Effects of Postectopic Heart Rate Turbulence on Measures of Heart Rate Variability in Patients after an Acute Myocardial Infarction

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Background: Heart rate (HR) turbulence lasting up to 15 beats after ventricular premature beats (VPBs) may have profound effects on HR variability measures. Aim of this study was to examine the effects of HR turbulence on HR variability measures.

Methods: We developed an algorithm, which deletes 15 consecutive RR intervals after VPBs and examined the effects of the HR turbulence removal on the HR variability measures in patients after an acute myocardial infarction (AMI). Two hundred and sixty seven patients with left ventricular ejection fraction (LVEF) ≤ 0.40 and occurrence of VPBs were included in the study. Differences (%) between original HR data and HR turbulence edited data were compared.

Results: HR turbulence editing had variable effects on different HR variability indexes. Ultra low (ULF) and very low frequency (VLF) spectral components were mostly affected by the HR turbulence removal. Both ULF and VLF decreased significantly both at baseline Holter recordings (ULF: $P = 0.006$, VLF: $P = 0.031$) and at 6 weeks from AMI (ULF: $P < 0.001$, VLF: $P = 0.001$). The number of VPBs had a marked influence on results, e.g., when the number of VPBs exceeded the highest decile (≈ 50 VPBs/hour), the ULF and VLF spectral component were $>30\%$ lower after removal of turbulence. In addition, the prediction of arrhythmic events by ULF component improved after turbulence removal (AUC: $0.69 \rightarrow 0.74$).

Conclusions: HR turbulence affects HR variability measures, especially the ULF and VLF spectral components. Editing of the HR turbulence should be considered when HR variability is measured from Holter recordings.

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Analysis of heart rate (HR) variability has been widely considered as a tool for evaluating the cardiac autonomic regulation from 24-hour ambulatory ECG recordings.^{1–6} Previous studies have shown the importance of the careful artifact editing of the RR interval time series to obtain more reliable results in the HR variability analysis.^{6,7} Frequent ectopic beats are the potential source of errors in the analysis of HR variability, especially in the power spectrum analysis of the HR time series.⁸

HR turbulence analysis is a method that quantifies the short-term RR interval oscillation instantly followed by a single ventricular premature beat (VPB).⁹ In the HR turbulence analysis, the presence of the VPBs is essential when analyzing the changes in the autonomic regulation. However, despite the presence of the turbulence behavior of the RR intervals followed the VPB, it has not been verified that the turbulence oscillation of the RR intervals does not produce bias into the other conventional

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Table 1. Characteristics of the Patients (n = 267)

Age (years)	64±11
Male gender	208 (78%)
Prior MI	100 (37%)
Prior CHF	20 (7%)
Diabetes	52 (19%)
Hypertension	118 (44%)
Beta-blocker	246 (92%)
ACE-inhibitor/AT blocker	227 (85%)
Statin	214 (80%)
Antiplatelet agent	246 (92%)
Ejection fraction (%)	33 ± 6

Values are reported as n patients (% of population) or as means ± SD; Abbreviations: ACE = angiotensin converting enzyme; AMI = acute; myocardial infarction; AT = angiotensin; CHF = congestive heart failure.

time and frequency domain and nonlinear HR variability analysis.

The aim of the present study was to develop an algorithm to diminish the effects of the turbulence behavior of the RR intervals on the HR variability analysis and to examine the effects of the HR turbulence exclusion on the different HR variability parameters. In addition, aim of the present study was to assess the possible significance of the HR turbulence editing algorithm in the risk evaluation of arrhythmic events in the population of patients with acute myocardial infarction (AMI) who had impaired left ventricular ejection fraction (LVEF ≤ 0.40) (CARISMA study).

STUDY POPULATION AND METHODS

Study population was collected from a Multicenter study including 10 European centers where a total of 5869 AMI patients were screened in the acute phase of AMI during 2–7 days after the event. Of these an impaired left ventricular function (LVEF ≤ 0.40) was defined in 1393 patients. After exclusions, the total number of patients who were included in the study was 267. The characteristics of the patient population are shown in Table 1. All participating patients in the study had an impaired LVEF (≤0.40) and in their ECG recording had an occurrence of VPBs.

