

EDITORIAL

# What Should Be Done With the Asymptomatic Patient With Right Bundle Branch Block?

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**R**ight bundle branch block (RBBB) is frequently found in the general healthy population. RBBB is caused by diseases that affect the right bundle branch or the myocardial region, where the right bundle branch is located. Possible causes include trauma, structural changes, infiltrative diseases (eg, sarcoidosis), myocarditis, and myocardial infarction. Right ventricular pressure and/or volume overload, either acutely or chronically, can stretch the right bundle branch leading to the RBBB pattern. Lenegre disease or Lev disease (progressive cardiac conduction system diseases) can cause RBBB, especially in elderly patients. In patients with underlying heart disease causing degeneration of the conduction pathway, a tachycardia-dependent RBBB can be seen.<sup>1</sup>

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**See Article by Gaba et al.**

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RBBB is generally a slowly progressive degenerative disease of the conductive system. The incidence of RBBB increases with age, reaching up to 11.3% of the population by the age of 80 years.<sup>1</sup> Many people with RBBB have no clinical evidence of structural heart disease or coronary artery disease. The relatively high prevalence of RBBB is related to the fragility of the right bundle branch, as RBBB often occurs after minor chest trauma<sup>2</sup> or after right heart catheterization.<sup>3</sup> Traditionally, it was accepted that in patients without evidence of cardiac disease, complete or incomplete

RBBB usually is not associated with increased risk of cardiac morbidity or mortality; however, this was based on a small cohorts of patients.<sup>1,4,5</sup>

Yet, over the years, conflicting data have emerged about the long-term prognostic significance of incidental RBBB in people without overt cardiac disease. Rotman and Triebwasser used the database of the US Air Force Central Electrocardiographic Library and reported on 394 individuals with RBBB with a mean age of 36.9 years (range, 17–58 years). Most of the subjects were asymptomatic at the time of diagnosis. During a mean follow-up of 10.8 years, 6% of the patients developed coronary artery disease and 4% died. Only one patient developed complete heart block. They concluded that, overall, the prognosis was good.<sup>4</sup> No increased mortality was reported in patients >85 years with RBBB.<sup>6</sup> Casiglia et al assessed the implications of BBB on mortality among 2254 elderly subjects included in the CASTEL (Cardiovascular Study in the Elderly) who were followed up for 7 years.<sup>7</sup> The presence of RBBB was associated with increased all-cause mortality in both men and women and with cardiovascular mortality only in men, but not in women.<sup>7</sup> Fahy et al reported on 310 individuals with bundle branch block (BBB) who were followed up for 9.5 years. Left BBB, but not RBBB, was associated with an increased prevalence of cardiovascular disease at the follow-up (21% versus 11%;  $P=0.04$ ).<sup>8</sup>

Eriksson et al used the Primary Prevention Study in Goteborg, Sweden. They included 7392 men without

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prior myocardial infarction or stroke born between 1915 and 1925 and initially evaluated between 1970 and 1973 (70 men had RBBB).<sup>9</sup> The patients were followed up until 1998. RBBB was not associated with increased risk of myocardial infarction, cardiovascular mortality, all-cause mortality, or heart failure. Yet, RBBB was associated with an increased risk for progression to high-degree atrioventricular block.<sup>9</sup>

Among the 9541 patients aged  $\geq 55$  years with established cardiovascular disease or diabetes mellitus with  $\geq 1$  risk factors who participated in the Heart Outcomes Prevention Evaluation trial and were followed up for a median of 4.5 years, a total of 428 (4.5%) had RBBB on their baseline ECG.<sup>10</sup> RBBB was not associated with increased risk of cardiovascular events.<sup>10</sup>

