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Retrospective Cohort Study

Improved scoring system for the electrocardiographic diagnosis of left ventricular hypertrophy

Eric D Braunstein, Lori B Croft, Jonathan L Halperin, Steve L Liao

ORCID number: Eric D Braunstein (0000-0001-5290-9089); Lori B Croft (0000-0003-3962-8922); Jonathan L Halperin (0000-0002-8318-5471); Steve L Liao (0000-0002-8161-0294).

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Eric D Braunstein, Division of Cardiology, Department of Medicine, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, New York, NY 10467, United States

Lori B Croft, Jonathan L Halperin, Steve L Liao, Division of Cardiology, Icahn School of Medicine at Mount Sinai, Mount Sinai Medical Center, New York, NY 10029, United States

Corresponding author: Steve L. Liao, MD, Assistant Professor, Division of Cardiology, Mount Sinai Medical Center, 1176 5th Avenue, New York, NY 10029, United States.

steve.liao@mountsinai.org

Telephone: +1-212-4271540

Fax: +1-212-4107196

Abstract

BACKGROUND

Left ventricular hypertrophy (LVH) is a common manifestation of cardiovascular disease and a risk factor for cardiovascular morbidity and mortality, but available methods for its electrocardiographic (ECG) diagnosis have limited accuracy.

AIM

To investigate findings associated with LVH on ECG and developed an improved system for the diagnosis of LVH.

METHODS

A cohort study comparing ECG data acquired within 30 days of transthoracic echocardiography (TTE) was performed. Multivariate regression analysis identified ECG findings associated with increased LV mass and mass index. A scoring system was derived and performance compared to established criteria for LVH.

RESULTS

Data from 5486 outpatients with TTEs and corresponding ECGs were included in the derivation cohort, 333 (6.1%) of whom had LVH by TTE. In the primary regression analysis, findings associated with LVH were amplitudes of Q in V3, R in V6, S in V3, T in V6, P' in V1, P in V6, as well as R and T-axis discordance, R peak time in V6, QRS duration, weight, height, sex, and age. From this we derived a score consisting of 5 criteria, and validated it in an independent cohort of 910 patients. With a threshold of 1.5 points, sensitivity and specificity were 67.9% and 81.4%, and 62.5% and 83.2% in the derivation and validation cohorts, respectively. With a threshold of 2 points, sensitivity and specificity were 42.3% and 93.0%, and 37.5% and 93.4% in these cohorts.

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CONCLUSIONS

This score had superior sensitivity for detection of LVH by ECG while making a modest sacrifice in specificity compared to conventional criteria.

Key words: Left ventricular hypertrophy; Electrocardiogram; Echocardiogram; Diagnostic criteria; Scoring system

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Core tip: In this study we performed analysis of a large number of echocardiograms with corresponding electrocardiographic (ECG), and though multivariate regression analysis identified ECG findings associated with left ventricular hypertrophy (LVH). Using these findings, a five-item scoring system was developed to diagnose LVH on ECG. The performance characteristics of the system were compared to several conventional criteria, and it was seen to have superior sensitivity, including in an independent validation cohort. Using this scoring system, we believe that the diagnosis of LVH on ECG will be more clinically applicable in certain patient populations given the enhanced sensitivity of this test.

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INTRODUCTION

Left ventricular hypertrophy (LVH) is a common consequence of various cardiovascular diseases, and has been associated with increased risks of morbidity and mortality. Specifically, LVH has been associated with several adverse cardiac outcomes including heart failure, angina pectoris, myocardial infarction, and sudden cardiac death^[1-5]. Upwards of 30 electrocardiographic (ECG) criteria have been proposed for diagnosis of LVH^[6], but most have low sensitivity in the general population. Transthoracic echocardiography (TTE) is often required to confirm the diagnosis^[7,8]. Antihypertensive treatment can promote regression of LVH and prevent adverse cardiovascular events in patients with hypertension^[9,10], and TTE is preferred over ECG to assess myocardial mass in this setting^[8,11], although detection of left ventricular electrical remodeling may have prognostic implications independent of mass^[12-16]. Despite the availability of multiple criteria for ECG diagnosis of LVH, relatively few are widely implemented in clinical practice. Several models have been correlated with echocardiographic, cardiac magnetic response imaging, and autopsy measurements of LV mass, but these have not been integrated into commonly used ECG analysis software, while others are too complex for practical use. The aim of this study was to identify ECG findings associated with increased LV mass and develop an improved and easy to use scoring system to facilitate the diagnosis of and screening for LVH.

MATERIALS AND METHODS

Data collection and processing

The Institutional Review Board approved the protocol in October 2015. Clinical data available in the information systems of the Mount Sinai Medical Center, a large urban academic medical center, were derived from two sources, one for ECGs, and another for echocardiographic data. Data from all standard 12-lead ECGs recorded between December 1, 2013 and January 31, 2015 was exported from the MUSE v8.0 SP2 system (GE Healthcare, Chicago, IL, United States). Computer performed measurements including ventricular rate, PR interval, QRS duration, R-axis, T-axis, P-, P'- (second phase of P-wave), Q-, R-, S-, R'- and T-wave maximum amplitude, duration, area and peak time, maximum and minimum ST-segment level, and ST-segment deviation at J-point, mid-ST-segment and end-ST-segment. Measurements in each standard lead

were averaged across the ECG by the MUSE software. ECGs were not manually verified or measured and all ECGs except for those noted below were included in analyses.

Data from all outpatient TTEs acquired from patients ≥ 18 yr of age between January 1, 2014 and December 31, 2014 were exported from a proprietary echocardiography reporting system. Two-dimensional echocardiograms were performed using Siemens SC-2000, Siemens Acuson Sequoia, Phillips IE-33 or GE Vivid 7 cardiac ultrasound equipment. Measurements of the left ventricle were made in the parasternal long-axis view perpendicular to the axis at or immediately below the level of the mitral valve leaflet tips. Internal ventricular dimensions were measured linearly from two dimensional (2D) echocardiographic images to avoid oblique sections, or from 2D-guided M-mode echocardiography. Posterior and septal wall thickness and left ventricular end-diastolic and end-systolic diameters were measured according to the recommendations of the American Society of Echocardiography^[17]. Measurements were made during routine clinical interpretation of the echocardiogram and were not repeated or verified for the purposes of this study. Demographic data including age, sex, height, and weight (patient reported at the time of the study) were also collected.

Left ventricular mass was calculated using the method of Devereux *et al*^[18]. Body mass index, body surface area, and LV mass index were calculated using the standard methods. LVH was defined by LV mass index one standard deviation above the mean, stratified by sex (145 g/m² for males, 125 g/m² for females). Data from the first 10 mo of the study period comprised the derivation set, while those from the final 2 mo were used to validate the derived model.

TTEs and ECGs were matched by selecting the ECG obtained most proximate to each TTE. When patients had more than one TTE during the study period, only the first was included for analyses. Echocardiograms with incomplete demographic or measurement data and those without a corresponding ECG within 30 d were excluded. Also excluded were ECGs showing complete (but not incomplete) left bundle branch block or a paced rhythm, as identified by the MUSE software and confirmed by a board-certified cardiologist.

Statistical analysis

A multivariate linear regression model was constructed using LV mass as the endpoint and covariates including P-, P'- (second phase of P-wave), Q-, R-, S-, R'- and T-wave amplitudes in each lead, R-wave peak time in each lead (intrinsicoid deflection), maximum and minimum ST levels in each lead, ST-segment deviation at the J-point and mid-ST-segment in each lead, QRS duration, PR interval, difference between R-axis and T-axis, and patient weight, height, sex and age (152 degrees of freedom). A similar model using LV mass index as the endpoint yielded similar output with reduced fit parameters. Another model constructed using wave-complex areas (as opposed to maximum amplitudes) was less strongly associated with the endpoint. Covariates most strongly correlated with LV mass (based on regression *P*- and *t*-values, and a *P*-value threshold set at $P \leq 0.005$ in the linear regression model) were retained for multivariate logistic regression analysis. Additional logistic regression models were constructed stratifying the data set by sex in order to assess differences in ECG findings between sexes.

As several of the amplitudes and durations included in the model are correlated, we minimized effects of multicollinearity by calculating variance inflation factors (VIF) for covariates likely to be correlated and manually removing colinear covariates (VIF > 5) in a stepwise fashion while maximizing fit parameters of the overall model. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, United States).

Scoring system development

A scoring system was derived using scaled and rounded regression Wald chi-square and beta-coefficients similar to the method of Sullivan *et al*^[19]. Thresholds for the prediction model were developed based on standard deviations of the covariates, established LVH criteria, and iteration. The derived diagnostic criteria as well as several accepted criteria for LVH (Cornell^[20], Sokolow-Lyon^[21], Cornell product^[22], Sokolow-Lyon product^[23], Gubner-Ungerleider^[24], Sum-of-12-lead^[25], Romhilt-Estes^[26], Framingham-adjusted Cornell^[27], R-wave amplitude in aVL, Peguero-Lo Presti^[28]) were evaluated. Sensitivity and specificity were calculated for each criterion in both cohorts, along with 95% confidence intervals using binomial proportions in the derivation cohort. Positive and negative predictive values were also calculated.

RESULTS

Patient characteristics

During the 1-yr inclusion period, 11087 outpatient TTEs were obtained, while 202706 ECGs were recorded during the bracketed 14-mo period for the study. After matching each TTE with available ECGs and excluding those with incomplete data ($n = 570$), subsequent TTE examinations in the same patients (695), those with left bundle-branch block (128) or paced rhythm (235), and those without corresponding ECGs within 30 days (1396), a total of 5486 cases were entered into the derivation cohort. Applying the same criteria, 910 cases comprised the validation cohort. Patients characteristics were similar between both cohorts, and patients included in analyses in the cohorts had mean age around 60, were on average overweight but not obese, and were about half male (Table 1).

Regression results

In the derivation cohort, 333 patients (6.1%) had LVH as defined by the foregoing TTE criteria. Utilizing the full set of 152 covariates available, multivariate logistic analysis for the endpoint of LV mass yielded a regression coefficient of 0.502. The most highly associated variables ($P \leq 0.005$) included Q-wave amplitude in V3, R-wave amplitude in V6, S-wave amplitude in V3, QRS duration, difference between R and T-wave axis, R-wave peak time in V6, T-wave peak amplitude in V6 (inversely associated with the outcome), P'-wave amplitude in V1 (inversely associated), P-wave amplitude in V6, weight, height, sex, and age. Using these covariates, a logistic regression model was constructed for LVH (Table 2) with area under the ROC curve estimated by the c-statistic at 0.867.

Scoring system development and evaluation

To derive a scoring system (Table 3), we summed the amplitude predictors and set a threshold of two standard deviations above the mean in the derivation cohort data, distinguished by sex. The QRS duration threshold was set arbitrarily at 100 ms, the upper limit of normal. The absence of a positive T-wave component in V6 was set based on the negative association of maximum T-wave amplitude in the regression model. Definition of R- and T-wave precordial axis discordance was set at $\pm 75^\circ$, although similar results were seen at $\pm 45^\circ$ and $\pm 90^\circ$. P-wave negative deflection greater than positive deflection in V1 was used due to the negative association of P'-wave amplitude in V1 in the model. Despite its association with LVH in the regression model, patient height was omitted from the scoring system to enhance clinical convenience.

Additional logistic regression models were constructed stratifying the data set by sex in order to assess differences in ECG findings between sexes (Table 4). Findings in these cohorts were similar to those in the overall analysis; however, notably discordance between R and T-wave axis was only found to be associated with LVH in men but not in women.

The derived prediction model and other criteria for ECG diagnosis of LVH were evaluated in the derivation and validation cohorts, calculating sensitivity and specificity as well as positive and negative predictive values (Table 5). Using a threshold of 2 points, the score exhibited sensitivity superior to previous methods while sacrificing little to no specificity; using a cutoff of 1.5 points, the score improved sensitivity while maintaining specificity $> 80\%$. Looked at another way, the score was also seen to have superior positive predictive values utilizing a cutoff of 2 points than established criteria while maintaining a high negative predictive value; all positive predictive values in this study for the derived and established criteria were relatively low because of the low overall prevalence of LVH in the studied population.

DISCUSSION

In this study of 5486 patients undergoing TTE within 30 d of a 12-lead ECG, several ECG findings were associated with increased LV mass from a set of 147 ECG variables, many of which are included in established criteria for LVH, along with several others heretofore unrecognized. In our model, QRS duration was independently associated with LVH, even when the voltage QRS duration products were tested as the other covariates. For this reason, we included QRS duration rather than a voltage duration product as an independent predictor. This independent association suggests that voltage duration products may not be optimal for identification of LVH. In contrast to established schema, R-wave amplitude in lead aVL was not independently associated with echocardiographic LVH in this analysis,

Table 1 Patient characteristics

Characteristic - no. (%) unless noted	Derivation cohort (n = 5486)	Validation cohort (n = 910)
Age (mean \pm SD)	59.1 \pm 15.8	58.6 \pm 15.2
18-29	265 (4.8)	30 (3.3)
30-39	408 (7.4)	91 (10.0)
40-49	708 (12.9)	105 (11.5)
50-59	1295 (23.6)	224 (24.6)
60-69	1358 (24.8)	242 (26.6)
70 +	1452 (26.5)	218 (24.0)
Male sex	2869 (52.3)	448 (49.2)
Body mass index		
mean \pm SD	28.0 \pm 6.6	28.5 \pm 6.5
Median (range)	26.9 (12.9-75.2)	27.5 (15.8-66.1)
Left ventricular mass by echocardiogram		
mean \pm SD	167.2 \pm 62.1	173.3 \pm 64.8
Median (intraquartile range)	155.4 (123.3-200.4)	163.0 (124.1-205.0)
Left ventricular hypertrophy present by echocardiogram	333 (6.1)	80 (8.6)
Time between echocardiogram and electrocardiogram in days (mean, intraquartile range)	6.7 (0-13)	5.9 (0-11)

possibly due to interactions with precordial lead amplitude.

P-wave amplitude in V6 and negative P-terminal force in V1 were associated with LVH, likely reflecting left atrial pathology. P-wave duration (encompassing both positive and negative components), however, was not associated with LVH. These variations suggest the need for further study of the ECG manifestations of left atrial conduction delay. Unlike previous systems for identification of LVH, which typically include only R and S-wave amplitudes, we found an association of Q-wave in addition to S-wave amplitude in V3 with LVH. This could indicate an association of the total negative QRS vector in this lead, rather than the S-wave alone, with LVH. Lead V3 was found to be more highly associated with LVH than lead V1 or V2 as is seen in many other LVH criteria; this may be due to the location of lead V3 being more in line with the LV septum and therefore a better representation of its thickness.

An additional analysis looking at differences in ECG findings associated with LVH between sexes found that although most factors remained similar, R- and T-axis discordance was found to be associated with LVH in men but not in women. This may highlight differences in electrical remodeling as it relates to repolarization between sexes, and could be the subject of further study.

Conventional ECG criteria have low sensitivity for diagnosis of LVH. Several regression equations have been developed to estimate LV mass directly, but are impractical except for implementation in computerized ECG software, and correlate poorly with measurements of LV mass made by echocardiography, cardiac magnetic resonance imaging (MRI), or autopsy. The scheme we derived was evaluated using two thresholds based on distinct objectives. A threshold of 2 points yielded high specificity (approximately 93%) with improved sensitivity (approximately 40%), while a cutoff of 1.5 points markedly improved sensitivity (approximately 65%) while maintaining sensitivity at $> 80\%$. The higher limit may be preferred for general use, while the lower value may be more applicable to patients with hypertension or clinical conditions associated with LVH. Further studies are needed to assess the utility of either cut-point for serial assessments in the same individual, or to identify those who may benefit from echocardiography or other imaging studies to assess LV mass or its response to therapeutic interventions.

The derived scoring system was compared to conventional criteria for the ECG diagnosis of LVH and our system was found to have increased sensitivity with a modest sacrifice in specificity. Most conventional LVH criteria have high specificity but low sensitivity which limits use as a screening test in a general population. The enhanced sensitivity of the presented scoring system may introduce improvement to clinical practice by aiding with patient risk stratification and preventing unnecessary additional testing.

