JACC Vol. 28, No. 3
September 1996:720–4

Determinants of Spontaneous Occurrence of Sustained Monomorphic Ventricular Tachycardia in Right Ventricular Dysplasia

JEAN FRANÇOIS LECLERCQ, MD, FESC, SERGIO POTENZA, MD,
PIERRE MAISON-BLANCHE, MD, CLAUDE CHASTANG, MD, PhD, PHILIPPE COUMEL, MD, FESC
Paris, France

Objectives. **We sought to demonstrate the determinants of spontaneous onset of ventricular tachycardia in right ventricular dysplasia.**

Background. **Sudden death during athletic activities has been described in patients with right ventricular dysplasia, but few data are available on the clinical circumstances of well tolerated ventricular tachycardias.**

Methods. **The spontaneous occurrence of 43 episodes of sustained monomorphic ventricular tachycardia was recorded during ambulatory electrocardiographic (Holter) monitoring in 12 patients.**

Results. **The ventricular tachycardia usually occurred without a significant immediate precipitating arrhythmic event: Atrial arrhythmia was never present, and long-short cycle sequences by postextrasystolic pauses or runs of polymorphic extrasystoles were also unusual (four episodes of ventricular tachycardia each). Finally, no arrhythmia was present immediately before the tachycardia in 36 (84%) of the 43 episodes and in 8 of 12 patients. Examination of the sinus rate before the initial episode of tachycardia in each patient showed a continuous increase from 30 min to the few cycles before the tachycardia (mean RR decrease from 876 ± 778 to 830.5 ± 189 ms, with a mean slope of −8.4 ms/min; both $p = 0.01$ by Wilcoxon test). A within-patient comparison showed that the first cycle of the ventricular tachycardia was shorter than that of runs or couplets (389 ± 88 vs. 453 ± 121 and 520 ± 133 ms, $p = 0.03$ and $p < 0.01$, respectively, by paired *t* test) and that the second cycle was shorter than that of runs (383 ± 96 vs. 435 ± 120 ms, $p = 0.03$). Sinus rate measured 15 beats before the event was higher for ventricular tachycardia than for isolated beats (mean RR interval 835 ± 184 vs. 908 ± 153 ms, $p < 0.01$).**

Conclusions. **Increased heart rate and shortening of the coupling intervals of the first cycles before the tachycardia are due to a change in the vagosympathetic balance with an increased sympathetic tone. This increase appears to be the main determinant of the ventricular tachycardia in this disease in contrast to the multifactorial origin of ventricular tachycardia due to coronary heart disease. It should be considered in patients participating in strenuous athletic activities.**

(J Am Coll Cardiol 1996;28:720–4)

The spontaneous onset of ventricular tachycardias has been recorded in a relatively large number of series, allowing a better understanding of their mechanism, especially of those leading to sudden death. However, these studies have concerned almost exclusively patients with coronary artery disease (1–5). The clinical characteristics of sustained ventricular tachycardias due to arrhythmogenic right ventricular dysplasia are now well known (6,7), but few examples of recordings of the spontaneous onset of the ventricular tachycardia in patients with this disease have been published (8). We prospectively recorded a series of spontaneous initiation of ventricular tachycardia due to arrhythmogenic right ventricular dysplasia by ambulatory electrocardic (Holter) monitoring and we report here the analysis of the short- and long-term determinants of ventricular tachycardia.

From the Department of Cardiology, Lariboisière University Hospital and Department of Biostatistics and Medical Computing, Saint-Louis University Hospital, Paris, France.

Manuscript received January 18, 1995; revised manuscript received April 10, 1996, accepted May 3, 1996.

Address for correspondence: Dr. Jean François Leclercq, Department of Cardiology, Lariboisière Hospital, 2 Rue Ambroise Paré, 75010 Paris, France.

Methods

Study patients. The study group comprised 12 patients (10 men and 2 women, mean age ±SD 39.9 ± 14.6 years) who were referred because of frequent symptomatic sustained monomorphic ventricular tachycardia due to arrhythmogenic right ventricular dysplasia and who had at least one episode recorded during Holter monitoring. Right ventricular disease was documented by cineangiograms showing localized abnormal kinetics of the right ventricular wall in seven patients, and diffuse dilation with increased right ventricular end-diastolic pressure in the remaining five. Ventricular late potentials were always present on the signal-averaged electrocardiogram (ECG), and a monomorphic ventricular tachycardia was inducible during electrophysiologic study in all patients. Holter tapes were recorded before antiarrhythmic therapy in eight patients, after discontinuation of class I drugs for >5 half-time elimination durations in two and after <6 days of amiodarone therapy in the remaining two.

