

# Association between complete right bundle branch block and atrial fibrillation development

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## Abstract

**Background:** Complete right bundle branch block (CRBBB) is an important predictor of atrial fibrillation (AF) recurrence after pulmonary vein isolation. However, the association between CRBBB and AF development remains unclear.

**Methods:** We performed a retrospective study of 2639 patients (male,  $n = 1549$ ; female,  $n = 1090$ ; mean age,  $58 \pm 13$  years). CRBBB was defined as a late R ( $R'$ ) wave in lead  $V_1$  or  $V_2$  with a slurred S wave in lead I and/or lead  $V_6$  with a prolonged QRS duration ( $\geq 120$  ms).

**Results:** Among the 2639 patients, CRBBB was detected in 40 patients (1.5%), and the prevalence of AF was 7.4% (196/2639). The proportion of patients with AF and CRBBB was higher than the proportion of patients with AF without CRBBB (22.5% vs. 7.2%;  $p = 0.001$ ). In the forward multivariate logistic analysis, CRBBB (odds ratio [OR], 3.329; 95% confidence interval [CI], 1.350–8.211;  $p = 0.009$ ), complete left bundle branch block (OR, 2.209; 95% CI, 1.238–3.940;  $p = 0.007$ ), age (OR, 1.020; 95% CI, 1.005–1.035;  $p = 0.009$ ), valvular heart disease (OR, 2.332; 95% CI, 1.531–3.552;  $p < 0.001$ ), left atrial diameter (OR, 1.133; 95% CI, 1.104–1.163;  $p < 0.001$ ), left ventricular ejection fraction (OR, 1.023; 95% CI, 1.006–1.041;  $p = 0.007$ ), and class I or III anti-arrhythmic drug use (OR, 10.534; 95% CI, 7.090–15.651;  $p < 0.001$ ) were associated with AF.

**Conclusion:** Complete right bundle branch block was significantly associated with AF development in hospitalized patients with cardiovascular diseases.

## KEYWORDS

atrial fibrillation, complete right bundle branch block, electrocardiography

## 1 | INTRODUCTION

Atrial fibrillation (AF) is a common cardiac arrhythmia in the general population (Kjerpeseth et al., 2021) and is associated with increased cardiovascular morbidity and mortality. (Tanaka et al., 2021) Early

recognition of AF could allow for more successful control of arrhythmia and protect the patient from adverse consequences. (Hindricks et al., 2021) Therefore, it is crucial to identify patients who are at an increased risk of developing AF. Complete right bundle branch block (CRBBB) is one of the most frequent alterations observed on

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electrocardiography (ECG). It is defined as a late R (R') wave presenting in lead V<sub>1</sub> or V<sub>2</sub> with a slurred S wave in lead I and/or lead V<sub>6</sub> with a prolonged QRS duration of  $\geq 120$  ms. (Surawicz et al., 2009) CRBBB is generally considered a benign finding that does not imply an increased risk of cardiovascular diseases when found in asymptomatic healthy individuals. (Eriksson, Hansson, Eriksson, & Dellborg, 1998; Fahy et al., 1996; Fleg et al., 1983) However, these findings are based on a few outdated studies with small sample sizes, and many recent cohort studies have found that CRBBB is significantly associated with cardiovascular risk and all-cause mortality. (Bussink et al., 2013; Cinca et al., 2013; Kleemann et al., 2008; Manzano et al., 2011; McCullough et al., 2005; Nakazawa et al., 2021; Widimsky et al., 2012; Wong et al., 2006) Furthermore, a recent study showed that CRBBB is an independent predictor of AF recurrence after pulmonary vein isolation. (Yano et al., 2021) In patients with CRBBB who have undergone AF ablation, most of the pathogenic factors for AF exist before ablation. It is reasonable to hypothesize that CRBBB is also associated with AF development. However, there is little information available on the association between CRBBB and AF development. Thus, the purpose of this retrospective study was to investigate the association between CRBBB and AF development.

