Correlation of Intracardiac Impedance and Right Ventricular Contractility during Dobutamine Stresstest

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Summary

Changes of the unipolar right ventricular impedance during the cardiac cycle are thought to correlate with right ventricular contractility, and thus, with the inotropic state of the heart. Aim of this study was to analyze the effect of increasing dobutamine challenge on RV contractility and the ventricular inotropic parameter (VIP) calculated from the measured impedance signals. In 12 patients (68 ± 12 years) undergoing implantation of an Inos² DDDR pacemaker (Biotronik), right ventricular dp/dtmax and impedance measurements during intrinsic and VVI paced rhythm were obtained during a stepwise increasing dobutamine stresstest (5-20 µg/kg/min). There was a strong and highly significant correlation between dp/dtmax and VIP for ventricular paced ($r^2 = 0.97$) as well as for intrinsic rhythm ($r^2 = 0.93$), although the morphologies of the original impedance curves differed quite substantially. We conclude that for both intrinsic and ventricular paced rhythm, sensor signals derived from right ventricular unipolar impedance curves closely correlate with dp/dtmax, and thus, with right ventricular contractility.

Keywords

Right ventricular contractility, intracardiac impedance

Introduction

Changes of the unipolar ventricular impedance during the cardiac cycle are thought to reflect the contraction process of the right ventricle (RV), thereby providing information about myocardial contractility and the inotropic state of the heart 1-6. The hypothesis is, that in patients with chronotropic incompetence, in whom cardiac output is mainly regulated via increased contractility (Frank Starling mechanism, sympathetic innervation), the changing intracardiac impedance may be used as an ideal sensor-principle to regulate the chronotropic response of a rate-adaptive pacemaker [2,3,7-10].

Aim of this study was to investigate the relationship between changes of intracardiac impedance and RV contractility during incremental dobutamine challenge.

Methods

Patients undergoing routine DDDR pacemaker implantation were selected for the study. All patients received an Inos² DDDR pacemaker (Biotronik, Germany) in combination with passive fixation leads (Polyrox, Biotronik, Germany) in the RV and right atrial appendice. In the rate-adaptive mode, this pacemaker is able to scan the unipolar ventricular impedance during a time window of 47 to 290 ms after a pacing spike (or occurrence of a sensed ven-tricular event) by delivery of 30 µs rectangular impulses of 600 µA at a rate of 128 Hz. These measurements are used to calculate intracardiac impedance curves and a mathematically derived sensor-signal (VIP).

After placement of the RV pacing lead, a RV pigtail catheter was positioned through an introducer sheath inserted into the vena subclavia, which was later used for definite insertion of the right atrial lead. For study purposes, continuos measurement of VIP signals (cus-tom-ized external Inos² pacemaker), RV pressure curves and dp/dt$_{max}$ were obtained and digitally stored on optical disk (CardioCath version 1.1, Prucka Inc., USA). After calibration, RV pressure and impedance curves were sampled during intrinsic and VVI paced rhythm (10 bpm above intrinsic rate). Then, a stresstest
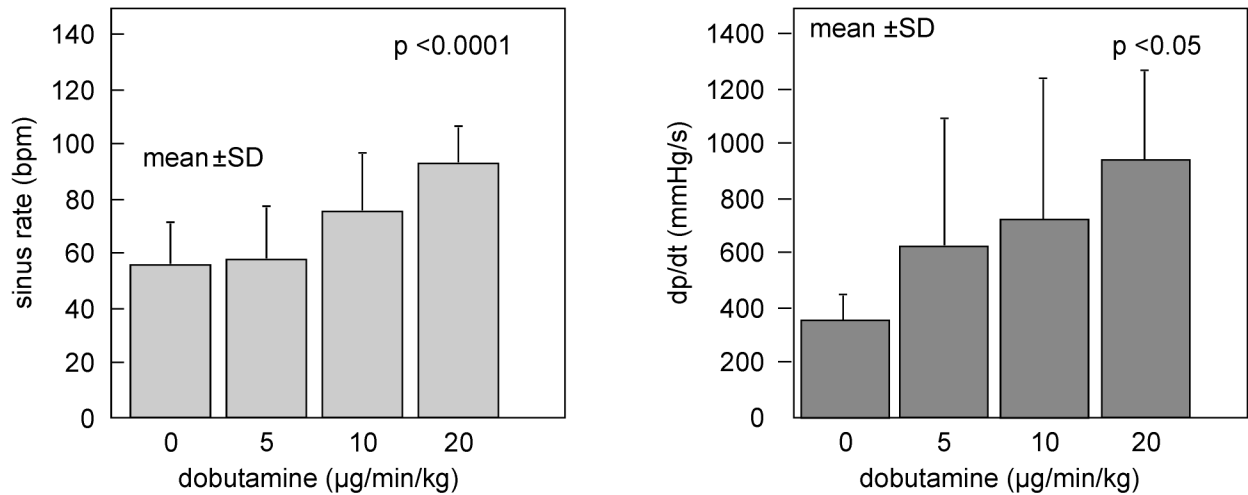
Figure 1. The graph shows the response of sinus rate (left) and right ventricular contractility measured as dp/dtmax (right) to stepwise increase of intravenous dobutamine (5 minute intervals). The values are depicted as mean ± standard deviation.

