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Improvements in implantable cardioverter defibrillator patient stratification

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Citation

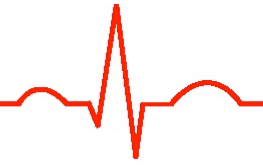
Welsenens, G. H. van. (2012, February 2). *Improvements in implantable cardioverter defibrillator patient stratification*. Retrieved from <https://hdl.handle.net/1887/18430>

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Chapter 7

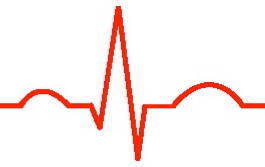
Predicting Ventricular Arrhythmias in Patients with Ischemic Heart Disease: Clinical Application of the ECG derived QRS-T Angle

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Circ Arrhythm Electrophysiol 2009; 2:548-554



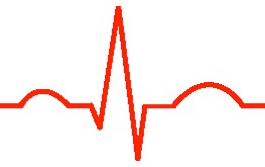
Abstract

Background: In primary prevention implantable cardioverter defibrillator (ICD) patients, the incidence of life-threatening ventricular arrhythmias resulting in ICD therapy is relatively low, prompting for better risk stratification. The aim of this study was to assess the value of the QRS-T angle for prediction of ICD therapy and mortality in primary prevention patients with ischemic heart disease (IHD).

Methods and results: ICD patients (n=412, 361 male, age 63±11 years) with IHD and a left ventricular ejection fraction $\leq 40\%$ were included. After device implantation, the occurrence of appropriate ICD therapy and mortality was noted. A survival analysis was performed comparing patients with a planar QRS-T angle $\leq 90^\circ$ (n=124, 30%) to patients with a planar QRS-T angle $> 90^\circ$ before device implantation. Furthermore, patients with a spatial QRS-T angle $\leq 100^\circ$ (n=56, 14%) were compared to patients with a spatial QRS-T angle $> 100^\circ$, prior to implant.

For patients with a planar QRS-T angle $>90^\circ$ as compared to $\leq 90^\circ$, the adjusted hazard ratio for the occurrence of appropriate device therapy was 2.4 (95% CI 1.1-5.2); a spatial QRS-T angle $> 100^\circ$ was associated with an adjusted hazard ratio of 7.3 (95% CI 1.0-53.8). Furthermore, a spatial QRS-T angle $\leq 100^\circ$ exhibited a positive predictive value of 98% (95% CI 95-100%) for the prediction of an appropriate therapy-free follow-up.

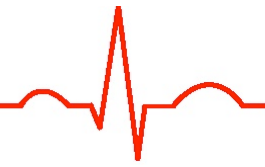
Conclusions: A wide QRS-T angle is a strong predictor of appropriate device therapy in primary prevention ICD recipients with IHD. Furthermore, a spatial QRS-T angle $\leq 100^\circ$ might be of value in the identification of patients in whom, although currently indicated, ICD treatment should be reconsidered.



Introduction

Sudden cardiac death (SCD), mainly caused by ventricular arrhythmias, accounts for approximately 50% of all cardiac mortality worldwide.¹⁻³ It is recognised that patients with ischemic heart disease and depressed left ventricular ejection fraction (LVEF) are at high risk of SCD,^{4, 5} and large randomised trials have demonstrated that implantable cardioverter defibrillator (ICD) therapy reduces all-cause mortality, as well as SCD.⁶⁻¹⁰ Implementation of these results in the international guidelines resulted in a significant increase of the number of ICD implantations.^{11, 12} However, long-term follow-up studies in currently indicated patients show a relatively low incidence of ventricular arrhythmias that trigger ICD therapy.¹³ Additionally, approximately 6% of ICD patients experience severe device-related adverse events (i.e. pocket infections, sepsis), causing the need for surgical re-intervention, additional hospitalization, or even death.^{14, 15} This led to critical appraisal of the wide-spread application of ICD therapy and stressed the need for more precise risk stratification criteria.¹⁶ In an attempt to identify those criteria, post-hoc analyses of the second Multicenter Automatic Defibrillator Implantation Trial (MADIT II) revealed several clinical criteria associated with an increased risk for ventricular arrhythmias resulting in appropriate device therapy.¹⁷⁻¹⁹ So far, however, in low LVEF patients no criteria have been recognised which may identify patients at low risk of ventricular arrhythmias during follow-up. If possible to identify a low risk population, ICD therapy in this group may be reconsidered.

Recently, a wide angle between the QRS and T axes, the QRS-T angle, on the standard 12-lead ECG was recognised as a novel and easy applicable marker of increased risk for cardiovascular mortality.^{20, 21} Subsequently, a wide QRS-T angle was found to be



associated with the increased incidence of appropriate device therapy and mortality in primary prevention ICD recipients with non-ischemic cardiomyopathy.²² However, no data are available on the value of the QRS-T angle in ICD patients with IHD.

The aim of the current study was, to assess the value of the QRS-T angle in predicting life threatening ventricular arrhythmias in primary prevention ICD patients with IHD. Furthermore the value of the QRS-T angle was evaluated as a parameter to identify patients at low risk for ventricular arrhythmias.

