

Value of the signal-averaged electrocardiogram in arrhythmogenic right ventricular cardiomyopathy/dysplasia

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BACKGROUND Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is an inherited disease that causes structural and functional abnormalities of the right ventricle (RV). The presence of late potentials as assessed by the signal-averaged electrocardiogram (SAECG) is a minor task force criterion.

OBJECTIVE The purpose of this study was to examine the diagnostic and clinical value of the SAECG in a large population of genotyped ARVC/D probands.

METHODS We compared the SAECGs of 87 ARVC/D probands (age 37 ± 13 years, 47 males) diagnosed as affected or borderline by task force criteria without using the SAECG criterion with 103 control subjects. The association of SAECG abnormalities was also correlated with clinical presentation, surface ECG, ventricular tachycardia (VT) inducibility at electrophysiologic testing, implantable cardioverter-defibrillator therapy for VT, and RV abnormalities as assessed by cardiac magnetic resonance imaging (cMRI).

RESULTS Compared with controls, all three components of the SAECG were highly associated with the diagnosis of ARVC/D ($P < .001$). They include the filtered QRS duration (97.8 ± 8.7 ms vs 119.6 ± 23.8 ms), low-amplitude signal (24.4 ± 9.2 ms vs 46.2 ± 23.7 ms), and root mean square amplitude of the last 40 ms of the QRS ($50.4 \pm 26.9 \mu\text{V}$ vs $27.9 \pm 36.3 \mu\text{V}$). The sensitivity of using SAECG for diagnosis of ARVC/D was increased from 47% using the established 2 of 3 criteria (i.e., late potentials) to 69% by using a

modified criterion of any 1 of 3 criteria, while maintaining a high specificity of 95%. Abnormal SAECG as defined by this modified criterion was associated with a dilated RV volume and decreased RV ejection fraction detected by cMRI ($P < .05$). SAECG abnormalities did not vary with clinical presentation or reliably predict spontaneous or inducible VT and had limited correlation with ECG findings.

CONCLUSION Using 1 of 3 SAECG criteria contributed to increased sensitivity and specificity for the diagnosis of ARVC/D. This finding is incorporated in the recent modification of the task force criteria.

KEYWORDS Arrhythmogenic right ventricular cardiomyopathy/dysplasia; Signal-averaged electrocardiogram

ABBREVIATIONS ARVC/D = arrhythmogenic right ventricular cardiomyopathy/dysplasia; cMRI = cardiac magnetic resonance imaging; fQRSd = filtered QRS duration; ICD = implantable cardioverter-defibrillator; LAS = low-amplitude signal; LP = late potential; LV = left ventricle; RMS-40 = root mean square voltage of last 40 ms of QRS; ROC = receiver operator characteristic; RV = right ventricle; SAECG = signal-averaged electrocardiogram; VF = ventricular fibrillation; VT = ventricular tachycardia (Heart Rhythm 2011;8:256–262) © 2011 Heart Rhythm Society. All rights reserved.

Introduction

Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is an inherited myocardial disease characterized pathologically by fibrofatty replacement that causes structural and functional abnormalities of the right ventricle

(RV). Clinical manifestations of the disease include ventricular arrhythmias, congestive heart failure, and sudden death. The diagnosis of ARVC/D is based on task force criteria established in 1994 that are divided into major and minor components.¹ Localized conduction delay by a variety of ECG measurements is seen in a large number of ARVC/D patients.^{2–4} The high-resolution signal-averaged electrocardiogram (SAECG) is particularly well suited to detect localized slowed conduction and has been viewed as an adjunct for the diagnosis of ARVC/D. Currently, the presence of late potentials on SAECG is a minor task force criterion; however, data corroborating its diagnostic value are limited.

