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Relation Between Heart Rate Variability and Spontaneous and Induced Ventricular Arrhythmias in Patients With Coronary Artery Disease

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Objectives. **The aim of this study was to determine the relation between autonomic control of heart rate and the spontaneous occurrence and inducibility of ventricular arrhythmias in patients with coronary artery disease.**

Background. **Low heart rate variability increases the risk of arrhythmic events. It is not known whether impaired autonomic heart rate control reflects alterations in functional factors that contribute to the initiation of spontaneous arrhythmias or whether it is the consequence of an anatomic substrate for reentrant tachyarrhythmias.**

Methods. **Fifty-four patients with coronary artery disease with a history of sustained ventricular tachycardia (n = 25) or cardiac arrest (n = 29) were studied by 24-h ambulatory electrocardiographic recording and by programmed electrical stimulation. Heart rate variability was compared among the patients with and without spontaneous ventricular arrhythmias and with and without inducibility of sustained ventricular tachyarrhythmias.**

Results. **Eight patients had a total of 21 episodes of sustained ventricular tachycardia on Holter recordings. Standard deviation of RR intervals and low frequency and very low frequency components of heart rate variability were significantly blunted in patients with sustained ventricular tachycardias compared with those without repetitive ventricular ectopic activity ($p < 0.05$, $p < 0.01$ and $p < 0.05$, respectively). However, no significant alterations were observed in heart rate variability before the onset of 21 episodes of sustained ventricular tachycardia. Heart rate variability did not differ between the patients with or without nonsustained episodes of ventricular tachycardia. In patients with frequent ventricular ectopic activity, low frequency and very low frequency power components were significantly blunted compared with those with infrequent ventricular ectopic activity ($p < 0.01$ and $p < 0.001$, respectively). Heart rate variability did not differ significantly between the patients with and without inducible sustained ventricular tachyarrhythmias.**

Conclusions. **Impaired very low and low frequency oscillation of heart rate reflects susceptibility to the spontaneous occurrence of ventricular arrhythmias but may not reflect the instantaneous triggers for life-threatening arrhythmias or a specific marker of the arrhythmic substrate for ventricular tachyarrhythmias.**

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Power spectral analysis of heart rate variability has the potential to quantify the activity and changes in cardiac autonomic function (1–3). Previous studies have shown that blunting of both total heart rate variability and measures of various frequency domain components of heart rate variability indicate an increased risk of arrhythmic events after myocardial infarction (4–6) and that spontaneous episodes of sustained ventricular tachycardia are preceded by low heart rate variability analyzed in the frequency domain (7).

There may be several mechanisms that can explain the association between low heart rate variability and the risk for life-threatening arrhythmias. One hypothesis is that low heart rate variability reflects the presence of other factors, such as left ventricular dysfunction or ventricular denervation, that can serve as a substrate for life-threatening arrhythmias. Another theory is that low heart rate variability actively participates in the pathophysiologic process, leading to the onset of arrhyhmias. The purpose of this research was to test these hypotheses in patients with coronary artery disease with a history of life-threatening arrhythmias by comparing the frequency-domain measures of heart rate variability in patients with and without spontaneous ventricular arrhythmias and in those with and without inducibility of sustained ventricular tachyarrhythmias during programmed electrical stimulation.

Methods

Patients. The study included 54 consecutive patients with coronary artery disease who were admitted to the Oulu University Central Hospital (49 patients) and University of

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Table 1. Clinical Characteristics of 54 Study Patients

Age (yr)	61 ± 8
Gender (F/M)	6/48
Clinical arrhythmia	
Sustained VT	25 (46%)
Cardiac arrest	29 (54%)
NYHA functional class	
I	7 (13%)
II	27 (50%)
III	17 (31%)
IV	3 (6%)
Previous MI	
Anterior	23 (43%)
Inferior	9 (17%)
≥2 MI	12 (22%)
No MI	10 (19%)
Ejection fraction (%)	44 ± 13
Angiographic data (n = 47)	
1-vessel disease	17 (36%)
2-vessel disease	16 (34%)
3-vessel disease	14 (30%)
Cardiac medication	
Digitalis	21 (39%)
Diuretic	18 (33%)
Beta-blocker	30 (56%)
Calcium antagonist	6 (11%)
ACE inhibitor	6 (11%)

Data presented are mean value ± SD or number (%) of patients. ACE = angiotensin-converting enzyme; F = female; M = male; MI = myocardial infarction; NYHA = New York Heart Association; VT = ventricular tachycardia.

