Natural history of left bundle-branch block*

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SUMMARY The purpose of this study was to examine factors associated with the development of complete left bundle-branch block and the prognosis in a group of people not in hospital, who had no clinical evidence of ischaemic or valvular heart disease. Twenty-nine cases of left bundle-branch block without clinical evidence of ischaemic heart disease were noted in the Manitoba cohort of 3983 men under observation since 1948. The most frequent electrocardiographic finding before development of left bundle-branch block was a normal electrocardiogram; left ventricular hypertrophy though infrequent, was the only abnormality significantly more common than in the rest of the group. The development of left bundle-branch block was associated with distinct leftward shift of the frontal plane mean QRS axis. The most frequent clinical cardiovascular event observed after development of the block was sudden death without previous clinical evidence of ischaemic heart disease. The five-year incidence of sudden death as the first manifestation of heart disease was 10 times greater in men with left bundle-branch block than in those without it.

Our knowledge of the natural history of complete left bundle-branch block has come almost entirely from patients in hospital with heart disease, because there are comparatively few data from apparently healthy populations. Because prognosis derived from clinical case studies may be inappropriate to the symptomless individual prognostic data from persons without clinical evidence of heart disease are also necessary. Little is known about the electrocardiographic antecedents of left bundle-branch block and the electrocardiographic abnormalities that accompany its development, and there is still controversy about its association with changes in the mean frontal plane QRS vector. We have examined data from the Manitoba study cohort of 3983 men (most of whom were between 25 and 34 years of age at entry in 1948) in order to assess these problems.

Methods

The details have been reported previously. We have examined the electrocardiograms at the time had a routine electrocardiogram in addition to the regular medical examination. After discharge from service, some continued to fly but most found different occupations and are in different strata of society. For each subject, the examination closest to 30 June 1948 (date population was defined) was selected as the entry examination. The mean age of the men was then 30-8 years. The age distribution was as follows: 318 men were between 15 and 24 years; 1479 were between 25 and 29 years; 1258 were between 30 and 34 years; 539 were between 35 and 39 years; 205 were between 40 and 44 years; 153 were between 45 and 54 years, and 31 were between 55 and 64 years. On the history, physical examination and electrocardiogram none had clinical manifestations of ischaemic heart disease at entry. Since then, they have been written to annually, with examinations and electrocardiograms at intervals of at first five years and later three years. The observation period was from 1 July 1948 until 30 June 1977, an average follow-up of 29 years. Annual contact has been lost with only one person.

DEFINITION AND CASE SELECTION

The electrocardiograms have been coded using rules for identification of deflections and measurement of intervals outlined by the American Heart Association committee on electrocardiography and elabor-
ated in the Minnesota code. Descriptions of such variables as ST segment and T wave were those of the Minnesota code. The criteria used for the diagnosis of left bundle-branch block and other conduction disturbances were those outlined by the New York Heart Association and the Minnesota code. The mean frontal plane QRS vector was determined for each electrocardiogram, from the limb leads, using the hexaxial reference system, calculated to the nearest 15° because this is a reasonable limit of precision of the method.

Cases of left bundle-branch block included in the analysis satisfied the following criteria: detection of this conduction defect at a routine examination, and no clinical evidence of ischaemic or valvar heart disease on that examination or previously. Cases of left bundle-branch block associated with ischaemic heart disease were excluded. Twenty-nine cases fulfilled the above criteria. The age distribution at the detection of left bundle-branch block as follows: 35 to 39 years 3 men, 40 to 44 years 3 men, 45 to 49 years 4 men, 50 to 54 years 4 men, 55 to 59 years 8 men, 60 to 64 years 7 men. Left bundle-branch block developed during the observation period in all but one case, in whom it was present at entry; that case was only included for the analysis of prognosis.

Reports from doctors and hospitals, death certificates, information from relatives or executors of the estate and, whenever possible, necropsy findings were used to determine the cause of death. The definition of sudden death was that proposed by the World Health Organisation, namely natural death occurring immediately or within an estimated 24 hours after onset of symptoms.