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The purpose of this study was to reexamine the value of SAECG in a large population of genotyped ARVC/D probands enrolled in the Multidisciplinary Study of ARVC/D.^{5,6} The specific aims of the present study were as follows: (1) to test the contribution of SAECG to the diagnosis of ARVC/D, (2) to determine the optimal cutoff values for the SAECG for the diagnosis of ARVC/D, and (3) to compare the diagnostic sensitivity and specificity of one, two, and three standard individual SAECG components. Additional substudies evaluated the association of the abnormalities of SAECG using the optimal criteria with (1) clinical presentation of ARVC/D, (2) abnormalities on the surface ECG, (3) ventricular tachycardia (VT) inducibility at electrophysiologic testing, (4) implantable cardioverter-defibrillator (ICD) therapy for sustained VT, and (5) volume/morphologic features as defined by cardiac magnetic resonance imaging (cMRI).

Methods

Clinical characteristics of study subjects

The study included 87 ARVC/D probands (age 37 ± 13 years, 47 males) diagnosed as affected ($n = 62$) or borderline ($n = 25$) by task force criteria¹ without using the SAECG criterion (Table 1). Probands were excluded if that test was crucial for the diagnosis of the individual patient. This was done to eliminate bias in estimating the sensitivity and specificity of that particular test. In general, when determining the sensitivity and specificity of a new screening test, it is recommended that none of the screening test elements be used in making the primary diagnosis. This principle also holds when establishing diagnostic criteria. At enrollment, 20 (23%) of the ARVC/D probands were asymptomatic. The most frequent presentation included palpitations in 52 (60%), syncope/presyncope in 43 (49%), and chest pain in 11 (13%). History of VT/ventricular fibrillation (VF) prior to enrollment was documented in 61 (70%) of probands. All patients underwent genotyping for known mutations associated with ARVC/D, and 30 patients (34%) had desmosome gene mutations. The controls were age and gender matched, and included 83 genotype-negative normal family members (age 30 ± 14 years, 34 males) who had undergone comprehensive genotypic and phenotypic analysis and 20 unaffected unrelated volunteers (age 37 ± 13 years, 10 males) for a total of 103 control subjects.

SAECG acquisition and analysis

QRS signals were acquired from standard X, Y, and Z orthogonal leads and recorded until low noise was achieved. Several commercial devices were used to record the SAECG. The individual leads were then combined into a vector magnitude, using the square root of the sum of the square signals of each of the three leads. Conventional time-domain analysis was obtained using a high-pass filter at 40 Hz. Vector magnitude composite was analyzed for filtered QRS duration (fQRSd), low-amplitude signal (LAS) duration below $40 \mu\text{V}$, and root mean square voltage

Table 1 Baseline characteristics of ARVC/D probands according to task force criteria ($n = 87$)*

Family History	
Familial disease confirmed at necropsy or surgery	13 (15%)
Family history (clinical diagnosis based on present criteria)	4 (5%)
ECG Depolarization/Conduction Abnormalities	
Epsilon waves or localized prolongation (>110 ms) of the QRS complex in the right precordial leads (V_1 - V_3)	3 (3%)
Late potentials seen on signal-averaged ECG	42 (48%)
Repolarization Abnormalities	
Inverted T waves in right precordial leads (V_2 - V_3) in people age >12 years and in the absence of right bundle branch block	61 (70%)
Tissue Characterization of Walls	
Fibrofatty replacement of myocardium on endomyocardial biopsy	9 (10%)
Global and/or Regional Dysfunction and Structural Alterations	
Severe dilation and reduction of RV ejection fraction with no (or only mild) LV impairment	14 (16%)
Localized RV aneurysms (akinetic or dyskinesic areas with diastolic bulging)	43 (49%)
Severe segmental dilation of the RV	2 (2%)
Mild global RV dilation and/or ejection fraction reduction with normal LV	19 (22%)
Mild segmental dilation of RV/ regional RV hypokinesia	5 (6%)
Arrhythmias	
Left bundle branch block type VT (sustained and nonsustained)	62 (71%)
Frequent ventricular extrasystoles ($>1,000/24$ hours) on Holter	19 (22%)

ARVC/D = arrhythmogenic right ventricular cardiomyopathy/dysplasia; LV = left ventricle; RV = right ventricle; VT = ventricular tachycardia.

