Automated Electrocardiographic Quantification of Myocardial Scar in Patients Undergoing Primary Prevention Implantable Cardioverter Defibrillator Implantation: Association with Mortality and Subsequent Appropriate and Inappropriate Therapies

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Abstract

Background: Myocardial scarring from infarction or non-ischemic fibrosis forms an arrhythmogenic substrate. The Selvester QRS-score has been developed to estimate myocardial scar from the 12-lead ECG.

Objective: We aimed to assess the value of an automated version of the Selvester QRS-score for prediction of ICD therapy and death in patients undergoing primary prevention ICD implantation.

Methods: Unselected patients undergoing primary prevention ICD implantation were included in this retrospective, observational, multicenter study. The QRS-score was calculated automatically from a digital standard pre-implant 12-lead ECG and was correlated to the occurrence of death, appropriate and inappropriate shocks during follow up. Analyses were performed in groups defined by QRS-duration <130ms vs. ≥130ms.

Results: Overall, 1047 patients (83% male; median age 64 years) with ischemic (62%) or non-ischemic cardiomyopathy (38%) were included. The median QRS-duration was 123ms (IQR 111-157) and the median QRS-score was 5 (IQR 2–8). QRS-duration was <130ms in 59% and ≥130ms in 41%. During a median follow-up of 45 months (IQR 24–72), a QRS-score ≥5 was independently associated with a significantly higher risk of mortality (HR 1.67, 95%CI 1.05–2.66, p=0.031), appropriate (HR 1.83, 95%CI 1.07–3.14, p=0.028) and inappropriate shocks (HR 2.32, 95%CI 1.04–5.17, p=0.039) in patients with a QRS-duration ≥130ms. No association of the QRS-score and outcome was observed in patients with QRS-duration <130ms (p>0.05).

Conclusion: The automatically calculated Selvester QRS-score, an indicator of myocardial scar burden, predicts mortality, appropriate and inappropriate shocks in patients undergoing primary prevention ICD implantation with prolonged QRS-duration.

Keywords: cardiac arrhythmia; cardiomyopathy; ECG; heart failure; sudden cardiac death; implantable cardioverter-defibrillator; risk stratification

Introduction

Sudden cardiac death (SCD) due to life-threatening ventricular arrhythmias is a major cause of death, accounting for around 50% of cardiovascular deaths and 20% of all natural deaths in Western societies.[1, 2] The risk of dying suddenly is particularly high in patients with reduced left ventricular ejection fraction (LVEF). Placement of implantable cardioverter-defibrillators (ICD) in these patients has been shown to improve survival in large clinical trials and subsequently in registry data analyses.[3-5] However, appropriate device interventions are only observed in 25% of patients with primary preventive ICD,[6] while a significant proportion of patients experience inappropriate shocks and device-related complications.[7] Given the global trends of population growth, increasing life expectancy, and the heart failure rates rising with the aging of the population,[8] better identification of patients at substantial risk for malignant ventricular arrhythmias who will benefit most from ICD implantation is necessary to improve patient selection and avoid unnecessary device implantations.

Myocardial scarring from infarction or non-ischemic fibrosis is the main substrate for reentry ventricular arrhythmias in patients with left ventricular remodeling. Previous studies have demonstrated that myocardial scar burden quantified by late gadolinium enhancement cardiac magnetic resonance imaging (LGE-CMR) is an independent predictor of appropriate device therapy[9] and of mortality in ICD recipients with ischemic cardiomyopathy (ICM)[10] and non-ischemic cardiomyopathy (NICM).[11] Therefore, quantification of myocardial scar burden allows improving the risk stratification in these patients.[11] Interestingly, the Selvester QRS-score, a score that quantifies the changes in the Q-, R-, and S-wave duration and amplitude on a routine 12-lead ECG, has been shown to strongly correlate with myocardial scar burden in ICM and NICM patients.[12] In a pilot study, Strauss et al.[13] showed that primary preventive ICD patients with no scar (QRS-score = 0) have a significantly lower risk of ventricular tachycardia (VT)/ventricular fibrillation (VF) than those with a myocardial scar (QRS-score ≥1). Manual calculation of the QRS-score, however, is difficult, tedious and may take up to 15 minutes per ECG, thereby limiting its application in clinical practice.[14] More recently, an automatically computed version of the Selvester QRS-score has been shown to correlate with myocardial scar burden and to predict mortality in patients with acute heart failure.[15]

In this study, we aimed to assess the utility of the automatically calculated version of this easy-to-use, non-invasive marker for predicting appropriate and inappropriate shocks and mortality in a contemporary, large, multicenter cohort of primary prophylactic ICD recipients included in the EU-CERT-ICD study.

