ECG Quantification of Myocardial Scar Does Not Differ between Primary and Secondary Prevention ICD Recipients with Ischemic Heart Disease

KARIN KRAAIER, M.D.,* PASCAL F.H.M. VAN DESSEL, M.D., PH.D.,*
JOB VAN DER PALEN, M.Sc., PH.D.,†,‡ ARTHUR A.M. WILDE, M.D., PH.D.,§
and MARCOEN F. SCHOLTEN, M.D., PH.D.*

From the *Department of Cardiology, Medisch Spectrum Twente, Enschede, The Netherlands; †Department of Epidemiology, Medisch Spectrum Twente, Enschede, The Netherlands; ‡Department of Research Methodology, Measurement and Data Analysis, University of Twente, Enschede, The Netherlands; and §Department of Cardiology, Academic Medical Centre, Amsterdam, The Netherlands

Background: *Myocardial scar is an anatomic substrate for potentially lethal arrhythmias. Recent study showed that higher QRS-estimated scar size using the Selvester QRS score was associated with increased arrhythmogenesis during electrophysiologic testing. Therefore, QRS scoring might play a potential role in risk stratification before implantable cardioverter defibrillator (ICD) implantation. In this study, we tested the hypothesis that QRS scores among ICD recipients for secondary prevention are higher than QRS scores in primary prevention patients.*

Methods and Results: *From the hospital database, 100 consecutive patients with ischemic heart disease and prior ICD implantation were selected. Twelve-lead electrocardiograms (ECGs) had been obtained before implantation. ECGs were scored following the 32-points Selvester QRS scoring system and corrected for underlying conduction defects and/or hypertrophy. Ninety-three ECGs were suitable for scoring; seven ECGs were rejected because of noise, missing leads, excessive ventricular extrasystoles, or ventricular pacing. No statistically significant difference in QRS score was found between the primary [6.90 (standard deviation [SD] 3.94), n = 63] and secondary prevention group [6.17 (SD 4.50) (P = 0.260), n = 30]. Left ventricular ejection fraction (LVEF) was significantly higher in the secondary prevention group [31% (SD 13.5) vs 24% (SD 11.7) (P = 0.015)]. When patients with LVEF ≥35% were excluded, QRS scores were still comparable, namely 7.02 (SD 4.04) in the primary prevention group (n = 52) and 6.28 (SD 4.24) in the secondary (P = 0.510) (n = 18).*

Conclusion: *We found no significant difference in QRS score between the ischemic primary and secondary prevention groups. Therefore, a role of the Selvester QRS score as a risk stratifier remains unlikely. (PACE 2010; 33:192–197)*

risk stratification, implantable cardioverter defibrillator, sudden cardiac death, electrocardiography

Background

With the introduction of the implantable cardioverter defibrillator (ICD), patients can be protected from sudden cardiac death (SCD) due to ventricular arrhythmia (VA).[1–5] In patients with ischemic cardiomyopathy (CMP), a low ejection fraction (EF) is a risk marker for SCD and the most important criterion to decide whether a patient will receive an ICD for primary prevention.[6] Given the fact that many patients who receive an ICD for primary prevention will never experience a life-threatening VA requiring antitachycardia pacing (ATP) or shock therapy,[3] better risk stratification is desirable to reduce the number of unnecessary device implants.

Both in patients with ischemic and nonischemic CMP, myocardial scar is an anatomical substrate for potentially lethal arrhythmias. Recently, Strauss et al. showed electrocardiogram quantification using the Selvester QRS score can identify and quantify scar size in both ischemic and nonischemic CMP patients. A higher QRS-estimated scar size was associated with increased arrhythmogenesis during electrophysiologic study (EPS) testing.[7] Therefore, there may be a potential role for the Selvester QRS score as an additional risk marker for the selection of candidates for primary prevention.

In this study, we tested the hypothesis that the Selvester QRS scores adapted for confounders among ICD recipients with ischemic heart disease

Financial Disclosure: None.

