Significance of Chronic Bifascicular Block Without Apparent Organic Heart Disease

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SUMMARY Eighty-six of 452 patients (19%) with chronic bifascicular block were found to have no clinically apparent associated organic heart disease (OHD) and were defined as having primary conduction disease (PCD). Comparison of patients with PCD and OHD revealed a significantly lower incidence of the following clinical variables in the PCD patients (p < 0.001): exertional angina, dyspnea, congestive heart failure, cardiomegaly, functional class I (all by study design), left bundle branch block and premature ventricular contractions. Both mean AH and HV intervals were significantly shorter in patients with PCD (p < 0.01). The incidence of HV prolongation was 21% in PCD and 41% in OHD patients (p < 0.001). All patients were prospectively followed for 21–2998 days with a mean ± SEM of 1209 ± 66 days for PCD and 1172 ± 36 days for OHD. Atrioventricular (AV) block developed in three patients from the PCD group and 26 from the OHD group (NS), with spontaneous block occurring in one (1%) PCD patient and 19 (5%) OHD patients (p < 0.05). Annual mortality due to sudden death as well as total cardiovascular mortality (including sudden death) for the 5-year follow-up was significantly lower in patients with PCD.

Patients with PCD have a significantly lower incidence of electrophysiologic abnormalities and subsequent spontaneous AV block as well as cardiovascular and sudden death mortality. The diagnosis of PCD based on clinical criteria probably understimates the presence of underlying OHD, as suggested by a small but definite risk of cardiovascular mortality.

IN PATIENTS with chronic bifascicular block, physical examination and chest roentgenogram allow subclassification of patients into those with apparent organic heart disease, and those with no evidence of organic heart disease. The latter group may be clinically categorized as having primary conduction disease. Rosenbaum suggested that patients with primary conduction disease could be further subcategorized into those with Lenegre's disease (idiopathic bilateral bundle branch sclerodegenerative disease) and Lev's disease (senile sclerosis and calcification of the left side of the cardiac skeleton with secondary involvement of the bi- or trifascicular conduction system). In the patients with chronic bifascicular block, little is known of how the presence or absence of apparent organic heart disease relates to the severity of conduction disease, or to the risk of developing progressive conduction disease.

In the present study, we report clinical, electrocardiographic, and electrophysiologic features of patients with chronic bifascicular block, contrasting patients with organic heart disease to those with primary conduction disease. In addition, we report prospective observations concerning the life history of both groups of patients.

Patients and Methods

Definitions

Definitions are based on the recommendations of the criteria committee of the New York Heart Association. The criteria for electrocardiographic diagnosis of right bundle branch block included a QRS duration of ≥0.12 second with an rSR or qR or a tall R wave in lead V1. The criteria for diagnosis of left bundle branch block were as follows: 1) QRS duration of ≥0.12 second; 2) the presence of a broad monophasic R or Rs in lead V6; 3) ST depression and T-wave inversion in lead V6.

In patients with right bundle branch block, left anterior hemiblock was diagnosed when the mean frontal QRS axis was more negative than −30°, with the presence of a small q and tall R waves in lead I and small r and deep S waves in lead III. Left posterior hemiblock was diagnosed when the mean frontal QRS axis was more positive than +90°, with the presence of a small r and deep S waves in lead I, a small q and tall R waves in lead III and absence of right ventricular hypertrophy.

Bifascicular block was defined as right bundle branch block with left anterior hemiblock, right bundle branch block with left posterior hemiblock or left bundle branch block.

Primary conduction disease was diagnosed when bifascicular block patients met the following criteria: 1) no history consistent with cardiovascular disease (hypertension, angina, dyspnea, etc.); 2) negative cardiovascular physical examination (patients with an in-
significant murmur or an audible fourth heart sound were not excluded from the primary conduction disease group; 3) normal heart size on chest x-ray (cardiothoracic ratio < 0.5). All patients fulfilling these criteria, by definition, were in New York Heart Association cardiac functional class I.

