Quantitative assessment of ST segment elevation in Brugada patients

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BACKGROUND ST segment elevation in the right precordial leads constitutes the electrocardiogram (ECG) hallmark of Brugada syndrome (BS). This pattern is variable and can be concealed, but the magnitude and the cause of ST segment fluctuations have been poorly investigated.

OBJECTIVE Our goal was to quantify ST changes and to assess rate and autonomic influences on ST level.

METHODS A 12-lead ECG was continuously recorded during 24 hours in 20 patients with BS (ages 49 ± 12) and 10 healthy subjects (ages 32 ± 7). Using two-dimensional binning we obtained average QRS-T complexes every 30 minutes (time bins) and at different RR intervals (rate bins) for each subject. ST level was measured at five different points located 90, 100, 110, 120, and 140 ms after Q onset (Qo). In BS patients, the highest ST elevation was measured 110 ms after Qo (Qo+110).

RESULTS ST level changes between time points were significantly greater in patients with BS compared with control subjects: on lead V2, the range of ST level at Qo+110 was 264 ± 85 μV in BS and 91 ± 22 μV in control subjects ($P < .01$). In BS, ST level decreased with heart rate acceleration: the difference in ST level at Qo+110 for RR = 900 and 600 ms was 55 ± 53 μV ($P < .01$). HFnu was positively, although weakly, correlated with ST level ($R^2 = 0.02$, $P < .01$).

CONCLUSIONS ECG changes observed in patients with BS are related in part to heart rate influences on ST segment level. These spontaneous fluctuations over a 24-hour time period suggest that Holter recordings may improve the ECG diagnosis sensitivity in BS.

KEYWORDS Electrocardiography; Heart rate; Brugada syndrome

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Brugada syndrome is characterized by an ST segment elevation in the right precordial leads and a high incidence of sudden death in patients with structurally normal hearts.[1] The electrocardiogram (ECG) pattern constitutes the hallmark of the syndrome, and a J point or an ST elevation ≥0.2 mV is mandatory for the diagnosis of the Brugada ECG pattern.[2,3] It has been long recognized that the Brugada ECG pattern is variable and can be concealed.[3–5] The spontaneous ECG changes represent a source of potential false-negative diagnosis. So far, the characteristics of these spontaneous ST segment fluctuations have not been quantified in Brugada patients.

In Brugada syndrome, ST elevation as well as the occurrence of cardiac events may be modulated by numerous conditions.[5,6] Since cardiac events occur preferentially during sleep, the influence of the autonomic nervous system (ANS) seems to be of the utmost importance in the syndrome.[7,8] The autonomic modulation of ST segment level in Brugada ECGs has been documented in both experimental models and clinical studies.[9,10] Isoproterenol reduces ST elevation, whereas acetylcholine amplifies the ECG abnormality.[9,10] Less is known about the effect of the ANS on the ST segment in physiological conditions. Experimental data suggest that the ST segment elevation observed in BS is a consequence of the loss of action potential dome in epicardial cells as a consequence of an increased transient outward potassium current (Ito1). The transmural gradient leads to the ST segment elevation observed on the transmural ECG.[10] Using this model, Yan and Antzelevitch[10] have shown that either a premature beat or a faster pacing could restore the epicardial dome and thus decrease ST elevation. This phenomenon could be explained by the gating properties of Ito, in particular its slowness to recover from inactivation.[11] We hypothesized that the spontaneous ST segment elevation recorded in Brugada patients could be related in part to heart rate changes.

In this study, we used long-term 12-lead ECG recordings during daily activities in Brugada patients to (1) quantify spontaneous ST segment changes and (2) assess rate and autonomic influences on the ST segment level.

