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Bundle branch block in cardiac arrest survivors without ischemic heart disease

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A R T I C L E   I N F O

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A B S T R A C T

Aims: Cardiac arrest (CA) survivors with left/right bundle branch block (LBBB/RBBB) and no ischemic heart disease (IHD) have not been previously characterized. The aim of this study was to describe heart failure, implantable cardioverter defibrillator (ICD) therapy and mortality in this population.

Methods: Between 2009 and 2019 we consecutively identified all CA survivors with a consistent bundle branch block (BBB) defined as a QRS ≥ 120 ms, who had a secondary prophylactic ICD implanted. Patients with congenital and ischemic heart disease (IHD) were excluded.

Results: Among 701 CA-survivors who survived to discharge and received an ICD, a total of 58 (8%) were free from IHD and had BBB; 46 (79%) had LBBB, 10 (17%) had RBBB and 2 (3%) had non-specific BBB (NSBBB). The prevalence of LBBB was 7%. Pre-arrest ECG were available in 34 (59%) patients; 20 patients (59%) had LBBB, 6 (18%) had RBBB, 2 (6%) had NSBBB, 1 had (3%) incomplete LBBB, and 4 (12%) without BBB. At discharge, patients with LBBB had a significantly lower left ventricular ejection fraction (LVEF) than patients with other types of BBB (P < 0.001). During follow-up, 7 (12%) died after a median of 3.6 years (IQR: 2.6–5.1) with no difference between BBB subtypes.

Conclusion: We identified 58 CA-survivors with BBB and no IHD. The prevalence of LBBB among all CA-survivors was high, 7%. During CA hospitalization LBBB patients presented with a significantly lower LVEF than patients with other types of BBB (P < 0.001). ICD treatment and mortality did not differ between BBB subtypes during follow-up.

1. Introduction

Patients with bundle branch block (BBB) and concomitant cardiovascular disease are known to have increased mortality [1–7]. However, patients with BBB and no ischemic heart disease (IHD), who survive a cardiac arrest have previously not been systematically described, and information about the natural history of BBB patients surviving a cardiac arrest (CA) is lacking. Isolated left bundle branch block (LBBB) is associated with reduced left ventricular ejection fraction (LVEF) [8–10], but a similar association with other types of BBB is to our knowledge yet to be investigated. Heart failure (HF) is known to increase patient mortality [11], though the association between BBB without IHD, left ventricular systolic dysfunction (LVSD) and CA, to our knowledge has never been described.

We aimed to describe and compare the prognostic impact of LBBB and other BBB types on mortality, LVSD and ICD therapy after CA, by characterizing and following all CA patients with BBB and no IHD, who had an implantable cardioverter defibrillator (ICD) implanted.

2. Methods

2.1. Study population

We performed a retrospective single-center study at Copenhagen...
University Hospital Rigshospitalet, Denmark, with a mean coverage area of 2.7 million people in the study-period. Through the Danish Pacemaker and ICD registry we identified all patients who had a secondary prophylactic ICD implanted at Rigshospitalet, in a 9.25-year study-period (January 2010 - March 2019). Among patients with a secondary prophylactic ICD, we then identified all CA survivors with consistent BBB in the baseline electrocardiograms (ECG). Generally, all CA survivors with suspected ST-segment-elevation myocardial infarction (STEMI) are admitted to our institution on recommendation of referring EMS doctor and/or consulted cardiologist whereas patients with other causes of cardiac arrest were unselected referred to our institution.

We excluded all patients with IHD; thus, all included patients were required to have a coronary angiography without stenosis ≥ 50% or indication for coronary intervention. Patients with previous myocardial infarction (MI) and/or with blood tests indicative of MI were also excluded. Additionally, patients with a previously known or later diagnosed congenital heart disease were excluded. All patients were followed regularly in the ICD outpatient clinic.

The study was approved by the Danish Data Protection Agency, I-Suite: VD-2019-215) and the Danish Patient Safety Authority (3-3013-2853/1).