Address for reprints: K. Kraaier, M.D., Medisch Spectrum Twente, Department of Cardiology, Haaksbergerstraat 55, 7513 ER Enschede, The Netherlands. Fax: 31 53 487 6162; e-mail: k.kraaier@mst.nl

Received June 19, 2009; revised August 11, 2009; accepted September 17, 2009.

doi: 10.1111/j.1540-8159.2009.02611.x

and prior life-threatening VA (secondary prevention group) are higher than the QRS scores in those who received prophylactic ICDs (primary prevention group).

Methods

Patients

From the hospital database, 100 consecutive patients with ischemic CMP and prior ICD implantation, according to the current guidelines of the Dutch (NVVC) and European society of Cardiology (ESC), were selected. The selected patients are all included in a single-center prospective cohort study (TICS—Twente ICD Cohort Study) in which the predictive value of several risk markers for VA are studied.

Electrocardiographic Analysis

Twelve-lead ECGs were obtained before ICD implantation and analyzed using the Selvester QRS criteria. The Selvester QRS criteria consist of 53 criteria which involve Q and R wave duration and R/Q and R/S amplitude ratios. A maximum of 32 possible points can be achieved, with each point representing 3% of the left ventricle mass. Confounders are left bundle branch block (LBBB), left anterior fascicular block (LAFB), right bundle branch block (RBBB), combination of LAFB and RBBB, and left ventricular hypertrophy (LVH). If any of these confounders was present, a modified QRS score was used.[8]

Statistical Analysis

Continuous variables are expressed as a mean [±standard deviation (SD)]. To compare the primary and secondary prevention groups; Student's *t*-test and Mann-Whitney U test were used to compare continuous variables, and χ^2 test and Fisher exact test were used to compare categorical variables. P values <0.05 were considered statistically significant.

Results

Study Patients

One hundred patients were selected. From these, 93 ECGs were suitable for scoring. Seven ECGs were rejected because of noise, missing leads, excessive ventricular extra systoles, or ventricular pacing. Of these 93 patients, 63 received their ICD for primary prevention, and 30 for secondary prevention. Baseline characteristics are presented in Table I. Baseline EF was significantly higher in the secondary prevention group compared with the primary prevention group, 30.7% versus 24.3% (P = 0.027). Infarct localization significantly differed between the secondary and primary prevention groups. If patients with EF >35% were excluded from analyses, no significant differences in any of the baseline characteristics remained.

Differences between Primary and Secondary Prevention Groups

Overall the QRS score was 6.90 (SD 3.94) in the primary prevention group, compared with 6.17 (SD 4.50) in the secondary prevention group, which is not significantly different (P = 0.26) (Table II, Fig. 1). The QRS scores in the primary and secondary prevention groups were comparable for both infarcts ≤12 months and >12 months (P = 0.32 and 0.87, respectively). There was no significant difference in QRS-estimated scar size between patients with anterior versus patients with an inferior infarction. In patients with anterior infarction, there was no significant difference in QRS scores between the primary and secondary prevention groups (P = 0.73). Likewise in patients with inferior infarction, no significant difference was found (P = 0.66). Patients with multiple infarctions had higher QRS scores, which did not prove statistically significant. Both for patients with a single or multiple infarctions, no significant difference in QRS scores between the primary and secondary prevention groups was found (P = 0.75 and 0.62, respectively). In the group of patients with normal conduction and without electrocardiographic signs of LVH, there was a trend which showed a lower QRS score in the secondary prevention group, [5.05 (SD 3.63) compared with 6.92 (SD 4.02)] in the primary prevention group (P = 0.08). Other ECG confounders were not analyzed due to the small amount of patients in those groups.