Methods

Patients

The study population included 20 patients with Brugada syndrome or a typical ECG pattern who were referred to the department. The ECG diagnosis of Brugada syndrome/pattern was accepted only if the ST segment elevation on right precordial leads was >200 μV together with a type 1 morphology.[2,3] An example of the typical pattern is shown

Fabio Badilini is vice president of AMPS LLC, New York. Part of the study was done using the Winatrec software commercialized by AMPS.
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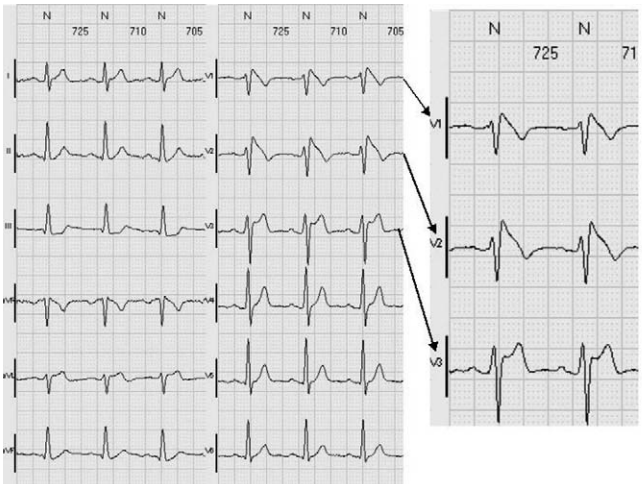

Figure 1 A 12-lead ECG extracted from the 24-hour recording in one Brugada patient.

in Figure 1. This typical ECG pattern could be recorded either spontaneously or after a class I antiarrhythmic drug challenge (intravenous ajmaline 1 mg/kg body weight/5 minutes). All patients had a structurally normal heart as assessed by transthoracic echocardiography and underwent an electrophysiological study. The programmed ventricular stimulation protocol included two basic cycle lengths (600 and 400 ms) with up to three extra stimuli delivered at the right ventricle apex and outflow track with a shortest RR interval of 200 ms.

A group of 10 healthy volunteers served as a control group. All control subjects had a normal clinical examination including normal blood pressure and ECG. None of them had a previous history of chronic disease.

ECG recording and analysis

The 12 standard ECG leads (six limb and six precordial leads) were continuously recorded using Holter technology in all patients during 24 hours (Ela Medical, Sorin Group, Le Plessis Robinson, France). Holter recordings were performed in drug-free conditions. ECG recordings were carefully edited to ensure that cardiac beats of sinus origin were accurately identified and that nonsinus beats as well as artifacts had been excluded for quantitative analysis. ECG recordings were then transferred to the dedicated software (Winatrec 7.0.0 beta release, AMPS LLC, NY) that was used in a beat-averaging approach, which has been called the "bin" method.[12–14] In this study, we used two different averaging processes (Figure 2).

To assess ST segment elevation at different time points during the 24 hours of the recordings, we constructed one template every 30 minutes from 30 seconds of consecutive cardiac complexes of sinus origin. We thus obtained 48 time bins for each patient (Figure 2A). Each time bin was classified as diurnal (6 consecutive hours with the fastest heart rates in the awake period) or nocturnal (6 consecutive hours with the slowest heart rates in the sleeping period) according to the mean hourly heart rate obtained from the 24-hour frequency table and subject diaries.

The second bin-averaging model aimed to evaluate heart rate influences on ST segment elevation. For each of the circadian periods as defined above, QRS-T complexes were classified according to their preceding RR interval and then averaged (rate bins). For each subject, diurnal rate bins were obtained within the range of RR intervals of 600–900 ms and nocturnal rate bins within the range of RR intervals of 800–1000 ms (100-ms step increment; Figure 2B).