**Data Analysis**
The Wilcoxon matched pair test was used to test differences of paired observations. To test proportions, the $x^2$ method was used. For analysis of prognosis, the life table method of Cutler and Ederer was used because it has several advantages, including the calculation of cases lost to follow-up, a category that incorporates cases of death not resulting from ischaemic heart disease. Thus the survival rate pertaining if ischaemic heart were the only cause of death can be determined.

**Results**

Factors Associated with Development of Complete Left Bundle-Branch Block
The most common electrocardiographic antecedent of left bundle-branch block was a normal electrocardiogram (Table 1). The next most frequent finding was left ventricular hypertrophy (satisfying

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Proportion</th>
</tr>
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<tbody>
<tr>
<td>None</td>
<td>15 (54%)</td>
</tr>
<tr>
<td>Left ventricular hypertrophy*</td>
<td>4 (14%)</td>
</tr>
<tr>
<td>ST and T abnormalities†</td>
<td>4 (14%)</td>
</tr>
<tr>
<td>Pronounced left axis deviation‡</td>
<td>1 (3.5%)</td>
</tr>
<tr>
<td>Prolonged PR interval§</td>
<td>1 (3.5%)</td>
</tr>
<tr>
<td>Pronounced left axis deviation plus prolonged PR interval</td>
<td>1 (3.5%)</td>
</tr>
<tr>
<td>Incomplete left bundle-branch block¶</td>
<td>1 (3.5%)</td>
</tr>
<tr>
<td>Intraventricular conduction defect of indeterminate type**</td>
<td>1 (3.5%)</td>
</tr>
</tbody>
</table>

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*Voltage criteria (Minn. 3-1 or 3-3 bł) plus ST and T abnormalities;
†ST and T abnormalities (Minnesota code 4-1 to 4-3, 5-1 to 3):
‡A QRS $-45^\circ$ to $-90^\circ$;
§PR 0-22 (Minn. 6-3);
¶QRS duration 0-10 to 0-11 s with A QRS $+75$ to $-75^\circ$.

There were no other cases with QRS duration 0-10 to 0-11 s;
**QRS duration 0-12 without QRS axis deviation or criteria for left or right bundle-branch block.

Minnesota code voltage criteria 3-1 or 3-3 plus ST and T wave changes Minn. 4-1 to 4-3 and 5-1 to 5-3) in 14 per cent of cases. This was significantly (P < 0.05) larger than the proportion of cases observed in the rest of the group without left bundle-branch block (14/100 versus 3-5/100). Pronounced left axis deviation or mean frontal plane QRS vector from $-45^\circ$ to $-90^\circ$ and incomplete left bundle-branch block seldom preceded the development of complete left bundle-bunch block. The proportion of ST segment and T wave abnormalities, pronounced left axis deviation, and prolonged PR interval in this group was not significantly different (P > 0.10) from the proportion in the rest of the group without left bundle-branch block.

The development of left bundle-branch block was associated with the characteristic QRS, ST, and T wave changes. It was also associated with a significant (P < 0.001) leftward shift in the mean frontal plane axis of QRS of $-22.0 \pm 5.5^\circ$ (mean $\pm$ SEM) from the last tracing (3.4 $\pm$ 0.2 years) before left bundle-branch block (Fig. 1). By comparison the mean change in frontal plane axis of QRS for the same ages in the entire group over the same time interval between electrocardiograms ranged from $-3^\circ$ to $-7^\circ$. In contrast and not unexpectedly there was no significant change (P > 0.05) in the PR interval from the tracing immediately before (PR = 16.2 $\pm$ 4 ms) to the electrocardiogram with the intraventricular conduction defect (PR 16.8 $\pm$ 4 ms).

**Prognosis of Left Bundle-Branch Block**
The cardiovascular morbidity and mortality after the development of complete left bundle-branch block was: 17.2 per cent (5/29) had sudden death.
without prior cardiovascular symptoms; 3.4 per cent (1/29) developed angina pectoris and later died suddenly; 3.4 (1/29) had a cerebrovascular accident; none had myocardial infarction (an episode of chest pain associated with increases in blood levels of cardiac enzymes).

