Background—Catheter ablation of the slow conducting pathway (SP) is treatment of choice for atrioventricular nodal reentrant tachycardia (AVNRT). Although there are abundant data on AVNRT ablation in adult patients, little is known about the long-term results ≥3 years after AVNRT ablation in pediatric patients.

Methods and Results—Follow-up data from 241 patients aged ≤18 years who had undergone successful AVNRT ablation were analyzed. Median age at ablation had been 12.5 years, and median follow-up was 5.9 years. Radiofrequency current had been used in 168 patients (70%), whereas cryoenergy had been used in 73 patients (30%). Procedural end point of AVNRT ablation had been either SP ablation (no residual dual atrioventricular nodal physiology) or SP modulation (residual SP conduction allowing for a maximum of one atrial echo beat). After the initial AVNRT ablation, calculated freedom from AVNRT was 96% at 1 year, 94% at 3 years, 93% at 5 years, and 89% at 8 years. Age, sex, body weight, the choice of ablation energy, and the procedural end point of AVNRT ablation did not impact freedom from AVNRT. Six of 22 AVNRT recurrences (27%) occurred ≥5 years after ablation. No late complications including atrioventricular block were noted.

Conclusions—Cumulatively, catheter ablation of AVNRT continued to be effective in >90% of our pediatric patients during the long-term course. A significant part of recurrences occurred ≥5 years post ablation. Body weight, energy source, and the end point of ablation had no impact on long-term results. No adverse sequelae were noted. (Circ Arrhythm Electrophysiol. 2016;9:e004264. DOI: 10.1161/CIRCEP.116.004264.)

Key Words: adolescent • atrioventricular node • AV nodal reentrant tachycardia • catheter ablation • children • long term course

Catheter ablation of the slow conducting pathway (SP) of the atrioventricular (AV) node is the recommended treatment for AV nodal reentrant tachycardia (AVNRT) in children and adults. With both radiofrequency and cryoenergy, high procedural success rates of 98% to 100% have been reported.1,2 In adult patients, freedom from AVNRT has been achieved in 95% after radiofrequency ablation and in 90% after the use of cryoenergy 1 year after the initial ablation procedure.3 In children and adolescents, data from the pediatric radiofrequency catheter ablation registry acquired more than a decade ago reported a significant number of recurrences with 71% freedom from AVNRT 3 years post ablation.4 However, recent follow-up studies of pediatric patients after AVNRT ablation reported freedom from AVNRT between 84% and 100% with radiofrequency,2,5 and between 78% and 93% with cryoenergy,2,6 respectively. These studies on a limited number of pediatric patients analyzed data on the follow-up of 1 to 3 years post ablation. Little information on the course beyond 3 years after AVNRT ablation in pediatric patients has been published.

The purpose of the present study was to evaluate the long-term course of pediatric patients after AVNRT ablation at our institution. Foci of interest were (1) impact of the primary procedural end point (SP ablation versus SP modulation) on long-term success, (2) impact of body weight on long-term safety and success, (3) incidence and timing of late AVNRT recurrence, and (4) incidence of late AV block or new tachyarrhythmias attributable to AVNRT ablation.

See Editorial by Kirsh

Methods

Patients

Between October 2002 and May 2014, a total of 249 children and adolescents <18 years of age had undergone catheter ablation for AVNRT at our institution. Procedural data and primary success rates and acute complications have recently been published.1 Patients, in whom AVNRT ablation failed (n=5), were not enrolled into the present study: although a repeat ablation was offered for all 5 subjects with procedural failure, 3 out of 5 patients were lost during follow-up and 1 individual decided against a repeat procedure. Additionally, 3 patients with permanent AV block immediately after radiofrequency ablation (n=3)7 were excluded. Finally, follow-up data ≥1 year after AVNRT ablation of 241 patients were included into this study. Follow-up data of patients after primary AVNRT ablation procedures were exclusively considered to avoid bias by including follow-up...
WHAT IS KNOWN

- Catheter ablation is an effective therapy for AVNRT in pediatric and adult patients.
- After AVNRT ablation in children, freedom from AVNRT is between 78% and 100% with a follow-up time of 1 to 3 years.
- Most AVNRT recurrences were noted within the first year after ablation.