Bansilal et al studied a cohort of 2271 consecutive patients who presented to 3 Olmsted County, Minnesota, emergency departments with angina from 1985 to 1992. Over a median follow-up of 7.3 years, the patients with RBBB had a higher risk for major adverse cardiac events (hazard ratio [HR], 1.85; 95% CI, 1.44–2.38;  $P < 0.001$ ) compared with patients without BBB. The survival rate after a median follow-up of 16.6 years was lower in patients with RBBB (23% versus 53%; HR, 2.19; 95% CI, 1.73–2.78;  $P < 0.001$ ); however, after adjustment for baseline risk factors, the risk associated with RBBB was no longer significant (HR, 1.10; 95% CI, 0.86–1.40;  $P = 0.45$ ).<sup>11</sup>

Zhang et al studied the prognostic significance of RBBB in women, using the WHI (Women's Health Initiative) study. A total of 66 450 women (832 with RBBB) were followed up for 14 years. The adjusted HR for coronary heart disease mortality with RBBB was 1.62 (95% CI, 1.08–2.43;  $P < 0.05$ ). Among the women without cardiovascular disease at baseline, RBBB was not associated with all-cause mortality or coronary heart disease mortality; yet, among those with cardiovascular disease at baseline RBBB, and especially RBBB+left anterior fascicular block (LAFB), was associated with increased all-cause mortality.<sup>12</sup> In another analysis of the same cohort, RBBB was not an independent predictor of increased risk of heart failure; however, when associated with LAFB, it was an independent predictor of heart failure (HR, 2.96; 95% CI, 1.77–4.93).<sup>13</sup>

Bussink et al reported on the outcomes of subjects with RBBB in the general population, using the CCHS (Copenhagen City Heart Study).<sup>14</sup> Among 18 441 participants without history of myocardial infarction, heart failure, or left BBB, 1.4% of the men and 0.5% of the women had RBBB and 4.7% and 2.3% had incomplete RBBB, respectively. RBBB was associated with increased risk of all-cause and cardiovascular mortality (the age-adjusted HR was 1.31 [95% CI, 1.11–1.54] and 1.87 [95% CI, 1.48–2.36], respectively). In addition, RBBB was associated with higher risk of myocardial

infarction and pacemaker implantation, but not with chronic heart failure. A similar risk was detected in men and women.<sup>14</sup> Incomplete RBBB was not associated with increased risk.<sup>14</sup>

In the ARIC (Atherosclerosis Risk in Communities) Study, a total of 159 patients of 14 478 patients included in the study had RBBB. Over a follow-up of 18 years, RBBB combined with either LAFB or left posterior fascicular block, but not lone RBBB, were predictors of heart failure.<sup>15</sup>

Among 2981 patients without baseline cardiovascular events followed up at primary health centers in Spain for 5 years, 4.6% had incomplete RBBB and 3.2% had complete RBBB. In univariate analysis, complete RBBB was associated with increased all-cause mortality, but only bifascicular block (RBBB with LAFB or left posterior fascicular block) was significant after adjusting for confounders.<sup>16</sup> Incomplete RBBB was not associated with increased risk.<sup>16</sup>

In a recently published study of 6299 subjects (mean age, 52.8 years), 75 (1.2%) had complete RBBB and 61 (1%) had incomplete RBBB at baseline.<sup>17</sup> During a median follow-up of 15.9 years, 1309 of the subjects (20.8%) died, and of these, 655 (10.4%) were cardiovascular deaths. Nonspecific intraventricular conduction delay and left BBB according to the Minnesota definition, but not complete or incomplete RBBB, were independently associated with cardiovascular mortality after adjustment for age and sex. The authors did not study the prognostic impact of combined intraventricular conduction disorders.

Thus, there have been conflicting data on the prognostic significance of isolated RBBB in patients without established heart disease. Yet, it seems that when combined with LAFB or left posterior fascicular block, RBBB is associated with increased risk.<sup>12,13,15,16</sup> The other studies did not separate between isolated RBBB and RBBB as part of a bifascicular block; therefore, we cannot exclude the possibility that the different results are related to different prevalence of concomitant fascicular blocks among the studies.