Methods

Patients

Patients with IHD who underwent implantation of an ICD, based on the international treatment guidelines, in the Leiden University Medical Center were selected for the current study.¹¹ Criterion for inclusion were a depressed LVEF (<40%) with or without a history of non sustained ventricular tachycardia. Since 1996, these patients were prospectively registered in the departmental Cardiology Information System (EPD-Vision[®]).²³ Prior to implantation, a comprehensive assessment of patient characteristics was performed as described previously.²⁴

During follow-up, the occurrence of appropriate ICD therapy and patient mortality was noted. In addition, for the purpose of this study, the ECG made before implantation was analyzed.

Implantable cardioverter defibrillator implantation and follow-up

All defibrillator systems were implanted transvenously without thoracotomy. Device follow-up was scheduled every three to six months. All printouts were carefully checked for appropriate and inappropriate ICD therapy. In case of any ICD therapy, an electrophysiologist, blinded to QRS-T measurements, determined whether or not the ICD therapy was appropriate. All therapies, either

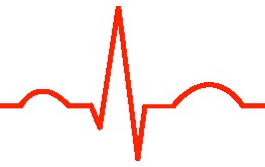


anti-tachycardia pacing (ATP) or shock, were classified as appropriate when they occurred in response to life threatening arrhythmias; ventricular tachycardia (VT) or ventricular fibrillation (VF) and as inappropriate when triggered by sinus or supraventricular tachycardia (SVT), T-wave oversensing, or electrode dysfunction.

Defibrillators were programmed as follows: ventricular arrhythmia faster than 150 bpm was monitored by the device without consequent defibrillator therapy. Ventricular arrhythmias faster than 188 bpm were initially attempted to be terminated with two bursts of ATP and, after continuation of the arrhythmia, with defibrillator shocks. In the case of a ventricular arrhythmia faster than 210 bpm, device shocks were the initial therapy. Furthermore, atrial arrhythmia detection was set to >170 bpm with SVT discriminators enabled. Settings were adapted, only when clinically indicated (i.e. hemodynamic well tolerated ventricular tachycardia at high rate; ventricular tachycardia in the monitor zone).

Electrocardiographical analysis

First, the quality of ECGs was evaluated. If electrode displacement, missing leads or signal noise was present, the ECGs were excluded from the analysis. Since right ventricular pacing alters normal cardiac conduction and results, by definition, in an abnormal QRS-T angle, patients with a pacemaker were excluded from the analysis.²⁵ Subsequently, the ECGs were analyzed with a dedicated computer program (LEADS, Leiden ECG Analysis and Decomposition Software).²⁶ Full details on the computation method and LEADS based values of vector characteristics in healthy subjects, have been extensively described earlier.²⁷ In short, the software converts the standard ECG into a vectorcardiogram and computes the three dimensional orientation of the QRS- and T-axes. Thereafter, the QRS-T angle is calculated in the plane formed by the QRS- and T-axes, the *spatial* QRS-T angle. In addition, the more commonly used but less precise projection of the spatial QRS-T angle in the frontal plane, the *planar* QRS-T angle, was computed. Previous



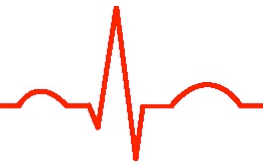
studies demonstrated that a spatial QRS-T angle wider than 100° is associated with the presence of cardiac disease and increased cardiovascular mortality.^{20, 21} Pavri et al. recently demonstrated that a planar QRS-T angle wider than 90° is associated with an increased incidence of appropriate device shocks and mortality²². In the present study, these cut-offs (100° for the spatial and 90° for the planar QRS-T angle) were applied.

Statistical analysis

A survival analysis, comprising of the following end-points, was performed: (1) first appropriate ICD therapy (ATP and/or shock); (2) all-cause mortality; and (3) a composite end-point of all-cause mortality and first appropriate device therapy, whichever occurs first. ICD recipients with a narrow QRS-T angle were compared to those with a wide QRS-T angle. The points of cut-off were pre-defined as described above, 100° for the spatial and 90° for the planar QRS-T angle. Cumulative event rates of end-points were analyzed by the method of Kaplan-Meier. Relationships between baseline parameters and end-points were assessed with Cox's proportional hazard regression analysis. For the composite end-point, survival time was defined as time to all-cause death or appropriate device therapy, whichever occurred first. For each variable a hazard ratio with a 95%-confidence interval (95% CI) was calculated. Therapy-free follow-up was defined as a study follow-up without the occurrence of appropriate ICD therapy.

Continuous data are expressed as mean \pm standard deviation or median and quartiles where appropriate; dichotomous data are presented as numbers and percentages. Comparison of data at baseline was performed with the Student's *t* test for unpaired data and Chi-square tests with Yates correction when appropriate.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.