WHAT THE STUDY ADDS

- Somewhat surprisingly, a substantial portion of AVNRT recurrences occurred late, sometimes even after 5 years after ablation.
- Age and body weight at the time of ablation, the choice of ablation energy source, and the acute procedural end point did not influence likelihood of AVNRT recurrence.

Data of repeat procedures. Data of patients with AVNRT recurrence and a repeat ablation procedure were, therefore, analyzed separately. Time of recurrence was defined as either first ECG documentation of supraventricular tachycardia (SVT) or inducibility of AVNRT on re-electrophysiological study (EPS) in patients with symptoms of tachycardia recurrence.

Follow-up data were obtained from follow-up visits at our institution, and questionnaires sent to the patients. In case of missing follow-up data, patients were additionally contacted by telephone.

Median age at the time of the procedure had been 12.5 years; median body weight had been 48.5 kg. Table 1 provides patients’ characteristics. Congenital heart disease (CHD) with potential impact on catheter ablation of AVNRT was present in 4 patients (complex CHD, n=2 and Ebstein anomaly of the tricuspid valve, n=2). Patients with repaired CHD and normal intracardiac anatomy (ie, patients after surgical or catheter-guided closure of atrial or ventricular septal defects, closed patent ductus arteriosus, and status post balloon valvuloplasty of aortic/pulmonic stenosis) were not considered to have CHD relevant to this study.

The study was approved by the institutional review board and fully complies with the Declaration of Helsinki. Informed consent was obtained from the study’s subjects.

Electrophysiological Study and Catheter Ablation

The institutional approach of EPS and catheter ablation of AVNRT has been described before. A nonfluoroscopic catheter navigation system (LocalA: Medtronic, Inc, Minneapolis, MN and Ensite NavX; St Jude Medical, St Paul, MN) had been used in all cases. Ablation was performed if dual AV node physiology allowing for more than one atrial echo beat was present or if AVNRT could be induced. A combined electroanatomic approach to identify target sites for ablation was used regardless of the energy source. This approach was not changed by time while all procedures were supervised by one senior operator (TP). Selection of the primary energy source had been at the discretion of the operator (n=4). Data were used for the purpose of the study, although cases were not contemporaneous.

Radiofrequency was primarily used until 2004; cryoenergy was the preferred energy source between 2004 and 2008. Afterward, again radiofrequency was used as primary energy source because of prolonged procedure duration and unproven superiority of cryoenergy and costs. Since then, indications for the use of cryoenergy included (1) patients with CHD, (2) uncertain or atypical localization of the conduction system, and (3) patients with structurally normal hearts and SP localization with presumed high risk of AV block. In patients in whom radiofrequency and cryoenergy had been used during the same procedure (n=281), the energy used to achieve the ablation end point was considered the relevant energy. Procedural end point of AVNRT ablation had been either SP ablation (no residual dual AV nodal physiology) or SP modulation (residual SP conduction allowing for a maximum of one atrial echo beat) isopropenol provocation (0.001 μg/kg/min). Diagnosis of AVNRT recurrence was established either by ECG documentation of typical SVT or—in patients with symptoms of AVNRT recurrence—presence of dual AV node physiology allowing for more than one atrial echo beat during repeat EPS.

Statistics

Statistical analysis was performed using SPSS 22.0 software (IBM, New York, NY). Numeric data are presented as median and interquartile range.

For freedom from AVNRT analyses, the Kaplan–Meier method was used with the time of AVNRT ablation serving as time 0. Subjects not experiencing AVNRT recurrence were censored event free at the time of the last clinical evaluation. The influence of additional variables on freedom from AVNRT was computed with Cox regression and log-rank test. A value of *P*<0.05 was defined as the level of statistical significance.