Reasons to exclude the patients from the study analysis were mainly the refusal of the patient or inability of the patient to participate in the study due to other serious illness, coronary bypass graft surgery or death before the implantation of loop-recorder. Other reasons to exclusion were

pregnancy, life expectancy <1 year for noncardiac cause. In addition, the exclusion of the patient from the study was done due the lack of VPBs or ECG recording failure. The inclusion and exclusion criteria are described in more detail in the previous study.¹⁰ Study patients were followed-up for 24 months and arrhythmic events were documented with an ECG loop-recorder that was implanted between 5 and 21 days after the AMI. Clinical follow-up was done in every three months during the two-year time period.

Fatal or near-fatal cardiac arrhythmia was the primary end point of this study. Arrhythmic events containing resuscitated cardiac arrest due to primary arrhythmia, symptomatic sustained ventricular tachycardia (VT), or arrhythmic death were obliged to be documented with the implanted loop-recorder, implanted cardioverter-defibrillator (ICD), pacemaker, Holter recording or with the telemetry slip. Programming of the implantable loop recorder has been previously described in details.¹⁰

Description of the Methods in Heart Rate Signal Processing

Holter Recordings and HR Signal Processing

Recordings of the 24-hour ambulatory 2- or 3-channel ECG were performed twice for study patients. The first, baseline ECG recording was performed instantly after the AMI, during 5 to 21 days and the second ECG recording was obtained after six weeks from the AMI.

For the processing of the ECG recordings, an Oxford Excel Holter system (Oxford Instruments, Abingdon, Oxfordshire, United Kingdom) was used. 24-hour ECG recordings were examined by an experienced technician and an individual classification of the QRS complexes was performed. QRS complexes were classified into different beat classes, such as normal sinus beats, VPBs, and supraventricular ectopic beats. Single VPBs were carefully verified and marked with a label. Next, the 24-hour RR interval time series containing labeled VPBs were obtained from the ECG recordings. 24-hour RR interval time series that could be HR variability analyzed were successfully obtained on 267 patients of which 237 patients at baseline phase and 220 patients after 6 weeks from the AMI. Discard or failure of the RR interval time series for the HR variability analysis was mainly due to appearance of large amount of

disturbances (>20% of RR intervals). Disturbances were, for instance, long episodes of atrial fibrillation (FA) or bigeminy or a large number of frequent ectopic beats.

HR Turbulence Editing Algorithm

VPBs are shown to be often followed by RR interval fluctuation including a pattern that starts with an acceleration of the sinus rhythm immediately after the VPB and lasts few RR intervals. After the acceleration, a gradual deceleration of the RR intervals takes part and usually lasts up to tenth to fifteenth cycle after a VPB. This type of RR interval fluctuation after a single VPB has been previously described with the HR turbulence method.⁹

In the present study the RR interval oscillation after every single VPB, determined as HR turbulence, was excluded from the HR variability analysis. Each verified and labeled single VPB and fifteen RR intervals immediately after each verified and labeled single VPB were edited with the deletion method. Other possible episodes of disturbances were also removed so that analyzed data included only RR intervals of pure sinus beats and verified single VPBs. Deletion method was used instead of different interpolation methods to avoid the production of the false trends into RR interval time series due to long segment of RR intervals in the HR turbulence phenomenon (VPB + turbulence = 17 RR intervals).

