

Neurovegetative Tests to Evaluate Rate Responsive Pace-Makers

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Abstract

Aim of this study is to design a procedure to evaluate rate-responsive Pace-Makers (PMK) featuring rate adaptation through autonomic inputs. The proposed procedure is based on a set of neurovegetative stressors and on the analysis of the heart rate variability (HRV). The selected stressors include: controlled respiration in supine position and during active standing; mental stress; hand-grip and non-invasive sinusoidal stimulation of carotid baroreceptors. Each test lasted 5 minutes. Complete or partial incompetent patients implanted with INOS²-CLS (Biotronik) were studied one month after the start of the rate modulating program. ECG, respiration activity and non-invasive blood pressure (Finapres) were monitored. We found that the most effective stressors were active standing and handgrip. Spectral analysis is of limited value due to the distortion introduced by spontaneous beats. In conclusion a procedure based on HRV analysis in response to selected neurovegetative stressors is able to quantify the rate adaptation of PMKs.

1. Introduction

Rate-responsive cardiac PMKs aim at having pacing rates as similar as physiological cardiac rhythms. Modern PMK implement a closed loop strategy (CLS) based on indirect measures of right ventricle contractility using intracardiac impedance signal [1]. The contractility is, in turn, related to the autonomic nervous system (ANS) control to the heart.

A standardized method to evaluate the performances of such devices after the first programming and also its long term stability, in each patient, has not been defined yet.

Aim of this study is to design a procedure to evaluate rate-responsive PMKs, based on the analysis of the heart rate variability (HRV) evoked by a set of neurovegetative stressors.

2. Methods and materials

2.1. Study population

We focused on complete or partial incompetent patients implanted with INOS²⁺-CLS (Biotronik, Germany). After the implant, PMKs were programmed in CLS mode, 70 bpm lower rate, 130 bpm upper CLS rate.

After 3 months patients with significant paced beats (>70%) were enrolled for the study. 10 patients were studied.

2.2. Neurovegetative stressors

The set of autonomic stressors were selected according to the following criteria: limited compliance of the patients due to their age; standardization and reproducibility of the tests; constraints imposed by signal processing of HRV series and physiological interpretation of the response. The following tests were selected:

- controlled breathing in supine position [2];
- active standing;
- sustained handgrip [3];
- mental stress;
- carotid stimulation by neck suction [4];

Each stage lasted 5 minutes, 1 minute of recovery was introduced between each stage. The sequence of the various stages was randomized. Controlled breathing was achieved by asking the patient to start the inspiration following an audible tone generated by a PC. Respiration frequency was set at 0.25 Hz. Controlled breathing was continued during active standing, but not for the other stages. Handgrip lasted 3 minutes, 2 minutes of recovery were included in the monitoring. Mental stress was provided by mathematical tasks including addition and subtraction. The task difficulty was modulated by the operator according to cultural level of the subject and to the response to the first calculations. Neck suction (NS) was applied to two cuffs posed on both sides of the neck (at the positions corresponding to the carotid baroreceptors). The cuffs were connected to a vacuum

source, whose power was modulated by a software-controlled feed-back sinusoidal control. The use of the cuffs instead of a molded collar (previously employed, [4]) is more comfortable for the patient, although providing the same stimulation. The protocol consisted in two stages lasting 5 minutes each. The NS stimulation frequency was set to 0.2 Hz in one stage and to 0.1 Hz in the other, in a random order.

2.3. Experimental protocol

Surface ECG (II lead), Respiration Activity (RA) and Blood Pressure (by Finapres, Ohmeda) were simultaneously recorded. RA was monitored by a pletismographic thoracic belt. Signals were sampled at 1000 Hz, 12 bit via an A/D converter board (DAQCard 1200, National Instruments).

PMKs were set to bipolar atrial stimulation, fixed atrio-ventricular interval and bipolar ventricular stimulation. This configuration makes the atrial spikes of the PMK easy to be detected, while reduces the amplitude of the ventricular pacing to conveniently lower values.

