

HEART RATE AND BLOOD PRESSURE TURBULENCE AFTER INDUCED SINGLE VENTRICULAR PREMATURE CONTRACTIONS IN PATIENTS WITH ICD

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Abstract: A single spontaneous ventricular premature complex (VPC) evokes heart rate turbulence (HRT) and turbulence of arterial blood pressure. We describe HRT and turbulence of both systolic and diastolic blood pressure (SBP & DBP) after a ventricular stimuli delivered by ICD in 5 post-MI male patients (59.5±10.2 years old). Twenty five out of the originally stimulated 125 VPCs had a normal HRT pattern and were selected for analysis. The highest range of changes relative to the last pre-VPC normal RR interval (RRI) was observed for DBP (28.1±11.1%), then for SBP (17.0±10.2%) and RRI (15.5±9.5%). The range of changes in DBP was significantly higher than for SBP (p=0.0001) and RRI (p=0.0004). It is known that HRT is caused by the post-VPC hemodynamic changes activating baroreflex. It is possible that changes in DBP and not SBP have stronger contribution in the induction of HRT.

INTRODUCTION

A phenomenon of an early acceleration and late deceleration of sinus rhythm following a ventricular premature complex (VPC) is termed heart rate turbulence (HRT) and was introduced in 1999 by Schmidt et al.¹ Two numerical HRT descriptors have been proposed, i.e. turbulence onset (TO), reflecting the early post-VPC acceleration of sinus rhythm, and turbulence slope (TS), quantifying its later deceleration.¹ With the use of the discriminating thresholds, 0% for TO and 2.5 ms/RR interval (RRI) for TS, any positive TO value or TS < 2.5 ms/RRI are considered abnormal in survivors of myocardial infarction (MI).¹

HRT has been shown to have an independent predictive value in post-MI patients both in retrospective and prospective analyses.¹⁻⁵ The presence of abnormal HRT predicts risk of total mortality in patients receiving conservative

therapy or treated mostly with invasive coronary revascularization during the acute phase of MI.¹⁻⁵

HRT is a measure of the autonomic response to perturbations of arterial blood pressure after a single VPC. Arterial baroreceptors recognize a drop of blood pressure accompanying VPC and change vagal tonic activity.⁶⁻¹³

There are suggestions that HRT is present not only after a VPC but after a supraventricular premature complex.¹⁴ Besides, HRT may be triggered by a premature ventricular stimuli during invasive EP study.^{9,15} Our group has reported that HRT may be also induced non-invasively by a delivery of premature stimuli in ICD patients.¹⁶

The aim of the current study was: (1) to describe HRT and turbulence of both systolic (SBP) and diastolic blood pressure (DBP) induced by single premature ventricular stimuli initiated by a telemetry in ICD patients; (2) to evaluate the association between post-VPC baroreflex and HRT.

SUBJECTS & METHODS

Subjects. Five consecutive patients (52.7±9.9 years old, all men, mean LVEF 34.6±8.8%) with spontaneous sinus rhythm and newly implanted ICD (GEM 3VR or GEM 3DR, Medtronic, USA) were recruited. All had a history of at least one MI, 2 individuals had survived at least one VF and 3 patients had repetitive, symptomatic and not tolerated sustained VT. All subjects gave their informed consent for stimulation of single VPCs during a routine predischarge evaluation of ICD.

Protocol of VPCs induction. The study was performed during a routine predischarge ICD evaluation. After 5 min rest, single premature ventricular stimuli were delivered by Medtronic CareLink® Programmer (Medtronic, USA) by telemetry. A stimulus (50 to 78% prematurity of the preceding RRI) was administered every 30

seconds, which totaled to 25 stimuli, after which the procedure was stopped. The pulse stimuli had a width of 1.6ms and an amplitude of 8V. To avoid ventricular or dual chamber pacing during the post-VPC compensatory pause, the pacing was turned off before the VPCs initiation and turned on after the whole protocol was finished. Regardless of the protocol phase, emergency VVI pacing was available all the time.

Heart rate and blood pressure. Three-channel chest ECG and non-invasive finger blood pressure (Portapres 2, FMS, The Netherlands) were recorded by an A/D converter (Porti 5, TMSI, The Netherlands). The records were evaluated with RASCHlab (v. 0.6.1; www.librasch.org, Germany) and values of RRIs, SBP and DBP were taken for further analysis.

Calculation of HRT. Most of 125 given extrastimuli produced VPCs. However, only 64 VPC-segments fulfilled the strict criteria used for HRT calculation according to published references.^{1,4,13} Finally, after visual inspection of all local post-VPC tachograms of RRIs and preliminary calculation of TO and TS, only 25 VPCs revealing a normal HRT pattern were accepted and taken for further analysis. Both TO and TS were calculated for all single VPCs.