Analysis of Holter tapes. A total of 43 episodes of sustained ventricular tachycardia were recorded on 15 Holter tapes. Analog recordings (ICR or ELA recorders, 1 mm/s)

0735-1097/96/$15.00
PII S0735-1097(96)00233-1

Table 1. Clinical Characteristics and Ventricular Arrhythmias Recorded in the 12 Study Patients

Pt No.	Age (yr)/Gender	Years of F-U	Angio Data	VT (episodes)	Pause	Burst	Runs	Couplets	PVCs
1	53/M	3	Loc	1	—	—	—	12	1,084
2	40/F	3	Loc	2	—	—	—	—	28
3	22/M	7	Loc	5	—	—	59	11	39
4	42/M	7	Diff	3	1	—	8	20	740
5	34/M	14	Diff	5	—	1	6	—	133
6	25/F	10	Diff	4	—	—	7	38	1,238
7	49/M	3	Loc	3	—	—	7	—	—
8	64/M	8	Diff	4	—	—	32	61	4
9	14/M	<1	Loc	8	2	2	—	4	230
10	42/M	1	Loc	3	—	—	87	2	309
11	56/M	20	Loc	2	—	—	13	100	1,197
12	38/M	12	Diff	3	1	1	—	—	23
Total				43			219	248	5,025

Angio = angiographic; Diff = diffuse alteration of right ventricular contractility; F = female; F-U = follow-up after the first tachycardia; Loc = localized akinesia; M = male; Pt = patient; PVCs = premature ventricular complexes; VT = ventricular tachycardia.

were processed on two channels on a Marquette Laser Holter system XP. After validation of the ventricular morphology classification, data were transferred to a personal computer (Olivetti M380/C) implemented with a specific software, the Atrec 2 system (9). This program allows a search on mean RR cycles in the 3 min, and on each cycle on the 15 cycles preceding and the 3 cycles following each defined type of ventricular arrhythmia.

Sustained ventricular tachycardia was defined as lasting >1 min, and its short-term determinants were compared with those of other ventricular arrhythmias having the same configuration in the two leads of the recording, that is, runs (n = 219), couplets (n = 248) and isolated premature ventricular complexes (n = 5,025). In all these arrhythmias, the following variables were measured: the mean RR cycle in the 3 min, the last min and the last 15 beats before the arrhythmia, the sinus cycle immediately before the arrhythmia (RR-1), the coupling interval of the first beat of the arrhythmia (RV1), the first cycle of the repetitive arrhythmias (V1V2) and the second cycle of runs and sustained ventricular tachycardia (V2V3).

Long-term analysis of sinus rhythm behavior before sustained ventricular tachycardia was performed in the first recorded episode of ventricular tachycardia for each patient (initial tachycardia). In all cases, at least 30 min of sinus rhythm without sustained ventricular tachycardia was available for analysis. The mean RR cycle of 1-min consecutive sinus cycles was measured at 30, 15, 5, 3 and 1 min before and immediately before the initial tachycardia in all 12 patients. It was necessary to eliminate some cycles corresponding to premature ventricular complexes and compensatory pauses and to replace them by adjacent sinus cycles in 14 of the 72 analyzed sequences.

Statistical analysis. Statistical analysis of the sinus rate changes before tachycardia was performed on a by-patient basis, using only the first episode of ventricular tachycardia when several episodes were observed for a same patient. The variation in RR cycle was studied by 1) the crude variation in RR cycle between 30 min and 1 min before ventricular tachycardia, and 2) the slope of the RR cycle assessed at 30, 15, 5, 3 and 1 min before ventricular tachycardia for each patient, through a linear regression model. These distributions were compared with 0 by the Wilcoxon nonparametric two-tailed test. A paired t test was used to compare the first two tachycardia cycles of episodes of ventricular tachycardia with those of minor arrhythmias present in the same Holter tape.

Results

Patients and tachycardias. Table 1 displays the clinical characteristics of the 12 patients and the number of ventricular arrhythmias with the same configuration as that of sustained ventricular tachycardia recorded in each. The number of episodes of sustained ventricular tachycardia varied from 1 to 8, and their duration from 2 min to 4 h. All 12 patients had several types of minor arrhythmias (isolated premature ventricular complexes, couplets or runs) with the same configuration.

