Subsidiary Pacemaker Function in Complete Heart Block After His-Bundle Ablation

Herwig Schmidinger, MD, Peter Probst, MD, Barbara Schneider, PhD, Heinz Weber, MD, and Josef Kaliman, MD

To investigate the electrophysiological properties of ventricular impulse formation after His-bundle ablation in 11 patients, incremental ventricular overdrive stimulation studies were performed. The studies, which were spread over a follow-up period of up to 601 days, were carried out invasively with temporary leads as well as noninvasively with the implanted pacemakers and chest wall inhibition. The overdrive pacing rate was increased in steps of 10 beats/min, and the pacing duration was 2 minutes at each level. Ten out of 11 patients had a reliable ventricular escape rhythm; in the remaining patient, consistently no subsidiary pacemaker function was observed up to 10 seconds. In 83% of the studies, incremental ventricular overdrive stimulation caused progressive suppression of ventricular impulse formation with exponential increase in ventricular recovery time and progressive postrecovery subsidiary pacemaker depression. In the remaining 17%, ventricular recovery time showed a heterogeneous response to overdrive stimulation—as possible cause alterations in the sympathetic tone and limitations attributable to the method used are discussed. The results of this study demonstrate a rate-dependent overdrive suppression of subsidiary ventricular pacemaker tissue. This can be of clinical importance in patients with complete heart block and rate-adaptive pacemakers because sudden pacemaker failure or temporary pacemaker inhibition at high stimulation rates may cause Stokes-Adams attacks not reproducible at lower pacing rates. (Circulation 1988;78:893–898)

Since its introduction in humans,1,2 closed-chest ablation of the atrioventricular conduction system has become a routine therapeutic alternative for the treatment of supraventricular tachycardias unresponsive to medical treatment. The purpose of the procedure is to create complete heart block to prevent rapid ventricular response during supraventricular tachycardias. In the setting of complete heart block, overdrive suppression of subsidiary pacemakers is abolished and ventricular tissue assumes the function of impulse formation initiating the activation of the heart. However, because the rate of the newly established subsidiary rhythm and its adaptation during physical activity usually does not meet the demand, the majority of these patients require permanent ventricular pacing, and some will become completely pacing dependent.

Sufficient data on ventricular impulse formation and its response to overdrive suppression have been obtained in experimental studies3–10; however, little information on subsidiary pacemaker function in humans3,9,11,12 is available. It was our purpose to evaluate the electrophysiological properties of ventricular pacemaker tissue and its response to incremental overdrive suppression in patients with complete heart block after His-bundle ablation.

Patients and Methods

Eleven patients (five women and six men; mean age, 59 years; range, 46–73 years) were studied. All had intractable paroxysmal supraventricular tachycardias. The electrophysiological diagnosis was atrial fibrillation in eight patients, atrioventricular-nodal reentry tachycardias in two patients, and atrioventricular reciprocating tachycardias attributable to a retrogradely conducting bypass tract in one patient. To control the tachyarythmias in all patients, catheter-induced ablation of the atrioventricular junction was performed with the method first described by Gallagher et al.1 After induction of complete heart block, ventricular pacing was initiated with temporary leads that were then replaced by implantable devices after a mean follow-up of 3 days (seven Vitatron TX 911 [Vitatron Medical BV, Dieren, The Netherlands], one Vitatron TX 915, one Cordis 334 A [Cordis, Miami, Florida], one Cordis 233 F, and

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ventricular overdrive stimulation (VOS) studies were carried out invasively with temporary leads as well as noninvasively with the implanted pacemakers and chest wall inhibition. In the follow-up period, the studies were carried out as an outpatient procedure. In all patients, the pacing site was the right ventricular apex, and pacing was performed at twofold to fourfold the diastolic threshold with stimuli 0.5–2.0 msec in duration. The pacing duration was 2 minutes at each level. Starting with ventricular stimulation (RR-STIM) at rates slightly above the intrinsic heart rate (RR-IHR), pacing was stopped after 2 minutes, and the ventricular recovery time (VRT) was assessed. Subsequently, the stimulation rate was increased in steps of 10 beats/min, and the recovery time was assessed in a similar manner. Pacing was reinstituted immediately if the patient became symptomatic.