HR Variability Analysis

After the removal of the HR turbulence, HR variability analysis was performed including analysis in the time and frequency domain and in addition a short-term detrended fluctuation analysis (DFA). These kinds of HR variability measures were chosen, as they have shown to possess the most powerful prognostic power in post-AMI populations. Time domain HR variability analysis contained the computation of the standard deviation of normal-to-normal RR intervals (SDNN). In the frequency domain, high (HF, 0.15–0.4 Hz) and low frequency (LF, 0.04–0.15 Hz) components of the HR variability power spectrum were estimated with the fast Fourier transform (FFT) method over a blocks of 512 RR intervals. In addition, in the spectrum analysis also very low (VLF, 0.005–0.04 Hz) and ultra low (>0.0033 Hz) frequency components were computed with Fourier transform method on the

entire HR time series. Frequency domain HR variability analysis provides information about the HR behavior related to specific frequencies. Spectral HR variability analysis can produce detailed view of the cardiac autonomic modulation and can be used as a predictor of mortality in AMI patients.¹¹ DFA concerned the computation of the fractal scaling exponent (α_1) for the short-term HR variability. Fractal scaling analysis has shown to have promising results as a predictor of mortality in AMI patients.^{12,13} The details of the DFA method have been described elsewhere.¹⁴

Statistical Analysis

Statistical analysis of the data was performed with the PASW Statistics software (PASW 18.0.1, SPSS Inc., Chicago, IL, USA). First, the effects of the HR turbulence editing were examined by computing the percentage differences between the HR variability results of the original (VPBs and other disturbances were edited) and HR turbulence edited (VPBs + 15 RR intervals and other disturbances were edited) RR interval time series. In addition, paired two-sample *t*-test was performed to analyze the differences of the HR variability results of the original and HR turbulence edited data. A values of $P < 0.05$ was considered statistically significant.

Next, the result data was split into deciles according to the amount of the VPBs. The percentage differences of the HR variability parameters between original and HR turbulence edited data were computed in every decile to examine the effects of the VPB amount in the HR turbulence removal process.

Lastly, the effects of the HR turbulence removal in the risk evaluation of the arrhythmic events were analyzed. The receiver operating characteristic curve (ROC) was graphed and the area under the curve (AUC) was computed for the HR variability analysis results with primary end point for normally edited and HR turbulence edited RR-interval time series.

RESULTS

Effects of the HR Turbulence Removal on the HR Variability Measures

First, the mean effects of the HR turbulence removal on the HR variability analysis were examined in the whole data. The absolute values of the

Table 2. Absolute Values and Percentage Differences of HR Variability Measures between Original and HR Turbulence Edited Data

	ULF (ms ²)	VLF (ms ²)	SDNN (ms)	α_1	LF (ms ²)	HF (ms ²)
Original						
Baseline	7304 ± 6000	856 ± 767	94 ± 32	1.12 ± 0.24	313 ± 328	205 ± 292
6 weeks	8737 ± 5698	1172 ± 920	111 ± 35	1.16 ± 0.23	508 ± 624	328 ± 526
HR turbulence edited						
Baseline	7102 ± 5936	842 ± 748	94 ± 33	1.13 ± 0.24	314 ± 330	203 ± 290
6 weeks	8279 ± 5558	1125 ± 920	111 ± 35	1.17 ± 0.22	504 ± 619	318 ± 514
Percentage difference (%)						
baseline	4.3 ± 1.8 P = 0.006	3.9 ± 1.7 P = 0.031	0.9 ± 0.0 P = 0.420	1.6 ± 1.5 P < 0.001	2.2 ± 2.2 P = 0.119	2.7 ± 1.9 P = 0.206
6 weeks	6.8 ± 5.3 P < 0.001	5.6 ± 3.3 P = 0.001	1.1 ± 0.8 P = 0.107	1.7 ± 1.5 P < 0.001	4.1 ± 3.1 P = 0.591	3.8 ± 3.1 P = 0.263

Absolute HR variability values are reported as mean ± standard deviation and percentage differences (%) are reported as mean ± interquartile range. Abbreviations: ULF = ultra low frequency power; VLF = very low frequency power; SDNN = standard deviation of normal-to-normal RR interval; α_1 = short term fractal scaling exponent of the detrended fluctuation analysis; LF = low frequency power; HF = high frequency power.