Short-term determinants of the ventricular tachycardias. Visual examination of the ECG immediately preceding each episode of ventricular tachycardia showed that sustained ventricular tachycardia was always monomorphic, and that no atrial arrhythmia was present. In only four cases, the monomorphic ventricular tachycardia was preceded by a burst of polymorphic premature ventricular complexes. The presence of short-long cycle sequences due to premature ventricular complexes and compensatory pauses was also unusual (four ventricular tachycardia episodes).

As shown in Table 1, when several ventricular tachycardias were recorded in the same patient, pauses or polymorphic bursts were not systematically present, and no arrhythmia was present immediately before the tachycardia in 36 (84%) of the 43 episodes of ventricular tachycardia and in 8 of 12 patients.

JACC Vol. 28, No. 3
September 1996:720–4

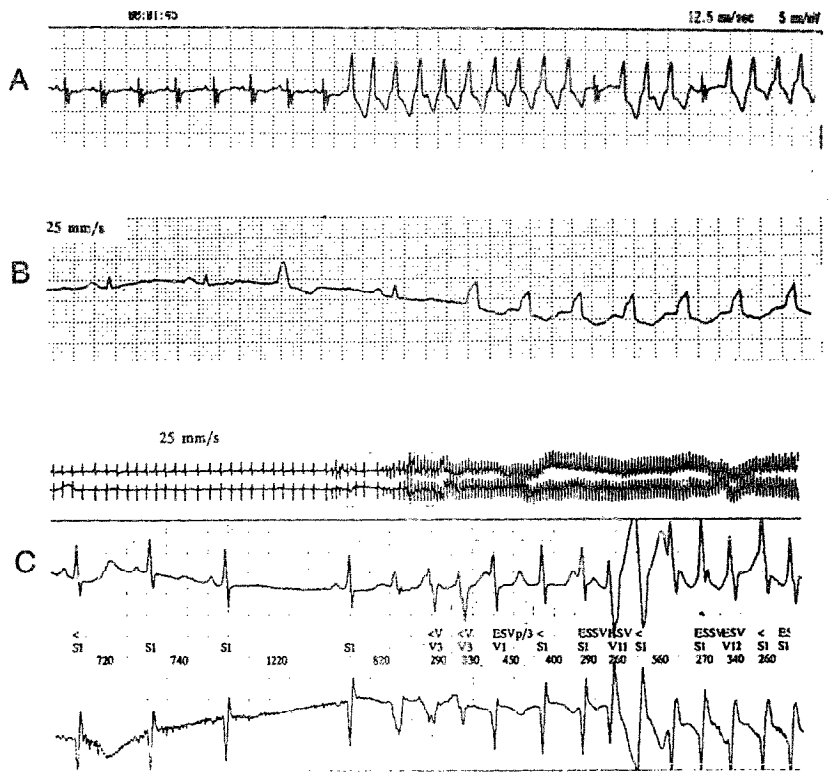

Figure 1. Three examples of spontaneous initiation of sustained monomorphic ventricular tachycardia in arrhythmogenic right ventricular dysplasia. **A,** Onset of ventricular tachycardia without any significant event. This type represents almost all cases (35 of 43 ventricular tachycardias). **B,** Onset of ventricular tachycardia preceded by a long-short cycle sequence due to a postextrasystolic pause, occurring in only 4 (10%) of 43 ventricular tachycardias. **C,** Onset of ventricular tachycardia preceded by a burst of polymorphic ventricular tachycardia, occurring in only 4 (10%) of 43 ventricular tachycardias. Numerical values = RR cycle length.

Figure 1 shows different examples of these possible types of initiation of ventricular tachycardia, the great majority occurring without significant preceding ventricular events (no premature ventricular complexes in the two RR cycles immediately before the onset of ventricular tachycardia). The circadian timing of tachycardia onset showed two peaks, both before 9 PM: 1) between 6 and 9 AM with six ventricular tachycardias, and 2) between 6 and 9 PM with seven ventricular tachycardias; in contrast, only three ventricular tachycardias occurred at night (9 PM to 3 AM).

Long-term determinants of the tachycardias. Table 2 shows the changes in sinus RR cycle before the initial tachycardia in the 12 patients. The mean crude variation between 30 min and 1 min before ventricular tachycardia was estimated at 98 ± 28 ms, with increases in cycle length in only two patients. The Wilcoxon test showed a significant difference ($p = 0.01$) between the 30-min and 1-min values. The same result was obtained when the slope of RR cycles was estimated by linear regression from all values from 30 min to 1 min before ventricular tachycardia; the mean slope was estimated at −8.4 ± 5.7 ms/min ($p = 0.01$ by Wilcoxon test), and the value was positive in only two patients.

