Serial Electrocardiologic Studies in Patients with Chronic Bundle Branch Block

ROBERT W. PETERS, M.D., MELVIN M. SCHEINMAN, M.D., RAMESH DHINGRA, M.D.,
KENNETH ROSEN, M.D., JOHN McANULTY, M.D., SHAHBUDIN H. RAHIMTOOLA, M.D.,
AND GUNNAR MODIN

SUMMARY Serial His bundle recordings were obtained during 1:1 atrioventricular (AV) conduction in 90 patients with chronic bundle branch block over a mean interval of 30 months. Atrioventricular conduction time (AH) increased ≥ 10 msec in 25 (28%) and infranodal conduction time (HV) increased ≥ 8 msec in 29 (32%), but only 10 patients had parallel increases in AH and HV intervals. Increases in conduction times were independent of age, time interval between studies, cause of heart disease or initial AH or HV intervals. Women were significantly more likely than men to show an increased HV interval and spontaneous trifascicular block. Spontaneous progression to second- or third-degree AV block occurred at the AV node in seven patients and below the node in 12 patients. The initial AH interval was prolonged in five of seven patients (71%) with AV nodal block and had increased further in only two at restudy. The initial HV interval was abnormal in eight of 12 patients (67%) who progressed to infranodal block and was prolonged further in eight at restudy.

We conclude that in patients with chronic bundle branch block, (1) approximately 33% show progressive AV conduction system disease and AV nodal and infranodal disease progress independently; (2) progression of infranodal disease is more common in women; (3) AV nodal disease is a common cause of AV block and can occur without further prolongation of the AH interval once a critical level of disease is attained, whereas infranodal block is usually accompanied by progressive lengthening of the HV interval; and (4) progression of AV conduction disease is not readily predictable from clinical and electrophysiologic variables.

PATIENTS with chronic bundle branch block are at risk of developing complete atrioventricular (AV) block. The incidence of this complication is extremely low, particularly in patients without organic cardiac disease; hence, prophylactic permanent pacemaker insertion for these patients is not justified. Three large prospective studies of patients with bundle branch block using His bundle recordings are being conducted, and the predictive value of the infranodal conduction time (HV interval) has not been determined. These studies show that the rate of progression of infranodal conduction system disease is highly variable. In the present study, we analyzed the clinical and electrophysiologic variables that appear to be associated with progressive disease in the ventricular specialized conduction system. Ninety patients in these three prospective studies underwent at least two electrophysiologic studies. We compared changes in AV nodal and infranodal conduction times in these 90 patients with clinical variables and progression to second- or third-degree AV block.

Methods

The patients were a composite group from three large prospective studies of patients with chronic intraventricular conduction disorders who underwent His bundle recordings. The criteria for admission to the studies have been reported. Two centers (University of Illinois and University of Oregon) included only patients with bifascicular block, i.e., left or right bundle branch block with either left anterior or posterior fascicular block. One center (University of California, San Francisco) included all patients with bundle branch block. Admission criteria for all three studies included a medical history, physical examination, chest roentgenogram, standard ECG and His bundle recording. Additional diagnostic studies were performed if clinically indicated. Intracardiac conduction times were analyzed in identical fashion. The AH interval was measured from the first rapid atrial deflection to the first rapid His bundle deflection, whereas the HV interval was measured from the initial rapid His bundle deflection to the earliest onset of ventricular activation determined by at least three orthogonal surface electrocardiographic recordings. The His bundle deflection was differentiated from that of the right bundle branch by its typical triphasic form and associated well-defined atrial depolarization. His bundle pacing was used in selected patients. Atrial overdrive pacing was not consistently performed, which precludes meaningful analysis of pacing-induced changes in AV conduction or sinus node function.