Results

Data from 241 patients with a median follow-up of 5.9 (25th–75th percentiles: 3.6–8.2) years after AVNRT ablation were analyzed. After the initial procedure, overall long-term freedom from AVNRT was noted in 219 individuals (90.9%), whereas AVNRT recurred in 22 patients (9.1%). Among these

### Table 1. Patients Characteristics (n=241)

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>All Patients, n=241</th>
<th>Long-Term Success (n=219)</th>
<th>Relapse (n=22)</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
<th>Cox Regression P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex, n (%)</td>
<td>129 (53)</td>
<td>115 (53)</td>
<td>14 (64)</td>
<td>1.75 (0.73–4.2)</td>
<td>0.20</td>
</tr>
<tr>
<td>Age (median), y (25th–75th percentiles)</td>
<td>12.5 (10.1–15.2)</td>
<td>12.5 (10.2–15.3)</td>
<td>11.7 (9.4–14.1)</td>
<td>0.96 (0.86–1.08)</td>
<td>0.53</td>
</tr>
<tr>
<td>Body weight (median), kg (25th–75th percentiles)</td>
<td>48.5 (25.2–60.3)</td>
<td>48.5 (35.4–60)</td>
<td>50 (30.5–61.3)</td>
<td>1.0 (0.98–1.02)</td>
<td>0.98</td>
</tr>
<tr>
<td>Body weight &lt;25 kg, n (%)</td>
<td>24 (10)</td>
<td>21 (9.6)</td>
<td>3 (14)</td>
<td>0.84 (0.25–2.84)</td>
<td>0.78</td>
</tr>
<tr>
<td>Body height (median), cm (25th–75th percentiles)</td>
<td>158 (140–170)</td>
<td>158 (140–170)</td>
<td>161 (139–169)</td>
<td>1.01 (0.98–1.03)</td>
<td>0.68</td>
</tr>
<tr>
<td>Congenital heart defects, n (%)</td>
<td>4 (1.6)</td>
<td>3 (1.3)</td>
<td>1 (0.4)</td>
<td>1.59 (0.21–11.86)</td>
<td>0.69</td>
</tr>
<tr>
<td>Complex cardiac malformation</td>
<td>2 (0.8)</td>
<td>1 (0.4)</td>
<td>1 (0.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ebstein anomaly</td>
<td>2 (0.8)</td>
<td>2 (0.9)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Number of patients and percentage (n [%]) or median and interquartile range (25th–75th percentiles) are shown where appropriate. The influence on AVNRT recurrence has been estimated with Cox regression. AVNRT indicates atrioventricular nodal reentrant tachycardia.

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**WHAT THE STUDY ADDS**

- Somewhat surprisingly, a substantial portion of AVNRT recurrences occurred late, sometimes even after 5 years after ablation.
- Age and body weight at the time of ablation, the choice of ablation energy source, and the acute procedural end point did not influence likelihood of AVNRT recurrence.

**Electrophysiological Study and Catheter Ablation**

The institutional approach of EPS and catheter ablation of AVNRT has been described before. A nonfluoroscopic catheter navigation system (LocalA: Medtronic, Inc, Minneapolis, MN and Ensite NavX; St Jude Medical, St Paul, MN) had been used in all cases. Ablation was performed if dual AV node physiology allowing for more than one atrial echo beat was present or if AVNRT could be induced. A combined electroanatomic approach to identify target sites for ablation was used regardless of the energy source. This approach was not changed by time while all procedures were supervised by one senior operator (TP). Selection of the primary energy source had been at the discretion of the operator (n=4). Data were used for the purpose of the study, although cases were not contemporaneous.