In order to exclude the statistical influence of the larger extent of patients with relatively preserved left ventricular (LV) function in the secondary prevention group, patients with a LVEF > 35% were omitted and the aforementioned analysis was repeated. After this exclusion, 52 and 18 patients remained in the primary and secondary prevention groups, respectively. Overall scores were 7.02 (SD 4.04) in the primary prevention group and 6.26 (SD 4.24) in the secondary prevention group, without statistical significance (P = 0.510) (Table III, Fig. 1). Again in this second analysis, we found no statistic differences between the primary and secondary prevention groups, regarding infarct age (≤12 months P = 0.83, >12 months P = 0.52), infarct localization (anterior P = 0.11, inferior P = 0.31), number of infarctions (single infarction P = 0.95, multiple infarction P = 0.23), or conduction (normal conduction with no electrocardiographic signs of LVH, P = 0.341).

Table I.

Patient Characteristics

	All Patients			Patients with LVEF ≤35%		
	Primary Prevention	Secondary Prevention	P	Primary Prevention	Secondary Prevention	P
Patients, n	63	30		52	18	
Men/Women	56/7	28/2	0.46	45/7	17/1	0.67
Age, years (±SD)	64.4 (9.0)	62.6 (8.8)	0.37	65.2 (8.6)	63.7 (7.9)	0.54
Infarct age, months (mean, range)	129 (0–459)	143 (0–491)	0.85	142 (1–459)	168 (1–491)	0.54
Infarct			0.76			0.73
Single	51 (81)	23 (77)		41 (79)	14 (78)	
Multiple	9 (14)	5 (17)		9 (17)	4 (22)	
Unknown	3 (5)	2 (7)		2 (4)	0 (0)	
Infarct localization			0.05			0.33
Anterior	36 (57)	9 (30)		28 (54)	7 (39)	
Inferior	18 (29)	12 (40)		16 (31)	6 (33)	
Both	7 (11)	7 (23)		7 (13)	5 (28)	
Unknown	2 (3)	2 (7)		1 (2)		
Baseline ejection fraction, % (SD)	24.1 (12)	31.0 (13,5)	0.015	20.4 (7.8)	22.4 (7.8)	0.33
Medication						
β-blocker	52 (83)	26 (86.7)	0.77	43 (82.7)	14 (77.8)	0.73
ACE inhibitor	50 (79)	22 (73.3)	0.52	40 (76.9)	14 (77.8)	1.00
AT-II inhibitor	9 (14)	3 (10.0)	0.75	9 (17.3)	3 (16.7)	1.00
QRS score	6.90 (3.94)	6.17 (4.50)	0.26	7.02 (4.04)	6.28 (4.24)	0.51
ECG confounders			0.16			0.16
No confounders	39 (62)	21 (70)		32 (62)	14 (78)	
LBBB	15 (24)	3 (10)		11 (34)	2 (11)	
LAFB	6 (10)	3 (10)		6 (12)	0 (0)	
RBBB	1 (2)	3 (10)		1 (2)	2 (11)	
RBBB + LAFB	0 (0)	0 (0)		0 (0)	0 (0)	
LVH	2 (3)	0 (0)		2 (4)	0 (0)	

Values are numbers (percentage) unless otherwise specified. ACE inhibitor = angiotensin-converting enzyme inhibitor, AT-II-inhibitor = angiotensin II inhibitor, LBBB = left bundle branch block, LAFB = left anterior fascicular block, RBBB = right bundle branch block, LVH = left ventricular hypertrophy.

Follow-Up

During follow-up (mean follow-up 13 months, range 5–21 months), 15 patients received appropriate therapy from their device. Shock therapy was delivered in five patients, ATP in five patients, and both ATP and shock in five patients. In the primary prevention group, six patients experienced appropriate ICD therapy, the QRS score [5.33 (SD 3.98) was not significantly different from primary prevention patients without appropriate therapy (7.07 (SD 3.93)] (P = 0.31). In the secondary group, nine patients received appropriate therapy. No significant difference in QRS score was found [5.89 (SD 4.40) vs 6.29 (SD 4.65), P = 0.83]. Of the patients with an LVEF ≤35%, 10 patients experienced appropriate therapy. Both in primary and secondary prevention groups, no significant differences in QRS scores were found (P = 0.28 and 0.60, respectively).