Results

Patients and follow-up

A total of 460 patients with ischemic heart disease and a LVEF \leq 40% underwent ICD implantation for primary prevention of sudden cardiac death in the Leiden University Medical Center. Thirty-two (7%) patients were excluded due to the presence of a pacemaker and 16 (3%) patients were excluded since their ECG prior to device implantation could not be analyzed because of technical reasons such as electrode displacement, missing leads, or signal noise. The remaining 412 (90%) ICD recipients (63 \pm 11 yrs, 88% male) were included in the analysis and were followed for 22 \pm 17 months (range 0 to 77 months). Baseline characteristics are summarised in Table 1.

During follow-up, 46 (11%) patients died, and a total of 482 episodes of appropriate device therapy for ventricular arrhythmias occurred in 56 (14%) patients; 386 episodes of ventricular arrhythmia, terminated by ATP in 35 (8%) patients, and 96 episodes triggering device shocks in 28 (7%) patients. During follow-up, the first end-point (first appropriate device therapy) was reached in 56 patients (24 shock, 32 ATP), the second end-point (all-cause death) was reached in 46 patients and the composite end-point (death or first appropriate device therapy) was reached in 96 patients (40 patients all cause deaths, 56 appropriate therapy).

**Table 1.** Patient characteristics

	All patients	Planar QRS-T angle ≤ 90°		Spatial QRS-T angle ≤ 100°	
		Yes	No	Yes	No
Patients	412	124 (30%)	288 (70%)	56 (14%)	356 (86%)
Clinical parameters					
Age (yrs)	63±11	61±11	64±10*	62±11	63±10
Male (%)	361 (88%)	110 (89%)	251 (87%)	51 (91%)	310 (87%)
Biventricular ICD (%)	194 (47%)	43 (35%)	151 (52%)†	22 (39%)	172 (48%)
LVEF (%)	26±7	28±7	25±7†	30±6	26±7†
NYHA functional class					
I-II	261 (63%)	92 (74%)	169 (59%)*	41 (73%)	220 (62%)
III-IV	151 (37%)	32 (26%)	119 (41%)*	15 (27%)	136 (38%)
History of diabetes mellitus (%)	110 (27%)	24 (19%)	86 (30%)*	6 (11%)	104 (29%)†
History of nicotine abuse (%)	190 (46%)	55 (44%)	135 (47%)	29 (52%)	161 (45%)
Current nicotine abuse (%)	86 (21%)	25 (20%)	60 (21%)	12 (21%)	74 (21%)
History of atrial fibrillation / flutter (%)	98 (24%)	24 (19%)	74 (26%)	10 (18%)	88 (25%)
Atrial fibrillation / flutter at implantation (%)	39 (9%)	8 (6%)	31 (11%)	2 (4%)	37 (10%)
History of nonsustained VT (%)	81 (20%)	24 (19%)	57 (20%)	10 (18%)	71 (20%)
Body mass index (kg/m ²)	27±4	26±4	27±5	27±3	27±4
Medication					
Beta blocker (%)	317 (77%)	99 (80%)	218 (76%)	42 (75%)	275 (77%)
ACE inhibitor / AT antagonist (%)	358 (87%)	110 (89%)	248 (86%)	49 (88%)	309 (87%)
Diuretics for CHF (%)	317 (77%)	90 (73%)	227 (79%)	38 (68%)	279 (78%)
Statins (%)	349 (85%)	111 (90%)	238 (83%)	53 (95%)	296 (83%)*
Amiodarone (%)	57 (14%)	15 (12%)	42 (15%)	1 (2%)	56 (16%)†
ECG parameters					
Heart rate (bpm)	66±16	66±15	66±16	67±16	66±15
QRS duration (ms)	130±33	120±29	134±34†	115±28	132±33†
QTc Bazett (ms)	431±51	431±52	431±51	434±50	431±52
Frontal QRS-T angle (°)	116±52	47±24	146±26†	62±33	125±50†
Spatial QRS-T angle (°)	139±32	112±35	151±22†	75±18	149±20†

* p<0.05; † p<0.01 as compared to patients with a narrow planar/spatial QRS-T angle.

ACE = angiotensin converting enzyme; AT = angiotensin; CHF = congestive heart failure; ICD = implantable cardioverter defibrillator; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; VT = ventricular tachycardia.



QRS-T angle and all-cause mortality

In 124 (30%) patients, a planar QRS-T angle smaller or equal to 90° was measured on the baseline ECG. As summarised in Table 1, patients with a narrow planar QRS-T angle were more likely to be younger (61 ± 11 yr vs. 64 ± 10 yr, $p < 0.05$), to have a better LVEF ($28 \pm 7\%$ vs. $25 \pm 7\%$, $p < 0.001$), and shorter QRS duration (120 ± 29 ms vs. 134 ± 34 ms, $p < 0.001$). The hazard ratio of a planar QRS-T angle $> 90^\circ$ for mortality was 3.1 (95% CI 1.3-7.3) as compared to patients with a narrow planar QRS-T angle. The cumulative event-free follow-up for all cause mortality in patients with a narrow planar QRS-T angle was 99% (95% CI 98-100%) at one year, 92% (95% CI 87-98%) at two years, and 92% (95% CI 87-98%) at four years of follow-up (Figure 1).