HR variability measures with standard deviation and the percentage differences with interquartile range between the HR variability values of the original data and HR turbulence edited data are shown in Table 2. The largest changes were found in the values of ULF and VLF components when analyzed both at the baseline phase and at 6 weeks after the AMI. ULF component reduced by 4.3% ($P = 0.006$) at the baseline analysis and 6.8% ($P < 0.001$) at 6 weeks analysis between the original and HR turbulence edited data. Respectively, reduction of the VLF values was 3.9% ($P = 0.031$) in the baseline phase and 5.6% ($P = 0.001$) at the 6 weeks analysis. Low (LF) and high (HF) frequency components diminished between 2.2% to 4.1% after the HR turbulence removal. SDNN was least affected by the HR turbulence editing so that the differences between the results of the original and HR turbulence edited data were around 1.0% in SDNN values. A slight significant increase in the α_1 values was observed after turbulence removal ($P < 0.001$).

Next, the effects of the HR turbulence editing were examined in more detail. HR variability analysis data was split into deciles, 10 quantiles, according to the VPB amount. The effects of the VPB amount in the HR turbulence editing process are presented in the Table 3 in which the percentage differences of the HR variability parameters between original and HR turbulence edited data are shown in deciles of different VPB amount. In

the lower half quantiles (Q1–Q5) at the baseline phase the VPBs are infrequent (Q5: 15–41 VPBs per 24h, 0.02–0.04%) and thus the effects of the HR turbulence editing for HR variability parameters were minor (percentage difference <1%). Correspondingly in the HR variability analysis after 6 weeks from AMI with about same small amount of VPBs (Q3: 10–40 VPBs per 24 hour, 0.013–0.03%) the percentage differences remained small between the original and HR turbulence edited data (<1%) with the exception in the LF values of which the difference was about 2%. The SDNN analysis was least affected by the HR turbulence removal. The differences in the SDNN values remained small up to 9th quantile in both phase, the baseline and after 6 weeks from the AMI. In addition to SDNN, also analysis of the α_1 was not remarkably affected by the HR turbulence removal until the 10th quantile (Table 3).

The ULF and VLF components were affected most notably by the HR turbulence removal. When the amount of the VPBs was over 0.44% (Q9: 339–1431 VPBs per 24h, 0.44–1.38%) in the baseline phase, the percentage difference was 6.41% ± 4.23% for ULF and 3.79% ± 3.18% for the VLF. In the phase of 6 weeks after AMI the changes in ULF and VLF component were notably changed due the HR turbulence removal already in the 6th quantile (Q6: 39–204 VPBs per 24 hour, 0.11–0.19%) of which the percentage differences

Table 3. Percentage Differences of the HR Variability Measures between Original and HR Turbulence Edited Data at Baseline Phase and after 6 Weeks from AMI split in 10 Quantiles according to the Percentage Amount of the VPBs