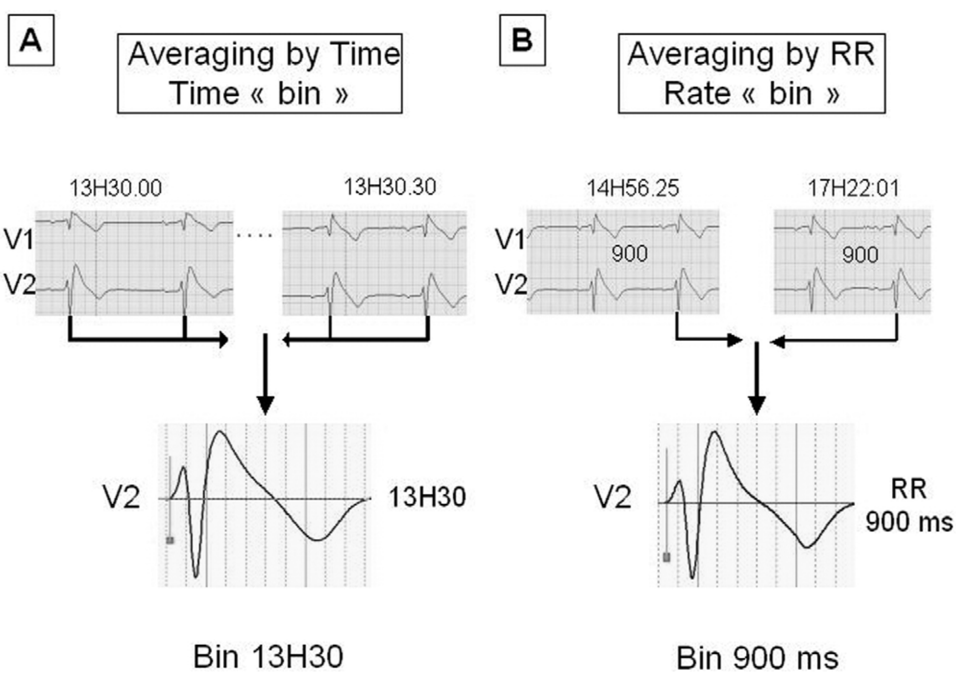

Figure 2 The two averaging processes: the two-dimensional binning. **A:** Each time bin was built using 30 seconds of consecutive sinus QRS-T complexes. The process was repeated every 30 minutes, thus leading to 48 time bins for each patient. **B:** To obtain rate bins, QRS-T complexes were classified according to their preceding RR interval and then averaged. This process led to the construction for each subject of diurnal and nocturnal rate bins for RR intervals ranging from 600 to 900 ms during the day and from 800 to 1000 ms at night with a 100-ms step.

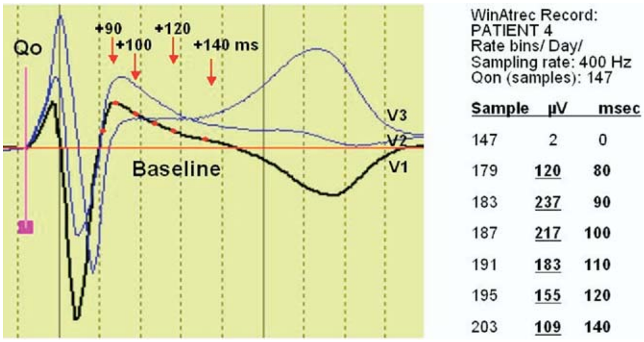

Figure 3 Qo and baseline assessment and measurement of ST segment level at the five different points. Overlap of three leads (V1, V2, and V3). Measures shown on the right panel were performed on the lead V1 recording. The position of Qo was defined as the beginning of the QRS complex assessed on three overlapped leads. Then the line on the horizontal crossing Qo defined the baseline. ST segment level was measured relative to the baseline at five different points located 90, 100, 110, 120, and 140 ms after Qo.

Whatever the averaging process considered, each bin was considered suitable for quantitative ECG measurement only if it was built from a minimum of 20 individual QRS-T complexes and if the level of residual noise was <3 μV. The position of Q onset point (Qo) was defined as the beginning of the QRS complex. The baseline was defined by the horizontal line crossing Qo (Figure 3). The Qo and the baseline position were validated and corrected when necessary. Both rate and time bins have been manually reviewed.

The primary ECG endpoints were the ST segment levels from baseline at five different points located 90, 100, 110, 120, and 140 ms after Qo (Qo+90, Qo+100, Qo+110, Qo+120, and Qo+140, respectively) (Figure 3). The analysis was performed separately on leads V1 and V2.

