Remote Monitoring Leads to Early Recognition and Treatment of Critical Arrhythmias in Adults After Atrial Switch Operation for Transposition of the Great Arteries

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Background: Adults with transposition of the great arteries (TGA) after atrial switch repair have an increased risk for arrhythmia and sudden cardiac death. We analyzed whether a remote monitoring (RM) system as part of an implantable cardiac device contributes to timely recognition and improved treatment of critical arrhythmias in these patients.

Methods and Results: All consecutive TGA patients (n=11) requiring a pacemaker or cardiac resynchronization therapy with or without implantable cardioverter defibrillator between 2008 and 2011 were included. RM-detected arrhythmia, abnormality of device integrity and reaction time from event transmission until acknowledgement via email and clinical decision making were analyzed and compared to a control group (n=21). In 10 patients (91%) 17 arrhythmias were detected, 8 patients (80%) indicated no symptoms. In the RM group time interval from transmission to acknowledgement was 2.4 days (range, 0–4.5 days). Clinical decision-making was advanced by a mean of 77.5 days (range, 10–197 days) compared with conventional follow-up and identified adaption of anti-arrhythmic medication in 8, electrical cardioversion in 2, overdrive pacing in 1 and radiofrequency ablation in 2 patients. A coronary sinus lead fracture was identified in 1 patient followed by successful replacement.

Conclusions: RM enables early detection of tachyarrhythmia followed by optimization of medical treatment and potentially life-saving anti-tachycardic intervention in adults after atrial repair of TGA. (Circ J 2014; 78: 450–456)

Key Words: Arrhythmia; Cardiac resynchronization therapy; Congenital heart disease; Pacemaker

After atrial switch operation (ASO; either the Mustard or Senning procedure for transposition of the great arteries; TGA), patients are at increased risk of arrhythmia. Ventricular and supraventricular arrhythmia as well as dysfunction of the systemic right ventricle (RV) have been shown to be associated with sudden death.3,4 Sick sinus syndrome and higher degree atrioventricular block may necessitate an anti-bradycardic pacemaker system.4 Implantable cardioverter defibrillators (ICD) may become necessary in selected patients with ventricular arrhythmia.5,6

Patients undergoing device implantation are followed up by a schedule that ranges from 3 to 6 months for ICD and up to 12 months for pacemakers.7 The absence of information about the occurrence or the progression of a tachyarrhythmia between scheduled outpatient visits is a major limitation of conventional follow-up. Important data, recorded and stored in the device memory, which may warrant further diagnostic or therapeutic interventions, remain concealed until the next visit.

Pacemakers, ICD and cardiac resynchronization therapy devices with (CRT-D) or without an ICD (CRT) equipped with a remote monitoring (RM) system are able to overcome this lack of information by providing automatically transmitted data about arrhythmias and about implant and lead status on a daily basis including storage and transmission of intracardiac electrocardiograms (ECG).8

The aim of the present study was to clarify if a cardiac device-integrated RM system in TGA patients following atrial switch repair enables physicians to improve medical care by early recognition of arrhythmias or lead-related problems.

Methods

Patients

After approval from the institutional ethics board, patients were
enrolled from 2 centers (Grown-up Congenital Heart Disease Unit, Medical University Graz and German Pediatric Heart Centre, St. Augustin). In total 11 consecutive adult patients who had ASO for TGA (mean age at operation, 0.6 years; range, 0.1–1.2 years) requiring implantation or revision of a pacemaker, CRT or CRT-D were included in this prospective observational cohort study. All patients gave informed consent before the study. The study group is a subset of 107 TGA patients after ASO who are regularly followed up at our institutions. A further subset of 21 TGA patients served as a control group. They all had a conventional cardiac device follow-up without RM on a 6-monthly basis during the study period.

Medical records of all patients were reviewed for collection of demographics, medical and surgical details including previous ECG and 24-h Holter ECG. Cardiac device follow-up visits were planned 4 weeks and 3 months after implantation followed by 6-monthly intervals including clinical examination, ECG and transthoracic echocardiography. In all patients systolic RV function was assessed on echocardiography via visual assessment as normal (ejection fraction ≥50%), mildly (40–49%), moderately (30–39%) or severely depressed (≤30%).

Values of 10–16 mm indicated mildly–moderately reduced; and <10 mm, moderately–severely reduced.

Tri-cuspid annular plane systolic excursion was measured as described previously. In patients with ASO the cuspid annular plane systolic excursion was measured as described previously.

