Complete Right Bundle Branch Block Predicts Mortality in Thai Patients with Chronic Heart Failure with Reduced Ejection Fraction

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Background: *Previous studies have shown that intraventricular conduction defect is associated with increased mortality in heart failure (HF) population. However, it is conflicting whether left bundle branch block (LBBB) or right bundle branch block (RBBB) is a better predictor for mortality.*
Objective: *To evaluate the relationship between patterns of bundle branch block (BBB) and all-cause mortality in Thai patients with chronic heart failure with reduced ejection fraction (HFrEF) and to compare the prognostic values of RBBB and LBBB in this population.*
Material and Method: *The authors retrospectively studied a cohort of 170 patients (age 58 $\pm$ 14 years, male = 117) with HFrEF requiring hospitalization and were followed-up in a heart failure clinic. Predictors of mortality were evaluated by Cox proportional hazard analysis.*
Results: *Wide QRS complex (duration > 120 ms) was present in 26% of patients, 15% with LBBB, 11% with RBBB. During an average follow-up of 1.8 $\pm$ 1.6 years, 22 patients (13%) died. By univariate analysis, presence of chronic renal insufficiency, chronic obstructive pulmonary disease, severe left ventricular systolic dysfunction and RBBB, but not LBBB were associated with increased mortality. After multivariate adjustment, the presence of RBBB was the only strong predictor of mortality in HF patients (OR 3.9, 95% CI 1.3-11.7, $p < 0.05$).*
Conclusion: *The presence of RBBB was the only independent predictor of mortality in Thai patients with HFrEF.*

Keywords: *Bundle branch block, Heart failure, Intraventricular conduction defect, Mortality predictor*

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Chronic heart failure with reduced ejection fraction (HFrEF) is common and it carries a poor prognosis even with optimal pharmacotherapy. The presence of IVCD was shown to be a significant predictor of mortality in patients with heart failure[1,2] and the prevalence of LBBB and right bundle branch block (RBBB) in heart failure patients ranged from 16-25% and 6-14%, respectively[3-7]. However, there has been conflicting data whether the presence of LBBB or RBBB provides a more powerful predictor of mortality in this group of patients[2-8].

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Chronic heart failure is the prevalent disease in Thailand. Nevertheless, there has been no data regarding the prevalence and prognostic value of bundle branch block (BBB) in Thai HFrEF patients reported previously. The purpose of the present study was to evaluate the relationship between patterns of BBB and all-cause mortality in Thai patients with HFrEF and to compare the prognostic values of RBBB and LBBB in the presented population. Other mortality predictors were also investigated.

Material and Method

The authors retrospectively studied a cohort of 170 patients (age 58 $\pm$ 14 years, male = 126) with HFrEF who were followed-up in the heart failure clinic

at Maharaj Nakorn Chiang Mai Hospital from January 2004 to December 2007. All patients were symptomatic with New York Heart Association (NYHA)-Functional class between III-IV and had left ventricular ejection fraction (LVEF) < 50% before recruitment into the clinic. All medical records were reviewed and patients were excluded if electrocardiograms and/or echocardiograms were not available. Those with implantable pacemakers were also excluded. Chronic renal dysfunction was defined as the averaged level (obtained from the first and second visits) of creatinine equal or more than 2 mg/dl. The authors used creatinine level, instead of creatinine clearance, to estimate renal function, due to the marked change in body weight of the presented patients. The history of atrial fibrillation (AF) was obtained from the medical records and ECG performed periodically during follow-up.

A cardiologist, who was blinded to the study protocol, reviewed the electrocardiograms and echocardiographic reports. The informed consents for data analysis were obtained in all patients.

Measurements

The electrocardiographic diagnosis of LBBB was based on standard diagnosis criteria *i.e.* (1) QRS duration > 120 ms (2) PQ interval > 120 ms, (3) predominantly upright complexes with slurred R waves in leads I, V5, and V6, and (4) QS or rS pattern in V1. The electrocardiographic diagnosis of RBBB was based on (1) QRS duration > 120 ms, (2) PQ interval > 120 ms, (3) rSR in leads V1 and V2, and (4) S wave in lead I and either lead V5 or V6. Those electrocardiograms with nonspecific intraventricular conduction delay (QRS duration > 120 ms) patterns were categorized into LBBB or RBBB patterns based on the predominant morphology (*e.g.* S wave in lead I and either lead V5 or V6 forced a categorization of RBBB).