Subsidiary pacemaker recovery time was taken as the time elapsing from the last pacemaker spike to the appearance of the earliest spontaneous electrogram. Electrocardiograms were recorded on a Siemens Mingograf three-channel recorder, and measurements were made at a paper speed of 50 mm/sec. VRT (msec) and RR-STIM (msec) were normalized to RR-IHR (msec) and plotted against each other. Values are mean ± SEM.

The procedure was explained, and informed consent was obtained. No arrhythmias or complications requiring therapy occurred in any patient either during or after the stimulation studies.

**Results**

The results were obtained from 46 investigations that were spread over a mean follow-up period of 258 days (range, 5–601 days). A total of 247 ventricular recovery time measurements were made. The pacing cycle lengths ranged between 440 and 1,520 msec.

In one patient who was studied on three different occasions, consistently no ventricular escape rhythm was observed up to 10 seconds. In another patient on one of three different occasions, VRT exceeded 5.7 seconds at the beginning of the study. Because this was associated with transient dizziness, no further VOS were performed on this day.

In the remaining 42 studies on 35 occasions (83%), incremental VOS resulted in an exponential increase in VRT. The results are summarized in Table 1 and illustrated in Figure 1. The mean RR interval of the intrinsic heart rate was 1,417.8 ± 36.5 msec. To demonstrate the individual increase in VRT with incremental VOS, two examples are outlined. The correlation between the variables VRT and RR-STIM was significantly defined by the non-linear regression equation $\text{VRT} = ae^{0.28 \times \text{RR-STIM}}$ (mean $r^2$, 0.92 ± 0.01). The shape of the regression curve demonstrates that after an initial gentle rise in VRT around a critical VOS rate, further shortening of RR-STIM will result in a marked increase in VRT. Overall, shortening of RR-STIM to 63.8 ± 2.2% of RR-IHR was associated with a gradual increase in VRT to 146.2 ± 5.8% of RR-IHR. Around this critical overdrive stimulation rate, further shortening of RR-STIM by 8.9 ± 0.6% of RR-IHR resulted in a marked increase in VRT to 325.5 ± 13.8% of RR-IHR.

When the QRS morphology of the escape rhythm is examined, three groups of patients can be distinguished: 1) those with narrow QRS complexes (four patients), 2) those with wide QRS complexes (five patients), and 3) one patient who had both wide and narrow QRS complexes. Group 2 can be subdivided into patients with predominantly uniform QRS complexes (three patients) and those with polymorphous QRS complexes (two patients). Neither the intrinsic heart rate nor subsidiary pacemaker suppression presented differences between patients with narrow QRS complexes and those with wide QRS complexes.

However, when the follow-up period was examined (pooled data from groups 1 and 2), differences were seen (Table 2): in the early follow-up period, the critical overdrive stimulation rate was reached at a lower VOS rate than during the late follow-up period, and the corresponding measured recovery times were shorter. Further shortening of RR-STIM resulted in a higher increase in VRT already at a lower RR-STIM. The remaining one patient (group 3) was studied in the late follow-up period only. After VOS at low rates, the escape rhythm consisted of wide QRS complexes (left bundle branch block pattern) with a mean RR-IHR of 1,527 msec. When VOS was slightly increased, the escape rhythm slowed down to a mean of 2,051 msec and consisted of narrow QRS complexes. In this patient, the marked increase in VRT (mean, 303.8% of RR-IHR) already occurred at a mean RR-STIM of 73.6% of RR-IHR.

On three occasions, VRT was biphasic. Lengthening exponentially at the beginning, it progressively shortened again at high stimulation rates (Table 1: patient 2 on day 47, patient 6 on day 89, and patient 9 on day 232).