Congestive heart failure was diagnosed based on the medical history, physical examination and chest roentgenogram, and patients were categorized according to the New York Heart Association's functional classification. Congenital heart disease or primary valvular disease was diagnosed based on the physical examination or results of cardiac catheterization. Hypertensive heart disease was diagnosed in patients with cardiac disease and systemic hypertension and no other obvious cause of cardiac disease. Primary conduction system disease was diagnosed in patients...
without evidence of cardiovascular disease based on the medical history, physical examination or chest roentgenogram, and on additional diagnostic tests if performed. Five hundred fifteen patients are being followed at the University of Illinois (mean follow-up 3.4 years); 380 patients are being followed at the University of California, San Francisco (mean follow-up 3.1 years); and 351 patients are being followed at the University of Oregon (mean follow-up 3.6 years). In each center, patients are examined at 3–6 month intervals at a special arrhythmia clinic and follow-up information is obtained from the personal physician at 3-month intervals. During the follow-up, 90 patients underwent at least two electrophysiologic studies: 37 patients from the University of California, San Francisco, 36 from the University of Illinois and 17 from the University of Oregon. The indications for repeat electrophysiologic study are presented in table 1.

Only patients who received no cardioactive drugs before either electrophysiologic study or who received an identical drug regimen during both studies were included. A significant increase in the AH interval was arbitrarily defined as $\geq 10$ msec, whereas a significant change in the HV interval was defined as changes $\geq 8$ msec. The latter was chosen because blinded measurements of HV by two observers from one center showed a maximal interobserver error of 7 msec in the HV interval. These 90 patients were representative of the larger population from which they were drawn. There was no significant difference in age, sex, severity of congestive heart failure (New York Heart Association classification), QRS configuration or AH and HV intervals between the larger and smaller groups. However, the incidence of syncope was significantly higher for the total patient population (303 of 1181, 26%) than for the restudy group (10 of 90, 11%) ($p < 0.005$).

Twelve patients had documented spontaneous episodes of second- or third-degree AV block and at restudy had evidence of infranodal block. The HV interval for this group was measured during 1:1 AV conduction. In seven patients with documented spontaneous second- or third-degree AV block, the block was located at the level of the AV node. Patients with persistent complete AV block were treated with pacemakers and were not included in the present study.

**Statistical Methods**

All data were stored on punch cards and specially designed programs were used for data recall and statistical analysis. Analysis of variance was used to analyze parametric data and chi-square analysis was used for nonparametric data.

**Results**

**General Characteristics of the Study Group**

Ninety patients underwent repeat electrophysiologic studies. The study population was predominantly male (78%), elderly (mean age 64 ± 11 years [± sd] and had a 92% incidence of organic cardiac disease. The mean interval between studies was 30 months (range 2–83 months). Most patients underwent the initial study (table 1) for medical investigation, whereas the second study was more often performed to elucidate the cause of transient neurologic symptoms (37 patients) or to determine the location of AV block (23 patients).

For the group as a whole, there was no significant change in mean AH or HV interval between studies. Similarly, there was no significant correlation between changes in either AH or HV interval and age, cause of heart disease, time between studies, type of bundle branch block pattern, or the initial AH and HV intervals. There was a positive trend (NS) between lengthening of the HV interval and increased severity of heart failure.

**Patients with Increased AH Interval**

Twenty-five patients had a significant increase in AH interval ($\geq 10$ msec) between studies. These patients were compared with 50 others who did not have such an increase. Fifteen patients with atrial flutter, fibrillation or atrial tachycardia were excluded from this analysis. There was no significant difference between groups with respect to age, sex, cardiac diagnosis, severity of heart failure or bundle branch block pattern. In addition, an abnormal AH interval at entry failed to distinguish those who showed progressive disease from those who did not. There was no significant change in heart rate between studies ($75.5 \pm 14.6$ vs $77.3 \pm 15.2$), and only nine patients showed a difference in heart rate greater than 10 beats/min between studies. Thus, changes in heart rate did not appear to be an important factor in explaining the changes in AH interval between studies. Lengthening of the AH interval between studies was not necessarily paralleled by progressive lengthening of the HV interval (fig. 1).

