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Electrocardiographic Identification of Abnormal Ventricular Depolarization and Repolarization in Patients With Idiopathic Ventricular Fibrillation

HEIDI A. P. PEETERS, MD,* ARNE SIPPENSGROENEWEGEN, MD,† ERIC F. D. WEVER, MD,* MARK POTSE, MSc,‡ MARCEL C. G. DANIËLS, MD,§ CORNELIS A. GRIMBERGEN, PhD,‡ RICHARD N. W. HAUER, MD,* ETIENNE O. ROBLES de MEDINA, MD, FACC*

Utrecht, Amsterdam and 's-Hertogenbosch, The Netherlands and San Francisco, California

Objectives. **We sought to gain more insight into the arrhythmogenic etiology of idiopathic ventricular fibrillation (VF) by assessing ventricular depolarization and repolarization properties by means of various electrocardiographic (ECG) techniques.**

Background. **Idiopathic VF occurs in the absence of demonstrable structural heart disease. Abnormalities in ventricular depolarization or repolarization have been related to increased vulnerability to VF in various cardiac disorders and are possibly also present in patients with idiopathic VF.**

Methods. **In 17 patients with a first episode of idiopathic VF, 62-lead body surface QRST integral maps, QT dispersion on the 12-lead ECG and XYZ-lead signal-averaged ECGs were computed.**

Results. **All subjects of a healthy control group had a normal dipolar QRST integral map. In patients with idiopathic VF, either a normal dipolar map (29%), a dipolar map with an abnormally large negative area on the right side of the thorax (24%) or a nondipolar map (47%) were recorded. Only four patients (24%) had increased QT dispersion on the 12-lead ECG and late potentials could be recorded in 6 (38%) of 16 patients. During a median follow-up duration of 56 months (range 9 to 136), a recurrent arrhythmic event occurred in 7 patients (41%), all of whom had an abnormal QRST integral map. Five of these patients had late potentials, and three showed increased QT dispersion on the 12-lead ECG.**

Conclusions. **In patients with idiopathic VF, ventricular areas of slow conduction, regionally delayed repolarization or dispersion in repolarization can be identified. Therefore, various electrophysiologic conditions, alone or in combination, may be responsible for the occurrence of idiopathic VF. Body surface QRST integral mapping may be a promising method to identify those patients who do not show a recurrent episode of VF.**

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Ventricular fibrillation (VF) is the most frequently observed mechanism of sudden cardiac death (1). The predominant underlying etiology is coronary artery disease, although other causes have been identified (2,3). In a small subset of patients, VF occurs in the absence of any detectable structural heart disease (4,5). These patients are believed to have primary electrical disease or idiopathic VF, although this diagnosis is arrived at by exclusion.

Programmed electrical stimulation has been used to assess vulnerability to life-threatening ventricular arrhythmias (6). However, this invasive technique has appeared to be of limited prognostic value in patients with idiopathic VF (5). Noninvasive methods to identify increased risk for ventricular arrhythmias include assessment of heart rate variability (7), baroreflex sensitivity testing (8), measurement of QT dispersion on the 12-lead electrocardiogram (ECG) (9), assessment of electrical alternans on the ECG (10), body surface QRST integral mapping (11) and the signal-averaged ECG (SAECG) (12). Measurement of QT dispersion on the 12-lead ECG and body surface QRST integral mapping can be applied to identify dispersion in ventricular repolarization, an arrhythmogenic condition favorable for the occurrence of reentry. The SAECG allows detection of late potentials, which have been related to delayed ventricular depolarization and are believed to represent a substrate for reentrant ventricular arrhythmias. Although the clinical significance of these methods has been demonstrated in patients with structural heart disease (9,11–16), studies about their value in patients with idiopathic VF have not yet been published.

The aim of the present study was to gain more insight into the arrhythmogenic etiology of idiopathic VF. For this pur-

From the *Department of Cardiology, Heart-Lung Institute, University Hospital Utrecht, Utrecht, The Netherlands; †Section of Cardiac Electrophysiology, Department of Medicine and Cardiovascular Research Institute, University of California San Francisco, San Francisco, California; ‡Department of Medical Physics, Academic Medical Center, Amsterdam and §Department of Cardiology, Bosch Medicentrum, 's-Hertogenbosch, The Netherlands. This study was supported by Grant 93.080 from The Netherlands Heart Foundation.