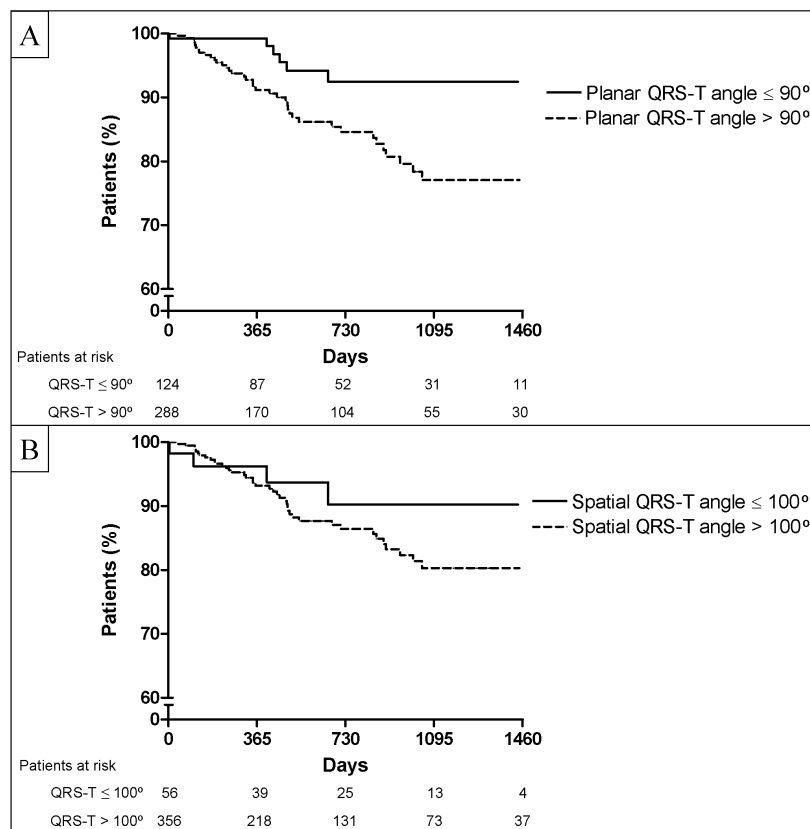


Figure 1. Kaplan-Meier curve for cumulative event rate for all cause mortality in patients with a planar QRS-T angle $\leq 90^\circ$ vs. a planar QRS-T angle $> 90^\circ$ (panel A) and with a spatial QRS-T angle $\leq 100^\circ$ vs. a spatial QRS-T angle $> 100^\circ$ (panel B).



Fifty-six (14%) patients had a baseline spatial QRS-T angle smaller than or equal to 100°. These patients were younger, had a more preserved LVEF (30±6% vs. 26±7%, $p<0.01$), a shorter QRS duration (115±28 ms vs. 132±33 ms, $p<0.01$), used statins more often (95% vs. 83%, $p<0.05$) and were using amiodarone less frequently (2% vs. 16%, $p<0.01$) (Table 1). As is shown in Table 2, patients with a wide spatial QRS-T angle exhibited a hazard ratio for all-cause mortality of 1.7 (95% CI 0.6-4.9).

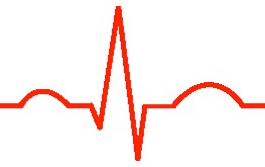
Table 2. Event rates, hazard ratios, and p-values for end-points

	Planar QRS-T angle $\leq 90^\circ$		HR (95% CI)	Adjusted HR (95% CI)*	Spatial QRS-T angle $\leq 100^\circ$		HR (95% CI)	Adjusted HR (95% CI)*
	Yes	No			Yes	No		
Appropriate therapy	8/124 (6.5%)	48/288 (16.7%)	2.9 (1.4-6.1)	2.4 (1.1-5.2)	1/56 (1.8%)	55/356 (15.4%)	9.9 (1.4-1.7)	7.3 (1.0-53.8)
All-cause mortality	6/124 (4.8%)	40/288 (13.9%)	3.1 (1.3-7.3)	2.3 (1.0-5.6)	4/56 (7.1%)	42/356 (11.8%)	1.7 (0.6-4.9)	1.0 (0.4-3.2)
Appropriate therapy and all-cause mortality	14/124 (11.3%)	82/288 (28.5%)	2.9 (1.6-5.0)	2.3 (1.3-4.1)	5/56 (8.9%)	91/356 (25.6%)	3.4 (1.4-8.3)	2.3 (0.9-5.9)

*Hazard ratio was adjusted for age, sex, LVEF, and QRS duration.
CI = confidence interval; HR = hazard ratio

QRS-T angle and ventricular arrhythmia

The hazard ratio of a planar QRS-T angle wider than 90° for the occurrence of ventricular arrhythmia triggering appropriate device therapy was 2.9 (95% CI 1.4-6.1). When adjusted for age, sex, LVEF and QRS duration, the hazard ratio was 2.4 (95% CI 1.1-5.2). Furthermore, this group demonstrated an almost threefold risk increase (hazard ratio 2.9, 95% CI 1.6-5.0) for the composite end-point of appropriate therapy and mortality (Table 2). The cumulative event-free follow-up for appropriate therapy in patients with a narrow planar QRS-T angle was 95% (95% CI 90-99%) at one year, 93% (95% CI 87-98%) at two years, and 89% (95% CI 81-98%) at four



years of follow-up (Figure 2).