*Excluding 11 patients in whom signal-averaged electrocardiogram was essential to meet 1994 task force criteria.

of the last 40 ms of the QRS (RMS-40). It has been suggested that the normal values for fQRSd are <114 ms, for LAS $40 <38$ ms, and for RMS-40 $>20 \mu\text{V}$.⁴ Although there are no guidelines for abnormal SAECG in patients with ARVC/D, it is common practice to categorize the SAECG as abnormal if two or more of these parameters are abnormal.^{7,8}

Electrocardiography

In addition to standard ECG measurements, the following parameters were evaluated: (1) extent of T-wave inversion in the precordial leads, (2) QRS duration in leads V_1 - V_3 (normal <110 ms), (3) prolonged S wave in leads V_1 - V_3 (normal ≤ 55 ms), (4) ratio of QRS duration in leads V_2/V_5 (normal <1.2), and (5) presence of epsilon waves, defined as notches/deflections occurring after QRS complex (in ST segment) in at least one of the V_1 - V_6 leads that occurred after the end of the QRS complex.^{9,10}

Table 2 SAECG parameters for ARVC/D probands and controls

	ARVC/D probands (n = 87)	Controls (n = 103)	P value
fQRS (ms)	119.6 ± 23.8	97.8 ± 8.7	<.001
LAS (ms)	46.2 ± 23.7	24.4 ± 9.2	<.001
RMS-40 (μV)	27.9 ± 36.3	50.4 ± 26.9	<.001

Values are given as mean ± SD. Normal values: fQRS <114 ms, LAS <38 ms, RMS-40 >20 μV.

ARVC/D = arrhythmogenic right ventricular cardiomyopathy/dysplasia; fQRS = filtered QRS duration; LAS = low-amplitude signal; RMS-40 = root mean square voltage of last 40 ms of QRS; SAECG = signal-averaged electrocardiogram.

Cardiac magnetic resonance imaging

cMRI was performed in 77 of the 87 ARVC/D probands at local centers and interpretation was performed at a core lab, according to a protocol described previously.¹¹ Major morphologic abnormalities by cMRI were defined using 1994 Task Force Criteria as (1) severe dilation and reduction of RV ejection fraction with minimal or absent left ventricular (LV) impairment, (2) localized RV aneurysms (akinetic or dyskinetic areas with diastolic bulging), and/or (3) severe segmental dilation of the RV. Minor morphologic abnormalities by cMRI were defined as (1) mild global RV dilation, (2) depressed RV ejection in the presence of normal LV function, and/or (3) mild segmental dilation of the RV and regional RV hypokinesia.

Statistical analysis

All continuous variables are expressed as mean ± SD. Categorical variables are summarized as absolute number and relative frequencies. Continuous variables were compared using the Student's t-test, and Chi-square test was used for categorical variables. Receiver operator characteristic (ROC) curves were plotted to determine the value of using SAECG parameters for the diagnosis of ARVC/D. Optimal cutoff points for individual or combination of SAECG parameters were evaluated at 90% to 95% specificity. $P < .05$ was considered significant.

Results

SAECG findings

Table 2 compares the individual SAECG parameters of 87 ARVC/D patients and 103 matched controls. All three SAECG parameters (fQRS, LAS, and RMS-40) were significantly more abnormal in ARVC/D probands than in controls. The difference for each parameter was highly significant ($P < .001$). The SAECG parameters fQRS (124.2 ± 27.4 ms vs 118.0 ± 22.7 ms, $P = .28$), LAS (52.4 ± 26.9 ms vs 44.5 ± 22.4 ms, $P = .16$), and RMS-40 (19.3 ± 15.4 μV vs 27.4 ± 30.1 μV, $P = .18$) were not significantly different in ARVC/D probands with and without desmosome gene mutations, respectively.

