Detection of Cardiac Allograft Rejection Using a pPhysios CTM 01 Pacemaker: A Preliminary Case Study

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Summary

VER processing from IEGM recorded with a pacemaker could be of interest for monitoring heart transplantation rejection. Physios CTM offers such a feature with the CHARM server. We report our experience with two patients implanted with this pacemaker soon after transplantation. The patients have been regularly followed up for more then six months.

Key Words

Heart transplantation, rejection monitoring, VER

Introduction

Orthotopic heart transplantation has been a routine procedure in our center since 1988. Among our patients, the implantation of a permanent pacemaker is a rare occurrence. This condition is based on a sinus node dysfunction or an atrioventricular conduction of the transplant that persists more than 21 days after the heart transplantation. We recently adopted the Physios CTM 01 pacemaker (BIOTRONIK, Germany) in such situations. According to preliminary studies, this device, which offers a high resolution IEGM, allows a non-invasive approach to diagnosing cardiac rejection. We report herein our preliminary results with Computerized Heart Rejection Monitoring (CHARM) based on two patients who were implanted with a Physios CTM 01 pacemaker and endocardial leads.

Materials and Methods

Since 1998, we have implanted two patients with the telemetric pacemaker Physios CTM 01 and fractal-coated, endomyocardial leads, immediately following heart transplantation. Both patients underwent total orthotopic heart transplantation according to the Shumway technique. Heart transplants were arrested with intra-aortic injection of 1 liter of Celsior® and then stored at 4°C in the same solution. During the transplantation, the heart transplant was regularly cooled with cold Ringer Lactate solution and the sinus node was carefully protected from injury during the atrial suture. Before unclamping the aorta, the heart transplant was re-perfused with pressure-controlled warm sanguine anterograde re-perfusion solution (Buckberg). A continuous perfusion of Isoproterenol was used in order to obtain a sinus rhythm with a frequency above 120 bpm. In case pharmacologically-induced frequency was too low, temporary epicardial pacing leads were used to maintain an adequate frequency until spontaneous recovery. Initially, patients were treated with cyclosporine (4 to 10 mg/kg/day) together with prednisolone (0.5 to 1 mg/kg/day) and azathioprine (0.1 to 0.2 mg/kg/day). Immunosuppressive treatment was then adjusted to the patient's tolerance and to the episodes of rejection diagnosed by scheduled EMB.

Patient 1: A 51-year-old man with severe chronic heart failure secondary to ischemic cardiomyopathy was transplanted on July 10, 1998. The total duration of transplant ischemia was 270 minutes. The hemodynamic outcome was simple despite a third degree AV block that occurred at the very beginning of the post-operative period. On July 22, he finally received a Physios CTM 01 telemetric pacemaker with a lead placed at the apex of the right ventricule. He was dis-

charged from the hospital on August 7 after an uneventful outcome.

Patient 2: A 68-year-old man with chronic heart failure due to severe pulmonary arterial hypertension secondary to ischemic cardiomyopathy was transplanted on February 13, 1999. The patient had undergone a previous multiple CABG four years earlier. The total duration of transplant ischemia was 240 minutes. Immediately following the procedure, the patient experienced right heart failure due to early and severe sinus bradycardia, which resulted in functional renal insufficiency. Due to lead dysfunction, bradycardia could be treated neither by increasing the regimen of isoproterenol nor by epicardial stimulation. However, a medically controlled septicemia temporarily contraindicated the PM implantation until March 5 when he received a Physios CTM 01 telemetric pacemaker with a lead placed in the medial portion of the right ventricular base. The patient was eventually discharged from hospital on March 19.

In both cases, an intracardiac electrogram (IEGM) analysis was performed the same day the patients were admitted to the Post-Transplantation Consultation Unit for their scheduled EMB. IEGM sequences with a duration of 60 seconds were recorded during ventricular pacing at 100 bpm using a portable PM programming system. All sequences were transmitted for analysis to the central workstation in Graz (Austria). However, due to the necessary learning curve, IEGM recordings for the first patient were not interpretable until the second postoperative month. All EMB results were classified according to the standardized grading system for EMBs established by the International Society of Heart and Lung Transplantation (ISHLT).

