

Cardiac structural and functional profile of patients with delayed QRS transition zone and sudden cardiac death

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Received 12 December 2015; accepted after revision 2 February 2016; online publish-ahead-of-print 19 March 2016

Aims

Delayed QRS transition zone in the precordial leads of the 12-lead electrocardiogram (ECG) has been recently associated with increased risk of sudden cardiac death (SCD), but the underlying mechanisms are unknown. We correlated echocardiographic findings with ECG and clinical characteristics to investigate how alterations in cardiac structure and function contribute to this risk marker.

Methods and results

From the ongoing population-based Oregon Sudden Unexpected Death Study (catchment population ~1 million), SCD cases with prior ECG available ($n = 627$) were compared with controls ($n = 801$). Subjects with delayed transition at V_5 or later were identified, and clinical and echocardiographic patterns associated with delayed transition were analysed. Delayed transition was present in 31% of the SCD cases and 17% of the controls. These subjects were older and more likely to have cardiovascular risk factors and history of myocardial infarction. Delayed transition was associated with increased left ventricular (LV) mass (122.7 ± 40.2 vs. 102.9 ± 33.7 g/m²; $P < 0.001$), larger LV diameter (53.3 ± 10.4 vs. 49.2 ± 8.0 mm; $P < 0.001$), and lower LV ejection fraction (LVEF) (46.4 ± 15.7 vs. $55.6 \pm 12.5\%$; $P < 0.001$). In multivariate analysis, delayed transition was independently associated with myocardial infarction, reduced LVEF, and LV hypertrophy. The association between delayed transition and SCD was independent of the LVEF (OR 1.57; 95% CI 1.04–2.38; $P = 0.032$).

Conclusion

The underpinnings of delayed QRS transition zone extend beyond previous myocardial infarction and reduced LVEF. Since the association with sudden death is independent of these factors, this novel marker of myocardial electrical remodelling should be explored as a potential risk predictor of SCD.

Keywords

Electrocardiography • Delayed QRS transition • Clockwise rotation • Sudden cardiac death • Population

Introduction

Sudden cardiac death (SCD) is a major public health concern worldwide, responsible for >300 000 out of hospital deaths annually in the USA alone.¹ Severely depressed left ventricular (LV) function and myocardial infarction are conditions with high attributable risk for SCD, and during the last decade the prophylactic implantable cardioverter defibrillator (ICD) has been established as the main

primary prevention modality for a selected group of these patients.² However, almost half of SCD victims are not previously diagnosed with heart disease and a sizeable proportion meeting current criteria for the prophylactic ICD may not receive therapies from the device. This has stimulated the search for novel risk markers that will identify individuals at increased risk of fatal arrhythmia.³

The 12-lead electrocardiogram (ECG) is a potentially attractive tool for large-scale screening because of its relatively low cost and

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What's new?

- Delayed QRS transition at V_5 or later is associated with increased risk of sudden cardiac death (SCD), independent of cardiac function.
- Overall, 31% of all SCD patients manifested with delayed QRS transition prior to their sudden cardiac arrest event.
- Delayed QRS transition in the electrocardiogram may represent an abnormal electrical response to several conditions such as higher prevalence of prior myocardial infarction, increased left ventricular (LV) mass, larger LV diameter, and reduced ejection fraction. Further investigation of this marker may be helpful for risk assessment and prevention of sudden cardiac arrest.

ubiquitous availability. Several ECG patterns that mark abnormalities of the depolarization and repolarization phases of the cardiac action potential have been found to be associated with SCD in the general population, but whether the ECG adds value to the current approaches to SCD risk stratification needs further investigation.^{3,4} QRS transition zone is an electrocardiographic parameter that can be easily determined from a standard ECG and is defined as the precordial lead in which the R wave equals or exceeds the S wave in amplitude. Until recently, the transition zone has attracted little attention beyond cardiac electrophysiologists assessing the origin of ectopic beats and tachycardias from the ventricular outflow tract. A recent study from Japan revived interest in the QRS transition zone by suggesting that delayed QRS transition, or clockwise rotation of the QRS complex, was associated with increased mortality.⁵ These findings were followed by a report from a large Finnish general population cohort demonstrating that delayed QRS transition was also associated with increased risk of SCD.⁶ However, the mechanisms behind this association have remained speculative since information on cardiac structure and function was not available in these studies. Furthermore, it would be important to evaluate whether the prognostic significance of delayed QRS transition extends beyond the LV ejection fraction (LVEF).