Figure 1 shows the ROC curve for the diagnosis of ARVC/D using the individual SAECG parameters. The

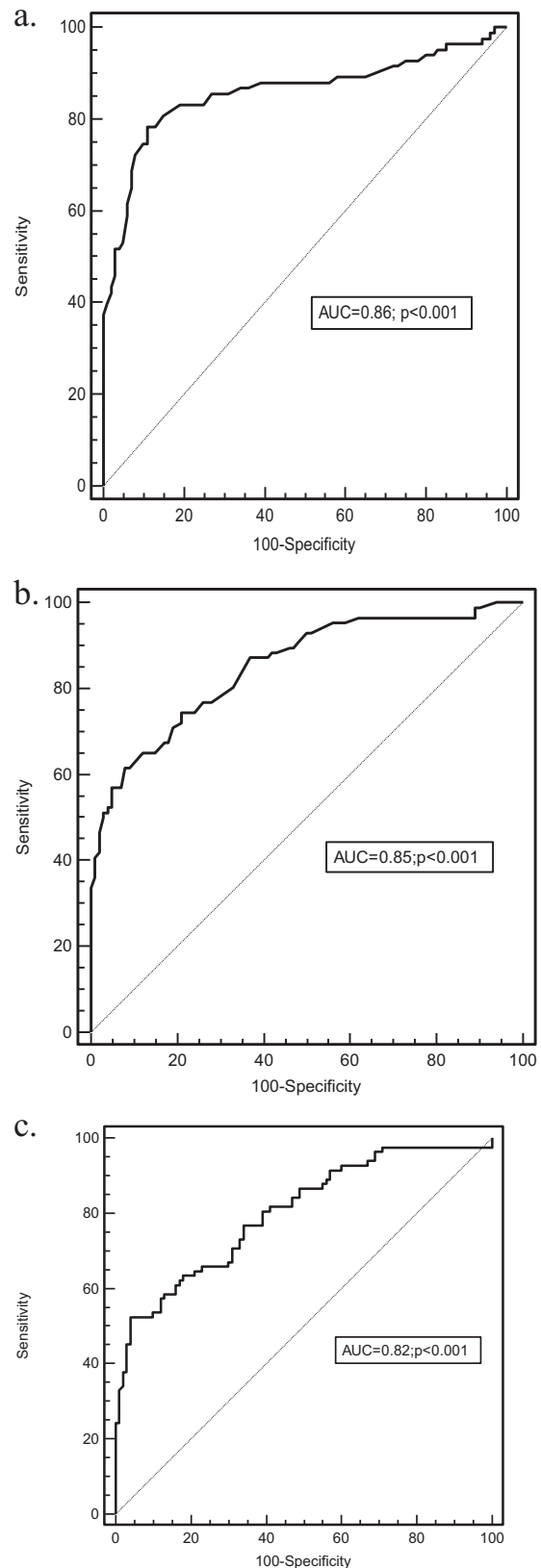


Figure 1 Receiver operator characteristic curve for the diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) using filtered QRS duration (ms; **A**), low-amplitude signal (ms; **B**), and root mean square voltage of last 40 ms of QRS (μV; **C**). ARVC/D :probands n = 87; controls: n = 103.

Table 3 Association of clinical presentation by abnormal SAECG*

Clinical symptoms at presentation	Normal SAECG (n = 29)	Abnormal SAECG (n = 58)	P value
Asymptomatic	9 (31%)	11 (19%)	.2
Syncope	6 (21%)	15 (26%)	1
Presyncope	5 (17%)	17 (29%)	.6
Palpitations	13 (45%)	39 (67%)	.4
Chest pain	3 (10%)	8 (14%)	1
Other	3 (10%)	4 (7%)	.4

fQRS = filtered QRS duration; LAS = low-amplitude signal; RMS-40 = root mean square voltage of last 40 ms of QRS; SAECG = signal-averaged electrocardiogram.

*Using 1 of 3 criteria: fQRS >114 ms, LAS >38 ms, RMS-40 <20 μV.

diagnostic accuracy of fQRS in identifying those with and without ARVC/D is represented by the area under curve and was 0.86. Similarly, the ROC curves for LAS (area under curve = 0.85) and RMS-40 (area under curve = 0.82) demonstrated high diagnostic accuracy. All were statistically significant ($P < .001$; Figure 1).