As is shown in Table 2, patients with a wide spatial QRS-T angle exhibited a near tenfold risk for the occurrence of ATP or shocks (hazard ratio 9.9, 95% CI 1.4-71.7) during follow-up. When adjusted for age, sex, LVEF, and QRS duration the hazard ratio was 7.3 (95% CI 1.0-53.8). Strikingly, the cumulative event-free follow-up for ventricular arrhythmia which triggered device therapy was 100% at two years and 96% (95% CI 87-100%) at four years of follow-up, as can be readily seen in Figure 2.

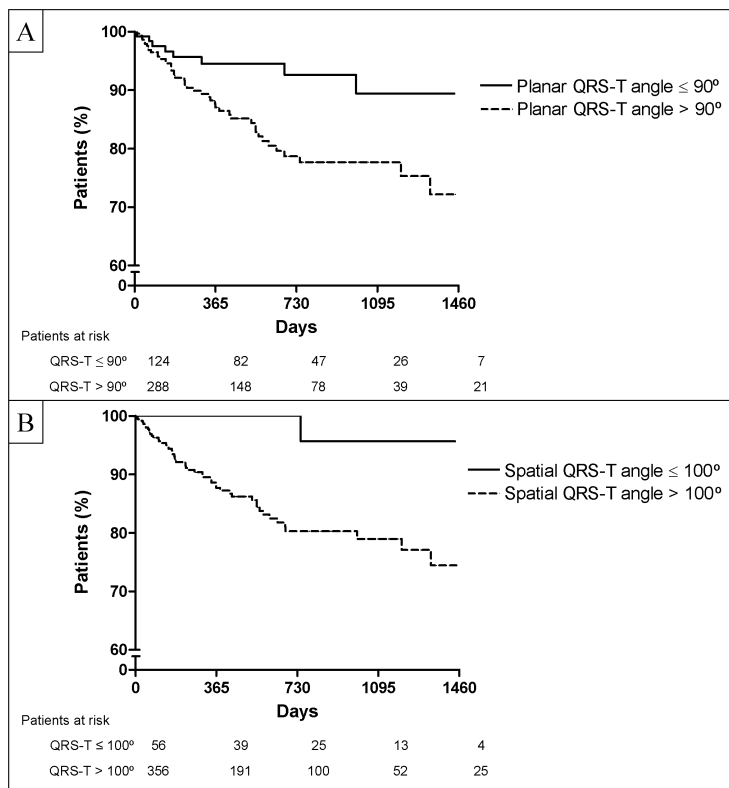
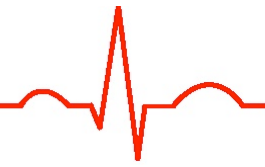


Figure 2. Kaplan-Meier curve for cumulative event rate for appropriate therapy in patients with a planar QRS-T angle $\leq 90^\circ$ vs. a planar QRS-T angle $> 90^\circ$ (panel A) and with a spatial QRS-T angle $\leq 100^\circ$ vs. a spatial QRS-T angle $> 100^\circ$ (panel B).



Identification of patients free of life-threatening arrhythmias

Evaluation of the usefulness of a planar QRS-T angle smaller than or equal to 90° at baseline in the prediction of an appropriate therapy-free follow-up revealed a positive predictive value of 94% (95% CI 89-98%) and a negative predictive value of 17% (95% CI 12-21%).

The spatial QRS-T angle had a positive predictive value of 98% (95% CI 95-100%) and a negative predictive value of 15% (95% CI 12-19%) for the prediction of an appropriate therapy-free follow-up. Most importantly, only 2% of the patients with a spatial QRS-T angle $\leq 100^\circ$ had appropriate device discharges during follow-up, the only event occurring after 745 days (Figure 2).

Discussion

In the current study on the clinical application of the planar and spatial QRS-T angle in the prediction of ventricular arrhythmias in ischemic primary prevention ICD patients, the main findings can be summarised as follows: after adjustment for age, sex, LVEF, and QRS-duration, 1) patients with a wide planar QRS-T angle exhibited a nearly 2.5-fold risk for mortality, as well as for appropriate device therapy; 2) patients with a wide spatial QRS-T angle had a sevenfold risk for ventricular arrhythmias triggering appropriate device therapy; and 3) patients with a spatial QRS-T $\leq 100^\circ$ prior to implantation, exhibited an absolute risk of 2% for appropriate therapy during follow-up.

With primary prevention ICD therapy as a class I indication in international guidelines in patients with a low LVEF, the indicated population, and therefore the worldwide defibrillator implantation rates, have increased significantly.^{11, 12} This expansion is of such magnitude that health care systems might lack the logistic capacity and financial means to meet the demand of



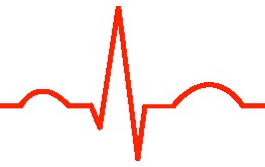
ICD implantations.^{16, 28} Furthermore, MADIT II demonstrated a cumulative incidence of the need for defibrillator back-up of only 35% of patients after three years.¹³ Moreover, 6% of ICD treated patients, experience severe device-related adverse events.¹⁴ These issues underscore the need for better risk stratification within the indicated population.