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Address for correspondence: Dr. Heidi A. P. Peeters, Department of Cardiology, Heart-Lung Institute, University Hospital Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands. E-mail: j.a.vangestel@hli.azu.nl.

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Abbreviations and Acronyms

ECG = electrocardiogram, electrocardiographic
ICD = implantable cardioverter-defibrillator
SAECG = signal-averaged electrocardiogram
VF = ventricular fibrillation

pose, we assessed whether late potentials or dispersion in ventricular repolarization could be identified in patients with a first documented episode of idiopathic VF using the SAECG, body surface QRST integral mapping and QT measurement on the 12-lead ECG. Moreover, we evaluated whether such abnormal findings in ventricular depolarization or repolarization could be related to the recurrence of a life-threatening ventricular arrhythmia.

Methods

Study cohort. *Patients with idiopathic VF.* Seventeen patients who had survived a first out of hospital cardiac arrest due to documented VF and were referred to the cardiac arrhythmia unit of the Heart-Lung Institute, University Hospital Utrecht, The Netherlands, between January 1986 and January 1997, were included. There were 13 men and 4 women, with a mean (±SD) age of 37 ± 14 years (range 17 to 67) at the time of the initial episode of cardiac arrest. Patient characteristics are shown in Table 1. No patient used any medication at the time of the episode of VF. Structural heart disease was excluded after extensive evaluation, which included clinical history, physical examination, 12-lead ECG, 24-h Holter recording, exercise testing and Valsalva maneuver, laboratory testing, chest X-ray film, two-dimensional and color Doppler echocardiography, cardiac catheterization with coronary angiography and cineangiography of both the left and right ventricle, nuclear scintigraphic assessment of left ventricular ejection fraction, multiple endomyocardial biopsies and a baseline electrophysiologic study, which included isoproterenol infusion (Table 1) (5). Ventricular pre-excitation and prolonged QT interval were excluded by analysis of serial 12-lead ECGs and 24-h telemetric and Holter recordings. Measurement of QT intervals corrected for heart rate was performed according to Bazett's formula ($QTc = QT/\sqrt{RR}$). Ergonovine testing for coronary spasm was negative in all patients. The aforementioned clinical evaluation comprised the necessary investigations to make the diagnosis of idiopathic VF according to a recently published consensus statement (17). In three of the 17 patients, the standard 12-lead ECG showed nonspecific abnormalities (Table 1). Patient 6 demonstrated the typical 12-lead ECG abnormalities, described by Brugada and Brugada (18), that have been associated with sudden cardiac death and are characterized by right bundle branch block and ST elevation in leads V_1 to V_3. The 12-lead ECG was normal in the other 13 patients. Serum potassium and magnesium values, determined within 24 h after admission, were normal in all patients. After the diagnostic evaluation, 15 patients underwent implantation of an implantable cardioverter-defibrillator (ICD), 1 patient received both an ICD and quinidine, and 1 patient was discharged with quinidine only. In all patients, the rate cutoff of the ICD was programmed at 200/min. In eight patients, the device had ECG storage capabilities. Each patient visited the outpatient clinic once every month during the first 3 months after discharge and every 2 to 6 months thereafter. History taking, physical examination and 12-lead ECG analysis were performed during each visit. Additionally, all patients underwent chest radiography and two-dimensional and color Doppler echocardiography at least once a year to exclude later development of underlying structural heart disease. All recordings for the present study were obtained while the patients abstained from antiarrhythmic drugs.

Control subjects. A previously reported (16) control group of 27 healthy volunteers (17 men, 10 women; mean age 33 ± 14 years, range 17 to 62) was included in the study. Physical examination, 12-lead ECG analysis and two-dimensional and color Doppler echocardiography were normal in all subjects.

