PREVALENCE AND CLINICAL SIGNIFICANCE OF ELECTROCARDIOGRAPHIC COMPLETE RIGHT BUNDLE BRANCH BLOCK IN YOUNG INDIVIDUALS

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ABSTRACT

Background and Aims: There is limited information on the clinical significance of complete right bundle branch block (CRBBB) in young individuals. The aim of this study was to determine the prevalence and significance of CRBBB in a large cohort of young individuals aged 14-35 years old.

Methods: From 2008 to 2018, 104,369 consecutive individuals underwent a cardiovascular assessment with a health questionnaire, electrocardiogram, clinical consultation, and selective echocardiography. Follow-up was obtained via direct telephone consultations. Mean follow-up was 7.3 ± 2.7 years.

Results: CRBBB was identified in 154 (0.1%) individuals and was more prevalent in males compared with females (0.20% vs. 0.06%; $p<0.05$) and in athletes compared with non-athletes (0.25% vs. 0.14%; $p<0.05$). CRBBB-related cardiac conditions were identified in 7 (5%) individuals (4 with atrial septal defect, 1 with Brugada syndrome, 1 with progressive cardiac conduction disease and 1 with atrial fibrillation). Pathology was more frequently identified in individuals with non-isolated CRBBB compared with individuals with isolated CRBBB (14% vs 1%; $p < 0.05$) and in individuals with a QRS duration of ≥130 milliseconds (ms) compared with individuals with a QRS of <130ms (10% vs 1%; $p<0.05$).

Conclusion: The prevalence of CRBBB in young individuals was 0.1% and was more prevalent in males and athletes. CRBBB-related conditions were identified in 5% of individuals and were more common in individuals with non-isolated CRBBB and more pronounced intraventricular conduction delay (QRS duration of ≥130ms). Secondary evaluation should be considered for young individuals with CRBBB with

symptoms, concerning family history, additional electrocardiographic anomalies or significant QRS prolongation (≥130ms).

LAY SUMMARY

There is limited information on the clinical significance of complete right bundle branch block (CRBBB) in young people (aged 14 to 35 years old).

- CRBBB is a rare finding in young individuals and is more common in male and athletic individuals.
- CRBBB related-conditions are found in 5% of young individuals with this electrocardiogram finding and are more common in those with additional heart symptoms, family history of premature heart disease, other abnormal electrocardiographic (ECG) findings and more pronounced forms of CRBBB (≥ 130 milliseconds). Further investigation, including at least an ultrasound of the heart (echocardiogram), is recommended for all young individuals with CRBBB with concerning symptoms, family history of heart disease, additional ECG anomalies or more pronounced CRBBB (≥130milliseconds).

KEYWORDS: athletes, cardiovascular disease, complete right bundle branch block, young

INTRODUCTION

Large observational studies suggest that the prevalence of complete right bundle branch block (CRBBB) in the general population is between 0.9% and 1.5%, and increases with age.[1–3] Among asymptomatic individuals with no prior heart disease, CRBBB has historically been considered a benign anomaly; however, this conclusion was derived from small cohort studies.[4–7] Larger population studies have returned conflicting results on the association of CRBBB with cardiac morbidity and mortality.[1–3,8] Young individuals (≤35 years) are poorly represented in these studies, and information pertaining to the prevalence and prognosis of CRBBB in this age group is commonly drawn from studies in young athletes. Datasets of young athletes suggest that the prevalence of CRBBB is higher compared to healthy members of the general population, and ranges between 0.5% and 3.1%.[9–15] Such studies are typically cross-sectional in nature and most report CRBBB in the context of many other ECG indices, making it challenging to decipher an association between CRBBB and cardiac pathology.

Uncertainty over the clinical significance of CRBBB in young athletes is reflected in the international criteria for electrocardiogram (ECG) interpretation in athletes which classifies CRBBB as a borderline feature requiring further evaluation only in the presence of additional ECG abnormalities.[16] This recommendation is based on a study of 13 athletes with CRBBB, where CRBBB was attributed to right ventricular dyssnchrony as a result of physiological cardiac remodelling.[10] The objective of this study was to investigate the prevalence and significance of CRBBB among individuals assessed in a nationwide cardiac screening programme for young individuals in the United Kingdom (UK).