The ongoing Oregon Sudden Unexpected Death Study (Oregon SUDS) provides a unique opportunity to perform a comprehensive evaluation of patients who suffered SCD, with access to ECGs and echocardiograms in a large proportion of patients. We therefore utilized this resource to study the association between delayed QRS transition zone and SCD in a contemporary population, while evaluating the underlying clinical, electrical, and cardiac structural abnormalities.

Methods

Study population

We performed a case-control analysis from the Oregon SUDS, an ongoing prospective population-based study of SCD based in Portland, Oregon (catchment population ~1 million). Detailed methods of this study have been published previously.⁷ Briefly, cases suffered out-of-hospital cardiac arrest and were identified through three main

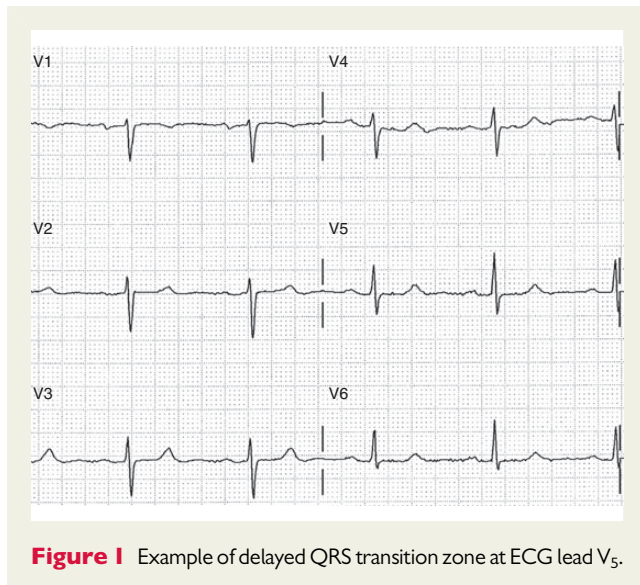
sources: emergency medical response system (including ambulance and fire services), county medical examiner's office, and local hospital emergency rooms. Sudden cardiac death was defined as sudden unexpected death if death occurred (i) within 1 h of symptom onset if witnessed, or (ii) within 24 h of last having been seen in the usual state of health if unwitnessed. Both survivors and non-survivors of the cardiac arrest event were included in the cases. Adjudication of SCD cases was performed by three physicians reviewing all available medical records/autopsy reports for each subject, and the non-cardiac causes of death such as trauma, drug overdose, or chronic terminal illness were excluded. Controls, also enrolled within Oregon SUDS, were subjects from the same geographical region as cases. They were recruited from medical clinics of participating health systems, from patients referred to coronary angiography, from patients transported by emergency medical services for symptoms suggestive of coronary ischaemia, and among members of a local health maintenance organization. Since coronary artery disease (CAD) is responsible for the vast majority of SCD,⁸ >80% of the controls were with a diagnosis of CAD, which was defined as having $\geq 50\%$ stenosis of a major coronary artery, history of coronary artery bypass grafting, or percutaneous coronary intervention. All controls had no history of prior ventricular arrhythmia or cardiac arrest.

Subjects included in the current analysis were aged ≥ 18 years with appropriate pre-arrest ECGs available, with the SCD events occurring between 1 February 2002 and 31 January 2015. Cases and controls with complete left or right bundle-branch block, second- or third-degree AV block, ventricular paced rhythm, or ventricular pre-excitation were excluded. Medical records were reviewed for baseline demographic data and clinical history. Where available, echocardiograms were reviewed for LV mass index, LVEF, and LV diameter. Left ventricular mass was calculated using the linear formula recommended by the American Society of Echocardiography.⁹ A cut-off of 134 g/m^2 for males and 110 g/m^2 for females was used to define an increased LV mass index,¹⁰ and a cut-off of $>60 \text{ mm}$ for males and $>54 \text{ mm}$ for females was used to define an enlarged LV diameter.

This study was approved by the Institutional Review Boards of Cedars-Sinai Medical Center, Oregon Health and Science University and all participating hospitals and health systems.

