

Prognostic impact of right bundle branch block in hospitalized patients with idiopathic dilated cardiomyopathy: a single-center cohort study Journal of International Medical Research 48(1) I-II © The Author(s) 2018 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/0300060518801478 journals.sagepub.com/home/imr



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### Abstract

**Objective:** Idiopathic dilated cardiomyopathy (IDCM) is a primary myocardial disease resulting in symptoms of heart failure. Right bundle branch block (RBBB) is associated with increased cardiovascular risk and all-cause mortality. Therefore, the present study was performed to identify the prognostic impact of RBBB in patients with IDCM.

**Methods:** In total, 165 hospitalized patients with IDCM were evaluated. Receiver operating characteristic curve analysis was used to determine the cutoff point, and Cox regression was used to assess risk factors.

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**Results:** After a median follow-up of 73.1 months (interquartile range, 36.1–88.7 months), 59 (35.8%) patients had died. All-cause mortality was significantly higher in patients with than without RBBB (log-rank  $\chi^2 = 9.400$ ), P<0.05. Significant independent predictors of all-cause mortality in patients with IDCM were RBBB (hazard ratio, 2.898; 95% confidence interval, 1.201–6.995) and the left ventricular end-diastolic dimension (LVEDD) (hazard ratio, 1.034; 95% confidence interval, 1.004–1.066) at admission. Patients with RBBB and an LVEDD of  $\geq$ 63 mm had the highest mortality (log-rank  $\chi^2 = 14.854$ ), P<0.05.

**Conclusion:** RBBB was an independent predictor of all-cause mortality, and the combination of RBBB and LVEDD provided more clinically relevant information than RBBB alone for assessing the risk of all-cause mortality in patients with IDCM.

### **Keywords**

Idiopathic dilated cardiomyopathy, right bundle branch block, mortality, prognosis, left ventricular end-diastolic dimension, cardiovascular risk

Date received: 24 July 2017; accepted: 28 August 2018

## Introduction

Idiopathic dilated cardiomyopathy (IDCM) is a myocardial disorder characterized by a dilated left ventricular chamber and systolic dysfunction that commonly results in congestive heart failure.<sup>1,2</sup> IDCM is currently the leading indication for heart transplantation and remains the third most common cause of heart failure after coronary artery disease and hypertension.<sup>2,3</sup> With an incidence of 5.5 cases per 100,000 individuals per year, IDCM is the most common form of cardiomyopathy, and it is diagnosed when no other cause of congestive heart failure is apparent.<sup>4,5</sup>

Right bundle branch block (RBBB) is defined as a QRS duration of  $\geq$ 120 ms in adults according to the American Heart Association recommendations for standardization of the electrocardiogram (ECG).<sup>6</sup> On the ECG, RBBB presents with a wide, blunt R or R' wave in lead V1 or aVR and a wide, blunt S wave in leads V5, I, and aVL.<sup>7</sup> The prevalence of RBBB in the general population ranges from 0.5% to 1.5%, shows male predominance (1.4% in men and 0.5% in women), and increases with age to 2.2% in patients aged >55 years.<sup>8,9</sup> Some previous studies have shown that RBBB is associated with right ventricular dysfunction in patients with congenital heart diseases and has been proven to be independently associated with adverse outcomes.<sup>10–12</sup> However, the relationship between RBBB and the prognosis of IDCM is unclear. Therefore, the aim of the present study was to define the clinical value of RBBB in predicting the outcome of IDCM.