	VPBs (%) min-max	VPBs/24h min-max	ULF	VLF	Percentage SDNN	differences α_1	(%) LF	HF
Baseline								
Q1	0.001–0.004	1–4	0.05 ± 0.05	0.28 ± 0.33	0.00 ± 0.00	0.23 ± 0.56	0.26 ± 0.57	0.33 ± 0.98
Q2	0.004–0.007	3–7	0.13 ± 0.15	0.65 ± 1.04	0.00 ± 0.00	1.16 ± 2.24	0.40 ± 0.42	0.16 ± 0.41
Q3	0.007–0.01	5–11	0.10 ± 0.07	0.43 ± 0.30	0.00 ± 0.00	0.43 ± 0.46	0.45 ± 0.53	0.23 ± 0.54
Q4	0.01–0.02	7–27	0.16 ± 0.14	0.47 ± 0.42	0.04 ± 0.18	0.80 ± 0.97	0.44 ± 0.72	0.62 ± 0.82
Q5	0.02–0.04	15–41	0.27 ± 0.24	0.50 ± 0.36	0.16 ± 0.46	0.77 ± 0.66	0.66 ± 0.70	0.60 ± 0.87
Q6	0.04–0.08	29–80	0.68 ± 0.60	1.01 ± 1.02	0.27 ± 0.52	0.59 ± 0.66	1.06 ± 1.20	0.83 ± 1.14
Q7	0.08–0.16	55–144	1.35 ± 0.93	1.30 ± 1.29	0.18 ± 0.47	1.00 ± 1.26	1.79 ± 1.65	1.49 ± 1.59
Q8	0.16–0.42	142–377	2.22 ± 1.93	2.84 ± 2.36	0.26 ± 0.53	1.63 ± 2.42	2.08 ± 1.88	2.31 ± 2.86
Q9	0.44–1.38	339–1431	6.41 ± 4.23	3.79 ± 3.18	0.83 ± 1.21	2.07 ± 1.60	4.39 ± 3.65	2.80 ± 3.01
Q10	1.39–10.12	1124–10322	34.7 ± 34.8	29.8 ± 39.9	7.37 ± 10.7	7.65 ± 9.95	11.5 ± 12.8	19.2 ± 21.6
6 weeks								
Q1	0.001–0.006	1–6	0.08 ± 0.07	0.26 ± 0.22	0.00 ± 0.00	0.86 ± 2.28	0.20 ± 0.31	0.25 ± 0.47
Q2	0.006–0.013	5–15	0.17 ± 0.14	0.50 ± 0.17	0.03 ± 0.16	0.53 ± 0.71	0.45 ± 0.45	0.42 ± 0.58
Q3	0.013–0.03	10–40	0.25 ± 0.22	0.61 ± 0.48	0.00 ± 0.00	0.58 ± 0.71	2.03 ± 7.02	0.39 ± 0.51
Q4	0.04–0.07	27–65	0.44 ± 0.39	0.62 ± 0.42	0.03 ± 0.13	1.14 ± 1.86	1.61 ± 2.24	0.98 ± 1.88
Q5	0.07–0.10	53–130	0.94 ± 0.75	0.98 ± 0.99	0.16 ± 0.37	1.10 ± 2.20	1.35 ± 1.57	1.87 ± 4.05
Q6	0.11–0.19	39–204	8.76 ± 23.4	8.64 ± 24.2	3.33 ± 11.2	1.86 ± 3.38	6.06 ± 19.4	6.23 ± 19.9
Q7	0.19–0.36	115–330	2.27 ± 2.25	2.11 ± 1.70	0.32 ± 0.61	1.12 ± 1.32	4.27 ± 8.12	4.30 ± 8.13
Q8	0.36–0.66	248–686	7.46 ± 4.86	4.72 ± 3.69	1.03 ± 1.39	2.18 ± 5.18	3.62 ± 3.34	3.81 ± 3.56
Q9	0.71–2.20	487–1983	10.1 ± 7.33	6.80 ± 5.09	1.21 ± 1.62	1.71 ± 2.58	5.46 ± 4.90	3.98 ± 3.07
Q10	2.21–9.96	1812–9265	38.7 ± 21.0	32.2 ± 22.0	4.81 ± 4.34	5.77 ± 6.66	16.7 ± 18.2	16.6 ± 14.8

Percentage differences (%) of the HR variability parameters are reported as mean ± standard deviation and amount of the VPBs during 24 hours are reported as range from minimum to maximum as percentage value (column 2) and absolute number (column 3). Quantiles are numbered as Q1...Q10. For other abbreviations see Table 2.

were $8.76\% \pm 23.4\%$ for the ULF and $8.64\% \pm 24.2\%$ for the VLF.

In the last 10th quantile the percentage differences were significantly increased for every HR variability parameter tested. The most remarkable changes were obtained in the ULF and VLF parameters in the 10th quantile in which the differences were at baseline 35% for ULF and 30% for VLF and after 6 weeks from AMI 39% for ULF and 32% for VLF. In addition, in the 10th quantile the percentage differences in the LF and HF components were considerable large ($>10\%$) at both baseline phase and after 6 weeks from the AMI (Table 3). Figure 1 displays the power spectra of a patient with frequent VPBs before and after the turbulence removal.