**Patients with Increased HV Interval (fig. 2)**

Twenty-nine patients had a significant ($\geq 8$ msec) increase in the HV interval between studies. There was no significant difference in age, cardiac diagnosis, New York Heart Association classification, or electrocardiographic patterns between those with and those without an increase in the HV interval. In addition, an abnormal initial HV interval ($\geq 55$ msec) did not distinguish between the groups. The percentage of females was significantly higher (14 of 29 [48%] vs six of 61 [10%], $p < 0.001$) among the patients with progressive disease than among those with nonpro-

<table>
<thead>
<tr>
<th>Table 1. Reasons for Electrophysiologic Study</th>
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</thead>
<tbody>
<tr>
<td>Study 1 (no. of pts)</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Transient neurologic symptoms*</td>
</tr>
<tr>
<td>Clinical investigation</td>
</tr>
<tr>
<td>Evaluation of tachycardia</td>
</tr>
<tr>
<td>Atrioventricular block</td>
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</tbody>
</table>

*Syncope, dizzy spells or seizures.
five of the seven patients, compared with 22 of 80 patients (28%) \((p < 0.05)\) without progression. The AH interval was unchanged in five patients at restudy and prolonged significantly (55 and 125 msec) in two of the patients who progressed to AV nodal block.

**Infranodal Block** (table 3)

Thirteen patients had documented progression to second- or third-degree AV block (table 3). One patient had progression during the course of an acute anterior myocardial infarction and was excluded from the study. The initial HV interval was abnormal (> 55 msec) in nine of 12 and was abnormal in 11 of 12 at the second study. There was a significantly higher percentage of women among those who progressed to second- or third-degree infranodal block than among those who did not develop AV block. A higher percentage of patients with left bundle branch block progressed to high-grade AV block (38%) than among those with right bundle branch block (17%), but this difference was not significant. Patients who progressed to second- or third-degree AV nodal block did not have an increased incidence of lengthening of the HV interval compared with those who did not have progression. The same was true with respect to the AH interval among those who had second- or third-degree infranodal block.

**Discussion**

Although intracardiac conduction times might have lengthened over the 2½-year mean interval between studies, such progression was not universal and could not be predicted from clinical and electrocardiographic variables. For example, some patients were followed for as long as 7 years without appreciable change in conduction times, whereas others, appar-

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**Figure 1.** Changes in AH and HV intervals in 25 patients with significant \((\geq 10\) msec) AH prolongation between studies.

**Patients with Spontaneous AV Block**

The site of spontaneous AV block was verified by His bundle recordings in 16 of 19 patients. Conduction times were measured during conducted beats in patients with type II second-degree AV block and after resumption of AV conduction in patients with intermittent AV block. In the remaining three patients, infranodal block was presumed because of type II second-degree AV block (one patient) or because of episodes of complete AV block with ventricular asystole and escape of a ventricular pacemaker of different morphology and a rate less than 40 beats/min. In two of these three patients, infranodal block was induced by atrial pacing during the second electrophysiologic study.

**AV Nodal Block** (table 2)

Ten patients progressed to second- or third-degree AV nodal block. Seven had spontaneous progression, two progressed during acute inferior wall myocardial infarction and one progressed secondary to digitalis toxicity. The last three patients were not included in this analysis. There were no significant changes in mean AH interval between studies for those who did or did not progress to AV nodal block. The initial AH interval was abnormally prolonged (> 120 msec) in

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**Figure 2.** Changes in AH and HV intervals in 29 patients with significant \((\geq 8\) msec) HV prolongation between studies.
Table 2. Clinical Data for Patients Who Did and Did Not Progress to Spontaneous Atrioventricular Nodal Block

<table>
<thead>
<tr>
<th></th>
<th>Atroventricular nodal block*</th>
<th>Nonprogressors</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of pts</td>
<td>7</td>
<td>80</td>
</tr>
<tr>
<td>Age (years)</td>
<td>67 ± 8</td>
<td>64 ± 13</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>6/1</td>
<td>60/19</td>
</tr>
<tr>
<td>NYHA functional class (mean)</td>
<td>1.9 ± 0.7</td>
<td>1.7 ± 0.8</td>
</tr>
<tr>
<td>AH (msec)</td>
<td>131 ± 35</td>
<td>110 ± 37</td>
</tr>
<tr>
<td>HV (msec)</td>
<td>48 ± 10</td>
<td>55 ± 11</td>
</tr>
<tr>
<td>AH t ≥ 10 msec</td>
<td>2/7 (29%)</td>
<td>22/62 (35%)</td>
</tr>
<tr>
<td>HV t ≥ 8 msec</td>
<td>1/7 (14%)</td>
<td>29/80 (37%)</td>
</tr>
<tr>
<td>Initial AH &gt; 120 msec</td>
<td>5/7 (71%)</td>
<td>22/80 (28%)‡</td>
</tr>
<tr>
<td>Initial HV &gt; 55 msec</td>
<td>2/7 (29%)</td>
<td>50/80 (63%)‡</td>
</tr>
</tbody>
</table>

*Excludes two patients with atrioventricular nodal block secondary to acute myocardial infarction and one patient with atrioventricular nodal block secondary to digitalis toxicity.
†HV interval at initial study, p < 0.05.
‡p < 0.05.

