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Full Length Research Paper

Diagnostic value of signal-averaged electrocardiogram in arrythmogenic right ventricular cardiomyopathy patients

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Arrythmogenic right ventricular cardiomyopathy (ARVC) is the leading cause of sudden cardiac death (SCD) in people aged <35 years. Accordingly, a successful early diagnosis of ARVC can be life saving. The aim of this study was to re-examine the diagnostic and clinical value of the signal-averaged electrocardiogram (SAECG) in patients with ARVC. This was a retrospective and prospective descriptive study conducted at Groote Schuur Hospital, Cape Town, South Africa. Fifty one patients who had been diagnosed as either definite or possible ARVC using the international task force criteria 2010. They underwent SAECG to obtain RMS (root mean square), LAS (low amplitude signal) and fQRS (filtered QRS) recordings, which were then compared to the Groote Schuur Hospital protocol normal values, thus re-evaluating the importance of a SAECG in ARVC. Thirty six (71%) of the ARVC patients had an overall abnormal SAECGs, while 15 (29%) had normal SAECGs. Twenty one (58.3%) of the patients with overall abnormal SAECGs had definite ARVC while 15 (41.6%) had possible ARVC. SAECG can be a useful initial test before performing other procedures on the patient in order to meet the criteria for ARVC. An early abnormal SAECG would mean that the patient should be referred immediately for further tests as ARVC is a condition that should be treated early due to the risk of SCD.

Keywords: Arrythmogenic right ventricular cardiomyopathy (ARVC), signal-averaged electrocardiogram (SAECG).

INTRODUCTION

Arryhythmogenic Right Ventricular Cardiomyopathy (ARVC) is a rare inherited autosomal dominant disorder with variable penetrance that mainly affects the right ventricle (RV) free wall and right ventricle outflow tract (RVOT). ARVC is hallmarked by fibro-fatty infiltration in the muscle of the RV that may cause supraventricular arrhythmias such as supraventricular tachycardia (SVT), ventricular tachycardia (VT) and sudden cardiac death (SCD). Although it is described as a disease of the RV, left ventricle (LV) involvement has also been observed. Later in the disease evolution, progression of RV muscle disease and LV involvement may result in heart failure (Swanton and Banerjee, 2008).

In 2004, Peters et al., discovered that ARVC is the leading cause of SCD in people aged <35 years. Approximately 40% of people with ARVC suffer sudden

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cardiac death as their first clinical manifestation of the disease (Peters et al., 2004). Accordingly, this statistic makes a successful diagnosis of ARVC early in its disease process a key to saving lives.

ARVC enters the differential diagnosis when there is an absence of other known cardiac disease and when the patient experiences palpitations or symptoms of impaired consciousness, sudden ventricular fibrillatory arrest and apparent myocarditis. Frequent ventricular extrasystoles and precordial T-wave inversion beyond V2 should warrant further investigation and should not be considered to be benign. Isolated RV failure in the absence of pulmonary hypertension is an unusual presentation of ARVC, but possible if the individual remained asymptomatic through the earlier arrhythmic phases of the disease (Sen-Chowdhry et al., 2004).

There is no single diagnostic test to establish or exclude the diagnosis of ARVC. The diagnosis may be very difficult due to several problems with the specificity of the electrocardiograph abnormalities, the different potential etiologies of ventricular arrhythmias with LBBB morphology, the assessment of RV function and structure and the interpretation of endomyocardial biopsy findings. Therefore standardized diagnostic criteria were proposed.

However, from 2001 to 2008, Dr Fran Marcus led a second task force with the aim of modifying the criteria, because even though the 1994 criteria were highly specific, it lacked sensitivity for early and familial disease. This study substantiated the need for multiple diagnostic tests. Revision of the 1994 diagnostic criteria provides guidance on the role of emerging diagnostic modalities and to recognize advances in the genetics of ARVC. The approach of classifying the disease as major and minor criteria has been maintained (Marcus et al., 2010).

The signal-averaged electrocardiogram (SAECG) is a special electrocardiographic technique in which multiple electrical signals from the heart are averaged to remove interference and reveal small variations in the QRS complex. These may represent a predisposition towards potentially dangerous tachyarrythmias (Kamath et al., 2011).

The main objective of this study is to test the contribution of SAECG in the diagnosis of ARVC. This study was conducted at Groote Schuur Hospital in Cape Town where patients who had been clinically assessed and diagnosed with ARVC, as either definite or possible, using international task force criteria, underwent a signal-averaged electrocardiogram (SAECG) in order to confirm the diagnosis, thus re-evaluating the importance of a SAECG in ARVC.

METHODS

The research design was retrospective and prospective in nature. It was a descriptive study of patients who were diagnosed as either definite or possible ARVC from 1991 till 2011. After obtaining a voluntary written consent from each patient, fifty one patients diagnosed with definite or possible RVC, based on international task force criteria from 1991 till 2011 at the cardiac clinic at Groote Schuur Hospital in Cape Town were included in the study.