Patient Selection
The study group consisted of 452 patients with chronic bifascicular block detected through screening of inpatient and outpatient ECGs at the Chicago West Side Medical Center (Cook County Hospital, the West Side Veterans Administration Hospital and the University of Illinois Hospital). In addition, some patients with bifascicular block were referred to us for electrophysiologic studies and follow-up in our conduction clinics from the Chicago area.

Criteria for inclusion were: 1) presence of chronic bifascicular block with intact anteroposterior (AV) conduction; 2) age 18 years or older; 3) giving informed consent for electrophysiologic studies; and 4) voluntary agreement to periodic follow-up in conduction disease clinics. Patients with a history of second- or third-degree AV block and patients with acute myocardial infarction were excluded. The patients of this study were detected, studied and followed between January 1970 and August 1978.

Patient Evaluation
Initial evaluation of patients included history, physical examination, chest x-ray and serial ECGs. A clinical diagnosis was established for each patient on the basis of this evaluation. Previously described criteria were used to diagnose organic heart disease.6 Arteriosclerotic heart disease was diagnosed if the patient had a history of typical exertional angina, or previous diagnosis of definite myocardial infarction and/or positive coronary arteriogram. Hypertensive heart disease was diagnosed if two or more blood pressure recordings indicated a systolic pressure > 140 mm Hg and diastolic pressure > 100 mm Hg. If a patient had both arteriosclerotic and hypertensive cardiovascular disease, the most clinically significant diagnosis (symptomatic) was listed. Valvular heart disease was diagnosed when a significant valvular lesion was detected by auscultation, radiological examination, echocardiographic evaluation and/or cardiac catheterization. Primary myocardial disease was diagnosed if the patient had cardiac enlargement without apparent cause.

The patients gave informed written consent before electrophysiologic study. His bundle electrograms were recorded in all patients, using previously described catheter techniques.7 Cardiac drugs were withheld for at least 48-72 hours before the study. Measurements of AH (AV nodal conduction) and HV (His-Purkinje conduction) intervals were made at paper speeds of 200 mm/sec, and reflect the mean of 10 consecutive sinus beats. Normal values (mean ± 2 SD) used for these intervals were as follows: AH, 92 ± 38 msec; and HV, 43 ± 12 msec.7 Sinus node recovery times (normal 988 ± 692 msec) were measured as the mean of three determinations after sudden cessation of atrial pacing (continued for longer than 30 seconds) at a rate of 130 beats/min.7

Refractory periods of the atrium and AV node were measured with the atrial extrastimulus technique as previously described by Denes and co-workers.8

Patient Follow-up
Patient follow-up was similar to that previously described by our laboratory.9,14 After initial study, all patients were prospectively followed in conduction disease clinics at intervals of 1-3 months. A complete history and physical examination, together with a 12-lead ECG, were performed at each clinic visit. Patients were hospitalized if they developed symptoms, and prolonged portable ECG monitoring was used to detect transient bradyarrhythmias. Symptomatic bradyarrhythmias were treated with permanent pacemaker insertion. After pacemaker insertion, the patients were continued on in the study to determine their final outcome. Sudden death was defined as unexpected death due to natural causes occurring within 24 hours of the onset of acute symptoms, or within 24 hours of being seen alive without symptoms.14 If death occurred outside the hospital, details of the death and copies of death certificate were obtained. Death was considered due to cardiovascular causes if the patient died of congestive heart failure or after an acute myocardial infarction in the absence of any other cause. In a selected number of patients, post mortem examination determined the cause of death. Nine patients were lost to follow-up.