Radiofrequency was primarily used until 2004; cryoenergy was the preferred energy source between 2004 and 2008. Afterward, again radiofrequency was used as primary energy source because of prolonged procedure duration and unproven superiority of cryoenergy and costs. Since then, indications for the use of cryoenergy included (1) patients with CHD, (2) uncertain or atypical localization of the conduction system, and (3) patients with structurally normal hearts and SP localization with presumed high risk of AV block. In patients in whom radiofrequency and cryoenergy had been used during the same procedure (n=281), the energy used to achieve the ablation end point was considered the relevant energy. Procedural end point of AVNRT ablation had been either SP ablation (no residual dual AV nodal physiology) or SP modulation (residual SP conduction allowing for a maximum of one atrial echo beat) isopropenol provocation (0.001 μg/kg/min).

Diagnosis of AVNRT recurrence was established either by ECG documentation of typical SVT or—in patients with symptoms of AVNRT recurrence—presence of dual AV node physiology allowing for more than one atrial echo beat during repeat EPS.

**Statistics**

Statistical analysis was performed using SPSS 22.0 software (IBM, New York, NY). Numeric data are presented as median and interquartile range.

For freedom from AVNRT analyses, the Kaplan–Meier method was used with the time of AVNRT ablation serving as time 0. Subjects not experiencing AVNRT recurrence were censored event free at the time of the last clinical evaluation. The influence of additional variables on freedom from AVNRT was computed with Cox regression and log-rank test. A value of *P*<0.05 was defined as the level of statistical significance.

**Results**

Data from 241 patients with a median follow-up of 5.9 (25th–75th percentiles: 3.6–8.2) years after AVNRT ablation were analyzed. After the initial procedure, overall long-term freedom from AVNRT was noted in 219 individuals (90.9%), whereas AVNRT recurred in 22 patients (9.1%). Among these...
22 subjects, AVNRT recurred between 36 days and 9.9 years. For the whole study cohort, calculated freedom from AVNRT was 96% at 1 year, 94% at 3 years, 93% at 5 years, and 89% at 8 years post ablation. A total of 9 out of 22 recurrences (41%) occurred within the first year post ablation, whereas 6 out of 22 recurrences (27%) occurred ≥5 years after the procedure. Table 2 depicts patients with AVNRT recurrence. Sex, age, and body weight at the time of ablation and the presence of CHD did not influence recurrence on Cox regression analysis (Table 1). The choice of ablation energy (radiofrequency energy versus cryoenergy) did not impact freedom from AVNRT (log-rank \( P=0.50 \); Figure [A]).

Impact of Low Body Weight
A total of 25 children had a body weight ≤25 kg at the time of AVNRT ablation. There was no difference in long-term freedom from AVNRT between children with a body weight ≤25 and >25 kg (Figure [B]).

Procedures With Radiofrequency Energy
In 168 patients (70%), radiofrequency energy had been used for AVNRT ablation. Figure [A] shows Kaplan–Meier analysis of freedom from AVNRT after catheter ablation. AVNRT recurred in 12 patients (7.1%) and in 6 out of 12 patients within the first 12 months post ablation. After radiofrequency ablation, calculated freedom from AVNRT was 96% at 1 year, 95% at 3 years, 95% at 5 years, and 90% at 8 years post ablation. The primary procedural end point (SP ablation versus SP modulation) using radiofrequency energy did not impact long-term freedom from AVNRT (Figure [C]; log-rank \( P=0.35 \)).

Procedures With Cryoenergy
Cryoenergy was used in 73 patients (30%). AVNRT recurred in 10 patients (13.7%) and in 3 out of 10 patients within the first 12 months post ablation. After cryoablation, calculated freedom from AVNRT was 96% at 1 year, 90% at 3 years, 89% at 5 years, and 85% at 8 years post ablation. As in the radiofrequency procedures, the primary procedural end point did not impact long-term freedom from AVNRT (Figure [D]; log-rank \( P=0.088 \)).

Long-Term Follow-Up of Patients With AVNRT Recurrence
After the initial catheter ablation, AVNRT recurred in 22 patients (Table 2). A second SP ablation was performed in 21 patients although 18 out of 21 patients underwent the procedure at our center. Of those, AVNRT recurred again in 5 out of 18 patients (28%), whereas long-term freedom from AVNRT was achieved in 13 out of 18 individuals (72%). Two out of 5 patients with a second AVNRT recurrence were either lost during further follow-up or underwent repeated ablations at another center. Two out of 5 patients decided deliberately against a third ablation. A third AVNRT ablation was performed in only one patient who is currently free from AVNRT for >1.6 years.