When activated following patient consent, Home monitoring (Biotronik, Berlin, Germany) transmits selected data to a home-based quad-band cellular phone (Cardiomessenger) on a daily basis. From there the data are transmitted to a dedicated service center located in Berlin via the GSM network, where it is stored on a secured internet platform. Data that exceed the limits set by the physician are immediately and automatically transmitted via email.

All messages created by the RM system were documented. Monthly recorded intracardiac electrograms and the first message received after each in-house follow-up were classified as routine message. Adverse events were defined as non-sustained (<30 s) or sustained (>30 s) ventricular or supraventricular tachycardia, atrial flutter, ventricular flutter or fibrillation, ventricular ectopics and abnormalities concerning the system integrity of the cardiac device. The parameters to initiate an event had been set to the most sensitive limits and modified individually during follow-up only if repeated messages of the same kind did not display additional information. In case of an event showing arrhythmias or changes of the device’s parameters, the patients were called by phone within 2 days following acknowledgement of the event via email. The date was defined according to clinical and diagnostic relevance.

The detection time from transmission of a message by the RM system via email (RM group) or occurrence of an arrhythmia stored in the device memory (control group) until acknowledgement by the physician was recorded (B.N., P.Z., M.K.) on the internet platform and during standard device follow-up, respectively, was documented. The reaction time from the transmission or occurrence of an adverse event until an advanced in-house visit as well as the gain of time between advanced and originally scheduled conventional follow-up were calculated for all events.

### Results

#### RM Group

From June 2008 to December 2011 11 adult patients (9 male;
Adverse Events
During a mean follow-up time of 1.9 years (range, 0.3–3.6 years) 99% of all transmissions reached the internet platform daily. Via email 313 RM transmissions were received, of which 262 were routine messages and 51 (16.2%) were about adverse events. Of the acknowledged 51 events 33 were repeated messages of the same kind without adding additional information. The remaining 18 adverse events were documented in 10 patients with up to 3 adverse events per patient occurring at a mean of 236 days (range, 3–918 days) after the implantation of the cardiac device (Table 3).

RM-related arrhythmia detection was followed by initiation

| Table 3. Adverse Events Documented by the RM System and Actions Taken |
|---------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Patient | 1st event After implant (days) | Actions taken After implant (days) | 2nd event | Actions taken | 3rd event | After implant (days) | Actions taken | Event-free follow-up (days) |
| 1 | Sustained SVT† | 45 | β-blocker suggested, refused | 1st event | 420 | Synchronized cardioversion AFI | 478 | Re-RFA | 289 |
| 2 | VT‡ | 12 | < β-blocker | 2nd event | 672 | Overdrive pacing; RFA | 95 |
| 3 | None | 2 | Overdrive pacing; β-blocker † | | | | |
| 4 | AFI | 278 | Synchronized cardioversion; β-blocker † | | | | |
| 5 | VT † | 3 | Overdrive pacing; β-blocker † | 2nd event | 208 | β-blocker † | 486 |
| 6 | VT | 34 | β-blocker→<Amiodarone> SVT † | | | |
| 7 | Sustained SVT† | 5 | β-blocker→<Amiodarone> | | | |
| 8 | AFI | 33 | Synchronized cardioversion; VFI self-limited† | | | |
| 9 | VEB=100 | 66 | β-blocker continued, flecainide | | | |
| 10 | VEB≤50/h | 20 | β-blocker> CS-lead fracture | | | |

†Newly detected arrhythmias; ‡symptomatic arrhythmias.
<, medication started; >, medication discontinued; †, dose increased; ‖, dose decreased; →, dose continued. CPR, cardiopulmonary resuscitation; CS, coronary sinus; RFA, radiofrequency ablation; SVT, supraventricular tachycardia; VFI, ventricular flutter. Other abbreviations as in Table 1.
Remote Monitoring After ASO

of anti-arrhythmic drug therapy or uptitration of the dosage in 8 patients. Medical therapy could be discontinued in 2 patients with CRT after RV function and functional NYHA class improved without recurrence of ventricular tachycardia (patient 7) and the RM system notified significant reduction of ventricular ectopics <50/h (patient 11). Despite a previous radiofrequency ablation (RFA), patient 4 required 2 consecutive synchronized cardioversions within 5 months for recurrent episodes of atrial flutter (Figure 1). RFA was performed successfully in patients 4 and 5, at 6 and 4 weeks, respectively, after RM transmission without recurrence of atrial flutter to date.