Electrocardiogram analysis

Electrocardiograms closest and prior but unrelated to the cardiac arrest event were reviewed in a blinded fashion by a trained physician reader (D.P.) to identify the transition zone in the precordial leads. To minimize errors in the evaluation process, a subset of ECGs was reviewed a second time in a blinded fashion by an experienced cardiologist (A.L.A.) for determination of inter-observer agreement (κ value 0.91 for determining delayed transition). The transition zone was defined as the precordial lead where QRS pattern had changed from an rS to an Rs configuration, or the lead where an isoelectric RS pattern was present. A delayed transition was defined as the transition occurring at V_5 or beyond. *Figure 1* shows an example of a delayed QRS transition at lead V_5 . Electrocardiogram data obtained included evaluation of LV hypertrophy (LVH), QTc, QRS duration, resting heart rate, QRS axis, T-wave axis, and evidence of myocardial infarction. Frontal QRS-T angle was calculated as the absolute value of difference of the QRS axis and T-wave axis. The resting heart rate was categorized as high or low based on the 75th percentile value in control subjects. Left ventricular hypertrophy was determined based on meeting either the Sokolow–Lyon criteria ($S V_1 + R V_5$ or $V_6 \geq 35 \text{ mm}$) or Cornell voltage criteria ($S V_3 + R$ in aVL $>28 \text{ mm}$ in men and $>20 \text{ mm}$ in women). The QT interval was automatically measured, and the QT was corrected using Bazett's formula. Evidence of myocardial infarction was determined based on the



presence of pathological Q waves, or the presence of ST-segment elevation corresponding to a coronary artery territory.

Statistical analysis

Cases and controls were compared using independent samples *t*-test and χ^2 test for continuous and categorical variables, respectively. Multivariable logistic regression was used to determine the odds ratio (OR) for independent association between delayed QRS transition and SCD. Multiple various models were performed adjusting for various variables. Comparisons (both univariate and multivariate) between delayed and non-delayed QRS transition were done to identify differences between the groups. A two-tailed *P*-value of ≤ 0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA).

Results

Characteristics of sudden cardiac death cases and controls

A total of 1428 subjects (627 SCD cases and 801 controls) were included in the study. The demographic and clinical characteristics of these subjects are presented in *Table 1*. Cases and controls were similar with respect to age (66.4 vs. 66.1 years; $P = 0.66$) and sex (67.5 vs. 67.9% male; $P = 0.86$), most of white European descent (83.5 vs. 92.2%; $P < 0.001$). Cases were more likely to have diabetes, hypertension, and history of myocardial infarction, and were more likely to smoke than the controls, but there were no differences in obesity rate and cholesterol levels between the groups. Heart rate was higher and electrocardiographic LVH was more common among cases than controls. Echocardiographic information was available from 327 (52.2%) cases and 476 (59.4%) controls. Among cases, LVEF was significantly lower, LV mass index higher, LV diastolic diameter wider, and severe LV dysfunction (LVEF $\leq 35\%$) more common than in controls.

Table 1 Baseline characteristics of subjects

	Case (n = 627)	Control (n = 801)	P-value
Age (year)	66.4 \pm 14.7	66.1 \pm 11.5	0.659
Male sex	423 (67.5)	544 (67.9)	0.856
Race			
Caucasian	518 (83.5)	724 (92.2)	<0.001
African American	60 (9.7)	27 (3.4)	<0.001
Other	42 (6.8)	34 (4.3)	0.044
Obesity ^a	135 (21.5)	143 (17.9)	0.086
Diabetes	250 (39.9)	208 (26.0)	<0.001
Hypertension	468 (74.6)	542 (67.8)	0.005
Cholesterol (mg/dL)	178.0 \pm 50.2	174.0 \pm 44.2	0.178
Current or former smoker	359 (72.5)	393 (64.1)	0.003
Heart rate (b.p.m.)	78.3 \pm 18.8	67.7 \pm 14.7	<0.001
LVH by ECG	93 (14.8)	74 (9.2)	0.001
Infarct on ECG	168 (29.4)	195 (24.9)	0.065
History of MI	256 (40.8)	277 (34.6)	0.015
LV mass index (g/m ²)	119.6 \pm 39.5	101.2 \pm 32.8	<0.001
LV diameter (mm)	51.4 \pm 10.0	49.7 \pm 8.1	0.039
LVEF (%)	49.3 \pm 15.5	55.6 \pm 12.4	<0.001
LVEF $\leq 35\%$	77 (23.5)	47 (9.9)	<0.001

Data are presented as mean \pm SD or n (%).