Ethical clearance for this study was obtained from the University of Cape Town's Health Sciences Faculty Research Ethics Committee and the Institutional Research Ethics Committee of the Durban University of Technology.

The patients had previously undergone various diagnostic procedures including echocardiograms, electrophysiology studies, biopsies, cardiac catheterization and/or MRI (magnetic resonance imaging) at Groote Schuur Hospital, where the results were present in the patients' folders and hospital archives.

The patients had to have been diagnosed without the use of the SAECG criterion, and had to be over 18 years of age. Then, all patients underwent a SAECG. QRS signals were acquired from standard X, Y and Z orthogonal leads and recorded until low noise was achieved.

The SAECG is a special elecrocardiographic technique in which multiple electrical signals from the heart are averaged to remove interference and reveal small variations in the QRS complex. These may represent a predisposition towards potentially dangerous tachyarrythmias. A resting ECG was recorded with the patient in the supine position, using an ECG machine equipped with SAECG software.

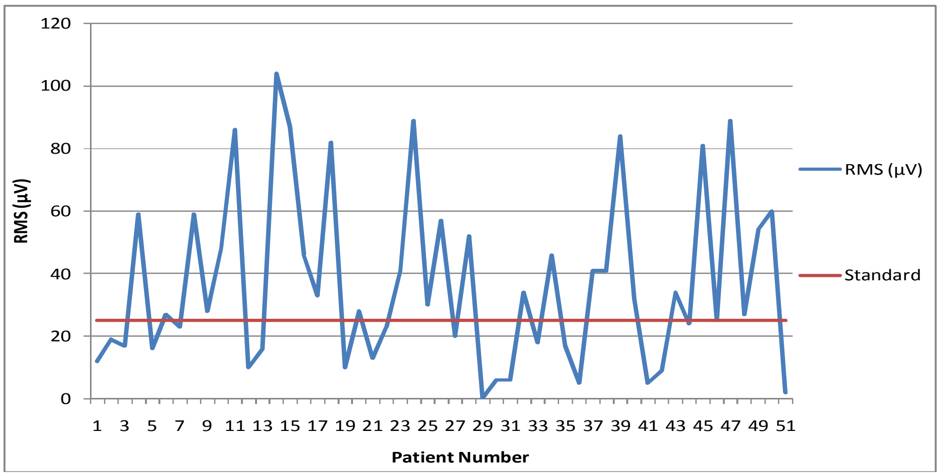
The individual leads were then combined into a vector magnitude, using the square root of the sum of the square signals of each of the 3 leads. Vector magnitude composite was analysed to obtain a filtered QRS dugration (fQRS), low amplitude signal (LAS) and root mean square voltage (RMS). These values were then compared to the hospital's protocol normal values in order to test their importance in the diagnosis of ARVC. Additional sub-studies evaluated the definite or possible diagnosis of the condition with echocardiographic findings, cardiac catheterization findings, VT and ICD implants, biopsy results and MRI findings. Statistical analysis was performed using SPSS version 18 software, Some of the data is presented as a mean with standard deviation, while the rest is presented as a percentage (%) of the patient data set.

The following normal ranges were taken from Groote Schuur Hospital's protocol for determining an abnormal SAECG: RMS $\leq$25 µV (microvolt), LAS $\geq$40 ms (millisecond) and fQRS $\geq$120 ms.

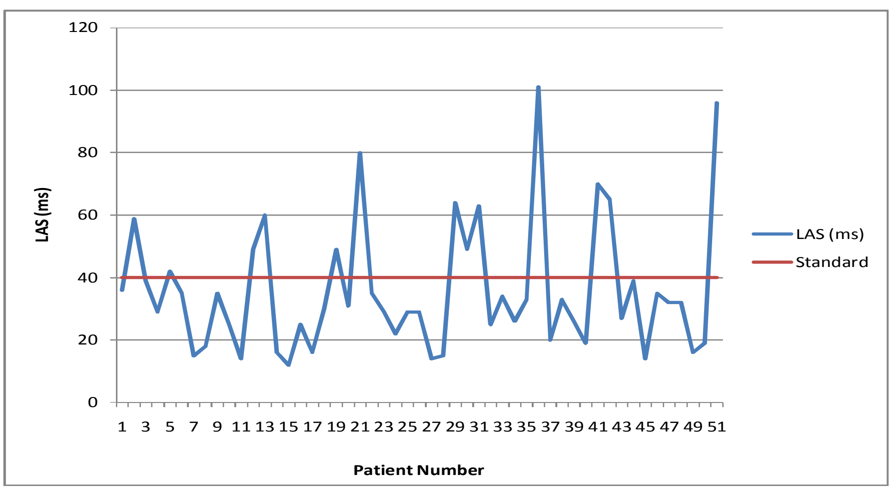
Statistical analysis was performed using SPSS version 18 software. Some of the data is presented as a mean with standard deviation, while the rest is presented as a percentage (%) of the patient data set.