This experience is in distinct contrast to the rest of the population. The proportion of sudden deaths in men without clinical evidence of previous myocardial infarction is not only significantly larger (P<0.01), but also is over 10 times greater in the group with left bundle-branch block compared with those in the rest of the group without left bundle-branch block (20.7/100 versus 1.6/100).

To focus on sudden death as the first manifestation of ischaemic heart disease and to standardise the length of follow-up as well as to examine age specific subgroups, two approaches were used. The life table method disclosed that for men 35 to 44 years of age at development of complete left bundle-branch block the five-year probability of survival without sudden death was 1.0, for men 45 to 54 years of age it was 0.85, and for men 55 to 64 years of age it was 0.75. Only two sudden deaths occurred after five years of observation and both were over 10 years later. Two individuals died from malignancies (12 and 28 years) and one from stroke (one year) after the development of left bundle-branch block. The five-year incidence of sudden death as the first manifestation of heart disease was calculated for men with left bundle-branch block onset between 45 and 54 years and 55 and 64 years of age at development of left bundle-branch block and compared with men in five-year age groups without left bundle-branch block. Though the incidence rates are based upon a small number of cases of left bundle-branch block, they are at least 10 times greater than the five-year incidence of sudden death as the first manifestation of ischaemic heart disease in the remainder of the series free of left bundle-branch block (Table 2).

Examining the mean frontal plane axis of QRS and QRS duration to determine whether these variables would identify subsets of left bundle-branch block with a poor prognosis, the ages 45 to 64 were combined because there was no significant correlation between age and either of these two electrocardiographic variables in the presence of left bundle-branch block. For QRS duration there was no difference in early mortality but there was a trend towards increased long-term mortality for wide QRS duration (Fig. 3); also two subjects with left bundle-branch block and QRS widening died after the first five years. The mean frontal plane axis of QRS did not differentiate those with an adverse or favourable prognosis (Fig. 3). Only two of those with a QRS axis of less than 0°, however, had pronounced left axis deviation, both of them had it
before the development of left bundle-branch block. One is still alive after nine years of follow-up and the other died of a stroke after one year of follow-up.

Table 2 Five-year incidence of sudden death as only manifestation of heart disease

<table>
<thead>
<tr>
<th>Complete left bundle-branch block (LBBB)</th>
<th>Five-year incidence sudden death/1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at LBBB</td>
<td></td>
</tr>
<tr>
<td>45 to 54</td>
<td>143</td>
</tr>
<tr>
<td>55 to 64</td>
<td>183</td>
</tr>
</tbody>
</table>

| No LBBB                                  |                                       |
| Age free of ischaemic heart disease and LBBB | Five-year incidence sudden death/1000 |
| 45           | 0.8                                    |
| 50           | 3.1                                    |
| 55           | 4.7                                    |
| 60           | 8.1                                    |
| 65           | 18.9                                   |

Discussion

PROGNOSIS

Discussion of the prognosis for left bundle-branch block in this series should be preceded by the examination of several factors including the population from which the data were derived. Though there is concern that none of the groups for study of cardiovascular disease is representative of general population, the Manitoba study is a highly selected series, and extrapolation of our findings to the general population must be done with caution. However, the relatively young age at entry and the repeated examinations permit identification of age at development and factors associated with the development of left bundle-branch block. The small number of cases of left bundle-branch block suggests caution in the extrapolation of the data. Clinically, occult ischaemic heart disease may have been responsible for the development of left bundle-branch block in some cases and thus have influenced the prognosis.

