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 electrocardiography.

Association between complete right bundle branch block and atrial fibrillation development

Fu-Tao Zhang MM¹ | Xiao-Jie Liu MM¹ | Dan-Qing Zhao MM¹ | Jin-Tao Wu MD² ☉ | Lei-Ming Zhang MM² | Juan Hu MD² | Xian-Wei Fan MM² | Hai-Tao Yang MD² | Li-Jie Yan MD² | Jing-Jing Liu MM² | Shan-Ling Wang MD²

¹Department of Cardiology, Henan University People’s Hospital, Henan Provincial People’s Hospital, Zhengzhou, China
²Heart Centre of Henan Provincial People’s Hospital, Central China Fuwai Hospital, Central China Fuwai Hospital of Zhengzhou University, Zhengzhou, China

Correspondence Jin-Tao Wu, Heart Centre of Henan Provincial People’s Hospital, Central China Fuwai Hospital, Central China Fuwai Hospital of Zhengzhou University, Zhengzhou, China. Email: wujintao666@126.com

Funding information Medical Science and Technology Project of Henan Province, Grant/Award Number: SBGJ202002030; Science and Technology Research Project of Henan Province, Grant/Award Number: 212102310793

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 ± 13 years). CRBBB was defined as a late R (R′) wave in lead V1 or V2 with a slurred S wave in lead I and/or lead V6 with a prolonged QRS duration (≥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
electrocardiography (ECG). It is defined as a late R (R’) wave presenting in lead V4 or V5, with a slurred S wave in lead I and/or lead V6, with a prolonged QRS duration of ≥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 CHA2DS2-VASc score, and thyroid dysfunction, as determined by an abnormal free thyroxine or thyroid-stimulating hormone concentration.

The CHA2DS2-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 ≥75 years. (Lip et al., 2010) Hypertension was defined as a systolic blood pressure of ≥140 mmHg, a diastolic blood pressure of ≥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-pass filter, 0.05 Hz; low-pass 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 V4 or V5 with a slurred S wave in lead I and/or lead V6 with a prolonged QRS duration of ≥120 ms, and complete left bundle branch block (CLBBB) was defined as QRS duration ≥120 ms; broad notched or slurred R waves in leads I, aVL, V5, and V6; and absent q waves in leads I, V5, and V6. (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 ± standard deviation, as appropriate. Continuous and categorical variables were compared between groups using the independent samples t-test and the χ2 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 ± 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 CHA2DS2-VASc score and a lower LVEF, as well as a higher rate of β-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, CHA2DS2-VASc score, congestive heart failure, valvular heart disease, left atrial diameter, and LVEF, as well as use of calcium channel blockers, β-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 = .001) (Figure 1).

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).

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).

| 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    |
| CHA2DS2-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   |
| β-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...
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 non-pulmonary 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.

### ACKNOWLEDGEMENT

We thank Emily Woodhouse, PhD, from Liwen Bianji (Edanz) (www.liwenbianji.cn) for editing the English text of a draft of this manuscript. This research was supported by Medical Science and Technology Project of Henan Province (No. SBCGJ202002030) and Science and Technology Research Project of Henan Province (No.212102310793).

### AUTHOR CONTRIBUTIONS

FTZ designed this study and wrote the manuscript. XJL, DQZ, LMZ, JH, XWF, HTY, LJY, JYL, 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.

### ORCID

Jin-Tao Wu https://orcid.org/0000-0003-0224-6920

### REFERENCES

Akutsu, Y., Kaneko, K., Kodama, Y., Suyama, J., Li, H. L., Hamazaki, Y., Tanno, K., Gokan, T., & Kobayashi, Y. (2011). Association between left and right atrial remodeling with atrial fibrillation recurrence after pulmonary vein catheter ablation in patients with paroxysmal atrial fibrillation: A pilot study. Circulation: Cardiovascular Imaging, 4(5), 524–531. https://doi.org/10.1161/CIRCIMAGING.110.962761

Baragan, J., Fernandez, F., Coblence, B., Saad, Y., & Lenegre, J. (1970). Left ventricular dynamics in complete right bundle-branch block with left axis deviation of QRS. Circulation, 42(5), 797–804. https://doi.org/10.1161/01.cir.42.5.797

Benjamin, E. J., Levy, D., Vaziri, S. M., D’Agostino, R. B., Belanger, A. J., & Wolf, P. A. (1994). Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. JAMA, 271(11), 840–844.