METHODS

The charitable organisation Cardiac Risk in the Young (CRY) offers cardiac screening to all individuals aged 14-35 years old in the UK. Screening events are held in locations around the UK (schools, youth clubs, sports clubs, and pavilions) and are advertised through social media platforms and on the CRY website (www.c-r-y.org). Young individuals can register on a voluntary basis for the cardiac screening event through an online platform. Elite athletes are usually screened in the context of a pre-participation cardiac screening programme according to the policy of their respective sporting organisation. The screening team includes a doctor, cardiac physiologists, and additional support staff. Cardiac screening consists of a health questionnaire (HQ) and a 12-lead ECG followed by clinical consultation. Transthoracic echocardiography (TTE) is offered selectively on the day to individuals with concerning symptoms, family history, abnormal physical signs, or ECG abnormalities, at the discretion of the consulting physician. Secondary cardiac evaluation is recommended for individuals with abnormal findings. A letter is written to the screened individual by the consulting physician, detailing the interpretation of tests and the outcome of the evaluation, including any recommendations for secondary evaluation. An additional copy of the letter is sent to the individual's primary care physician if secondary evaluation is recommended.

For the purpose of this study, we considered electrocardiographic CRBBB as an rSR' pattern in lead V1 with an S wave wider than the R wave in V6 and a QRS duration of ≥120 milliseconds (ms). We considered individuals as athletes if their evaluation was part of a sporting organisation's mandatory pre-participation cardiac screening programme. This typically included amateur or professional athletes participating at regional, national, or international level. CRBBB was classified as 'isolated' or 'non-isolated' based on the absence or presence, respectively, of concomitant cardiovascular symptoms (typically syncope, chest pain, palpitation and/or dyspnoea), relevant family history of inherited cardiac conditions or young (aged <50 years) sudden cardiac death (SCD), and other ECG abnormalities. Anterior T wave inversion was considered discordant if confined between V1 and V3, but not V4.

Follow-up data pertaining to additional secondary investigations and final diagnoses was obtained via direct telephone consultations using the contact details provided at the time of preliminary evaluation. Self-reported cardiac diagnoses and interventions were cross-referenced through request of clinical correspondence from cardiology services. Calculation of the follow-up period for each individual was based on the number of years between screening and telephone consultation.

Written informed consent for cardiac screening was obtained from all participants, or a guardian if aged under 16 years, prior to completing their screening investigations. Follow-up of screened individuals was within the remit of CRY's audit of their screening programme conducted in 2022.

Data analysis was performed using SPSS software, V.26.0 (Chicago, Illinois, USA). Values are presented as mean and standard deviation (SD) or as percentages where more appropriate.

RESULTS

Between 2007 and 2018, 104,369 consecutive young individuals (aged 14 to 35 years) underwent voluntary cardiac evaluation. The mean age was 20.2 ± 6.2 years.

The majority were male (n = 64,708; 62%) and white (n = 92,708; 89%). The cohort included 9,745 (9%) competitive athletes who represented 22 different sporting disciplines, predominantly rugby (66%) and cricket (13%).

CRBBB was reported in 154 (0.1%) individuals (Figure 1) who all underwent a one-off assessment. CRBBB was more prevalent in males compared with females (0.20% vs. 0.06%, $p < 0.05$) and in athletes compared with non-athletes (0.25% vs. 0.14%, $p < 0.05$). There was no significant difference in terms of age (0.11% for <16 years vs 0.16% for ≥16 years; $p > 0.05$) or ethnicity (0.15% for white vs 0.09% for non-white, $p > 0.05$).

- **Insert Figure 1**

Characteristics of CRBBB

The mean QRS duration was 131 ± 12 ms. Most individuals with CRBBB had isolated CRBBB (n = 112, 73%), with a QRS duration of < 130 ms (n = 92, 60%), and either absent or discordant anterior T wave inversion (n = 151, 98%).

Of the 42 (27%) individuals with non-isolated CRBBB, 2 (1%) reported significant symptoms, including 1 individual with palpitation and 1 individual with syncope. Two (1%) individuals reported significant symptoms or family history and additional ECG findings, including 1 with palpitation and right axis deviation on their ECG, and 1 with pre-syncope, family history of premature conduction disease in a first-degree relative, and left axis deviation on their ECG. The remaining 38 (25%) individuals were classified as non-isolated CRBBB based on additional ECG findings, including axis deviation or indeterminate axis (n = 35), atrial enlargement (n=4), non-discordant T wave inversion (n=3) and 1st-degree heart block (n=5) (Table 1).