Severe LV dysfunction was defined as an EF < 25%. Chronic renal dysfunction was defined as serum creatinine level $\geq$ 2 mg/dl.

Statistical analysis

Baseline characteristics were reported with means $\pm$ standard deviation or counts and proportions with 95% confidence intervals, as appropriate. The demographic and baseline characteristics of the patients with RBBB, LBBB and without BBB were compared with the Chi-square test for categorical variables and one-way analysis of variance test for continuous variables. Survival was estimated from the date the patient referred to the heart failure specialty clinic to the date of death; living patients were censored at the last date of follow-up. Cox proportional hazard modeling was used to examine associations between independent factors and survival with adjustment for potential confounders. All p-values are two-tailed and considered significant at p-value < 0.05. SPSS version 11.5 software (SPSS, Chicago, Illinois) was used for all statistical analysis.

Results

Of 190 patients, 20 patients were excluded from the present study (15 had missing electrocardiograms, eight had missing echocardiographic data, and one patient received pacemaker implantation). The patient population was divided into three groups based on baseline electrocardiogram, comprising of no BBB (QRS duration < 120 ms), LBBB, and RBBB. The prevalence of LBBB and RBBB in the presented heart failure population was 15% and 11%, respectively. The demographic and baseline characteristics of the three study groups were compared as shown in Table 1. The mean age of the overall population was 58 $\pm$ 14 years and there were no significant age differences between groups. The majority of the patients in the present study was male (69%) and the patients with LBBB tended to have a higher proportion of men (88.5%) than other groups (p = 0.053). There were no significant differences across the groups with respect to the prevalence of diabetes mellitus, hypertension, dyslipidemia, and chronic renal dysfunction. The patients without BBB had a trend of higher prevalence of chronic obstructive pulmonary disease (COPD) and coronary artery disease (CAD) than those with BBB. The prevalence of AF was not different among three groups. Of 27 (16.1%) patients who had the history of AF, only one patient was in chronic AF. Notably, the patients with LBBB significantly had poorer EF (p = 0.006) and had larger LV dimension (p < 0.001) than did the other two groups.

During the median follow-up duration of 1.8 $\pm$ 1.6 years, 22 (13%) patients died. The causes of death are shown in Table 2. The authors demonstrated that the presence of RBBB, but not LBBB, was associated with the increase in mortality (OR 3.9, 95% CI 1.3-11.7, p = 0.021). The authors analyzed the other potential variables in addition to BBB patter including age, sex, comorbidities, and LV function by univariate analysis as predictors of mortality (Table 3). The presence of RBBB and renal dysfunction were significantly associated with higher mortality risk by univariate analysis (p = 0.021 and 0.034, respectively).

Table 1. Demographic and clinical characteristics

Variable	Total (n = 170) (100%)	RBBB (n = 19) (11%)	LBBB (n = 26) (15%)	No BBB (n = 125) (74%)	p-value
Age (years)	58 ± 14	54 ± 13	59 ± 14	58 ± 14	0.483
Male	69.0%	72.2%	88.5%	64.5%	0.053
DM	29.8%	44.4%	19.2%	29.8%	0.198
HT	31.0%	44.4%	26.9%	29.8%	0.406
Dyslipidemia	43.5%	44.4%	38.5%	44.4%	0.856
Chronic renal dysfunction	38.1%	33.3%	42.3%	37.9%	0.831
COPD	14.3%	5.6%	3.8%	17.7%	0.098
CAD	45.1%	35.3%	26.1%	50.0%	0.074
History of AF	16.1%	14.8%	11.1%	16.1%	0.637
Systolic PAP (mmHg)	45 ± 14	46 ± 16	45 ± 14	46 ± 15	0.966
LVEF (%)	30 ± 12	28 ± 13	24 ± 8	32 ± 12	0.006
Severe LV dysfunction	38.5%	47.4%	78.3%	29.4%	<0.001
LVDD (mm)	63 ± 10	62 ± 9	70 ± 11	62 ± 9	<0.001
Long-term medications					
Lipid-lowering	44.7%	26.3%	34.6%	49.6%	0.087
Beta-blockers	77.6%	63.2%	92.3%	76.8%	0.062
ACEI or ARB	77.1%	84.2%	80.8%	75.2%	0.608
Diuretics	92.4%	100.0%	92.3%	91.2%	0.405
CCB	5.9%	10.5%	3.8%	5.6%	0.621
Spironolactone	69.4%	84.2%	69.2%	67.2%	0.325
Mortality (%)	22 (13.0%)	6 (31.6%)	5 (19.2%)	11 (8.8%)	0.013