## 2 | METHODS

### 2.1 | Study subjects

Our prospectively established database of ECG recordings from patients who were hospitalized at the Heart Center of Henan Provincial People's Hospital for diagnosis and treatment between 1 March 2018 and 31 March 2018 was retrospectively reviewed. If patients underwent more than one ECG examination during the index hospitalization, only the first ECG recording was analyzed. The clinical records of all patients were reviewed. Patients with confirmed AF lasting longer than 30 seconds documented by ECG and/or Holter recordings (Hindricks et al., 2021) or with a history of AF were considered to have AF. We excluded patients with congenital heart disease and previous cardiac surgery, missing data for calculation of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, and thyroid dysfunction, as determined by an abnormal free thyroxine or thyroid-stimulating hormone concentration.

The CHA<sub>2</sub>DS<sub>2</sub>-VASc score was calculated for each patient by assigning 1 point each for age 65–74 years, hypertension, diabetes mellitus, congestive heart failure, vascular disease, and female sex, and 2 points for previous stroke or transient ischemic attack and age  $\geq 75$  years. (Lip et al., 2010) Hypertension was defined as a systolic blood pressure of  $\geq 140$  mmHg, a diastolic blood pressure of  $\geq 90$  mmHg, or treatment with antihypertensive drugs. Congestive heart failure was considered present for patients with a history of heart failure or a left ventricular ejection fraction (LVEF) of  $< 35\%$ . Diabetes mellitus was defined as a fasting blood glucose concentration of  $> 126$  mg/dl or treatment with hypoglycemic agents. The study protocol conformed to the ethical guidelines of the Declaration of

Helsinki. The study protocol was approved by the local institutional review board, and the requirement for informed consent was waived because of the retrospective nature of the study.

### 2.2 | ECG analysis

For all patients, CRBBB was assessed from resting 12-lead ECG recordings in sinus rhythm (high-bandpass filter, 0.05 Hz; low-bandpass filter, 150 Hz; 25 mm/s, 10 mm/mV). ECG recordings were manually analyzed on a computer screen using digital calipers with scanning at 300 dots per square inch and four-fold image amplification. CRBBB was defined as a late R (R') wave presenting in lead V<sub>1</sub> or V<sub>2</sub> with a slurred S wave in lead I and/or lead V<sub>6</sub> with a prolonged QRS duration of  $\geq 120$  ms, and complete left bundle branch block (CLBBB) was defined as QRS duration  $\geq 120$  ms; broad notched or slurred R waves in leads I, aVL, V<sub>5</sub>, and V<sub>6</sub>; and absent q waves in leads I, V<sub>5</sub>, and V<sub>6</sub>. (Perez-Riera et al., 2019; Surawicz et al., 2009) The QRS duration was measured from the beginning of the QRS complex to the J point, which was defined as the point of transition from the R wave to the ST segment. (Rosso et al., 2008; Wong et al., 2006) ECG analysis was performed independently by two observers who were blinded to patients' details, and any differences between observers were resolved by consensus.

### 2.3 | Statistical analysis

Data analysis was performed using SPSS software (SPSS, version 26.0; IBM Corp.). Data are expressed as percentage or mean  $\pm$  standard deviation, as appropriate. Continuous and categorical variables were compared between groups using the independent samples *t*-test and the  $\chi^2$  test, respectively. The univariate analysis was performed using logistic regression. For each variable, the odds ratio (OR), 95% confidence interval (CI), and *p* value are provided. Variables that significantly correlated in the univariate analysis were further analyzed using a forward multiple logistic regression analysis to identify factors associated with AF. All probability values were two-sided. A *p* value of  $< .05$  was considered statistically significant.

## 3 | RESULTS

### 3.1 | Patient characteristics

A total of 2639 patients (male,  $n = 1,549$ ; female,  $n = 1,090$ ; mean age,  $58 \pm 13$  years) were included in the study. AF was detected in 196 patients (7.4%). The clinical characteristics of patients with and without AF are listed in Table 1. Compared with patients without AF, patients with AF were older and had a larger left atrial diameter, a higher CHA<sub>2</sub>DS<sub>2</sub>-VASc score and a lower LVEF, as well as a higher rate of  $\beta$ -blocker and class I or III anti-arrhythmic drug use on

admission. The prevalence of congestive heart failure, valvular heart disease, CLBBB, and CRBBB was significantly higher in patients with AF compared with those without AF.