Miami Medical Center (5 patients) because of life-threatening ventricular arrhythmias. Twenty-five patients had documented episodes of sustained ventricular tachycardia, and 29 had been resuscitated from cardiac arrest. All patients had clinical or angiographic evidence of coronary artery disease. Forty-four patients (81%) had a history of previous myocardial infarction. None of the patients had an acute myocardial infarction. The clinical characteristics are presented in Table 1. The patients provided informed consent for the studies.

Electrophysiologic and angiographic studies. Fifty-one patients underwent electrophysiologic testing, which included incremental ventricular pacing and programmed ventricular stimulation using up to three extrastimuli and two basic drive cycle lengths (600 and 400 ms) from the right ventricular apex and outflow tract. Induced ventricular tachyarrhythmias were defined as described previously (8). Left-sided catheterization was performed by the Judkins technique. Left ventricular cineangiograms were recorded in the 45° anterior oblique projection and calculated by the biplane area–length method.

Holter recordings. All patients underwent 24-h ambulatory electrocardiographic (ECG) recordings. The Delmar Avionics electroscanner was used for analysis of tape recordings. For the detection and quantification of arrhythmias, a two-channel oscilloscopic display and an arrhythmia analyzer were used. In addition, all tapes were scanned manually by an experienced observer, and all areas of questionable accuracy were verified by direct printout. All recordings were made with two-channel tape recorders and two bipolar leads. Ventricular extrasystoles were identified on the basis of the width of the QRS complex and prematurity of the QRS complex of at least 30%. Ventricular tachycardia was defined as nonsustained if it lasted >4 beats but <30 s and as sustained when its duration was >30 s. The patients were classified into three groups according to the number of premature ventricular beats: infrequent (0 to 9/h), moderate (10 to 29/h) and frequent (≥30/h).

Analysis of heart rate variability. The ECG data were digitally sampled and transferred from the Delmar Avionics scanner to a microcomputer for analysis of heart rate variability. The details of the analysis of frequency domain measures of heart rate variability have been described previously (7). A linear detrend was applied to the RR interval data segments of 512 samples to make the data more stationary. This was implemented by first fitting a straight line to a segment by a standard least-squares method and then subtracting it from the sample values. The RR interval series was passed through a filter that eliminates unwanted premature beats and noise and fills the resulting gaps with an average computed in the local neighborhood. An RR interval is interpreted as a premature beat if it deviates from the previous qualified interval value by more than a given tolerance (e.g., 30%), which is a programmable variable depending on the prematurity index of ectopic beats in each patient. With this filtering technique, abrupt temporary changes in RR interval sequence representing noise or ectopic beats were removed, and a more stationary data set was available for analysis. In addition, the RR intervals were reviewed on the computer display by an experienced observer, and the questionable portions were compared with the printouts of the Holter ECG recordings. Only those RR intervals related to normal sinus beats in a stationary state were included in the final analysis, and only those segments with >85% of qualified beats.

An autoregressive model was used to estimate the power spectral densities of the RR interval variability (9). The size of 10 was used for the model order in the analysis of the RR data. The computer program automatically calculates the autoregressive coefficients to define the power spectral density. Power spectra were quantified by measuring the area in four bands: total power <0.40 Hz, high frequency power from 0.15 to 0.40 Hz, low frequency power from 0.04 to 0.15 Hz and very low frequency power from 0.005 to 0.04 Hz.