ACEI = angiotensin converting enzyme inhibitor; ARB = antiogensin receptor blocker; AF = atrial fibrillation; CAD = coronary artery disease; CCB = calcium channel blockers; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; HT = hypertension; LBBB = left bundle branch block; LVDD = left ventricular diastolic dimension; LVEF = left ventricular ejection fraction; PAP = pulmonary arterial pressure; RBBB = right bundle branch block

Table 2. Causes of death

Causes of death	Number (%) (total = 22)
Decompensated heart failure	15 (68%)
Sudden cardiac death	6 (27%)
COPD with respiratory failure	1 (5%)

COPD = chronic obstructive pulmonary disease

There was also a trend toward the increased mortality in the patients with COPD compared with those without COPD (p = 0.093). Similarly, the patients with severe LV dysfunction tended to have a higher mortality risk than those without (p = 0.090). After the multivariate analysis, the presence of RBBB was the only independent predictors of mortality in the authors' studied population (Table 4). Among 19 patients with RBBB, 13 (68%) patients had concomitant left fascicular hemi-block. Interestingly, six (46%) of 13 patients with RBBB associated with left fascicular hemiblock did not survive while all patients with RBBB without concomitant left fascicular hemiblock survived (p = 0.1). Of six patients with RBBB who died, two died due to arrhythmic death and the other four died because of worsening heart failure. Fig. 1 shows the adjusted survival curves stratified by the BBB pattern. The relative effect of RBBB on the worse prognosis in comparison with LBBB was enhanced after Cox proportional hazards model adjusting for heart failure prognostic variables including age, gender, comorbidities, and LV function.

Discussion

The authors demonstrated that the presence of RBBB, but not LBBB, was associated with the increase in mortality in heart failure patients, which was in accordance with the findings of Mueller et al and Barsheshet et al[6,7]. On the contrary, other investigators found that the presence of LBBB, but not RBBB predicts mortality[4,5]. The inconsistent findings may

Table 3. Univariate analysis-predictors of mortality in heart failure patients with reduced ejection fraction

Variables	Survived (n = 148, 87%)	Dead (n = 22, 13%)	p-value	Odd ratio (95% CI)
Age (years)	57 ± 14	61 ± 13	0.241	
Male	68.9%	72.7%	0.909	0.8 (0.3-2.3)
DM	28.4%	36.4%	0.606	1.4 (0.6-3.7)
HT	29.1%	40.9%	0.380	1.7 (0.7-4.2)
Dyslipidimia	40.5%	59.1%	0.159	2.1 (0.8-5.3)
Chronic renal dysfunction	34.5%	59.1%	0.034	2.7 (1.1-6.8)
COPD	12.2%	27.3%	0.093	2.7 (0.9-7.8)
CAD	43.7%	50.0%	0.744	1.3 (0.5-3.2)
History of AF	16.2%	13.6%	1.000	0.8 (0.2-3.0)
Systolic PAP (mmHg)	46 ± 14	42 ± 16	0.359	
LVEF (%)	26 ± 9	24 ± 8	0.703	
Severe LV dysfunction	35.7%	57.1%	0.090	2.4 (0.9-6.1)
LVDD (mm)	63 ± 10	63 ± 8	0.896	
RBBB	8.8%	31.6%	0.021	3.9 (1.3-11.7)
LBBB	12.8%	19.2%	0.204	2.0 (0.7-6.0)

Table 4. Univariate and multivariate analysis of right bundle brunch block (RBBB) as a predictor of all-cause mortality

Univariate P	0.021
HR (95% CI)	3.89 (1.30-11.67)
Model 1[a]	
Multivariate P	0.001
HR (95% CI)	6.60 (2.17-20.0)
Model 2[b]	
Multivariate P	0.001
HR (95% CI)	6.43 (2.06-20.0)
Model 3[c]	
Multivariate P	0.047
HR (95% CI)	4.03 (1.02-15.91)

HR, hazard ratio

[a] Adjusting for age, gender and comorbidities

[b] Adjusting for age, gender, comorbidities and left ventricular function

[c] Adjusting for age, gender, comorbidities, left ventricular function and medications