Baroreflex sensitivity (BRS). The spontaneous BRS was estimated in the post-VPC local RRI tachograms using the sequence method.¹¹ We computed the linear regression of RRIs as a function of SBP or DBP for the first 15 sinus beats after the VPC. The maximum positive slope of the regression line assessed over any sequence of 3 to 6 consecutive differences of SBP or DBP and RRIs represented the BRS, separately for SBP (BRS_{SBP}) and DBP (BRS_{DBP}).

Relative values of blood pressure and RRIs. The absolute values of SBP, DBP and RRI for the last sinus beat before the VPC were taken as the reference to calculate relative values (presented in %) of all series of SBP, DBP and RRIs. The maximal change of the relative values of SBP, DBP and RRIs within the post-VPC tachogram for 15 consecutive sinus beats were calculated as well.

Statistical analysis. Nonparametric Wilcoxon test for paired data was used for the comparison of continuous data. Spearman correlation was used for: (1) the evaluation of association of TO and TS with BRS_{SBP} and BRS_{DBP} ; (2) the analysis of mutual relationship of the maximal change of

relative post-VPC data. Only $p < 0.05$ was considered significant.

RESULTS

Safety. Neither life threatening arrhythmia (VF/VT, asystole) was induced nor ICD shocks were delivered during the study. Neither ventricular triplets nor nonsustained VT were induced. The longest post-VPC compensatory pause did not exceed 2100 ms. No external cardioversion and/or defibrillation was necessary. The emergency VVI pacing was not used. Except of the induced single VPCs, spontaneous single VPCs, occasionally as bigeminy or trigeminy, and ventricular pairs were observed. These additional VPCs were the most frequent cause of rejection of the induced single VPCs from the analysis.

Heart rate and blood pressure turbulence. The mean TO is for: SBP: $-4.9 \pm 5.6\%$, DBP: $-11.2 \pm 7.0\%$ and RRI: $-5.0 \pm 5.5\%$. The mean TS is for: SBP: 3.3 ± 2.2 mmHg/RRI, DBP: 2.5 ± 1.0 mmHg/RRI and RRI: 25.2 ± 11.6 ms/RRI. Figure 1 presents HRT and blood pressure turbulence for relative values.

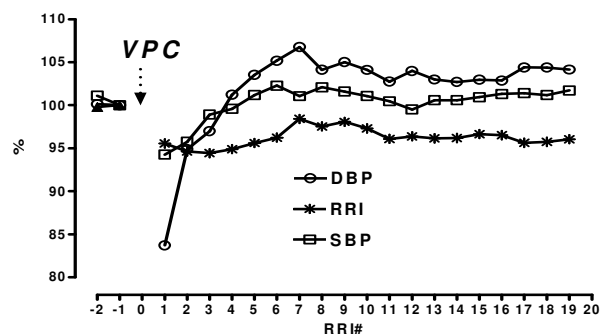


Figure 1. Local tachograms for pooled relative data of RRI, SBP and DBP for consecutive sinus beats before and after the VPCs. DBP - open circles; SBP - open squares; RRI - asterisks. See text for abbreviations.

The calculated TO for relative values is the same as for absolute ones. TO for relative DBP is significantly higher than for SBP ($p < 0.0001$) and RRIs ($p = 0.0043$) with no significant difference between SBP and RRI. TS for relative values is 2.9 ± 2.1 %/RRI for SBP, 5.1 ± 2.2 %/RRI for DBP and 2.3 ± 1.2 %/RRI for RR intervals. TS for relative DBP is significantly higher than for SBP ($p < 0.0001$) and RRIs ($p = 0.0002$) with no significant difference between SBP and RRI.

Baroreflex sensitivity. The mean BRS_{SBP} is 26.8 ± 22.1 ms/mmHg and BRS_{DBP} is 23.5 ± 14.5 ms/mmHg (not significant difference).

Maximal change of the relative values. The mean maximal change of relative values is 15.4±/8.2% for SBP, 28.11±/11.1% for DBP and 16.6%±/6.7% for RRI within the first 15 sinus beats after the VPC. The change for DBP is significantly higher than for SBP ($p<0.0001$) and RRI ($p<0.0001$). The changes for SBP and RRI are not different.

Correlation analysis. The results of correlation analysis between HRT and BRS are shown in Figure 2. There is a significant positive correlation between BRS_{DBP} and TS (Panel B: $p=0.0077$) and a negative correlation between TO and BRS_{SBP} (Panel C: $r=-0.4004$; $p=0.0473$).