Statistical methods. Analysis of variance was used first to compare the groups defined according to the number of premature ventricular beats and the three groups defined according to repetitive ventricular activity, followed by Scheffé tests and the *t* test for equality of mean values. Analysis of variance followed by the *t* test was also used to compare the groups with and without inducibility to ventricular tachycardia during programmed electrical stimulation. Because of the skewness of distribution of the frequency-domain measures, log transformation was used to produce a normal distribution before the statistical analyses were performed. Analysis of variance for repeated measurements was used to estimate the

Table 2. Heart Rate Variability in Relation to Ventricular Ectopic Activity

	0–9 VPBs/h (n = 32)	10–29 VPBs/h (n = 5)	≥30 VPBs/h (n = 17)
Total power (ms^2)	1,958 ± 2,262	1,890 ± 1,586	939 ± 1,257
ln total power	8.1 ± 0.8	8.0 ± 4.0	7.4 ± 0.9*
VLF (ms^2)	1,365 ± 1,577	1,300 ± 1,091	496 ± 664
ln VLF	6.7 ± 1.0	6.6 ± 1.3	5.5 ± 1.4†
LF (ms^2)	316 ± 305	300 ± 390	213 ± 330
ln LF	5.4 ± 1.0	5.3 ± 1.3	4.6 ± 1.2*
HF (ms^2)	277 ± 331	290 ± 343	230 ± 305
ln HF	5.2 ± 1.0	5.2 ± 1.0	4.9 ± 0.8
RRI (ms)	962 ± 167	887 ± 152	844 ± 130*
SD of RRI (ms)	61 ± 23	55 ± 34	45 ± 21*

*$p < 0.01$, †$p < 0.001$ between groups with ≥30 and 0 to 9 ventricular premature beats (VPBs)/h. Data presented are mean value ± SD. HF (LF) = high (low) frequency power; SD of RRI = standard deviation of RR intervals; VLF = very low frequency power.

trends in heart rate variability variables before the onset of sustained ventricular tachycardia episodes. Linear stepwise multiple regression analysis was performed to assess the independent values of different component variables for predicting the occurrence of sustained ventricular tachycardia or frequent ectopic beats, respectively.

Results

Patients. Sustained ventricular tachycardia (≥30 s) was the clinical arrhythmic event in 25 patients (46%) and cardiac arrest in 29 patients (54%) (Table 1). Most patients had a history of previous myocardial infarction (81%). The average heart rate and frequency domain measures of heart rate variability did not differ between the patients with clinical sustained ventricular tachycardia and those with cardiac arrest.

Frequency domain measures of heart rate variability and occurrence of premature beats. Standard deviation of RR intervals, total power, low frequency power and very low frequency power were significantly lower in the patients with frequent premature ventricular beats than in those with infrequent ventricular events ($p < 0.01$, $p < 0.01$, $p < 0.01$ and $p < 0.001$, respectively) (Table 2, Fig. 1). After exclusion of patients with sustained ventricular tachycardias from the group of frequent ventricular premature beats, the very low frequency power was still significantly blunted in this group compared with patients with infrequent premature beats ($p < 0.01$). Heart rate was also significantly higher in the patients with frequent premature ventricular beats ($p < 0.001$), but ejection fraction or angiographic severity of coronary artery disease did not differ between the groups. In multiple regression analysis, including age, medication, ejection fraction, New York Heart Association functional class, location of myocardial infarction, standard deviation of RR intervals and frequency domain measures of heart rate variability, the very low frequency power of heart rate variability was the only significant predictor of frequent premature ventricular impulses ($p < 0.01$).