An important limitation of this study was inclusion of only ambulatory outpatients. This was because fluctuating clinical circumstances in acute ill hospital inpatient could influence echocardiographic measurements of wall thickness or produce

Table 2 Multivariate logistic regression analysis for left ventricular hypertrophy

Characteristic	Wald Chi-Square	P value
Q-wave amplitude in V3	19.3	$P < 0.0001$
R-wave amplitude in V6	39.7	$P < 0.0001$
S-wave amplitude in V3	135	$P < 0.0001$
QRS Duration	115.4	$P < 0.0001$
Discordant R-axis and T-axis (difference ≤ 75 or > 75)	14.6	$P = 0.0001$
Maximum (positive deflection) T-wave amplitude in V6	38.5	$P < 0.0001$
Maximum P'-wave amplitude in V1	18.5	$P < 0.0001$
P-wave peak amplitude in V6	0.19	$P = 0.659$
Weight	0.008	$P = 0.927$
Height	25.2	$P < 0.0001$
Sex	6.3	$P = 0.012$
Age	0.03	$P = 0.864$

discordance with ECG's recorded within the requisite 30-d window. It is also worth noting that the ECG data we used was measured automatically, while the echocardiographic measurements were obtained manually. Echocardiographic measurement, while regarded as being relatively accurate, are not the gold standard for LV mass measurement; more accurate measurements of LV mass such as cardiac MRI were not able to be used in this study. We also were not able to collect data on patient race, cardiovascular risk factors, or comorbidities (*e.g.*, hypertension, diabetes), all of which are factors that may influence ECG estimations of LVH. Finally, while the Working Group on ECG diagnosis of LVH suggested that research on LVH focus on the potential relationship of electrical remodeling to clinical outcomes^[13], we lack long-term clinical follow-up of patients to correlate the LVH score with such outcomes.

In conclusion, we identified several ECG findings that are associated with LVH and incorporated them into a score to improve the ECG diagnosis of this common condition. The scoring system may help improve clinical utility by enhancing sensitivity whilst displaying a modest sacrifice in specificity compared to conventional criteria. Further studies are needed to determine whether this scheme optimally reflects changes in the electrical characteristics of the myocardium over time, and whether it may have value for predicting cardiovascular events that are not exposed by measurement of ventricular mass alone.

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Table 3 Components of the electrocardiographic diagnostic score for left ventricular hypertrophy

Criteria	Number of points
Sum of R-wave amplitude in V6 + S-wave amplitude in V3 + Q-wave amplitude in V3 > 4.0 mV in males and 3.2 mV in females	1
QRS duration > 100 ms	1
Absence of positive component of T-wave in V6 (maximum T-wave amplitude < 0) when overall QRS vector in V6 positive (i.e., R-wave larger than S-wave)	1
Discordant limb lead R- and T-wave axis (R- minus T-wave axis ≤ 75 or > 75 degrees)	0.5
Amplitude of negative terminal p-wave deflection in V1 greater than amplitude of positive deflection	0.5

Table 4 Multivariate logistic regression analysis for left ventricular hypertrophy stratified by sex

Characteristic	Male (n = 2869)		Female (n = 2617)	
	Wald Chi-Square	P value	Wald Chi-Square	P value
Q-wave amplitude in V3	14.7	P = 0.0001	5.0	P = 0.025
R-wave amplitude in V6	25.5	P < 0.0001	10.0	P = 0.001
S-wave amplitude in V3	77.0	P < 0.0001	53.6	P < 0.0001
QRS Duration	62.2	P < 0.0001	51.2	P < 0.0001
Discordant R-axis and T-axis (difference ≤ 75 or > 75)	17.8	P < 0.0001	0.63	P = 0.426
Maximum (positive deflection) T-wave amplitude in V6	16.0	P < 0.0001	26.1	P < 0.0001
Maximum P'-wave amplitude in V1	9.4	P = 0.002	4.6	P = 0.031
P-wave peak amplitude in V6	1.0	P = 0.314	3.5	P = 0.061
Weight	0.50	P = 0.477	0.9	P = 0.340
Height	6.8	P = 0.009	21.8	P < 0.0001
Age	1.4	P = 0.245	1.06	P = 0.303

Table 5 Sensitivity, specificity, and positive and negative predictive values of selected electrocardiographic criteria for left ventricular hypertrophy

Criteria	Cutoff	Derivation cohort				Validation cohort	
		Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV	Sensitivity	Specificity
Derived Criteria	1.5 points	67.9 (62.6-72.9)	81.4 (80.3-82.4)	19.0	97.5	62.5	83.2
""	2 points	42.3 (37.0-47.7)	93.0 (92.3-93.7)	28.2	96.2	37.5	93.4
""	2.5 points	30.0 (25.2-35.3)	96.6 (96.1-97.1)	37.6	95.6	30.0	96.8
Cornell	-	37.8 (32.6-43.1)	92.3 (91.6-93.0)	24.1	95.8	36.2	90.3
Sokolow-Lyon	-	16.5 (12.5-20.5)	95.9 (95.4-96.5)	20.7	94.7	20.0	96.3
Cornell Product		55.0 (49.6-60.3)	88.3 (87.5-89.2)	23.3	96.8	53.8	88.1
Sokolow-Lyon Product		22.5 (18.0-27.0)	95.9 (95.3-96.4)	26.0	95.0	23.8	95.6
Gubner-Ungerleider		27.0 (22.3-31.8)	88.9 (88.0-89.8)	13.6	95.0	27.5	87.7
Sum-of-12-Lead		57.4 (51.9-62.7)	76.1 (74.9-77.3)	13.4	96.5	57.5	77.1
Romhilt-Estes	5 points	35.4 (30.3-40.8)	94.4 (93.7-95.0)	26.2	95.8	35.0	95.0
""	4 points	51.1 (45.5-56.5)	88.2 (87.3-89.0)	21.8	96.5	57.5	90.0
Framingham-adjusted Cornell		42.3 (37.0-47.7)	90.1 (89.3-90.9)	21.7	96.0	51.3	87.6
R-wave amplitude in aVL	1.1 mV	20.1 (16.0-24.8)	92.6 (91.8-93.3)	14.9	94.7	21.3	92.1
Peguero-Lo Presti		24.9 (20.3-29.6)	94.7 (94.1-95.3)	23.3	95.1	26.3	93.5

CI: Confidence interval; PPV: Positive predictive values; NPV: Negative predictive values.

ARTICLE HIGHLIGHTS

Research background

Left ventricular hypertrophy (LVH) is a common manifestation of cardiovascular disease and a risk factor for cardiovascular morbidity and mortality, but available methods for its electrocardiographic (ECG) diagnosis have limited accuracy.

Research motivation

Improvement in the ability of clinicians to diagnose LVH on ECG could aid with patient risk stratification and prevent unnecessary additional testing.

Research objectives

The aim of this study was to investigate findings associated with LVH on ECG and develop an improved system for the diagnosis of LVH.

Research methods

A cohort study comparing ECG data acquired within 30 days of transthoracic echocardiography was performed. Multivariate regression analysis identified ECG findings associated with increased LV mass and mass index. A scoring system was derived and performance compared to established criteria for LVH.

Research results

In regression analysis, findings associated with LVH were amplitudes of Q in V3, R in V6, S in V3, T in V6, P' in V1, P in V6, as well as R and T-axis discordance, R peak time in V6, QRS duration, weight, height, sex, and age. A score consisting of 5 criteria was derived and validated it in an independent cohort. This score had superior sensitivity for detection of LVH by ECG compared to conventional criteria whilst making a modest sacrifice in specificity compared to conventional criteria.

Research conclusions

We identified several ECG findings that are associated with LVH and incorporated them into a score to improve the ECG diagnosis of this common condition. The scoring system may help improve clinical utility by enhancing sensitivity whilst displaying a modest sacrifice in specificity compared to conventional criteria.

Research perspectives

Further studies are needed to determine whether this scheme optimally reflects changes in the electrical characteristics of the myocardium over time, and whether it may have value for predicting cardiovascular events that are not exposed by measurement of ventricular mass alone.

REFERENCES

- 1 Casale PN, Devereux RB, Milner M, Zullo G, Harshfield GA, Pickering TG, Laragh JH. Value of echocardiographic measurement of left ventricular mass in predicting cardiovascular morbid events in hypertensive men. *Ann Intern Med* 1986; **105**: 173-178 [PMID: 2942070 DOI: 10.7326/0003-4819-105-2-173]
- 2 Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Left ventricular mass and incidence of coronary heart disease in an elderly cohort. The Framingham Heart Study. *Ann Intern Med* 1989; **110**: 101-107 [PMID: 2521199 DOI: 10.7326/0003-4819-110-2-101]
- 3 Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med* 1990; **322**: 1561-1566 [PMID: 2139921 DOI: 10.1056/NEJM199005313222203]
- 4 Koren MJ, Devereux RB, Casale PN, Savage DD, Laragh JH. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. *Ann Intern Med* 1991; **114**: 345-352 [PMID: 1825164 DOI: 10.7326/0003-4819-114-5-345]
- 5 Kannel WB, Cobb J. Left ventricular hypertrophy and mortality--results from the Framingham Study. *Cardiology* 1992; **81**: 291-298 [PMID: 1301257 DOI: 10.1159/000175819]
- 6 Hancock EW, Deal BJ, Mirvis DM, Okin P, Kligfield P, Gettes LS, Bailey JJ, Childers R, Gorgels A, Josephson M, Kors JA, Macfarlane P, Mason JW, Pahlm O, Rautaharju PM, Surawicz B, van Herpen G, Wagner GS, Wellens H; American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; American College of Cardiology Foundation; Heart Rhythm Society. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: Part V: electrocardiogram changes associated with cardiac chamber hypertrophy: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol* 2009; **53**: 992-1002 [PMID: 19281932 DOI: 10.1016/j.jacc.2008.12.015]
- 7 Ang D, Lang C. The prognostic value of the ECG in hypertension: Where are we now? *J Hum Hypertens* 2008; **22**: 460-467 [PMID: 18432258 DOI: 10.1038/jhh.2008.24]
- 8 Bauml MA, Underwood DA. Left ventricular hypertrophy: An overlooked cardiovascular risk factor. *Cleve Clin J Med* 2010; **77**: 381-387 [PMID: 20516249 DOI: 10.3949/ccjm.77a.09158]
- 9 Schiattarella GG, Hill JA. Inhibition of hypertrophy is a good therapeutic strategy in ventricular pressure overload. *Circulation* 2015; **131**: 1435-1447 [PMID: 25901069 DOI: 10.1161/CIRCULATIONAHA.115.013894]
- 10 Okin PM, Devereux RB, Jern S, Kjeldsen SE, Julius S, Nieminen MS, Snapinn S, Harris KE, Aurup P,

- Edelman JM, Wedel H, Lindholm LH, Dahlöf B; LIFE Study Investigators. Regression of electrocardiographic left ventricular hypertrophy during antihypertensive treatment and the prediction of major cardiovascular events. *JAMA* 2004; **292**: 2343-2349 [PMID: [15547161](#) DOI: [10.1001/jama.292.19.2343](#)]
- 11 **Pewsnar D**, Jüni P, Egger M, Battaglia M, Sundström J, Bachmann LM. Accuracy of electrocardiography in diagnosis of left ventricular hypertrophy in arterial hypertension: systematic review. *BMJ* 2007; **335**: 711 [PMID: [17726091](#) DOI: [10.1136/bmj.39276.636354.AE](#)]
- 12 **Bacharova L**, Schocken D, Estes EH, Strauss D. The role of ECG in the diagnosis of left ventricular hypertrophy. *Curr Cardiol Rev* 2014; **10**: 257-261 [PMID: [24827796](#) DOI: [10.2174/1573403X10666140514103220](#)]
- 13 **Bacharova L**, Estes EH, Schocken DD, Ugander M, Soliman EZ, Hill JA, Bang LE, Schlegel TT. The 4th Report of the Working Group on ECG diagnosis of Left Ventricular Hypertrophy. *J Electrocardiol* 2017; **50**: 11-15 [PMID: [27890283](#) DOI: [10.1016/j.jelectrocard.2016.11.003](#)]
- 14 **Rautaharju PM**, Soliman EZ. Electrocardiographic left ventricular hypertrophy and the risk of adverse cardiovascular events: a critical appraisal. *J Electrocardiol* 2014; **47**: 649-654 [PMID: [25012077](#) DOI: [10.1016/j.jelectrocard.2014.06.002](#)]
- 15 **Estes EH**, Zhang ZM, Li Y, Tereshchenko LG, Soliman EZ. The Romhilt-Estes left ventricular hypertrophy score and its components predict all-cause mortality in the general population. *Am Heart J* 2015; **170**: 104-109 [PMID: [26093870](#) DOI: [10.1016/j.ahj.2015.04.004](#)]
- 16 **Leigh JA**, O'Neal WT, Soliman EZ. Electrocardiographic Left Ventricular Hypertrophy as a Predictor of Cardiovascular Disease Independent of Left Ventricular Anatomy in Subjects Aged \geq 65 Years. *Am J Cardiol* 2016; **117**: 1831-1835 [PMID: [27067620](#) DOI: [10.1016/j.amjcard.2016.03.020](#)]
- 17 **Lang RM**, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ; Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005; **18**: 1440-1463 [PMID: [16376782](#) DOI: [10.1016/j.echo.2005.10.005](#)]
- 18 **Devereux RB**, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, Reichek N. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol* 1986; **57**: 450-458 [PMID: [2936235](#) DOI: [10.1016/0002-9149\(86\)90771-X](#)]
- 19 **Sullivan LM**, Massaro JM, D'Agostino RB Sr. Presentation of multivariate data for clinical use: The Framingham Study risk score functions. *Stat Med* 2004; **23**: 1631-1660 [PMID: [15122742](#) DOI: [10.1002/sim.1742](#)]
- 20 **Casale PN**, Devereux RB, Alonso DR, Campo E, Kligfield P. Improved sex-specific criteria of left ventricular hypertrophy for clinical and computer interpretation of electrocardiograms: Validation with autopsy findings. *Circulation* 1987; **75**: 565-572 [PMID: [2949887](#) DOI: [10.1161/01.cir.75.3.565](#)]
- 21 **SOKOLOW M**, LYON TP. The ventricular complex in left ventricular hypertrophy as obtained by unipolar precordial and limb leads. *Am Heart J* 1949; **37**: 161-186 [PMID: [18107386](#) DOI: [10.1016/0002-8703\(49\)90562-1](#)]
- 22 **Molloy TJ**, Okin PM, Devereux RB, Kligfield P. Electrocardiographic detection of left ventricular hypertrophy by the simple QRS voltage-duration product. *J Am Coll Cardiol* 1992; **20**: 1180-1186 [PMID: [1401620](#) DOI: [10.1016/0735-1097\(92\)90376-X](#)]
- 23 **Okin PM**, Roman MJ, Devereux RB, Kligfield P. Electrocardiographic identification of increased left ventricular mass by simple voltage-duration products. *J Am Coll Cardiol* 1995; **25**: 417-423 [PMID: [7829796](#) DOI: [10.1016/0735-1097\(94\)00371-V](#)]
- 24 **Ungerleider HE**, Gubner R. The Q3 and QS3 deflections in the electrocardiogram; criteria and significance. *Am Heart J* 1947; **33**: 807-818 [PMID: [20242367](#) DOI: [10.1016/0002-8703\(47\)90026-4](#)]
- 25 **Dollar AL**, Roberts WC. Usefulness of total 12-lead QRS voltage compared with other criteria for determining left ventricular hypertrophy in hypertrophic cardiomyopathy: analysis of 57 patients studied at necropsy. *Am J Med* 1989; **87**: 377-381 [PMID: [2529761](#) DOI: [10.1016/S0002-9343\(89\)80817-4](#)]
- 26 **Romhilt DW**, Estes EH. A point-score system for the ECG diagnosis of left ventricular hypertrophy. *Am Heart J* 1968; **75**: 752-758 [PMID: [4231231](#) DOI: [10.1016/0002-8703\(68\)90035-5](#)]
- 27 **Norman JE**, Levy D, Campbell G, Bailey JJ. Improved detection of echocardiographic left ventricular hypertrophy using a new electrocardiographic algorithm. *J Am Coll Cardiol* 1993; **21**: 1680-1686 [PMID: [8496537](#) DOI: [10.1016/0735-1097\(93\)90387-G](#)]
- 28 **Peguero JG**, Lo Presti S, Perez J, Issa O, Brenes JC, Tolentino A. Electrocardiographic Criteria for the Diagnosis of Left Ventricular Hypertrophy. *J Am Coll Cardiol* 2017; **69**: 1694-1703 [PMID: [28359515](#) DOI: [10.1016/j.jacc.2017.01.037](#)]



Risk factors for sudden cardiac death to determine high risk patients in specific patient populations that may benefit from a wearable defibrillator

Hilal Mohammed Khan, Stephen J Leslie

ORCID number: Hilal Mohammed Khan (0000-0003-0412-2227); Stephen J Leslie (0000-0002-1403-4733).