On seven total occasions in four patients, incremental VOS was associated with a heterogeneous increase in VRT. Two patients had narrow and two patients had wide QRS complexes (Table 3 and Figure 2). Because of a low intrinsic heart rate (mean RR-IHR, 2,044 msec) and a limited rate programmability of the pacemakers used on four of the seven occasions, VOS could not be started at lower pacing rates than, on average, 44.5% of RR-IHR (Table 3: patient 5 on days 0, 2, and 5 and patient 1 on day 25). At this level, mean VRT was already 252.0% of RR-IHR. It further lengthened to a mean of 415.4% of RR-IHR when RR-STIM was shortened to, on average, 28.5% of RR-IHR. On the
other hand, on three occasions VOS could not be performed at higher rates than, on average, 39.0% of RR-IHR (mean, RR-IHR 1,452 msec) because at higher stimulation rates chest wall stimuli randomly fell within the pacemaker refractory period, making reliable pacemaker inhibition and VRT determination impossible (Table 3: patient 6 on day 49 and patient 9 on days 113 and 134). In these three patients, VRT gradually increased to, on average, 138.4% of RR-IHR.

On 25 occasions, the ventricular escape rhythm consisted exclusively of one type of QRS complex. The first five RR intervals were normalized to RR-IHR and plotted against the different VOS rates. As illustrated in Figure 3, incremental VOS caused progressive postrecovery subsidiary pacemaker sup-
pression with increasing temporary instability of ventricular impulse formation. However, during the first six QRS complexes of the escape rhythm, a tendency toward stabilization and return to prepa-
ing control values can be observed.

Discussion

Our data demonstrate that a majority (91%) of patients with complete heart block after His-bundle ablation have a reliable subsidiary ventricular escape rhythm. Only one out of 11 patients (9%) consistently had no escape rhythm when pacing was stopped up to 10 seconds and was considered completely pacing dependent.

In 83% of the studies performed, incremental VOS was associated with an exponential increase in VRT. Although the exponential increase in impulse suppression was strikingly uniform, there was a wide range of the critical overdrive stimulation rate around which only a minor increase in the stimulation rate resulted in a marked increase in VRT. This was true for both individual patients as well as the total patient population, and there was no difference in ventricular impulse suppression between subsidiary pacemakers with wide and those with narrow QRS complexes. With regard to the QRS morphology of the escape rhythm, it should be emphasized that the precise site of origin of the subsidiary pacemakers was not documented by bundle of His recordings; however, in all probability, they were located at a comparatively distal site in the His-Purkinje system because shocks for His-bundle ablation were delivered at the site of maximal His deflection.

In good agreement with experimental findings,8,10 in our study, the recovery interval after overdrive suppression was directly related to the cycle length of the spontaneous idioventricular rhythm. This is in contrast to the findings of Narula and Narula,12 who did not find any definite correlation between these two variables in the patients they studied.

In experimental studies,3,8,9,10 as well as in humans,3,8,9,11,12 a direct relation between overdrive pacing rate and escape interval was observed; however, the correlation between these two variables was precisely defined by only Jordan et al.9 In this study, a biphasic increase in the escape interval was observed in humans, whereas in dogs, a linear relation between pacing rate and recovery time was found. Contrary to these observations, in the present study, incremental VOS was associated with an exponential increase in VRT, and on only three out of 42 occasions after an initial exponential increase, a sudden decrease in VRT was observed at high stimulation rates. The differences between the pres-

**TABLE 2.** Incremental Ventricular Overdrive Suppression—Comparison Between Early and Late Follow-up Period After His-Bundle Ablation