Before inclusion into the study 2 patients had a persistent episode of atrial flutter of unknown duration (Table 1). Patient 4 was noted to have a thrombus formation on his atrial pacemaker lead when he came for a routine follow-up visit and required warfarin therapy before his first RFA could be performed. Patient 5 presented in cardiac failure requiring intensive care management and had to be hospitalized for 19 days.

**Figure 1.** (A) Patient 4 with 3 recurrent episodes of atrial flutter. Sinus rhythm was achieved after synchronized cardioversion at subsequent follow-up. Aburd, mean atrial burden per week; FU, follow-up; P-IEGM, periodic intracardiac electrogram. (B) Intracardiac electrogram of patient 4 that documents atrial flutter. Ars, atrial refractory sense; As, atrial sense; FFP, far field protection; Vp, ventricular pace.
In patient 11 a sudden increase in the coronary sinus lead impedance was noticed 918 days after implantation of CRT device. A lead fracture was able to be confirmed at an advanced in-house visit. Given that he had significant reduction of ventricular ectopics after device implantation it was decided to replace the lead. Patient 7 had a syncope during his work as a lumberman, requiring cardiopulmonary resuscitation 680 days following implantation of a CRT-D, but no adverse event was documented by the RM system. On that day the patient had febrile diarrhea with only minimal fluid intake while he continued to take his diuretics. This episode was interpreted as syncope due to acute hypovolemia.

In the control group 16 tachyarrhythmias (atrial, n=10; ventricular, n=6) occurred in 12 patients. In 2 patients with previously documented asymptomatic non-sustained supraventricular tachycardia, sudden cardiac death occurred during the follow-up period. Three patients presented with symptoms, 2 of them with cardiac failure due to long-standing atrial tachycardia and 1 with stroke after persistent asymptomatic atrial fibrillation.

Detection and Reaction Times

In the RM group the acknowledged routine intracardiac electrograms confirmed normal pacemaker function in all cardiac devices. The 18 adverse events (5.8% of all transmissions, 35% of all adverse events) resulted in 18 advanced in-house visits and could be approved as correctly transmitted in all cases by analyzing the respective intracardiac electrograms and the device settings. Detection and reaction times for all messages are shown in Figure 2. In the 3 patients with first episodes of atrial flutter and in the patient with self-limiting ventricular flutter the reaction time was ≤7 days. Longest reaction time was 32 days in patient 4 with a third recurrence of atrial flutter 8 weeks after preceding synchronized cardioversion despite high-dose β-blocker therapy. Because of his good clinical condition we decided to wait for RFA, which was performed with success 6 weeks later. Tachyarrhythmia diagnosis and thus clinical decision-making could be carried out up to 6 months earlier as a consequence of RM detection (mean gain of time, 77.5 days; range, 10–197 days) if compared to a conventional standard follow-up schedule in the
same RM patients. In the control group there was a time gain in 3 patients coming for an advanced in-house follow-up visit due to symptoms. In the other 9 patients the arrhythmias were diagnosed a mean of 108.5 days after occurrence during subsequent follow-up visits (Table 4).

Discussion

In this study, we have investigated the benefit of a wireless remote RM system as part of a cardiac device for adult patients with TGA following atrial switch repair. We found tachyarrhythmias in 10 of the 11 investigated patients (91%), which is a higher incidence of arrhythmias than previously reported.1-4,15 Half of the arrhythmias (53%) were documented for the first time. Short RM-triggered detection times allowed rapid acknowledgement of actionable events and potentially life-saving interventions.

With a mean gain of time of 77.5 days clinical decisions could be made much earlier when compared to a standard follow-up within the RM group. A previous multicenter trial was able to show that RM led to early detection of adverse events by up to within the RM group. A previous multicenter trial was able to be made much earlier when compared to a standard follow-up interventions.

In the control group tachyarrhythmias were noticed early only when patients presented with symptoms. As a consequence detection time in asymptomatic patients was much longer compared to the RM group. The majority of the study patients (80%) as well as the control group (75%) were asymptomatic during sustained or non-sustained arrhythmias. Absence of symptoms does not seem to rule out potentially life-threatening tachyarrhythmias. This was documented by the RM system in this group of asymptomatic patients as atrial flutter, sustained supraventricular tachycardia and even short ventricular flutter. The 2 symptomatic patients (20%) conceded symptoms only after they were asked at the time they were contacted after an adverse event alert. A study that investigated asymptomatic pediatric patients after the Mustard operation noted that absence of symptoms did not rule out relevant arrhythmias.17 Kohno et al reported on 20 adult patients with a DDD pacemaker system, of whom 75% developed asymptomatic atrial tachycardia or atrial flutter/fibrillation during a mean follow-up period of 17 months.18 Two of the present 3 RM patients with atrial flutter presented with a thrombus formation on an atrial lead and in cardiac failure, respectively, due to unrecognized atrial flutter before inclusion into the study.