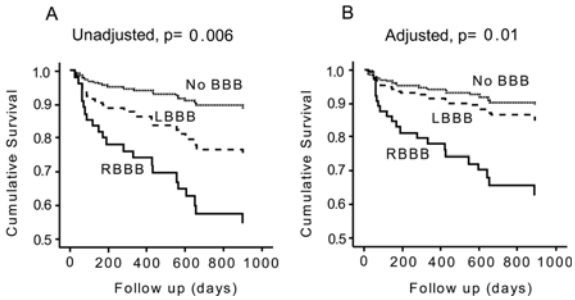

Fig. 1 Cox proportional-hazard regression survival curves for patients with systolic heart failure analyzed according to bundle branch block patterns: RBBB = right bundle branch block; LBBB = left bundle branch block, Panel A) displays survival curves before adjusting for heart failure prognostic variables. Panel B) displays survival curves after adjusting for heart failure prognostic variables including age, gender, comorbidities and left ventricular function

be explained by the fact that there were variations among those studies regarding the prevalence of BBB and the characteristics of the studied populations. Several studies had included the heart failure patients with preserved LV systolic function, which were excluded in the present study[4,5]. Barsheshet et al showed that RBBB was a strong predictor of mortality in heart failure patients with impaired systolic function but not in patients with preserved LV systolic function[7]. In addition, the prevalence of LBBB (15%) and RBBB (11%) in the authors' studied population was similar to those reported by Mueller et al (17% and 14%, respectively)[6] and Barsheshet et al (16% and 10%, respectively)[7]. However, there were more LBBB (23-25%) and less RBBB (6-7%) in other studies[3-5].

In general, RBBB was frequently associated with pulmonary hypertension and chronic pulmonary disease, which may contribute to right ventricular (RV)

dysfunction and worsening outcome of patients with heart failure. Mueller et al has shown that the patients with RBBB more often had pulmonary comorbidities[6]. Similarly, Barsheshet et al found that the patients with RBBB had a slightly higher prevalence of COPD and had higher pulmonary arterial (PA) pressure, compared to those with LBBB and without BBB[7]. However, in the present study, the authors did not find the higher prevalence of COPD in the RBBB group. In addition, the PA systolic pressure did not differ between the patients with and without RBBB.

It has been shown that cardiac resynchronization therapy (CRT) can improve symptoms and reduce morbidity and mortality in patients with heart failure and intraventricular conduction defect[9]. The benefit of CRT has been well-established in the patients with LBBB, but only a few studies had included patients with RBBB[9,10]. Fantoni et al[11] used three-dimensional electroanatomical mapping to characterize RV and LV activation in heart failure patients with RBBB, compared to those with LBBB. They demonstrated that the patients with RBBB had greater right-sided conduction delay than did the patients with LBBB. Interestingly, the degree of LV activation delay was found similar between the patients with RBBB and LBBB. With this regard, RBBB may be the marker not only of RV dysfunction, but also of the severe degree of both left and right ventricular dyssynchrony in the patients with systolic heart failure. Of note, all of their patients with RBBB had concomitant left fascicular block. Consistently, a total of six patients with RBBB in the present study who died, were all associated with concomitant left fascicular hemiblock, indicating the presence of 'not only right-sided' but a diffuse disease of the conduction system and working myocardium in this group of patients. This may have partly explained why the patients with RBBB in the present study who had neither higher prevalence of pulmonary comorbidities nor higher systolic PA pressure, still carried a higher mortality risk, compared to those without RBBB. It is conceivable that the use of CRT may also be beneficial in this group of patients. Long-term studies addressing the benefit of CRT in the patients with RBBB are warranted. Of 170 patients, six patients (3.5%) died due to sudden cardiac arrest. According to the current guidelines, the implantation of automatic implantable cardiac defibrillator (AICD) is recommended for primary prophylaxis in the majority of our patients[12]. However, these high cost devices are not affordable by most patients and Thai clinicians preferred to continue the optimal medical therapy for a certain period before making the decision for AICD implantation. Future studies regarding the cost-effectiveness of AICD implantation for primary prophylaxis in Thai population may be needed.

In the present study, LBBB was associated with larger LV size and poorer LV systolic function. However, LBBB was not an independent predictor of mortality in the HFrEF patients in the present study. This may be attributable to the fact that LBBB is an indicator of advanced LV disease, therefore, it did not provide additional prognostic information in these patients.

The population studied comprised of patients with relatively severe heart failure. All of them had severe heart failure symptoms and had been hospitalized from worsening heart failure before entering the study. The extrapolation of the present results to other heart failure populations with less severe symptoms should be made with caution.

Conclusion

The authors demonstrated that the presence of RBBB was a powerful independent predictor of mortality in Thai patients with chronic heart failure with reduced ejection fraction. Therefore, the management of this group of patients should be more aggressively addressed.