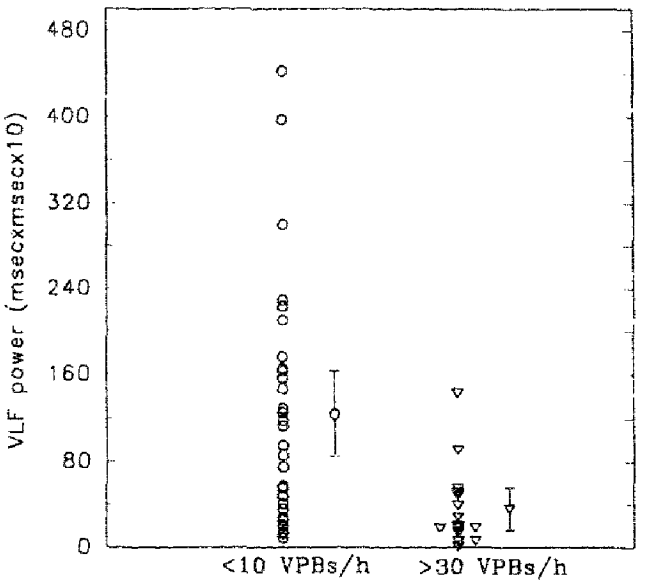

Figure 1. Very low frequency (VLF) power of heart rate variability in patients with infrequent (**circles**) and frequent (**triangles**) ventricular premature beats (VPBs). **Vertical bars** = 95% confidence intervals of the mean values.

Frequency domain measures of heart rate variability and occurrence of ventricular tachycardia. Standard deviation of RR intervals and the low frequency and very low frequency components of heart rate variability were significantly lower in the eight patients with sustained ventricular tachycardia than in those without repetitive ventricular ectopic beats ($p < 0.05$, $p < 0.01$ and $p < 0.05$, respectively) (Fig. 2, Table 3). Ejection fraction and angiographic severity did not differ between these

Figure 2. Low frequency (LF) power of heart rate variability in patients with (**solid circles**) and without (**open circles**) spontaneous sustained ventricular tachycardia (VT). **Vertical bars** = 95% confidence intervals of the mean values.

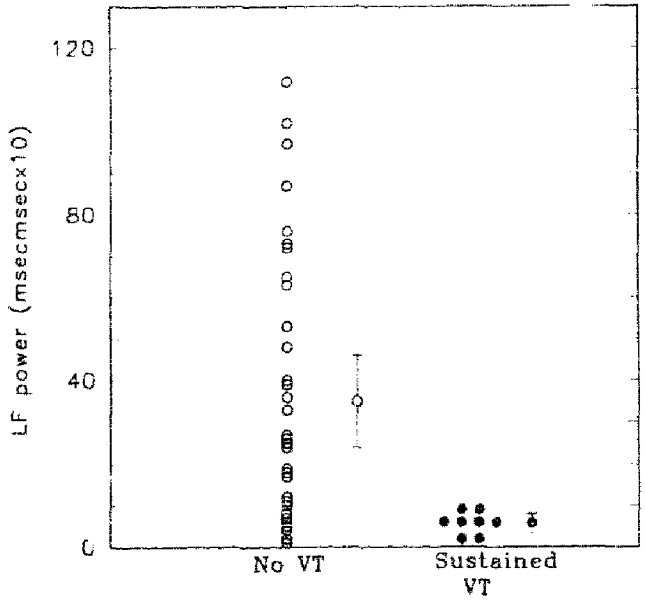

Table 3. Heart Rate Variability in Relation to Spontaneous Ventricular Tachycardia

	No VT (n = 38)	Nonsustained VT (n = 8)	Sustained VT (n = 8)
Total power (ms^2)	1,910 ± 2,237	1,830 ± 1,177	408 ± 276
ln total power	8.0 ± 0.9	7.9 ± 1.1	7.2 ± 0.5*
VLF (ms^2)	1,272 ± 1,490	1,280 ± 1,132	217 ± 147
ln VLF	6.5 ± 1.3	6.5 ± 1.3	5.2 ± 0.7*
LF (ms^2)	341 ± 334	330 ± 343	55 ± 26
ln LF	5.4 ± 1.1	4.9 ± 1.4	3.9 ± 0.6†
HF (ms^2)	297 ± 349	220 ± 298	136 ± 130
ln HF	5.2 ± 0.9	4.8 ± 0.9	4.7 ± 0.8
RRI (ms)	935 ± 174	914 ± 146	818 ± 70
SD of RRI (ms)	60 ± 23	58 ± 25	42 ± 13*

*$p < 0.05$, †$p < 0.01$ between groups with sustained and no ventricular tachycardia (VT). Data presented are mean value ± SD. Abbreviations as in Table 2.

groups. Frequency domain measures of heart rate variability did not differ between patients with nonsustained ventricular tachycardia and those without ventricular tachycardia. In multiple regression analysis, including age, medication, ejection fraction, functional class, location of myocardial infarction, severity of coronary artery disease and measures of heart rate variability, the low frequency power was the strongest predictor of the occurrence of sustained ventricular tachycardia ($p < 0.0001$). Figures 3 and 4 show examples of spectral analysis of heart rate variability in two patients with and without spontaneous ventricular arrhythmias during 24-h ECG recording.