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Hilal Mohammed Khan, Stephen J Leslie, Cardiac Unit, Raigmore Hospital, Inverness IV2 3UJ, United Kingdom

Stephen J Leslie, Department of Diabetes and Cardiovascular Science, University of the Highlands and Islands, The Centre for Health Science, Old Perth Road, Inverness IV2 3JH, United Kingdom

Corresponding author: Stephen J Leslie, FRCP (C), MBBS, MRCP, PhD, Professor, Cardiac Unit, Raigmore Hospital, Inverness IV2 3UJ, United Kingdom. stephen.leslie@nhs.net
Telephone: +44-1463-705459

Abstract

BACKGROUND

There is a high risk for sudden cardiac death (SCD) in certain patient groups that would not meet criteria for implantable cardioverter defibrillator (ICD) therapy. In conditions such as hypertrophic cardiomyopathy (HCM) there are clear risk scores that help define patients who are high risk for SCD and would benefit from ICD therapy. There are however many areas of uncertainty such as certain patients post myocardial infarction (MI). These patients are high risk for SCD but there is no clear tool for risk stratifying such patients.

AIM

To assess risk factors for sudden cardiac death in major cardiac disorders and to help select patients who might benefit from Wearable cardiac defibrillators (WCD).

METHODS

A literature search was performed looking for risk factors for SCD in patients post-MI, patients with left ventricular systolic dysfunction (LVSD), HCM, long QT syndrome (LQTS). There were 41 studies included and risk factors and the relative risks for SCD were compiled in table form.

RESULTS

We extracted data on relative risk for SCD of specific variables such as age, gender, ejection fraction. The greatest risk factors for SCD in post MI patients was the presence of diabetes [Hazard ratio (HR) 1.90-3.80], in patient with LVSD was ventricular tachycardia (Relative risk 3.50), in LQTS was a prolonged QTc (HR 36.53) and in patients with HCM was LVH greater than 20 mm (HR 3.10). A proportion of patients currently not suitable for ICD might benefit from a WCD

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CONCLUSION

There is a very high risk of SCD post MI, in patients with LVSD, HCM and LQTS even in those who do not meet criteria for ICD implantation. These patients may be candidates for a WCD. The development of more sensitive risk calculators to predict SCD is necessary in these patients to help guide treatment.

Key words: Sudden cardiac death; Wearable cardiac defibrillators; Myocardial infarction; Hypertrophic cardiomyopathy; Left ventricular systolic dysfunction

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Core tip: This article looks at the risk factors for sudden cardiac death (SCD) in patients post myocardial infarction, patients with left ventricular systolic dysfunction, patients with hypertrophic cardiomyopathy, patients with long QT syndrome and the relative risk for sudden cardiac death of these risk factors. This is compared to the absolute risk of SCD for these conditions. We reviewed the recommendations from current guidelines and we outline where patients are at high risk for SCD but are not eligible for implantable cardioverter defibrillator implantation. The risk factors identified in this study can be used to select patients who may benefit from Wearable cardiac defibrillators therapy.

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INTRODUCTION

Sudden cardiac death (SCD) is a major global health problem estimated to account for 15%-20% of death^[1]. The mechanism of SCD has changed substantially over the last decade with ventricular fibrillation (VF) and pulseless ventricular tachycardia (VT) accounting for between 23%-36% of out-of-hospital cardiac arrests^[2,3]. This compares to 75% of cases of SCD in the 1980's and early 1990's^[4,5]. The decline in SCD due to VT/VF is partly due to improved medical care such as the use of beta blockers and implantable cardioverter defibrillators (ICD)^[6,7]. Thus VF and pulseless VT are potentially treatable heart rhythms particularly if patients are given an early DC shock with return of an organised rhythm in up to 70% of cases after a single biphasic shock^[8]. This has led to the development of multiple measures such as automated external defibrillators in public places, ICD therapy and wearable cardioverter defibrillators (WCD) to reduce the rate of preventable death from VF/VT.

History of defibrillation

The first successful closed chest direct current cardioversion of ventricular fibrillation was performed by Paul Zoll in the 1950's^[9]. This was initially a monophasic shock but more recently biphasic shocks are used. Biphasic waveforms have superior efficacy to monophasic pulses^[8] and the European resuscitation council recommend a first shock at 150-200 J with subsequent shocks at a higher energy level if the device allows and the arrhythmia remains uncorrected^[10]. Return of sinus rhythm and spontaneous circulation after administration of biphasic shocks occurs in up to 70% in patients with VF or VT^[8]. This highlights the high efficacy of this relatively simple treatment.

The first ICD was implanted in a patient in 1980 by Mirowski *et al*^[11]. There have since been multiple studies proving the benefit of ICDs in preventing SCD and reducing all-cause mortality. These include primary prevention studies which show a reduction in mortality from SCD of between 23%-54%^[12-16] (Table 1) and secondary prevention studies which show a reduction in mortality from SCD of between 20%-28%^[17-19] (Table 2). Current guidelines based on the results of these and other studies recommend the insertion of ICD in patients more than 40 d post myocardial infarction (MI) with severe LVSD (ejection fraction less than 35%), patients with severe LVSD and in several other situations such as high risk hypertrophic cardiomyopathy (HCM) patients, patients with long QT syndrome (LQTS) with a history of cardiac arrest.

These guidelines advise against inserting an ICD for patients who survive sustained VT or VF within the first 48 h of an MI unless they have pre-existing LV impairment and are on optimal medical therapy already or they have incomplete revascularisation, as it is felt that tachyarrhythmia within this period is most likely due to the acute coronary obstruction and cardiac injury^[20].

In other patients an ICD may not be possible due to infection or lack of vascular access or patient preference. Thus, some high risk patients who would warrant an ICD do not have one. In order to address this, the WCD was developed. The WCD has been in development since 1986 and had been tested for 17 years prior to it receiving the Food and Drug Administration approval in 2002^[21]. The WCD is a device contained within a vest worn under a patient's clothes which records a patient's rhythm and delivers a shock if a shockable rhythm occurs^[22]. This has provided a much lower risk solution to ICD implantation in selected patients. Current guidelines recommend considering a WCD or ICD post MI within 40 d of their MI in patients with incomplete revascularisation, VT or VF > 48 h post MI or pre-existing LVSD^[23]. Additional groups of patients that could benefit from a WCD include patients with channelopathies such as LQTS who have not suffered a VT or VF event but have high risk features, patients with HCM who have intermediate risk features but not yet achieving criteria for ICD implantation, and also patients with infected ICDs could be offered a WCD once their ICD has been removed and they are awaiting ICD re-implantation. WCD do however come with a risk of inappropriate shocks and their efficacy can be reduced due to a lack of patient compliance.

The aim of this review is to use existing literature to identify risk factors for SCD that may help identify patients who may benefit from a WCD and to discuss the potential role that WCDs could play in reducing the risk of SCD in selected patient groups who do not currently meet guidelines for ICD implantation.

MATERIALS AND METHODS

Study design

This review included available data on risk factors for SCD in predefined patient groups. All odds ratio (OR), relative risk (RR), Exp(b) and hazard ratio (HR) were rounded to 2 decimal places for consistency. OR is a statistic defined as the ratio of the odds of variable A in the presence of variable B and the odds of variable A without the presence of variable B. RR is the ratio of the probability of an outcome in an exposed group to the probability of an outcome in an unexposed group. The HR is an expression of the hazard or chance of events occurring in the treatment arm as a ratio of the hazard of the events occurring in the control arm.

Inclusion and exclusion criteria

All studies that reported risk factors for SCD in patients with LVSD, LQTS, HCM or post MI. There was no restriction on age, gender, geographical area or date of publication. Studies reported in English. Any studies where the risk of SCD was not quantified by either a HR, OR or RR were excluded.

Search strategy

A literature search was performed in 4 main groups of patients: Search terms included: (risk of SCD* or risk factors for SCD* or SCD* or female gender and outcome* or mortality in patients* or mortality in women* or risk stratification for SCD* or risk of cardiac arrest* or atrial fibrillation and mortality* or echocardiographic predictors of outcome* or risk of death* or COPD and mortality* or prognosis of heart failure* or risk of death in patients*) and (post myocardial infarction* or after myocardial infarction* or after acute st elevation myocardial infarction* or after ST elevation myocardial infarction* or with inferior myocardial infarction* or following myocardial infarction* or after myocardial infarction* or myocardial scarring* or electrocardiographic abnormalities* or patients with hypertrophic cardiomyopathy* or heart failure* or patients with heart failure* or left ventricular dysfunction* or after hospitalization for heart failure* or in the community* or new diagnosis of heart failure* or LQTS*).

The risk factor in each group that was associated with SCD, was then tabulated along with the relevant studies that supported this finding.

RESULTS

Results of literature search

Table 1 Primary prevention implantable cardioverter defibrillator studies

Study	Intervention/control group	Inclusion criteria	Risk reduction of SCD with ICD
Multicenter Automatic Defibrillator Implantation Trial ^[12]	ICD <i>vs</i> antiarrhythmic drug	Previous MI; EF≤35%; nsVT; positive findings on EPS	54% (<i>P</i> = 0.001)
Multicenter Unsustained Tachycardia Trial ^[13]	EP-guided therapy <i>vs</i> placebo	Coronary disease; EF≤40%; Non-sustained VT; inducible VT at EPS	51% (<i>P</i> = 0.001)
Multicenter Automatic Defibrillator Implantation Trial 2 ^[14]	ICD <i>vs</i> optimal pharmacological treatment	Prior MI EF≤30%	31% (<i>P</i> = 0.02)
Sudden Cardiac Death in Heart Failure Trial ^[15]	ICD <i>vs</i> optimal pharmacological therapy <i>vs</i> optimal pharmacological therapy + amiodarone	Ischaemic and non-ischaemic cardiomyopathy; EF≤35%	23% (<i>P</i> = 0.007)
Defibrillator implantation in patients with nonischemic systolic heart failure ^[16]	ICD <i>vs</i> optimal pharmacological therapy	Non-ischaemic cardiomyopathy; EF≤35%	50% (<i>P</i> = 0.005)

SCD: Sudden cardiac death; ICD: Implantable cardioverter defibrillator; EF: Ejection fraction; EP: Electrophysiology; MI: Myocardial infarction; EPS: Electrophysiology studies; VT: Ventricular tachycardia.

The initial search strategy produced 21620 articles. Removal of duplicates and screening of the papers reduced the number to 480 articles. A further 435 papers were removed after reading of the full text. During data extraction an additional 4 papers were removed as a result of not having the prerequisite data available in the correct form. Forty one papers were included in the final data analysis (Figure 1)

Risk of sudden cardiac death post myocardial infarction

In patients post MI, 16 studies were identified involving a total of 250766 patients^[24-39](Table 3). The absolute risk of SCD in these studies varied from around 4.9%-8%^[24,26,30,33]. The absolute risk of SCD was 4.9% in the first month post-MI and decreased thereafter^[24]. Another study showed a cumulative risk of SCD at 1 year to be 5.3%^[26]. One study showed a risk of SCD of 7% at 30 d and 11% at 2 years^[30]. Another study showed a risk of SCD at 4% in those with EF > 35% and 8% in those with EF < 35% at one year^[33].

Several risk factors for SCD were identified post MI in order of decreasing magnitude: diabetes (HR 1.90-3.80), LVSD (HR 1.21 to 3.64), NSVT (HR 3.30), right ventricular involvement (OR 3.20), premature ventricular complexes occurring at a frequency of 10 or more per hour (HR 2.40), female gender (OR 1.09-1.76), older age (OR 1.03-1.56), LBBB (HR 1.49), non-specific intraventricular conduction delay (HR 1.44) and LVH (OR 1.40)^[24-39].

Risk factors for sudden cardiac death in heart failure

In patients with heart failure, 15 studies were identified involving a total of 65182 patients^[40-54](Table 4). The absolute risk of SCD in these studies varied from 8.8%-23.7%^[49,50]. Doval *et al*^[49] showed that in patients with NSVT the risk of SCD at 2 year was 23.7% compared to 8.8% in those who do not have NSVT at 2 years. Teerlink *et al*^[50] showed that the risk of SCD was 13% at 2 years.

Several features increasing the risk of SCD were identified in order of decreasing magnitude: VT (RR 3.50), NSVT (RR 2.77-3.89), couplets (RR 3.37), cirrhosis (OR 3.22), 1-SD difference in LV Mass (RR 2.75), a 1-SD difference in LV end systolic dimension (RR 2.73), deranged kidney function (HR 2.02-2.64), dementia (OR 2.54), cancer (OR 1.86), the degree of left ventricular impairment(less than 40%) (HR 1.29-1.80), older age (OR 1.70), COPD (OR 1.66), atrial fibrillation (HR 0.89-1.55), male gender (HR 1.21-1.50) and cerebrovascular disease (OR 1.43)^[40-54].

Risk of sudden cardiac death in the long QT syndrome

In patients with LQTS, 5 studies were identified with a total of 9758 patients^[55-59](Table 5). The absolute risk of SCD in these studies varied from 4.9%-13%^[55,57]. Sauer *et al*^[55] showed that the risk of SCD from the age of 18 until follow-up at the age of 40 was 4.9% in LQTS1, 8.0% in LQTS2 and 4.9% in LQTS3. Priori *et al*^[57] showed that the risk of SCD was 13% over 28 years of follow-up before the age of 40.

Several risk factors for SCD were identified in order of decreasing magnitude including: LQTS with a prolonged QTc interval (HR 36.53), LQTS with a normal range QTc interval (HR 10.25), LQTS 1 (HR 9.88), length of QTc interval (RR 5.34-8.36), consistent QTc interval prolongation (HR 2.23-6.67), previous history of cardiac events (syncope or aborted SCA) (HR 3.10-5.10), LQTS 3 (RR 1.80-2.76), female gender (HR 2.68), LQTS 2 (RR 1.61) and bradycardia (HR 1.02)^[55-59].

Table 2 Secondary prevention implantable cardioverter defibrillator studies

Study	Intervention/control group	Inclusion criteria	Risk reduction with ICD
Antiarrhythmics Versus Implantable Defibrillators study ^[17]	ICD <i>vs</i> antiarrhythmic drugs	Resuscitated from near-fatal VF or post-cardioversion from sustained VT	28% ($P = 0.02$)
Canadian Implantable Defibrillator Study ^[18]	ICD <i>vs</i> amiodarone	Resuscitated VF or VT or with unmonitored syncope	20% ($P = 0.14$)
Cardiac Arrest Study Hamburg ^[19]	ICD <i>vs</i> amiodarone <i>vs</i> metoprolol	Survivors of cardiac arrest secondary to documented ventricular arrhythmias	23% ($P = 0.08$)

ICD: Implantable cardioverter defibrillator; VF: Ventricular fibrillation; VT: Ventricular tachycardia.

Risk of sudden cardiac death in patients with HCM

In HCM there were 5 studies involving a total of 25823 patients^[60-64] (Table 6). The risk of SCD in HCM was about 5% over 5 years^[60].

The following risk factors for SCD in order of decreasing magnitude were identified including: LVH (highest risk when greater than 20 mm) (HR 1.05-3.17), NSVT (HR 2.53-2.92), syncope (HR 2.31-2.68), left ventricular outflow tract obstruction (HR 1.01-2.41), family history of SCD (HR 1.27-2.34), abnormal blood pressure response during exercise (HR 1.30-1.38) and an enlarged left atrial diameter (HR 1.04)^[60-64].

Wearable cardioverter defibrillator studies

There are currently only a few published outcome studies of WCDs. The WCD use in patients perceived to be at high risk, early post-MI study showed that 1.6% of patients received an appropriate shock for VT/VF and up to 67% of patients with VT/VF survived because of an appropriate shock^[65]. Inappropriate shocks occurred in 1.1% of patients; none of the inappropriate shocks induced an arrhythmia.