Table 1. Number and Percentage of Definite and Possible ARVC Males and Females

		Male	Female	Total
Possible	Count	14	5	19
	% of Total	27.50%	9.80%	37.30%
Definite	Count	21	11	32
	% of Total	41.20%	21.60%	62.70%
Total	Count	35	16	51
	% of Total	68.60%	31.40%	100.00%



Graph 1. Plot of RMS Voltages of Each Patient



Graph 2. Plot of LAS of Each Patient

RESULTS

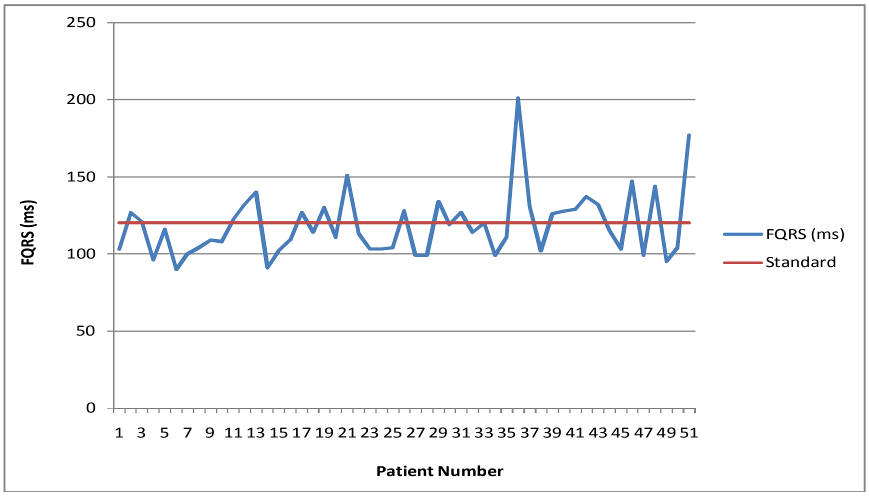
The study consisted of 51 patients that underwent a SAECG in 2011. There were 35 (68.6%) males and 16 (31.4%) females. Table 1 shows number and percentages of Definite and possible ARVC males and females.

Graphs 1, 2 and 3 show the results of the SAECG performed on the 51 study patients.

The number and percentage of definite and possible ARVC patients with normal and abnormal RMS voltages are represented in Table 2 below.

Twenty one (41%) of patients had normal RMS voltages while 30 (59%) had abnormal values. Also, of the 30 abnormal RMS patients, 13 (25%) had possible ARVC while 17 (34%) had definite ARVC (Table 2).

The number and percentage of definite and possible ARVC patients with normal and abnormal LAS values are



Graph 3. Plot of fQRS Durations of Each Patient

Table 2. Number and Percentage of Definite and Possible ARVC Patients with Normal and Abnormal RMS Voltages.

RMS (µV)		Possible	Definite	Total
=< 25	Count	6	15	21
	% of Total	11%	30%	41%
> 25	Count	13	17	30
	% of Total	25%	34%	59%

Table 3. Number and Percentage of Definite and Possible ARVC Patients with Normal and Abnormal LAS Values.

LAS (ms)		Possible	Definite	Total
< 40	Count	15	23	38
	% of Total	30%	45%	75%
>= 40	Count	4	9	13
	% of Total	8%	17%	25%

represented in Table 3.

From Table 3, it is apparent that 13 (25%) of patients had normal LAS values while 38 (75%) had abnormal values. Also, of the 38 abnormal LAS patients, 15 (30%) had possible ARVC while 23 (45%) had definite ARVC.

The number and percentage of definite and possible ARVC patients with normal and abnormal fQRS durations are represented in Table 4 below.

From Table 4, it can be seen that 22 (44%) of patients had normal fQRS durations while 29 (56%) had abnormal values. Also, of the 29 abnormal fQRS patients, 13 (26%) had possible ARVC while 16 (31%) had definite ARVC.

The mean ± standard deviation for RMS, LAS and fQRS for all the patients is summarized in Table 5.

SAECGs are considered abnormal if 2 or more variables (RMS, LAS, fQRS) fall within the abnormal range (Table 6) (Kamath et al., 2011).

The observation was that 36 (71%) of the ARVC patients had an overall abnormal SAECGs, while 15 (29%) had normal SAECGs. Twenty one (58.3%) of the patients with overall abnormal SAECGs had definite ARVC while 15 (41.6%) had possible ARVC.