Dynamics of heart rate variability before onset of sustained ventricular tachycardia. Changes in heart rate variability were analyzed in 1-h, 15-min and 5-min periods before the spontaneous onset of 21 sustained ventricular tachycardias in eight patients. The mean rate of the ventricular tachycardias was 189 ± 24 beats/min, and the length 279 ± 163 beats. No significant trends or alterations were observed in the measures of heart rate variability before these arrhythmic episodes, but the average heart rate was higher in the 5-min period before the onset of sustained ventricular tachycardia than 5 to 10 min and 10 to 15 min before the arrhythmic episode ($p < 0.01$) (Table 4).

Frequency domain measures of heart rate variability and inducibility to ventricular tachycardia during programmed electrical stimulation. Sustained ventricular tachycardia was induced in 30 (59%) of 51 patients and ventricular fibrillation in 5 patients (10%) during programmed electrical stimulation (Table 5). No significant correlations were found in the frequency domain measures of heart rate variability between patients with inducibility to sustained ventricular tachycardia or ventricular fibrillation compared with those without inducible arrhythmias or with inducible nonsustained ventricular tachycardia during programmed electrical stimulation. However, high frequency power was significantly lower in patients with induced ventricular fibrillation than in those with induced sustained ventricular tachycardia ($p < 0.02$) (Table 6).

Discussion

Heart rate variability and occurrence of spontaneous ventricular arrhythmias. The very low frequency and low frequency powers of heart rate variability were predictors of the occurrence of frequent ventricular premature beats and sustained ventricular tachycardia in this study. Standard deviation of RR intervals was also lower in patients with episodes of

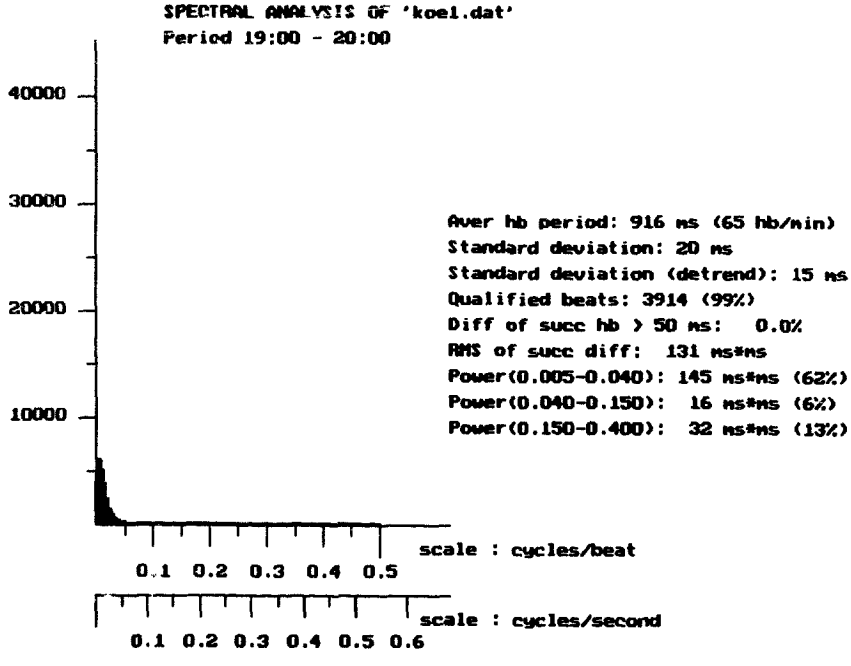

Figure 3. Power spectral analysis of heart rate variability in a patient with several spontaneous episodes of sustained ventricular tachycardia during 24-h electrocardiographic recording and who had inducible sustained ventricular tachycardia. Aver hb = average heartbeat; Diff, diff = difference; koe1.dat = patient code; hb = heart beat; RMS = root-mean-square; succ = successive.