The software for the signal acquisition and for neck suction control was developed using LabView (National Instruments).

2.4. Signal pre-processing

Pre-processing of ECG included the recognition of atrial-to-atrial and ventricular-to-ventricular PMK spikes.

ECG was band-pass filtered to enhance the PMK spike [5]. Cut-off frequencies were chosen at 30 and 45 Hz, on empirical basis. HRV series were expressed as a function of beat number (tachogram, RR). According to this approach, the series of systolic values were obtained from the blood pressure signal (systogram, SS) [6]. Power spectrum densities were estimated by autoregressive modelling. Model orders were chosen according to Anderson's whiteness test and Akaike's optimal criteria [7].

The algorithms for PMK spikes detection, tachogram and systogram construction and spectral analysis were developed in Matlab (The MathWorks).

3. Results

All patients completed the controlled breathing, the active standing and the mental stress. Handgrip was performed by 9 out of 10 patients; 7 out of 10 underwent the neck suction.

Significant increases of heart rate, respect to basal values were observed during active standing, handgrip and, to a minor extent, during mental stress.

Figure 1 shows these results in one patient. Histograms include only RR intervals from stimulated beats. It is clear a progressive decrease in the RR intervals passing from resting condition to mental stress and active standing.

Figure 2 illustrates the dynamical behavior of systolic values and stimulated RR intervals during the handgrip, in a subject featuring 100% of stimulated beats. Handgrip lasted 3 minutes. One minute of the recovery period is also showed. Note the progressive decreasing in the RR interval, as the blood pressure increases. The rapid drop of the systolic values at the end of the test is followed by a sudden increase in the RR intervals.

Figure 3 shows the same data plotted in a Heart Rate vs Systolic Pressure plane. Note the correlation between systolic values and heart rate, for a relatively large range of systolic values.

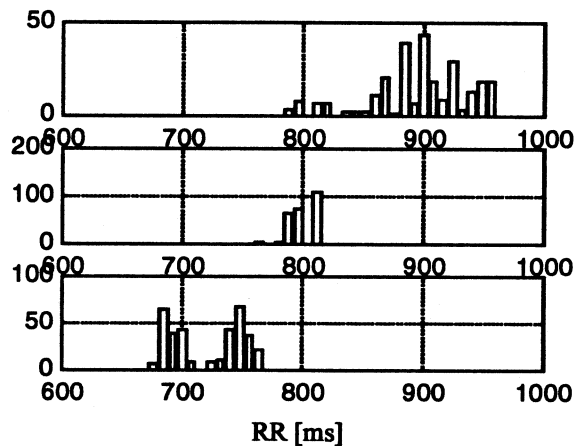


Fig. 1. Histograms of stimulated RR interval during basal (upper panel), mental (mid panel) and active standing (lower panel), in one subject.

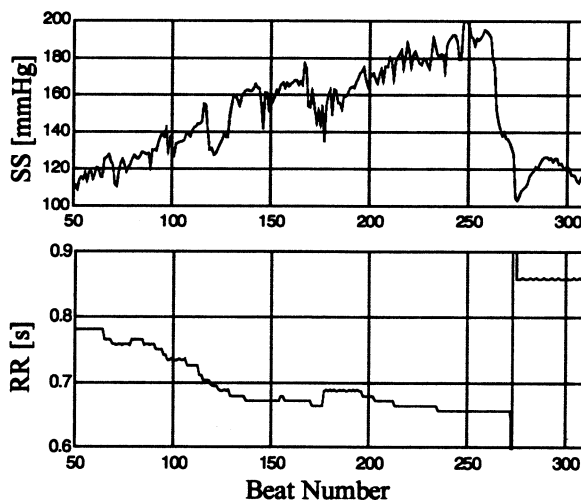


Fig. 2. Systolic values (upper panel) and stimulated RR intervals (lower panel) and systolic values, in one subject, during the handgrip test and the following recovery period.