Heart rate variability (HRV) parameters were used as autonomic surrogates and calculated from both time domain and frequency domain approaches.[15] Three time domain parameters were calculated: (1) the standard deviation of all normal RR intervals (SDNN), (2) the percentage of interval differences of successive normal RR intervals difference >50 ms (PNN50), and (3) the square root of the mean squared differences of successive normal RR intervals (RMSSD). The frequency domain analysis was performed using autoregressive models, and both low-frequency (LF) and high-frequency (HF) corresponding data were reported as normalized units (LFnu, HFnu); we also calculated the LF/HF ratio.[16] HRV parameters were computed on a 5-minute basis. To match the QRS-T time bins and HRV parameters, the 5-minute periods used for HRV analysis were centered on the 30 seconds used for the time bin–averaging process.

Statistical analysis

Data are presented as mean ± SD. ST segment changes are expressed by the within-subject standard deviation (SD_{within}) and by the maximal difference within a subject (Δmax). Comparisons between groups were performed by analysis of variance (ANOVA) with a Scheffe post-test when applicable. Rate influences as well as circadian influences were assessed using ANOVA for repeated measures. Statistical analysis was performed using Statview 5.0 (SAS Institute, Cary, NC).

Results

Patients

Table 1 displays the clinical characteristics of the 20 Brugada patients. All of them were males with a mean age of 48.8 ± 12 years. Out of the 20 patients, 12 were asymptomatic patients. The disease had been discovered fortuitously in 10 and because of a family history of sudden cardiac death in the two others. The remaining eight patients were symptomatic (one patient presenting with aborted sudden cardiac death and seven patients with syncope and/or near syncope). After electrophysiological testing, we proposed an implantable cardioverter defibrillator for 10 of the 20 patients and nine were implanted. The group of healthy volunteers included nine males and one female, and their mean age was 32 ± 7 years.

ST segment elevation in healthy subjects and in Brugada patients

At all five ST points considered, the 24-hour average ST segment elevation was significantly higher in Brugada patients than in control subjects on both V1 and V2 leads (Table 2). On lead V2, averaged ST segment elevation was above 200 μV 100, 110, and 120 ms after Qo in Brugada patients. Whatever the lead considered (V1 or V2), the averaged highest ST segment elevation was observed at ECG sample occurring 110 ms after Qo in Brugada patients.

Symptomatic patients showed a nonsignificant trend toward a higher ST segment elevation when compared with asymptomatic patients. For instance, on lead V2, the ST segment level measured 110 ms after Qo was 320 ± 134 μV in symptomatic patients versus 222 ± 81 μV in asymptomatic patients ($P = .08$) and 305 ± 126 μV in symptomatic patients versus 217 ± 53 μV in asymptomatic patients 120 ms after Qo ($P = .06$).

ST segment elevation changes over 24 hours

Figure 4A shows the individual pattern of ST segment fluctuation in a Brugada patient and a control subject during the 24-hour time course of the recording. In that specific case, ST segment elevation at the Qo+110 ms sample ranged from 300 to 700 μV in the Brugada patient, whereas it was always below 100 μV in the control subject.

ST level changes between time points were significantly greater in Brugada patients when compared with control subjects (Table 3). For instance, on lead V2, the range of ST segment level at the Qo+110 ms sample was 264 ± 85 μV in Brugada patients and 91 ± 22 μV in control subjects ($P < .01$).

It should be pointed out that in Brugada patients, the level of ST segment showed a nonsignificant but unexpected trend toward a reduced ST elevation at night (Figure 4B). No significant differences in the amplitude of ST fluctuations were evidenced between symptomatic and asymptomatic Brugada patients.

Table 1 Clinical characteristics of Brugada patients

Patient no.	Age	Symptoms	EP study	Family history	Implantable cardioverter defibrillator
1	35	SCD	VF	SCD (cousin, 25 years)*	Yes
2	41	0	VF	SCD (brother, 43 years)*	Yes
3	53	0	EP−	0	No
4	56	0	VF	0	No
5	50	Syncope	EP−	SCD (father, 56 years)*	Yes
6	59	0	VF	Syncope (brother)	No
7	42	0	EP−	0	No
8	42	Syncope	VF	SCD (brother, 1 year)*	Yes
9	19	Near syncope	VF	SCD (father, 42 years)*	No
10	78	Syncope	VF	0	Yes
11	39	Syncope	VF	SCD (uncle, 42 years)*	No
12	47	0	VF	0	No
13	42	Syncope	VF	0	Yes
14	42	0	VF	0	No
15	49	0	EP−	0	No
16	57	0	EP−	0	No
17	56	Syncope	VF	0	Yes
18	50	0	VF	SCD (father, 58 years)	Yes
19	59	0	VF	SCD (nephew)	No
20	59	0	VF	0	Yes

EP study = electrophysiological study; EP− = negative EP study; SCD = sudden cardiac death; VF = ventricular fibrillation.
*Age at occurrence of symptom.