ECG data acquisition, processing and analysis. *Body surface mapping.* Body surface QRST integral maps were obtained both in patients and in control subjects. The median time interval between the index arrhythmic episode and the acquisition of body surface maps in the patient group was 2 months (range 1 to 81). Our methods of data recording and processing have been described elsewhere (16). Briefly, body surface mapping was performed during sinus rhythm with a portable mapping system and a 62-lead electrode array (Fig. 1A). The 62 ECG signals were recorded with Wilson's central terminal as reference. These signals were amplified, digitized at a rate of 1 kHz and then transmitted to a 486 microcomputer for data recording and storage. Subsequent processing, analysis and display of data were performed with a directly connected Amiga 1200 microcomputer (Commodore-Amiga, Ltd.). Baseline drifting or offset differences was corrected by an interpolation algorithm. A mean of 2.0 ± 1.3 leads/map with signals of unacceptable quality was rejected and replaced by values calculated from surrounding leads. QRS onset and T wave offset were defined at the instant when an extreme value exceeded 0.05 mV or declined below −0.05 mV, respectively. QRST integral maps were computed, and hard copies of each map were produced (Fig. 1B). QRST integral maps were analyzed visually by two observers who had no knowledge of patient information. Visual analysis was focused on the location and mutual distance of the extremes and the configuration of the zero line. The QRST integral map of each patient was compared with the maps of the other patients and with the computed mean QRST integral map of the control group. The mean QRST integral map of the control group was calculated by dividing the sum of the values obtained at each lead point by the number of subjects. Visual analysis classified body surface map patterns as *normal dipolar*, *abnormal dipolar* or *nondipolar*. A QRST integral map was defined as nondipolar if three or more extremes could be identified. An extreme was considered

Table 1. Patient Characteristics

Pt No.	Age (yr)/ Gender	Exercise Related VF	Syncope Before Index Episode*	12-Lead ECG	QTc (s)	LVEF (%)	LVEDP (mm Hg)	Holter Recording	Inducibility at PES	Treatment	Follow-Up Events	Total Follow-Up (mo)
1	27/M	−	−	Normal	0.40	57	3	VES	—	ICD	Shock (at 18 mo)	98
2	29/M	−	−	Normal	0.40	55	7	—	—	ICD	—	41
3	33/F	−	+	Normal	0.43	68	3	NS-PVT	NS-PVT	ICD	Shock (at 6 mo)	52
4	17/F	−	+	Normal	0.40	58	5	—	—	ICD	—	76
5	52/M	−	+	Normal	0.36	59	3	VES	VF	ICD	Shock (at 3 mo)	136
6	53/M	−	−	LAD; RBBB; ST elevation in leads V_1–V_3; inverted T wave in leads V_1–V_3	0.45†	56	10	—	NS-MVT	ICD	—	86
7	29/M	+	+	Normal	0.42	59	6	—	—	ICD	Shock (at 19 mo)	56
8	32/F	−	+	Normal	0.43	52	10	—	—	ICD	Shock (at 21 mo)	77
9	47/M	−	−	Normal	0.40	70	12	—	—	ICD	—	57
10	43/M	+	+	Low voltage ECG; LAD; flat T wave in leads II, III, aVF	0.40	59	12	—	—	ICD	2 shocks (at 37 and 43 mo)	98
11	25/F	−	−	Normal	0.38	55	10	—	—	ICD	—	43
12	27/M	−	−	Ectopic atrial rhythm; LAD; QRS fractionation in leads III, aVL, aVF	0.41	74	6	—	NS-PVT; VF	ICD + Quin	—	35
13	21/M	−	−	Normal	0.43	83	9	—	NS/S-PVT; VF	Quin	—	31
14	32/M	−	+	Normal	0.38	66	10	NS-PVT	NS-PVT	ICD	—	28
15	50/M	−	+	Normal	0.38	62	10	—	—	ICD	Shock (at 6 mo)	9
16	43/M	−	−	Normal	0.43	64	10	—	NS-PVT; VF	ICD	—	80
17	67/M	−	−	LAD	0.40	73	7	—	NS-PVT; VF	ICD	—	41

*Presyncope, dizziness or near syncope. †QRS width of 160 ms. ECG = electrocardiogram; F = female; ICD = implantable cardioverter-defibrillator; LAD = left-axis deviation; LVEDP = left ventricular end-diastolic pressure; LVEF = left ventricular ejection fraction; M = male; NS-MVT = nonsustained monomorphic ventricular tachycardia; NS-PVT = nonsustained polymorphic ventricular tachycardia; NS/S = nonsustained and sustained; PES = programmed electrical stimulation using up to three extrastimuli, delivered at two right ventricular sites; Pt = patient; QTc = corrected QT interval duration; RBBB = right bundle branch block; VF = ventricular fibrillation; + = yes; − = no; — = no arrhythmia or shock observed.