Based on the ROC curves, various cutpoints for fQRS and for the other parameters were evaluated to obtain the optimal sensitivity and specificity. In accordance with the task force criteria, we aimed to maximize specificity at 90% to 95%. All three individual SAECG parameters had high specificity (95%) for the diagnosis of ARVC/D. The sensitivity of fQRS >114 ms was 53%, LAS >38 ms was 52%, and RMS-40 <20 μV was 52%.

The utility of using a combination of the traditional criteria (fQRS >114 ms, LAS >38 ms, RMS-40 <20 μV) was examined by using any 1 of the 3, 2 of the 3, or 3 of the 3 for diagnosis of ARVC/D. Using 1 of the 3 had sensitivity of 69% and specificity of 92%; using 2 of the 3 had sensitivity of 47% and specificity of 95%; and using all 3 had sensitivity of 33% and specificity of 100%.

Using 1 of the 3 criteria modified the diagnosis of the 25 borderline probands to affected in 9 (36%), 2 of the 3 criteria in 6 (24%), and 3 of the 3 criteria in 5 (20%). Several new cutoff points were examined based on the ROC curves. None of these alternative cutoff values had superior sensitivity and specificity (95%) compared to using traditional values of the SAECG. Therefore we elected to utilize modified SAECG optimal criteria as defined by abnormalities of any 1 of the 3 traditional criteria (fQRS >114 ms, LAS >38 ms, RMS-40 <20 μV).

Clinical presentation of ARVC/D and SAECG findings

The presence of palpitations was not significantly different in the normal and abnormal SAECG groups (45% vs 67%, $P = .4$). Similarly, the frequency of abnormal SAECG was not significantly different with other clinical presentations (Table 3).

Association of abnormal SAECG with surface ECG abnormalities

The presence of T-wave inversions limited to V₁-V₃ (59% vs 36%, $P = .05$) and beyond V₃ (17% vs 41%, $P = .02$) was significantly associated with abnormal SAECG. The presence of other ECG abnormalities was not associated with greater frequency relative to SAECG abnormality (Table 4).

VT inducibility at electrophysiologic study and SAECG

Eighty-seven patients in the cohort underwent both programmed electrical stimulation and SAECG. At electrophysiologic study, 50 (57%) were found to have inducible VT. There were no significant differences in each of the three SAECG parameters between those with and those without VT inducibility (Table 5). For 1 of 3 abnormal SAECG parameters, sensitivity was 76% and specificity was 40%. These values resulted in a positive predictive value of 63% and negative predictive value of 56%. When examining for 2 of 3 or 3 of 3 parameters, the positive and negative predictive values remained essentially unchanged.

Implantable cardioverter-defibrillator therapy for sustained VT and the SAECG

Appropriate ICD therapy for sustained VT during follow-up (mean 3.6 ± 1.3 yrs) was documented in 27 (31%) patients. The individual SAECG parameters did not significantly differ between those with and without appropriate ICD therapy (Table 5).

Table 4 Association of ECG abnormalities by abnormal SAECG*

ECG abnormalities	Normal SAECG (n = 29)	Abnormal SAECG (n = 58)	P value
Negative T wave in V ₁ only†	7 (24%)	10 (17%)	.4
Negative T wave in V ₁ -V ₂ only†	11 (38%)	14 (24%)	.2
Negative T wave in V ₁ -V ₃ only†	17 (59%)	21 (36%)	.05
Negative T wave in V ₁ -V ₃ ‡	22 (76%)	42 (72%)	.7
Negative T wave beyond V ₃	5 (17%)	24 (41%)	.02
Negative T in V ₄ -V ₆ only†	0 (0%)	3 (5%)	.5
QRS in V ₁ -V ₃ >110 ms	4 (14%)	11 (19%)	.5
QRS in V ₂ >110 ms	4 (14%)	18 (31%)	.1
V ₂ /V ₅ ≥ 1.2	10 (34%)	13 (22%)	.2
S wave in V ₁ -V ₃ ≥ 55 ms	13 (45%)	19 (33%)	.2
QRS dispersion >40 ms	0 (0%)	4 (7%)	.3
QT dispersion >65 ms	2 (8%)	6 (10%)	1

fQRS = filtered QRS duration; LAS = low-amplitude signal; RMS-40 = root mean square voltage of last 40 ms of QRS; SAECG = signal-averaged electrocardiogram.