Methods

Study design, setting, and selection of participants

The EU-CERT-ICD collaborative project (ClinicalTrials.gov Identifier: NCT02064192) aims to analyze the clinical effectiveness of primary preventive ICD therapy. The retrospective arm of the project includes a compilation of 14 locally existing registries of primary prevention ICD implantations from 11 countries between 2002 and 2014. The study design has been described previously.[16] From the total cohort of 5111 patients, 1948 had a digital pre-implantation ECG available for analysis. For this analysis, patients with missing clinical or follow-up information were excluded (n=650). Patients with non-specific bundle branch block were also excluded because the Selvester QRS-score provides no classification for this type of ECG confounder (n=251). After exclusions, a total of 1047 patients from four centers were included in the analyses.

Baseline data were collected at each participating center. The data quality of clinical parameters and outcome variables were assessed by the coordinating clinical trial unit of the University Hospital of Basel, Switzerland, as described elsewhere.[16] All participants provided written, informed consent and the study was approved by local ethics committees.

Principle of the Selvester QRS-score

The principle applied in the Selvester QRS-score to quantify myocardial scar burden from the 12-lead ECG has previously been reported in detail.[15, 17, 18] In brief, ECGs are first classified into six confounder categories: left bundle branch block (LBBB), right bundle branch block (RBBB) and left anterior fascicular block (LAFB), isolated RBBB, isolated LAFB, left ventricular hypertrophy (LVH) or no confounders. Second, points for Q-, R-, and S-wave amplitudes, durations, amplitude ratios, and notches in 10 of the 12 standard ECG leads (excluding leads III and aVR) are awarded according to six confounder categories. With a total of 54 criteria, a maximum QRS-score of 32 points can be reached, with each point representing 3% of the LV with myocardial scar. In addition, age and sex adjustments are made to the score criteria, as the normal limits of Q-, R-, and S-wave amplitudes and durations may differ by age and sex. For illustration and a better understanding of the Selvester QRS-score, a sample scoring sheet and additional details are provided in the supplementary material.

Recording of ECGs and automated calculation of the Selvester QRS-score

Standard resting 12-lead ECGs were acquired prior to ICD implantation locally as part of the standard clinical assessment. The raw data of the digital 12-lead ECGs collected from the registry were analyzed using the Schiller ECG analysis program (ETM V01.12.09.00, Schiller AG, Baar, Switzerland). Automated Q-, R-, and S-amplitude and duration measurements along with diagnostic statement codes were extracted and used for analysis. The criteria used to classify automatically ECG confounder types for QRS-scoring have been published before[19] and are listed in the supplementary material.

Study outcomes and follow-up

The primary study outcomes were death, appropriate and inappropriate ICD shock. The follow-up started at the time of the ICD implantation. Although the original cohort provides follow-up for longer periods, for the purpose of this analysis an administrative censoring was performed at 5 years of follow-up.

Statistics

Standard test were used for statistical analysis. Details are summarized in the supplementary material.

Results

Patient characteristics

Of the 1047 patients included in the study, 83% were male. The median age at ICD implantation was 64 (IQR 55–71) years; 62% suffered from ICM, and 37% received a CRT-D. Patients with NICM were younger (59 vs. 67 years, $p<0.001$), more likely to be female (26% vs. 11%, $p<0.001$), had a lower left ventricular ejection fraction (LVEF, 25 vs. 28, $p=0.015$), a wider QRS-duration (130 vs 120 ms, $p<0.001$) and more often received a CRT-D (48% vs. 30%, $p<0.001$), while patients with ICM were more likely to have diabetes (30% vs. 16%, $p<0.001$), serum creatinine >1.2 mg/dl (39% vs. 27%, $p<0.001$), or be treated with ACE inhibitor/angiotensin II receptor blocker (93% vs. 84%, $p<0.001$). Patients with CRT-D were more likely to have NYHA class III/IV as opposed to NYHA class I/II heart failure, than the non-CRT-D group (86% vs. 25%, $p<0.001$).