was started with stepwise increase of intravenous dobutamine ranging from 5-20 µg/min/kg. At the end of each dosing step, sinus rate, blood pres-sure, RV pres-sure, dp/dt_{max} and VIP were measured during 10-second periods of intrinsic rhythm and VVI paced rhythm. For comparison of dp/dt_{max} and VIP measurements, normalized values were computed (0.00 = baseline value, 1.00 = maximally achieved value in a particular patient). Regression analysis was used to investigate the relationship between normalized dp/dt_{max} and VIP values. A p-value of < 0.05 was considered to indicate statistical significance.

Results

In total, 12 patients (68 ± 12 years) completed the study. Indication for pacemaker implantation was sick sinus syndrome in 5 and AV-block in 7 patients, with all patients having narrow complex rhythm at implantation. In 4 patients, chronotropic incompetence was documented.

There was a significant increase of both sinus rate and right ventricular contractility with increasing dobutamine doses (Figure 1). Figure 2 shows a typical example of impedance curves at three different dobutamine doses in the same patient during intrinsic (left) and VVI paced rhythm (right). As shown in this example, the curve morphologies differed quite substantially between intrinsic and VVI paced rhythm. For calcula-

tion of VIP, the maximal slope of the curve in a predefined region of interest was used. The time window for this region of interest was patient specific, and in addition, different for intrinsic and VVI paced rhythm, in order to facilitate optimal curve separation.

If the normalized values of dp/dtmax and VIP were plotted in a linear regression model, there was a strong and highly significant correlation between myocardial contractility and the derived sensor signal ($r^2 = 0.923$ for all events, Figure 3). If intrinsic rhythm and VVI paced rhythm were analyzed separately, there was a comparably strong correlation between dp/dtmax and VIP for both types of rhythm (Figure 4) suggesting a good robustness of the derived sensor parameter despite the fact of substantially differing raw data information (Figure 2). Furthermore, there was a strong non-linear correlation between normalized sinus rate and VIP at increasing dobutamine doses (Figure 5), although there were at least 4 patients with documented chronotropic incompetence during daily life exercise.

Discussion

The integrated information of rapid impedance changes during the ventricular contraction process closely correlated with dp/dtmax values at different inotropic states of the heart. This correlation was equally strong for intrinsic rhythm as well as VVI
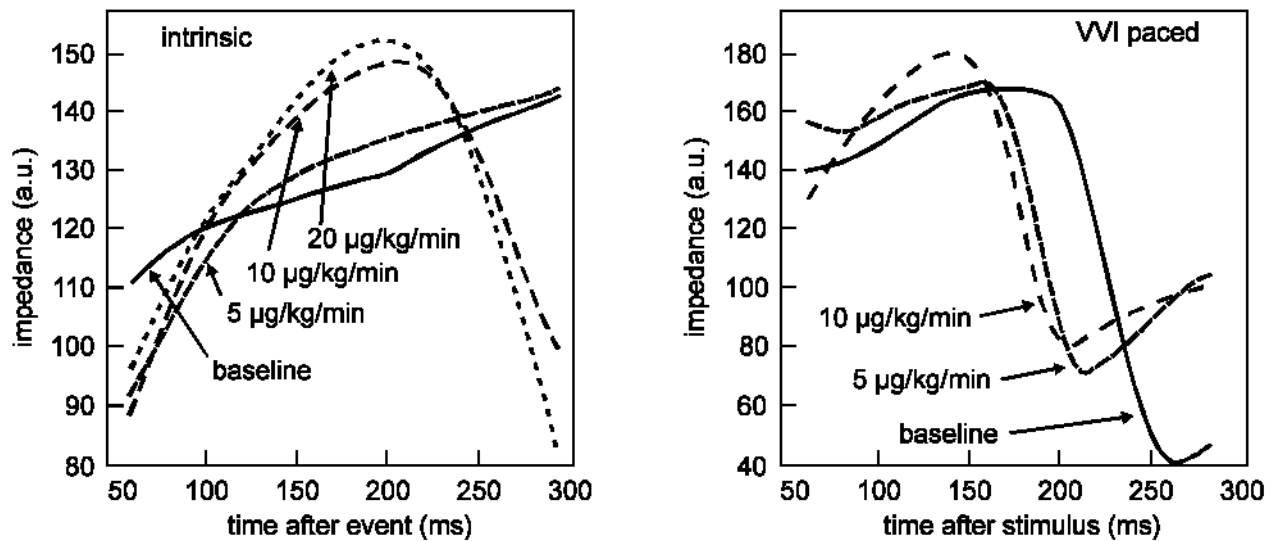
Figure 2. The curves on the left show typical impedance curves at different dobutamine doses in the same patient (arbitrary units). Note that the shape of the impedance curve is substantially different during intrinsic (left) as compared to ventricular paced rhythm (right) in the same patient. However, in both diagrams a region of interests can be defined, where the slope of the curves can be differentiated. This allows to calculate a sensor signal for both, intrinsic and VVI paced rhythm, that reflects the inotropic state of the heart.

