The Influence of Pacing Rate on Intramyocardial Electrograms

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Summary

In 13 heart transplant patients, stimulated intramyocardial electrograms were recorded during the posttransplant period using telemetric pacemakers and two epimyocardial electrodes. One electrode was used for stimulation and the other electrode for sensing the electrical activity of the heart and vice versa. The signals recorded in this manner are designated as crossed ventricular evoked responses (VERX). Pacing rates (PR) of 90, 100, 110, 120 and 130 pulses per minute (ppm) were applied. The different PR were applied in a randomly selected order. The influence of PR on parameters of interest extracted from the VERX was analyzed (Q_x-, R_x- and T_x-wave amplitudes, propagation time, duration, and the maximum slope during the repolarization phase). Statistical analysis showed that the PR has a significant and distinct influence on some of those parameters.

Key Words

Pacing rate, evoked response, intramyocardial electrogram, pacemaker telemetry

Introduction

Intramyocardial electrograms, particularly recordings of evoked responses during pacing, offer a noninvasive method for patient monitoring after heart transplantation [1]. Therefore, all patients of the University of Graz heart transplant program receive telemetric pacemakers and epimyocardial electrodes in the course of the transplant procedure.

Two ventricular leads are used. They not only allow recording of ventricular evoked responses (VER) from two different ventricular sites, but also using one electrode to stimulate and the other electrode to sense the electrical activity of the heart. In this case, the resulting signals are designated as crossed ventricular evoked responses (VERX).

At present, the VERX signals are not as well studied as the VER signals. However, they may contain important clinical information not observable in the VER signals. The most obvious of this supplementary information is the propagation time, related to the propagation velocity of the depolarization wavefront [2,3].

Due to different individual spontaneous heart rates, it is not possible to stimulate all patients at the same pacing rate (PR), as would be desirable. Some of the parameters obtained from the VERs may be affected by the PR. The objective of the present study was to investigate the influence of PR on parameters of interest obtained from the VERX signal.

Methods

Data Acquisition

Unipolar intramyocardial electrograms were obtained using dual-chamber pacemakers with extended bandwidth capability between 0.3 and 200 Hz (Physios CTM 01), and fractal coated epimyocardial electrodes (ELC 54-UP). The first electrode (E1) was placed at the right ventricular outflow tract and connected to the ventricular channel of the pacemaker. The second electrode (E2) was implanted at the right or at the left ventricle with a distance of at least 4 cm to E1 (Figure 1). The measuring session was performed not earlier than three months after the transplantation, and the patients

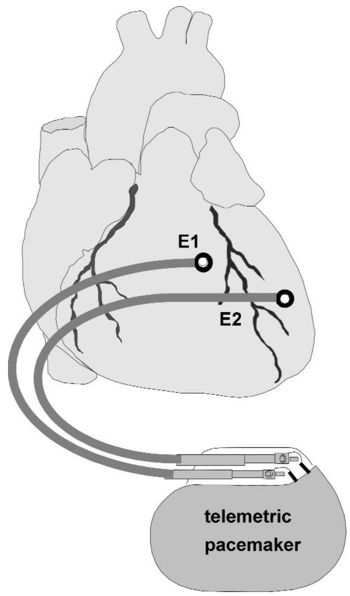

Figure 1. Pacemaker implant configuration with a telemetric dual-chamber pacemaker and two epimyocardial screw-in electrodes, placed on the right and the left ventricle.

were clinically inconspicuous at the time of measurement. During each measuring session, sequences of intramyocardial electrograms were recorded from the paced heart at rates of 90, 100, 110, 120, and 130 ppm. For the present study, the VERXs stimulated at the first electrode E1 and sensed at the second electrode E2 (VER1X2) and vice versa, stimulated at E2 and sensed at E1 (VER2X1), were analyzed. The order in which the PRs were applied was randomly selected for each patient. The recordings were telemetrically received and sampled with 667 Hz, thus resulting in a temporal resolution of 1.5 ms. The digitized signals were stored in a special data acquisition unit (SWM/SWD 1000, all equipment and devices so far: BIOTRONIK, Berlin, Germany).

Signal Analysis

The usual signal analysis consisted of signal processing and parameter extraction. Signal processing was performed in the following steps [4]:
- event detection,
- event classification,
- averaging of all events assigned to the same class.