## Patients and methods

### Patients

We retrospectively reviewed the data of patients admitted to our cardiology department with IDCM from February 2004 to July 2011. All patients recruited into this study provided verbal informed consent. This research was approved by the Ethics Committee of Fuwai Hospital. For all patients, we obtained an extensive baseline clinical history, performed a physical examination, and obtained a 12-lead ECG and 2-dimensional Doppler echocardiogram. The definition of IDCM was based on the World Health Organization criteria: presentation with both a left ventricular enddiastolic dimension (LVEDD) of  $\geq$ 55 mm and a left ventricular ejection fraction (LVEF) of <50% in the absence of a possible known cause.<sup>13</sup> The exclusion criteria were as follows:

- A history of severe systemic hypertension (>160/100 mmHg), diabetic heart diseases, and other cardiomyopathies with LVEDD dilation, including alcoholic cardiomyopathy and peripartum cardiomyopathy
- (II) An ischemic etiology (ruled out by coronary angiography or computed tomography angiography)
- (III) Organic valve diseases, tachycardiainduced cardiomyopathy, congenital heart diseases, hyperthyroidism, and advanced systemic diseases

## Echocardiography

Because the pulmonary artery systolic pressure (PASP) is equal to the right ventricular systolic pressure in the absence of pulmonary stenosis, the PASP was estimated using Doppler echocardiography by calculating the right ventricular to right atrial pressure gradient during systole (approximated by the modified Bernoulli equation as 4v<sup>2</sup>, where v is the velocity of the tricuspid regurgitation jet in m/s). The right atrial pressure, estimated based on the echocardiographic characteristics of the inferior vena cava and assigned a standardized value, was then added to the calculated gradient to give the PASP. According to the new guideline, the presence of a PASP of  $\geq$ 40 mmHg was likely to be pulmonary hypertension.<sup>14</sup>

### Follow-up and endpoint

Follow-up was performed until November 2016. Data on the occurrence of all-cause mortality at follow-up were collected by

reviewing the medical records (outpatient clinic attendance and hospitalization), telephone interviews, and retrieval of survival status through the police station. The primary endpoint in this study was all-cause mortality. This study was approved by the Ethics Commission of Fuwai Hospital.

#### Statistical analysis

Baseline demographic data, risk factors, and clinical variables are descriptively summarized. Variables with a normal distribution are presented as mean  $\pm$  standard deviation, whereas those with a non-normal distribution are presented as median and interquartile range (IQR). Categorical variables are presented as percentage frequency. The t test was used to compare differences in continuous variables, and the chi-square ( $\chi^2$ ) test was used to compare differences in categorical variables.

To predict all-cause mortality from the baseline variables, a univariate Cox regression screening of all parameters at enrollment was initially performed. For the multivariable Cox proportional hazards analysis, we included only those variables with a p value of <0.05 in the univariate analysis as well as the N-terminal fragment pro-brain natriuretic peptide (NT-pro BNP) level because it is a well-known prognostic indicator in patients with IDCM.

On the basis of the multivariate Cox regression analysis, continuous variables were categorized by receiver operating characteristic (ROC) curve analysis, which was used to optimize the cutoff level of continuous variables. Survival curves were generated by the Kaplan–Meier method and compared by the log-rank test. The level of statistical significance was set at p < 0.05. All hypothesis tests were two-sided. The entire analysis was performed using SPSS Statistics for Windows, Version 17.0 (SPSS Inc., Chicago, IL, USA).

## Results

## Study population

In total, 165 patients who were hospitalized from February 2004 to July 2011 were included in this study. Twenty patients were lost to follow-up, which was performed until November 2016. Of the 165 patients included in the study, 107 (64.8%) were men and 58 (35.1%) were women. The age of the patients at diagnosis of IDCM ranged from 19 to 80 years (mean,  $56.9 \pm 12.3$  years), and the median disease duration was 2 years (IQR, 0.35-5 years). One hundred two (61.8%) patients had New York Heart Association (NYHA) functional class III/IV heart failure. Forty-six patients had a QRS duration of  $\geq$ 150 mm and 83 had a duration of  $\geq$ 120 mm, among whom 12 patients had RBBB. During a median follow-up time of 73.1 months (IQR, 36.1-88.7 months), 59 patients with IDCM (35.8%) died.