“The aggregate national experience with the WCD vest: event rates, compliance and survival study” showed that 1.7% of patients received an appropriate shock for VT/VF. It also showed that 90% of patients survived because of an appropriate shock for VT/VF^[66]. Inappropriate shocks occurred in 1.9% of patients^[66].

The Vest Prevention of Early Sudden Death Trial compared WCD therapy to optimal medical therapy that was the control group. This trial showed that 0.6% of patients received an inappropriate shock. 1.4% of patients received an appropriate shock. The number of hours per day, the WCD was worn was 14.1 h. The risk of SCD was 1.6% in the WCD group compared to 2.4% in the control group ($P = 0.18$). All-cause mortality in the WCD group was 3.1% compared to 4.9% in the control group ($P = 0.04$)^[67] (Table 7).

DISCUSSION

The risk of SCD in various groups of patients has been well studied. This has led to the development of clear criteria for ICD implantation^[23]. There is data on various subgroups of patients that quantifies the magnitude of known risk factors for SCD (post MI, LQTS, HCM and LVSD). There are clear guidelines on the use of ICD in these groups of patients but a lack of clear guidelines for WCD therapy. This study has identified risk factors for several groups of patients who may not qualify for an ICD (due to the risk associated with implantation) but could benefit from WCD. These risk factors may help select patient for WCD therapy.

In patients who have recently had an MI with severe LVSD, guidelines recommend primary prevention with an ICD should be delayed for 40 d as the degree of myocardial recovery is uncertain in the acute period. This leaves certain patients without the best possible treatment if they were to have a further episode of VT/VF or patients who develop VT/VF later as a result of left ventricular dysfunction resulting from an MI. Patients post-MI are at increased risk of SCD. Several factors are associated with this increased risk of SCD. These risk factors could be used to select patient who may benefit from WCD post MI and if their risk remains high, they could be offered an ICD at 40 d. In addition, the DINAMIT study looked at early ICD implantation within 6-40 d *vs* optimal medical therapy. The DINAMIT study showed a reduction in arrhythmic death with early ICD implantation but no effect on overall mortality^[68]. These results do raise the question of whether there are device related

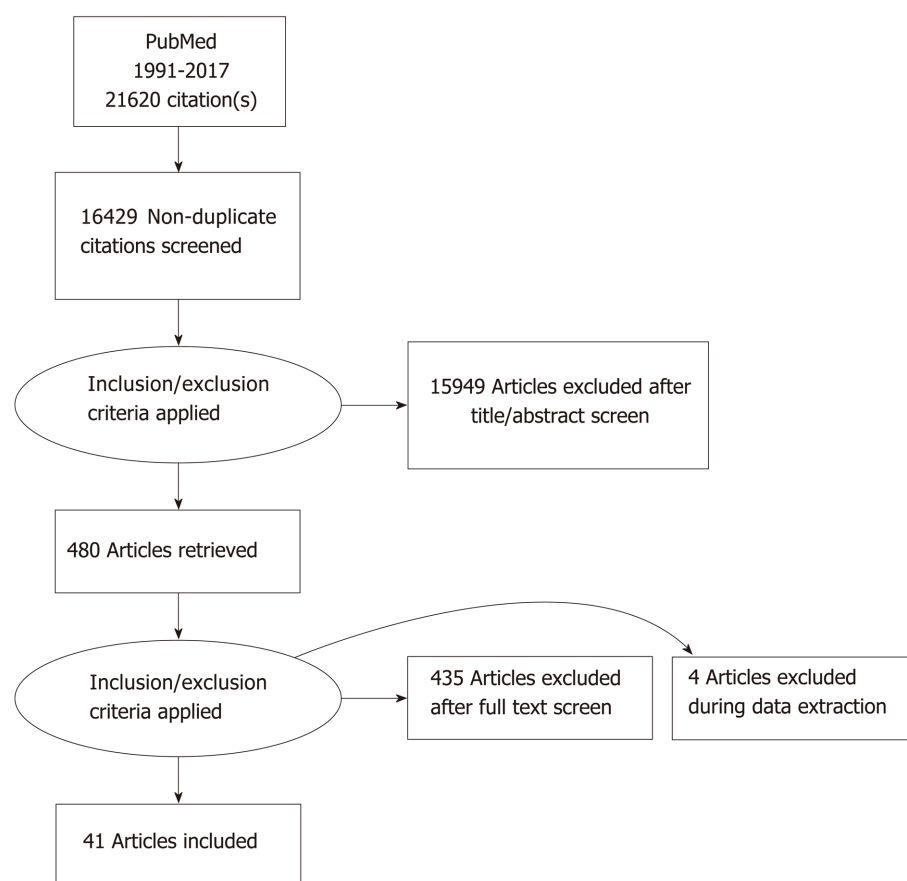


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

deaths that may reduce the overall mortality benefit such as device infections, procedural complications *etc.* These risks would not be present with WCD as there are no procedural risks associated with these devices. Some studies have advocated differentiating ICD implantation in the setting of acute MI based on whether the VT/VF occurred within 48 h in which case it could be attributed to acute MI and the treatment was revascularisation or if it occurred after 48 h in the absence of recurrent ischemia then these patients needed ICD implantation on the basis of secondary prevention and the 40 d rule in guidelines shouldn't apply^[69]. These patients could also potentially be covered by using a WCD until the 40 d window has elapsed. In addition, the highest risk of SCD is within the first 30 d of an MI and so high-risk patients who have not yet suffered VT/VF may benefit from a WCD during this period^[30]. The risk factors identified in this study could be used to help select such patients.

In patients with LVSD, guidelines only recommend an ICD if EF is less than 35 percent. This is the group of patients who are at the highest risk of SCD from LVSD. Studies of heart failure patients with an EF between 30% and 35% have shown that these patients also benefit from ICD therapy and have a lower mortality than the same group of patients without an ICD^[70]. This would also lead one to believe that patients at higher EF with more high risk features may also benefit from having a defibrillator such patients could be offered a WCD as a lower risk option than ICD implantation. Similarly patients post-MI who develop severe LVSD are not offered a ICD and are sent home for a clinic review in 40 d to assess the degree of myocardial recovery during this period. This is potentially dangerous as the absolute risk of SCD during this period is about 4.9% which is similar to the risk of SCD in patients with HCM at which an ICD would be implanted these patients should probably all be offered a WCD during this time period^[24,60]. It is important to note, however, the results of the recent VEST trial looking at the risk of SCD in WCD patient *vs* controls in the first 90 d post MI. It did not show a statistically significant reduction in SCD (1.6% *vs* 2.4%, $P = 0.18$) but there was a trend to lower risk of SCD in the WCD group. It did show a reduction in overall mortality (3.1% *vs* 4.9%, $P = 0.04$). These results are the opposite

Table 3 Risk factors for sudden cardiac death post myocardial infarction

Risk factor studied	Relative risk of SCD	P value	Absolute SCD risk in cohort	Study size	Year	Country
Age						
Rao <i>et al</i> ^[24]	OR 1.03 (1.00-1.05) (Increasing age)	0.0163	4.9% in the 1 st month post MI	929	2012	India
Mehta <i>et al</i> ^[25]	OR 0.12; Standard error = 0.02 (Age per 1 year increase)	0.0001		2948	2001	North America
Abildstrom <i>et al</i> ^[26]	OR 1.56 (1.43-1.70) (Age per 10 years)	< 0.0001	5.3% at 1 year	5983	2002	Denmark
Female gender						
Rao <i>et al</i> ^[24]	OR 1.78 (1.02-2.85)	0.0042	4.9% in the 1st month post MI	929	2012	India
Greenland <i>et al</i> ^[27]	OR 1.72 (1.45-2.04)	< 0.0005		5839	1991	Israel
Greenland <i>et al</i> ^[27]	OR 1.32 (1.05-1.66) (Death at 1 year)	< 0.03		5839	1991	Israel
Ghaffari <i>et al</i> ^[28]	OR 1.76 (1.22-2.54) (univariate analysis)	0.002		1017	2017	Iran
Ghaffari <i>et al</i> ^[28]	OR 1.19 (0.77-1.8) (multivariate analysis)	0.407		1017	2017	Iran
Macintyre <i>et al</i> ^[29]	OR 1.09 (1.06 to 1.13) (Death at 1 year)	< 0.00001		201114	2001	UK
Male gender						
Abildstrom <i>et al</i> ^[26]	OR 1.34 (1.11-1.63)	< 0.005	5.3% at 1 year	5983	2002	Denmark
LV dysfunction						
Rao <i>et al</i> ^[24]	OR 2.35 (1.09-5.03) (Severe LV dysfunction ≤ 30%)	0.0292	4.9% in the 1st month post MI	929	2012	India
Solomon <i>et al</i> ^[30]	HR 1.21 (1.10 to 1.30) (LV depression by each 5 percentage points)		7% at 1 month post MI; 11% at 2 years post MI	14609	2005	North America, Europe and New Zealand
Klem <i>et al</i> ^[31]	HR 6.30 (1.40-28.00) (LVEF > 30% and significant scarring > 5% on CMRI compared to no scarring)	0.02		137	2012	USA
Klem <i>et al</i> ^[31]	HR 3.90 (1.20-13.10) (LVEF ≤ 30% and those with scar > 5% on CMRI compared to those with scarring)	0.03		137	2012	USA
Yeung <i>et al</i> ^[32]	HR 3.60 (1.46-8.75) (LVEF ≤ 30%)	< 0.01		610	2012	China
Chitnis <i>et al</i> ^[33]	OR 4.51 (2.20-9.24) (LVEF ≤ 35%)	< 0.0001	4% in those with EF > 35% at 1 year post MI; 8% in those with EF ≤ 35% at 1 year post MI	929	2014	India
Adabag <i>et al</i> ^[34]	HR 3.64 (1.71-7.75) (presence of heart failure based on the framingham criteria)	< 0.001		693	2008	USA
Right ventricular involvement						
Mehta <i>et al</i> ^[25]	OR 3.20 (2.40-4.10)	< 0.00001		2948	2001	Canada
Diabetes						
Yeung <i>et al</i> ^[32]	HR 1.90 (1.04-3.40)	0.04		610	2012	China
Junttila <i>et al</i> ^[35]	HR 3.80 (2.40-5.80)	< 0.001		3276	2010	Finland
Ventricular arrhythmia						

Maggioni <i>et al</i> ^[36]	RR 2.24 (1.22-4.08) (more than 10 premature ventricular beats per hour)	0.002	8676	1993	Italy
Maggioni <i>et al</i> ^[36]	RR 1.20 (0.80-1.79) (NSVT)		8676	1993	Italy
Mäkikallio <i>et al</i> ^[37]	HR 2.40 (1.30-4.40) (Ventricular premature complexes 10/h)	0.0049	2130	2005	Finland
Mäkikallio <i>et al</i> ^[37]	HR 3.30 (1.70-6.50) (NSVT)	< 0.0005	2130	2005	Finland
ECG features					
Mäkikallio <i>et al</i> ^[37]	HR 3.30 (1.70-6.50) (QRS ≥ 120 ms)	0.0004	2130	2005	Finland
Zimetbaum <i>et al</i> ^[38]	HR 1.44 (1.11-1.88) (Non-specific intraventricular conduction delay)	0.0069	1638	2004	USA
Zimetbaum <i>et al</i> ^[38]	HR 1.49 (1.02-2.17) (LBBB)	0.0400	1638	2004	USA
Zimetbaum <i>et al</i> ^[38]	HR 1.35 (1.08-1.69) (LVH)	0.0082	1638	2004	USA
Siscovick <i>et al</i> ^[39]	OR 1.40 (1.00-2.00) (LVH)	0.02	688	1996	USA

SCD: Sudden cardiac death; MI: Myocardial infarction; HR: Hazard ratio; OR: Odds ratio; LV: Left ventricular; EF: Ejection fraction.

of the DINAMIT study this may be due to poor patient compliance with compliance decreasing with time during the study, which may have contributed to the lack of a significant reduction in SCD. It is important to note that at the time of SCD only 8 of 25 patients in the treatment group were wearing their WCD^[67]. Another group of patient who may benefit from a WCD are those who are awaiting heart transplantation. These patients should be offered an ICD based on current guidelines pre-transplantation; however, a WCD could be used as an alternative in these patients while they await their heart transplant.

In patients with non-ischaemic cardiomyopathy, the risk for SCD appears to be lower than those with ischaemic cardiomyopathy. They also do not appear to benefit from ICD therapy in the same way as patients with ischaemic cardiomyopathy as was shown by the recent defibrillator implantation in patients with nonischemic systolic heart failure (DANISH) study. The DANISH study showed no significant reduction in all-cause mortality between the ICD therapy and standard care group (21.6% *vs* 23.4%, $P = 0.28$). It did show a reduction in sudden cardiac death in the ICD group when compared to the standard care group ((4.3% *vs* 8.2%, $P = 0.005$)^[6]. This reinforces the need for a risk stratification tool to help determine individual risk factors that would make patients at higher risk for SCD. This study does help provide data that could be used to select not only patients for WCD but also patients who might benefit from an ICD in this patient group.

In patients with LQTS guidelines only recommend an ICD in these patients if they have survived an episode of VT/VF. This may be an unacceptable risk for some patients and a WCD could afford these patients with some protection until they meet criteria for a permanent ICD. One large study used 4 variables which included age, length of QTc, symptoms and the presence of cardiac arrest to determine the decision on whether patients were likely to benefit from therapy with an ICD in LQTS^[71]. Such a risk score could also be used to offer patients a choice between an ICD or a WCD.

Patients with HCM who have 5 year risk of death of less than 6% could be offered a WCD if they find the risk of SCD unacceptable. The ESC HCM risk-SCD calculator has a cut off of > 6% at which an ICD should be implanted. There may be patients who do not want an ICD and these patients could also be offered a WCD as an alternative.

A large WCD registry showed that WCD usage in patients with HCM and LQTS was safe, effective and associated with a high rate of compliance^[72]. A further large meta-analysis of WCD showed that WCD have a 95% success rate at terminating arrhythmias^[73]. The HCM risk-SCD calculator provides a very helpful measure of assessing a patient's risk of SCD and making treatment decisions in patients with HCM. It would be useful to develop risk calculators for SCD in other conditions,

Table 4 Risk factors for sudden cardiac death in heart failure

Risk factor studies	Relative risk of SCD	P value	Absolute SCD risk in cohort	Study size	Year	Country
Age						
Lee <i>et al</i> ^[40]	OR 1.70 (1.45-1.99) (Age per 10 unit increase)	< 0.001		4031	2003	Canada
Cowie <i>et al</i> ^[41]	HR 1.26 (1.01 to 1.57) (Age per 10 year increase)	0.04		220	2000	UK
Taylor <i>et al</i> ^[42]	HR 1.10 CI 1.09-1.10 (Increasing age)			6162	2012	UK
Male gender						
Taylor <i>et al</i> ^[42]	HR 1.50 (1.36-1.66)			6162	2012	UK
Vaartjes <i>et al</i> ^[43]	HR 1.21 (1.14-1.28) at 28 d; HR 1.26 (1.21-1.31) at 1 year; HR 1.28 (1.24-1.31) at year 5			29053	2010	Netherlands
Comorbidities						
Lee <i>et al</i> ^[40]	OR 1.43 (1.03-1.98) 30-day mortality (Cerebrovascular disease)	0.03		4031	2003	Canada
Lee <i>et al</i> ^[40]	OR 1.66 (1.22-2.27) (COPD)	0.002		4031	2003	Canada
Lee <i>et al</i> ^[40]	OR, 3.22 (1.08-9.65) (Cirrhosis)	0.04		4031	2003	Canada
Lee <i>et al</i> ^[40]	OR 2.54 (1.77-3.65) (Dementia)	< 0.001		4031	2003	Canada
Lee <i>et al</i> ^[40]	OR 1.86 (1.28-2.70) (Cancer)	0.001		4031	2003	Canada
Yoshihisa <i>et al</i> ^[44]	HR 3.01 (1.11-8.63) (COPD)	0.038		378	2014	Japan
Fisher <i>et al</i> ^[45]	RR 1.10 (1.06-1.14) Death at 1 year; RR 1.40 (1.28-1.52) death at 5 years (COPD)			9748	2015	USA
Atrial fibrillation						
Taylor <i>et al</i> ^[44]	HR 1.55 (1.26-1.92)			6162	2012	UK
Ahmed <i>et al</i> ^[46]	HR 1.41 (1.08-1.83)			944	2005	USA
Corell <i>et al</i> ^[47]	HR 1.38 (1.07-1.78)	0.01		1019	2007	Denmark
Middlekauff <i>et al</i> ^[48]	HR 0.89 (0.55-1.23)	0.013		390	1991	USA
Ventricular arrhythmia						
Doval <i>et al</i> ^[49]	RR 2.77 (1.78-4.44) (NSVT)	< 0.001	23.7% at 2 years in those with NSVT; 8.8% at 2 years in those without NSVT	516	1996	Argentina
Doval <i>et al</i> ^[49]	RR 3.37 (1.57-7.25) (Couplets)	< 0.0005	23.7% at 2 years in those with NSVT; 8.8% at 2 years in those without NSVT	516	1996	Argentina
Teerlink <i>et al</i> ^[50]	RR 1.16 (1.09-1.24) (NSVT)	0.001	13% at 2 years	1080	2000	USA
Szabó <i>et al</i> ^[51]	RR 3.50 (1.54-7.98) (VT)	0.003		211	1994	Netherlands
Szabó <i>et al</i> ^[51]	RR 2.68 (1.11-6.48) (Freq. VT > 144 beats/min)	0.029		211	1994	Netherlands
Szabó <i>et al</i> ^[51]	RR 3.89 (1.61-9.43) (Length VT > 2s)	0.003		211	1994	Netherlands
Echocardiographic variables						
Taylor <i>et al</i> ^[42]	HR 1.80 (1.55-2.10) (EF < 40% vs > 50%)			6162	2012	UK