Brooks, N., Leech, G., & Leatham, A. (1979). Complete right bundle-branch block: Echophonocardiographic study of first heart sound and right ventricular contraction times. British Heart Journal, 41(6), 637–646. https://doi.org/10.1136/hrt.41.6.637

Bussink, B. E., Holst, A. G., Jespersen, L., Deckers, J. W., Jensen, G. B., & Prescott, E. (2013). Right bundle branch block: Prevalence, risk factors, and outcome in the general population: results from the Copenhagen City Heart Study. European Heart Journal, 34(2), 138–146. https://doi.org/10.1093/eurheartj/ehs291

Cabrera-Bueno, F., Molina-Mora, M. J., Alzueta, J., Pena-Hernandez, J., Jimenez-Navarro, M., Fernandez-Pastor, J., Barrera, A., & de
Surawicz, B., Childers, R., Deal, B. J., & Gettes, L. S. (2009). AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: Part III: Intraventricular conduction disturbances: A scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society: endorsed by the International Society for Computerized Electrocardiology. *Circulation*, 119(10), e235–e240. https://doi.org/10.1161/CIRCULATIONAHA.108.191095

Tanaka, Y., Shah, N. S., Passman, R., Greenland, P., Lloyd-Jones, D. M., & Khan, S. S. (2021). Trends in cardiovascular mortality related to atrial fibrillation in the United States, 2011 to 2018. *Journal of the American Heart Association*, 10(15), e020163. https://doi.org/10.1161/JAHA.120.020163

Widimsky, P., Rohac, F., Stasek, J., Kala, P., Rokyta, R., Kuzmanov, B., ... Lorencoova, A. (2012). Primary angioplasty in acute myocardial infarction with right bundle branch block: should new onset right bundle branch block be added to future guidelines as an indication for reperfusion therapy? *European Heart Journal*, 33(1), 86–95. https://doi.org/10.1093/eurheartj/ehr291

Wong, C. K., Stewart, R. A., Gao, W., French, J. K., Raffel, C., & White, H. D. (2006). Prognostic differences between different types of bundle branch block during the early phase of acute myocardial infarction: insights from the Hirulog and Early Reperfusion or Occlusion (HERO)-2 trial. *European Heart Journal*, 27(1), 21–28. https://doi.org/10.1093/eurheartj/ehi622

Yano, M., Egami, Y., Ukita, K., Kawamura, A., Nakamura, H., Matsuhiro, Y., Yasumoto, K., Tsuda, M., Okamoto, N., Tanaka, A., & Matsunaga-Lee, Y. (2021). Impact of baseline right bundle branch block on outcomes after pulmonary vein isolation in patients with atrial fibrillation. *The American Journal of Cardiology*, 144, 60–66. https://doi.org/10.1016/j.amjcard.2020.12.051

Zu, L., Wang, Z., Hang, F., Jiang, Y., Wang, X., Cheng, L., Zhang, J., & Wu, Y. (2021). Cardiac resynchronization performed by LBBaP-CRT in patients with cardiac insufficiency and left bundle branch block. *Annals of Noninvasive Electrocardiology*, 26(6), e12898. https://doi.org/10.1111/anec.12898

How to cite this article: Zhang, F-T, Liu, X-J, Zhao, D-Q, Wu, J-T, Zhang, L-M, Hu, J., Fan, X-W, Yang, H-T, Yan, L-J, Liu, J-J, Wang, S-L (2022). Association between complete right bundle branch block and atrial fibrillation development. *Annals of Noninvasive Electrocardiology*, 27, e12966. https://doi.org/10.1111/anec.12966