- **Insert Table 1**

Further evaluation and follow-up

After initial evaluation with a HQ, ECG, clinical consultation, a TTE was performed on the day in 144 (94%) individuals with CRBBB. Sixty (39%) individuals were recommended secondary evaluation and/or follow-up by their local cardiology service (Figure 1).

Of the 154 individuals with CRBBB, follow-up was available in 149 (97%). During a mean follow-up period of 7.3 ± 2.7 years, 7 (5%) individuals were identified with a CRBBB-related condition. Four (3%) individuals were diagnosed with an atrial septal defect (ASD) on TTE at screening. Three individuals were diagnosed on subsequent secondary evaluation; 1 with Brugada syndrome, 1 with progressive cardiac conduction disease (PCCD) and 1 with atrial fibrillation (AF). An additional 2 individuals were identified with cardiac conditions which were considered incidental findings; including 1 with mitral valve prolapse, and 1 with coarctation of the aorta (Figure 1).

Five (3%) individuals required cardiac intervention including 3 individuals who underwent percutaneous ASD closure, 1 individual was implanted with a primary prevention implantable cardioverter defibrillator (ICD) for a diagnosis of Brugada syndrome and 1 individual was implanted with a permanent pacemaker (PPM) for PCCD (Figure 1).

The prevalence of CRBBB-related cardiac conditions was significantly greater in individuals with non-isolated CRBBB compared to individuals with isolated CRBBB (14% vs 1%; $p < 0.05$), and in individuals with a QRS duration of ≥ 130 ms compared to those with a QRS of < 130ms (10% vs 1%; $p < 0.05$) (Figure 2). Concomitant anterior T wave inversion did not correlate with pathology.

- **Insert Figure 2**

Retrospective application of the international criteria for ECG interpretation in athletes would consider the ECG as abnormal in 6 of the 7 individuals with CRBBB-related conditions (Table 2).[15] The individual with a CRBBB-related condition who may not have been identified using these criteria, refers to a 17-year-old, white, male, non-athlete, who presented with isolated CRBBB with QRS of 141ms and T wave inversion V1-V2 (Supplementary Figure 1 – ECG number 2) who was diagnosed with an ASD following an on-site TTE (Table 2 – individual number 2).

- **Insert Table 2**

DISCUSSION

The prevalence of CRBBB in a large cohort of young individuals who underwent cardiac screening in the UK was 0.1%. The prevalence of CRBBB was 4-fold greater in men (1 in 490) compared with women (1 in 1,803) and almost 2-fold greater in athletes (1 in 406) compared with non-athletes (1 in 728). Seven (5%) individuals with CRBBB were identified with a cardiac condition, with the presence of additional abnormalities and a broad QRS (≥130ms) emerging as markers of pathology.

The prevalence of CRBBB in this study is lower than that reported in large studies of the general population which range between 0.9% to 1.5%. This difference may be accounted for by age when one considers that the prevalence of CRBBB increases with age, and that this cohort was much younger (mean age 21 years) than those in the large population studies (mean age > 50 years).[1–3]

Our findings support the notion that CRBBB is more common in young athletes than healthy members of the general population. However, the prevalence of CRBBB in young athletes in this study was 0.25% which is lower than the range reported in the literature (0.5% - 3.1%).[9–15] One possible explanation for this is the relatively small proportion of athletes engaging in pure endurance forms of sport in our cohort of 9,745 athletes. Based on the ESC classification of sports,[17] only 12% of athletes in this study were engaged in high-intensity endurance sports that are more likely to be associated with a greater magnitude of right ventricular remodelling which has been proposed as a mechanism for CRBBB in healthy young athletes through stretching of the terminal RV Purkinje fibres.[10,18]

Seven (5%) individuals with CRBBB were identified with a cardiac condition commonly associated with this ECG pattern, of which 2 required potentially life-saving intervention; including one individual with Brugada syndrome implanted with a primary prevention ICD and one individual with PCCD implanted with a PPM. Indeed, CRBBB can obscure the diagnosis of Brugada syndrome,[19,20] and is also more common in patients with idiopathic ventricular fibrillation,[21] which may partially account for the increased risk of cardiovascular morbidity and mortality associated with this anomaly in large community studies.[1,2] The findings from this study underscores the importance of primary electrical disorders associated with CRBBB and SCD, and suggests that screening may promote early detection of disease.