Table 3 displays the mean values for RR intervals within the 3 min before the ventricular arrhythmias and for coupling intervals for the four types of arrhythmia examined. By comparison with sustained ventricular tachycardia, isolated prema-

Table 2. Sinus Cycle Changes Before the Initial Ventricular Tachycardia

	Minutes					
RR Interval	30	15	5	3	1	VT*
Mean	876	877	824	801	778	791
Median	857	896	863	773	785	763
SD	143	170	187	203	191	194
Minimal	600	566	415	388	382	387
Maximal	1,071	1,093	1,089	1,092	1,095	1,065

*Immediately before ventricular tachycardia onset. All values are in ms.

Table 3. RR Cycles Preceding the Different Ventricular Arrhythmias

Cycles	VT	Runs	Couplets	PVCs
RR-3 min	819 ± 161	786 ± 234	845 ± 192	846 ± 160
RR-1 min	818 ± 181	794 ± 203	839 ± 188	884 ± 145†
RR-15	835 ± 184	831 ± 200	848 ± 177	908 ± 153†
RR-1	847 ± 167	859 ± 233	857 ± 149	904 ± 165
RV1	653 ± 197	633 ± 228	562 ± 106	613 ± 141
V1V2	389 ± 88	453 ± 121*	520 ± 133‡	—
V2V3	383 ± 96	435 ± 120*	—	—

*$p < 0.05$, †$p < 0.01$, ‡$p < 0.001$ versus ventricular tachycardia (VT). All values are in ms (mean ± SD). PVCs = premature ventricular complexes; RR-3 min, RR-1 min, RR-15, RR-1 = values of sinus cycles 3 min, 1 min, 15 cycles and immediately before the first complex of the ventricular arrhythmia; RV1 = coupling interval of the first beat of the ventricular arrhythmia; V1V2, V2V3 = values of the first and the second cycles, respectively, of the repetitive ventricular arrhythmias.

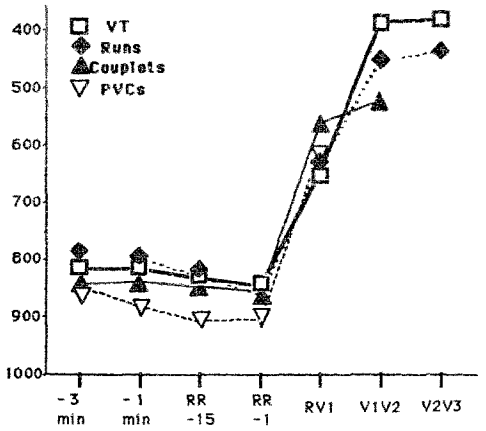

Figure 2. Schematic representation of sinus rate in the preceding 3 min and of coupling intervals (RV1) and the first (V1V2) and the second (V2V3) cycles of the arrhythmias. Repetitive arrhythmias are preceded by shorter sinus RR cycles, 1 min and 15 cycles before the event, by comparison with isolated premature ventricular complexes (PVCs). Sustained episodes of ventricular tachycardia are initiated by shorter V1V2 and V2V3 cycles than those initiating couplets or runs (see also Table 2).

ture ventricular complexes were preceded by longer RR cycles from 1 min to the 15th RR interval, whereas no difference existed between couplets or runs and ventricular tachycardia, or between premature ventricular complexes and ventricular tachycardia for other values. For example, values for the last RR cycle and for the coupling interval of the first premature ventricular complexes do not differ significantly from one type of arrhythmia to another even when the same trend is observed. Values for the coupling interval (RV1) of the first beat of the arrhythmia were also not significantly different among arrhythmias, but a significant difference appears in the values for the second (V1V2) and the third (V2V3) cycles of the repetitive arrhythmia: Sustained episodes of ventricular tachycardia were triggered by shorter cycles than were couplets or runs. When analyzing by patient instead of by tachycardia episodes, a difference was still present for the RR cycle measured 1 min before the event (754 ± 208 versus 809 ± 157 ms, $p < 0.05$). Additionally, there was a general trend to a decrease in sinus cycle length within the 3 min preceding each type of ventricular arrhythmia. All these differences are schematically depicted in Figure 2.