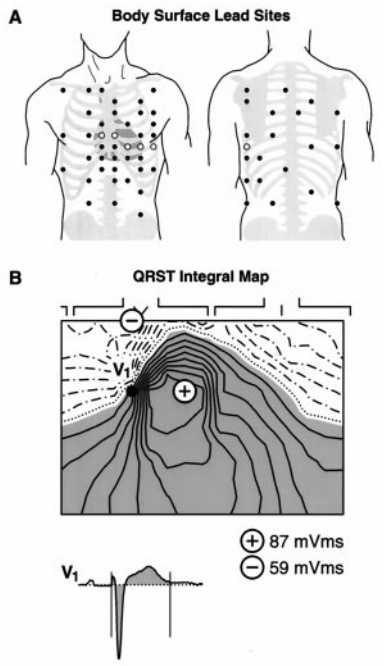

Figure 1. A, Diagram showing the positions of the 62 electrodes in relation to the thoracic anatomy. The set consists of 14 straps with 41 electrodes placed on the front and 21 on the back of the thorax. The sites of the standard precordial leads V_1 to V_6 are included in the array and are indicated by **open circles**. Note that the density of the electrodes is high in the precordial region. **B,** Normal dipolar QRST integral map obtained in one of the control subjects. The **hatched area** in lead V_1 between the **vertical lines** indicates the period of integration of this map. The position of lead V_1 is also shown on the map. The left and right sides of the map correspond to the front and back of the patient, respectively. The position of the jugular notch and vertebral column are indicated at the top of the map. **Solid lines** in the **shaded area** represent positive isointegral lines, and the **dashed lines** represent negative isointegral lines. The **dotted line** indicates the zero isointegral line. The position of the positive and negative extremes are displayed by a **plus** and **minus** sign, respectively. Their values are shown below the map. In this control subject, a normal dipolar map pattern can be observed with a maximum in the left mammary region and a minimum at the right upper sternal area.

to be present if the area of the extreme value comprised at least two unipolar lead sites. In case of discrepancy in opinions, discussion between the two observers led to consensus. The degree of nondipolarity of the QRST integral maps was also determined quantitatively by means of principal component analysis to substantiate our qualitative findings. A covariance matrix was estimated from the set of recordings of the normal control group, and the eigenvectors of this matrix were derived as described by Lux et al (19). The percentage contribution of nondipolar eigenvectors was then computed according to the method developed by Abildskov et al (20). This analysis was performed on a Sun Sparc Station 4 computer (Sun Microsystems, Inc.) using Matlab software (The MathWorks, Inc.). Using this method, a QRST integral map was designated as nondipolar if the nondipolar content exceeded the mean nondipolar content of the control group by more than two times the standard deviation of the control group. In five patients, the nondipolar content of the QRST integral map was again determined 1 year after the initial recording to assess the reproducibility of this technique.

Twelve-lead ECG. Twelve-lead ECGs in the patient and control groups were obtained during body surface mapping. These ECGs were randomly analyzed by two observers who had no knowledge of patient information. In case of conflicting analysis, discussion led to mutual consensus. The paper speed of the 12-lead ECG was 25 mm/s; amplification was set at 10 mm/mV; and all 12 leads were acquired simultaneously. The QT interval was measured manually. The end of the T wave was determined by drawing a tangent to the steepest section of the descending limb of the T wave. In 0.8 ± 0.9 leads/subject, the QT interval could not be reliably determined; therefore, these leads were not included in the analysis. QT dispersion on the 12-lead ECG was determined for each individual by subtracting the shortest QT interval from the longest QT interval (9). QT dispersion of more than the mean value plus 2 SD of the control group was considered abnormal.

SAECG. SAECGs were recorded from the Frank X, Y and Z leads during sinus rhythm with an ART 1200 EPX system (Arrhythmia Research Technology, Inc.) in 16 of the 17 patients. The median time interval between the index arrhythmic episode and the SAECG recording was 2 months (range 1 to 76). A mean of 231 ± 32 cycles were averaged to obtain a noise level ≤0.3 μV. The signals were amplified, digitized, averaged and bidirectionally filtered with a high pass filter at frequencies between 40 and 250 Hz. In Patient 6, an SAECG was not obtained because of the presence of a complete right bundle branch block on the 12-lead ECG with a QRS duration of 160 ms. Late potentials were considered to be present if two or three of the following criteria were met: 1) filtered QRS duration >114 ms; 2) duration of low amplitude signals <40 μV for >38 ms; and 3) root-mean-square voltage of the last 40 ms <20 μV (21).

Definition of arrhythmia recurrence. A *recurrence* was defined as present when an appropriate shock was delivered by the ICD. An *appropriate shock* was defined as a documented shock that terminated a syncopal attack, sudden and transient dizziness (presyncope) or palpitations. In those cases in which the device had storage capabilities, an appropriate shock was defined as shock delivery associated with documentation of ventricular tachycardia or VF.