*Using 1 of 3 criteria: fQRS >114 ms, LAS >38 ms, RMS-40 <20 μV.

†Patients have negative T wave in the designated lead(s) and do not have negative T wave in the other precordial leads.

‡Patients have negative T wave in V₁-V₃ and may or may not have negative T wave in V₄-V₆.

Table 5 SAECG parameters for ARVC/D probands with inducible VT and appropriate ICD therapy

	fQRS (ms)	LAS (ms)	RMS-40 (μ V)
Induced VT			
No (n = 37)	117.5 \pm 25.5	43.4 \pm 24.1	29.4 \pm 17.6
Yes (n = 50)	121.2 \pm 22.5	48.3 \pm 23.4	26.9 \pm 45.3
P value	.5	.3	.8
Appropriate ICD therapy			
No (n = 60)	119.1 \pm 28.8	49.0 \pm 27.3	26.2 \pm 40.5
Yes (n = 27)	120.6 \pm 20.2	43.5 \pm 21.4	33.4 \pm 37.8
P value	.8	.4	.5

ARVC/D = arrhythmogenic right ventricular cardiomyopathy/dysplasia; fQRS = filtered QRS duration; ICD = implantable cardioverter-defibrillator; LAS = low-amplitude signal; RMS-40 = root mean square voltage of last 40 ms of QRS; SAECG = signal-averaged electrocardiogram; VT = ventricular tachycardia.

cMRI and SAECG

This substudy included 77 ARVC/D probands who underwent cMRI. Based on cMRI results, major morphologic abnormalities of the RV were present in 50 (65%) of 77 and minor abnormalities were present in 31 (40%) of 77 ARVC/D probands. ARVC/D probands with abnormal SAECG had significantly larger RV systolic and diastolic diameters (38 ± 9 mm vs 30 ± 7 mm, $P = .001$; and 45 mm \pm 8 vs 39 ± 8 mm, $P = .005$, respectively), larger RV end-diastolic volumes (190 ± 68 cc vs 149 ± 42 cc, $P = .04$), and lower RV ejection fraction ($40\% \pm 11\%$ vs $49\% \pm 6\%$, $P = .02$; Figure 2).

Discussion

This study is the largest to date to examine the diagnostic value of SAECG in ARVC/D and the association of clinical parameters with abnormal SAECG. In the present study, the SAECG and its components fQRS, LAS, and RMS-40 were highly associated with the diagnosis of ARVC/D. The sensitivity of using SAECG for diagnosis of ARVC/D was increased from 47% using 2 of the 3 criteria to 69% by using any 1 of the 3 criteria while maintaining high specificity of 90% to 95%. Abnormal SAECG as defined by this modified criteria was strongly associated with dilated RV volumes and decreased RV ejection fraction detected by cMRI. SAECG abnormalities did not vary with clinical presentation or reliably predict spontaneous or inducible VT, and had limited correlation with ECG findings.

SAECG detects delayed ventricular activation signals on the body surface referred to as *late potentials* (LPs). LPs reflect the slow conduction in the ventricular myocardium and electrical potentials that extend beyond the activation time of normal myocardium,^{12,13} a potential substrate for reentrant arrhythmias. It has been reported that LPs in patients with ARVC/D ranges from 50% to 100%,^{4,14,15} with higher prevalence of LPs in patients with sustained VT. The cutoff values for LPs have been derived from studies in postinfarction patients with ischemic cardiomyopathy.

