Role of hypotension in heart rate turbulence physiology

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BACKGROUND Heart rate turbulence is a recently described cardiac prognostic marker that may be mediated by arterial baroreceptor sensitivity, suggesting it is induced by a brief initial hypotension.
OBJECTIVES The purpose of this study was to assess whether heart rate turbulence could be noninvasively induced through a previously implanted defibrillator and whether hypotension modulates turbulence physiology.
METHODS Premature ventricular paced beats was delivered during continuous ECG and blood pressure monitoring in patients with implanted defibrillators. Heart rate turbulence parameters from paced beats were compared with those from spontaneous premature ventricular beats. Subsequently, turbulence hemodynamic parameters were compared in 11 subjects with turbulence induced by pacing trains of 1, 3, 5, and 8 beats at a cycle length of 400 ms.
RESULTS Heart rate turbulence was very similar whether it followed a spontaneous premature ventricular complex or a paced beat. Induced and spontaneous turbulence slopes correlated well (R_s = 0.917, P = .001). With increasing pacing train length, the magnitude of hypotension, cumulative hypotension time from the last sinus beat, turbulence tachycardia magnitude, magnitude of hypertension in recovery, and turbulence onset (but not turbulence slope) all increased. The cumulative hypotension time, but not the magnitude of hypotension, was tightly correlated with the magnitude of tachycardia (R^2 = 0.999, P = .003) and turbulence onset (R^2 = 0.975, P = .01).
CONCLUSION Heart rate turbulence can be induced noninvasively through an implanted device. Turbulence parameters are physiologically modulated by the duration of the initial hypotension, suggesting a possible important role for arterial baroreceptors.

KEYWORDS Heart rate turbulence; Baroreceptor; Implanted defibrillator; Physiology; Hypotension; Tachycardia

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Introduction

Heart rate turbulence (HRT) is a transient coupled tachycardia-bradycardia complex that follows premature ventricular complexes (PVCs).[1] It is an initial 2- to 3-beat tachycardia, followed by a 10- to 20-beat bradycardia, before a return to the baseline heart rate. Blunted HRT has been found to be a strong predictor of cardiac arrest,[2] heart failure death and hospitalization,[3] and mortality following a myocardial infarction.[1,4,5] Successful cardiac reperfusion with percutaneous coronary intervention improves HRT parameters acutely.[6,7]

Given these findings, the physiologic origin of turbulence is of some importance. Its study has been facilitated by the observation[8–12] that HRT can be induced by programmed stimulation in the electrophysiology laboratory, with characteristics similar to HRT following premature ventricular complexes.[9] It can be blocked with atropine, indicating a vagal dependence.[11–13] Savelieva et al[14] reported that delivering more premature ventricular beats (shorter coupling intervals with a longer postpacing interval) correlates with HRT parameters in patients with a normal ejection fraction. HRT parameters correlate with baroreceptor sensitivity when they occur spontaneously[2,15] and when they are induced[8–12] in the elec-

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trophysiology laboratory. These findings suggested that both early tachycardia and delayed bradycardia are responses mediated by the arterial baroreceptor to (documented) blood pressure changes.

To test this hypothesis, we aimed to measure turbulence morphometric parameters in response to gradations in the initial transient hypotension. We used rapid pacing trains to vary the hypotension, reasoning that longer pacing trains would induce greater sustained hypotension and subsequently alter the turbulence tachycardia, turbulence bradycardia, turbulence onset, and possibly turbulence slope. Our primary goal was to assess the effects of pacing trains (simulating nonsustained ventricular tachycardia) on HRT physiology and parameters. A second goal was to show that HRT could be induced noninvasively using previously implanted pacemakers and defibrillators.

Methods

Subjects and data acquisition

The study was approved by the University of Calgary Medical Research Ethics Board. A total of 21 subjects were recruited from the University of Calgary Arrhythmia Clinic population. Of these 21 subjects, 4 were referred for clinically indicated electrophysiologic studies for ventricular or supraventricular tachycardia, and 17 had previously received an implantable cardioverter-defibrillator (ICD) for treatment of ventricular tachycardia.

Subjects were instrumented[8] with ECG leads and the Finapres noninvasive finger cuff blood pressure monitor (Ohmeda, Englewood, CO). ECG and blood pressure outputs were digitally sampled at 500 Hz using Matlab (The MathWorks, Natick, MA) data acquisition software. RR interval and mean arterial pressure (MAP) sequence were determined using in-house software written for Matlab. The time of the second R wave of each RR interval was used as the time of that beat's RR interval. All RR interval sequences were screened for atrial or ventricular ectopy and discarded if spontaneous ectopy occurred within 15 seconds before or 20 beats after the early depolarization. This process was used to avoid the potentially confounding effects of these collateral beats on HRT.[8]

Protocol 1: Spontaneous HRT vs ICD-induced HRT

With the subject seated comfortably, up to four single extrastimuli were delivered through their ICD once per minute at a coupling interval of 400 ms to the preceding beat. Heart rate and blood pressure recordings were continued for at least 10 minutes in an effort to record a spontaneous PVC. HRT parameters were compared for the spontaneous and induced extra beats.

Protocol 2: Effect of pacing train on HRT

Subjects either were seated comfortably or were supine. Ventricular pacing trains that were 1 beat (T1), 3 beats (T3), 5 beats (T5), and 8 beats (T8) in length were given three times at 1-minute intervals. The coupling interval between paced beats was 400 ms.

HRT description

Turbulence onset was defined[1] as the mean of the first 2 post-pacing (or spontaneous PVC) sinus RR intervals (after the compensatory pause) minus the mean of the last 2 pre-pacing (or spontaneous PVC) sinus RR intervals, rather than this value normalized by baseline heart rate. Turbulence slope was defined in the conventional manner as the maximum positive slope (ms per beat) of a regression line obtained over any sequence of five sinus RR intervals within the 20 beats following completion of the pacing train (or spontaneous PVC). Positive turbulence onset and turbulence slope were defined by Schmidt et al[1] as turbulence onset <0 and turbulence slope >2.5 ms/beat.

For each patient at each pacing train length, we determined the average RR interval and blood pressure responses using a time basis with a 100-ms interpolation grid[8,9] to allow for analysis of these data on a time basis rather than a beat basis. This method permitted interpatient hemodynamic comparisons without undue influences from varying baseline RR intervals. Figure 1 shows a schematic RR interval and blood pressure trace with labels defining our time-based morphometric parameters. *Baseline RR* is the average of the last two sinus RR intervals prior to pacing, with a similar definition for baseline MAP. *HRT hypotension* was defined as the baseline MAP minus the minimum MAP within 5 seconds of the last paced beat m. *HRT tachycardia* is the baseline RR minus the minimum RR within 6.5 seconds of the last paced beat. *HRT hypertension* was defined as the maximum MAP to occur between 5 and 13 seconds after the last paced beat minus the HRT hypotension MAP minimum. *HRT bradycardia* was defined as the maximum RR interval to occur in the window between 6.5 and 13 seconds after the last paced beat minus the HRT tachycardia RR minimum. Times to events (HRT tachycardia, HRT bradycardia, HRT hypotension, HRT hypertension) were measured using a 100-ms interpolation grid relative to the last paced beat. *Cumulative hypotension time* was defined as the time from the initial paced beat to the HRT hypotension.

Statistical analysis

The primary unit of analysis was the patient, not the individual sequence. This was done to avoid overweighting patients with higher numbers of analyzable sequences. For protocol 1, a Spearman rank order correlation was performed to determine the relationship between spontaneous and ICD-induced HRT parameters (turbulence onset and turbulence slope).