QRS-duration and Selvester QRS-score

12-lead ECGs were recorded within a median of 1 (IQR 1–8) days prior to ICD implantation. The median automatically calculated Selvester QRS-score was 5 (IQR 2–8) (Table 1). Only 8% of the patients had a QRS-score of 0. The QRS-score was higher in ICM patients compared to NICM patients (median 6 (IQR 3-9) vs. 3 (IQR 1-6), $p<0.001$). The median QRS-duration was 123 ms (IQR 111-157), and 41% of the patients had a QRS-duration of ≥130 ms (Table 2). More details on the distribution of QRS-scores according to QRS-duration and underlying disease etiology are shown in Figure S1.

Mortality, appropriate and inappropriate shocks during follow-up

During a median follow-up of 45 months (IQR 24–60), 156 (15%) patients experienced an appropriate shock, 82 (8%) patients had an inappropriate ICD shock and 150 (14%) patients died with a median time to death of 33 months (IQR 15–43). The rates of appropriate (14% vs. 15%, $p=0.64$) and inappropriate shocks (7% vs. 9%, $p=0.24$) were similar among patients with QRS-duration ≥130 ms and those with QRS-duration <130 ms, but patients with a QRS-duration ≥130 ms had a higher mortality during the follow-up (18% vs. 11%, $p=0.001$). Appropriate ICD shocks occurred at similar rates in ICM and NICM groups (17% vs. 12%, respectively, $p=0.06$), while inappropriate shocks were more common in NICM patients (6% vs. 11%, p=0.003) and death in the ICM patients (19% vs. 8%, p<0.001).

Association of the automatically calculated Selvester QRS-score with mortality, appropriate and inappropriate shocks during follow-up

A QRS-score ≥5 (the median) was associated with a significantly higher risk of mortality (p=0.033), appropriate shock (p=0.006) and inappropriate shock (p=0.047) in patients with QRS-duration ≥130 ms, but not in those with a QRS-duration <130 ms (Figure 1). For patients with QRS-duration ≥130 ms, a QRS-score ≥5 remained independently associated with mortality (HR 1.67, 95%CI 1.05–2.66, p=0.031), appropriate shock (HR 1.85, 95%CI 1.08–3.18, p=0.026) and inappropriate shock (HR 2.32, 95%CI 1.04–5.17, p=0.039) also after adjustment for other confounders in multivariable analysis (Table 3).

In an exploratory subgroup analysis of patients with ICM and NICM and QRS-duration ≥130 ms, both groups showed trends of potential association of QRS-score of ≥5 with higher rates of mortality, appropriate and inappropriate ICD shocks, but the associations did not reach statistical significance due to the limited sample size in the etiological subgroups (p>0.05, Figure S2).

Discussion

In this study, by using data of a large retrospective, multicenter, observational registry, we explored the potential of an automatically calculated version of the Selvester QRS-score, an ECG indicator of myocardial scar burden, to predict mortality and appropriate and inappropriate ICD shocks in a contemporary, real-world cohort of patients undergoing primary prevention ICD implantation. We report several novel, clinically relevant findings that might improve the risk assessment in candidates for a primary prevention ICD.

First, the automatically calculated Selvester QRS-score is a predictor of mortality, appropriate and inappropriate ICD shocks in primary preventive ICD patients with prolonged QRS-duration, but not in patients with normal QRS (Figure 2). Second, after adjustment in a multivariate analysis model in patients with prolonged QRS-duration, a QRS-score ≥5 remained an independent predictor and was associated with a 67% higher likelihood of mortality, 85% higher risk of appropriate ICD shock, and 132% higher probability of inappropriate ICD shocks during follow-up as compared to patients with QRS-score <5. Of important note, the use of cardiac resynchronization therapie (CRT) did not affect the predictive value of the QRS-score. And third, subgroup analysis of cases with prolonged QRS-duration according to heart failure etiology showed consistent trends for the association of QRS-score ≥5 with mortality, appropriate and inappropriate shocks in both patients with ICM and NICM. However, this study was not powered to detect the differences in risk driven by the QRS-score in disease etiology subgroups. This finding therefore has to be considered as preliminary and the differences between ICM and NICM should be further investigated.