Ideally, a parameter for the identification of a population at high or at low risk for the need for defibrillator back-up should be non-invasive and easily acquired. An ECG derived parameter such as the QRS-T angle, validated in the current analysis, would fit these demands.

Risk stratification with the QRS-T angle

The QRS-T angle is the angle between the electrical axes of depolarisation and repolarisation. In the present study, clinical application of both the planar as well as the spatial QRS-T angle has been investigated in primary prevention ICD recipients with ischemic heart disease. The planar QRS-T angle is the projection of the spatial QRS-T angle in the frontal plane. As with any projection, it is sensitive to variations of the anatomical position of the heart in thorax. Therefore, the spatial QRS-T angle, which is calculated in the plane that the QRS- and T-axes form, is a more robust clinical tool. This is an important issue as the results from this study demonstrate that a narrow spatial angle is associated with a lower risk of ventricular arrhythmias. And although the spatial QRS-T angle cannot be derived directly from the surface ECG, recent studies have provided easy methods to acquire the spatial QRS-T angle from the standard 12-lead ECG.²⁹

In our population of ischemic primary prevention ICD recipients, patients with a wide planar QRS-T angle demonstrated a hazard ratio of 2.5 for the need of defibrillator back-up and 3.1 for all-cause mortality. In the recently published post hoc analysis of the DEFINITE trial, by Pavri and co-workers²², the planar QRS-T angle was analyzed as a predictor of the composite end-point of appropriate device therapy, mortality, and resuscitated cardiac arrest in a population

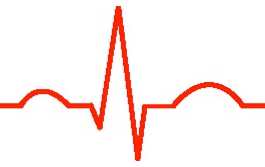


with *non*-ischemic cardiomyopathy. In this study, the hazard ratio of a planar QRS-T angle wider than 90° for the occurrence of appropriate device therapy was 1.95 (95% CI 1.24-3.08). The hazard ratio for all-cause mortality was 1.81 (95% CI 1.04-3.13).

After adjustment for other commonly used risk factors, the presence of a spatial QRS-T angle wider than 100° was associated with a hazard ratio of 7.3 for the occurrence of device therapy for ventricular arrhythmias as compared to patients with a spatial QRS-T angle $\leq 100^\circ$, in our population. More importantly, all patients with a spatial QRS-T angle $\leq 100^\circ$ were free of device generated therapy during two years following implantation. This indicates that the spatial QRS-T angle may have an important potential for risk stratification in patients with ischemic heart disease.

Previous studies on the spatial QRS-T angle have already indicated its high value in the risk stratification for cardiac death in a population without ICDs.^{20, 21} In a large cohort of patients, Yamazaki et al. observed a hazard ratio of 1.9 (95% CI 1.7-2.1) on cardiovascular death for a spatial QRS-T angle $> 100^\circ$ after correction for other ECG parameters.²¹

As a consequence of the balanced regulation of electrical activation and recovery of the ventricles, a narrow QRS-T angle is generally observed in healthy individuals.²⁷ Ventricular scar or residual ischemia, which is the arrhythmic substrate in ischemic cardiomyopathy, causes a disbalance of this process, sometimes referred to as electrical heterogeneity or discordance of de- and repolarisation.³⁰ Vectorcardiographically, these alterations in cardiac electrophysiology become, amongst others, apparent through directional changes of the QRS and T vectors and consequent widening of the QRS-T angle. When patients with ischemic cardiomyopathy have a narrow QRS-T angle, which is then associated with electrical homogeneity, it could be postulated that the amount of arrhythmic substrate is limited and may even be absent. The high incidence of ventricular arrhythmias in patients with a wide QRS-T angle and the low incidence in patients with a narrow QRS-T angle, as observed in the current study, underscores this principle.

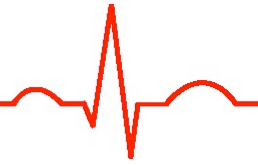


Clinical implications

Several non-invasive parameters that could improve patient selection for ICD therapy have been proposed. These include LVEF, QRS duration, QT interval, heart rate variability, ventricular ectopy on ambulatory monitoring, exercise capacity, and T-wave alternans.³¹ In addition, total cosine R to T, which is also a measure of QRS-T concordance like the QRS-T angle, has been proven a promising parameter in the mortality risk stratification in patients following myocardial infarction.^{32, 33} However, this variable has not been assessed in an ICD treated population, to our knowledge. Although the majority of these parameters appear promising, only LVEF has proven its usefulness in patient selection for ICD implantation and is currently the most important factor in the clinician's choice whether or not an ICD is indicated.¹¹ Still, in the implanted ischemic population, identified as being at high risk for ventricular arrhythmia based on depressed LVEF, 35% of patients actually experiences appropriate device therapy during follow-up, prompting for the identification of a sub-population at low risk.¹³ In our population of ischemic primary prevention ICD recipients, patients with a spatial QRS-T angle $\leq 100^\circ$ demonstrated no ventricular arrhythmias during the first two years following implantation and only 2% during further follow-up. These results imply that this parameter could be used in the discrimination of patients in whom the beneficial effects of an ICD might not exceed the costs and potential morbidity accompanying ICD therapy.