In this issue of the *Journal of the American Heart Association (JAHA)*, Gaba et al<sup>18</sup> used a cohort of patients who underwent exercise stress tests at the Mayo Clinic Integrated Stress Center between 1993 and 2010. They selected only Minnesota residents and excluded patients with known cardiovascular disease.<sup>18</sup> The authors did not specify whether cardiovascular disease included hypertensive heart disease. It is unclear whether they included only patients who underwent plain ECG stress test or also patients who underwent exercise stress test together with imaging (stress echocardiography or single-photon emission computed tomography). In addition, it is unclear whether patients with left BBB or nonspecific intraventricular conduction delay were included.

A total of 220 patients (0.96%) of the 22 806 patients included had RBBB. Patients were followed up for 6 to 23 years (mean duration, 12.4 years). The authors found that RBBB was associated with all-cause (HR, 1.5; 95% CI, 1.1–2.0;  $P=0.0058$ ) and cardiovascular-related mortality (HR, 1.7; 95% CI, 1.1–2.8;  $P=0.0178$ ) after adjusting for age, sex, diabetes mellitus, hypertension, obesity, current and past history of smoking, and use of a heart rate lowering drug.<sup>18</sup> This is a distinct and selective population of patients without known heart disease, who underwent an exercise stress test for various reasons. In a considerable proportion (>50%) of patients, the reason for the test was screening for coronary artery disease, whereas only ≈30% had symptoms. The index stress test was positive for ischemia in only 4.8% of the patients without RBBB and in 3.2% of the patients with RBBB. Yet, the presence of RBBB was associated with a significant increased risk for all-cause and cardiovascular mortality. The exact causes of cardiovascular death are not specified (coronary artery disease, heart failure, or arrhythmic death); thus, we cannot conclude whether the sensitivity of the stress test for detection of ischemia is low in the presence of RBBB, or that non-ischemia-related causes were more prevalent as a cause of death in these patients.

If patients with concomitant imaging stress test had been included, reporting the data could have shed light on the issue of sensitivity to detect ischemia. Confirming the findings in previous studies, Gaba et al<sup>18</sup> reported that patients with RBBB were older than those without RBBB. In addition, peak heart rate was significantly lower and metabolic equivalents achieved was significantly lower. The percentage of the patients reaching target heart rate and the average percentage of the age-adjusted maximal heart rate reached are not reported. With an average peak heart rate of 134.4 beats per minute and average age of 59 years (Tables 1 and 3), it is possible that a higher percentage of patients with RBBB did not reach target heart rate and, therefore, significant ischemia could have been missed. Moreover, patients with RBBB often have ST depression in the right precordial leads that become deeper during exercise. Isolated ST depression in V1 to V3 in patients with RBBB is usually not interpreted as a sign of ischemia. Studying a cohort of patients who underwent pharmacologic stress test could answer the question of whether RBBB at rest is associated with extensive coronary artery disease and worse prognosis, as was recently suggested for patients with acute coronary syndromes.<sup>19–21</sup>

In the current cohort, patients with RBBB had lower exercise capacity, had slower heart rate recovery, and more often need to stop the test because of dyspnea compared with the patients without RBBB.<sup>18</sup> Thus, RBBB can be a marker for underlying subclinical

cardiac conditions, including diastolic dysfunction with preserved systolic function; hypertension was more frequent in the patients with RBBB than in those without.

In addition, it is unclear whether the study included only patients with RBBB at baseline ECG in the RBBB group or also those with exercise-induced RBBB. Stein et al reported that the mortality of patients with exercise-induced RBBB during a stress test is relatively high.<sup>22</sup> However, these patients were older and had significantly more comorbidities than patients without exercise-induced RBBB. After adjusting for age, exercise-induced RBBB was no longer significantly associated with all-cause mortality or cardiovascular mortality.<sup>22</sup>

Moreover, the authors did not analyze patients with isolated RBBB versus those with concomitant fascicular blocks (see above). Thus, we do not know if it is the RBBB itself or only RBBB associated with fascicular block that predicts mortality.

Thus, the current study of mostly asymptomatic patients added an important piece of information about the long-term significance of RBBB in patients without known heart disease; yet, it has not solved the mystery as to the underlying pathophysiological characteristics and the mechanism of increased mortality in these patients.

## ARTICLE INFORMATION

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### Disclosures

None.

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