Statistical analysis. Results are given as mean value ± SD. Body surface QRST integral maps were quantitatively compared using correlation coefficients. Mean correlation coefficients and significance levels of differences in correlation coefficients between groups were computed after applying the Fisher z-transform. The sign test was used to determine whether the ability to identify patients with an arrhythmia recurrence using QRST integral mapping or the SAECG was statistically different. The initial and second body surface mapping recordings were compared using the paired Student *t* test. A p value ≤0.05 was considered statistically significant.

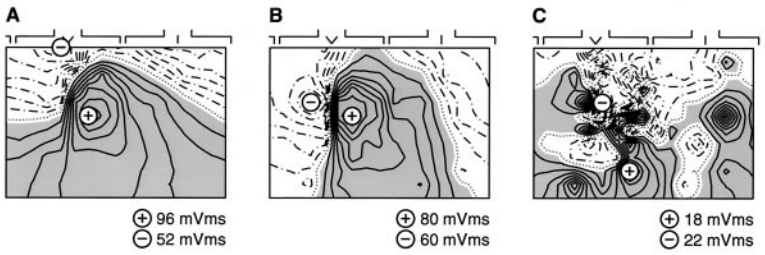

Figure 2. A, Normal dipolar QRST integral map obtained in Patient 11 with idiopathic ventricular fibrillation (VF). This normal map pattern was highly comparable with the maps obtained in the control group (see Fig. 1B). **B,** Abnormal dipolar QRST integral map from Patient 14 with idiopathic VF. There is an abnormally large negative area on the right superior and inferior side of the thorax. In addition, the negative extreme has a more inferior position than in the normal map pattern. Therefore, the electromotive repolarization force has a leftward and only slightly inferior direction. **C,** Nondipolar QRST integral map acquired in Patient 4 with idiopathic VF. There are six positive extremes, five on the front and one on the back of the torso. There are seven negative extremes, six of which are located anteriorly and one posteriorly. Only the highest positive and negative values are indicated by the **plus** and **minus signs**. The nondipolar content of this map was 65%.

Results

Body surface QRST integral mapping. The QRST integral maps of all control subjects demonstrated the characteristic normal dipolar repolarization pattern with a negative extreme in the right upper sternal area and a positive extreme in the left mammary region (22). An example of a normal QRST integral map pattern obtained in one of the control subjects is displayed in Figure 1B.

Visual analysis revealed a dipolar QRST integral map pattern in 9 (53%) of 17 patients with idiopathic VF. Five of these nine patients (29% of all patients) demonstrated the same normal dipolar QRST integral map pattern as the control subjects (Fig. 2A). However, in four patients (24% of all patients), the QRST integral map was dipolar but showed an abnormally large area with negative potentials, covering the right superior and inferior thorax. In addition, the negative extreme was located more inferiorly, at the middle right anterior part of the torso (Fig. 2B). In 8 (47%) of 17 patients, a nondipolar QRST integral map was obtained (Fig. 2C). Thus, 12 (71%) of 17 patients demonstrated an abnormal QRST integral map. The results are summarized in Table 2.

The correlation coefficients of the mean QRST integral map of the control group with the individual integral maps of the group of five patients with a normal dipolar QRST integral map, the group of four patients with an abnormal dipolar map and the group of eight patients with a nondipolar map were 0.94 ± 0.03, 0.84 ± 0.07 and 0.16 ± 0.59, respectively. The correlation coefficients of the groups with an abnormal dipolar and nondipolar map showed a statistically significant difference from the control group (both $p < 0.002$). There was no significant difference between the patient group with a normal dipolar map and the control group ($p = 0.24$).

The mean nondipolar content of the control group was 5.0 ± 2.6%. Therefore, a QRST integral map of a patient with idiopathic VF was defined nondipolar if the nondipolar content exceeded 10.2%. In accordance with the visual analysis, Table 2 shows that 8 (47%) of 17 patients with idiopathic VF had an abnormally high nondipolar content of the QRST integral map. In five patients with a nondipolar map (Patients 4 to 7 and 9) (mean nondipolar content 38 ± 23%), body surface mapping was repeated 1 year after the first recording. No patient presented any significant difference in map pattern (mean nondipolar content 43 ± 18%, $p = 0.25$).