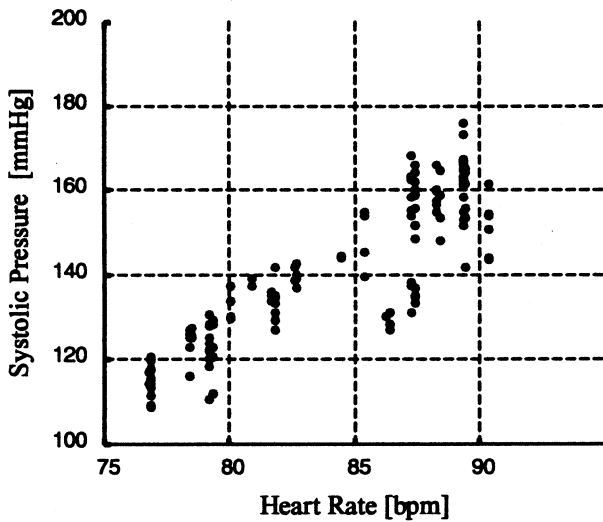


Fig. 3. Plot of systolic values (vertical axis) vs instantaneous heart rate (horizontal axis) during the handgrip, in one subject.

The estimation of the power spectra during the various stages turned out to be unreliable in most of the patients. In fact, tachograms were significantly affected by the presence of spontaneous beats. Although our protocol selected patients with significant paced beats (>70%), still proper methods for spontaneous beats interpolation are needed.

Figure 4 shows the tachogram and systogram spectra for one patient with 100% of stimulated beats. Systogram spectrum shows the physiological components at the respiratory frequency (HF, 0.25 Hz) and in the low frequency (0.1 Hz, LF) band. A component centered at twice the respiratory component is also detected, being a second harmonic of the respiratory component. Tachogram spectrum shows a significant component in the LF band, while no contributions were detected in the respiratory band.

4. Discussion

Rate responsive PMKs based on estimation of the sympathetic drive to the heart require specific methods for the evaluation of their adaptation to meet the haemodynamic challenges of the normal life. We hereby evaluated the response to a set of tests consisting in both physical and emotional inputs to the ANS.

The results obtained during active standing and handgrip showed an increase in heart rate respect to basal conditions, in most of the patients. Handgrip turned out to be the best stressor in terms of increase in blood pressure and seems the most convenient for a clinical evaluation of these PMKs. The recovery phase after the handgrip highlighted the quick adaptation of the heart rate at the end of the stressors.