Results

A total of 17 IEGM recordings and 27 EMBs were performed during the follow-up.

Patient 1: A total of 8 IEGM recordings and 16 EMBs were used for analysis. During the 9 months of a clinically uneventful follow-up, the patient presented two episodes of rejection as assessed by EMB: one was a grade 1B and occurred within the first two postoperative months, and the second was a grade 1A. During the entire recorded outcome, VER T-slew values were never below 100 mV/s. The trend curve of VER T-slew suggest that even a low grade episode of rejection is related to a decrease of the VER (Figure 1).

Patient 2: A total of 9 IEGM recordings and 11 EMBs were used for analysis. During the 3 months of follow-up, the patient exhibited two episodes of grade 1A rejection. VER T-slew values were never below 50 mV/s. Trend curves of VER T-slew showed an initial rapid decrease of T-slew value followed by a plateau with a secondary, slight increase after a few weeks (Figure 2). At the same time as the initial decrease, the patient received anti-CMV prophylactic therapy because of a severe neutropenia.

Discussion

Previous studies have shown that the Physios CTM 01 telemetric pacemaker, due to its superb sensitivity and reproducibility, is a promising device for non-invasive

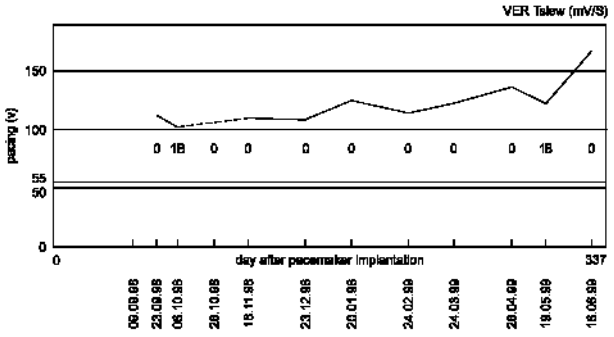

Figure 1. Patient 1 VER, T-slew and EMB grades (Dotted lines indicate missing data).

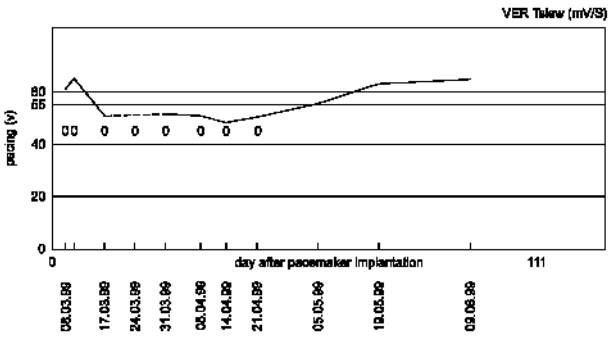

Figure 2. Patient 2 VER, T-slew and EMB grades (Dotted lines indicate missing data).

detection of rejection in heart transplants. Therefore, a beneficial effect could be to limit the necessity of using EMB to detect heart rejection. The key to interpreting these reports is simply this: decreasing VER amplitudes indicates a deterioration, increasing VER amplitudes indicates an improvement. Basically, the rejection sensitive parameter as extracted from the VER corresponds to the maximum slew rate of the failing part of the repolarization phase of the VER (VER T-slew). Since all our recordings have been performed with the same pacing rate, the corrected trend curve and the trend curve of the VER T-slew parallel each other very well for our two patients. However, due to the lack of high-grade rejection during the follow-up of both patients, significant correlation between EMB and IEGM could not be achieved. For the first patient, a slight decrease of VER T-slew was possibly related to the episodes of low-grade rejection as detected by EMBs, as opposed to the second patient for whom the lead position was only suboptimal. For the latter, the low level of depolarization amplitude of VER could also be related to the end diastolic dilatation of the right ventricle as assessed through a systematic echocardiography follow-up. Although our results are only preliminary, they do make us confident to pursue a clinical trial on our heart transplant population.

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