Despite the incessant search for novel clinical, easy-to-use indicators of high arrhythmic risk, global LVEF ≤35% remains the only established criteria for ICD implantation for primary prevention of SCD (except for cardiac laminopathies, where specific criteria exist).[3, 6] As a large proportion of these patients will not experience therapeutic intervention from the device, it is well appreciated that the absence of proper risk estimation model leads to ICD implantation in patients at lower risk for SCD, potentially resulting in reduced benefit from a mismatch between risk and treatment. Cardiac imaging, in particular LGE-CMR, has been established as a valuable tool for quantification of myocardial scar burden and prediction of ICD therapy and mortality in both patients with ICM and NICM.[9-11]

These high end cardiac imaging technologies, however, are costly and not always available. To address this challenge, Strauss et al. first evaluated the utility of Selvester QRS-score for identifying patients at high-risk for a composite endpoint of appropriate ICD intervention or arrhythmic SCD in a cohort of 797 primary preventive ICD recipients (SCD-HEFT study).[13] Patients with no myocardial scar, as indicated by a QRS-score of 0 (13% of the population), experienced 48% fewer VT/VF events than patients with QRS-score ≥1. A QRS-score of ≥1 remained a significant predictor of arrhythmic events even when controlled for 10 clinically relevant variables,[13] indicating a potential causal relationship between the Selvester QRS-score-determined myocardial scar burden and arrhythmic events. . In contrast to the latter study, we further developed the methods of Strauss and colleagues and applied a previously developed automated version of the Selvester QRS-score.[15] While the manual calculation of the QRS-scores requires significant knowledge and takes about 15 minutes,[14] the automated version used in our approach is observer-independent and available immediately after recording the ECG. Accordingly, this approach could be integrated into routine clinical practice relatively easily. Furthermore, no CRT devices were included in SCD-HEFT or another study by Hiraiwa et al,[6, 13, 20] while resynchronization was used in 37% of the patients in the current study. Accordingly, our study better reflects the population of patients undergoing ICD implantation nowadays.

We found that the combination of a prolonged QRS duration and a QRS-score higher than the median identifies a high-risk group of roughly 20% of all primary prophylactic ICD recipients. Those patients are at highest risk for both death and appropriate ICD-shocks. As previous studies reported inconsistent findings regarding the association of prolonged QRS-duration with appropriate ICD therapy,[21-23] differences in myocardial scar burden might have contributed to the variation between cohorts.

Another remarkable finding of our study was the fact that the QRS-score predicted outcomes in patients with QRS-duration ≥130ms, but not in those with a normal QRS duration. Some clinical characteristics of the two groups were quite different and might have played a role: patients with QRS-duration ≥130ms were 5 years older (median 67 vs. 62 years), were more often in NYHA classes III and IV (69% vs. 27%) and more often received CRT-therapy (74% vs. 11%).

On the other hand, ECG confounders were present in 91% as opposed to 19%. Given that the criteria for calculation of the QRS score vary depending on the ECG confounder type present in the ECG, this difference was certainly relevant.

Even though several other ECG-based risk stratifiers such as heart rate variability (HRV), signal averaged ECG (SAECG), QT dispersion, microvolt T-wave alternans (MTWA) or QT variability have been studied in the past, very few, if any, made it into routine clinical practice.[24] Two main reasons might have contributed to this lack of translation: First, the inter-study reproducibility of the results has been rather poor und accordingly, the true value for SCD risk stratification is still incompletely understood for several of the markers proposed in the past. Second, several of the markers require time-consuming measurements at times requiring non-standard equipment.