All information at the time of initial evaluation and subsequent clinic visits was keypunched and stored on IRS database discs. For data recall and statistical analysis, specifically designed programs were used. A standard t test was used to test the significance of differences in means and two by two chi-square method for frequency data analysis. Data on survival rates were analyzed using previously described life table methods.15

Results
Clinical Data (table 1)
Of the 452 patients with chronic bifascicular block, 86 (19%) had no apparent organic heart disease and were categorized as the primary conduction disease group. Three hundred sixty-six (81%) had organic heart disease, and were classified as the heart disease group.

The clinical diagnoses in the patients of the heart disease group were as follows: hypertensive cardiovascular disease in 146 (40%), arteriosclerotic heart disease in 140 (38%), primary myocardial disease in 34 (9%) valvular heart disease in 25 (7%) and miscellaneous heart disease in 21 (6%).

There were 71 (83%) males and 15 (17%) females in the primary conduction disease group and 289 (79%) males and 77 (21%) females in the heart disease group.
TABLE 1. Comparative Clinical Data in Primary Conduction Disease and Organic Heart Disease Patients

<table>
<thead>
<tr>
<th></th>
<th>PCD (n = 86)</th>
<th>OHD (n = 366)</th>
<th>p</th>
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<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>71 (83)</td>
<td>289 (79)</td>
<td>NS</td>
</tr>
<tr>
<td>Female</td>
<td>15 (17)</td>
<td>77 (21)</td>
<td>NS</td>
</tr>
<tr>
<td>Clinical finding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td>0 (0)</td>
<td>100 (27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dizziness</td>
<td>25 (29)</td>
<td>99 (27)</td>
<td>NS</td>
</tr>
<tr>
<td>Syncope</td>
<td>7 (7)</td>
<td>46 (12)</td>
<td>NS</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>0 (0)</td>
<td>177 (48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHF</td>
<td>0 (0)</td>
<td>150 (41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>0 (0)</td>
<td>252 (70)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NYHA class I</td>
<td>86 (100)</td>
<td>172 (47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NYHA class II to IV</td>
<td>0 (0)</td>
<td>194 (53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9 (10)</td>
<td>65 (18)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviations: PCD = primary conduction disease; OHD = organic heart disease; CHF = congestive heart failure; NYHA = New York Heart Association.

The mean age (± SEM) was 61 ± 2.0 years for the organic heart disease group (range 18–93 years) and 62 ± 0.7 years for the primary conduction disease group (range 18–91 years) (NS). The frequency of selected clinical findings in the two groups is presented in table 1.

Electrocardiographic Data (table 2)

There was no significant difference between the two groups in regard to PR interval and QRS duration. The incidence of right bundle branch block was significantly higher in the primary conduction disease group (p < 0.001). Left bundle branch block was more frequent in the group with organic heart disease (p < 0.001). Premature ventricular contractions, detected on resting 12-lead ECG, were significantly less common in the primary conduction disease group (p < 0.001).

Electrophysiologic Data (table 3)

There was no significant difference in heart rate between the bifascicular block patients with and without organic heart disease at the time of electrophysiologic study. Both mean AH interval and incidence of AH prolongation were significantly lower in patients with primary conduction disease (p < 0.01 and p < 0.02). The mean HV interval was significantly shorter in the patients with primary conduction disease (p < 0.005). In addition, the incidence of HV prolongation was lower in this group (p < 0.001). The effective refractory periods of the atrium, AV node, and ventricular specialized conduction system were not significantly different in the two groups. Also, there was no significant difference between the two groups in the mean sinus node recovery time.

AV Block

The overall follow-up period ranged from 21–2998 days, with a mean ± SEM of 1209 ± 66 days for the primary conduction disease group and 1172 ± 36 days for the heart disease group.