### 3.2 | Clinical correlates for atrial fibrillation

Determinants of AF development in all patients are shown in Table 2. In the univariate analysis, AF was significantly associated with CRBBB, CLBBB, age, CHA<sub>2</sub>DS<sub>2</sub>-VASc score, congestive heart failure, valvular heart disease, left atrial diameter, and LVEF, as well as use of calcium channel blockers,  $\beta$ -blockers, and class I or III anti-arrhythmic drugs on admission. In the forward multivariate logistic analysis, CRBBB (OR, 3.329; 95% CI, 1.350–8.211;  $p = .009$ ), CLBBB (OR, 2.209; 95% CI, 1.238–3.940;  $p = .007$ ), age (OR, 1.020; 95% CI, 1.005–1.035;  $p = .009$ ), valvular heart disease (OR, 2.332; 95% CI, 1.531–3.552;  $p < .001$ ), left atrial diameter (OR, 1.133; 95% CI, 1.104–1.163;  $p < .001$ ), LVEF (OR, 1.023; 95% CI, 1.006–1.041;  $p = .007$ ), and class I or III anti-arrhythmic drug use (OR, 10.534; 95% CI, 7.090–15.651;  $p < .001$ ) were associated with AF.

### 3.3 | Comparison of AF development

The percentage of patients with AF with and without CRBBB is shown in Figure 1. The proportion of patients with AF with CRBBB was higher than the proportion of patients with AF without CRBBB (22.5% vs. 7.2%;  $p = .001$ ) (Figure 1).

TABLE 1 Baseline clinical characteristics of patients with and without AF

Parameters	AF (n = 196)	No AF (n = 2,443)	p Value
Age (years)	63 ± 12	58 ± 13	<.001
Male, n (%)	117 (59.7%)	1,432 (58.6%)	.768
Coronary artery disease, n (%)	64 (32.7%)	754 (30.9%)	.602
Diabetes mellitus, n (%)	41 (20.9%)	520 (21.3%)	.904
Hypertension, n (%)	86 (43.9%)	1,199 (49.1)	.161
Congestive heart failure, n (%)	23 (11.7%)	102 (4.2%)	<.001
Prior stroke or TIA, n (%)	27 (13.8%)	303 (12.4%)	.576
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	2.4 ± 1.8	2.1 ± 1.6	.017
Valvular heart disease, n (%)	110 (56.1%)	299 (12.2%)	<.001
Left atrial diameter (mm)	46.0 ± 9.0	36.3 ± 6.3	<.001
LVEF, %	56.2 ± 12.2	60.1 ± 9.5	<.001
CRBBB, n (%)	9 (4.6%)	31 (1.3%)	.001
CLBBB, n (%)	6 (3.1%)	18 (0.7%)	.004
Anti-arrhythmic drugs on admission, n (%)			
None	30 (15.3%)	782 (32.0%)	<.001
Class I or III, n (%)	86 (43.9%)	103 (4.2%)	<.001
$\beta$ -blockers, n (%)	122 (62.2%)	1,327 (54.3%)	.032
Calcium channel blockers, n (%)	44 (22.4%)	715 (29.3%)	.042

Abbreviations: AF, atrial fibrillation; CLBBB, complete left bundle branch block; CRBBB, complete right bundle branch block; LVEF, left ventricular ejection fraction; TIA, transient ischemic attack.

## 4 | DISCUSSION

The main findings of this study were as follows. First, the prevalence of CRBBB was 1.5% in patients hospitalized for cardiovascular disease who were enrolled from our registry. Second, CRBBB was independently associated with AF in this study population. Third, CLBBB, age, valvular heart disease, left atrial diameter, LVEF, and class I or III anti-arrhythmic drug use were significantly correlated with AF.