QT dispersion on 12-lead ECG. The mean QT dispersion in the control group was 32 ± 12 ms. Thus, the cutoff value for abnormal QT dispersion was defined at 56 ms. Table 2 shows that increased QT dispersion on the 12-lead ECG could be demonstrated in only 4 (24%) of 17 patients with idiopathic VF. Three of these patients also demonstrated a nondipolar

Table 2. Summary of Results

Pt No.	QRST Integral Map: Visual Analysis*	QRST Integral Map: Eigenvector Analysis† (%)	12-Lead ECG: QT Dispersion‡ (ms)	SAECG: Late Potentials§ (No abn criteria)
1	+	39.9 +	68 +	3 +
2	−(*)	6.5 −	40 −	0 −
3	+	14.9 +	63 +	3 +
4	+	64.8 +	48 −	0 −
5	+	63.8 +	52 −	3 +
6	+	33.1 +	67 +	NP NP
7	+	28.3 +	19 −	2 +
8	−(*)	6.6 −	60 +	0 −
9	+	29.0 +	40 −	3 +
10	+	24.2 +	48 −	3 +
11	−	4.8 −	20 −	0 −
12	−	9.4 −	32 −	0 −
13	−	4.6 −	19 −	0 −
14	−(*)	9.6 −	48 −	0 −
15	−(*)	7.5 −	52 −	0 −
16	−	4.9 −	54 −	0 −
17	−	7.7 −	27 −	0 −

*+ = nondipolar; − = dipolar; −(*) = abnormally dipolar. †+ = nondipolar content >10.2%; − = nondipolar content ≤10.2%. ‡+ = QT dispersion >56 ms; − = QT dispersion ≤56 ms. §+ = presence; − = absence. abn = abnormal; NP = not performed; SAECG = signal-averaged electrocardiogram; other abbreviations and symbols as in Table 1.

QRST integral map (Patients 1, 3, and 6), whereas the fourth patient had an abnormal dipolar QRST integral map pattern (Patient 8).

SAECG. The mean values of the filtered QRS duration, duration of low amplitude signals and root-mean-square voltage for the terminal 40 ms of the total group were 106 ± 15 ms, 37 ± 11 ms, and 25 ± 13 μV, respectively. Six (38%) of 16 patients with idiopathic VF (38%) who underwent SAECG recording demonstrated late potentials. Two and three abnormal criteria were met in one and five patients, respectively (Table 2). Table 2 also illustrates that in all six patients with late potentials, the QRST integral map revealed a nondipolar pattern.

Follow-up. The median follow-up duration of the patient group was 56 months (range 9 to 136). During follow-up, seven patients (41%) had appropriate shock delivery by their ICD. In three of these patients, a stored electrogram was available that demonstrated VF terminated by a shock. In the two patients who received quinidine, no recurrence occurred. All seven patients with a shock during follow-up demonstrated an abnormal body surface QRST integral map pattern. This pattern was nondipolar in five patients and showed an abnormal dipolar pattern in two patients. Moreover, five of the seven patients with a recurrent arrhythmic episode had late potentials on the SAECG, whereas only three patients demonstrated increased QT dispersion on the 12-lead ECG. Although QRST integral mapping was able to identify more patients with a recurrence than the SAECG (seven vs. five patients), this difference was not statistically significant ($p = 0.50$).

Discussion

Body surface QRST integral mapping. It has been postulated that the QRST integral reflects intrinsic ventricular repolarization properties and is largely independent of the activation sequence (23). Direct evidence for this hypothesis was given by Abildskov et al. (24), who showed that changes in QRST integrals of canine epicardial electrograms were related to local changes in the refractory period. Thereafter, Kubota et al. (25) demonstrated in dogs that increased dispersion in refractory periods and changes in QRST area of the electrogram at the site of localized myocardial heating were highly related to decreased VF induction threshold. These studies resulted in the introduction of body surface QRST integral mapping as a noninvasive tool to identify patients with vulnerability to ventricular arrhythmias. In subsequent clinical studies, the risk of developing life-threatening ventricular arrhythmias was related to a nondipolar body surface QRST integral map pattern, representing inhomogeneous ventricular repolarization (11,13). In the present study, nondipolar QRST integral maps were obtained in a considerable number of patients with idiopathic VF (47%). However, an abnormal dipolar QRST integral map with a negative area covering the right superior and inferior thorax was additionally identified in 4 (24%) of these 17 patients. Thus, an abnormal but dipolar map pattern may also be related to an increased risk for ventricular arrhythmias. Similar findings were described by De Ambroggi et al. (26) in patients with the long QT syndrome and recently also by our group (16) in patients with arrhythmogenic right ventricular dysplasia or idiopathic ventricular tachycardia originating from the right ventricular outflow tract. It has been hypothesized that the abnormally large negative area on the right superior and inferior part of the torso may be related to regionally delayed repolarization of the underlying ventricular myocardium (i.e., the anterior wall of the right ventricle or interventricular septum) (26). Because this pattern can be obtained in different groups of patients, one may postulate that the delayed repolarization may be caused by different underlying etiologies. In the long QT syndrome, the regionally delayed repolarization process has been attributed to lower than normal right sympathetic activity (26). In patients with idiopathic right ventricular tachycardia, the abnormal negative area was suggested to be related to structural abnormalities that are undetectable by current routine diagnostic techniques (16). The abnormal negative area on the QRST integral map in the four patients with idiopathic VF suggests the presence of delayed repolarization in the right ventricular wall or interventricular septum, but the underlying mechanism remains unknown. It is possible that cardiomyopathy will develop in these patients during further follow-up. However, after a median follow-up period of 53 months, no evidence of structural heart disease could be found in these four patients.