Discussion

Although ICDs are effective in preventing SCD, better risk stratification is warranted because many ICD recipients will never experience a life-threatening VA. Several potential indices for SCD are under evaluation,[9] and recently Strauss et al. proposed the Selvester QRS score as a new potential risk factor.[7] Although calculating the QRS score is time consuming, it remains an appealing method because ECGs are not expensive and usually obtained in every patient. Besides, software for automatic scoring is available. The prognostic use of the Selvester QRS score was studied in the Framingham cohort, where a higher

Table II.

QRS Scores

	QRS Score				
	Primary Prevention	n	Secondary Prevention	n	P
Overall	6.90 (3.94)	63	6.17 (4.50)	30	0.26
Infarct age					
≤12 months	5.80 (3.64)	10	4.17 (1.47)	6	0.32
>12 months	7.33 (3.85)	45	7.15 (4.67)	20	0.87
Infarct					
Single	6.67 (3.71)	51	6.35 (4.36)	23	0.75
Multiple	8.78 (4.60)	9	7.40 (5.18)	5	0.62
Infarct localization					
Anterior	7.17 (3.68)	36	6.67 (4.27)	9	0.73
Inferior	5.56 (3.97)	18	4.92 (3.55)	12	0.66
ECG confounders					
No confounders	6.92 (4.02)	39	5.05 (3.63)	21	0.08

All values are mean ± SD.

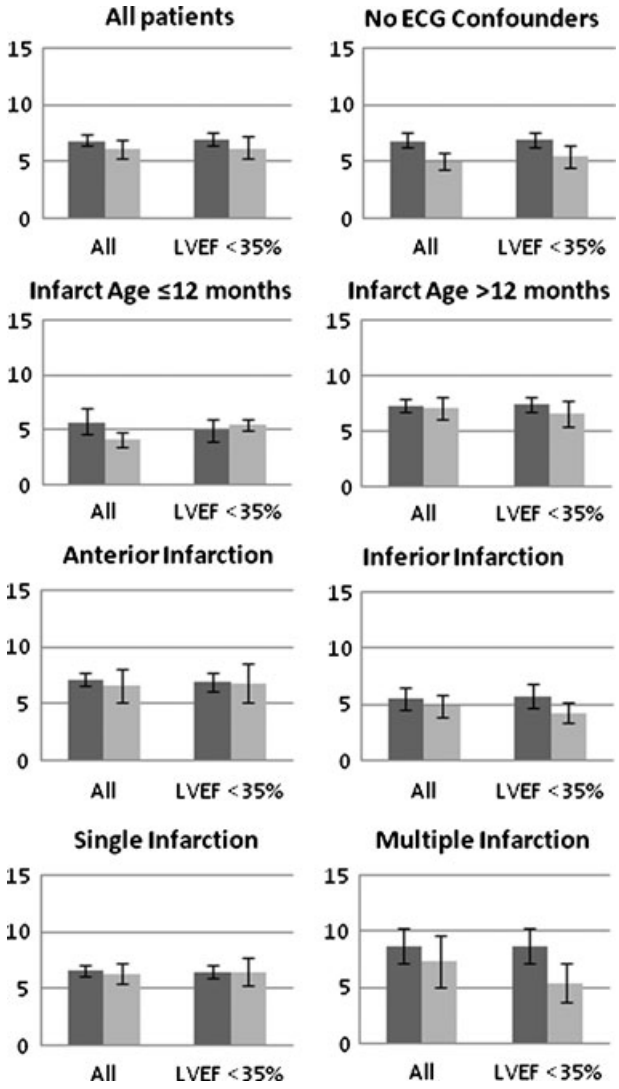

Figure 1. *Selvester QRS scores in the complete group, and in group with LVEF ≤35% for both primary (dark grey) and secondary (light grey) prevention groups. On the vertical axis Selvester QRS score in points [mean (±standard error of mean)].*

QRS score proved to be associated with poor outcome.[10] Strauss et al. found a relation between the QRS score and inducible monomorphic ventricular tachycardia during EPS in patients with CMP (n = 162, of which 95 with ischemic CMP).[7] In their study, higher QRS estimated scar size was associated with increased arrhythmogenesis. They suggested that the QRS score can be a potential risk marker to identify patients at high risk for life-threatening VA.