2.2. Danish registries and medical journals

All persons born in Denmark and residents of Denmark are assigned a unique civil registration number that allows for unambiguous linkage of all national healthcare- and administrative registries, and medical reports. We included all relevant data including demography, comorbidities, medication and diagnostic tests and results from the medical reports. Data was obtained from three time periods; (i) prior to CA, (ii) at CA Hospitalization, and (iii) at follow-up.

2.3. Clinical assessment

Permanent BBB was defined as a sustained BBB, either discovered at hospitalization in conjunction with CA or prior to CA. The ECGs were stratified according to the presence of LBBB, RBBB or non-specific BBB (NSBBB). RBBB and NSBBB were categorized together as other BBB. LBBB was defined as: (i) QRS ≥ 120 ms, (ii) Broad monophasic R-wave in leads I, V5, and V6, and (iii) Absence of Q-waves in leads V5 and V6 [14]. RBBB was defined as (i) QRS ≥ 120 ms, (ii) A secondary R-wave (R’) in V1 or V2, and (iii) Wide slurred S wave in leads I, V5, and V6 [12].

Echocardiographic data from all three periods was collected. Additionally, echocardiography performed at CA hospitalization should preferably be a minimum of 7 days after CA, in an effort to avoid the known possible decrease in LVEF within the first 48 h after CA due to stunning [13,14], and before ICD implant. Patients were followed regarding development of LVSD during the follow-up period. LVSD was defined as LVEF ≤ 40% [15]. Appropriate ICD therapy was defined as shock or anti-tachycardia pacing (ATP) due to ventricular tachycardia (VT) or ventricular fibrillation (VF) during the follow-up period.

2.4. Statistics

Baseline characteristics were described by use of proportions for categorical variables and means with standard deviations or medians with quartile 1 and 3 for continuous variables. Significance of associations was tested using the Wilcoxon rank-sum test for continuous variables and the χ2 test or Fisher exact test (as appropriate) for categorical variables. The cumulative death rate is illustrated in a Kaplan-Meier plot. The prevalence of BBB among CA patients was compared to the general population using data collected from the same coverage area [16]. Statistical calculations and analysis were performed in R version 4.2.2 (R development Core Team) [17]. A P-value of < 0.05 was considered statistically significant.

3. Results

3.1. Study population

In a 9.25-year study period a total of 2621 first ICD implantations were performed at our institution, among those we identified 701 CA survivors of whom 58 (8%) had BBB and no IHD (Fig. 1). LBBB was predominant and accounted for 46 (79%) of all CA patients with BBB, resulting in a LBBB prevalence of 7% (46/701) among all CA survivors. RBBB was identified in 10 (17%) patients, and the prevalence of RBBB among all CA survivors was 1% (10/701). A total of 2 (3%) had NSBBB (Table 2). An overall male predominance (79%) was found, and the median age at CA was 59.3 years (IQR: 51.0–64.7) with no detectable difference between patients with LBBB and patients with other BBB (Table 1). At the time of CA, previous cardiovascular disease was known in 33 patients (57%), of whom 12 patients (21%) had a HF diagnosis, 9 patients (16%) had hypertension, and 6 patients (10%) suffered from atrial fibrillation, also with no difference between the two groups (Table 1).

3.2. ECG prior to cardiac arrest

A total of 34 patients (59%) had an ECG recorded a median of 3.2 years (IQR 1.1–5.5) prior to CA and among these BBB was present in 28 patients (82%); 20 patients (59%) had LBBB, 6 patients (18%) had RBBB and 2 patients (6%) had NSBBB. Furthermore, 5 patients (15%) had an ECG without BBB and 1 patient (3%) had incomplete LBBB prior to CA. The ECG of one patient was missing, however, an adequate ECG description was available in the medical reports. Per the inclusion criteria, all 34 patients had developed either LBBB (77%) or RBBB (24%) at CA hospitalization. The median QRS-duration increased from 142 ms to 151 ms from prior ECG to CA hospitalization, no differences in rhythm, heart rate, or AV-block was observed (Table 3).