paced rhythm, although the shape of the original impedance curves differed quite substantially [11]. These observations suggest, that VIP sensing closely correlates with right ventricular contractilit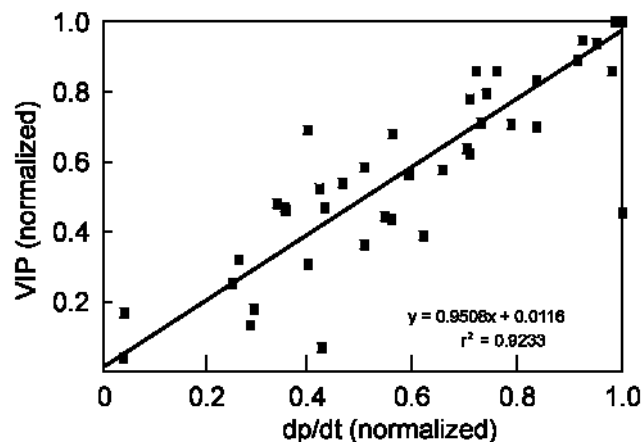y, and therefore, may be interpreted as a surrogate of sympathetic cardiac innervation. Furthermore, VIP also correlated in a non-linear fashion with the normal response of sinus rhythm.

Based on the concept that, in chronotropically incompetent patients, cardiac output is mainly regulated via increased contractility and sympathetic cardiac tone, the intracardiac impedance appears to be a ideal sensor principle for closed-loop stimulation [2-7]. For example, if right ventricular contractility increases in order to maintain or increase cardiac output in a chronotropically incompetent patient, the sensed VIP increases in parallel, which allows to calculate an appropriate increase in pacing rate. Once the hemodynamic demands are met, the sympathetic adrenergic tone will be down regulated, which secondarily will initiate a negative feedback effect on the pacemaker [4, 7]. This dual response of VIP sensing imitates the physiologic hemodynamic feedback regulation of the cardiovascular system making this sensor principle an integrated part of the neuro-humoral cardiovascular reflex that regulates cardiac output [7].