Abbreviations: NYHA = New York Heart Association; t = increase.

ently comparable in age, sex, and cause of cardiac disease, had dramatic lengthening in the AH or HV interval. Although we found no specific clinical or electrophysiologic predictors of progressive infranodal conduction system disease, certain findings are of note. We did find a significantly higher percentage of women among subjects who had progression, despite the younger ages and shorter HV interval for this group compared with those who did not have progression. The reason for this finding is not clear, and the relatively small sample size precludes definitive conclusions. Of interest, however, is the different pattern of conduction system disease described for women by Kulbertus. For example, autopsy findings suggested that Lev's disease is more common in women and causes left bundle branch block and a long PR interval, whereas Lenegre's disease is more common in men and is manifested by right bundle branch block and left anterior fascicular block. Similarly, although the incidence of increasing congestive heart failure and

Table 3. Clinical Data for Patients Who Did and Did Not Progress to Spontaneous Infranodal Block

<table>
<thead>
<tr>
<th></th>
<th>Infranodal block*</th>
<th>Nonprogressors</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of pts</td>
<td>12</td>
<td>77</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63 ± 15</td>
<td>65 ± 12</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>6/6</td>
<td>64/13†</td>
</tr>
<tr>
<td>NYHA functional class (mean)</td>
<td>1.6 ± 0.8</td>
<td>1.7 ± 0.8</td>
</tr>
<tr>
<td>ECG pattern</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RBBB</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>RBBB/LAH</td>
<td>8</td>
<td>53</td>
</tr>
<tr>
<td>RBBB/LPH</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>LBBB</td>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td>AH (msec)</td>
<td>117 ± 43</td>
<td>113 ± 39</td>
</tr>
<tr>
<td>HV (msec)</td>
<td>58 ± 18</td>
<td>59 ± 15</td>
</tr>
<tr>
<td>AH t ≥ 10 msec</td>
<td>3/12 (25%)</td>
<td>19/60 (32%)§</td>
</tr>
<tr>
<td>HV t ≥ 8 msec</td>
<td>8/12 (67%)†</td>
<td>20/77 (26%)†</td>
</tr>
<tr>
<td>Initial AH &gt; 120 msec</td>
<td>4/12 (33%)</td>
<td>23/69 (33%)§</td>
</tr>
<tr>
<td>Initial HV &gt; 55 msec</td>
<td>8/12 (67%)</td>
<td>43/77 (56%)§</td>
</tr>
</tbody>
</table>

*One patient with infranodal block secondary to acute anteroseptal myocardial infarction was excluded.
†p < 0.01.
‡Difference in HV interval between studies, p < 0.05 for both patient groups.
§Not significant.

Abbreviations: NYHA = New York Heart Association; RBBB = right bundle branch block, LAH = left anterior hemiblock; LPH = left posterior hemiblock; LBBB = left bundle branch block; t = increase.
the left bundle branch block pattern was higher among those who had progression than in those who did not, the differences were not statistically significant.

**AV Nodal Block**

In seven of the 19 patients who spontaneously progressed to second- or third-degree AV block, the block was localized to the AV node. This finding emphasizes the importance of panconduction disturbances in patients with bundle branch block. The high incidence of AV nodal block in our patients was similar to that found for the composite group; thus, this finding is not a result of the selection process. We also found an abnormal control AH interval in five of seven patients and lengthening of AH interval in only two patients at restudy. This finding suggests that AV nodal block may, for most patients, represent an all-or-none phenomenon once a critical degree of AV nodal tissue is involved.