![Fig. 1. Patient identification flowchart. Among all first implantable cardioverter-defibrillator (ICD) implantations at our institution, we identified all cardiac arrest survivors (secondary ICD indication) with a consistent non-ischemic bundle branch block.](ClinicalKey.com)
Table 1
Baseline characteristics among 58 patients with out of hospital cardiac arrest and non-ischemic bundle branch block, patients with left bundle branch block compared to patients with other bundle branch block morphologies.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (n = 58)</th>
<th>LBBB (n = 46)</th>
<th>Other BBB (n = 12)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demography</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at CA (years), median (IQR)</td>
<td>59.3 (51.0–64.7)</td>
<td>59.9 (53.2–64.7)</td>
<td>57.0 (45.0–63.6)</td>
<td>0.508</td>
</tr>
<tr>
<td>Male sex</td>
<td>46 (79%)</td>
<td>35 (76%)</td>
<td>11 (92%)</td>
<td></td>
</tr>
<tr>
<td>BM1, median (IQR)</td>
<td>25.5 (23.4–29.4)</td>
<td>25.9 (23.2–29.6)</td>
<td>24.8 (24.5–25.0)</td>
<td>0.482</td>
</tr>
<tr>
<td>Pre-arrest comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>9 (16%)</td>
<td>6 (13%)</td>
<td>3 (25%)</td>
<td>0.375</td>
</tr>
<tr>
<td>Heart failure</td>
<td>12 (21%)</td>
<td>10 (22%)</td>
<td>2 (17%)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>6 (10%)</td>
<td>3 (7%)</td>
<td>3 (25%)</td>
<td>0.096</td>
</tr>
<tr>
<td>Psychiatric disorder</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>6 (10%)</td>
<td>3 (7%)</td>
<td>3 (25%)</td>
<td>0.096</td>
</tr>
<tr>
<td>Type 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>5 (8.6%)</td>
<td>5 (10.8%)</td>
<td>0 (0%)</td>
<td>0.542</td>
</tr>
<tr>
<td>No smoker</td>
<td>22 (38%)</td>
<td>16 (35%)</td>
<td>6 (50%)</td>
<td></td>
</tr>
<tr>
<td>Former or Current smoker</td>
<td>28 (48%)</td>
<td>24 (52%)</td>
<td>4 (33%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>8 (14%)</td>
<td>6 (13%)</td>
<td>2 (17%)</td>
<td></td>
</tr>
<tr>
<td>Pre-arrest medication, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betablockers</td>
<td>13 (22%)</td>
<td>9 (20%)</td>
<td>4 (33%)</td>
<td>0.437</td>
</tr>
<tr>
<td>Ace-inhibitor/ARB</td>
<td>15 (26%)</td>
<td>13 (28%)</td>
<td>2 (17%)</td>
<td>0.712</td>
</tr>
<tr>
<td>Diuretics</td>
<td>15 (26%)</td>
<td>13 (28%)</td>
<td>2 (17%)</td>
<td>0.712</td>
</tr>
<tr>
<td>Years follow-up, median (IQR)</td>
<td>4.3 (2.7, 6.2)</td>
<td>3.9 (2.3–6.2)</td>
<td>5.5 (4.4–6.2)</td>
<td>0.198</td>
</tr>
</tbody>
</table>

P-value < 0.05. LBBB, left bundle branch block; Other BBB, other bundle branch block; CA, cardiac arrest; IQR, interquartile range; ARB, angiotensin receptor blocker.

Table 2
Electrocardiogram parameters at cardiac arrest hospitalization among all 58 patients, patients with left bundle branch block compared to patients with other bundle branch block morphologies.