The concept of closed-stimulation based on inotropy sensing is not new [2, 3], and many different approaches have been tried in the past [9, 10]. However, the main innovation of this sensor principle is the density
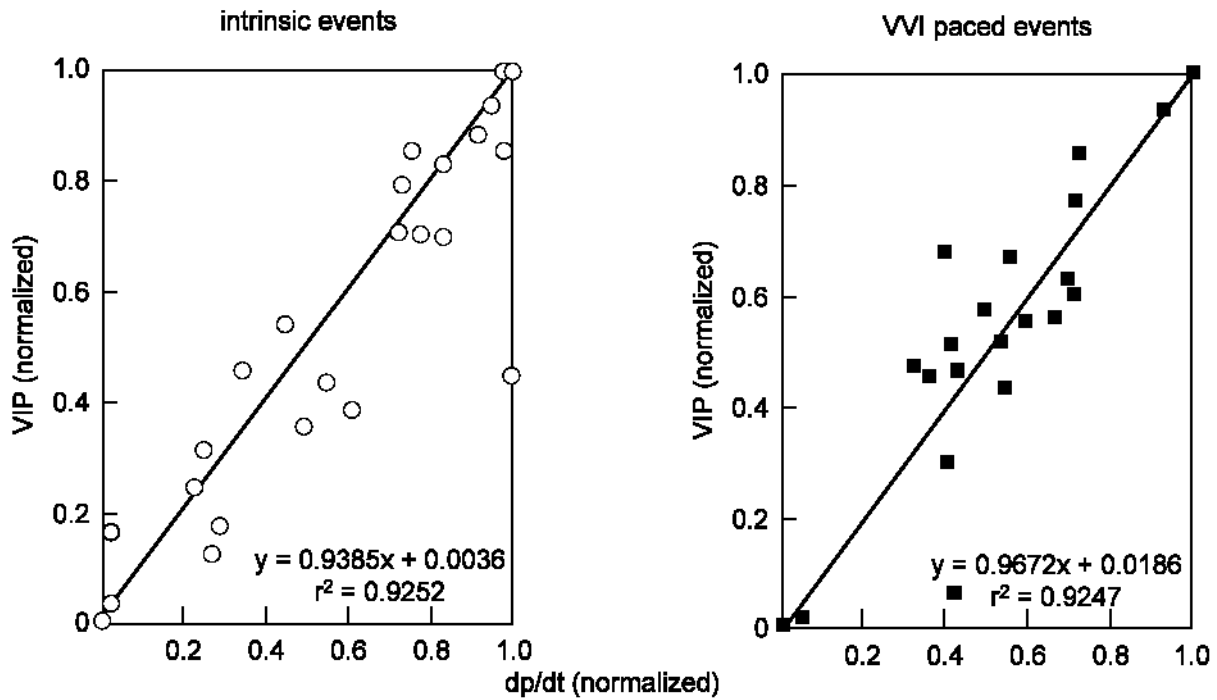

Figure 3. The correlation between normalized ventricular impedance signals (VIP) and right ventricular contractility measured as dp/dt_{max} are depicted for all cardiac events (intrinsic and VVI paced rhythm).

intrinsic events

$$y = 0.9385x + 0.0036$$
$$r^2 = 0.9252$$

VVI paced events

$$y = 0.9672x + 0.0186$$
$$r^2 = 0.9247$$

Figure 4. This graph shows the correlation between VIP and dp/dt$_{max}$ separated for intrinsic (left) and VVI paced rhythm (right). There was a comparably strong correlation between the VIP signal and right ventricular contractility for both types of rhythm, although the morphologies of the impedance curves, on which calculation was based, were substantially different.

$$Y = 1.0516x^2 - 0.1851x + 0.0368$$
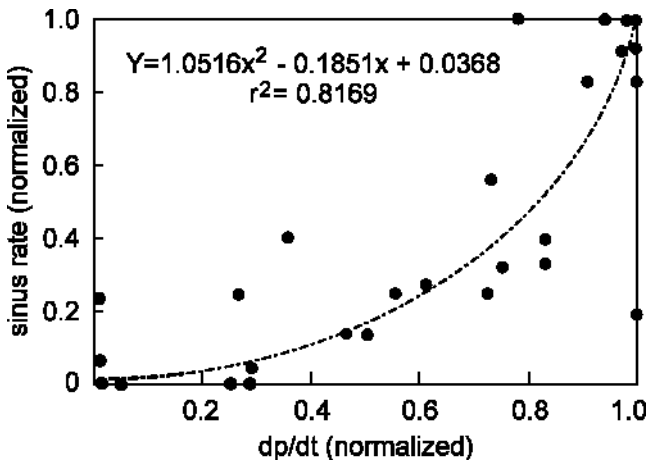$$r^2 = 0.8169$$

Figure 5. Normalized values of sinus rate and the VIP signal in response to dobutamine are depicted. This relationship was best described by a non-linear function, which may be explained by the fact, that there were some patients with virtually no sinus rate acceleration in response to dobutamine due to chronotropic incompetence.

and accuracy of data acquisition, and in particular, how this information is being processed by a complex algorithm. Although, calibration of this first generation algorithm was fairly complex and certainly not very user friendly, a new algorithm with autocalibration is available. First clinical evaluation of this new algorithm (treadmill testing and daily life exercise) seem to confirm our excellent results of acute dobutamine testing in the intraoperative setting [12,13]. Furthermore, comparison with other sensor principles showed that VIP sensing is comparable to minute-ventilation sensing in terms of its physiologic response to different forms of exercise, and clearly superior to the rate response of piezo sensors and accelerometers [13,14].

The dual response of this new sensor principle, which is capable of sensing a surrogate of sympathetic cardiac innervation, provides the unique opportunity to integrate technical rate support in the physiologic reflex arch of cardiac output regulation. With such potential, this sensor technology may significantly

add to the world of rate-adaptive pacing, where non-physiologic rate response with most of currently available technologies remains the main dilemma.

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