QT dispersion on 12-lead ECG. The present study clearly demonstrated a discrepancy in identifying dispersed ventricular repolarization in patients with idiopathic VF by means of the body surface QRST integral mapping technique and the standard 12-lead ECG. Only 4 (24%) of 17 patients demonstrated increased QT dispersion on the standard 12-lead ECG. In contrast, body surface QRST integral mapping was able to demonstrate dispersed repolarization, represented by a nondipolar map, in twice as many patients. Previous studies (9,15) have reported statistically significant higher mean QT dispersion on the 12-lead ECG in patients with structural heart disease or the idiopathic long QT syndrome and life-threatening ventricular arrhythmias than the mean QT dispersion in control groups without ventricular arrhythmias. However, these studies focused on the mean QT dispersion in the patient groups and did not discuss the value of individual QT dispersion values. Our results show that measurement of QT dispersion appears to be of little clinical value in the individual patient with idiopathic VF.

SAECG. In the present study, late potentials could be identified in 6 (38%) of 16 patients in whom a SAECG recording was performed. These findings suggest the presence of a substrate with areas of slow conduction that may lead to ventricular arrhythmias based on a reentrant mechanism. It is well documented that ventricular arrhythmias based on reentry can often be induced by programmed electrical stimulation. Previous studies (14,27) have demonstrated that the SAECG is capable of identifying patients in whom ventricular arrhythmias are likely to be induced during an electrophysiological study. However, ventricular arrhythmias were inducible by

programmed electrical stimulation with up to three extrastimuli and including isoproterenol infusion in only two (33%) of six patients with idiopathic VF showing late potentials in the present study. In the previous studies (14,27), most patients had structural heart disease, which may suggest the presence of a different type of reentrant circuit in patients with ventricular arrhythmias unrelated to structural heart disease. It is possible that the excitable gap in such a reentrant circuit is too short to allow the induction of ventricular arrhythmias by current programmed electrical stimulation techniques.

Possible mechanisms. Our results strongly suggest that idiopathic VF is probably not caused by a single specific underlying etiology. One might assume that patients with idiopathic VF will develop different forms of structural heart disease in the future. However, during a median follow-up period of 56 months since the initial episode of VF, none of our patients developed demonstrable structural heart disease. An alternative explanation for the three different QRST integral map patterns and the presence or absence of late potentials in our patient group may be that idiopathic VF is a genetic disorder showing heterogeneous expression just as in the idiopathic long QT syndrome (28). De Ambroggi et al. (26) have recorded QRST integral maps in patients with the long QT syndrome and found the same three map patterns as those in the present study. It is possible that their patient group comprised genetically different forms of the long QT syndrome. Thus, our patients with idiopathic VF may also represent a heterogeneous group with different mutations in cardiac ion channel genes, all leading to a propensity for VF.