The prevalence of CRBBB varies by age and population. The prevalence of CRBBB is approximately twice as high in men than in women, and ranges from 0.6% in women aged <40 years to 14.3% in men aged >80 years. (Bussink et al., 2013) Furthermore, the prevalence of CRBBB may be higher in patients with hypertension, diabetes mellitus, and AF. (Miller et al., 2008; Movahed, 2007; Yano et al., 2021) In a recent large community-based cohort study of 90,022 individuals aged 40–79 years who participated in annual community-based health check-ups, the prevalence of CRBBB was 1.5%. (Nakazawa et al., 2021) In our study, the prevalence of CRBBB was also 1.5%, but our study population included patients aged <40 years, all of whom were hospitalized at the Heart Center of Henan Provincial People's Hospital and the majority of whom had cardiovascular diseases.

Several studies have also investigated the association between CRBBB and AF. Bussink et al. (Bussink et al., 2013) evaluated the prognostic value of CRBBB on resting 12-lead ECG in the general population. They concluded that CRBBB was not associated with the risk of AF. In contrast, in a study by Nielsen et al., (Nielsen

Parameters	Univariate		Multivariate (Forward)	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Age (years)	1.035(1.023–1.048)	<.001	1.020 (1.005–1.035)	.009
Male, n (%)	1.046(0.777–1.407)	.768		
Coronary artery disease, n (%)	1.086(0.796–1.482)	.602		
Diabetes mellitus, n (%)	0.978(0.684–1.399)	.904		
Hypertension, n (%)	0.811(0.605–1.087)	.162		
Congestive heart failure, n (%)	3.051(1.892–4.921)	<.001		
Prior stroke or TIA, n (%)	1.128(0.739–1.724)	.576		
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	1.124(1.031–1.226)	.008		
Valvular heart disease, n (%)	9.172(6.747–12.467)	<.001	2.332 (1.531–3.552)	<.001
Left atrial diameter (mm)	1.165(1.142–1.189)	<.001	1.133 (1.104–1.163)	<.001
LVEF, %	0.967(0.955–0.979)	<.001	1.023 (1.006–1.041)	.007
CRBBB, n (%)	3.745(1.757–7.982)	.001	3.329 (1.350–8.211)	.009
CLBBB, n (%)	2.063(1.292–3.293)	.002	2.209 (1.238–3.940)	.007
Class I or III, n (%)	17.762(12.588–25.061)	<.001	10.534 (7.090–15.651)	<.001
$\beta$ -blockers, n (%)	1.387(1.028–1.871)	.033		
Calcium channel blockers, n (%)	0.700 (0.495–0.989)	.043		

TABLE 2 Determinants of AF in the study population

Abbreviations: CI, confidence interval; CLBBB, complete left bundle branch block; CRBBB, complete right bundle branch block; LVEF, left ventricular ejection fraction; OR, odds ratio; TIA, transient ischemic attack.

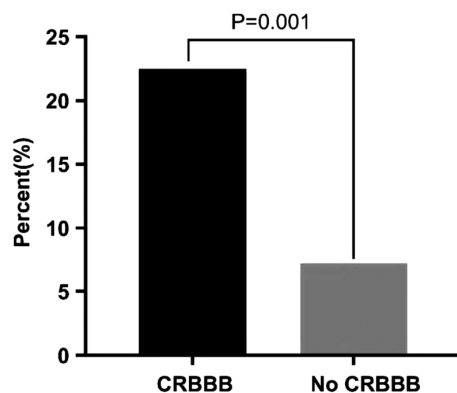


FIGURE 1 Percentage of patients with AF among those with and without CRBBB. AF, atrial fibrillation; CRBBB, complete right bundle branch block

et al., 2011) incomplete right bundle branch block was strongly and independently associated with early-onset AF. In addition, a recent study evaluated the impact of baseline CRBBB on outcomes after pulmonary vein isolation in patients with AF and found that CRBBB was an independent predictor of AF recurrence after