Second- or third-degree AV block developed in 26 patients with heart disease (7%) and in three patients (3%) with primary conduction disease (NS). The incidence of AV block with right bundle branch block (with either left- or right-axis deviation) and left bundle branch block in the two groups was as follows: The incidence was 9% (24 of 262 patients) with right bundle branch block and 2% (two of 104 patients) with left bundle branch block in the organic heart disease group and 4% (three of 77 patients) with right bundle branch block and none with left bundle branch block in the primary conduction disease group. These differences were not statistically significant. AV block was further subcategorized by whether it occurred spontaneously (no precipitating cause) or due to apparent cause (e.g., acute myocardial infarction, drug intoxication or hyperkalemia). Spontaneous AV block was noted in 19 patients (5%) with heart disease and one patient (1%) with primary conduction disease (p < 0.05). Of the 19 patients with organic heart disease who developed spontaneous AV block, the incidence of AV block with various heart diseases was as follows: nine of 140 (6%) patients with arteriosclerotic heart disease; eight of 146 (6%) with hypertensive heart disease; none of 34 (0%) with primary myocardial disease; and none of 25 (0%) with valvular heart disease. Two patients with spontaneous AV block had myotonia dystrophica. Syncope was the presenting symptom during AV block in seven of 19 patients with organic heart disease.

TABLE 2. Comparative Electrocardiographic Findings in Primary Conduction Disease and Organic Heart Disease Patients

<table>
<thead>
<tr>
<th></th>
<th>PCD (n = 86)</th>
<th>OHD (n = 366)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean ± SEM</td>
<td>No. (%)</td>
</tr>
<tr>
<td>PR Interval (sec)</td>
<td>0.11–0.28</td>
<td>0.18 ± 0.003</td>
<td>77 (90)</td>
</tr>
<tr>
<td>QRS duration (sec)</td>
<td>0.12–0.18</td>
<td>0.13 ± 0.002</td>
<td>21 (10)</td>
</tr>
<tr>
<td>PVC</td>
<td>7 (8)</td>
<td></td>
<td></td>
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</table>

Abbreviations: PCD = primary conduction disease; OHD = organic heart disease; RBBB = right bundle branch block; LBBB = left bundle branch block; PVC = premature ventricular contraction.
heart disease and in the only patient with primary conduction disease. AV block due to apparent cause was noted in seven patients (2%) with heart disease and two patients (2%) with primary conduction disease (NS) (hyperlakemia in both). Permanent pacemakers were implanted in all the patients with symptomatic AV block: 17 in the organic heart disease group and one in the primary conduction disease group.

In summary, the risk of total AV block in both groups was similar, but the risk of spontaneous AV block was significantly greater in the organic heart disease group, occurring in 5% of these patients, compared with 1% in the primary conduction disease group (p < 0.05).

Mortality

Cardiovascular mortality (including sudden death) occurred in 105 patients (29%) with organic heart disease and in 10 (12%) with primary conduction disease (p < 0.001). Sudden death was noted in 61 patients (17%) with heart disease and in six patients (7%) with primary conduction disease (p < 0.01). Cumulative cardiovascular mortality (including sudden death) as well as mortality due to sudden death (through 5 years), using actuarial methods, is presented in table 4 and figure 1. Both the cardiovascular and sudden death mortality rates for all 5 years of follow-up were significantly lower in patients with primary conduction disease.

Discussion

Early studies of the natural history of patients with chronic bundle branch block suggested that bundle branch block was often a manifestation of serious underlying heart disease.17-19 Studies by Graybiel and Sprague,17 Perera et al.,18 Messer et al.19 and Campbell20 in a large number of patients with chronic bundle branch block (both right and left) revealed a mean survival period ranging from 14 months to 3.9 years. These studies were based on bundle branch block detected in hospital patients. Recent studies concerning bundle branch block detected in healthy young subjects, including military service personnel, reveal that intraventricular conduction defects, if not associated with organic heart disease, are compatible with normal longevity.21-23

It is apparent that patients with bundle branch block or bifascicular block may or may not have associated clinically apparent organic heart disease. The prognosis of bifascicular block should be at least partially dependent upon the presence or absence of underlying organic heart disease. There is no information available using prospective follow-up regarding the presence or absence of complicating heart disease on the prognosis of bifascicular block.