As a consequence of these changes, the level of ST segment could be below the 200-μV cutoff value at some time points in a given patient. None of the control subjects had an ST segment sample measured 110 ms after Qo that was above 200 μV. In Brugada patients, 57% ± 42% of ECG time points (Qo+110 ms sample) in lead V1 and 31% ± 32% in lead V2 showed ST segment elevation below 200 μV.

Heart rate influences on ST segment level

In control subjects, no significant rate effect was evidenced on lead V1 whatever the circadian period considered. On lead V2, the ST segment level 110 ms after Qo decreased by 25.5 ± 19 μV when the RR interval increased from 600 to 900 ms (P <.01) during the day, but increased by 21 ± 14 μV when RR increased from 800 to 1000 ms at night (P <.01).

The rate influences on ST segment level in Brugada patients are shown Table 4. During the diurnal period, the lowest ST segment elevation was observed for a 600-ms RR interval. On lead V1, ST level rate dependence was bell shaped with a peak around 700 ms. On lead V2, ST segment level showed a clear rate dependence with a decreased ST elevation when heart rate accelerates. This phenomenon was consistent at all ST segment points (Table 4). For instance, the mean difference in ST segment level at sample Qo+110 ms between RR bin 900 and RR bin 600 ms was 55 ± 53 μV (P <.01) on lead V2. Figure 5 shows representative examples of ST level changes in two Brugada patients and one control subject. This rate influence was no more evidenced during the nocturnal period.

As a consequence of the rate influence, the level of ST segment points could be below the 200-μV cutoff value at some specific rate bins in a given patient. On lead V2, the diurnal level of ST segment elevation was <200 μV in 50% of patients for RR bins of 600 ms and only in 20% patients for RR bins of 900 ms (Qo+110 ms sample).

HRV parameters and ST segment level

Among the "parasympathetic" HRV parameters, only the HFnu was positively correlated with ST level (Qo+110 = 0.77 × HFnu+248, P <.01, R^2 = 0.02). The level of

Table 2 ST segment elevation on leads V1 and V2 in healthy subjects and in Brugada patients

	Lead V1		Lead V2	
ST level (μV) at	Controls	Brugada	Controls	Brugada
Qo+90	−60 ± 93	149 ± 179*	−61 ± 136	133 ± 218†
Qo+100	8 ± 33	198 ± 137*	53 ± 52	231 ± 148*
Qo+110	33 ± 21	201 ± 122*	92 ± 34	264 ± 114*
Qo+120	44 ± 19	179 ± 114*	115 ± 33	254 ± 99*
Qo+140	55 ± 24	114 ± 69†	146 ± 39	197 ± 70†

*P <.01 versus controls.
†P <.05 versus controls.