Without respect to follow-up time, overall freedom from AVNRT was achieved in 233 out of 241 patients (97%), with 8 out of 241 individuals (3%) who were either lost to follow-up or decided against a repeat AVNRT ablation.

Patients With Late AVNRT Recurrence
Late AVNRT recurrence, that is, >5 years after primary ablation, was noted in 6 patients (Table 2). A total of 4 individuals underwent repeat EPS and ablation, whereas 2 patients underwent a repeat AVNRT ablation at another center. In all those 4 patients, who had a repeat procedure at our institution, dual AV nodal physiology with more than a single atrial echo beat was evident, and typical AVNRT could be induced in 3 of them. Repeat radiofrequency ablation was performed in 2 patients, resulting in SP ablation, whereas SP modulation by cryoenergy application was achieved in the remaining 2 individuals of whom 1 had Ebstein anomaly of the tricuspid valve.

Late Complications/Secondary Arrhythmias
In the total group of 241 patients, no late AV block occurred during follow-up.

Palpitations reported by the patients without ECG documentation of SVT lead to a total of 7 repeat EPS. Dual AV node physiology allowing for a maximum of one atrial echo beat was found in 5 out of 7 patients. In the remaining 2 out of 7 patients, no dual AV node physiology was found on EPS. By definition, all those 7 patients were not considered to have AVNRT recurrence.11

In 2 additional patients, arrhythmias other than AVNRT occurred during follow-up: SVT occurred in a 15-year-old boy 4 years after AVNRT ablation. In this patient, SVT was caused by a left lateral accessory pathway, which had not been noted during primary EPS. Successful ablation of the pathway was performed. There was no evidence for dual AV nodal physiology in this patient. The second patient (female patient, 13 years old) had already undergone repeat SP ablation for AVNRT recurrence. Six months later, she presented again with SVT. During the third EPS, however, focal atrial tachycardia arising from the lateral left atrium was noted. In both cases, secondary arrhythmia was not attributable to AVNRT ablation.

Discussion
Most studies focusing on mid- or long-term success of catheter ablation for AVNRT in children and adolescents showed higher recurrence rates when compared with data from adult populations. Although radiofrequency/cryoablation of AVNRT continued to be successful in 95% and 90% of adult patients, respectively3 (median follow-up of 10.5 months), a recent nationwide multicenter analysis on radiofrequency ablations of AVNRT in pediatric patients in the Czech Republic yielded a long-term success of 84.4% of the initial procedures and an overall success of 95.8% when including repeat procedures (median follow-up 14 months).3 In line with this report, long-term success rate after AVNRT ablation in our center was almost 91% after the initial procedure and 97% when including repeat procedures.

Previous studies reported AVNRT recurrence predominantly within the first year after ablation.8,11,12 Providing data on a significantly longer follow-up, we found a substantial portion of late recurrences even >5 years after ablation.
As previous studies reported on a follow-up of 2 to 3 years post ablation,2,5–7 long-term freedom from AVNRT >3 years after ablation might have been systematically overestimated. A similar high rate of late AVNRT recurrence has not yet been described in adult cohorts with comparatively long follow-up.13

This new finding raises some questions about the pathogenesis of AVNRT. Although AVNRT is rare in infancy, the incidence of AVNRT increases during the first decade of life.14,15 The current concept of AVNRT depends on the presence of a slow (SP) and fast (FP) conducting AV pathway with a longer fast pathway effective refractory period.11,16 With growth, the distance between the SP and FP areas representing 2 sides of Koch triangle and 2 geometrically distant yet electrically interacting pathways increases.17 In a computer model of the AV node, AVNRT could only be induced when the SP area was made wide enough.18 Developmental changes of the geometry of Koch triangle could, therefore, be responsible for AVNRT occurrence and for late recurrence of AVNRT.