Taylor <i>et al</i> ^[42]	HR 1.29 (1.11–1.50) (EF 40%–50% <i>vs</i> > 50%)		6162	2012	UK
Shadman <i>et al</i> ^[52]	OR 1.15 (EF per 10% decrease)	0.005	9885	2015	USA
Quiñones <i>et al</i> ^[53]	RR 2.75 (1.62–4.66) (1-SD difference in LV Mass)	0.0002	1209	2000	USA
Quiñones <i>et al</i> ^[53]	RR 1.84 (1.08–3.15) (1-SD difference in LA Diameter)	0.03	1209	2000	USA
Quiñones <i>et al</i> ^[53]	RR 2.73 (1.43–5.20) (1-SD difference in lv end systolic dimension)	0.003	1209	2000	USA
Grayburn <i>et al</i> ^[54]	HR 1.01 (1.00–1.01) (LV end-diastolic volume index)	0.0012	336	2005	USA
Deranged kidney function					
Grayburn <i>et al</i> ^[54]	HR 2.023 (1.24–3.32)	0.0052	336	2005	USA
Cowie <i>et al</i> ^[41]	HR 2.64 (1.87–3.74)	< 0.001	220	2000	UK

SCD: Sudden cardiac death; HR: Hazard ratio; OR: Odds ratio; LV: Left ventricular; EF: Ejection fraction.

which are more common and have a much larger impact on global mortality. This would provide patients and doctors with more information to make the best decision regarding their care.

The following groups of patients could also benefit from WCD therapy; patients who have an explanted ICD for infective endocarditis and must wait a certain time period before reinsertion, patients who have a risk of SCD but have a lower absolute risk such that the cost and risk of ICD insertion can't be justified, patients in remote areas where there is no expertise for ICD insertion, patients with myocarditis, patients with takotsubo cardiomyopathy, patients with peripartum cardiomyopathy, patients with advanced stage chronic kidney disease and children and young adults with channelopathies. The risk factors compiled in this review article could be used to help risk stratify many of these patients. The risk factors for patients post MI could be extrapolated to patients with takotsubo cardiomyopathy and myocarditis as all these processes involve an acute myocardial injury and so could be expected to have similar risk factors for SCD. In addition, the risk factors for LVSD could be extrapolated to patients with peripartum cardiomyopathy and those awaiting heart transplantation to determine high risk patients who may benefit from a WCD. There is potentially large scope for the use of WCD in carefully selected patient populations. One of the key disadvantages to WCD is the dependence on patient compliance for successful therapy as patients may decide to not wear the WCD, which can be a key limiting factor in its success.

In conclusion, we have identified multiple risk factors for sudden cardiac death in various conditions that could be used to help select patients for WCD therapy. The WCD is a landmark development that provides patients and physicians an additional therapy for the treatment of SCD; however, it is underutilized due to a lack of clear guidelines governing its usage^[74]. SCD remains a common cause of death and continued effort must be made to try and develop more targeted approaches to treatment for SCD.

Table 5 Risk factors for sudden cardiac death in the long QT syndrome

Risk factor studied	Relative risk of SCD	P value	Absolute SCD risk in cohort	Study size	Year	Country
Female gender						
Sauer <i>et al</i> ^[55]	HR 2.68 (1.10–6.50)	< 0.05	Risk between ages of 18–40: LQTS1 4.9%; LQTS2 8.0%; LQTS3 4.9%	812	2007	USA
QTc interval						
Sauer <i>et al</i> ^[55]	HR 3.34 (1.49–7.49) (QTc 500–549 ms <i>vs</i> ≤ 499 ms)	< 0.01	Risk between ages of 18–40: LQTS1 4.9%; LQTS2 8.0%; LQTS3 4.9%	812	2007	USA
Sauer <i>et al</i> ^[55]	HR 6.35 (2.82–14.32) (QTc ≥ 550 ms <i>vs</i> ≤ 499 ms)	< 0.01	Risk between ages of 18–40: LQTS1 4.9%; LQTS2 8.0%; LQTS3 4.9%	812	2007	USA
Moss <i>et al</i> ^[56]	HR 1.05 (1.02–1.09) (QTc per 0.01 units)	< 0.01		1496	1991	USA
Priori <i>et al</i> ^[57]	RR 5.34 (2.82–10.13) [QTc in the third quartile (469 to 498 ms)]		Risk between ages 12–40 was 13% over 28 years	580	2003	Italy
Priori <i>et al</i> ^[57]	RR 8.36 (2.53–27.21) [QTc in the highest quartile (more than 498 ms)]		Risk between ages 12–40 was 13% over 28 years	580	2003	Italy
Goldenberg <i>et al</i> ^[58]	HR 36.53 (13.35–99.95) (LQTS with prolonged QTc interval <i>vs</i> unaffected family members)	< 0.001		3386	2012	USA, Europe, Japan and Israel
Goldenberg <i>et al</i> ^[58]	HR 10.25 (3.34–31.46) (LQTS with normal-range QTc interval <i>vs</i> unaffected family members)	< 0.001		3386	2012	USA, Europe, Japan and Israel
Previous history of cardiac events						
Sauer <i>et al</i> ^[55]	HR 5.10 (2.50–10.39) (Interim time dependant syncope <i>vs</i> no interim syncope)	< 0.01	Risk between ages of 18–40: LQTS1 4.9%; LQTS2 8.0%; LQTS3 4.9%	812	2007	USA
Moss <i>et al</i> ^[56]	HR 3.10 (1.30–7.20) (History of cardiac event)	< 0.01		1496	1991	USA
Genotype						
LQTS 3						
Priori <i>et al</i> ^[57]	RR 2.76 (1.01–7.51) (Male sex)		Risk between ages 12–40 was 13% over 28 years	580	2003	Italy
Priori <i>et al</i> ^[57]	RR of 1.80 (1.07–3.04) (mutation at the LQT3 locus)		Risk between ages 12–40 was 13% over 28 years	580	2003	Italy
LQTS 2						
Priori <i>et al</i> ^[57]	RR 1.61 (1.16–2.25) (LQT2 locus)		Risk between ages 12–40 was 13% over 28 years	580	2003	Italy
LQTS 1						
Goldenberg <i>et al</i> ^[58]	HR 9.88 (1.26–37.63) (LQTS 1 mutation and normal QTc)	0.03		3386	2012	USA, Europe, Japan and Israel
Heart rate						

Moss <i>et al</i> ^[56]	HR 1.02 (1.00-1.03) (Resting heart rate less than 60 beats/min)	0.01	1496	1991	USA
Niemeijer <i>et al</i> ^[59]	Bazett: HR 2.23 (1.17-4.24) Fridericia: HR 6.67 (2.96-15.06) (Consistent Qtc interval prolongation)		3484	2015	Netherlands

SCD: Sudden cardiac death; LQTS: Long QT syndrome; QTc: QT corrected interval; HR: Hazard ratio; OR: Odds ratio; LV: Left ventricular; EF: Ejection fraction.

Table 6 Risk factors for sudden cardiac death in patients with hypertrophic cardiomyopathy

Risk factor studied	Relative risk of SCD	P value	Absolute SCD risk in cohort	Study size	Year	Country
Age						
O'Mahony <i>et al</i> ^[60]	HR 0.99 (0.98-1.00) (Age 42 ± 15)	0.007	5% at 5 years	3675	2014	Europe
Syncope						
Liu <i>et al</i> ^[61]	HR 2.31 (1.22-4.38)			12146	2017	USA, China
O'Mahony <i>et al</i> ^[60]	HR 2.33 (1.69-3.19)	< 0.001	5% at 5 years	3675	2014	Europe
Christiaans <i>et al</i> ^[62]	HR 2.68 (0.97-4.38)			9357	2010	Netherlands, UK
Family history of SCD						
Christiaans <i>et al</i> ^[62]	HR 1.27 (1.16-1.38)			9357	2010	Netherlands, UK
O'Mahony <i>et al</i> ^[60]	HR 1.76 (1.32-2.24)	<0.001	5% at 5 years	3675	2014	Europe
Liu <i>et al</i> ^[61]	HR 2.34 (1.46- 3.75)			12146	2017	USA, China
Abnormal blood pressure response during exercise						
Liu <i>et al</i> ^[61]	HR 1.38 (0.65-2.89) (BP dropping on exercise)			12146	2017	USA, China
Christiaans <i>et al</i> ^[62]	HR 1.30 (0.64-1.96) (BP dropping on exercise)			9357	2010	Netherlands, UK
Non sustained ventricular tachycardia						
Liu <i>et al</i> ^[61]	HR 2.92 (1.97-4.33)			12146	2017	USA, China
Sugrue <i>et al</i> ^[63]	HR 3.36 (1.00-11.35)	0.05		52	2017	USA
O'Mahony <i>et al</i> ^[60]	HR 2.53 (1.85-3.47)	< 0.001	5% at 5 years	3675	2014	Europe
Christiaans <i>et al</i> ^[62]	HR 2.89 (2.21-3.58)			9357	2010	Netherlands, UK
Left ventricular wall thickness/hypertrophy						
Liu <i>et al</i> ^[61]	HR3.17 (1.64-6.12) (Maximum LV wall thickness ≥ 30 mm)			12146	2017	USA, China
Maeda <i>et al</i> ^[64]	HR 1.21 (1.04-1.39) (Maximum left ventricular wall thickness per 1-mm increase)	0.011		593	2016	Japan
O'Mahony <i>et al</i> ^[60]	HR 1.05 (1.03-1.07) (Maximal LV wall thickness in mm 21.5 ± 6)	< 0.001	5% at 5 years	3675	2014	Europe
Christiaans <i>et al</i> ^[62]	HR 3.10 (1.81-4.40) (LVH ≥ 20 mm)			9357	2010	Netherlands, UK
Left ventricular outflow tract obstruction						
Liu <i>et al</i> ^[61]	HR 2.41 (1.55-3.73)			12146	2017	USA, China
O'Mahony <i>et al</i> ^[60]	HR 1.01 (1.00-1.01) [LVOT Gradient mmHG 18 (6-58)]	0.005	5% at 5 years	3675	2014	Europe
Left atrial diameter						

O'Mahony <i>et al</i> ^[60]	HR 1.04 (1.02-1.05) (LA diameter in mm 46.2 ± 9)	< 0.001	5% at 5 years	3675	2014	Europe
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SCD: Sudden cardiac death; LVOT: Left ventricular outflow tract; HR: Hazard ratio; OR: Odds ratio; LV: Left ventricular; EF: Ejection fraction.

Table 7 Summary of wearable cardioverter defibrillator studies

Study	General findings	Survival post shock
Wearable cardioverter-defibrillator use in patients perceived to be at high risk early post-myocardial infarction ^[65]	99 out of 8453 patients received 114 inappropriate shocks. None of the inappropriate shocks induced arrhythmias. The inappropriate shock rate was 0.006 shocks per patient month of use.	67% for those with VT/VF; 62% for those treated for PMVT/VF
Aggregate national experience with the wearable cardioverter defibrillator vest: event rates, compliance and survival ^[66]	Inappropriate shocks occurred in 67/3569 (1.9%) patients	90% for VT/VF events; 73.6% for all events
Vest Prevention of Early Sudden Death Trial ^[67]	Inappropriate shocks: 0.6%; Appropriate shocks: 1.4%; Hours/day WCD worn: 14.1	Risk of SCD (WCD <i>vs</i> Control): 1.6% <i>vs</i> 2.4%, <i>P</i> = 0.18. All-cause mortality (WCD <i>vs</i> Control): 3.1% <i>vs</i> 4.9%, <i>P</i> = 0.04

VT: Ventricular tachycardia; VF: Ventricular fibrillation; WCD: Wearable cardioverter defibrillator; SCD: Sudden cardiac death.

ARTICLE HIGHLIGHTS

Research background

There are many groups of patients including those post myocardial infarction (MI), patients with hypertrophic cardiomyopathy (HCM), patients with left ventricular systolic dysfunction (LVSD) and patients with long QT syndrome (LQTS) who are at high risk of sudden cardiac death (SCD) that do not meet criteria for implantable cardioverter defibrillator (ICD) implantation. This study looked at risk factors for SCD in these patient groups, which could be used as a method for identifying patients at high risk for SCD. Patients at high risk for SCD but not meeting conventional indications for ICD therapy could be offered a WCD until an ICD was indicated.

Research motivation

There is a need for more refined risk calculators to determine the risk of SCD in various conditions as is already present for patients with HCM. There is a requisite for more refined risk calculators to determine the risk of SCD in various conditions such as patients post MI, patients with LVSD, patients with LQTS and other channelopathies, patients with post-partum cardiomyopathy, patients with takotsubo cardiomyopathy, patients with myocarditis and patients with advanced chronic renal failure. This would allow better selection of patients at high risk of SCD and allow physicians to offer their patients the best treatment for each specific patient based on their individual risk.

Research objectives

The main objectives of our study were to collate the risk factors for SCD in specific patient groups as mentioned previously. These risk factors were to be used as a guide to help in determining high-risk patients that may benefit from WCD therapy. This to the best of our knowledge is the first attempt made at collating risk factors for SCD for various conditions in one place. This should help future studies to build on this data and hopefully give rise to risk calculators for SCD in these and many more conditions.

Research methods

We performed a literature search on PubMed. The studies were then selected according to whether they met the inclusion criteria for our review article. The inclusion criteria were any study that reported risk factors for SCD in patients with LVSD, LQTS, HCM or post MI. There was no restriction on age, gender, geographical area or date of publication. Studies had to be reported in English. Any studies where the risk of SCD was not quantified by either a hazard ratio, odds ratio or relative risk were excluded. The relevant risk factors for SCD in the 4 main conditions were then collected and tabulated in table format.

Research results

We collected a large number of risk factors for SCD in all 4 patients groups. These risk factors provide a robust method of assessing a patients risk for SCD. The study also looked at several WCD studies which showed that WCD were effective at terminating VT/VF but were limited in their effectiveness by patient compliance.

Research conclusions

This review shows that there are many risk factors for SCD that to the best of our knowledge

have never been compiled together in one place such as this study has done. We also show that WCD are effective therapies for ventricular tachycardia/ventricular fibrillation, but are limited by patient compliance.

This should help in the development of more precise risk calculators for sudden cardiac death such as the existing risk calculator for HCM. This should also help select patients who may benefit from WCD.

Research perspectives

This study demonstrates the wealth of data present that could be used to create precise risk calculators for SCD. These risk calculators could be used to determine patients at high risk for SCD. It could be used to select which patients need an ICD and which could benefit from a WCD. Further study should be in the form of a meta-analysis to allow this area of research to move forward.