Effects of the HR turbulence removal on the risk evaluation

During the follow-up of 22 months, 20 patients experienced the primary end point (7.4%) of the 267 enrolled patients. Ten of these were due to symptomatic sustained monomorphic VT and ten were sudden cardiac deaths (SCD) or resuscitated cardiac arrests due to ventricular fibrillation. The characteristics of the patient population and those

who experienced a primary end point are shown in Table 1.

The prediction of primary end point was evaluated by the values of area under the curve (AUC) for SDNN, spectrum parameters (HF, LF, VLF, ULF) and fractal scaling exponent for the short-term HR variability (α_1) analyzed from 24-hour Holter recordings. The values of the AUC for the original data and HR turbulence edited data are listed in Table 4. The HR turbulence removal slightly improved the predictive value of ULF spectral component, analyzed 6 weeks post-AMI (AUC: 0.69->0.74). Likewise, the predictive power of VLF component slightly improved (AUC: 0.69->0.71). No noticeable differences were observed in other HR variability indexes in the ability to predict the primary end point after turbulence removal (Table 4).

DISCUSSION

ECG signals are in most cases imperfect containing disturbances and abnormal RR intervals. Usually, long term (~24hour) HR variability signals include different amount of ectopic beats, which are associated as a one source of error in the HR variability analysis, especially in the

Figure 1. Power spectra of RR interval time series of a patient with frequent ventricular premature beats (>50/h). The upper curve represents the spectrum where only premature beat and the compensatory pause after the premature beat are edited. The lower curve represents the spectrum after removal of premature beat and 15 consecutive RR intervals after premature beat.

analysis in the frequency domain.^{7,8,15} VPBs appear almost in every human being along the phase of life, but especially in patients with cardiac diseases VPBs occur commonly. In most cases, HR variability analyzing requires and it is recommended using RR interval data that is free of artifacts and ectopic beats. However, RR interval data free of ectopy is achieved usually only in short term ECG recordings under laboratory conditions lasting only a few minutes. On this account, a careful editing is evidenced to be necessary particularly for the spectrum analysis of the HR variability signals with ectopic beats and other disturbances.¹⁵ It has been recommended that such RR interval time series with over 20 VPBs per hour should be excluded from the HR variability analysis.¹⁶

It has been verified that after a VPB, the RR intervals of sinus rhythm oscillate briefly with a certain physiologic pattern due to the phenomenon of the HR turbulence.⁹ After the VPB, the sinus heart rhythm first shortly accelerates, followed by a deceleration and at the end a return to the baseline rhythm appearing before the VPB.⁹ Despite the fact, the RR interval rhythm after the VPB oscillates according to the HR turbulence pattern, it

has not been studied in detail if the turbulence behavior of the RR intervals has effects on the other HR variability measures. It should be taken into consideration, that in the editing process of the individual ectopic beats, most of the commercial HR variability editing methods deletes or replaces with interpolating merely the premature RR interval and the following compensatory pause.

In this study it was found that different HR variability parameters were differently sensitive to the HR turbulence removal. Studied parameters reacted differently also to the increase of the VPB amount on the HR turbulence removal process. SDNN and α_1 were the least affected by the HR turbulence removal so that the percentage differences remained small even with the large amount of VPBs. HR variability power frequency components, especially at ultra low and very low frequencies were the most sensitive to the HR turbulence removal in this study. The changes in the ULF and VLF parameters were prominent due to HR turbulence removal since the 9th quantile (339–1431 VPBs, 0.44%–1.38%) at the baseline phase and since the 6th quantile (39–204 VPBs, 0.11%–0.19%) after six weeks from AMI (Table 3). Also the