The value of the Selvester score in several patient groups has been studied. In patients with anterior, posterolateral, or inferior myocardial infarction, the correlation coefficient between total QRS score and percentage infarction of the left ventricle estimated by autopsy was 0.80, 0.72, and 0.74, respectively.[11–13] The correlation values for delayed enhancement magnetic resonance imaging (DE-MRI) compared with the Selvester score were reported to be 0.33–0.74, and are higher for anterior infarction compared with inferior infarction.[7,14,15] All these results were based on studies in which patients only had a single infarction. Correlation value of QRS score and infarct size estimated by autopsy in patients with multiple infarctions is lower r = 0.44.[16] Originally, the Selvester Scoring System was only applicable in patients with normal conduction. However, after taking the specific underlying activation sequence in account, modified criteria for use in patients with conduction abnormalities were proposed.[7] These modified criteria were tested by Strauss et al., and a QRS score correlation for scar size of r = 0.74 as compared with DE-MRI was found, with a range from r = 0.66 to r = 0.80.[7]

After myocardial infarction a healing process starts. During this process structural and mechanical changes in the infarcted area will take place, which all may influence the infarction size. This means that there is a possibility that the QRS scores will also change over time succeeding infarction, as demonstrated by Bang et al.[15]

In our study, the QRS scores in the primary prevention group are not significantly different from QRS scores in the secondary prevention group, even if patients with a LVEF >35% were

Table III.

QRS Scores in Patients with LVEF ≤35%

	QRS Score				
	Primary Prevention	n	Secondary Prevention	n	P
Overall	7.02 (4.04)	52	6.26 (4.24)	18	0.51
Infarct age					
≤12 months	5.00 (2.98)	8	5.50 (0.71)	2	0.83
>12 months	7.51 (4.11)	37	6.67 (4.50)	15	0.52
Infarct					
Single	6.59 (3.90)	41	6.50 (4.54)	14	0.95
Multiple	8.78 (4.60)	9	5.50 (3.42)	4	0.232
Infarct localization					
Anterior	6.96 (3.95)	28	6.86 (4.60)	7	0.11
Inferior	5.81 (4.15)	16	4.33 (2.07)	6	0.31
ECG confounders					
No confounders	6.94 (4.02)	32	5.50 (3.59)	14	0.341

All values are mean ± SD.

excluded. During short-term follow-up, no differences in QRS score are found between the primary and secondary groups. This implicates that there must be other factors interfering with the risk of VA besides the size of the myocardial scar, for example, transmurality, localization, and heterogeneity.

In the study by Strauss et al.,[7] the Selvester QRS score was related to increased arrhythmogenesis during EPS and was therefore stated as a potential risk stratifier. EPS is a possible risk stratifier for VA; however, its negative predictive value is poor. A large percentage of patients with a negative EPS will experience life-threatening VA.[17] This could explain the difference between our hypothesis and our findings.

The fact that QRS scores do not vary between two groups, even if not taking possible confounders in account, implies that its prognostic role seems unlikely.

Limitations

The relative small number of patients in combination with the short duration (12 months) of follow-up makes it not entirely possible to judge the real prognostic value of the Selvester QRS score. However, by excluding patients with LVEF >35%, an estimation of the prognostic value of the Selvester QRS score for predicting VA is possible, since both groups are then comparable, and following MADIT II criteria for implantation. The number of patients is low in both the primary and secondary groups, especially during subdivision. The results must therefore be taken with care and larger studies must be performed.