These cutoff values have not been tested specifically in ARVC/D. In this study, SAECG data on ARVC/D probands provided detailed information to examine cutoff points to best define how the SAECG can be used for diagnosis.

In our cohort of patients with ARVC, 38 (44 %) probands had T-wave inversion in leads V_1 - V_3 only and 29 (33%) beyond lead V_3 , observations that significantly correlated with the presence of abnormal SAECG. The epsilon wave is specific but less sensitive and has been described 9% to 36% of ARVC/D.^{3,16} The presence of epsilon wave (3% of ARVC/D probands) was present at a lower rate than those reported in other studies.^{3,17-19} Nasir et al⁴ proposed prolonged S-wave upstroke to baseline in V_1 - $V_3 \geq 55$ ms as the most prevalent ECG feature, and this finding correlated with disease severity and induction of VT at electrophysiologic study. In that study, ECG intervals were measured using digital calipers capable of measuring to within 1 ms after enlarging the ECG two times. The cutoff of >55 ms was based on the best value that differentiated ARVC/D from patients with idiopathic VT and normal controls.⁴ The presence of prolonged S-wave upstroke (37% of genotyped ARVC/D probands) was lower than the previously reported

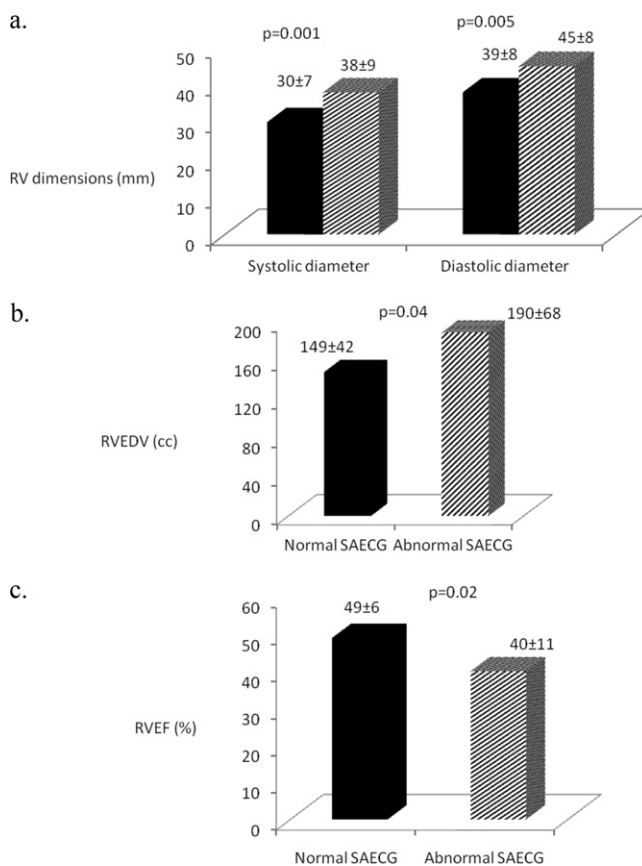


Figure 2 Comparison of RV diastolic and systolic diameter (mm; **A**), RVEDV (mL; **B**), and RV ejection fraction (%) (**C**) in normal (solid black bars) and abnormal (hatched bars) signal-averaged electrocardiogram (SAECG; using 1 of 3 criteria: filtered QRS duration >114 ms, low-amplitude signal >38 ms, root mean square voltage of last 40 ms of QRS <20 μ V) by cardiac magnetic resonance imaging. Arrhythmogenic right ventricular cardiomyopathy/dysplasia probands: n = 77. RV = right ventricular; RVEDV = right ventricular end-diastolic volume.

rates of 60% to 95%.^{4,18} The heterogeneity of the clinical presentations (all patients in the study by Nasir et al were symptomatic at presentation, and 67% had inducible VT) and variations in the definition of the S wave may explain this difference.

cMRI is an important imaging modality for the diagnosis of patients with ARVC/D. RV quantitative analysis as assessed by cMRI is useful in the diagnosis and follow-up of ARVC/D patients.^{20–24} In this study, probands with SAECG abnormalities had increased RV end-systolic and end-diastolic diameters, RV end-diastolic volume, and depressed RV ejection fraction compared to those with normal SAECG. Thus, abnormalities in structural and functional indices were accompanied by abnormal electrical substrate in our cohort.