Table 4. HR Variability Measures as Predictor of Primary End Point

		HR turbulence edited data: AUC $\pm$ SD, P-value	Original data: AUC $\pm$ SD, P-value
ULF	Baseline	0.71 $\pm$ 0.06, P = 0.002	0.72 $\pm$ 0.06, P = 0.002
	6 weeks	0.74 $\pm$ 0.07, P = 0.003	0.69 $\pm$ 0.08, P = 0.02
VLF	Baseline	0.63 $\pm$ 0.07, P = 0.068	0.64 $\pm$ 0.05, P = 0.11
	6 weeks	0.71 $\pm$ 0.07, P = 0.008	0.69 $\pm$ 0.07, P = 0.02
SDNN	Baseline	0.65 $\pm$ 0.07, P = 0.03	0.65 $\pm$ 0.07, P = 0.03
	6 weeks	0.65 $\pm$ 0.09, P = 0.07	0.66 $\pm$ 0.08, P = 0.05
α_1	Baseline	0.63 $\pm$ 0.09, P = 0.06	0.60 $\pm$ 0.08, P = 0.13
	6 weeks	0.57 $\pm$ 0.10, P = 0.37	0.59 $\pm$ 0.09, P = 0.25
LF	Baseline	0.51 $\pm$ 0.08, P = 0.94	0.51 $\pm$ 0.08, P = 0.92
	6 weeks	0.59 $\pm$ 0.09, P = 0.25	0.61 $\pm$ 0.09, P = 0.18
HF	Baseline	0.42 $\pm$ 0.07, P = 0.22	0.43 $\pm$ 0.07, P = 0.29
	6 weeks	0.57 $\pm$ 0.10, P = 0.40	0.58 $\pm$ 0.10, P = 0.29

AUC values are reported as means $\pm$ standard deviation. Baseline is tested 5–14 days after AMI. Abbreviations: AUC = area under receiver operating characteristics curve. For other abbreviations see Table 2.

LF and HF components were notably affected by the HR turbulence removal especially in the phase of 6 weeks after AMI since the 6th quantile (39–204 VPBs, 0.11%–0.19%). Recommendation that VPB amount should be less than 20 VPBs per hour¹⁶ corresponds to the maximum of 480 VPBs per 24 hours. The results of this study support this recommendation of the maximum VPB amount in the RR interval data. However, the VPB amount less than 480 VPBs caused significant changes especially in the HR variability spectrum analysis. Thus, the limit of the maximum number being 20 VPBs per hour¹⁶ could be even tighten up according to the results of this study especially in the phase of 6 weeks after the AMI. A stricter limit with a maximum of 10 premature beats per hour¹⁷ has also been recommended; this would correspond better to our results, especially in the analysis conducted at 6 weeks after AMI. The present result support the view that at least in cases with frequent ectopic beats, HR turbulence of 15 beats should ideally be deleted from the analysis.

Normal pattern of the HR turbulence involving a short acceleration followed by a gradual deceleration can be suggested to correspond to a slow frequency RR interval fluctuation. Therefore, in an RR interval time series containing a large number of VPBs, HR turbulence phenomenon presumably produces a low frequency trend into the RR interval time series leading to an increase of the power in the lower frequencies of the HR variability power spectrum.

In previous studies, a careful editing in the HR variability analysis, especially in the frequency do-

main analysis^{7,8} has been recommended. HR variability analysis as a risk predictor for SCD in AMI patients has been evidenced to be improved with properly chosen editing method and with accurate editing.¹⁸ This study showed that editing the HR turbulence by deletion method slightly improved the prediction of primary end point especially with the spectrum analysis including analysis of ULF and VLF spectral components. These findings in the risk analysis of this study are in agreement with the previous findings about the importance of the careful editing of RR interval data when spectral measures of HR variability are used in risk stratification.^{7,8,18}

Results of this study implicate that even a moderate number of VPBs in the 24-hour RR interval time series may cause distorted decreases in the spectrum parameters due to HR turbulence and may lead to biased interpretation of the spectrum results. According to these results, it can be recommended, when analyzing other HR variability parameters than HR turbulence and especially the spectrum HR variability parameters, it should be considered carefully with single HR variability analysis if it would be necessary to edit or remove also the 10 to 15 following RR intervals after a VBP in the 24 hour RR interval data with substantial number of VPBs (>0.11%). In the future, it would be important to do more investigation about the HR turbulence effects on the other HR variability parameters in different patient populations and standardize the accurate maximum level of the VPBs in the RR interval time series.

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