While the QRS-score corroborates earlier findings,[6, 13, 20] its major advantage over the aforementioned ECG-markers might be that it can be easily and automatically calculated from a standard 10 seconds 12-lead ECG and does not require neither a 24h holter ECG nor non-standard equipment. Doing so, it could serve as an additional tool in patients with borderline ICD indications such as in patients with NICMP or in those with EF 30-35%. Patients with wide QRS and a QRS-score ≥5 have a clearly elevated risk for SCD and should receive an ICD. In those with a QRS-score <5 however, additional examinations such as a cardiac MRI for more accurate quantification of myocardial fibrosis might be considered to further refine risk stratification.

Limitations

The findings of this study should be viewed in light of some limitations. First, this was a non-randomized study. Accordingly, our findings can only be considered hypothesis generating. For the least, additional external validation in other non-randomized studies is needed to corroborate further our findings. Second, because no data on mechanism and cause of death were available, we were unable to establish the potential association of automatically calculated Selvester QRS-score with risk of arrhythmic SCD. Third, patients with non-specific bundle branch block were excluded because the Selvester QRS-score provides no classification for this type of ECG confounder.

Conclusion

The automatically calculated Selvester QRS-score, an indicator of myocardial scar burden, predicts mortality, appropriate and inappropriate shocks in patients with prolonged QRS-duration undergoing primary prevention ICD implantation. These findings require prospective validation in cohorts of ICM and NICM patients.

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Appendix

Supplementary material associated with this article can be found in the online version of the manuscript.

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Table 1. Baseline characteristics of patients grouped based on QRS-score.

	All patients n=1047	**QRS-score <5 n=490**	**QRS-score ≥5 n=557**	**p-value**
Age, years, median (IQR)	64 (55 – 71)	65 (54 – 71)	64 (55 – 70)	0.37
Male	872 (83%)	407 (83%)	465 (83%)	0.46
Heart disease				
ICM	648 (62%)	242 (49%)	406 (73%)	<0.001
NICM	399 (38%)	248 (51%)	151 (27%)	
LVEF, median (IQR)	27 (22 – 32)	27 (22 – 32)	27 (23 – 32)	0.92
CRT-D	386 (37%)	211 (43%)	175 (31%)	<0.001
QRS (ms), median (IQR)	123 (111 – 157)	125 (112 – 161)	122 (110 – 153)	0.02
Serum creatinine (mg/dL), median (IQR)	0.9 (1.1 – 1-3)	0.9 (1.1 – 1-3)	0.9 (1.1 – 1-3)	0.34
Serum creatinine >1.2 mg/dL	360 (34%)	161 (33%)	199 (36%)	0.18
Diabetes	259 (25%)	117 (24%)	142 (25%)	0.49
Missing	22 (2%)	9 (2%)	13 (2%)	
NYHA class	961 (92%)	453 (92%)	508 (91%)	
I/II	495 (47%)	209 (43%)	286 (51%)	0.001
III/IV	466 (45%)	244 (50%)	222 (40%)	
missing	86 (8%)	37 (8%)	49 (9%)	
ECG confounders	511 (49%)	273 (56%)	238 (43%)	<0.001
No ECG confounder	536 (51%)	217 (44%)	319 (57%)	
LBBB	354 (34%)	214 (44%)	140 (25%)	<0.001
RBBB & LAFB	22 (2%)	3 (1%)	19 (3%)	0.001
RBBB	42 (4%)	5 (1%)	37 (7%)	<0.001
LAFB	24 (2%)	7 (1%)	17 (3%)	0.06
LVH	69 (7%)	44 (9%)	25 (6%)	0.03

Data are presented as median (interquartile range) or as n (%).

AF = atrial fibrillation; CRT-D = cardiac resynchronization therapy implantable cardioverter-defibrillator; ICM = ischaemic cardiomyopathy; LAFB = left-anterior fascicular block; LBBB = right bundle branch block; LVEF = left ventricular ejection fraction; LVH = left ventricular hypertrophy; NA = not applicable; NICM = non-ischemic cardiomyopathy; NYHA = New York York AssocIation; RBBB = right bundle branch block.

Table 2. Baseline characteristics of patients grouped based on QRS-duration and QRS-score.