The most common presentations of ARVC/D in studies have been palpitations, syncope, and atypical chest pain.²⁵ We studied the presenting symptoms of all ARVC/D probands and tabulated the frequency of abnormal SAECG using the modified criteria and hypothesized that certain clinical presentations (e.g., arrhythmia) may be more common with SAECG abnormalities. However, no clinical symptoms were associated with the presence of abnormal SAECG. This may be related to the fact that our cohort included newly diagnosed patients. Patients included in the other studies had long-standing diagnosis.

The utility of SAECG for predicting inducible VT in ARVC/D is uncertain. Nasir et al²⁶ reported that fQRS >110 ms was found to be predictive of inducible VT in ARVC/D with a positive predictive value of 95% and a negative predictive value of 82%. The presence of abnormal late potentials yielded sensitivity of 62% and specificity of 90%.²⁶ In a small cohort of 34 patients, VT was inducible in 68% of cases with LPs compared to 32% in noninducible patients, yielding a positive predictive value of 63% and a negative predictive value of 93% ($P < .001$).²⁷ Using the modified or traditional SAECG criteria in our study, the values for fQRS, RMS, and LAS did not differ between the inducible and noninducible patients, yielding low sensitivity and specificity. The rates of inducible VT in published reports were higher than in our cohort (57%), which may explain the variations in sensitivity and specificity when using the SAECG.

Data are sparse with regard to whether ARVC/D with LPs on SAECG correlates with sustained VT. In the study by Pezawas et al,²⁷ LPs on SAECG were highly correlated with spontaneous VT events. Folino et al²⁸ found that those with sustained VT events had greater prolongation of fQRS (130.3 ms vs 116.9 ms, $P < .05$) over 8-year follow-up; however, the presence of LPs was unable to predict arrhythmic events. Nava et al found that only a reduced RMS-40 correlated with VT events.^{15,29} In our cohort, there was no association between an abnormal SAECG and appropriate ICD therapy for sustained VT. The individual SAECG parameters also did not differ between the two groups.

From our cMRI data and that reported by Nava et al, it appears that SAECG is related to severity of disease.^{15,30} The SAECG did not correlate with induced VT. However, the risk of VT is not entirely dependent on disease severity, as shown by an autopsy study. Dalal et al³¹ found that among patients whose first presentation was sudden cardiac death, the RV was only mildly involved in 65% of cases. Among studies examining risk factors for appropriate ICD therapy in patients with ARVC/D, the results are discordant, and disease severity is not consistently related to arrhythmic events.^{32–36} Many patients with ARVC/D have an early risk of VT/VF events, as documented by the patients who initially present with sudden cardiac death. The arrhythmic risk in ARVC/D likely is multifactorial, a combination of both deranged gap junctions and scar-induced microreentrant and macroreentrant circuits.^{37,38} For those patients with a low scar burden, the malfunctioning gap junctions could explain the arrhythmic risk. Another possible explanation for the discordance between SAECG and risk of arrhythmic events may be related to the location and the heterogeneity of VT observed in ARVC/D patients. Although the VT in ARVC/D most often is a macroreentrant mechanism, it is possible that microreentrant or focal mechanisms may not be associated with an abnormal SAECG.^{39–41}

Conclusion

The SAECG was shown to contribute to the diagnosis of ARVC/D in a well-characterized population of ARVC/D patients with diagnosis within 3 years of onset. Using any 1 of the 3 SAECG criteria provided optimal sensitivity and specificity. This finding is incorporated in the current recent modification of the task force criteria.^{42,43} The evidence that abnormal SAECG reflects functional abnormalities of the RV and RV enlargement suggests that the SAECG correlates with disease severity; however, VT events were not more prevalent when the SAECG was more normal.

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