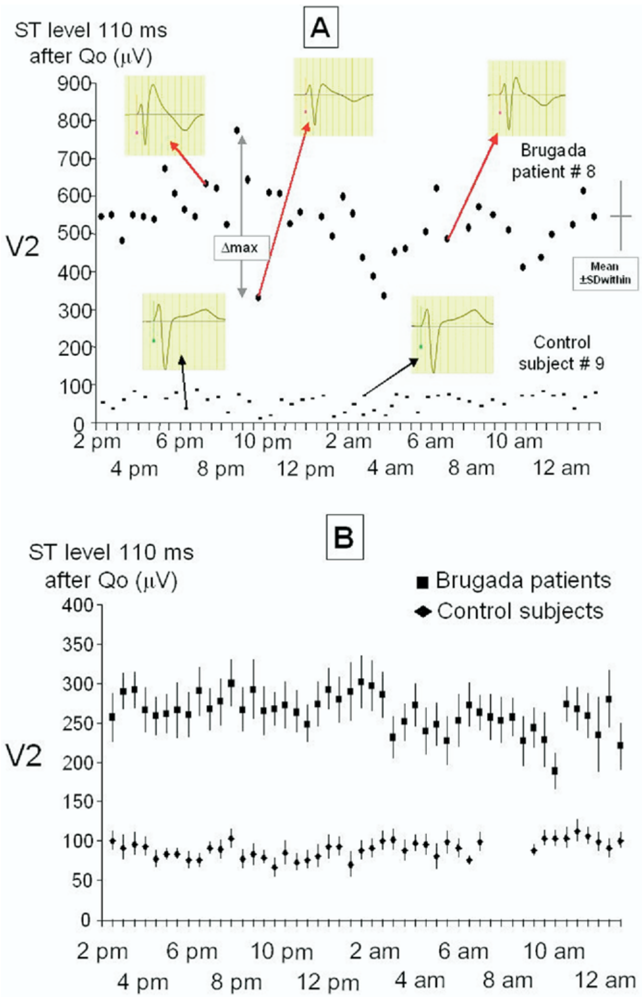

Figure 4 ST level fluctuation over 24 hours. The ST levels were measured after a time-binning procedure. The horizontal axis represents the time of day. **A:** Individual examples in one Brugada patient (*circles*) and one control subject (*lines*). The Brugada patient displayed a highly variable ST segment level associated with QRS-T complex morphology changes (*inserts*). The control subject showed only little ST level variability without obvious changes in QRS-T morphology. **B:** Average data (mean ± SEM) of Brugada patients and control subjects.

ST segment was also negatively correlated with LFnu (Qo+110 = −0.79 × LFnu+329, P <.01, R^2 = 0.02). Although these relations were statistically significant, the correlations were weak.

Discussion

Using continuous 12-lead ECG recordings, we could quantify ST segment elevation in Brugada patients at multiple different time points and different heart rates. We showed that ST segment elevation was highly variable over a 24-hour period, thus leading to a potential false-negative ECG diagnosis of the Brugada syndrome. We have also showed that these fluctuations were related to changes in heart rate (ST segment level decreased with increasing heart rate) but showed only a weak correlation with HRV parameters.

Relation to previous clinical studies

Although it is well established that the ST segment elevation observed in Brugada syndrome may change over time, this phenomenon has been poorly quantified.[2,6,9,17,18] Mizumaki et al[18] showed that the level of ST segment evaluated 40 ms after the J wave change was on average around 200 μV. In the present study, we found that the average magnitude of ST segment elevation changes observed within 24 hours was between 200 and 300 μV, which is close to Mizumaki et al's results.[18] However, in opposition to Mizumaki et al's findings, we found a nonsignificant but unexpected trend toward a reduced ST elevation at night. This trend was still observed when ST segment level was compared between circadian periods at identical heart rates (Table 4).

However, the methodology in Mizumaki et al's paper suffers important technical limitations since the findings were obtained using software developed for identification of ischemic episodes.[18] The main concern with such tools is that it is not possible to manually edit all the measures of ST segment level. Another confounding factor is related to the definition of the J point. On ECGs with overt Brugada patterns, it is not always easy to determine the position of the transition between the QRS and the ST, especially in right precordial leads. In addition, it has not been yet demonstrated that the position of the J point is stable.

To overcome such limitations, in this study, we quantified the level of the ST segment from baseline at five different ECG samples with respect to the onset of the QRS complex. Quantitative evaluation was made on averaged ECG templates, thus minimizing the signal-to-noise ratio. In addition, we controlled and manually corrected if needed the position of the Qo and of the baseline for each single template. Therefore, we believe that the quantitative ECG data reported in this study were robust, at least not jeopardized by weak ECG processing.