	QRS <130 ms			QRS ≥130 ms		
	QRS-score <5 n=266	**QRS-score ≥5 n=347**	**p-value**	**QRS-score <5 n=224**	**QRS-score ≥5 n=210**	**p-value**
Age, years, median (IQR)	62 (52 – 70)	62 (52 – 68)	0.36	67 (58 – 72)	68 (60 – 73)	0.36
Male	230 (86%)	300 (86%)	0.55	177 (79%)	165 (79%)	0.50
Heart disease						
ICM	137 (52%)	279 (80%)	<0.001	105 (47%)	127 (60%)	0.003
NICM	129 (48%)	68 (20%)		119 (53%)	83 (40%)	
LVEF, median (IQR)	29 (24 – 35)	30 (25 – 33)	0.44	25 (20 – 30)	25 (20 – 30)	0.71
CRT-D	42 (16%)	24 (7%)	<0.001	169 (76%)	151 (72%)	0.4
QRS (ms), median (IQR)	113 (107 – 120)	114 (106 – 121)	0.589	164 (150 – 173)	164 (147 – 176)	0.8
Serum creatinine (mg/dL), median (IQR)	1.0 (0.9 – 1.3)	1.0 (0.9 – 1.3)	0.579	1.1 (0.9 – 1.3)	1.2 (1.0 – 1.4)	0.06
Serum creatinine >1.2 mg/dL	81 (30%)	100 (29%)	0.363	80 (36%)	99 (47%)	0.02
Diabetes	59 (23%)	86 (25%)	0.657	58 (26%)	56 (27%)	0.72
missing	6 (%)	8 (%)		3 (%)	5 (%)	
NYHA class	242 (91%)	306 (88%)	0.018	211 (94%)	202 (96%)	
I/II	156 (64%)	224 (73%)		53 (25%)	62 (31%)	0.12
III/IV	86 (36%)	82 (27%)		158 (75%)	140 (69%)	
missing	24 (9%)	41 (12%)		13 (6%)	8 (4%)	
ECG confounders	61 (23%)	54 (16%)	0.014	212 (95%)	184 (88%)	0.008
No ECG confounder	205 (77%)	293 (84%)		12 (5%)	26 (12%)	
LBBB	17 (6%)	10 (3%)	0.029	197 (88%)	130 (70%)	<0.001
RBBB & LAFB	0	1 (0%)	0.38	3 (1%)	18 (9%)	<0.001
RBBB	0	4 (1%)	0.08	5 (2%)	33 (16%)	<0.001
LAFB	7 (3%)	16 (5%)	0.14	0	1 (0%)	0.3
LVH	37 (14%)	23 (7%)	0.002	7 (3%)	2 (1%)	0.11

Data are presented as median (interquartile range) or as n (%).

See Table 1 for abbreviations.

Table 3. Predictors of mortality, appropriate and inappropriate ICD shocks in primary prophylactic ICD patients with QRS-duration ≥130 ms.

	Univariate		**Multivariate**	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Death				
Age at implantation (y)	1.04 (1.02-1.07)	0.001	1.04 (1.01-1.07)	0.004
Sex (male vs. female)	1.44 (0.78-2.66)	0.24		
LVEF (%)	0.96 (0.93-0.99)	0.02	0.95 (0.92-0.99)	0.01
Heart disease (ICM vs. NICM)	2.14 (1.31-3.5)	0.002	1.71 (1.03-2.85)	0.04
NYHA class (III/IV vs. I/II)	2.07 (1.09-3.92)	0.03	1.65 (0.85-3.18)	0.14
CRT-D vs. ICD	0.89 (0.55-1.44)	0.62		
QRS-score (≥ 5 vs. <5)	1.62 (1.04-2.53)	0.03	1.67 (1.05-2.66)	0.03
Appropriate Shock				
Age at implantation (y)	0.99 (0.97-1.02)	0.57		
Sex (male vs. female)	1.81 (0.86-3.80)	0.12		
LVEF (%)	0.98 (0.95-1.02)	0.34		
Heart disease (ICM vs. NICM)	1.85 (1.08-3.14)	0.02	1.53 (0.87-2.69)	0.14
NYHA class (III/IV vs. I/II)	0.58 (0.34-0.99)	0.05	0.69 (0.37-1.29)	0.25
CRT-D vs. ICD	0.58 (0.35-0.97)	0.04	0.77 (0.41-1.46)	0.43
QRS-score (≥ 5 vs. <5)	2.07 (1.23-3.49)	0.006	1.85 (1.08-3.18)	0.03
Inappropriate Shock				
Age at implantation (y)	0.96 (0.93-0.99)	0.009	0.96 (0.93-0.99)	0.008
Sex (male vs. female)	1.53 (0.53-4.43)	0.43		
LVEF (%)	0.99 (0.94-1.05)	0.74		
Heart disease (ICM vs. NICM)	0.55 (0.26-1.19)	0.13		
NYHA class (III/IV vs. I/II)	1.23 (0.50-3.07)	0.65		
CRT-D vs. ICD	1.28 (0.52-3.16)	0.6		
QRS-score (≥ 5 vs. <5)	2.25 (1.01-5.01)	0.05	2.32 (1.04-5.17)	0.04