Of the 35 (69%) male patients participating in the study, 26 (51% of total patients) had abnormal SAECGs and 9 (18% of total patients) had normal SAECGs. Also, of the 16 (31%) female patients, 10 (20% of total patients) had abnormal SAECGs and 6 (12% of total patients) had normal SAECGs.

Table 7 further breaks down the male and female patients with normal and abnormal SAECGs into definite or possible ARVC patients.

Of the 35 (100%) males with ARVC, 21 (60% of all males) had definite ARVC and 14 (40% of all males) had possible ARVC. Also, 26 (74%) had abnormal SAECGs

Table 4. Number and Percentage of Definite and Possible ARVC Patients with Normal and Abnormal fQRS Durations.

FQRS (ms)		Possible	Definite	Total
< 120	Count	13	16	29
	% of Total	26%	31%	56%
>= 120	Count	6	16	22
	% of Total	12%	32%	44%

Table 5. RMS, LAS and fQRS represented as a Mean with Standard Deviation.

		RMS (µV)	LAS (ms)	FQRS (ms)
N	Valid	51	51	51
	Missing	0	0	0
Mean		36.7647	35.8039	118.5490
Std. Deviation		27.40262	20.66787	21.04691

Table 6. Number and Percentage of Males and Females with Normal and Abnormal SAECGs.

			Gender		Total
			Male	Female	
Classification	Normal	Count	9	6	15
		% of Total	18%	12%	29%
	Abnormal	Count	26	10	36
		% of Total	51%	20%	71%
Total		Count	35	16	51
		% of Total	69%	31%	100%

Table 7. Number and Percentage of Definite and Possible ARVC Male and Female Patients with Normal and Abnormal SAECGs.

				Definite or Possible ARVC		Total
Gender				Possible	Definite	
Male	Classification	Normal	Count	4	5	9
			% of Total	11%	14%	26%
		Abnormal	Count	10	16	26
			% of Total	29%	46%	74%
	Total		Count	14	21	35
			% of Total	40%	60%	100%
Female	Classification	Normal	Count	0	6	6
			% of Total	0%	38%	38%
		Abnormal	Count	5	5	10
			% of Total	31%	31%	63%
	Total		Count	5	11	16
			% of Total	31%	69%	100%

and 9 (26%) had normal SAECGs. Of the 26 males with abnormal SAECGs, 16 (46%) had definite ARVC while 10 (29%) had possible ARVC. The same statistics can be checked for females.

DISCUSSION

Out of the 51 patients in the study, there were 35 males and 16 females (Table 1). This shows a 2:1

predominance in males. Also, when considering the definite ARVC patients with the confirmed diagnosis, 21 were males and 11 were females which are shown in Table 1, again showing a 2:1 predominance in males. This is in keeping with the literature presented by Tabib et al, 2003 (Tabib et al., 2003).

From Graphs 1, 2 and 3, it can clearly be seen that the majority of the plot lies within the abnormal region indicating that most of the patients in this study had abnormal values for RMS, LAS and fQRS. From Tables 2, 3 and 4, it can be deduced that the majority of the abnormal RMS and LAS measurements occurred in the definite ARVC patients while with fQRS, the number of normal and abnormal measurements were equal at 16. But when considering the possible ARVC patients, the fQRS results leaned more towards abnormal. When examining the data on Table 5, the mean for all 3 variables was in the abnormal range and when taking into consideration the standard deviation, the majority of the readings were all abnormal. When taking into account that 2 or more abnormal parameters result in an abnormal SAECG, as per GSH's protocol, 71% of the SAECGs in this study were abnormal (Table 6).

The results of definite ARVC patients in Table 7, one can see that of the 32 patients, 21 had abnormal SAECGs. This yields a percentage of 66% of definite ARVC patients having abnormal SAECGs. With the possible ARVC patients, 15 of the 19 had abnormal SAECGs yielding 79%. These percentages provide an understanding of the importance of a SAECG in diagnosing ARVC and this adheres to the findings of Kamath et al., 2011; Steriotis et al., 2009; Tabib et al., 2003.

In the study by Kamath *et al.* the value of the SAECG was assessed as a diagnostic tool. Compared with controls, all three components of the SAECG were highly associated with the diagnoses of ARVC ($P<0.001$) (Tabib et al., 2003).

Steriotis *et al.* determined the diagnostic capability of ECG's and SAECG's. ECG's were abnormal in 74% of patients and SAECG's were positive in 60%. Normal ECG's were mostly related to mild forms of the disease (Steriotis et al., 2009).

In conclusion, ARVC patients have common signs and symptoms that one should look for. Thus an easy and reliable preliminary procedure to start diagnosing with would be a SAECG. An early abnormal SAECG would mean that the patient should be sent immediately for further tests as ARVC is a condition that must be treated early due to the risk of sudden cardiac death.

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