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การปิดกั้นการเดินไฟฟ้าด้านขวา พยากรณ์การเสียชีวิตในผู้ป่วยหัวใจล้มเหลวเรื้อรังที่มีการบีบตัวของหัวใจลดลง

วรรณวรางค์ วงศ์เจริญ, อรินทยา พรหมินธิกุล, รังสฤษฎ์ กาญจนะวณิชย์, อนงค์ อมฤตโกมล, ปาลีรัฐ โตไพบูลย์, วรินทร เวียงโอสถ, ศรันย์ ควรประเสริฐ, อภิชาต สุคนธสรรพ์

ภูมิหลัง: *ข้อมูลจากหลายการศึกษาระบุว่าการปิดกั้นทางเดินไฟฟ้าในหัวใจห้องล่าง (intraventricular conduction defect) มีความสัมพันธ์กับการเสียชีวิตที่เพิ่มขึ้นของผู้ป่วยหัวใจล้มเหลว แต่ยังไม่ชัดเจนว่าการปิดกั้นการเดินไฟฟ้าด้านซ้ายหรือด้านขวามีความแม่นยำในการพยากรณ์การเสียชีวิตมากกว่า*

วัตถุประสงค์: *เพื่อประเมินความสัมพันธ์ระหว่างชนิดของการปิดกั้นทางเดินไฟฟ้า และการเสียชีวิตในผู้ป่วยชาวไทยหัวใจล้มเหลวเรื้อรังที่มีการบีบตัวของหัวใจลดลง และเปรียบเทียบความแม่นยำในการพยากรณ์การเสียชีวิตระหว่างการปิดกั้นการเดินไฟฟ้าด้านซ้ายและด้านขวา*

วัสดุและวิธีการ: *เป็นการศึกษาแบบย้อนหลังในผู้ป่วย 170 ราย (อายุเฉลี่ย 50 $\pm$ 14 ปี, ชาย = 117 คน) ซึ่งมีภาวะหัวใจล้มเหลวเรื้อรังที่มีการบีบตัวของหัวใจลดลง ร่วมกับมีประวัติเข้ารับการรักษาในโรงพยาบาล และได้รับการติดตามต่อเนื่องในคลินิกผู้ป่วยหัวใจล้มเหลว ข้อมูลทางคลินิกได้ถูกนำมาวิเคราะห์ โดยการใช้ Cox proportional hazard analysis เพื่อศึกษาปัจจัยที่มีผลต่อการพยากรณ์การเสียชีวิต*

ผลการศึกษา: *ผู้ป่วยร้อยละ 26 มี QRS complex กว้าง (ระยะเวลา > 120 วินาที), ร้อยละ 15 มีการปิดกั้นทางเดินไฟฟ้าด้านซ้าย, ร้อยละ 11 มีการปิดกั้นทางเดินไฟฟ้าด้านขวา โดยมีผู้ป่วยร้อยละ 13 (22 คน) เสียชีวิตระหว่างการติดตามรักษาต่อเนื่องในระยะเวลา 1.8 $\pm$ 1.6 ปี จากการวิเคราะห์ โดยใช้การวิเคราะห์แบบ univariate analysis พบว่า การมีภาวะไตเสื่อมเรื้อรัง, โรคปอดอุดกั้นเรื้อรัง, การทำงานของหัวใจห้องล่างซ้ายลดลงอย่างรุนแรง และมีการปิดกั้นการเดินไฟฟ้าด้านขวา มีความสัมพันธ์กับการเพิ่มขึ้นของการเสียชีวิต ในขณะที่การปิดกั้นทางเดินไฟฟ้าด้านซ้ายไม่มีความสัมพันธ์ และหลังจากใช้การวิเคราะห์แบบ multivariate พบว่าการมีการปิดกั้นทางเดินไฟฟ้าด้านขวาเป็นปัจจัยเดียวที่สามารพยากรณ์การเสียชีวิต ในผู้ป่วยหัวใจล้มเหลวเรื้อรังได้แม่นยำที่สุด (OR 3.9, 95% CI 1.3-11.7, $p < 0.05$)*

สรุป: *การปิดกั้นทางเดินไฟฟ้าด้านขวาเป็นเป็นปัจจัยอิสระ ที่สามารถพยากรณ์การเสียชีวิตในผู้ป่วยชาวไทยหัวใจล้มเหลวเรื้อรังที่มีการบีบตัวของหัวใจลดลง*