CI = confidence interval; HR = hazard ratio; CRT-D = cardiac resynchronization therapy with defibrillator; HR = hazard ratio; ICD = implantable cardioverter defibrillator; ICM = ischemic cardiomyopathy; LVEF = left ventricular ejection fraction; NA = not applicable; NICM = non-ischemic cardiomyopathy; NYHA = New York Heart Association.

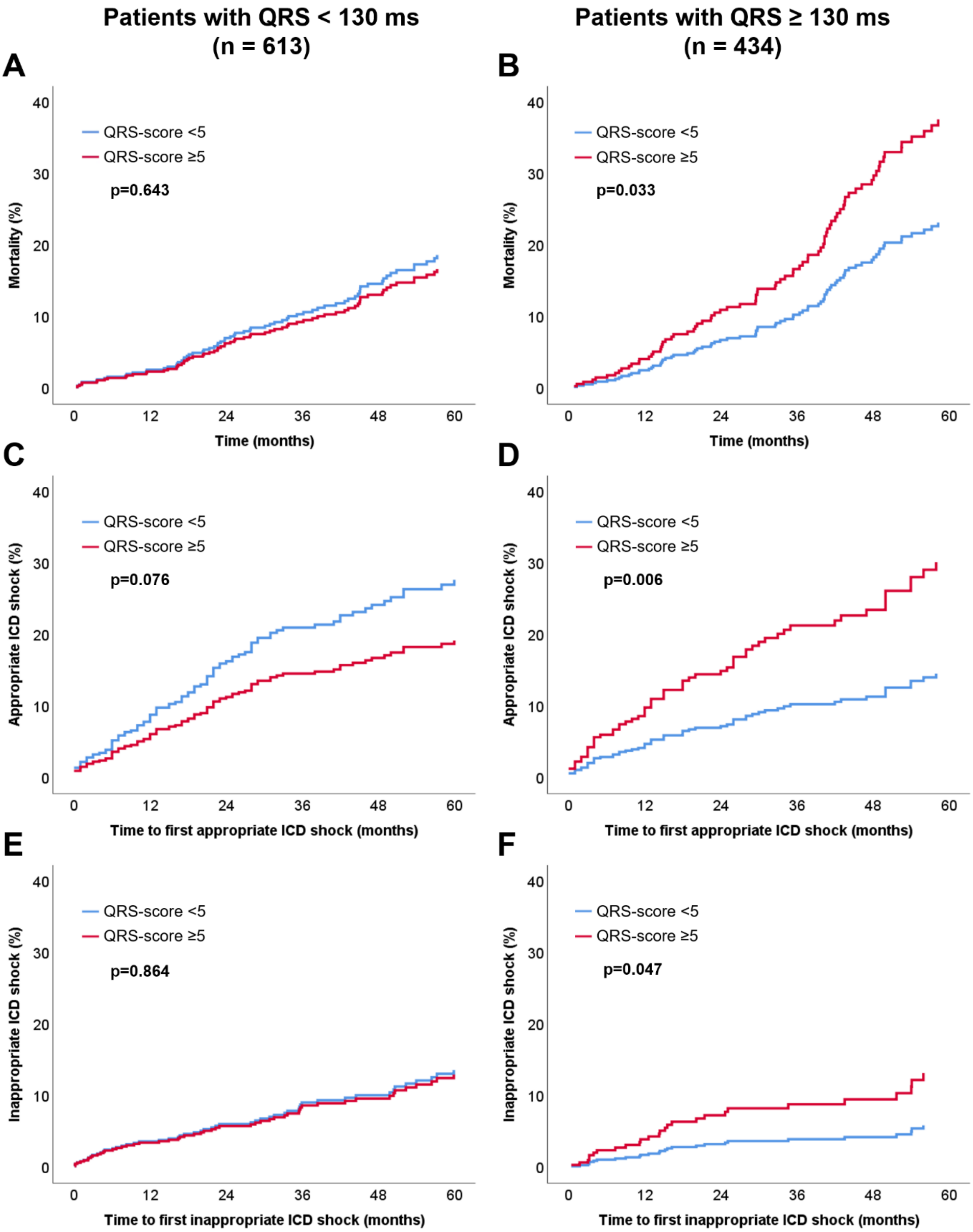

Figure 1. Cox regression analyses for the cumulative probability of death (A and B), first appropriate ICD shock (C and D), and