Atrial septal defect (n=4; 57%) accounted for most of the CRBBB-related conditions which were all detected at screening through assessment with TTE.

These findings highlight the enhanced sensitivity offered by TTE in the context of CRBBB although this must be carefully weighed against available resources and incremental costs.

CRBBB-related conditions were significantly more likely in individuals with a broad QRS duration of ≥130 ms compared to those with a narrow QRS of <130 ms (10% vs 1%; $p < 0.05$), and in those with non-isolated CRBBB compared to isolated CRBBB (14% vs 1%; $p < 0.05$). These results suggest that secondary cardiac evaluation with at least TTE should be considered for all young individuals with CRBBB and more pronounced intraventricular conduction delay (QRS duration ≥130 ms), and certainly those with CRBBB and associated symptoms or additional ECG anomalies.

The international criteria for ECG interpretation in athletes consider CRBBB as a borderline variant and recommend further evaluation for those with additional ECG abnormalities (considered borderline or pathological) and/or symptoms, signs or family history of cardiovascular disease or premature sudden cardiac death.[16] When applying these criteria to the ECGs of all 154 individuals with CRBBB, the prevalence of CRBBB-related conditions was significantly more likely in those with an abnormal ECG compared to those with a normal ECG (16% vs 1%; $p < 0.05$). The one individual identified with an ASD but had a normal ECG, according to the international criteria, was a male, non-athlete with isolated CRBB and a QRS duration of 141msec (Table 2). It is worth highlighting, however, that the international ECG criteria recommend further evaluation for all athletes with QRS duration ≥140 ms regardless of QRS morphology. Our results suggest that CRBBB is a rare finding in young athletes which is often (5% of subjects) associated with cardiovascular disease, including conditions associated with SCD. Regarding the current international criteria for ECG interpretation in athletes,[16] our findings suggest that CRBBB should remain as a 'borderline' finding but only if the QRS duration is < 130ms. CRBBB of ≥130 ms should be considered as an 'abnormal' finding, warranting secondary evaluation for all with at least an echocardiogram. No equivalent guidelines exist for the interpretation of non-athletes. However, we believe findings from this predominantly non-athletic cohort support the same recommendation for such individuals.

<u>Limitations</u>

Several limitations of this study should be noted. Selection bias, inherent to any voluntary screening programme, may have contributed to the reported prevalence of CRBBB-related conditions. However, only 2% of all screened individuals were deemed to have significant cardiovascular symptoms and/or family history, suggestive of a low-risk cohort, reflective of the general population. The reported prevalence of CRBBB-related conditions may represent an underestimate when one considers the potential for quiescent cardiovascular disease in the 94 (61%) of individuals with CRBBB who did not undergo secondary cardiac evaluation. However, it is unlikely that a significant number of CRBBB-related conditions were not detected by the programme, when one considers that 86 (91%) of the 94 individuals not referred for secondary evaluation underwent assessment with TTE at screening, and that structural heart disease accounted for the majority of CRBBB-related conditions identified by the programme. Lastly, each subject underwent a one-off assessment and as such it is unclear if these individuals harboured CRBBB from infancy or acquired it later in life. Large observational studies suggest that the prevalence of complete right bundle branch block (CRBBB) increases with age, which supports the notion that this ECG finding is acquired over time.[1–3] In the context of ECG screening, this raises important questions about the timing and frequency of assessments.

Conclusions

The prevalence of CRBBB in a large cohort of young individuals was 0.1%. CRBBB-related cardiac conditions were identified in 5% of young individuals with CRBBB and were more likely in individuals with non-isolated CRBBB and QRS duration of ≥ 130 ms. These findings highlight the clinical significance of CRBBB in young individuals and suggest that secondary cardiac evaluation with an echocardiogram, and targeted further evaluation, should be considered for young individuals with CRBBB with symptoms, concerning family history, additional electrocardiographic anomalies or significant QRS prolongation (≥130ms).

DATA AVAILABILITY STATEMENT

The data underlying this article were provided by Cardiac Risk in the Young by permission. Data will be shared on request to the corresponding author with permission of Cardiac Risk in the Young.