REFERENCES

- 1 Myerburg RJ, Castellanos A. Sudden cardiac death, Cardiac electrophysiology: From cell to bedside. Philadelphia: Saunders Elsevier 2009; 797–808
- 2 Nadkarni VM, Larkin GL, Peberdy MA, Carey SM, Kaye W, Mancini ME, Nichol G, Lane-Truitt T, Potts J, Ornato JP, Berg RA; National Registry of Cardiopulmonary Resuscitation Investigators. First documented rhythm and clinical outcome from in-hospital cardiac arrest among children and adults. *JAMA* 2006; **295**: 50-57 [PMID: 16391216 DOI: 10.1001/jama.295.1.50]
- 3 Meaney PA, Nadkarni VM, Kern KB, Indik JH, Halperin HR, Berg RA. Rhythms and outcomes of adult in-hospital cardiac arrest. *Crit Care Med* 2010; **38**: 101-108 [PMID: 19770741 DOI: 10.1097/CCM.0b013e3181b43282]
- 4 Bayés de Luna A, Coumel P, Leclercq JF. Ambulatory sudden cardiac death: mechanisms of production of fatal arrhythmia on the basis of data from 157 cases. *Am Heart J* 1989; **117**: 151-159 [PMID: 2911968 DOI: 10.1016/0002-8703(89)90670-4]
- 5 Myerburg RJ, Kessler KM, Castellanos A. Sudden cardiac death. Structure, function, and time-dependence of risk. *Circulation* 1992; **85**: 12-10 [PMID: 1728501]
- 6 Chadda K, Goldstein S, Byington R, Curb JD. Effect of propranolol after acute myocardial infarction in patients with congestive heart failure. *Circulation* 1986; **73**: 503-510 [PMID: 3948357 DOI: 10.1161/01.CIR.73.3.503]
- 7 Hulleman M, Berdowski J, de Groot JR, van Dessel PF, Borleffs CJ, Blom MT, Bardai A, de Cock CC, Tan HL, Tijssen JG, Koster RW. Implantable cardioverter-defibrillators have reduced the incidence of resuscitation for out-of-hospital cardiac arrest caused by lethal arrhythmias. *Circulation* 2012; **126**: 815-821 [PMID: 22869841 DOI: 10.1161/CIRCULATIONAHA.111.089425]
- 8 van Alem AP, Chapman FW, Lank P, Hart AA, Koster RW. A prospective, randomised and blinded comparison of first shock success of monophasic and biphasic waveforms in out-of-hospital cardiac arrest. *Resuscitation* 2003; **58**: 17-24 [PMID: 12867305 DOI: 10.1016/S0300-9572(03)00106-0]
- 9 Zoll PM, Linenthal AJ, Gibson W, Paul MH, Norman LR. Termination of ventricular fibrillation in man by externally applied electric countershock. *N Engl J Med* 1956; **254**: 727-732 [PMID: 13309666 DOI: 10.1056/NEJM195604192541601]
- 10 Soar J, Nolan JP, Böttiger BW, Perkins GD, Lott C, Carli P, Pellis T, Sandroni C, Skrifvars MB, Smith GB, Sunde K, Deakin CD; Adult advanced life support section Collaborators. European Resuscitation Council Guidelines for Resuscitation 2015: Section 3. Adult advanced life support. *Resuscitation* 2015; **95**: 100-147 [PMID: 26477701 DOI: 10.1016/j.resuscitation.2015.07.016]
- 11 Mirowski M, Reid PR, Mower MM, Watkins L, Gott VL, Schauble JF, Langer A, Heilman MS, Kolenik SA, Fischell RE, Weisfeldt ML. Termination of malignant ventricular arrhythmias with an implanted automatic defibrillator in human beings. *N Engl J Med* 1980; **303**: 322-324 [PMID: 6991948 DOI: 10.1056/NEJM198008073030607]
- 12 Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, Levine JH, Saksena S, Waldo AL, Wilber D, Brown MW, Heo M. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. *N Engl J Med* 1996; **335**: 1933-1940 [PMID: 8960472 DOI: 10.1056/NEJM199612263352601]
- 13 Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G. A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. *N Engl J Med* 1999; **341**: 1882-1890 [PMID: 10601507 DOI: 10.1056/NEJM199912163412503]
- 14 Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, Daubert JP, Higgins SL, Brown MW, Andrews ML; Multicenter Automatic Defibrillator Implantation Trial II Investigators. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med* 2002; **346**: 877-883 [PMID: 11907286 DOI: 10.1056/NEJMoa013474]
- 15 Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, Domanski M, Troutman C, Anderson J, Johnson G, McNulty SE, Clapp-Channing N, Davidson-Ray LD, Fraulo ES, Fishbein DP, Luceri RM, Ip JH; Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med* 2005; **352**: 225-237 [PMID: 15659722 DOI: 10.1056/NEJMoa043399]
- 16 Køber L, Thune JJ, Nielsen JC, Haarbø J, Videbæk L, Korup E, Jensen G, Hildebrandt P, Steffensen FH, Bruun NE, Eiskjær H, Brandes A, Thøgersen AM, Gustafsson F, Egstrup K, Videbæk R, Hassager C, Svendsen JH, Høfsten DE, Torp-Pedersen C, Pehrson S; DANISH Investigators. Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure. *N Engl J Med* 2016; **375**: 1221-1230 [PMID: 27571011 DOI: 10.1056/NEJMoa1608029]
- 17 Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. *N Engl J Med* 1997; **337**: 1576-1583 [PMID: 9411221 DOI: 10.1056/NEJM199711273372202]

- 18 **Connolly SJ**, Gent M, Roberts RS, Dorian P, Roy D, Sheldon RS, Mitchell LB, Green MS, Klein GJ, O'Brien B. Canadian implantable defibrillator study (CIDS): a randomized trial of the implantable cardioverter defibrillator against amiodarone. *Circulation* 2000; **101**: 1297-1302 [PMID: [10725290](#) DOI: [10.1161/01.CIR.101.11.1297](#)]
- 19 **Kuck KH**, Cappato R, Siebels J, Ruppel R. Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest: the Cardiac Arrest Study Hamburg (CASH). *Circulation* 2000; **102**: 748-754 [PMID: [10942742](#) DOI: [10.1161/01.CIR.102.7.748](#)]
- 20 **Kusumoto FM**, Calkins H, Boehmer J, Buxton AE, Chung MK, Gold MR, Hohnloser SH, Indik J, Lee R, Mehra MR, Menon V, Page RL, Shen WK, Slotwimer DJ, Stevenson LW, Varosy PD, Welikovich L. HRS/ACC/AHA expert consensus statement on the use of implantable cardioverter-defibrillator therapy in patients who are not included or not well represented in clinical trials. *Circulation* 2014; **130**: 94-125 [PMID: [24815500](#) DOI: [10.1161/CIR.0000000000000056](#)]
- 21 **Food and Drug Administration**. FDA Approves First Wearable Defibrillator. Available from: http://permanent.access.gpo.gov/lps1609/www.fda.gov/fdacs/departs/2002/202_upd.html#defib
- 22 **Francis J**, Reek S. Wearable cardioverter defibrillator: a life vest till the life boat (ICD) arrives. *Indian Heart J* 2014; **66**: 68-72 [PMID: [24581099](#) DOI: [10.1016/j.ihj.2013.12.050](#)]
- 23 **Priori SG**, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, Elliott PM, Fitzsimons D, Hatala R, Hindricks G, Kirchhof P, Kjeldsen K, Kuck KH, Hernandez-Madrid A, Nikolaou N, Norekvål TM, Spaulding C, Van Veldhuisen DJ; ESC Scientific Document Group. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). *Eur Heart J* 2015; **36**: 2793-2867 [PMID: [26320108](#) DOI: [10.1093/eurheartj/ehv316](#)]
- 24 **Rao HB**, Sastry BK, Korabathina R, Raju KP. Sudden cardiac death after acute ST elevation myocardial infarction: insight from a developing country. *Heart Asia* 2012; **4**: 83-89 [PMID: [27326036](#) DOI: [10.1136/heartasia-2012-010114](#)]
- 25 **Mehta SR**, Eikelboom JW, Natarajan MK, Diaz R, Yi C, Gibbons RJ, Yusuf S. Impact of right ventricular involvement on mortality and morbidity in patients with inferior myocardial infarction. *J Am Coll Cardiol* 2001; **37**: 37-43 [PMID: [11153770](#) DOI: [10.1016/S0735-1097\(00\)01089-5](#)]
- 26 **Abildstrom SZ**, Rask-Madsen C, Ottesen MM, Andersen PK, Rosthøj S, Torp-Pedersen C, Køber L; TRACE Study Group. Trandolapril cardiac evaluation. Impact of age and sex on sudden cardiovascular death following myocardial infarction. *Heart* 2002; **88**: 573-578 [PMID: [12433881](#) DOI: [10.1136/heart.88.6.573](#)]
- 27 **Greenland P**, Reicher-Reiss H, Goldbourt U, Behar S. In-hospital and 1-year mortality in 1,524 women after myocardial infarction. Comparison with 4,315 men. *Circulation* 1991; **83**: 484-491 [PMID: [1991367](#) DOI: [10.1161/01.CIR.83.2.484](#)]
- 28 **Ghaffari S**, Pourafkari L, Tajlil A, Bahmani-Oskoui R, Nader ND. Is female gender associated with worse outcome after ST elevation myocardial infarction? *Indian Heart J* 2017; **69** Suppl 1: S28-S33 [PMID: [28400036](#) DOI: [10.1016/j.ihj.2016.12.003](#)]
- 29 **MacIntyre K**, Stewart S, Capewell S, Chalmers JW, Pell JP, Boyd J, Finlayson A, Redpath A, Gilmour H, McMurray JJ. Gender and survival: a population-based study of 201,114 men and women following a first acute myocardial infarction. *J Am Coll Cardiol* 2001; **38**: 729-735 [PMID: [11527625](#) DOI: [10.1016/S0735-1097\(01\)01465-6](#)]
- 30 **Solomon SD**, Zelenkofske S, McMurray JJ, Finn PV, Velazquez E, Ertl G, Harsanyi A, Rouleau JL, Maggioni A, Kober L, White H, Van de Werf F, Pieper K, Califf RM, Pfeffer MA; Valsartan in Acute Myocardial Infarction Trial (VALIANT) Investigators. Sudden death in patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. *N Engl J Med* 2005; **352**: 2581-2588 [PMID: [15972864](#) DOI: [10.1056/NEJMoa043938](#)]
- 31 **Klem I**, Weinsaft JW, Bahnson TD, Hegland D, Kim HW, Hayes B, Parker MA, Judd RM, Kim RJ. Assessment of myocardial scarring improves risk stratification in patients evaluated for cardiac defibrillator implantation. *J Am Coll Cardiol* 2012; **60**: 408-420 [PMID: [22835669](#) DOI: [10.1016/j.jacc.2012.02.070](#)]
- 32 **Yeung CY**, Lam KS, Li SW, Lam KF, Tse HF, Siu CW. Sudden cardiac death after myocardial infarction in type 2 diabetic patients with no residual myocardial ischemia. *Diabetes Care* 2012; **35**: 2564-2569 [PMID: [22875229](#) DOI: [10.2337/dc12-0118](#)]
- 33 **Chitnis N**, Vooturi S, Hygriv Rao B. Sudden cardiac death early after ST elevation myocardial infarction with and without severe left ventricular dysfunction. *Indian Heart J* 2014; **66**: 569-573 [PMID: [25634386](#) DOI: [10.1016/j.ihj.2014.10.416](#)]
- 34 **Adabag AS**, Therneau TM, Gersh BJ, Weston SA, Roger VL. Sudden death after myocardial infarction. *JAMA* 2008; **300**: 2022-2029 [PMID: [18984889](#) DOI: [10.1001/jama.2008.553](#)]
- 35 **Junttila MJ**, Barthel P, Myerburg RJ, Mäkitallio TH, Bauer A, Ulm K, Kiviniemi A, Tulppo M, Perkiömäki JS, Schmidt G, Huikuri HV. Sudden cardiac death after myocardial infarction in patients with type 2 diabetes. *Heart Rhythm* 2010; **7**: 1396-1403 [PMID: [20682359](#) DOI: [10.1016/j.hrthm.2010.07.031](#)]
- 36 **Maggioni AP**, Zuanetti G, Franzosi MG, Rovelli F, Santoro E, Staszewsky L, Tavazzi L, Tognoni G. Prevalence and prognostic significance of ventricular arrhythmias after acute myocardial infarction in the fibrinolytic era. GISSI-2 results. *Circulation* 1993; **87**: 312-322 [PMID: [8093865](#) DOI: [10.1161/01.CIR.87.2.312](#)]
- 37 **Mäkitallio TH**, Barthel P, Schneider R, Bauer A, Tapanainen JM, Tulppo MP, Schmidt G, Huikuri HV. Prediction of sudden cardiac death after acute myocardial infarction: role of Holter monitoring in the modern treatment era. *Eur Heart J* 2005; **26**: 762-769 [PMID: [15778204](#) DOI: [10.1093/eurheartj/ehi188](#)]
- 38 **Zimetbaum PJ**, Buxton AE, Batsford W, Fisher JD, Hafley GE, Lee KL, O'Toole MF, Page RL, Reynolds M, Josephson ME. Electrocardiographic predictors of arrhythmic death and total mortality in the multicenter unsustained tachycardia trial. *Circulation* 2004; **110**: 766-769 [PMID: [15289365](#) DOI: [10.1161/01.CIR.0000139311.32278.32](#)]
- 39 **Siscovick DS**, Raghunathan TE, Rautaharju P, Psaty BM, Cobb LA, Wagner EH. Clinically silent electrocardiographic abnormalities and risk of primary cardiac arrest among hypertensive patients. *Circulation* 1996; **94**: 1329-1333 [PMID: [8822988](#) DOI: [10.1161/01.CIR.94.6.1329](#)]
- 40 **Lee DS**, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. *JAMA* 2003; **290**: 2581-2587 [PMID: [14625335](#) DOI: [10.1001/jama.290.19.2581](#)]