**Infranodal AV Block**

In contrast to patients with AV nodal block, patients who progressed to infranodal block showed a statistically significant increase in HV interval between studies. The control HV interval was abnormal in nine of 12 who had progression and was abnormal in all but one at restudy. These findings suggest a different pattern of development of infranodal block; that is, these patients appear to have a progressive disease involving the His-Purkinje system. Although the increase in HV interval was significant for those with progressive infranodal block, this finding is of limited clinical value. Among patients who had lengthening of the HV interval, we found no significant difference in the absolute or percent increase in HV interval between those who progressed to AV block and those who did not. Thus, perhaps because of the small sample size, we cannot use the magnitude of HV progression to predict progression to second- or third-degree block.

**Patterns of Progression**

Patients who had a significant increase in the AH interval between studies had no significant change in the HV interval. Although eight of 24 (33%) with an increasing AH interval showed parallel lengthening of both AH and HV intervals, 16 had no significant change in HV interval. Similarly, of 30 patients with an increased HV interval between studies, only eight (27%) had a significant increase in the AH interval. These findings suggest a varying pattern of progressive AV conduction disease. A minority of patients appear to have symmetric involvement of both AV nodal and infranodal structures; the rates of progression for the most part occur independently.

There is little information regarding the progression of conduction system disease as assessed by serial electrophysiologic studies. Schoenfeld et al. reported their experience in six patients with bundle branch block complicating acute myocardial infarction who were restudied 5-90 days after the acute event. Abnormalities in infranodal conduction persisted in five of the patients, including three in whom bundle branch block had since disappeared. Prystowsky et al. described nine patients with myotonic muscular dystrophy who had serial electrophysiologic studies conducted a mean of 35 months apart. Infranodal conduction time was prolonged in three at the initial study and was prolonged in an additional four at the second study; all but one had a narrow QRS complex. These investigators were unable to identify any electrocardiographic or electrophysiologic factors that correlated with progression of conduction system disease. Narula described serial studies in 13 patients with bundle branch block (six of whom had the onset of the conduction defect in the setting of acute myocardial infarction) at intervals of 6 months to 2 years. Only one patient (who had a permanent pacemaker implanted between studies for unspecified reasons) had prolongation of the infranodal conduction time, whereas nine patients had an unchanged HV interval, two patients had complete AV block at the time of the second study and one patient had infranodal block induced by atrial pacing, but the HV interval was not reported. Foster et al. reported the results of serial electrophysiologic studies in eight asymptomatic patients with right bundle branch block and left anterior hemiblock. The infranodal conduction time was unchanged in seven and had increased 10 msec in conducted beats in the one patient who progressed to AV block.

**Limitations**

Our findings must be interpreted cautiously. First, agreement by the subjects to be restudied introduces a bias toward inclusion of patients with either transient neurologic symptoms of those who were highly motivated to participate in research studies. The extent to which these factors affect the apparent natural history of AV conduction disease is not known. It is likely that the inclusion of a high incidence of patients with neurologic symptoms introduces a bias resulting in overestimation of progression of the conduction system disease. A second important limitation is the inability to restudy those patients who progressed to persistent third-degree AV block or those who died shortly after entering the study. Exclusion of these patients would tend to bias our data and perhaps result in underestimation of progression of AV conduction disease. Finally, the definition of AH progression (≥ 10 msec) was entirely arbitrary. Changes in autonomic tone during or between studies can produce changes in AV nodal conduction time. These changes in autonomic tone could not be assessed in the present study. A more precise definition of the changes in AH interval would require simultaneous sympathetic and parasympathetic blockade.

Nevertheless, the present study is the largest and most comprehensive serial electrophysiologic study of patients with bundle branch block. We found significant AV nodal or infranodal prolongation in approximately 33% of patients and found no correlation between changes in AH vs HV intervals. Similarly, the pattern of progression to second- or third-degree AV
block appeared to differ between those progressing to AV nodal and those progressing to infranodal block. We cannot explain the tendency for women to have enhanced prolongation of infranodal conduction time and progress to second- or third-degree infranodal block. Finally, we could not identify baseline clinical, electrocardiographic and electrophysiologic factors that predict progressive AV conduction system disease.

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Serial electrophysiologic studies in patients with chronic bundle branch block.
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