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DISCLOSURE OF INTEREST

No conflict to interest to declare

AUTHORSHIP

M.P. conceived and designed the analysis. H.M, R.B, S.F, N.C, M.A, S.M, J.B, C.M, H.D, A.Z, N.C, N.S, S.G, A.M and G.F collected the primary source data. H.M conducted follow-up consultations and analysed the data. H.M, S.S and M.P contributed to writing the manuscript. All authors reviewed the manuscript.

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FIGURE LEGENDS

Figure 1 - **Flow chart of study including clinical outcomes of individuals with complete right bundle branch block.** ASD: atrial septal defect; CRBBB: complete right bundle branch block; ECG: 12-lead electrocardiogram ; HQ: health questionnaire; ICD: implantable cardioverter defibrillator; TTE: transthoracic echocardiography.

Figure 2 - **Complete right bundle branch block-related cardiac conditions identified in individuals based on the presence of isolated and non-isolated complete right bundle branch block and QRS duration.** AF: atrial fibrillation; ASD: atrial septal defect; CRBBB: complete right bundle branch block; ECG: 12-lead electrocardiogram; HQ: health questionnaire; ICD: implantable cardioverter defibrillator; PCCD: progressive cardiac conduction disease; TTE: transthoracic echocardiography.

APPENDICES

Not available. Supplementary material uploaded separately.

TABLES

Characteristics of 154 individuals with CRBBB	Number (%)	Number of identified CRBBB-related cardiac conditions (%)	CRBBB-related cardiac condition
Isolated or non-isolated CRBBB			
Isolated	112 (73)	1 (1)	ASD
Non-isolated	42 (27)	6 (14)	ASD (3), AF, BrS, PCCD
CRBBB + abnormal HQ	2 (1)	0 (0)	-
CRBBB + other ECG finding*	38 (25)	4 (11)	ASD (3), BrS
CRBBB + abnormal HQ + other ECG finding	2 (1)	2 (100)	AF, PCCD
QRS duration			
<130 ms	92 (60)	1 (1)	ASD,
≥130 ms	62 (40)	6 (10)	AF, ASD (3), BrS, PCCD
Anterior T wave inversion			
No anterior T wave inversion/present in V1 only	96 (62)	2 (2)	AF, PCCD
V1 to V2	43 (28)	4 (9)	ASD (3), BrS
V1 to V3	12 (8)	1 (8)	ASD
V1 to V4	3 (2)	0 (0)	-
*ECG findings identified in non-isolated CRBBB			
1^{st} degree AV block (PR > 200ms)	5 (3)	0 (0)	-
Left axis deviation (-30 to -90)	11 (7)	1 (9)	PCCD
Right axis deviation (+120 to +180)	15 (10)	3 (20)	ASD (2), AF
Extreme axis deviation (-90 to + 180)	2 (1)	2 (100)	ASD, BrS
Indeterminate axis (equiphasic)	7 (5)	0 (0)	-
Left atrial enlargement	3 (2)	0 (0)	-
Right atrial enlargement	1 (1)	1 (100)	ASD
Abnormal T wave inversion (not considered discordant)	3 (2)	0 (0)	-

Table 1 - **Characteristics of individuals identified with complete right bundle branch block at screening.** AF: atrial fibrillation; ASD: atrial septal defect; AV: atrioventricular; BrS: Brugada Syndrome; CRBBB: complete right bundle branch block; ECG: 12-lead electrocardiogram; HQ: health questionnaire; Ms: millisecond; PCCD: progressive cardiac conduction disease. * = International criteria for ECG interpretation in athletes.[16]