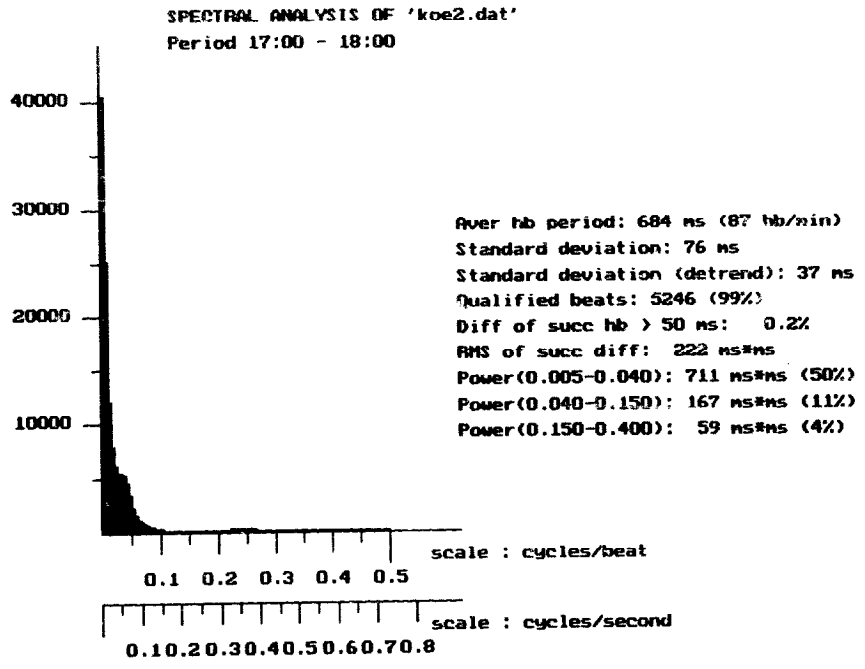

Figure 4. Power spectral analysis of heart rate variability in a patient with only occasional premature ventricular beats during 24-h electrocardiographic recording and who had inducible sustained ventricular tachycardia. Abbreviations as in Figure 3.

sustained ventricular tachycardia and frequent ectopic beats, but in multiple regression analysis the very low and low frequency power of heart rate variability were stronger predictors of arrhythmic susceptibility than the time domain measures of heart rate variability. We also previously showed (7) that sustained ventricular tachycardia episodes are preceded by reduced low frequency components of heart rate variability. A retrospective analysis of heart rate variability in postinfarction patients has demonstrated that very low frequency power is the strongest predictor of arrhythmic death (6). These findings imply that impaired very low and low frequency oscillations of heart rate are strongly related to a risk for spontaneous arrhythmic events.

A recent study (10) reported that spontaneous episodes of ventricular fibrillation are not preceded by low measures of heart rate variability analyzed in the time domain. In the present series of patients with coronary artery disease with documented episodes of life-threatening arrhythmias, an impaired low frequency component of heart rate variability was the strongest predictor of the occurrence of sustained ventricular tachycardia. However, no significant trends or alterations were observed immediately before the onset of sustained ventricular tachycardia episodes, suggesting that impaired autonomic control may not be directly related to the process that initiates the tachyarrhythmias. In our previous study (7), total heart rate variability was reduced in the hour preceding the

Table 4. Heart Rate Variability Before Onset of 21 Spontaneous Episodes of Sustained Ventricular Tachycardia