<table>
<thead>
<tr>
<th>ECG at CA hospitalization</th>
<th>Overall (n = 58)</th>
<th>LBBB (n = 46)</th>
<th>Other BBB (n = 12, 21%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, bpm median (IQR)</td>
<td>72 (65.5–89.0)</td>
<td>73.5</td>
<td>71.0</td>
<td>0.630</td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>49 (84%)</td>
<td>40 (87%)</td>
<td>9 (75%)</td>
<td>0.374</td>
</tr>
<tr>
<td>QRSl median (IQR)</td>
<td>154.0 (98%)</td>
<td>156.0</td>
<td>148.0</td>
<td>0.262</td>
</tr>
<tr>
<td>AV-block type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st degree</td>
<td>3 (6%)</td>
<td>2 (5%)</td>
<td>1 (9%)</td>
<td></td>
</tr>
<tr>
<td>2nd degree</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Mobitz I</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Mobitz II</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

Other BBB (n = 12, 21%) includes RBBB (n = 10, 17%) and Non-specific BBB (n = 2, 3%). LBBB, left bundle branch block; Other BBB, other bundle branch block; AV-block, atrioventricular block; IQR, interquartile range.

3.3. Left ventricular systolic dysfunction, recurrent arrhythmia, and mortality

At CA hospitalization, patients with LBBB had a significantly lower LVEF than patients with other types of BBB, a median of 6 days (IQR: 3–9) after CA. Among patients with LBBB (n = 46), a total of 32 patients (67%) had LVEF < 40%. This was significantly lower than patients with other BBB, where none had an LVEF < 40% (P < 0.0001) (Table 4). Among the 32 patients with LVSD, the discharge diagnosis of 28 (87.5%) patients was dilated cardiomyopathy, 4 (12.5%) had an unspecified cardiomyopathy, and none had a diagnosis of hypertrophic cardiomyopathy. Most patients with LBBB (63%) were implanted with a cardiac resynchronization therapy (CRT) device at CA hospitalization while the remaining had either a VVI-ICD or a DDD-ICD device implanted.

A total of 20 BBB patients had an echocardiography performed prior to CA. In the LBBB group, 6 patients (46%) had LVEF < 40% compared to none of patients with other types of BBB. A follow-up echocardiography was performed in 48 patients after a median of 3 months (IQR: 6.1–46.1) after CA. The majority of patients with LBBB (60%) had LVEF > 40% and all patients (100%) with other types of BBB had LVEF ≥ 40% (Table 4).

During 4.3 years of follow-up, 6 patients (6/58, 10%) received appropriate ICD therapy after a median of 3.6 months (IQR: 2.6–16.0) from CA. Among the 46 patients with LBBB, 4 had appropriate ICD implantation.
therapy (4/46, 9%), and among the 12 patients with other BBB, 2 patients had appropriate ICD therapy (2/12, 17%). There was no significant difference between patients with LBBB and patients with other BBB, and appropriate ICD therapy was not associated with reduced LVEF. Shock therapy counted for 66% of all appropriate ICD therapy cases. No patients with appropriate ICD therapy died during follow-up (Table 5).

A total of 7 patients (12%) died during follow-up after a median of 3.6 years (IQR: 2.6–5.1) from CA (Fig. 2). Among these, 1 patient died a sudden death, 1 had a terminal cancer diagnosis. In the remaining 5 deaths we did not have information available as the patient was not brought to the hospital. The most common BBB morphology among the deceased was LBBB which was present in 5 of the deceased (5/7, 71%). The remaining 2 deceased patients (2/7, 28.5%) had other BBB, and there was no significant difference in mortality between the two groups (Table 5).

4. Discussion

In a 9.25-year study-period we identified 58 CA survivors with BBB and no IHD (8%) (Fig. 1). The most predominant BBB type was LBBB (79%), and the prevalence of LBBB among all CA survivors receiving an ICD was 7%. There were no significant differences between patients with LBBB and other BBB regarding pre-arrest comorbidities and medications (Table 1), but at CA hospitalization the LBBB group had significantly lower LVEF than patients with other types of BBB (Table 4). It is worth noticing that only 6 patients had LVSD before CA (Table 4), and all 6 were LBBB patients, supported by previous observations [8–10].

4.1. Left ventricular systolic dysfunction at CA hospitalization

Patients with LBBB presented with a significantly lower LVEF than patients with other types of BBB at CA hospitalization, as none of the patients with other types of BBB had LVSD. Similarly, LBBB patients had lower LVEF prior to CA and at follow-up compared to patients with other types of BBB, though this difference was not significant (Table 4). In a recent Danish study, a significant association between HF and both LBBB and RBBB was found, and LBBB had the largest risk of HF [16]. Furthermore, it is known that patients with low LVEF have a higher mortality than patients with a normal LVEF [11]. We found a prevalence of LBBB (7%) among all CA survivors which is consistent with the treatment of the present cohort.