Additionally, adolescents were found to have a significantly longer fast pathway effective refractory period when compared with small children,19 whereas a substantial shortening of the fast pathway effective refractory period after successful SP ablation has been described in children.20 It might be possible that an increase of fast pathway effective refractory period several years after AVNRT ablation together with geometric changes of Koch triangle contributes to late AVNRT recurrence. However, no distinct anatomic structures representing SP or FP have yet been identified, and both structures are thought to be clusters of transitional cells adjacent to the compact AV node.21 At the present time, it is unknown, how much of these cell clusters have to be destroyed entirely by ablation to reach the desired result of SP modulation or ablation, respectively. Finally, it may be argued that the main effect of ablation is the modification of electric interaction between the SP and FP.

In this context, it is seems possible that something that has been ablated and presumably healed for years suddenly becomes active again >5 years later.

Many studies have tried to identify risk factors for recurrence after AVNRT ablation in children. Although no difference was found about ablation end point, that is, complete SP ablation versus SP modulation,6,22 the choice of ablation energy has been proven to influence long-term efficacy: cryoenergy was associated with a higher AVNRT recurrence rate, but the procedural risk of permanent AV block was lower.
when compared with radiofrequency energy.\textsuperscript{6,23,24} In accordance with previous reports,\textsuperscript{22,25,26} we did not find any difference in long-term recurrence rates between patients with SP ablation versus SP modulation at the end of the procedure. Because the number of patients with AVNRT recurrence was low (n=22), any analysis on factors for recurrence has low statistical power.

Previous studies identified low body weight as an independent risk factor for procedure-related complications during pediatric radiofrequency ablation.\textsuperscript{27,28} Our long-term follow-up data, however, do not show any late complications attributable to AVNRT ablation. Additionally, low body weight was not associated with AVNRT recurrence in the present study. It is an important finding that no late AV block occurred in our pediatric cohort during a median follow-up of almost 6 years. In elderly patients, development of late AV block years after AVNRT ablation has been described.\textsuperscript{29} Secondary arrhythmias, which might have been induced by atrial scarring after ablation,\textsuperscript{30} were not observed among our patients. According to our findings, AVNRT ablation in pediatric patients was a safe procedure with no relevant late morbidity.

Figure. Kaplan–Meier curves depicting freedom from atrioventricular nodal reentrant tachycardia (AVNRT) 10 y post ablation. Vertical bars denote censored data.
Limitations
The study is limited by its retrospective design and the number of patients enrolled. There was 1 out of 22 patients with AVNRT recurrence who refused repeat EPS. A different SVT substrate (not noted at the initial EPS) cannot completely be excluded in this individual. Additionally, 3 out of 22 patients with AVNRT recurrence underwent a repeat EPS at another center using another EP protocol.

Because AVNRT recurrence was noted in ≈9% of the patients during the long-term course, large pediatric patient cohorts have to be followed up to reliably evaluate factors associated with AVNRT recurrence. A multicenter study would, therefore, provide the framework for this purpose.

Conclusions
In a considerable number of pediatric patients with significantly longer follow-up than previously described, AVNRT ablation in children was associated with cumulative long-term outcome. Late A VNRT recurrence >5 years after ablation in children was associated with cumulative long-term outcome. A VNRT ablation in children and adolescents with A VNRT recurrence underwent a repeat EPS at another center. Additionally, 3 out of 22 patients with AVNRT recurrence who refused repeat EPS. A different SVT substrate in children and adolescents with A VNRT recurrence would, therefore, provide the framework for this purpose.

Disclosures
None.

References


Long-Term Follow-Up After Catheter Ablation of Atrioventricular Nodal Reentrant Tachycardia in Children
David Backhoff, Sophia Klehs, Matthias J. Müller, Heike E. Schneider, Thomas Kriebel, Thomas Paul and Ulrich Krause

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