	RRI (ms)	SD of RRI (ms)	VLF (ln ms^2)	LF (ln ms^2)	HF (ln ms^2)	LF/HF Ratio
Hours before VT (n = 14)						
5–4	854 ± 137	44 ± 20	5.7 ± 1.1	4.2 ± 1.1	4.7 ± 1.0	0.9 ± 1.0
4–3	842 ± 135	42 ± 25	5.5 ± 1.4	4.1 ± 1.3	4.5 ± 1.0	0.9 ± 1.0
3–2	833 ± 113	41 ± 24	5.5 ± 1.4	3.9 ± 1.4	4.3 ± 0.9	0.9 ± 1.0
2–1	818 ± 124	36 ± 22	5.3 ± 1.3	4.0 ± 1.4	4.5 ± 1.1	0.9 ± 1.2
1–0	830 ± 125	41 ± 25	5.2 ± 1.5	3.7 ± 1.8	4.7 ± 1.0	0.8 ± 1.3
15-min periods before VT (n = 18)						
60–45	809 ± 88	31 ± 23	4.9 ± 1.5	3.9 ± 1.3	4.6 ± 1.2	0.8 ± 0.6
45–30	812 ± 112	30 ± 13	5.2 ± 1.3	4.0 ± 1.4	4.7 ± 1.1	0.9 ± 0.7
30–15	809 ± 116	29 ± 13	5.0 ± 1.4	3.9 ± 1.6	4.8 ± 1.0	0.8 ± 1.2
15–0	790 ± 117	41 ± 23	5.4 ± 1.3	4.1 ± 1.3	4.6 ± 1.2	0.9 ± 0.7
5-min periods before VT (n = 21)						
15–10	784 ± 73	22 ± 10	4.7 ± 1.1	3.4 ± 1.4	4.4 ± 1.1	0.8 ± 1.3
10–5	775 ± 72	25 ± 15	4.8 ± 1.2	3.5 ± 1.1	4.4 ± 1.0	0.8 ± 1.2
5–0	756 ± 67*	27 ± 13	4.7 ± 1.5	3.6 ± 1.0	4.5 ± 0.9	0.8 ± 1.5

*$p < 0.01$ in RR interval with repeated measures analysis of variance. Data presented are mean value ± SD. Abbreviations as in Table 2.

Table 5. Type and Mode of Induction of Sustained Ventricular Tachyarrhythmias During Programmed Electrical Stimulation in 35 Patients

	Monomorphic VT (n = 27)	Polymorphic VT (n = 3)	VF (n = 5)
No. of extrastimuli			
1	2	0	0
2	10	2	0
3	15	1	5
Mean (±SD) VT rate (ms)	350 ± 53	287 ± 25	

VF = ventricular fibrillation; VT = ventricular tachycardia.

onset of sustained ventricular tachycardia, and a substantial increase in the low frequency/high frequency ratio was observed before the onset of ventricular tachycardia episodes. In the present study, which included a larger number of sustained ventricular tachycardia episodes, these observations could not be confirmed. The increase in total heart rate variability and low frequency/high frequency ratio seem to be more evident before nonsustained than sustained ventricular tachycardia episodes (7,11,12), and reduced heart rate variability is a more specific finding in the hours preceding sustained ventricular tachycardia episodes (7). It is not known at what time the dynamics of heart rate variability change before the onset of sustained ventricular tachycardia. It was not possible to record long time periods before the occurrence of spontaneous ventricular tachycardia episodes in this study. Therefore, it remains uncertain whether there exists a temporal relation between low heart rate variability and onset of sustained ventricular tachycardia episodes or whether low heart rate variability is a marker of susceptibility to sustained ventricular tachycardias only.

Heart rate variability and inducibility during programmed electrical stimulation. Many clinical variables can predict the inducibility of sustained ventricular arrhythmias during programmed electrical stimulation, including male gender (13–15), history of previous myocardial infarction with or without myocardial aneurysm (14), documentation of ventricular tachycardia at the time of cardiac arrest (15), intraventricular conduction delay (14) and the signal-averaged ECG (16–20). In our study, none of the components of frequency-domain measures of heart rate variability could predict the inducibility to sustained ventricular arrhythmias.