Primary or idiopathic conduction disease is defined as chronic bundle branch or bifascicular block without demonstrable organic heart disease. Data concerning the natural history of patients with primary conduction disease are limited to a few retrospective studies, some involving military personnel.21,22 Rotman and Triebwasser22 reported 348 Air Force personnel with right bundle branch block (104 with either right- or left-axis deviation) and 101 subjects with left bundle branch block who were asymptomatic and had no demonstrable heart disease at the time of inclusion into the study. During a mean follow-up period ranging from 8.8–10.8 years, two patients developed complete AV block. Fourteen patients with right bundle branch block (4%) and nine with left bundle branch block (8%) died during the follow-up period. Rotman and Triebwasser concluded that patients with primary conduction disease usually have a benign clinical course and low risk of progression to higher grades of AV block. Studies by Smith et al.,24 Wood et al.,25 Rodstein et al.25 and Reusch and Vivas26 in a limited number of asymptomatic subjects tend to support the above conclusions.

In contrast to asymptomatic outpatient population, Scanlon and colleagues27 reported results of retrospective follow up in 209 patients with chronic bifascicular
block (right bundle branch block with both left anterior and posterior hemiblock). Out of these, 30 (15%) had no demonstrable organic heart disease (primary conduction disease). Complete AV block developed in eight of 30 (26%) patients with no heart disease, compared with 22 of 179 (12%) with organic heart disease over an average follow-up period of about 2 years. The results of that study suggested that risk of progression to higher grades of AV block was greater in patients with primary conduction disease than in those with associated organic heart disease. Recently McAnulty and co-workers\(^2\) reported results of a 2-year follow up in 58 patients with primary conduction disease. Mortality rate due to sudden death was 9 ± 5.1% and total mortality, 15 ± 5.6%. These mortality rates were similar to those due to organic

<table>
<thead>
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<th>Mortality due to sudden death</th>
<th>PCD (n = 86)</th>
<th>OHD (n = 366)</th>
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<tr>
<td>1st year</td>
<td>1 ± 1.2</td>
<td>9 ± 1.5</td>
</tr>
<tr>
<td>2nd year</td>
<td>4 ± 2.4</td>
<td>13 ± 1.9</td>
</tr>
<tr>
<td>3rd year</td>
<td>6 ± 3.0</td>
<td>17 ± 2.2</td>
</tr>
<tr>
<td>4th year</td>
<td>11 ± 4.6</td>
<td>22 ± 2.6</td>
</tr>
<tr>
<td>5th year</td>
<td>11 ± 4.6</td>
<td>23 ± 2.8</td>
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<table>
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<tr>
<th>Cardiovascular mortality</th>
<th>PCD (n = 86)</th>
<th>OHD (n = 366)</th>
</tr>
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<tbody>
<tr>
<td>1st year</td>
<td>2 ± 1.7</td>
<td>14 ± 1.8</td>
</tr>
<tr>
<td>2nd year</td>
<td>7 ± 3.0</td>
<td>22 ± 2.2</td>
</tr>
<tr>
<td>3rd year</td>
<td>11 ± 3.8</td>
<td>29 ± 2.6</td>
</tr>
<tr>
<td>4th year</td>
<td>18 ± 5.4</td>
<td>33 ± 2.9</td>
</tr>
<tr>
<td>5th year</td>
<td>18 ± 5.4</td>
<td>39 ± 3.3</td>
</tr>
</tbody>
</table>

Abbreviations: PCD = primary conduction disease; OHD = organic heart disease.
heart disease. No information was supplied regarding the comparative incidence of AV block in the two groups.