Table 3 ST level changes over the 24 hours of the recordings in control subjects and Brugada patients

	Δmax		SD within	
ST point	Controls	Brugada	Controls	Brugada
V1				
Qo+90	134 ± 82	262 ± 159*	30 ± 23	58 ± 30*
Qo+100	71 ± 34	235 ± 153†	16 ± 9	50 ± 28†
Qo+110	58 ± 23	214 ± 176*	13 ± 4	46 ± 34*
Qo+120	57 ± 25	192 ± 146*	13 ± 5	41 ± 29†
Qo+140	67 ± 30	141 ± 72*	15 ± 5	31 ± 14†
V2				
Qo+90	208 ± 108	330 ± 157*	48 ± 27	80 ± 34*
Qo+100	109 ± 35	286 ± 109†	25 ± 9	69 ± 22†
Qo+110	91 ± 22	264 ± 85†	21 ± 4	61 ± 16†
Qo+120	96 ± 21	242 ± 87†	21 ± 5	57 ± 17†
Qo+140	106 ± 26	219 ± 99†	24 ± 6	52 ± 20†

Δmax = maximal range.
*P < .05 versus controls.
†P < .01 versus controls.

Table 4 ST segment level (μV) according to the RR interval in Brugada patients

ST level (μV) at	Diurnal period RR600	RR700	RR800	RR900	ANOVA P	Nocturnal period RR800	RR900	RR1000	ANOVA P
V1									
Qo+100	165 ± 127	188 ± 123	173 ± 103	166 ± 101	<.05	173 ± 69	158 ± 70	150 ± 86	.32
Qo+110	174 ± 117	197 ± 122	186 ± 104	178 ± 108	<.05	185 ± 73	183 ± 75	171 ± 82	.15
Qo+120	153 ± 130	180 ± 142	176 ± 125	169 ± 128	<.01	175 ± 98	176 ± 99	167 ± 105	.26
V2									
Qo+100	192 ± 126	232 ± 119	249 ± 116	254 ± 119	<.0001	199 ± 128	201 ± 132	212 ± 156	.67
Qo+110	217 ± 113	255 ± 109	274 ± 112	272 ± 103	<.0001	226 ± 100	235 ± 96	243 ± 106	.29
Qo+120	199 ± 115	239 ± 110	260 ± 114	255 ± 103	<.0001	227 ± 92	238 ± 93	247 ± 97	.09

The boxes highlight the circadian differences in ST segment elevation at identical heart rate (i.e., 800 and 900 RR bins).

Rate dependence of ST segment elevation in Brugada patients

In experimental models of Brugada syndrome, the relationship between the amplitude of phase 1 of the epicardial action potential and the level of the J point/ST segment on the transmural wedge ECG is well demonstrated.[10,19–21] The Ito1 current, which is mainly responsible for phase 1 of the action potential, is characterized by a long recovery from inactivation. Hence, shorter RR intervals are associated with a decrease in Ito1 that in turn induces a decreasing in action potential phase 1 amplitude. Therefore, the findings from Yan et al[10] that either a premature beat or a faster pacing could restore the dome and thus decrease ST elevation in a Brugada wedge model were not surprising. However, the wedge ECG despite numerous similarities is only a surrogate of the human surface ECG, and the role of Ito1 on ST segment elevation on Brugada ECGs has not been fully demonstrated in humans. Our results strongly support this hypothesis since we demonstrated that, as in the transmural wedge ECG, the ST segment elevation recorded in Brugada patients is dependent on heart rate with a decrease in ST level with heart rate acceleration. In addition, our data suggest that this phenomenon is not linear but is more pronounced for RR intervals between 600 and 800 ms. Again these data are in accordance with experimental data showing that heart rate influence on Ito1, and as a consequence on the phase 1 action potential amplitude, is small for RR intervals above 1000 ms.[11,22] To the best of our knowledge, our study is the first to quantify heart rate influences on ST segment elevation in Brugada patients.

Autonomic modulation of ECG pattern

We found a very tenuous, although statistically significant, positive correlation between HFnu and the level of ST segment. This correlation was expected to be stronger. However, HRV parameters illustrate the influence of the ANS on the sinus node. It is well established that the effect of the ANS on the sinus node is not equivalent to its effect on the ventricle.[23] Therefore, HRV parameters in daily conditions may be poor tools to assess autonomic effects on the ventricle. In addition, it has been suggested that the LF component of the HRV frequency domain spectrum (LFnu) could also contain information related to the parasympathetic limb of the ANS. The poor correlation we found might thus be a consequence of our inability to reliably quantify the parasympathetic tone using ECG recordings during daily activities.