<table>
<thead>
<tr>
<th></th>
<th>RR_{IHRR} (msec)</th>
<th>RR_{STIMx} (% of RR_{IHRR})</th>
<th>VRT, (of RR_{IHRR})</th>
<th>RR_{STIMx} (% of RR_{IHRR})</th>
<th>VRT, (of RR_{IHRR})</th>
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<td>Early follow-up ≤7 days</td>
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<td>(mean, 2.4±0.5 days)</td>
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<tr>
<td>(n = 16)</td>
<td>1,414.7±81.9</td>
<td>66.7±3.1</td>
<td>122.7±3.0</td>
<td>57.1±2.5</td>
<td>366.6±29.2</td>
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<td>Late follow-up ≥47 days</td>
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<tr>
<td>(mean, 249.5±30.8 days)</td>
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<tr>
<td>(n = 23)</td>
<td>1,405.6±35.6</td>
<td>58.3±2.4</td>
<td>164.9±8.3</td>
<td>50.9±1.9</td>
<td>299.6±12.6</td>
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</tbody>
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n, number of measurements; RR-IHR, RR interval of intrinsic heart rate; RR-STIMx, critical overdrive stimulation rate around which further shortening of the stimulated RR interval (RR-STIM y) resulted in a marked increase in ventricular recovery time (VRT y); VRT x, ventricular recovery time after RR-STIM x.
ent study and the observations by Jordan et al.9 may be either species-dependent or method related. In the study by Jordan et al.,9 overdrive pacing was started at a pacing rate of 90 beats/min, and an increase in subsidiary pacemaker recovery time was found up to a pacing rate of 150 beats/min, at which a decrease was observed. In our study, the pacing rate did not exceed 135 beats/min; thus, the occurrence of a decrease in VRT at higher stimulation rates may have been missed in the majority of our studies performed. Similar observations were made in some patients by Narula and Narula,12 and in accordance with these authors, we believe that the occurrence of a conduction block between the pacing site and the site of origin of the escape pacemaker probably accounts for this phenomenon.

The influence of the vegetative tone on idioventricular pacemakers has been demonstrated previously.7 However, the sympathetic system conditions but does not determine the events after overdrive stimulation.13 As major mechanism responsible for subsidiary pacemaker overdrive suppression rate-dependent and pacing duration-dependent changes in cellular ionic balance and subsequent activation of an electrogenic sodium pump have been identified that cause suppression by shifting the time course of diastolic depolarization to more negative values.5,6,13 Because in the present study the pacing duration was held constant, it seems reasonable to conclude that changes in the sympathetic tone accounted for the wide (interpatient and intrapatient) range of the critical overdrive stimulation rate, which may explain the differences between inpatient and outpatient studies. The same applies to the seven instances where no exponential increases in VRT were observed. The slow intrinsic heart rate (mean, RR-IHR 2,044 msec) and the initial long recovery time of, on average, 252% of RR-IHR probably reflected a reduced sympathetic drive on four occasions. On the other hand, the opposite may have been true in the remaining three patients in whom the mean RR-IHR was rather short (mean, RR-IHR 1,452 msec) and the mean recovery time increased to only 138.4% of RR-IHR. In addition, one might speculate that because of the limited rate programmability of the implanted devices, only a part of a hypothetical exponential recovery curve (either before or beyond the critical overdrive stimulation rate) was covered by incremental VOS, resulting in a pseudolinear increase in VRT.

In conclusion, 1) a majority of patients with complete heart block after His-bundle ablation have a reliable ventricular escape rhythm; 2) incremental VOS causes progressive suppression of subsidiary ventricular pacemakers with exponential increase in ventricular recovery time and progressive postrecovery subsidiary pacemaker suppression; and 3) the clinical implication is that in patients with rate-adaptive pacing devices, sudden pacemaker failure or temporary pacemaker inhibition at high stimulation rates can cause Stokes-Adams attacks because of temporary ventricular standstill that cannot be reproduced at low pacing rates.

References
2. Schleiming MM, Morady F, Hess DS, Gonzalez R: Catheter-induced ablation of the atrioventricular junction to control

![FIGURE 3. Bar charts of ventricular escape rhythm with uniform QRS morphology after incremental overdrive stimulation. Bars symbolize the first five RR intervals of the escape rhythm—the recovery times are omitted. RR-STIM, RR interval of stimulated heart rate; RR-IHR, RR interval of intrinsic heart rate.](image-url)
refractory supraventricular arrhythmias. JAMA 1982;248:851–855

KEY WORDS • noninvasive programmed stimulation • overdrive suppression • ventricular recovery time
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