^aBody mass index ≥ 30 kg/m².

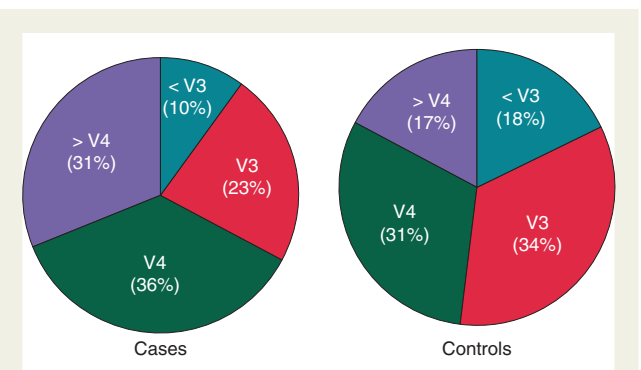


Figure 2 Distribution of QRS transition zones between cases and controls. For differences between cases and controls for $< V_3$, V_3 , and $> V_4$, $P < 0.001$; for V_4 , $P = 0.052$.

Demographic and clinical characteristics associated with delayed QRS transition zone

The distribution of QRS transition zones in cases and controls is shown in *Figure 2*. Delayed QRS transition was present in 192 cases and 137 controls (30.6 vs. 17.1%; $P < 0.001$). *Table 2* demonstrates the differences between individuals with delayed QRS transition and rest of the subjects, cases, and controls combined together. Subjects with QRS transition at V_5 or beyond were older (67.8 vs. 65.0 years;

Table 2 Demographic and echocardiographic characteristics between subjects with delayed and normal QRS transition, and the odds ratios (95% CI) for delayed QRS transition associated with each variable

	Delayed QRS transition (n = 329)	Normal QRS transition (n = 1099)	OR	95% CI	P-value
Age (year)	67.8 ± 13.3	65.0 ± 12.8	1.01	1.00–1.02	0.014
Male sex	206 (62.6)	761 (69.2)	0.74	0.58–0.96	0.024
Race					
Caucasian	280 (85.6)	962 (89.2)	–	–	0.074
African American	30 (9.2)	57 (5.3)	–	–	0.011
Other	59 (5.2)	17 (5.5)	–	–	0.848
Obesity ^a	70 (21.3)	208 (19)	1.16	0.85–1.57	0.353
Diabetes	137 (41.6)	321 (29.3)	1.73	1.34–2.23	<0.001
Hypertension	253 (76.9)	757 (69)	1.50	1.12–1.99	0.006
Cholesterol (mg/dL)	167.2 ± 46.0	177.8 ± 46.5	0.99	0.99–1.00	0.003
Current or former smoker	172 (69.9)	580 (67.3)	1.13	0.83–1.54	0.435
History of MI	183 (55.6)	350 (31.8)	2.68	2.09–3.45	<0.001
LV mass index (g/m ²)	122.7 ± 40.2	102.9 ± 33.7	1.01	1.01–1.02	<0.001
Increased LV mass index	71 (43.0)	74 (9.8)	3.05	2.05–4.55	<0.001
LV diameter (mm)	53.3 ± 10.4	49.2 ± 8.0	1.05	1.03–1.08	<0.001
Enlarged LV diameter	43 (24.7)	49 (12.4)	2.33	1.47–3.67	<0.001
LVEF (%)	46.4 ± 15.7	55.6 ± 12.5	0.96	0.94–0.97	<0.001
LVEF ≤35%	68 (30.6)	56 (9.6)	4.14	2.78–6.16	<0.001

Data are presented as mean ± SD or n (%). Echocardiographic data were available for 222 subjects with delayed QRS transition, and for 581 without delayed transition.

^aBody mass index ≥30 kg/m².

$P = 0.01$) and less likely to be male (62.6 vs. 69.2%; $P = 0.02$) than rest of the subjects. The proportion of African Americans was greater among subjects with delayed transition (9.2 vs. 5.3%; $P = 0.01$). Cardiovascular risk factors such as diabetes and hypertension were more common among subjects with delayed transition, and they were also more likely to have a history of myocardial infarction (55.6 vs. 31.8%; $P < 0.001$).