Regarding the trend to a lower ST segment elevation at night, a potential hypothesis is represented by the concept of accentuated antagonism proposed by Levy et al.[24,25] The absolute level of acetylcholine might be higher during the day than at night despite a relative predominant vagal tone at night. More specifically, Litovsky and Antzelevitch[26] have demonstrated that, on the canine right ventricle, the effect of acetylcholine on the calcium current was more pronounced in the presence of isoproterenol.[26] Hence, the effect of acetylcholine on the level of ST segment may be related to both an increase in Ito and a decrease in the calcium channel current. The former effect would be more pronounced in adrenergic conditions than at rest or during sleep. We must, however, acknowledge that this argument is speculative.

Clinical implications

Our results have primarily diagnostic consequences. Two-thirds of our Brugada patients had only an intermittent ST segment elevation >200 μV. Therefore, in such patients the risk of a false-negative ECG diagnosis is very high. This risk is further increased if the ECGs are recorded at relatively rapid heart rates (i.e., RR <700 ms). These data emphasize the potential added value of continuous 12-lead ECG recordings compared with 20-second strip ECG recordings. In case of a negative ECG, the diagnosis can be rescued by a sodium channel blocker challenge.[2,3,5,9] However, clinical data suggest that the spontaneous presence of a type 1 ECG pattern may be associated with a higher arrhythmia risk.[3,17] In this regard, Holter ECG may be a useful tool to better characterize this phenotypic trait, to better define a spontaneous Brugada ECG pattern, and thus to possibly help improve the arrhythmia risk stratification in Brugada patients. Further studies are, however, needed to demonstrate such an improvement.

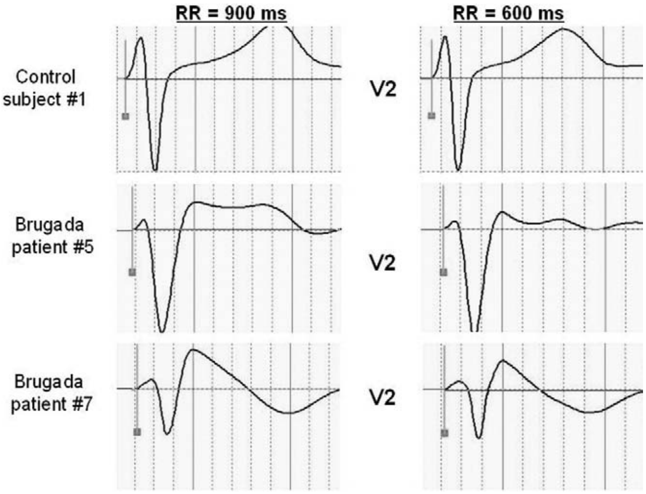

Figure 5 QRS-T morphology at RR = 900 ms (*left panels*) and RR = 600 ms (*right panels*). The templates were obtained after a rate-binning procedure. Upper panels: control subject; middle panels: type 2 Brugada pattern; lower panels: type 1 Brugada pattern.

Study limitations

The number of patients included in our study was relatively small, and we thus cannot exclude a lack of statistical power to demonstrate ECG differences according to the symptomatic status.

The present study was not intended to assess beat-to-beat changes in ST segment level. Such changes might be important in the genesis of arrhythmias in Brugada syndrome. In addition, taking into account the short time constant of parasympathetic effect on heart rate, we cannot exclude that vagal effects on ST level might have been better addressed using a beat-to-beat approach.

Finally, the genotype of each of our patients was not known. We cannot exclude a gene-specific ST segment behavior.

Conclusion

In accordance with experimental Brugada models, our clinical data showed that spontaneous ECG changes observed in Brugada patients are related in part to heart rate influences on the ST segment level. These spontaneous fluctuations suggest that Holter recordings may improve the ECG diagnosis sensitivity in Brugada syndrome.

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