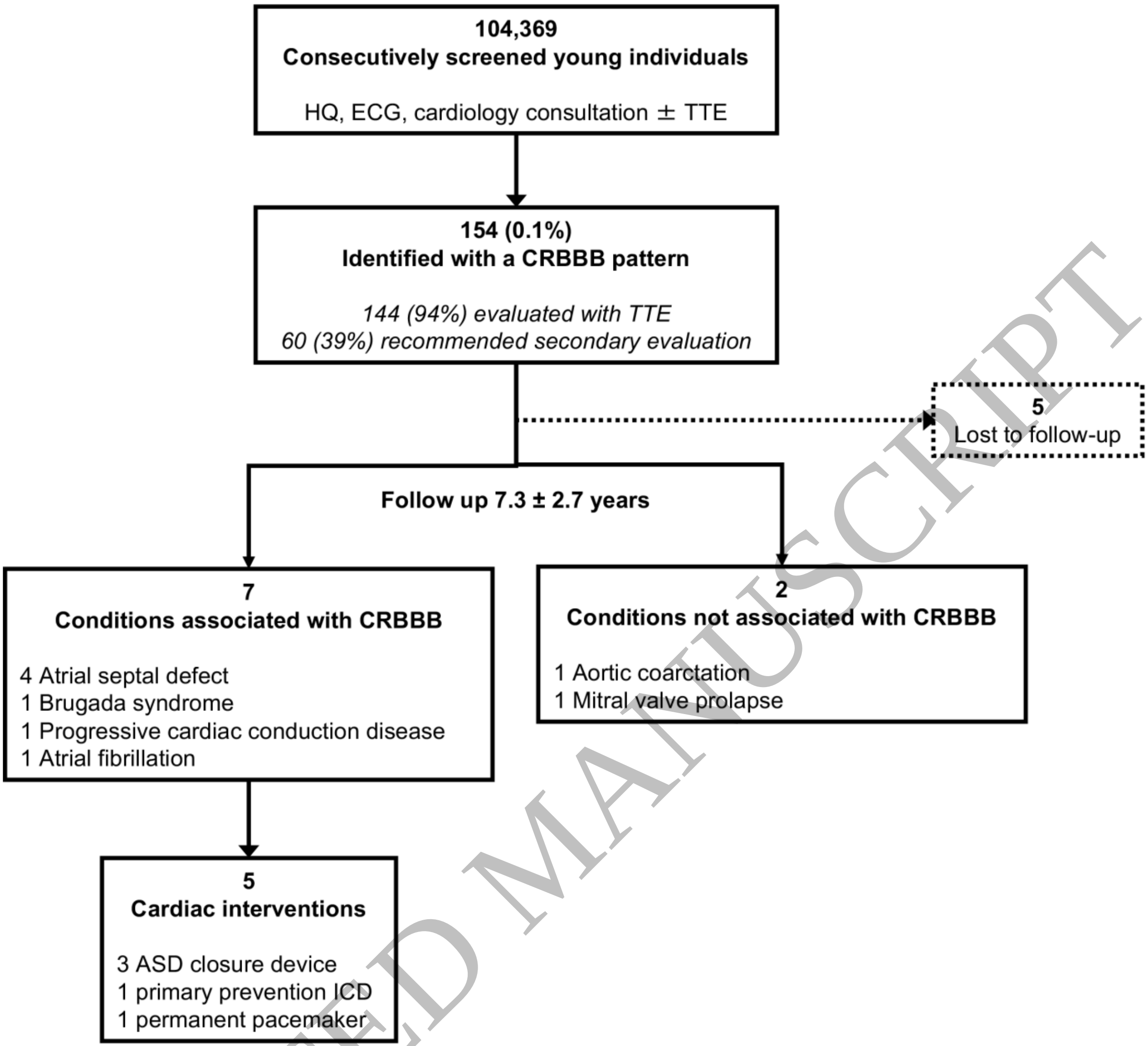
Individual number	Condition	Athletic status	Isolated or non-isolated CRBBB	Findings at screening	QRS duration (ms)	International ECG criteria for athletes*	Comments
1	ASD	Athlete	Non-isolated	HQ: Nil ECG: CRBBB + right axis deviation TTE: ASD	133	Abnormal	Diagnosed with ASD through on-site selective assessment with TTE. Implanted with percutaneous ASD closure device over follow-up period.
2	ASD	Non-athlete	Isolated	HQ: Nil ECG: CRBBB TTE: ASD	141	Normal	Diagnosed with ASD through on-site selective assessment with TTE. Implanted with percutaneous ASD closure device over follow-up period.
3	ASD	Non-athlete	Non-isolated	HQ: Nil ECG: CRBBB + right axis deviation TTE: ASD	146	Abnormal	Diagnosed with ASD through on-site selective assessment with TTE.
4	ASD	Non-athlete	Non-isolated	HQ: Nil ECG: CRBBB + extreme axis deviation + right atrial enlargement TTE: ASD	120	Abnormal	Diagnosed with ASD through on-site selective assessment with TTE. Implanted with percutaneous ASD closure device over follow-up period.
5	PCCD	Non-athlete	Non-isolated	HQ: Pre-syncope + chest pain + dyspnoea + family history of PCCD ECG: CRBBB + left axis deviation TTE: Nil	138	Abnormal	Discharged after initial secondary evaluation which included an ECG, 24-hour Holter and TTE. The patient presented 6 months later with recurrent syncope and was implanted with a permanent pacemaker.
6	AF	Non-athlete	Non-isolated	HQ: Palpitation ECG: CRBBB + right axis deviation TTE: Nil	140	Abnormal	Symptomatic paroxysmal atrial fibrillation diagnosed on 24-hour Holter monitor at secondary evaluation. No associated structural heart disease. Participant opted for pharmacological rhythm-control strategy.
7A/B	Brugada Syndrome	Non-athlete	Non-isolated	HQ: Nil ECG: CRBBB + borderline Type 1 Brugada pattern + extreme axis TTE: Nil	130	Abnormal	Positive ajmaline provocation study at secondary evaluation. Primary prevention ICD implanted approximately 7 years later following episode of syncope.