The baseline clinical, ECG, and echocardiographic characteristics of patients with IDCM are shown in Table 1. Among all patients with IDCM, differences in the baseline age, diastolic blood pressure (DBP), RBBB, and atrial fibrillation were observed between those who died and those who survived. Age and DBP at admission were higher in patients who died than in those who survived. RBBB and atrial fibrillation were more frequent in patients who died. Table 2 shows the baseline clinical, ECG, and echocardiographic characteristics of patients divided by RBBB. Patients with RBBB had a higher NTpro BNP level, QRS duration, and right ventricular (RV) diameter. The frequency of left bundle branch block was lower in the RBBBpositive than -negative group.

# Relationship between RBBB and all-cause mortality

The Kaplan-Meier survival probability estimate was 96.4% at 1 year and 70.4%

at 5 years. In our IDCM cohort, patients with RBBB had higher all-cause mortality than patients without RBBB (log-rank  $\chi^2 = 9.400, p = 0.002$ ) (Figure 1).

## ROC analysis of LVEDD and QRS

According to the ROC curve analysis, the optimal cutoff value of the LVEDD and QRS was 63 mm [area under the curve (AUC), 0.616; 95% confidence interval (CI), 0.523–0.709; p = 0.017] and 115 ms (AUC, 0.610; 95% CI, 0.519–0.701; p = 0.024), respectively (Figure 2).

# Predictors of all-cause mortality in patients with IDCM

The univariate analysis revealed the following predictors of all-cause mortality in patients with IDCM: age (hazard ratio (HR), 95% CI. 1.008-1.056; 1.031; p = 0.009), NYHA class (HR, 1.486; 95%) CI, 1.062-2.081; p = 0.021), DBP (HR, 0.974; 95% CI, 0.953–0.995; p = 0.016), RBBB (HR, 2.987; 95% CI, 1.411-6.323; p =0.004), LVEDD (HR, 1.029; 95% CI, 1.001–1.057; p = 0.042), and right atrial diameter (HR, 2.208; 95% CI, 1.037-4.702; p = 0.040). Independent predictors of all-cause mortality in the multiple Cox regression analysis were RBBB (HR, 2.898; 95% CI, 1.201–6.995; p = 0.018) and LVEDD (HR, 1.034; 95% CI, 1.004-1.066; p = 0.029) at admission (Table 3).

## Relationship between RBBB + increasedLVEDD ( $\geq$ 63 mm) and survival

Twelve patients had RBBB (7.3%) and 91 patients had an LVEDD of  $\geq 63$  mm (55.2%). Figure 3 shows the long-term event-free survival of patients with or without RBBB and an LVEDD of  $\geq 63$  mm. Patients with RBBB + an LVEDD of  $\geq 63$  mm had the highest mortality (logrank  $\chi^2 = 14.854$ , p = 0.002).