All patients who had at least one appropriate ICD shock showed an abnormal QRST integral map. The map pattern was nondipolar in five patients and abnormally dipolar in two. Five of seven patients who had a recurrent arrhythmic episode demonstrated late potentials on the SAECG in addition to their abnormally configured body surface QRST integral map pattern. Thus, it appears that patients who demonstrate both abnormal depolarization and repolarization characteristics are at particularly high risk for recurrent episodes of a life-threatening ventricular arrhythmia. It is remarkable that all six patients with late potentials on the SAECG also demonstrated nondipolar QRST integral maps (Table 2). This finding suggests that in the presence of areas with slow conduction, additional inhomogeneous ventricular repolarization may facilitate the occurrence of a reentrant ventricular arrhythmia. An alternative hypothesis is that these patients have a common origin of the repolarization abnormality and late potentials. De Bakker et al. (29) demonstrated in patients with a previous myocardial infarction that the mechanism of "slow conduction" is not decreased conduction velocity; rather, it is a "zigzag" course of activation. It is possible that in patients with idiopathic VF, inhomogeneous repolarization representing local dispersion in refractory periods may be responsible for a similar "zigzag" conduction. Saumarez et al. (30) measured local electrograms after pacing with decreasing S_1S_2 coupling intervals in patients with idiopathic VF and found that the local electrograms became wider and more fractionated at shorter coupling intervals than those in the control group, suggesting that slow conduction is due to activation over small separated strands of muscle fibers, causing inhomogeneity of intraventricular conduction. This dispersion in ventricular activation may be due to dispersion in ventricular refractoriness. Unfortunately, no published data appear to be available on the etiology of the substrate that is responsible for slow conduction and inhomogeneous repolarization in patients with idiopathic VF.

Because no patient with a normal QRST integral map had a recurrence, one may speculate that these patients had a temporary electrical instability that led to the episode of VF. The possible causes of such an electrical instability are still unknown, but subclinical myocarditis may be considered. Because of the patchy involvement of the myocardium in this disease, even multiple biopsy specimens may have a low sensitivity, and therefore a negative biopsy cannot be considered a definitive criterion for exclusion of myocarditis (31). Other causes of transient cardiac electrical instability include electrolyte disturbances, such as hypokalemia and hypomagnesemia. However, repeated measurements of these electrolytes yielded normal values in our patient cohort.

Study limitations. The QRST integral map is largely but not entirely independent of the activation sequence (32). Local electrotonic interactions caused by an altered activation sequence have minor effects on the primary repolarization process. Therefore, the possibility exists that certain depolarization abnormalities may have slightly influenced the QRST integral map pattern. However, 4 of our 17 patients demonstrated ventricular conduction abnormalities with or without changes in the QRS axis, such as right bundle branch block and left axis deviation, that could not be related to a specific QRST integral map pattern (Tables 1 and 2).

Body surface mapping and SAECG recording were performed at a time point during the hospital stay or the follow-up period in each patient. Therefore, we cannot exclude that time-dependent effects may have affected our findings. However, in the five patients that underwent a second body surface map recording after 1 year, no significant changes in map patterns were observed (mean nondipolar content 38 ± 23% vs. 43 ± 18%, $p = 0.25$).

In four of the seven patients with shock delivery during follow-up, the ICD was incapable of recording an electrogram before the discharge. These shocks were associated with termination of presyncope or syncope. However, we cannot exclude with certainty that a shock may have been delivered for a nonfatal arrhythmia or that in patients without documented ICD discharge, an arrhythmia might have occurred that ended spontaneously before ICD discharge. In the other three patients who experienced a shock delivery, the ICD stored electrogram demonstrated VF terminated by a shock.

Clinical implications. The clinical importance of using body surface QRST integral mapping relates to the ability to prospectively identify the subset of patients who will not show a recurrence of VF in the future. These patients may not need lifelong therapy with antiarrhythmic drugs or an ICD. The

SAECG provides an additional tool to clinically identify patients with a high risk for a recurrent event, especially when body surface mapping is not available. However, given the life-threatening nature of the disease, extensive further follow-up and a prospective study in a larger group of patients are needed to verify our findings before the aforementioned suggestions can be translated into therapeutic guidelines. Therefore, the present report must be regarded as an observational study whose exact clinical relevance requires further investigation.

Conclusions. To our knowledge, the present study is the first in a large group of patients with idiopathic VF to undergo body surface QRST integral mapping, measurement of QT dispersion on the 12-lead ECG and SAECG recordings. The results show that these noninvasive diagnostic techniques are able to identify delayed depolarization and inhomogeneous or delayed repolarization of the ventricular myocardium in a subset of patients with idiopathic VF. In view of the varying findings with regard to depolarization and repolarization, different underlying etiologies may be responsible for the occurrence of VF in these patients. Body surface QRST integral mapping, in particular, but also the SAECG seem to be promising noninvasive methods for identifying patients with a low recurrence risk.

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