The extracted parameters were the Q_x-, R_x-, and T_x-wave amplitudes, the propagation time (t_x), the duration (DUR), and the maximum slope during the repolarization phase (MRS) of the averaged VERX. Figure 2

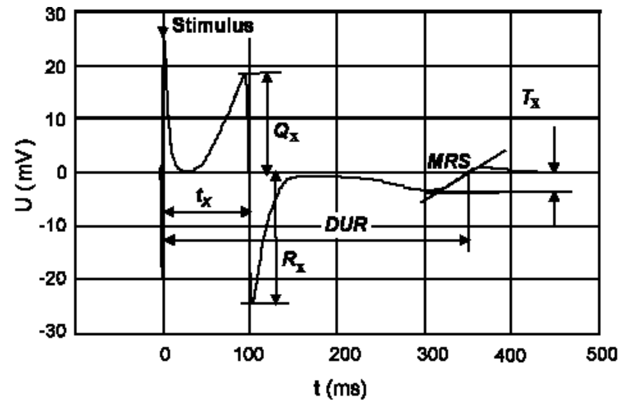

Figure 2. Typical averaged VERX signal. The definitions of the extracted parameters are shown: the Q_x, R_x and T_x wave amplitudes, the propagation time (t_x), the duration (DUR), and the maximum repolarization slope (MRS).

shows the definitions of these parameters. The x subindex is used to indicate that the Q_x, R_x and T_x waves are not identical with the corresponding Q, R and T waves in the spontaneous surface ECG.

The Q_x-wave amplitude is defined as the positive maximum during the depolarization phase. The R_x-wave amplitude is defined as the minimum during the depolarization phase. The T_x-wave amplitude is defined as the maximum (positive or negative) during the repolarization phase. The propagation time (t_x) is defined as the time interval between the application of the stimulus at one electrode and the arrival of the excitation at the other electrode [2,3]. As can be seen from Figure 2, the typical shape of the evoked response following the crosstalking of the stimulus shows a slow upward deflection, then a rapid downward deflection, and finally, again a slow upward deflection. The duration (DUR) is defined as the time interval between the stimulus and the crossing of the maximum slope line with the baseline (zero volts, the offset was corrected). The maximum repolarization slope (MRS) is defined as the maximum of the first derivative (positive or negative) after the maximum of the T_x wave.

Statistics

The Friedman test was applied to all analyzed parameters for the VER1X2 and VER2X1 signals, grouped by PR. A p value < 0.05 was considered statistically significant. Additionally, a linear regression analysis between the PR and each of the analyzed parameters was performed. The means and standard deviations of all analyzed parameters at each PR were calculated.

PR (ppm)	90	100	110	120	130
VER1X2	6	10	11	12	12
VER2X1	6	10	10	11	11

Table 1. Number of patients in whom the VERX measurements were performed with the respective PRs.

Results

Table 1 shows the number of patients for whom measurements were available at different PRs. In total, 99 measurements were made in 12 patients, 51 VER1X2 signals and 48 VER2X1 signals.

For a number of patients, the VERX could not be measured at a PR of 90 ppm because their spontaneous heart rates were higher than the PR. Therefore, this PR was not further considered in the analysis. For 10 patients, all the VER1X2 signals between 100 and 130 ppm were available. In case of the VER2X1, signals at all these PRs were available in only 8 patients. We provide detailed results for the VER1X2 signals.

Figure 3 shows the VER1X2 signals measured at different PRs for the same patient. Decreases in duration and propagation time can be observed when the PR increases.

The Friedman test showed a significant influence of the PR on the T_x-wave amplitude, t_x, DUR and MRS, but not on the Q_x-wave amplitude (Table 2). The R_x-wave amplitude was not included because the pacemaker amplifier was overdriven during the R_x wave for some of the VER1X2 signals. Table 2 shows detailed results. The values are the means and the standard deviations of the analyzed parameters for the 10 patients for whom VER1X2 signals are available at all PRs between 100 and 130 ppm. Figure 4 shows the influence of PR on the duration of the VER1X2.

Prior to regression analysis, each of the analyzed parameters was normalized by expressing the values for a certain PR as a percentage with respect to the average value as calculated from all 4 PRs for each patient.

Figures 5 and 6 show the results for the regression analysis between the PR and the parameters t_x and DUR, respectively.