Echocardiographic and electrocardiographic findings associated with delayed QRS transition

As presented in Table 2, there were multiple differences in cardiac structural abnormalities between the subjects with delayed QRS transition compared with the rest of the study population. Left ventricular ejection fraction was lower (46.4 vs. 55.6%; $P < 0.001$) and the proportion of severely reduced LVEF higher (30.6 vs. 9.6%; $P < 0.001$) in the group with delayed QRS transition. Adjusted LV mass index was significantly greater in subjects with delayed transition, and 43.0% of them had anatomical LVH compared with 19.8% subjects with non-delayed transition ($P < 0.001$). Moreover, LV diameter was significantly wider in the group with delayed transition, with a higher prevalence of LV dilatation (24.7 vs. 12.4%; $P < 0.001$).

Similarly, a wide range of electrocardiographic findings was associated with delayed QRS transition zone, as summarized in Table 3. Subjects with delayed transition had higher heart rates, and longer QRS width and QTc intervals than rest of the subjects. They also

had a higher prevalence of prolonged QRS duration, electrocardiographic LVH, and signs of myocardial infarction than other subjects. There were also significant differences in the frontal plane electrical axes, with a significantly wider QRS-T angle and higher prevalence of leftward frontal QRS axis in the group with delayed QRS transition.

As displayed in Tables 2 and 3, multiple clinical, echocardiographic, and ECG variables were associated with significant OR for delayed QRS transition in univariate analysis. When several of these factors were combined in a multivariate model (Table 4), reduced LVEF, increased LV mass, prolonged QTc interval, and electrocardiographic or clinical evidence of myocardial infarction were independently predictive of delayed QRS transition.

Risk of sudden cardiac death associated with delayed QRS transition zone

In an unadjusted analysis, delayed QRS transition at V₅ or later more than doubled the odds for SCD (OR 2.14; 95% CI 1.67–2.75; $P < 0.001$). We studied the association between delayed QRS transition and SCD also in several multivariable models (Table 5). When adjustments were made for several clinical and demographic factors, reduced LVEF and history of myocardial infarction, delayed transition remained significantly associated with SCD (OR 1.57; 95% CI 1.04–2.38; $P = 0.03$).

Discussion

Delayed QRS transition zone, also referred to as clockwise rotation of the heart in the horizontal plane, can be easily determined from

Table 3 Electrocardiogram characteristics in subjects with delayed versus normal QRS transition, and the odds ratios (95% CI) for delayed QRS transition associated with each variable

	Delayed QRS transition (n = 329)	Normal QRS transition (n = 1099)	OR	95% CI	P-value
QTc duration (ms)	439 ± 42	425 ± 42	1.01	1.01–1.01	<0.001
QTc ≥450 ms	119 (36.7)	205 (18.8)	2.52	1.92–3.30	<0.001
QRS duration (ms)	100 ± 20	93 ± 15	1.03	1.02–1.03	<0.001
Heart rate (b.p.m.)	78 ± 20	71 ± 16	1.02	1.01–1.03	<0.001
Heart rate >75th quartile	160 (48.8)	358 (32.6)	1.97	1.53–2.53	<0.001
LVH by ECG	69 (21.0)	98 (8.9)	2.71	1.94–3.80	<0.001
QRS axis (degrees)	15 ± 66	26 ± 39	0.99	0.99–1.00	<0.001
QRS axis < -30°	77 (23.7)	60 (5.5)	5.36	3.72–7.72	<0.001
T-wave axis (degrees)	69 ± 64	52 ± 55	1.01	1.00–1.01	<0.001
QRS-T angle (degrees)	89 ± 66	49 ± 50	1.01	1.01–1.01	<0.001
Infarct on ECG	140 (46.2)	223 (21.2)	3.20	2.44–4.19	<0.001

Data are presented as mean ± SD or n (%).