Table 2: **Characteristics of seven young individuals identified with complete right bundle branch block-related cardiac conditions.** AF: atrial fibrillation; ASD: atrial septal defect; CRBBB: complete right bundle branch block; ECG: 12-lead

electrocardiogram; HQ: health questionnaire; ICD: implantable cardioverter defibrillator; Ms: milliseconds; PCCD: progressive cardiac conduction disease; TTE: transthoracic echocardiography.

FIGURES

Figure 1 and 2 have been uploaded as separate image files in accordance with the instructions to authors.



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2 **Figure 1**

3 **159x145 mm (x DPI)**

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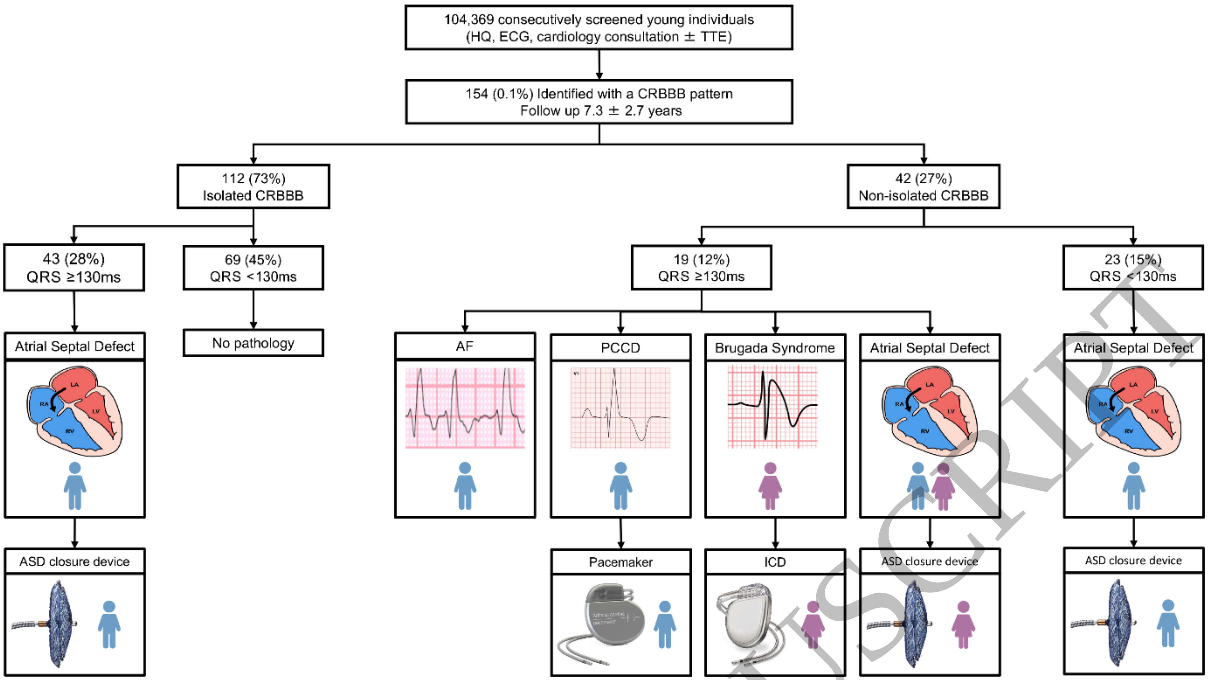