The clinical significance of non-sustained vs. sustained tachyarrhythmias in patients with TGA following atrial switch repair remains unclear, but RM-related continuous monitoring of the heart rhythm gave important information about progression or decrease of arrhythmias and effectiveness of any type of anti-arrhythmic therapy in the present patients. The present study has found that RM-based monitoring is able to prevent morbidity by reducing the number of potentially life-threatening complications of long-standing tachycardia such as cardiac failure or thromboembolic events. To date, however, it is unclear if it has an impact on mortality by decreasing the risk of sudden cardiac death in comparison with a conventional control group.

It has been shown that remote technology can save on costs for follow-up evaluation or hospitalization.19,20 In the present study additional in-house visits were necessary because of adverse events. This improves care, but to date it is unclear if prevention of acute events may be associated with reduction of follow-up visits and hospital admissions and thus cost-saving in the long term in this high-risk patient group.21 A recent randomized trial of long-term RM showed that RM is as safe as standard follow-up in adult pacemaker patients with structurally normal hearts as well as those with structural heart disease.22 It enables the early detection of adverse events such as arrhythmias and lead-related complications compared with conventional monitoring and allows early optimization of medical therapy in patients with ICD, CRT and pacemakers.20,22-25

In patients with congenital heart defects experience with an RM system is limited. Zartner et al showed that an RM system was favorable for modifying anti-arrhythmic therapy in 8 children and young adults with various forms of congenital heart disease.26 To our knowledge the present study shows for the first time that an RM system is useful for physicians caring for patients with TGA after ASO.

The RM system had been proven to be technically reliable.27,28 During the study period 18 adverse events with 17 tachyarrhythmias and 1 lead fracture could be confirmed precisely in all 10 affected patients after they were called in for an advanced in-house visit for analysis of the appropriate intracardiac electrograms and the device settings. During the scheduled follow-up visits no actionable events were noted, apart from the already known previously transmitted events. Continuous RM may also have the advantage of better classification of unexplained events. In 1 of the present patients with syncope we were able to exclude an arrhythmia as a possible cause.

Patient compliance was good, with 99% of daily transmissions reaching the internet platform, which is likely to be attributable to the mobile wireless RM system used. This is similar to the 91% of daily transmissions reported in the TRUST trial using the same system as in our study.29 Relevant non-compliance was seen in other RM systems requiring patient interaction for manual transmissions.29

Only 2 of the 5 patients with a CRT device had a ventricular tachycardia documented during the study period, and 2 patients had reduction of ventricular ectopics. This may be a consequence of an improvement of RV function observed in the present patients, similarly to the results of CRT in congenital heart defects previously published.30,31 Intrathoracic impedance monitoring in CRT-D may become an additional tool for early recognition of congestive heart failure, arrhythmic events and preemptive anti-arrhythmic therapy in the future.32,33

Study Limitations

This was a prospective observational cohort study with a small patient number that did not allow randomization between remote control and standard follow-up. A selection bias cannot be excluded because the present patients with CRT or CRT-D may have had a higher risk for ventricular tachyarrhythmias compared to patients with pacemakers only or without any device. Criteria to select event alerts, adjust device programming and to modify anti-arrhythmic drug therapy were defined at the beginning of the study and may in part have depended on subjective clinical assessment.

Conclusions

A continuous wireless RM system allows reliable and early diagnosis of tachyarrhythmias compared to conventional follow-up in TGA patients following atrial switch repair requiring implantable cardiac devices. The majority of patients were asymptomatic at the time of adverse events. Future use of RM devices may lead to improved anti-arrhythmic treatment and enhanced safety of cardiac device function in the long term for
these patients.

Disclosures

B.N.: none; J.J.: supported by the project (Ministry of Health, Czech Repub-

clic) for conceptual development of research organization 00064203 (Uni-

versity Hospital Motol, Prague, Czech Republic); M.K., R.M., W.S.,

V.S., A.G., P.Z.: none. The authors declare that they have no conflict of

interest.

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