As a summary, Figure 3 presents a typical example of a sustained ventricular tachycardia episode recorded in a young patient, preceded by a progressive and continuous sinus rate increase and initiated directly without previous premature ventricular complexes or morphologic changes of the ventricular tachycardia beats.

Discussion

Differences in short-term determinants between ventricular tachycardias of coronary artery disease and those of right ventricular dysplasia. The clinical characteristics of sustained monomorphic ventricular tachycardia in arrhythmogenic right

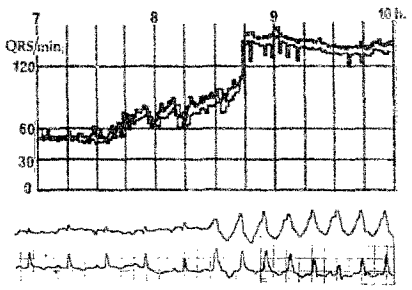

Figure 3. Typical example of the first sustained ventricular tachycardia episode recorded in a young patient who had nondiagnosed episodes of palpitation. The sustained ventricular tachycardia is preceded by a progressive and continuous increase in sinus rate during morning physical activities (**top**) and is initiated directly from sinus rhythm without previous significant premature ventricular complexes or morphologic changes of the first ventricular tachycardia beats (**bottom**).

ventricular dysplasia have been previously published, as they permitted the original description of the disease (6). However, no reports were available on the recordings of their spontaneous onset. Our series, although limited, shows several important characteristics: 1) Despite the polymorphism, classically observed (6,8) and present in the premature ventricular complexes of our patients, the sustained ventricular tachycardias were monomorphic, even though one patient may have had two or three different monomorphic ventricular tachycardias. Moreover, few monomorphic episodes of ventricular tachycardia were triggered by a burst of polymorphic ventricular tachycardia. This finding contrasts with data previously reported in patients with coronary artery disease, who had a high proportion of monomorphic ventricular tachycardias initiated by at least some beats of a different configuration (1,4). 2) The incidence of the long-short sequences due to postextrasystolic pauses was also surprisingly low in these patients with numerous premature ventricular complexes, and it contrasts again with the incidence rate of 30% to 45% of such pauses immediately before episodes of ventricular tachycardia/ventricular fibrillation reported in patients with coronary artery disease (4,5,10). 3) Finally, no ventricular tachycardia was triggered during an atrial arrhythmia in our small series, whereas it is usually evidenced before 25% to 33% of ventricular tachycardias in patients with coronary disease (1,4,11).

These important differences between the tachycardias of patients with arrhythmogenic right ventricular dysplasia and postmyocardial infarction probably mean that in arrhythmogenic right ventricular dysplasia, the initiation of ventricular tachycardia is usually related to changes within the electrophysiologic tachycardia substrate, without a significant role of external triggering factors as in the ventricular tachycardia of patients with coronary disease.

Sympathetic stimulation as a main determinant in ventricular tachycardias due to right ventricular dysplasia. The shortening of the first and the second cycles of the ventricular tachycardia, by comparison with those of runs and couplets, probably reflects an enhanced sympathetic tone, because no change in the site of origin seems conceivable in these monomor-

phic arrhythmias and because no short-long RR sequence was usually seen before the tachycardia. The same applies to the progressive increase in sinus rate, beginning 30 min before the ventricular tachycardia, and to the two diurnal peaks in the nycthemeral distribution of the tachycardias. The published descriptions of sudden death in young subjects with arrhythmogenic right ventricular dysplasia (12) included a high proportion of death occurring during athletic activities, and the frequent occurrence of ventricular tachycardia during exercise has been already mentioned in this disease (8). It thus seems probable that increased sympathetic stimulation is the main determinant of spontaneous initiation of ventricular tachycardia in arrhythmogenic right ventricular dysplasia, allowing the necessary change in electrophysiologic ventricular tachycardia substrate. A stronger sympathetic stimulation is needed to produce sustained ventricular tachycardia than to produce couplets or runs. This stimulation is maximal <3 min before ventricular tachycardia, as judged by the effect on sinus rate, but it is in fact progressive within the 30-min time interval before tachycardia, thus explaining the correlation between time and sinus rate. This time constant is consistent with a progressive increase in humoral sympathetic tone (and then to the occurrence of ventricular tachycardia during exercise) rather than with abrupt changes in neurogenic sympathetic tone.