Even though LBBB patients presented with a significantly lower LVEF than patients with other types of BBB, the distribution of LBBB and other BBB among the deceased was equal. Although more research is needed on the prognosis of CA survivors, one could conjure that having BBB and no IHD may impact the prognosis after surviving a CA, given the relatively high mortality found in this study. Patients could possibly benefit from earlier onset of prophylactic treatment, which would be an interesting scope of a prospective study. This study revealed that >50% of patients were known in the healthcare system before CA, which could make early preventive measures possible.

4.2. Recurrent arrhythmia and mortality

A total of 10% of patients received appropriate therapy from the ICD, and 66% of these were shock therapies. None of the deceased patients received appropriate ICD therapy. The low number of patients with appropriate ICD therapy in this study could be due to the relatively short follow-up period, or medical treatment. In the ESC (European Society of Cardiology) guidelines, CRT therapy is recommended in patients with LVSD (LVEF ≤ 35%), NYHA (New York Heart Association) class II–IV and LBBB and is well-documented to reduce mortality rates in patients which is consistent with the treatment of the present cohort.

BBB in otherwise healthy individuals has until now been considered without any specific risk for the patient [6], but our results indicate that there might be an association between LBBB and CA. Although literature on BBB without IHD is sparse, mortality and prognosis of LBBB without IHD has previously been described, and the most frequent cardiovascular event observed after development of LBBB was sudden cardiac death (SCD). A significant increase of SCD was observed in the first 5 years after the onset of LBBB [8]. Another study proposed that the prognosis of LBBB is determined by the presence or absence and also the severity of associated cardiovascular disease, and that LBBB per se appears to have a minimal effect on mortality for healthy subject [20].

We found a prevalence of LBBB (7%) among all CA survivors which was significantly higher than the prevalence of LBBB in the general population (0.5%). In contrast, the prevalence of RBBB in the general population was 1.7% [16] compared to a prevalence of 1% among CA survivors which is similar to a recent study, where RBBB without IHD was not associated with increased all-cause mortality [21]. A study of CA survivors with BBB including ischemic causes of CA did not find an increased 180-days mortality among LBBB or RBBB, but found that the neurologic prognosis after 180-days of CA with RBBB was worse when compared to CA with no BBB [22]. In contrast, there has been a reported significant association between RBBB and increased all-cause mortality, albeit only in a univariate analysis [3]. Some studies support both LBBB and RBBB to increase the risk of all-cause mortality [3–6], but most of these studies included patients with IHD. Previous studies on BBB without IHD are few and inconsistent. Further studies are needed to address the impact of BBB.

4.3. Strength and limitations

Exclusion of patients with ischemic and congenital heart disease makes this the first study that systematically identified and followed patients with BBB and CA with an ICD implanted in the absence of IHD. Furthermore, the Danish registries and medical reports provided a unique possibility to collect data on CA survivors with non-ischemic BBB before and after a CA. Beyond the scope of this study it would be of interest to perform a longer follow-up on these patients in the future. The retrospective design of this study is a limitation. Additionally, the population size was limited by the single center study design and low number of events, however, all possible patients were included in this study. Furthermore, we did not have access to the causes of death in all cases in this study.

5. Conclusion

Among CA survivors without IHD, 58% (8%) had BBB and more than half were known to have BBB prior to CA. The prevalence of LBBB among CA survivors was 7% compared to only 0.5% in the general population, and LBBB patients presented with a significantly lower LVEF.
than patients with other types of BBB at CA hospitalization. However, during follow-up, ICD treatment and mortality did not differ between BBB subtypes. Mortality of patients with BBB was 12% during 3.6-year follow-up period. Further studies are warranted to determine the severity of a BBB in non-IHD patients.

The authors report no relationships that could be construed as a conflict of interest.

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**Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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