Table 6. Heart Rate Variability in Relation to Inducibility of Ventricular Tachyarrhythmias in 51 Patients

	Inducibility During PES			
	No VT (n = 11)	Nonsustained VT (n = 5)	Sustained VT (n = 30)	VF (n = 5)
Total power (ln ms²)	8.3 ± 0.8	8.2 ± 0.9	7.9 ± 0.7	7.6 ± 1.9
VLF (ln ms²)	6.7 ± 1.1	6.4 ± 1.4	6.4 ± 1.4	6.2 ± 1.0
LF (ln ms²)	5.5 ± 1.4	5.4 ± 1.3	5.2 ± 1.1	4.2 ± 1.2
HF (ln ms²)	5.2 ± 0.8	5.5 ± 1.3	5.2 ± 0.9	4.2 ± 0.6*
RRI (ms)	1,012 ± 126	918 ± 115	921 ± 178	833 ± 100*
SD of RRI (ms)	69 ± 25	65 ± 31	55 ± 21	54 ± 20

*$p < 0.02$ between groups with sustained ventricular tachycardia (VT) and ventricular fibrillation (VF) in the high frequency power (HF) component and between the groups with ventricular fibrillation and no inducibility in RR interval measures. Data presented are mean value ± SD. PES = programmed electrical stimulation; other abbreviations as in Table 2.

Patients with inducible ventricular fibrillation had lower high frequency power and a higher basal heart rate than those with inducible sustained ventricular tachycardia, suggesting impaired vagal or increased sympathetic, or both, tone in patients with inducible ventricular fibrillation. We previously showed (8) that beta-adrenergic blocking agents can suppress the inducibility of fast, unstable ventricular tachyarrhythmias in patients with a high basal heart rate (8). In addition to antiadrenergic properties, beta-blockers may also enhance vagal tone, which can protect the patient from the inducibility of ventricular fibrillation (21,22). However, the number of patients with inducible ventricular fibrillation in the present series was too small to make firm conclusions in this respect.

Possible arrhythmogenic mechanisms of low heart rate variability. Impaired very low frequency and low frequency components, but not the high frequency power, of heart rate variability were strongly associated with the occurrence of spontaneous arrhythmias. Atropine abolishes all frequency-domain components almost completely (23), suggesting that vagal efferent activity is also a significant modulating factor for the very low and low frequency components of heart rate variability. However, the afferent limb or stimulus to the high frequency components is different because high frequency oscillation is related to respiration and is mediated primarily by pulmonary afferent stimuli (24). The afferent stimuli of lower frequency components may arise from the large vessels and the ventricles of the heart. These differences in sensory input may explain the relative importance of different frequency-domain components for the risk of arrhythmic episodes.

Methodologic considerations. Ventricular ectopic beats may potentially invalidate measurements of heart rate variability in the frequency domain. Ventricular premature beats were carefully excluded from the analysis of heart rate variability and replaced by an average of neighborhood RR intervals. In our experiments (7), eliminating randomly different numbers of RR intervals has allowed reliable measurements of spectral components of heart rate variability to be achieved by this technique (<5% error) if <15% of impulses are excluded from the analysis. Therefore, only those segments with >85% of qualified beats were included in the analysis, which eliminates the significant effects of the density of ectopic beats on the results.

The spectral components of heart rate variability did not change significantly, but heart rate had a tendency to increase before the onset of spontaneous episodes of sustained ventricular tachycardia. This might implicate sympathetic activation as a trigger of sustained arrhythmic episodes. Power spectral components of heart rate variability may not be accurate measures of temporal changes in sympathetic activity. Further-

more, heart rate variability reflects autonomic modulation at the sinus node level but not at the ventricular level. Therefore, unaltered measures of heart rate variability do not exclude the significance of autonomic fluctuation, especially adrenergic inluences, as a triggering or contributing factor for spontaneous life-threatening arrhythmias.

Clinical implications. The results of this study imply a functional relation between abnormal autonomic control of heart rate and the spontaneous occurrence of ventricular arrhythmias. However, further research will be needed to confirm these observations in larger groups of patients with different risks of ventricular arrhythmias. The pathophysiology of the reduction in very low and low frequency oscillations of heart rate and their significance in arrhythmogenesis also warrants further research.

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