inappropriate shock (E and F) according to the median QRS-score, <5 vs. ≥5, respectively in patients with QRS-interval duration <130 ms (left panels) and those with ≥130 ms (right panels). Patients who died were censored for the analyses regarding appropriate and inappropriate shocks.

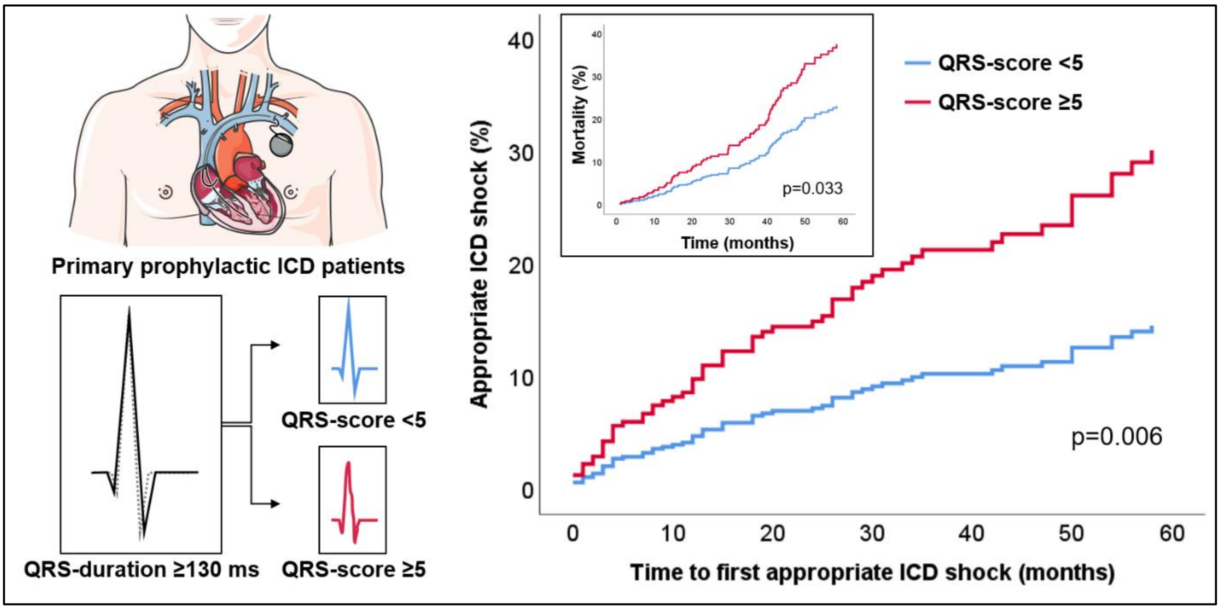

Figure 2 (Graphical abstract). Selvester QRS-score predicts appropriate shocks and mortality in patients with QRS-duration ≥130 ms undergoing primary prevention ICD implantation.