Figure 2
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STRUCTURED GRAPHICAL ABSTRACT

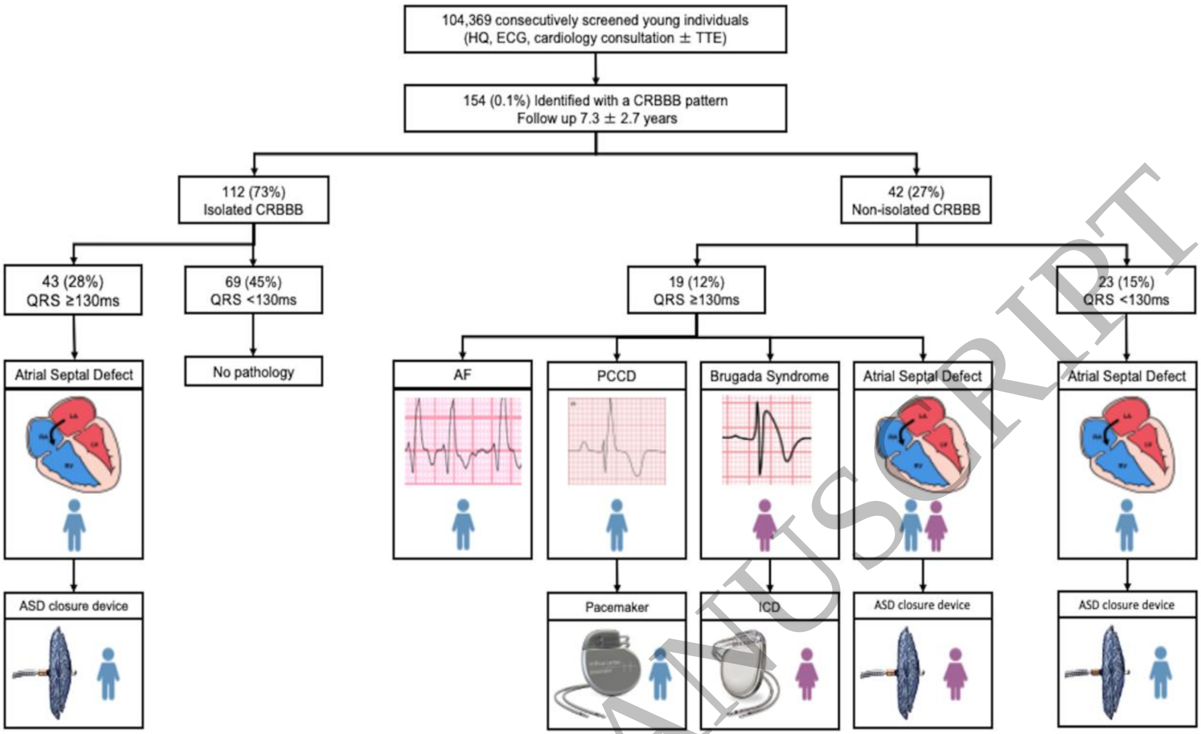
KEY QUESTION What is the prevalence and clinical significance of complete right bundle branch block (CRBBB) in a large population (n=104,369) of young individuals aged between 14 and 35 years?

KEY FINDING

- The prevalence of CRBBB was 0.1% and was more common in males and athletes.
- CRBBB-related conditions were identified in 5% of individuals.
- CRBBB-related conditions were more common in those with non-isolated CRBBB and pronounced intraventricular conduction delay (QRS duration ≥130ms).

TAKE-HOME MESSAGE

Secondary evaluation should be considered for young individuals with CRBBB, particularly those with symptoms, concerning family history, additional electrocardiographic anomalies or more pronounced intraventricular conduction delay (QRS duration ≥130ms).



Complete right bundle branch block-related cardiac conditions identified in individuals based on the presence of isolated and non-isolated complete right bundle branch block and QRS duration. AF: atrial fibrillation; ASD: atrial septal defect; CRBBB: complete right bundle branch block; ECG: 12-lead electrocardiogram; HQ: health questionnaire; ICD: implantable cardioverter defibrillator; PCCD: progressive cardiac conduction disease; TTE: transthoracic echocardiography.