Conclusion

We found no significant difference in the QRS score between the primary and secondary prevention groups with ischemic CMP; therefore, a role of the Selvester QRS score as risk marker in the risk stratification for predicting ventricular arrhythmia remains unlikely.

References

1. Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, Levine JH, et al. 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.
2. The 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.
3. Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, Domanski M, et al. Amiodarone or an implantable cardioverter defibrillator for congestive heart failure. N Engl J Med 2005; 352: 225–237.
4. 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.
5. Connolly SJ, Gent M, Roberts RS, Dorian P, Roy D, Sheldon RS, Mitchell LB, et al. Canadian implantable defibrillator study (CIDS): A randomized trial of the implantable cardioverter defibrillator against amiodarone. Circulation 2000; 101:1297–1302.
6. Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, Gregoratos G, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: A report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death): Developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Circulation 2006; 114:e385–e484.
7. Strauss DG, Selvester RH, Lima JAC, Arheden H, Miller JM, Gerstenblith G, Marban E, et al. ECG quantification of myocardial scar in cardiomyopathy patients with or without conduction defects. Circ Arrhythmia Electrophysiol 2008; 1:327–336.
8. Strauss DG, Selvester RH. The QRS complex—a biomarker that "images" the heart: QRS scores to quantify myocardial scar in the presence of normal and abnormal ventricular conduction. J Electrocardiol 2009; 42:85–96.
9. Kraaier K, Verhorst PM, van Dessel PF, Wilde AA, Scholten MF. Towards a better risk stratification for sudden cardiac death in patients with structural heart disease. Neth Heart J 2009; 17:101–106.
10. Jones MG, Anderson KM, Wilson PW, Kannel WB, Wagner NB, Wagner GS. Prognostic use of a QRS scoring system after hospital discharge for initial acute myocardial infarction in the Framingham cohort. Am J Cardiol 1990; 66:546–550.
11. Ideker RE, Wagner GS, Ruth WK, Alonso DR, Bishop SP, Bloor CM, Fallon JT, et al. Evaluation of a QRS scoring system for estimating myocardial infarct size. II. Correlation with quantitative anatomic findings for anterior infarcts. Am J Cardiol 1982; 49:1604–1614.
12. Ward RM, White RD, Ideker RE, Hindman NB, Alonso DR, Bishop SP, Bloor CM, et al. Evaluation of a QRS scoring system for estimating myocardial infarct size. IV. Correlation with quantitative anatomic findings for posterolateral infarcts. Am J Cardiol 1984; 53:706–714.
13. Roark SF, Ideker RE, Wagner GS, Alonso DR, Bishop SP, Bloor CM, Bramlet DA, et al. Evaluation of a QRS scoring system for estimating

myocardial infarct size. III. Correlation with quantitative anatomic findings for inferior infarcts. Am J Cardiol 1983; 51:382–389.
14. Engblom H, Wagner GS, Setser RM, Selvester RH, Billgren T, Kasper JM, Maynard C, et al. Quantitative clinical assessment of chronic anterior myocardial infarction with delayed enhancement magnetic resonance imaging and QRS scoring. Am Heart J 2003; 146:359–366.
15. Bang LE, Ripa RS, Grande P, Kastrup J, Clemmensen PM, Wagner GS. Comparison of infarct size changes with delayed contrast-enhanced magnetic resonance imaging and electrocardiogram QRS scoring during the 6 months after acutely reperfused myocardial infarction. J Electrocardiol 2008; 41:609–613.
16. Sevilla DC, Wagner NB, Pegues R, Peck SL, Mikat EM, Ideker RE, Hutchins G, et al. Correlation of the complete version of the Selvester QRS scoring system with quantitative anatomic findings for multiple left ventricular myocardial infarcts. Am J Cardiol 1992; 69:465–469.
17. Thomas KE, Josephson ME. The role of electrophysiology study in risk stratification of sudden cardiac death. Prog Cardiovasc Dis 2008; 51:97–105.