- 41 **Cowie MR**, Wood DA, Coats AJ, Thompson SG, Suresh V, Poole-Wilson PA, Sutton GC. Survival of patients with a new diagnosis of heart failure: a population based study. *Heart* 2000; **83**: 505-510 [PMID: 10768897 DOI: 10.1136/heart.83.5.505]
- 42 **Taylor CJ**, Roalfe AK, Iles R, Hobbs FD. Ten-year prognosis of heart failure in the community: follow-up data from the Echocardiographic Heart of England Screening (ECHOES) study. *Eur J Heart Fail* 2012; **14**: 176-184 [PMID: 22253455 DOI: 10.1093/eurjhf/hfr170]
- 43 **Vaartjes I**, Hoes AW, Reitsma JB, de Bruin A, Grobbee DE, Mosterd A, Bots MI. Age- and gender-specific risk of death after first hospitalization for heart failure. *BMC Public Health* 2010; **10**: 637 [PMID: 20969758 DOI: 10.1186/1471-2458-10-637]
- 44 **Yoshihisa A**, Takiguchi M, Shimizu T, Nakamura Y, Yamauchi H, Iwaya S, Owada T, Miyata M, Abe S, Sato T, Suzuki S, Oikawa M, Kobayashi A, Yamaki T, Sugimoto K, Kunii H, Nakazato K, Suzuki H, Saitoh S, Takeishi Y. Cardiovascular function and prognosis of patients with heart failure coexistent with chronic obstructive pulmonary disease. *J Cardiol* 2014; **64**: 256-264 [PMID: 24674751 DOI: 10.1016/j.jjcc.2014.02.003]
- 45 **Fisher KA**, Stefan MS, Darling C, Lessard D, Goldberg RJ. Impact of COPD on the mortality and treatment of patients hospitalized with acute decompensated heart failure: the Worcester Heart Failure Study. *Chest* 2015; **147**: 637-645 [PMID: 25188234 DOI: 10.1378/chest.14-0607]
- 46 **Ahmed A**, Perry GJ. Incident atrial fibrillation and mortality in older adults with heart failure. *Eur J Heart Fail* 2005; **7**: 1118-1121 [PMID: 16326363 DOI: 10.1016/j.ejheart.2004.12.004]
- 47 **Corell P**, Gustafsson F, Schou M, Markenvard J, Nielsen T, Hildebrandt P. Prevalence and prognostic significance of atrial fibrillation in outpatients with heart failure due to left ventricular systolic dysfunction. *Eur J Heart Fail* 2007; **9**: 258-265 [PMID: 17027330 DOI: 10.1016/j.ejheart.2006.08.004]
- 48 **Middlekauff HR**, Stevenson WG, Stevenson LW. Prognostic significance of atrial fibrillation in advanced heart failure. A study of 390 patients. *Circulation* 1991; **84**: 40-48 [PMID: 2060110 DOI: 10.1161/01.CIR.84.1.40]
- 49 **Doval HC**, Nul DR, Grancelli HO, Varini SD, Soifer S, Corrado G, Dubner S, Scapin O, Perrone SV. Nonsustained ventricular tachycardia in severe heart failure. Independent marker of increased mortality due to sudden death. GESICA-GEMA Investigators. *Circulation* 1996; **94**: 3198-3203 [PMID: 8989129 DOI: 10.1161/01.CIR.94.12.3198]
- 50 **Teerlink JR**, Jalaluddin M, Anderson S, Kukin ML, Eichhorn EJ, Francis G, Packer M, Massie BM. Ambulatory ventricular arrhythmias in patients with heart failure do not specifically predict an increased risk of sudden death. PROMISE (Prospective Randomized Milrinone Survival Evaluation) Investigators. *Circulation* 2000; **101**: 40-46 [PMID: 10618302 DOI: 10.1161/01.CIR.101.1.40]
- 51 **Szabó BM**, van Veldhuisen DJ, Crijns HJ, Wiesfeld AC, Hillege HL, Lie KI. Value of ambulatory electrocardiographic monitoring to identify increased risk of sudden death in patients with left ventricular dysfunction and heart failure. *Eur Heart J* 1994; **15**: 928-933 [PMID: 7925514 DOI: 10.1093/oxfordjournals.eurheartj.a060612]
- 52 **Shadman R**, Poole JE, Dardas TF, Mozaffarian D, Cleland JG, Swedberg K, Maggioni AP, Anand IS, Carson PE, Miller AB, Levy WC. A novel method to predict the proportional risk of sudden cardiac death in heart failure: Derivation of the Seattle Proportional Risk Model. *Heart Rhythm* 2015; **12**: 2069-2077 [PMID: 26142301 DOI: 10.1016/j.hrthm.2015.06.039]
- 53 **Quiñones MA**, Greenberg BH, Kopelen HA, Koipillai C, Limacher MC, Shindler DM, Shelton BJ, Weiner DH. Echocardiographic predictors of clinical outcome in patients with left ventricular dysfunction enrolled in the SOLVD registry and trials: significance of left ventricular hypertrophy. Studies of Left Ventricular Dysfunction. *J Am Coll Cardiol* 2000; **35**: 1237-1244 [PMID: 10758966 DOI: 10.1016/S0735-1097(00)00511-8]
- 54 **Grayburn PA**, Appleton CP, DeMaria AN, Greenberg B, Lowes B, Oh J, Plehn JF, Rahko P, St John Sutton M, Eichhorn EJ; BEST Trial Echocardiographic Substudy Investigators. Echocardiographic predictors of morbidity and mortality in patients with advanced heart failure: the Beta-blocker Evaluation of Survival Trial (BEST). *J Am Coll Cardiol* 2005; **45**: 1064-1071 [PMID: 15808765 DOI: 10.1016/j.jacc.2004.12.069]
- 55 **Sauer AJ**, Moss AJ, McNitt S, Peterson DR, Zareba W, Robinson JL, Qi M, Goldenberg I, Hobbs JB, Ackerman MJ, Benhorin J, Hall WJ, Kaufman ES, Locati EH, Napolitano C, Priori SG, Schwartz PJ, Towbin JA, Vincent GM, Zhang L. Long QT syndrome in adults. *J Am Coll Cardiol* 2007; **49**: 329-337 [PMID: 17239714 DOI: 10.1016/j.jacc.2006.08.057]
- 56 **Moss AJ**, Schwartz PJ, Crampton RS, Tzivoni D, Locati EH, MacCluer J, Hall WJ, Weitkamp L, Vincent GM, Garson A. The long QT syndrome. Prospective longitudinal study of 328 families. *Circulation* 1991; **84**: 1136-1144 [PMID: 1884444 DOI: 10.1161/01.CIR.84.3.1136]
- 57 **Priori SG**, Schwartz PJ, Napolitano C, Bloise R, Ronchetti E, Grillo M, Vicentini A, Spazzolini C, Nastoli J, Bottelli G, Folli R, Cappelletti D. Risk stratification in the long-QT syndrome. *N Engl J Med* 2003; **348**: 1866-1874 [PMID: 12736279 DOI: 10.1056/NEJMoa022147]
- 58 **Goldenberg I**, Horr S, Moss AJ, Lopes CM, Barsheshet A, McNitt S, Zareba W, Andrews ML, Robinson JL, Locati EH, Ackerman MJ, Benhorin J, Kaufman ES, Napolitano C, Platonov PG, Priori SG, Qi M, Schwartz PJ, Shimizu W, Towbin JA, Vincent GM, Wilde AA, Zhang L. Risk for life-threatening cardiac events in patients with genotype-confirmed long-QT syndrome and normal-range corrected QT intervals. *J Am Coll Cardiol* 2011; **57**: 51-59 [PMID: 21185501 DOI: 10.1016/j.jacc.2010.07.038]
- 59 **Niemeijer MN**, van den Berg ME, Deckers JW, Franco OH, Hofman A, Kors JA, Stricker BH, Rijnbeek PR, Eijgelsheim M. Consistency of heart rate-QTc prolongation consistency and sudden cardiac death: The Rotterdam Study. *Heart Rhythm* 2015; **12**: 2078-2085 [PMID: 26165945 DOI: 10.1016/j.hrthm.2015.07.011]
- 60 **O'Mahony C**, Jichi F, Pavlou M, Monserrat L, Anastasakis A, Rapezzi C, Biagini E, Gimeno JR, Limongelli G, McKenna WJ, Omar RZ, Elliott PM; Hypertrophic Cardiomyopathy Outcomes Investigators. A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCM risk-SCD). *Eur Heart J* 2014; **35**: 2010-2020 [PMID: 24126876 DOI: 10.1093/eurheartj/ehf439]
- 61 **Liu Q**, Li D, Berger AE, Johns RA, Gao L. Survival and prognostic factors in hypertrophic cardiomyopathy: a meta-analysis. *Sci Rep* 2017; **7**: 11957 [PMID: 28931939 DOI: 10.1038/s41598-017-12289-4]
- 62 **Christiaans I**, van Engelen K, van Langen IM, Birnie E, Bonzel GJ, Elliott PM, Wilde AA. Risk stratification for sudden cardiac death in hypertrophic cardiomyopathy: systematic review of clinical risk markers. *Europace* 2010; **12**: 313-321 [PMID: 20118111 DOI: 10.1093/europace/eup431]

- 63 **Sugrue A**, Killu AM, DeSimone CV, Chahal AA, Vogt JC, Kremen V, Hai J, Hodge DO, Acker NG, Geske JB, Ackerman MJ, Ommen SR, Lin G, Noseworthy PA, Brady PA. Utility of T-wave amplitude as a non-invasive risk marker of sudden cardiac death in hypertrophic cardiomyopathy. *Open Heart* 2017; **4**: e000561 [PMID: [28409011](#) DOI: [10.1136/openhrt-2016-000561](#)]
- 64 **Maeda R**, Minami Y, Haruki S, Kanbayashi K, Itani R, Suzuki A, Ejima K, Shiga T, Shoda M, Hagiwara N. Implantable cardioverter defibrillator therapy and sudden death risk stratification in hypertrophic cardiomyopathy patients with midventricular obstruction: A single-center experience. *Int J Cardiol* 2016; **214**: 419-422 [PMID: [27088403](#) DOI: [10.1016/j.ijcard.2016.03.231](#)]
- 65 **Epstein AE**, Abraham WT, Bianco NR, Kern KB, Mirro M, Rao SV, Rhee EK, Solomon SD, Szymkiewicz SJ. Wearable cardioverter-defibrillator use in patients perceived to be at high risk early post-myocardial infarction. *J Am Coll Cardiol* 2013; **62**: 2000-2007 [PMID: [23916930](#) DOI: [10.1016/j.jacc.2013.05.086](#)]
- 66 **Chung MK**, Szymkiewicz SJ, Shao M, Zishiri E, Niebauer MJ, Lindsay BD, Tchou PJ. Aggregate national experience with the wearable cardioverter-defibrillator: event rates, compliance, and survival. *J Am Coll Cardiol* 2010; **56**: 194-203 [PMID: [20620738](#) DOI: [10.1016/j.jacc.2010.04.016](#)]
- 67 **Olgin JE**, Pletcher MJ, Vittinghoff E, Wranicz J, Malik R, Morin DP, Zweibel S, Buxton AE, Elayi CS, Chung EH, Rashba E, Borggreffe M, Hue TF, Maguire C, Lin F, Simon JA, Hulley S, Lee BK; VEST Investigators. Wearable Cardioverter-Defibrillator after Myocardial Infarction. *N Engl J Med* 2018; **379**: 1205-1215 [PMID: [30280654](#) DOI: [10.1056/NEJMoa1800781](#)]
- 68 **Hohnloser SH**, Kuck KH, Dorian P, Roberts RS, Hampton JR, Hatala R, Fain E, Gent M, Connolly SJ; DINAMIT Investigators. Prophylactic use of an implantable cardioverter-defibrillator after acute myocardial infarction. *N Engl J Med* 2004; **351**: 2481-2488 [PMID: [15590950](#) DOI: [10.1056/NEJMoa041489](#)]
- 69 **Lim HS**, Lip GY, Tse HF. Implantable cardioverter defibrillator following acute myocardial infarction: the '48-hour' and '40-day' rule. *Europace* 2008; **10**: 536-539 [PMID: [18367548](#) DOI: [10.1093/europace/eun070](#)]
- 70 **Al-Khatib SM**, Hellkamp AS, Fonarow GC, Mark DB, Curtis LH, Hernandez AF, Anstrom KJ, Peterson ED, Sanders GD, Al-Khalidi HR, Hammill BG, Heidenreich PA, Hammill SC. Association between prophylactic implantable cardioverter-defibrillators and survival in patients with left ventricular ejection fraction between 30% and 35%. *JAMA* 2014; **311**: 2209-2215 [PMID: [24893088](#) DOI: [10.1001/jama.2014.5310](#)]
- 71 **Schwartz PJ**, Spazzolini C, Priori SG, Crotti L, Vicentini A, Landolina M, Gasparini M, Wilde AA, Knops RE, Denjoy I, Toivonen L, Mönnig G, Al-Fayyadh M, Jordaens L, Borggreffe M, Holmgren C, Brugada P, De Roy L, Hohnloser SH, Brink PA. Who are the long-QT syndrome patients who receive an implantable cardioverter-defibrillator and what happens to them?: data from the European Long-QT Syndrome Implantable Cardioverter-Defibrillator (LQTS ICD) Registry. *Circulation* 2010; **122**: 1272-1282 [PMID: [20837891](#) DOI: [10.1161/CIRCULATIONAHA.110.950147](#)]
- 72 **Kutyifa V**, Moss AJ, Klein H, Biton Y, McNitt S, MacKecknie B, Zareba W, Goldenberg I. Use of the wearable cardioverter defibrillator in high-risk cardiac patients: data from the Prospective Registry of Patients Using the Wearable Cardioverter Defibrillator (WEARIT-II Registry). *Circulation* 2015; **132**: 1613-1619 [PMID: [26316618](#) DOI: [10.1161/CIRCULATIONAHA.115.015677](#)]
- 73 **Nguyen E**. Wearable Cardioverter-defibrillators for the Prevention of Sudden Cardiac Death: A Meta-analysis. *J Innov Card Rhythm Manag* 2018 [DOI: [10.19102/icrm.2018.090506](#)]
- 74 **Pillarisetti J**, Emert M, Biria M, Chotia R, Guda R, Bommana S, Pimentel R, Vacek J, Dendi R, Berenbom L, Dawn B, Lakkireddy D. Under-Utilization of Implantable Cardioverter Defibrillators in Patients with Heart Failure - The Current State of Sudden Cardiac Death Prophylaxis. *Indian Pacing Electrophysiol J* 2016; **15**: 20-29 [PMID: [27186055](#) DOI: [10.1016/S0972-6292\(16\)30838-5](#)]

Utility of recognizing early electrocardiogram changes in bronchogenic Takotsubo cardiomyopathy: A case report

Maria Khan, Husam Watti, Khagendra Dahal, Paari Dominic

ORCID number: Maria Khan (0000-0002-4949-1221); Husam Watti (0000-0002-4234-1431); Khagendra Dahal (0000-0001-5335-0846); Paari Dominic (0000-0002-7843-375X).

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Maria Khan, Department of Internal Medicine, Louisiana State University Health Sciences Center Shreveport, Shreveport, LA 71130, United States

Husam Watti, Khagendra Dahal, Paari Dominic, Department of Cardiology, Louisiana State University Health Sciences Center Shreveport, Shreveport, LA 71130, United States

Corresponding author: Maria Khan, MD, Doctor, Department of Internal Medicine, Louisiana State University Health Sciences Center Shreveport, 1501 Kings Highway, Shreveport, LA 71130, United States. mkhan9@lsuhsc.edu

Telephone: +1-816-8638730

Abstract

BACKGROUND

Takotsubo cardiomyopathy (TCM) is a transient reversible systolic dysfunction, estimated to be the culprit in 1%-2% of patients presenting with clinical symptoms of acute coronary syndrome (ACS). TCM was previously thought to be indistinguishable from ACS on the basis of electrocardiogram (EKG) findings; many authors now describe specific EKG changes that distinguish TCM from ACS as well as aid in early recognition of TCM.

CASE SUMMARY

This unique case presentation illustrates an uncommon subtype of TCM, and very clearly exemplifies the specific EKG changes meant to aid in distinguishing TCM from ACS. A bronchogenic subtype of TCM has been proposed, given its prevalence and distinguishing features from TCM without pulmonary pathology; this case exemplifies that notion. The specific EKG changes of low QRS voltage and attenuation of the amplitude of the QRS complex are now being noted in the EKGs of TCM patients. This patient presented for worsening shortness of breath and increased productive cough; her EKG revealed ST elevations in leads V3-V6, and low voltage QRS complexes when compared to previous EKG from 12 wk ago; troponin peaked at 5.16 ng/mL. Left heart catheterization did not reveal significant lesions and left ventriculogram findings were consistent with TCM. Patient was treated for COPD exacerbation, her symptoms improved significantly; she was sent home on the appropriate medications.

CONCLUSION

This case exemplifies EKG changes noted in TCM patients who may aid in early detection and appropriate treatment of TCM.

Key words: Takotsubo cardiomyopathy; Apical ballooning; Case report; Early

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Core tip: This case report presents a unique opportunity to exemplify specific electrocardiogram (EKG) changes noted in patients with Takotsubo cardiomyopathy (TCM). Low QRS voltage and attenuation of the amplitude of the QRS complex have been noted in the EKGs of TCM patients. This case report presents a patient who had an EKG performed 12 wk prior to developing TCM and thus provides a recent EKG to compare the EKG changes noted during TCM.

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INTRODUCTION

Takotsubo cardiomyopathy (TCM) is characterized by reversible systolic dysfunction of the left ventricle in the absence of any significant obstructive coronary artery disease^[1]. Most commonly, the apical and the middle segments of the left ventricle are seen to be akinetic^[1]. Its clinical presentation is said to be indistinguishable from myocardial infarct^[2]. The gold standard used to differentiate acute coronary syndrome (ACS) from TCM is coronary angiography as it clearly shows if a significant obstructive lesion is present^[1]. Although some authors believe that it is not possible to differentiate ACS from TCM based of electrocardiogram (EKG) alone, many new case reports have been published that support the existence of unique EKG changes present only in TCM. This is a unique case presentation as it not only illustrates an uncommon subtype of TCM, but also very clearly exemplifies specific EKG changes meant to aid in distinguishing TCM from ACS. This was previously thought to be indistinguishable on the basis of electrocardiogram (EKG).

CASE PRESENTATION

Chief complaints

A 63 year-old Caucasian female presented to the emergency department for acute exacerbation of her chronic obstructive pulmonary disease (COPD). The patient had been experiencing 2 wk of worsening shortness of breath, productive cough and increased sputum production.