The prognosis reported for complete left bundle-branch block has varied widely, mainly as a result of the different populations from which the cases were selected, presence or absence of heart disease, and the type and severity of heart disease. Initial studies from hospital-based populations of ill patients disclosed a high prevalence of disease, with an average survival of 1·5 to 4·0 years. Later studies of armed forces personnel and outpatients with left bundle-branch block with no evidence of heart disease disclosed no adverse prognosis. Population studies have reported conflicting findings. Two studies reported an increased mortality while another two found little or no increased risk of death from ischaemic heart disease. In our study left bundle-branch block, developing in men over 45 years of age, is associated with an increased mortality usually within the first five years of development. One possible explanation for the apparently conflicting observations is that mortality rate is influenced by the proportion of left bundle-branch block of recent onset.

Electrocardiographic features such as QRS duration and frontal plane QRS axis did not identify subgroups with a significantly different outcome though a wide QRS duration may point to an unfavourable long-term prognosis. Johnson et al.,18 studying left bundle-branch block in patients with relatively severe heart disease, observed that survival was inversely proportional to QRS duration which they believed reflected the severity of the heart disease. For persons without apparent heart disease the electrocardiographic measurement of QRS duration was not a powerful prognostic factor. Electrophysiological intracardiac measurements of intraventricular conduction times are undoubtedly a more sensitive indicator of the severity of conduction system disease and prognosis.

Fig. 3 The proportion surviving after detection of left bundle-branch block according to QRS duration (upper panel) and mean frontal plane QRS vector (A QRS).
In this study, cardiac mortality consisted of sudden death mainly in persons who developed no clinical evidence of ischaemic heart disease in the interval between development of left bundle-branch block and death. Left bundle-branch block after myocardial infarction or in patients with angina pectoris has been identified as a predictor of sudden death, but a similar relation has not been observed in the absence of ischaemic heart disease.

It is important to recognise and define high-risk groups and the nature of the relation between left bundle-branch block and sudden death remains to be determined. Speculations on this relation include the possibility that persons with left bundle-branch block are more likely to develop complete heart block or fatal arrhythmias should ischaemic heart disease subsequently occur. In addition, though cardiovascular epidemiological studies label sudden death as one form of ischaemic heart disease, sudden death in left bundle-branch block may result from heart block or arrhythmias unrelated to ischaemic heart disease.

ANTECEDENT ELECTROCARDIOGRAPHIC FINDINGS

The electrocardiogram was of limited value in predicting the development of left bundle-branch block. The majority of previous electrocardiograms in this group had been normal. Left ventricular hypertrophy, though relatively infrequent, was the only electrocardiographic abnormality that was an important antecedent of left bundle-branch block. This is consistent with the data of Bauer whose much smaller group, however, consisted of patients with clinical evidence of heart disease. Of interest is the low proportion of cases with previous electrocardiographic findings of incomplete left bundle-branch block or pronounced left axis deviation referred to as left anterior hemiblock. The 7 per cent prevalence of previous distinct left axis deviation in this study is similar to that in preliminary reports from Framingham. The small proportion with earlier distinct left axis deviation suggests that the site of the block may not involve the anterior part of the left bundle and is proximal—predivisional, as suggested by Rosenbaum. An equally acceptable explanation, however, is that left bundle-branch block occurs without warning signs.

CHANGES ASSOCIATED WITH OCCURRENCE OF LEFT BUNDLE-BRANCH BLOCK

In the early days of electrocardiography it was believed that the development of left bundle-branch block was associated with changes in mean frontal QRS vector. Later investigators disputed these findings and reported that development of left bundle-branch block was infrequently associated with obvious shifts in QRS axis. The present investigation has shown a statistically significant mean leftward shift in the QRS axis of 22 degrees with the development of left bundle-branch block. This was considerably greater than the expected change in the QRS axis over a similar time interval in men who did not develop this intraventricular conduction defect.

The development of left bundle-branch block thus usually occurs without preceding electrocardiographic abnormalities. Previous left ventricular hypertrophy, though infrequent, is the only significant antecedent finding. In the absence of clinical evidence of ischaemic or valvar heart disease the prognosis of left bundle-branch block is more favourable than in patients with heart disease with this conduction disturbance. However, a significant increased proportion of sudden deaths was observed in this group mainly in the first few years after the onset of left bundle-branch block.

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