Little information is available regarding the comparative incidence of AV nodal and trifascicular disease (as detected with electrophysiologic studies) in bifascicular block patients with and without organic heart disease. McAnulty et al.24 reported a 49% incidence (28 of 58 patients) of trifascicular disease in their patients with primary conduction disease. In the present series, we noted a 21% incidence of trifascicular disease in our patients with primary conduction disease as diagnosed by the presence of a prolonged HV interval. In contrast, the incidence of HV prolongation was 41% in patients with organic heart disease. Also, AV nodal dysfunction (prolonged AH interval) was more frequent in patients with organic heart disease. Thus, bifascicular block patients with organic heart disease have more widespread conduction disease than bifascicular block patients with primary conduction disease. One would therefore suspect that development of AV block would be more common in the former group.

In the present study, documented spontaneous progression of conduction disease was relatively uncommon, occurring in only 4.4% of all patients, over a mean follow-up period of about 3.5 years. However, the risk of developing spontaneous AV block in patients with primary conduction disease was significantly lower than in those with organic heart disease (1% vs 5%). This is consistent with our electrophysiologic findings and with the studies of Smith et al.21 and Rotman and Triebwasser26 and inconsistent with the study of Scanlon and co-workers.27 The incidence of AV block secondary to apparent cause was not significantly different in the present series (2% in both organic heart disease and primary conduction disease groups). This suggests that both groups are at identical risk for development of AV block, if exposed to a noxious influence.

The incidence of AV block reported in the present series reflects what was documented during the follow-up. Some instances of AV block may be either asymptomatic or associated with the occurrence of sudden death, and thus escaped detection. The prospective nature of our study, coupled with careful patient follow-up should limit the first possibility. As for sudden death, we have suggested previously that the most common cause of sudden death in patients with bifascicular block was ventricular dysrhythmia rather than trifascicular block.14 Information about the prognostic significance of primary conduction disease is limited. Scanlon and co-workers27 reported two deaths among 30 patients with primary conduction disease (7%), compared with 29 deaths among 179 (17%) bifascicular block patients with organic heart disease. There was no information as to whether the deaths were due to cardiovascular causes, sudden or non-sudden. In the present study both the cardiovascular mortality and mortality due to sudden death were significantly lower among patients with primary conduction disease, suggesting that the prognosis of individuals with bifascicular block is at least partially determined by the presence or absence of underlying cardiovascular disease. The occurrence of cardiovascular mortality (though less frequent) in our patients with primary conduction disease suggests subclinical organic heart disease in at least some primary conduction disease patients which escaped detection by simple clinical means. Noninvasive techniques such as stress testing, echocardiography, and nuclear scanning may be helpful in detecting subclinical organic heart disease in patients with chronic bifascicular block without apparent cardiac disease.

Based on our experience and the present study, we could not identify any variables (other than organic heart disease) which were helpful in determining a propensity to AV block and sudden death.6,9,14,16 The surface ECG patterns of bifascicular block were of no prognostic help, since the incidence of AV block was similar with right bundle branch block (with left- or right-axis deviation) and left bundle branch block. Comparison of patients with and without syncope, in our previous study, did not reveal any clinical electrocardiographic or electrophysiologic differences.6 The incidence of sudden and non-sudden deaths was also identical in patients with and without syncope. Prolongation of the HV interval was also not a useful indicator, since the incidence of AV block was similar in patients with or without HV prolongation.6

Conclusions

Several conclusions are suggested from this study of patients with primary conduction disease: 1) The incidence of primary conduction disease in hospitalized patients with chronic bifascicular block is approximately 20%. 2) Although similar in age to organic heart disease patients, the primary conduction disease patients have a significantly lower incidence of electrophysiologic abnormalities and subsequent spontaneous AV block. 3) Total cardiovascular and sudden death mortality is significantly lower in patients with primary conduction disease compared with those with organic heart disease. 4) The diagnosis of primary conduction disease based on simple clinical criteria probably underestimates the presence of underlying organic heart disease, as manifested by a small but definite risk of cardiovascular mortality. In patients with apparent primary bifascicular block, additional noninvasive techniques such as echocardiography and nuclear scanning may be helpful in identifying patients with subclinical organic heart disease.

Acknowledgement

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