pulmonary vein isolation. (Yano et al., 2021) In the present study, the univariate and multivariate analyses showed that CRBBB was independently associated with AF development. Several mechanisms may account for the relationship between CRBBB and AF development. First, CRBBB induces an abnormal electrical and mechanical activation pattern in the ventricles, dividing the ventricles into early- and late-activated regions, resulting in ventricular dyssynchrony. (Baragan et al., 1970; Sillanmaki et al., 2020) CRBBB also leads to abnormal atrioventricular coupling. (Baragan et al., 1970; Miller et al., 2015) These factors result in decreased right ventricular systolic function, diastolic tricuspid regurgitation, and higher right atrial (RA) pressure. (Brooks et al. 1979; Miller et al., 2015) Increased RA pressure is associated with increased RA volume, which is associated with AF. (Akutsu et al., 2011; Nattel et al. 2008) Second, CRBBB might be associated with an increased risk of nonpulmonary vein AF triggers, such as the superior vena cava. This is supported by the findings of a recent study, which showed that with repeated AF ablation, the incidence of nonpulmonary vein AF triggers (confirmed firing to AF), especially in the superior vena cava, was significantly higher in patients with CRBBB than in those without CRBBB. (Yano et al., 2021) Third,

because the prevalence of CRBBB increases with age, CRBBB may be a marker of a slowly progressing degenerative disease, such as Purkinje system fibrosis or myocardial fibrosis. (Koshiyama et al. 2021) Fibrosis of the atrial tissue predisposes an individual to AF development.

In the present study, CRBBB was independently associated with AF; however, in a study by (Bussink et al., 2013) the risk of AF in patients with CRBBB was also increased (hazard ratio 1.10; 95% CI, 0.73–1.67), but this difference did not reach statistical significance. A likely explanation for this is that Bussink et al.'s study examined the general population, while we included patients who were hospitalized at the Heart Center of our hospital, the majority of whom had cardiovascular diseases. These two studies, therefore, addressed issues in different populations.

Additionally, our study showed that CLBBB significantly correlated with AF. In agreement with this finding, it has previously been reported that CLBBB induces and aggravates mitral regurgitation (Cabrera-Bueno et al., 2010; Kanzaki et al., 2004), left ventricular systolic dysfunction and diastolic dysfunction (Ozdemir et al., 2001; Zu et al., 2021), which result in left atrial volume and pressure overload and progressive left atrial fibrosis and dilation (Khan et al., 2004; Nattel et al., 2008). These resultant left atrial electroanatomical remodelings were associated with AF development. Moreover, our study found that age and left atrial diameter significantly correlated with AF, which is in accordance with the findings of previous studies. (Koshiyama et al., 2021; Laredo et al., 2018; Nattel et al., 2008) Because more patients with AF were taking class I or III anti-arrhythmic drugs on admission than in the non-AF group, class I or III anti-arrhythmic drug use was associated with AF in the present study. We also found that valvular heart disease was independently associated with AF, which is supported by previous studies showing that valvular regurgitation and valvular stenosis are associated with an increased risk of developing AF. (Benjamin et al., 1994).

This study has some limitations. First, because the study was a cross-sectional study, we could only confirm the presence of a significant association between CRBBB and AF. We were unable to determine a true cause-effect relationship between these two variables. Second, because RA dilation inclines to asymmetry, the RA volume is superior to RA diameter in assessing RA size. However, unfortunately, information on RA volume was not available in this retrospective study. Thus, whether patients with CRBBB have a larger RA size could not be assessed. Further prospective studies may be required to assess the association between CRBBB and RA size. Finally, this was a single-center hospital-based study, and the characteristics of the study population might differ from the general population, meaning that any generalizations should be made with caution.

## 5 | CONCLUSION

Complete right bundle branch block was significantly associated with AF development in this study. Screening of a resting 12-lead

ECG may help to identify patients who are at a high risk of developing AF in hospitalized patients with cardiovascular diseases.

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## AUTHOR CONTRIBUTIONS

FTZ designed this study and wrote the manuscript. XJL, DQZ, LMZ, JH, XWF, HTY, LJY, JLL, and SLW carried out the data collection and data analysis. JTW designed this study and made critical revisions of the manuscript. All authors read and approved the final manuscript.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ETHICAL APPROVAL

The study complied with the Declaration of Helsinki and the study protocol was approved by the local institutional review board.

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