our study was a retrospective single tertiary centre research involving a total of 356 HFrEF patients, we had managed to collect the risk variables that may predict SCD in HFrEF. The collected variables were the demographics, drug therapy and ECG parameters which were analysed revealed various important findings. Firstly, we managed to identify parameters that can estimate risk of SCD. Secondly, we manage to curate an ECG risk score model to predict risk of SCD.

Our study demonstrated that ischemic HFrEF have lowest association with SCD as compared to survivor and non-SCD group. An existing study of 3078 patients from Denmark showed that ischemic HFrEF predicts poorer prognosis.[8] Another study from China enrolled 873 patients which further divided into ischemic and non-ischemic HFrEF shown that HFrEF was associated with higher SCD and all-cause mortality.[9] Ischemic cardiomyopathy is the result of disturbance in between myocardial contractility and perfusion.

A permanent damage to myocardium following myocardial infarction will lead to gradual remodelling process and eventually myocardial fibrosis. In this situation, a revascularization therapy would not be beneficial as the tissues were no longer viable. As a result, the myocardial scarring may cause ventricular arrhythmia and sudden cardiac death. However, certain studies have found contrary result.

A study conducted in Portugal in 2011 enrolling a total of 286 heart failure patients with ischemic and non-ischemic aetiology shown that ischemic heart failure was not a predictor of mortality and the differences appears to fade along time.[10] The findings which contradicted previous studies indirectly highlighted that genetic variance and ethnicity could be a strong influencing factor for HF patients in different regions especially in multi-racial country such as Malaysia.

Our study also showed that male gender has higher association with sudden cardiac death. A previous study in Ireland which shown that incidence of SCD in male was 4.36 in 100,000 person-years which is higher than female which was 1.3 in 100,000 person-years.[11] Possible explanations for this result is the presence of coronary artery disease. Coronary artery disease is the commonest cause of SCD, contributing up to 80% of SCD. Male tend to be smoker and underwent more stress resulting in acceleration of cardiovascular risk such as diabetes mellitus, hypertension and dyslipidaemia, leading to the development of coronary artery disease which indirectly leading to SCD.

Our study revealed that several ECG parameters were proven to be significant in predicting SCD with bundle branch block proven to be one of the independent predictors. Our study included both right bundle branch (RBBB) and left bundle branch block (LBBB) in the analysis. A study conducted in Spain revealed that eight patients from different centres who contracted multiple aborted SCD shared similar ECG parameters. The patients had normal QTc interval but RBBB was persistent in all cases.[12] Another multi-centre study from seven countries (Denmark, Ireland, Finland, Germany, Norway, Sweden, and the United Kingdom), demonstrated that LBBB and RBBB which developed during follow-up was significantly associated with SCD.[13]

However, the mechanism of conduction problem leading to malignant arrhythmia remained speculative at present.

PR interval is another parameter that was shown to predict SCD in HFrEF patients. Our study divided PR interval into short PR <120ms and prolonged PR >220ms in which both were statistically significant to increase risk of developing SCD in our study population. However, the evidence for direct correlation between PR interval and SCD prediction is still lacking. A previous study conducted in Finland in 2014 revealed that prolonged PR interval was not associated with all-cause cardiovascular death.[14] However based on various studies, a wide QRS complex >120ms was widely approved as a risk of SCD. Another prospective study conducted in Finland in 2012 involving 2049 men aged 42 to 60 years were followed up for 19 years revealed 156 SCD among the enrolled patients. The study also demonstrated that the QRS duration was associated with 27% higher risk of developing SCD.[15] The potential mechanisms involved would be a delayed electrical conduction due to left ventricular dysfunction that lead to malignant arrhythmia.

Prolonged QTc had a long debate since a decade ago regarding its association with SCD. A study conducted in Netherland in 2006 enrolled 3,105 men and 4,878 women aged more than 55 years old. The study revealed that QTc >450ms in men and QTc >470ms in women was significantly associated with 3-fold increase in SCD risk.[16] Another study conducted in 2015, recruited a total of 195 clinical hypertrophic cardiomyopathy patients showed that QTC >460ms was associated with ventricular tachyarrhythmia or SCD.[17] However, in another study involving 254 initial ECGs of hypertrophic cardiomyopathy patients revealed no significant difference in QTc interval and SCD.[18]

Another ECG parameter related to SCD is the TpTe interval. Recently, studies are blooming gradually from various centre to prove that TpTe is a universal predictor of SCD. Mechanism leading to SCD is related to delay in repolarization phase from epi-myocardium to endo-myocardium which opens a probability of arrhythmia pre-excitation. Oregon Sudden Unexpected Death study conducted in Portland evaluated TpTe interval and other ECG parameters showed that TpTe interval is an independent predictor of SCD.[19]

Current guidelines, recommended that implantable cardioverter defibrillator (ICD) insertion in HFrEF should primarily be based on LVEF and NYHA classification. If this recommendation is to be applied in our local setting, a large number of HFrEF population would indirectly eligible for the ICD, Thus, the condition would give an impact to healthcare system expenses. MADIT-I trial showed ICD saves lives in high-risk patients with coronary heart disease whereas MADIT-II trial showed that prophylactic ICD therapy was associated with significantly improved survival in patients with ischemic cardiomyopathy. The study population in these trials was primarily confined to United States and Europe and the conventional treatment in non-ICD group was not optimal whereas the ICD group has better overall condition. Thus, there was significant difference between both groups.[20]

To date, evidence of such studies in Asian HFrEF population remains scarce and this open a wide realm for future study. To the best of our knowledge, this is the first study in Malaysia describing prevalence, demographics, and risk predictor model of SCD in HFrEF. From our ECG risk score model, subjects with ≥2 ECG abnormalities had more than 3-fold increased risk for SCD and the risk proportionately increased with an increased in ECG abnormalities. However, the predictive value remained relatively low, despite its significant. Thus, a larger sample size and a multi-center involvement is recommended to further strengthen the result. By application of this score, we managed to filter and prioritize our patient for ICD insertion, and in a long term it will be able to help in reducing healthcare expenses. Parameters listed in our risk score are relatively easily obtained from standard 12-lead ECG, making this risk score relevant for clinical use.

LIMITATIONS

Firstly, the optimization of medications in SCD group was very low, this may be the confounding factor for the

outcome. Secondly, both SCD and no SCD death group have very low intention to treat medications which may lead to selection bias. These two factors could be explained by poor insight and lack of awareness among our patients which need to be overcome in near future. Although including atrial fibrillation in abnormal P waves parameter may lead to significant confounding factors that affect mortality and morbidity rate, we would like to emphasize that our patients' selection processes were random. As the symptoms preceding the SCD occurred in patients outside hospital were clarified from the family or eye witness, this could potentially lead to overestimation of SCD as well.

CONCLUSION

This cumulative ECG risk score model was independently associated with SCD and particularly effective for LVEF <40% where risk stratification model remained scarce. These findings warrant further evaluation in prospective study to further clarify our outcome.

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