Limitations

This was a non-randomised prospective observational study, performed to assess the long-term follow-up in ischemic primary prevention ICD recipients and to assess the value of the planar and spatial QRS-T angle in baseline risk stratification. Adjustment for additional variables in the multivariable Cox model was limited by the number of end-points reached. Furthermore, some



patients without therapy during study follow-up might have reached an end-point, had follow-up been longer. Additionally, since not all patients had post-mortem ICD interrogation, some cases of death might have been arrhythmic. Finally, since patients were included over a period of 11 years, expanding guidelines for the implantation of defibrillators, treatment of acute myocardial infarction, and pharmacological anti-arrhythmic therapy could have created an inhomogeneous population.

Conclusion

In patients with ischemic heart disease, currently indicated for primary prevention ICD therapy, a baseline spatial QRS-T angle $> 100^\circ$ is associated with a sevenfold risk for the occurrence of appropriate device therapy, even after adjustment for commonly used risk factors. More importantly, a spatial QRS-T angle $\leq 100^\circ$ on the ECG prior to implantation can identify patients with very low risk of life-threatening ventricular arrhythmias in whom the beneficial effect of ICD treatment might not exceed the costs and potential complications.



Reference List

1. Huikuri HV, Castellanos A, Myerburg RJ. Sudden death due to cardiac arrhythmias. *N Engl J Med.* 2001; 345:1473-82.
2. Josephson M, Wellens HJ. Implantable defibrillators and sudden cardiac death. *Circulation.* 2004; 109:2685-91.
3. Zipes DP, Wellens HJ. Sudden cardiac death. *Circulation.* 1998; 98:2334-51.
4. Risk stratification and survival after myocardial infarction. *N Engl J Med.* 1983; 309:331-6
5. Rouleau JL, Talajic M, Sussex B, Potvin L, Warnica W, Davies RF, Gardner M, Stewart D, Plante S, Dupuis R, Lauzon C, Ferguson J, Mikes E, Balnozan V, Savard P. Myocardial infarction patients in the 1990s--their risk factors, stratification and survival in Canada: the Canadian Assessment of Myocardial Infarction (CAMI) Study. *J Am Coll Cardiol.* 1996; 27:1119-27.
6. 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, Vidson-Ray LD, Fraulo ES, Fishbein DP, Luceri RM, Ip JH. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med.* 2005; 352:225-37.
7. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De MT, Carson P, DiCarlo L, DeMets D, White BG, DeVries DW, Feldman AM. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med.* 2004; 350:2140-50.
8. 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; 341:1882-90.
9. 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; 335:1933-40.
10. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, Daubert JP, Higgins SL, Brown MW, Andrews ML. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med.* 2002; 346:877-83.
11. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA, III, Freedman RA, Gettes LS, Gillinov AM, Gregoratos G, Hammill SC, Hayes DL, Hlatky MA, Newby LK, Page RL, Schoenfeld MH, Silka MJ, Stevenson LW, Sweeney MO, Smith SC, Jr., Jacobs AK, Adams CD, Anderson JL, Buller CE, Creager MA, Ettinger SM, Faxon DP, Halperin JL, Hiratzka LF, Hunt SA, Krumholz HM, Kushner FG, Lytle BW, Nishimura RA, Ornato JP, Page RL, Riegel B, Tarkington LG, Yancy CW. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices): developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. *Circulation.* 2008; 117:e350-e408.
12. Maisel WH, Moynahan M, Zuckerman BD, Gross TP, Tovar OH, Tillman DB, Schultz DB. Pacemaker and ICD generator malfunctions: analysis of Food and Drug Administration annual reports. *JAMA.* 2006; 295:1901-6.