Table 4 Multivariate analysis of clinical factors associated with delayed QRS duration

	OR	95% CI	P-value
Infarct on ECG	2.52	1.50–4.24	<0.001
History of MI	1.77	1.06–2.96	0.029
Increased LV mass index	2.23	1.35–3.67	0.002
Enlarged LV diameter	0.73	0.39–1.37	0.333
LVEF ≤35%	2.40	1.34–4.27	0.003
QTc ≥450 ms	1.79	1.11–2.87	0.017
Heart rate >75th quartile	1.50	0.96–2.35	0.079
LVH by ECG	1.70	0.96–3.01	0.070
Diabetes	1.12	0.72–1.74	0.611

the precordial leads of a standard 12-lead ECG, but is often neglected in clinical practice. Our findings reinforce the potential utility of this marker for assessment of SCD risk, and to our knowledge this is the first study to evaluate the clinical underpinnings of this phenomenon. Besides myocardial infarction, delayed QRS transition was associated with multiple cardiac structural alterations such as increased LV mass, enlarged LV diameter, and reduced LV function, and was often accompanied by a wide range of other electrocardiographic abnormalities. However, in multivariate analysis, the association between delayed QRS transition and increased SCD risk was independent of depressed LV function or history of myocardial infarction, suggesting that the prognostic significance of delayed QRS transition extends beyond these established clinical risk markers.

Since the QRS transition zone is related to the position of the heart in the chest, conditions that cause the heart to shift leftward, such as left-sided lung resection, directly impact precordial R-wave transition causing clockwise rotation of the horizontal axis.¹¹ However, the QRS transition zone is only partly attributable to the actual anatomical rotation of the heart. When Tahara *et al.* studied groups of subjects with normal transition zone, clockwise rotation or

Table 5 Multivariate analysis of the association between SCD and delayed QRS transition

Delayed QRS transition	OR	95% CI	P-value
Unadjusted	2.14	1.67–2.75	<0.001
Model 1	1.73	1.26–2.35	<0.001
Model 2	1.60	1.15–2.23	0.005
Model 3	1.57	1.04–2.38	0.032

Model 1: adjusted for age, sex, obesity, diabetes, hypertension, smoking status, and heart rate.

Model 2: Model 1 + infarct on ECG + history of MI.

Model 3: Model 1 + infarct on ECG + history of MI + LVEF ≤35%.

counterclockwise rotation by cardiac computed tomography, only two-thirds of the cases with abnormal transition zone in ECG had actual anatomical rotation of the heart around the long axis.¹² Clockwise rotation of the heart can occur in several pathological conditions responsible of enlargement of the right ventricle, such as in severe chronic obstructive pulmonary disease¹³ or in the setting of acute massive pulmonary thromboembolism.¹⁴ Dilatation of the left ventricle may also cause posterior shift of the depolarizing electrical vector, which can be depicted as delayed QRS transition zone in the surface ECG.¹⁵ In heart failure patients, this posterior shift of the horizontal QRS axis has been associated also with increased mortality.¹⁶

Previously, only a few studies have examined the prognostic significance of delayed QRS transition zone.¹⁷ In 1987, a Finnish study on electrocardiographic findings in a geriatric population demonstrated that this marker was strongly associated with stroke mortality.¹⁸ More recently, a Japanese study from the NIPPON DATA80 cohort on subjects who were examined in 1980, reported among other ECG findings, that delayed QRS transition was associated with increased mortality.¹⁹ These findings were studied closer by Nakamura *et al.* in 2012 using the same database.⁵ With a 24-year follow-up of >9000 subjects, they showed that delayed QRS transition zone

was associated with 15% higher all-cause and 28% higher cardiovascular mortality in this Japanese population. Recently, the association between mortality and QRS transition zone was confirmed using data from the US Third National Health and Nutrition Examination Survey (NHANES III) conducted from 1988 to 1994 including >5000 subjects free of cardiovascular disease with a mean follow-up of almost 15 years.²⁰ The study demonstrated that clockwise rotation was associated with 43% increase in all-cause mortality and 61% increase in cardiovascular mortality during the follow-up.

Until now, the only data on delayed QRS transition zone and risk of SCD have come from a Finnish cohort of >10 000 middle-aged subjects examined in the 1960s and 1970s, and followed up for a mean of 30 years. Recently, the Finnish group reported that delayed QRS transition at V₄ or later was moderately associated with SCD, and when QRS transition was more delayed occurring at V₅ or later, the risk of SCD was 89% higher than in the group with normal transition zone.⁶ Our results are in line with these data. In the present study population, delayed QRS transition at or beyond V₅ was a relatively common phenomenon occurring in nearly one-third of SCD cases. The unadjusted OR for SCD was over two-fold in these individuals, but even after adjusting for several clinical variables, reduced LVEF and history of myocardial infarction, the risk of SCD associated with delayed QRS transition remained almost 60% higher than in subjects with normal transition zone.