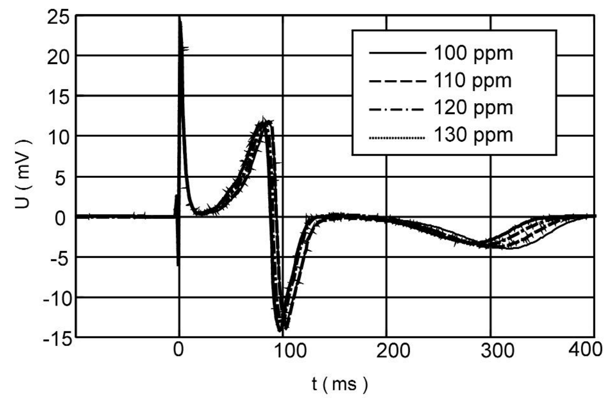

Figure 3. Averaged VER1X2 signals obtained at different pacing rates from a single patient. The most obvious differences in the signals are observed during the repolarization phase.

PR (ppm)	Q_x (mV)	T_x (mV)	t_x (ms)	DUR (ms)	MRS (mV/s)
100	7.17	1.76	73.1	377	-24.1
	±5.5	±3.6	±25	±18	±67
110	7.14	1.89	72.5	363	-28.0
	±5.6	±3.7	±26	±16	±68
120	7.04	2.10	70.8	349	-31.5
	±5.5	±3.5	±25	±18	±66
130	7.19	2.12	69.8	340	-31.1
	±5.6	±3.5	±25	±15	±66
p <	0.4	0.05	0.002	0.0001	0.0001

Table 2. Mean ± standard deviation of the Q_x- and T_x-wave amplitude, propagation time (t_x), duration (DUR), maximum repolarization slope (MRS) of the VER1X2, and the p values (Friedman test).

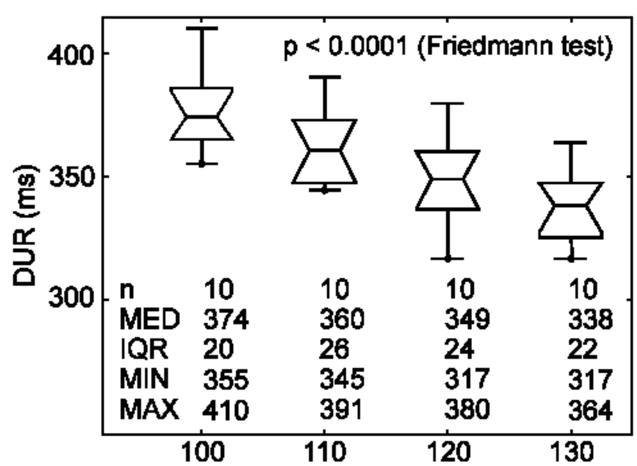

Figure 4. Boxplots showing the influence of pacing rate (PR) on the duration (DUR) of the VER1X2. The number of patients measured (n), the medians (MED), the interquartile ranges (IQR), the minima (MIN) and maxima (MAX), and the p value are displayed.

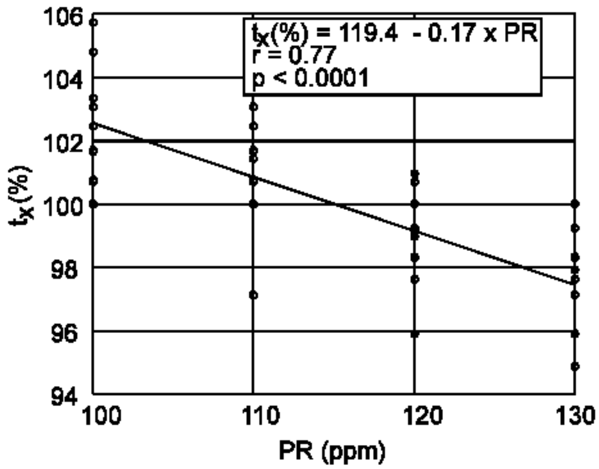

Figure 5. Regression analysis between the pacing rate (PR) and the normalized propagation time (t_x (%)) indicating a significant correlation and a correlation coefficient of 0.77.