13. Moss AJ, Greenberg H, Case RB, Zareba W, Hall WJ, Brown MW, Daubert JP, McNitt S, Andrews ML, Elkin AD. Long-term clinical course of patients after termination of ventricular tachyarrhythmia by an implanted defibrillator. *Circulation*. 2004; 110:3760-5.
14. Rosenqvist M, Beyer T, Block M, den DK, Minten J, Lindemans F. Adverse events with transvenous implantable cardioverter-defibrillators: a prospective multicenter study. European 7219 Jewel ICD investigators. *Circulation*. 1998; 98:663-70.
15. Sweeney MO, Wathen MS, Volosin K, Abdalla I, DeGroot PJ, Otterness MF, Stark AJ. Appropriate and inappropriate ventricular therapies, quality of life, and mortality among primary and secondary prevention implantable cardioverter defibrillator patients: results from the Pacing Fast VT REduces Shock ThERapies (PainFREE Rx II) trial. *Circulation*. 2005; 111:2898-905.
16. Tung R, Zimetbaum P, Josephson ME. A critical appraisal of implantable cardioverter-defibrillator therapy for the prevention of sudden cardiac death. *J Am Coll Cardiol*. 2008; 52:1111-21.
17. Brodine WN, Tung RT, Lee JK, Hockstad ES, Moss AJ, Zareba W, Hall WJ, Andrews M, McNitt S, Daubert JP. Effects of beta-blockers on implantable cardioverter defibrillator therapy and survival in the patients with ischemic cardiomyopathy (from the Multicenter Automatic Defibrillator Implantation Trial-II). *Am J Cardiol*. 2005; 96:691-5.
18. Goldenberg I, Moss AJ, McNitt S, Zareba W, Daubert JP, Hall WJ, Andrews ML. Cigarette smoking and the risk of supraventricular and ventricular tachyarrhythmias in high-risk cardiac patients with implantable cardioverter defibrillators. *J Cardiovasc Electrophysiol*. 2006; 17:931-6.
19. Pietrasik G, Goldenberg I, McNitt S, Moss AJ, Zareba W. Obesity as a risk factor for sustained ventricular tachyarrhythmias in MADIT II patients. *J Cardiovasc Electrophysiol*. 2007; 18:181-4.
20. Kardys I, Kors JA, van dM, I, Hofman A, van der Kuip DA, Witteman JC. Spatial QRS-T angle predicts cardiac death in a general population. *Eur Heart J*. 2003; 24:1357-64.
21. Yamazaki T, Froelicher VF, Myers J, Chun S, Wang P. Spatial QRS-T angle predicts cardiac death in a clinical population. *Heart Rhythm*. 2005; 2:73-8.
22. Pavri BB, Hillis MB, Subacius H, Brumberg GE, Schaechter A, Levine JH, Kadish A. Prognostic value and temporal behavior of the planar QRS-T angle in patients with nonischemic cardiomyopathy. *Circulation*. 2008; 117:3181-6.
23. van der Velde ET, Atsma DE, Schalij MJ, Witteman JC, Fogel RI, de Bruijn FDB. Development and Implementation of a Fully Paperless Cardiology Information System (EPD-Vision). *Computers in Cardiology*. 2006; 33:849-52.
24. van der Burg AE, Bax JJ, Boersma E, van EL, Bootsma M, van der Wall EE, Schalij MJ. Standardized screening and treatment of patients with life-threatening arrhythmias: the Leiden out-of-hospital cardiac arrest evaluation study. *Heart Rhythm*. 2004; 1:51-7.
25. van Huysduynen BH, Swenne CA, Bax JJ, Bleeker GB, Draisma HH, van EL, Molhoek SG, van d, V, van der Wall EE, Schalij MJ. Dispersion of repolarization in cardiac resynchronization therapy. *Heart Rhythm*. 2005; 2:1286-93.
26. Draisma HHM, Swenne CA, van de Vooren H, Maan AC, van Huysduynen BH, van der Wall EE, Schalij MJ. LEADS: An Interactive Research Oriented ECG/VCG Analysis System. *Computers in Cardiology*. 2005; 32:515-8.
27. Scherptong RW, Henkens IR, Man SC, Le CS, Vliegen HW, Draisma HH, Maan AC, Schalij MJ, Swenne CA. Normal limits of the spatial QRS-T angle and ventricular gradient in 12-lead electrocardiograms of young adults: dependence on sex and heart rate. *J Electrocardiol*. 2008; 41:648-55.



28. Borleffs CJ, Wilde AA, Cramer MJ, Wever E, Mosterd A. Clinical implementation of guidelines for cardioverter defibrillator implantation: lost in translation? *Neth Heart J*. 2007; 15:129-3
29. Rautaharju PM, Prineas RJ, Zhang ZM. A simple procedure for estimation of the spatial QRS/T angle from the standard 12-lead electrocardiogram. *J Electrocardiol*. 2007; 40:300-4.
30. Draisma HH, Schaliij MJ, van der Wall EE, Swenne CA. Elucidation of the spatial ventricular gradient and its link with dispersion of repolarization. *Heart Rhythm*. 2006; 3:1092-9.
31. Goldberger JJ, Cain ME, Hohnloser SH, Kadish AH, Knight BP, Lauer MS, Maron BJ, Page RL, Passman RS, Siscovick D, Siscovick D, Stevenson WG, Zipes DP. American Heart Association/American College of Cardiology Foundation/Heart Rhythm Society scientific statement on noninvasive risk stratification techniques for identifying patients at risk for sudden cardiac death: a scientific statement from the American Heart Association Council on Clinical Cardiology Committee on Electrocardiography and Arrhythmias and Council on Epidemiology and Prevention. *Circulation*. 2008; 118:1497-518.
32. Perkiomaki JS, Hyytinen-Oinas M, Karsikas M, Seppanen T, Hnatkova K, Malik M, Huikuri HV. Usefulness of T-wave loop and QRS complex loop to predict mortality after acute myocardial infarction. *Am J Cardiol*. 2006; 97:353-60.
33. Zabel M, Acar B, Klingenhoben T, Franz MR, Hohnloser SH, Malik M. Analysis of 12-lead T-wave morphology for risk stratification after myocardial infarction. *Circulation*. 2000; 102:1252-7.