The increase in sinus rate before the onset of sustained tachycardia was present in this series of patients with arrhythmogenic right ventricular dysplasia and occurred in those with ventricular tachycardia due to coronary heart disease when no long-short RR sequence was present immediately before the tachycardia (4). However, the mean value of this increase differed (7.3 beats/min in arrhythmogenic right ventricular dysplasia versus 13.3 beats/min in coronary disease). Even if a direct comparison is probably difficult in these different diseases, these data may indicate that the ventricular tachycardia substrate is more sensitive to sympathetic tone elevation in arrhythmogenic right ventricular dysplasia: A less pronounced sympathetic stimulation is sufficient to trigger the arrhythmia.

Conclusions. An enhanced humoral sympathetic tone seems to be the main determining factor in the spontaneous occurrence of sustained ventricular tachycardia in arrhythmogenic right ventricular dysplasia, and the role of other precipitating factors seem less important than in other situations such as coronary heart disease. This observation could explain why arrhythmogenic right ventricular dysplasia is often discovered in athletes, who may achieve a sufficient level of stimulation of the sympathetic system during exercise to modify their ventricular tachycardia substrate. The risk of sudden death reported in this disease should encourage a systematic search for arrhythmogenic right ventricular dysplasia in subjects who wish to be athletes, using primarily noninvasive techniques such as the signal-averaged ECG, which has an interesting predictive value in this situation (13,14).

References

1. Pratt CM, Francis MJ, Luck JC, Wyndham CR, Miller RR, Quinones MA. Analysis of ambulatory electrocardiograms in 15 patients during spontaneous ventricular fibrillation with special reference to preceding arrhythmic events. J Am Coll Cardiol 1983;2:789–97.
2. Bayes de Luna A, Coumel P, Leclercq JF. Ambulatory sudden cardiac death: mechanisms of production of fatal arrhythmia on the basis of data from 157 cases. Am Heart J 1989;117:151–9.
3. Roelandt J, Klootwijk P, Lubsen J, Janse MJ. Sudden death during longterm ambulatory monitoring. Eur Heart J 1984;5:7–20.
4. Leclercq JF, Maisonblanche P, Cauchemez B, Coumel P. Respective role of sympathetic tone and of cardiac pauses in the genesis of 62 cases of ventricular fibrillation recorded during Holter monitoring. Eur Heart J 1988;9:1276–83.
5. Gomes JA, Alexopoulos D, Winters SL, Deshmukh P, Fuster V, Suh K. The role of silent ischemia, the arrhythmic substrate and the long-short sequence in the genesis of sudden cardiac death. J Am Coll Cardiol 1989;14:1618–25.
6. Marcus FI, Fontaine GH, Guiraudon G, et al. Right ventricular dysplasia: a report of 24 adult cases. Circulation 1982;65:384–98.
7. Blomström-Lundqvist C, Sabel KG, Olsson B. The long-term follow-up of 15 patients with arrhythmogenic right ventricular dysplasia. Br Heart J 1987;58: 477–88.
8. Leclercq JF, Coumel P. Characteristics, prognosis and treatment of the ventricular arrhythmias of right ventricular dysplasia. Eur Heart J 1989; Suppl D:61–7.
9. Zimmermann M, Maisonblanche P, Cauchemez B, Leclercq JF, Coumel P. Determinants of the spontaneous ectopic activity in repetitive monomorphic idiopathic ventricular tachycardia. J Am Coll Cardiol 1986;7:1219–27.
10. Hook BG, Marchlinski FE. Value of ventricular electrogram recordings in the diagnosis of arrhythmias precipitating electrical device shock therapy. J Am Coll Cardiol 1991;17:985–90.
11. Olshausen KV, Witt T, Pop T, Treese N, Bethge KP, Meyer J. Sudden cardiac death while wearing a Holter monitor. Am J Cardiol 1991;67:381–6.
12. Thiene G, Nava A, Corrado D, Rossi L, Pennelli N. Right ventricular cardiomyopathy and sudden death in young people. N Engl J Med 1988;318:129–33.
13. Blomström-Lundqvist C, Hirsch I, Olsson SB, Edvardsson N. Quantitative analysis of the signal-averaged QRS in patients with arrhythmogenic right ventricular dysplasia. Eur Heart J 1988;9:301–12.
14. Leclercq JF, Coumel P. Late potentials in arrhythmogenic right ventricular dysplasia. Prevalence, diagnostic and prognostic values. Eur Heart J 1993;14 Suppl E:E80–3.