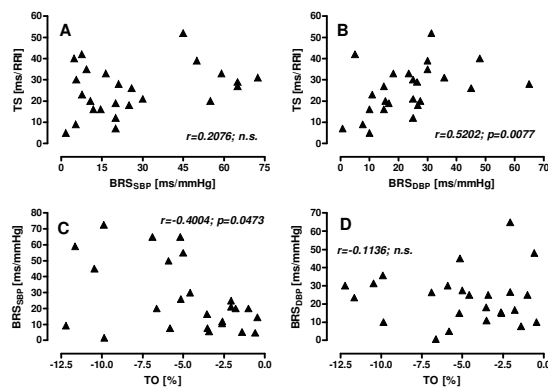


Figure 2. The associations between BRS and HRT. Panel A – between BRS_{SBP} and TS. Panel B – between BRS_{DBP} and TS. Panel C – between TO and BRS_{SBP} . Panel D – between TO and BRS_{DBP} . See text for abbreviations.

The results of correlation analysis between the maximal changes of relative values of blood pressure and RRIs are shown in Figure 3. Only the changes of DBP are significantly correlated with RRIs changes ($r=0.4769$; $p=0.0159$).

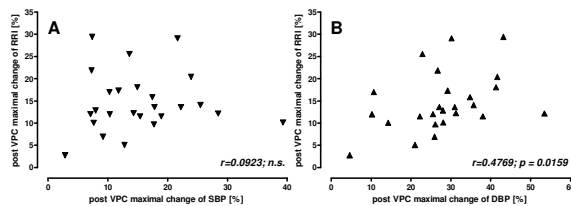


Figure 3. The associations between the maximal changes of relative values of blood pressure and RRIs after the VPC. Panel A – presents the results for SBP whereas Panel B for DBP. See text for abbreviations.

DISCUSSION

This study was performed in post-MI patients with compromised left ventricular function and newly implanted ICD. The main findings of this study are: (1) an ICD-induced single VPC may produce HRT and the turbulence of systolic and diastolic

blood pressure; (2) it appears that HRT is affected more by the changes in DBP than in SBP.

Hemodynamic perturbations caused by a single VPC are responsible for induction of HRT.⁶⁻¹² It was demonstrated that HRT is accompanied by blood pressure turbulence, is strongly correlated with BRS and is abolished by atropine.⁶⁻¹¹ In of the previous studies heart rate and mostly SBP or mean blood pressure were analyzed. Roach et al. reported the presence of transient relative hypertension caused by mean blood pressure overshoot.¹¹ In our study we concentrated on both SBP and DBP in a model of non-invasive induction of HRT by a single ventricular stimuli delivered by patient's ICD. We have also found the post-VPC overshoot effect of SBP (105.9±/4.1% of the pre-VPC reference) and DBP (110.4±/7.2%). Nevertheless, the diastolic relative hypertension was significantly higher than the systolic one ($p=0.0009$).

In contrast to others, we have not found any significant association between BRS derived from SBP and TS in our patients. But a similar relationship exists for TS and BRS calculated for DBP. Moreover, within the first 15 sinus beats after the VPC, there is a significant association between the relative changes of DBP and RRIs but not between corresponding changes of SBP and RRIs. The noticed significant link between TO and SBP-derived BRS suggests that the initial change of heart rate after the VPC (the early acceleration) modulates the activity of baroreceptors. The calculation of TO is based on heart rate both before and immediately after the VPC while BRS is computed only on the series of postectopic sinus beats and is not limited to the first two beats (as TO is). The more pronounced the early heart rate acceleration (the cause) is, the better BRS_{SBP} (the effect) is evoked, which results in a positive feedback. Another plausible explanation is that the sudden post-VPC reduction of blood pressure unloads baroreceptors, which in turn decrease vagal activity. The rapid reaction of baroreceptors to unloading suggests that they may have a potential for a fast response to the loading caused by rising blood pressure. We do not know why this association works only for TO and BRS_{SBP} and does not work for BRS_{DBP} . Perhaps this is a sample size effect and a higher number of analyzed VPCs would allow to observe a

significant correlation between TO and DBP-derived BRS as well?

Our patients had left ventricle dysfunction and were on a standard multi drug therapy used in post-MI survivors (all of them on ACE inhibitors, statins, beta-blockers, and amiodarone - stopped 3-4 days before the study, just after the successive ICD implantation - and some of them diuretics). Both clinical presentation and the administered therapy might have influenced the results. Therefore we are not able to extrapolate our observations to healthy people and to compare them with other reports. Although it was shown that HRT may be induced by an artificial ventricular stimuli but, as Watanabe wrote, HRT is "nature's own autonomic perturbation experiment and is non-invasive" when natural VPCs are evaluated. However, it was shown that HRT and blood pressure turbulence induced in the EP lab are similar to those following spontaneous VPCs and induced turbulence is a valid model for research studies.

CONCLUSIONS.

Changes in DBP have a stronger contribution in the induction of HRT than SBP in post-MI patients with ICD and impaired left ventricular function.

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