History of present illness

She had been using her inhalers more frequently at home and had increased her home oxygen to 3 liters, still with only minimal relief. On the day of presentation to the emergency department, the patient called an ambulance as she was concerned about her breathing.

History of past illness

She was noted to have a past medical history of COPD (on 2 liters home oxygen), coronary artery disease [status post right coronary artery (RCA) stent in 2000's], subarachnoid hemorrhage and tobacco abuse.

Personal and family history

No other family history or personal history was reported.

Physical examination upon admission

When the patient arrived in the emergency department, her physical exam revealed a blood pressure of 98/74 mmHg, pulse 101, temperature 97.5 °F (36.4 °C), temperature source Oral, respiratory rate of 27, and oxygen saturation of 95% on 3-4 liters of

oxygen. Scoliosis of spine was also noted. Patient was noted to be in respiratory distress.

Laboratory examinations

Initial troponin on presentation was 2.74 ng/mL and peaked at 5.16 ng/mL. Her renal function and hemoglobin were within normal limits. Her EKG showed sinus tachycardia with ST elevations in leads V3-V6 as well as low voltage QRS complexes when compared to previous EKG from 12 wk prior (Figures 1 and 2).

Cardiology was consulted for evaluation. The patient was advised to have an emergent left heart catheterization (LHC). However, the patient refused initially and wanted only medical management. She was not a candidate for thrombolysis due to history of subarachnoid hemorrhage.

Imaging examinations

A 2-D echocardiogram was done which showed mid and distal septal, anterior, lateral and apical wall akinesis concerning for ischemia in the left anterior descending (LAD) territory (Figure 3). The patient was then agreeable to have the cardiac angiogram 3 days after the initial presentation. Cardiac angiogram showed patent RCA stent with only mild luminal irregularities noted in the RCA. Left main was angiographically normal, as was the left circumflex. Mild to moderate stenotic lesions were noted in LAD, Diagonal 1 and Ramus Intermedius (Figure 4). A Left ventriculogram revealed hyperkinetic basal segments and akinesis of the apex and periapical segments consistent with TCM (Figure 5).

FINAL DIAGNOSIS

Based on the findings of the left ventriculogram, the LHC, and the EKG findings the patient was diagnosed with TCM.

TREATMENT

The patient was treated for COPD exacerbation. Her breathing improved, and she was back to her baseline 2 liters oxygen use. She was discharged to a long term acute care facility with medications ASA 81mg, Atorvastatin 80 mg, carvedilol 12.5 mg BID and losartan 25 mg. Her inhalers included tiotropium, fluticasone-salmeterol and ipratropium-albuterol. The patient was also started on sertraline 50 mg and instructed to continue her home medication of lorazepam 0.5 mg every 6 h as needed for anxiety.

OUTCOME AND FOLLOW-UP

Follow up Echo and EKG were planned; however, patient had passed away due to worsening of the pulmonary disease.

DISCUSSION

The Mayo Clinic diagnostic criteria, proposes that 4 criteria must be met in order to diagnose TCM: These criteria are, transient hypokinesis, akinesis or dyskinesis of the left ventricular mid segments, new ECG changes mimicking acute MI, absence of angiographic evidence of obstructive coronary disease, and absence of pheochromocytoma and myocarditis^[2].

It has been widely suggested that a bronchogenic sub type of TCM exists^[3]. Although not as common, there have been some reported cases of TCM in the setting of COPD or asthma^[4,5]. Some authors even estimate that pulmonary pathologies are suspected to be found in as high as 44% of TCM cases^[6], thus justifying the creation of a separate classification as a bronchogenic subtype. The disproportionate predominance of sympathetic activity during a COPD exacerbation has been noted as a possible trigger for TCM^[4]. Rajwani *et al*^[3] described 5 specific cases of bronchogenic TCM and noted some distinguishing features. The absence of chest pain, as with our patient, is noted as a main distinguishing feature of the bronchogenic subgroup of TCM. Progressive dyspnea was also a commonality noted in all 5 cases; this was also present in our patient.

TCM is commonly seen in postmenopausal women, as with our patient^[2]. Also in the setting of TCM, wall motion abnormalities are seen to extend beyond the

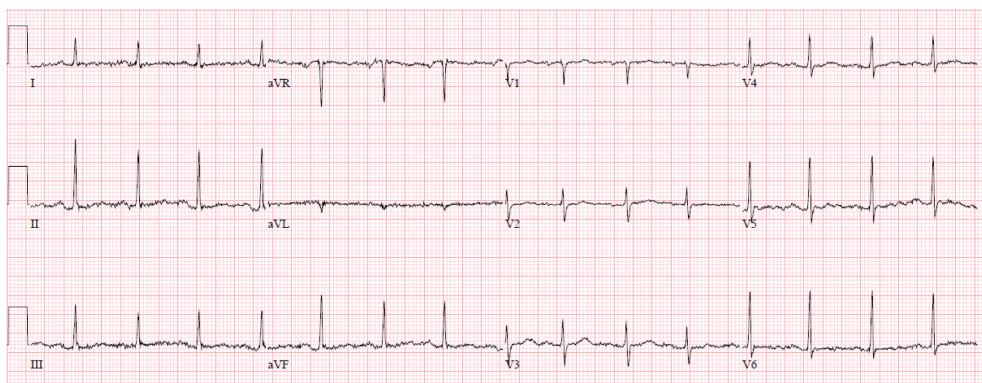


Figure 1 Electrocardiogram 12 wk before initial presentation.

distribution pattern of any single epicardial coronary artery, as seen in our case report^[2]. Though TCM is thought to be indistinguishable from ACS on the basis of EKG findings, Madias *et al*^[7] described a noticeably low voltage and attenuated QRS complexes in association with TCM seen in over 90% of the EKGs reviewed for published literature of TCM cases. Since then, many other cases have been reported showing marked QRS complex attenuation in the setting of TCM. In our case, a previous EKG from 12 wk before the patient presentation was available for comparison (Figures 1 and 2). Low QRS voltage (LQRSV), which is defined as ≤ 5 mm in limb leads and/or ≤ 10 mm in precordial leads, and significant attenuation of QRS complexes was appreciated. The likely mechanisms of this phenomenon was explained by author Madias who explored myocardial edema versus counterbalancing of depolarization vectors as the likely mechanisms and concluded that myocardial edema is the most likely cause of the LQRSV appreciated in EKGs of TCM patients^[7]. This was supported by review of multiple TCM cases where patients had cardiac MRI performed that revealed myocardial edema^[7]. Madias used Ohm's law (Voltage = Current \times Resistance) to explain how changes in the resistance of the electric conductor caused by myocardial edema can account for this phenomenon of LQRSV and attenuation of the amplitude of the QRS complex (AAQRS) since anything that alters resistance or current will result in changes in voltage^[7]. Extracardiac pathologies such as pulmonary congestion and pleural effusion, would also influence these changes^[7].

TCM is a transient reversible systolic dysfunction and is estimated to be the culprit in 1%-2% of patient presenting with clinical symptoms of a ACS^[2]. These patients do not require treatment with heparin drip and antiplatelet therapy thus it is important for clinicians to have a high level of suspicion to identify the correct etiology. As suggested by author Madias, utilizing EKG changes can aid in early identification of TCM and differentiation of TCM from ACS.

CONCLUSION

Though traditionally TCM was thought to be indistinguishable from ACS, many new case reports and papers have discussed using novel EKG criteria to aid in early recognition of TCM; this case exemplifies the characteristic EKG changes seen in TCM.

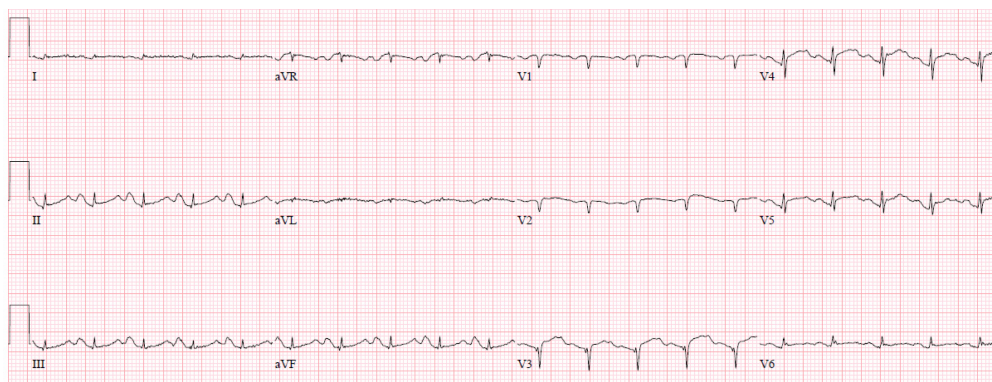


Figure 2 Electrocardiogram with acute changes on initial presentation. Significant attenuation of amplitude of QRS complexes noted diffusely.

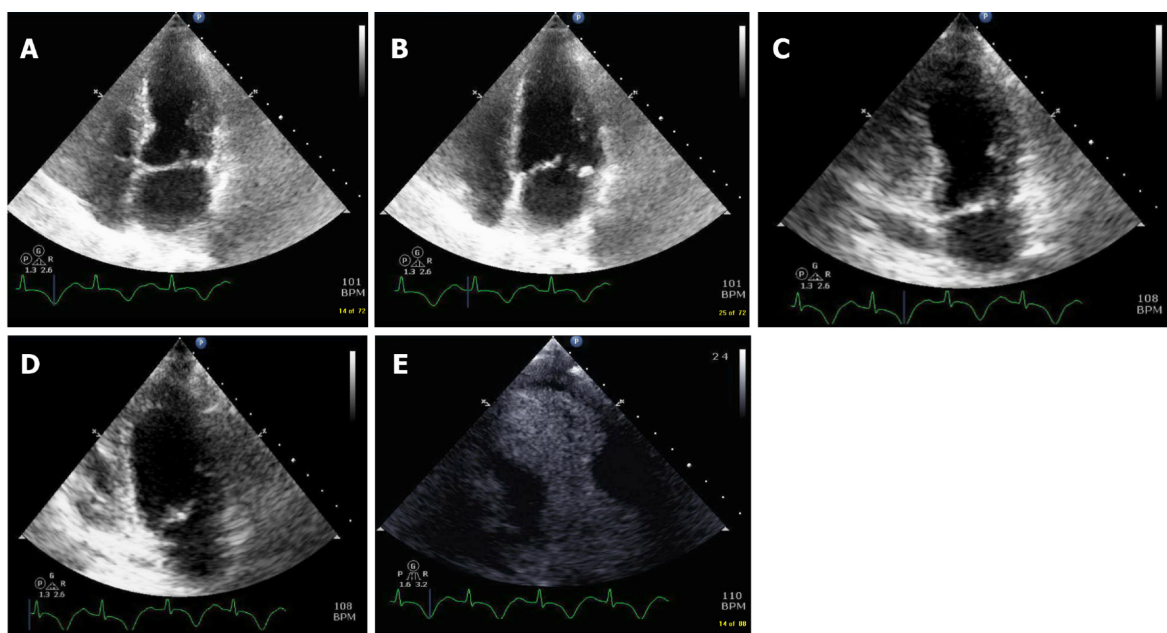


Figure 3 Four and 2 chamber view. A: 4 chamber view demonstrating akinesis of the septal and lateral apical segments; B: 4 chamber view demonstrating akinesis of the septal and lateral apical segments; C: 2-chamber view showing akinesis of anterior-inferior apical segments during systole; D: 2-chamber view showing akinesis of anterior and inferior apical segments during diastole; E: Contrast echocardiography showing akinesis of anterior and inferior apical segments.

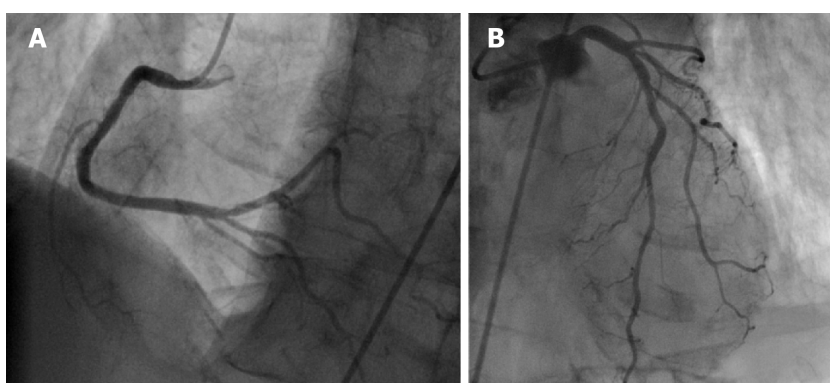


Figure 4 Coronary angiography of right coronary artery and left system demonstrating non obstructive coronary artery disease. A: Coronary angiography of right coronary artery demonstrating non obstructive coronary artery disease; B: Coronary angiography of the left system demonstrating non obstructive coronary artery disease.

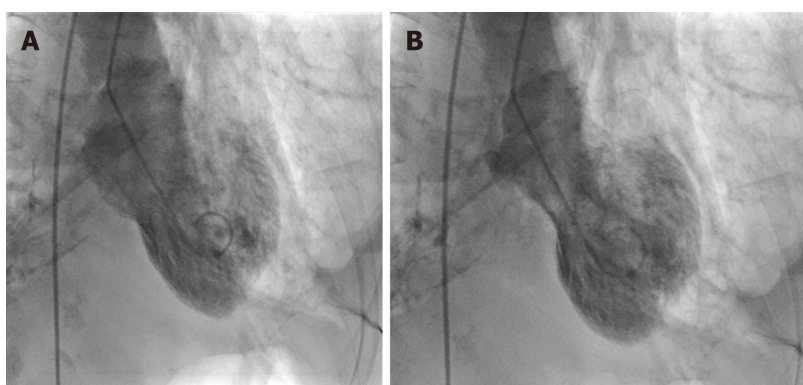


Figure 5 Left ventriculography demonstrating hyperkinetic basal segments and akinetic apex during diastole and systole. A: Left ventriculography demonstrating hyperkinetic basal segments and akinetic apex during diastole; B: Left ventriculogram demonstrating hyperkinetic basal segments and akinetic apex during systole.

REFERENCES

- 1 **Demirelli S**, Ermis E, Hatem E, Uslu A, Askin L. Focal mid-ventricular anterior ballooning: An unusual pattern of Takotsubo cardiomyopathy. *Intractable Rare Dis Res* 2015; **4**: 108-110 [PMID: [25984431](#) DOI: [10.5582/irdr.2015.01012](#)]
- 2 **Madhavan M**, Prasad A. Proposed Mayo Clinic criteria for the diagnosis of Tako-Tsubo cardiomyopathy and long-term prognosis. *Herz* 2010; **35**: 240-243 [PMID: [20582391](#) DOI: [10.1007/s00059-010-3339-x](#)]
- 3 **Rajwani A**, Adam Z, Hall JA. Bronchogenic stress cardiomyopathy: a case series. *Cardiology* 2015; **130**: 106-111 [PMID: [25612607](#) DOI: [10.1159/000369296](#)]
- 4 **Katsa I**, Christia P, Massera D, Faillace R. Recurrent Stress Cardiomyopathy During COPD Exacerbation: Are Beta-adrenergic Agonists Only to Blame? *Cureus* 2017; **9**: e1166 [PMID: [28507838](#) DOI: [10.7759/cureus.1166](#)]
- 5 **Manfredini R**, Fabbian F, Giorgi AD, Pala M, Menegatti AM, Parisi C, Misurati E, Tiseo R, Gallerani M, Salmi R, Bossone E. Heart and lung, a dangerous liaison-Tako-tsubo cardiomyopathy and respiratory diseases: A systematic review. *World J Cardiol* 2014; **6**: 338-344 [PMID: [24944763](#) DOI: [10.4330/wjc.v6.i5.338](#)]
- 6 **Hertting K**, Krause K, Härle T, Boczor S, Reimers J, Kuck KH. Transient left ventricular apical ballooning in a community hospital in Germany. *Int J Cardiol* 2006; **112**: 282-288 [PMID: [16325287](#) DOI: [10.1016/j.ijcard.2005.09.006](#)]
- 7 **Madias JE**. Transient attenuation of the amplitude of the QRS complexes in the diagnosis of Takotsubo syndrome. *Eur Heart J Acute Cardiovasc Care* 2014; **3**: 28-36 [PMID: [24562801](#) DOI: [10.1177/2048872613504311](#)]



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