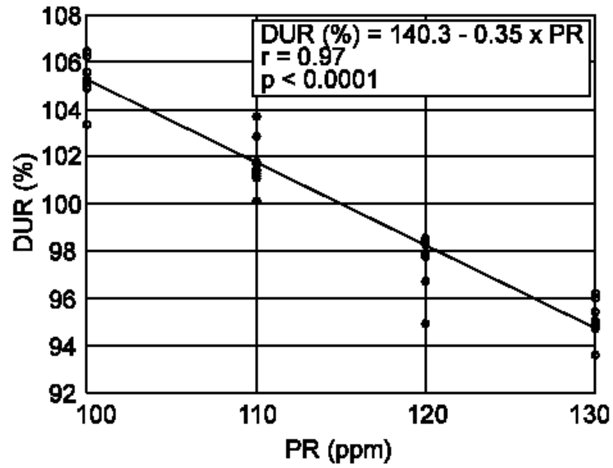

Figure 6. Regression analysis between the pacing rate (PR) and the normalized duration (DUR (%)) indicating a significant correlation and a correlation coefficient of 0.97.

Similar results were obtained for the VER2X1 signals. In this case, the pacemaker amplifier was not overdriven by the R_x-wave. Therefore, these R_x-wave amplitudes were included in the analysis. The Friedman test showed a significant influence of the PR on the R_x- and T_x-wave amplitudes ($p<0.01$), the t_x ($p<0.01$), the DUR ($p<0.0001$), and the MRS ($p<0.005$), but not on the Q_x-wave amplitude. The regression analysis showed a significant correlation for the R_x-wave amplitude, t_x and DUR, but not for the other parameters.

Discussion

The influence of PR on the rejection-sensitive parameter (RSP) and the infection-specific parameter (ISP), both obtained from the VER signals, has been demonstrated previously [5,6]. In the present study, the influence of PR on parameters extracted from the VERX signals has been shown.

Table 2 shows that the parameters t_x and DUR significantly decrease as the PR increases. In accordance with basic theory, these results are to be expected, because t_x contains information on two important factors:

- the distance between both electrodes (independent of PR).
- the propagation velocity which ultimately depends on the depolarization velocity, and, therefore, is influenced by the PR.

DUR depends on the action potential duration, which decreases as the PR increases.

The standard deviation of t_x is larger than the respective values for the standard deviation of DUR (Table 2). This result is not surprising, because DUR depends mainly on intrinsic properties of the heart, whereas t_x depends also on the distance between the electrodes, which differs from patient to patient.

There is a significant correlation between the PR and some of the analyzed parameters. This fact has to be considered when evaluating the results for a particular patient. In particular, it is useful to define correction factors for the parameters that showed a significant correlation with the PR (t_x and DUR) in order to compare the results measured at different PRs. For example, consider that a propagation time of t_{x130} = 70 ms and a duration DUR_{130} = 340 ms are measured for a certain patient at a PR of 130 ppm. The correction factors to be applied are the slopes of the regression lines calculated earlier (Figures 5 and 6). From these figures it can be seen that the correction factor for the propagation time is -0.17 %/ppm and the correction factor for the duration is -0.35 %/ppm. For an arbitrary parameter PAR with the correction factor CF, the value of the parameter referring to PR2 when it was measured at PR1 can be calculated by

$$PAR_{PR2} = [1 + CF/100 \times (PR1 - PR2)] \times PAR_{PR1}$$

Using the above equation, the propagation time (t_{x100}) and the duration (DUR100) referring to 100 ppm are

$$t_{x100} = [1 + (-0.17)/100 \times (100-130)] \times 70 = 73.6 \text{ ms}$$

$$DUR_{100} = [1 + (-0.35)/100 \times (100-130)] \times 340 = 376 \text{ ms}$$

Using this method, the results measured at different PRs can be directly compared. The correction factors for the propagation time and the duration for the VER2X1 signal are similar to the values calculated earlier for the VER1X2 signal: -0.15 %/ppm and -0.34 %/ppm, respectively.

Conclusion

Statistical analysis showed that the PR has a significant influence on the T_x-wave amplitude, the t_x, the DUR, and the MRS, but not on the Q_x-wave amplitude of the VERX signals. Regression analysis showed a significant correlation between the PR and two of the analyzed parameters: the propagation time and the duration. Correction factors for these two parameters were determined in order to allow direct comparison of measurements performed at different PRs.

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