The mechanisms behind this consistent association between delayed transition zone and adverse prognosis have remained speculative. Previous reports from the diverse general population samples described earlier have suggested that prevalence of delayed QRS transition becomes higher as age and body mass index increase,^{6,20} and delayed transition has been associated with several cardiovascular risk factors and incident cardiac disease as well.^{5,6} Our results are in agreement with these demographic data, as we found delayed QRS transition to be often accompanied by increased age, hypertension, diabetes, and history of myocardial infarction. However, no association between obesity and transition zone was observed in our study population. In accordance with previous studies,^{5,6} delayed QRS transition was associated also with multiple other abnormal ECG patterns associated with adverse prognosis. Together these demographic differences indicated that delayed QRS transition may be a marker of underlying structural cardiac pathology responsible for the increased SCD risk.

Previous studies on the prognostic significance of delayed QRS transition did not have echocardiographic data available thus precluding the possibility to correlate their findings with LV function, dimensions, and mass. Since information on echocardiography was available for a large proportion of subjects in the present study, we had an opportunity to look at structural changes in cardiac anatomy and function associated with delayed transition zone. Increased LV mass, larger LV diameter, and reduced LV function correlated strongly with delayed QRS transition zone, suggesting that increased thickness of the LV wall and dilatation of the left ventricle are responsible for the leftward shift of the horizontal QRS axis in many of these subjects. Moreover, as delayed QRS transition was significantly more common in subjects with myocardial infarction, diminished anterior depolarization forces due to distant anterior myocardial infarction may explain delayed QRS transition in some of these patients. Since all these aforementioned factors have

been associated with increased risk of SCD,^{21,22} it is likely that these structural alterations largely account for the adverse prognostic impact observed with delayed QRS transition. Moreover, when history of myocardial infarction and reduced LV function were considered in the analysis, the association between delayed QRS transition and SCD remained significant. This implies that the underpinnings of delayed QRS transition extend beyond previous myocardial infarction and LVEF, and may specifically reflect altered electrical forces and electrical remodelling that promote ventricular arrhythmias and SCD. Since myocardial infarction and severely reduced LV function also predict overall mortality, delayed QRS transition could represent a more specific marker of sudden arrhythmic death.

There are certain inherent limitations of a case-control community-based design that need to be considered while interpreting the findings of this study. Selecting appropriate controls is a vital part of any case-control study. In Oregon SUDS, controls are carefully chosen from the same geographical area with a similar distribution of CAD as SCD victims, making it likely that any differences observed between the groups would be specific for SCD. However, since SCD is the first manifestation of cardiac disease in a large proportion of subjects, ECGs may not have been uniformly available from all SCD cases, leading to certain bias in patient selection. Only a single 12-lead ECG was used to estimate the QRS transition zone, so we could not take into account the potential time-dependent variability in the transition zone. As the ECGs were recorded as part of routine clinical workup, it was not possible to ensure the correct placement of precordial ECG leads. However, inaccurate lead positioning would be more likely to result in conservative bias and attenuate the differences between groups. Moreover, echocardiographic data were collected from existing hospital records and were thus available only from a subgroup of patients.

Conclusions

In conclusion, delayed QRS transition at V₅ or beyond is associated with SCD in the community independent of several clinical factors, suggesting that determining the transition zone may potentially supplement the process of SCD risk stratification. It is likely that delayed QRS transition zone reflects a higher burden of cardiac structural abnormalities such as reduced LV systolic function and increased LV mass, but further research is warranted to unravel the complete electrical and anatomical basis of this phenomenon.

Funding

A.L.A. is funded by grants from the Finnish Cultural Foundation and the Finnish Foundation for Cardiovascular Research. This work was funded in part by National Heart Lung and Blood Institute grant R01HL122492 to S.S.C, who also holds the Pauline and Harold Price Chair in Electrophysiology at Cedars-Sinai, Los Angeles, CA, USA.

Conflict of interest: none declared.

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