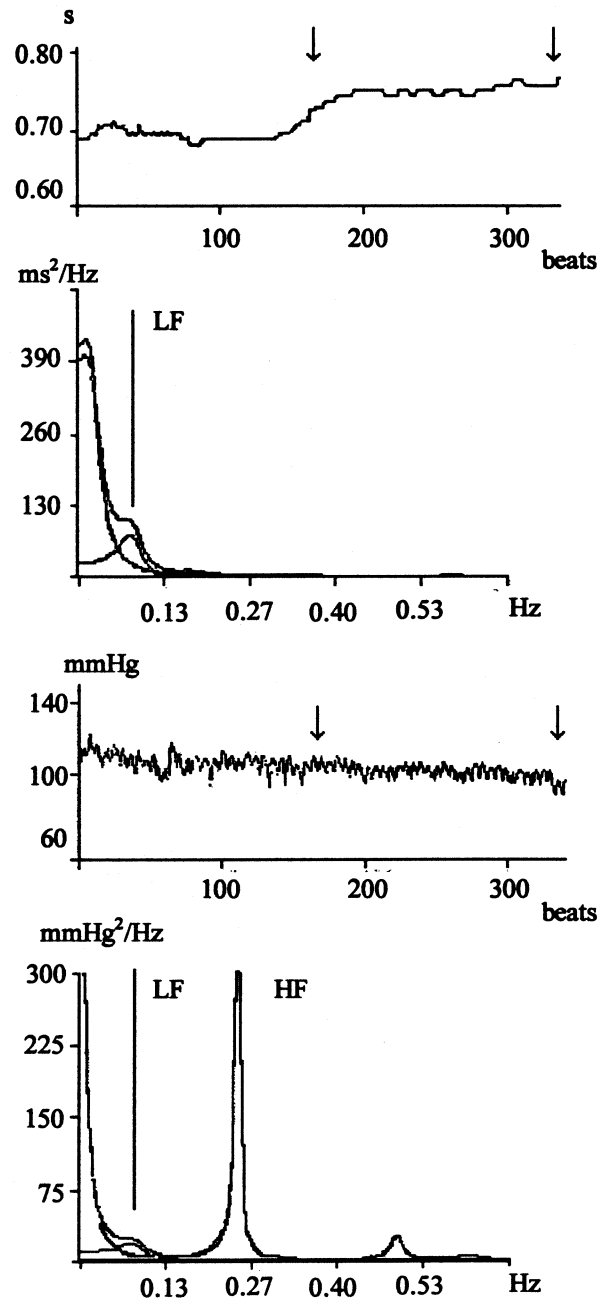


Fig. 4. From up to down, time series and their power spectrum density (right) of stimulated RR intervals (upper panel) and systolic values (lower panel) in one subject, during active standing. Arrows indicate the beginning and the end of the data interval used in the estimation of the spectra.

Mental stress did not evoke a strong response in blood pressure in all the patients, and thus it provides little help in the evaluation of the PMKs. Nevertheless in those patients who reacted to this stressor with significant increase in blood pressure, it showed the ability of these

PMKs to react to emotional stressors.

In most of the patients tachograms featured a not negligible presence of spontaneous beats. These beats play a minor role in time domain analysis (such as in the comparison of the mean RR values or in their histograms), provided that they are detected, classified as spontaneous and eliminated.

We also found that the percentage of spontaneous beats changed in the different stages. The sympathetic response evoked by the stressors may determine a temporary increase in the chronotropic function of the heart and thus may increase the spontaneous activity. When data are analyzed in the frequency domain, spontaneous beats may play a crucial role. Simple elimination of these beats can not be operated, because it would cause a severe spectrum distortion in the high frequency band.

In one patient with 100% of stimulated beats, we detected a low frequency component in the tachogram spectrum, during the active standing stage; no respiratory components were observed in the HRV spectrum, neither in basal nor in active standing, in this patient. The inotropic function of the ventricle is usually considered under the control of the sympathetic branch of the ANS. This may explain the finding of a modulation in the RR interval in the LF band. This modulating rhythm is present in various sympathetic fibers and in the spontaneous variability of heart period and systolic pressure [8][9]. The analysis of the neck suction stimulation data turned out to be extremely difficult. First, some patients were excluded because of concomitant or previous pathology to the carotid vessels or thyroid. Second, because analysis of such data is usually obtained by spectral analysis, a significant number of stimulated beats and proper techniques for spontaneous beat interpolation are needed.

5. Conclusion

In conclusion, we tested various procedures based on HRV analysis in response to selected neurovegetative stressors to quantify the rate adaptation of the INOS²⁺-CLS PMK. From a clinical point of view, active standing and handgrip seem to be the most appropriate tests for the evaluation of the rate adaptation feature of this class of PMKs. Spectral analysis during active standing, mental and neck suction may play a major role to assess the ability of the closed loop stimulation to mimic the physiological behavior in response to various stressors, beyond the simple increase/decrease of the average heart rate. A careful correction of spontaneous beats appears to be crucial for reliable spectral estimates. Nevertheless, this PMK seems able in imposing heart period modulation synchronous to the physiologic LF modulation in the systolic blood pressure.

6. Study limitations

In the present study various tachograms were not analyzed because were corrupted by spontaneous beats. In the comparison of the histograms, spontaneous beats were simply neglected, whilst they cause a relatively large number of series be discharged from frequency domain analysis. In the interpretation of the fluctuations in the stimulated beats we did not make use of any information concerning the filtering and decision rules the INOS²⁺-CLS implements. We only used information from the literature reported in the references.

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