	All patients (n = 165)	Death (n $=$ 59)	Survival (n = 106)	þ value
Mean age, years	$\textbf{56.9} \pm \textbf{12.3}$	$\textbf{60.9} \pm \textbf{11.6}$	$\textbf{54.7} \pm \textbf{12.1}$	0.002
Disease duration, years	2 (0.35–5)	3 (0.5–7)	2 (0.3–5)	0.365
Smoking	67 (40.6)	25 (42.4)	42 (39.6)	0.897
Syncope	9 (5.5)	4 (6.8)	5 (4.7)	0.576
Heart rate, bpm	$77.9 \pm 15.9$	$75.2\pm16.8$	$79.4 \pm 15.4$	0.105
Sex				0.668
Male	107 (64.8)	37 (62.7)	70 (66.0)	
Female	58 (35.2)	22 (37.3)	36 (34.0)	
NYHA functional class				0.122
I	6 (3.6)	0 (0.0)	6 (5.7)	
II	57 (34.4)	18 (30.5)	39 (36.8)	
III	73 (44.2)	27 (45.8)	46 (43.4)	
IV	29 (17.8)	14 (23.7)	15 (14.1)	
Blood pressure				
SBP, mmHg	$118.3 \pm 17.1$	116.6 $\pm$ 16.7	$119.2 \pm 17.2$	0.348
DBP, mmHg	$\textbf{74.8} \pm \textbf{I3.2}$	$71.2\pm12.2$	$\textbf{76.8} \pm \textbf{I3.4}$	0.008
Blood test results				
Cr, μmol/L	87 (70.6–98.1)	89.6 (75.5–102.9)	85.4 (68.5–97.4)	0.098
BUN, μmol/L	6.7 (5.5–8.7)	6.57 (5.6–8.9)	6.67 (5.4–8.35)	0.450
NT-pro BNP, fmol/mL	1173.1 (602.5–2186.1)	1278.6 (627–2305.9)	1087.8 (575.9-2057.6)	0.263
cTnl	0.05 (0.32-0.05)	0.05 (0.05-0.1)	0.05 (0.025-0.05)	0.363
ECG test results	· · · ·			
QRS duration, ms	$126.3\pm32.8$	$\textbf{I32.8} \pm \textbf{32.3}$	$\textbf{122.8} \pm \textbf{32.7}$	0.066
RBBB	12 (7.3)	8 (13.6)	4 (3.7)	0.020
LBBB	53 (32.1)	19 (32.2)	34 (32.1)	0.987
AF	9 (5.5)	6 (10.2)	3 (2.8)	0.047
Echocardiography results				
LVEF, %	$\textbf{34.6} \pm \textbf{8.9}$	$\textbf{33.6} \pm \textbf{8.5}$	$\textbf{35.2} \pm \textbf{9.1}$	0.250
LVEDD, mm	$65.4 \pm 8.6$	$67.1 \pm 8.8$	$64.5 \pm 8.3$	0.066
RV, mm	$\textbf{21.9} \pm \textbf{4.0}$	$\textbf{22.5} \pm \textbf{3.8}$	$21.5\pm4.1$	0.124
LA, mm	$\textbf{43.2} \pm \textbf{7.9}$	$\textbf{44.4} \pm \textbf{8.2}$	$\textbf{42.5} \pm \textbf{7.8}$	0.161
PH, mmHg	19 (11.5)	9 (15.3)	10 (9.4)	0.946

Table 1. Patient characteristics categorized according to survival and death.

Data are expressed as mean  $\pm$  standard deviation, median (interquartile range), or n (%); p values were calculated from independent-samples t-tests or  $\chi^2$  tests for categorical data. Bold data indicate p < 0.05.

Five patients lacked LVEDD data, 16 lacked RV data, 7 lacked LA data, 4 lacked LVEF data, 33 lacked NT-pro-BNP data, 7 lacked Cr data, 8 lacked BUN data, and 103 lacked cTnl data.

RBBB, right bundle branch block; NYHA, New York Heart Association; SBP, systolic blood pressure; DBP, diastolic blood pressure; Cr, creatinine; BUN, blood urea nitrogen; NT-pro BNP, N-terminal fragment pro-brain natriuretic peptide; cTnl, cardiac troponin; LBBB, left bundle branch block; AF, atrial fibrillation; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; RV, right ventricle; LA, left atrium; PH, pulmonary hypertension.

## Discussion

In the present study, the most relevant finding was that **RBBB** at admission was an independent predictor of all-cause mortality in patients with **IDCM**, and the combination of RBBB and LVEDD provides more clinically relevant information than RBBB alone for assessing the risk of all-cause mortality in patients with IDCM.

RBBB patterns are relatively rare in ECGs in the general population, and

	RBBB-positive (n = 12)	RBBB-negative (n = 153)	p value
Mean age, years	$\textbf{58.2} \pm \textbf{14.8}$	56.8±12.1	0.712
Disease duration, years	3.5 (1-5)	2 (0.3–5.5)	0.656
Smoking	6 (60.0)	61 (39.8)	0.491
Syncope	l (8.33)	8 (5.22)	0.648
Heart rate, bpm	$75.7 \pm 16.8$	78.I ± 15.9	0.618
Sex			0.444
Male	9 (75.0)	98 (64.1.0)	
Female	3 (25.0)	55 (35.9.0)	
NYHA functional class		× ,	0.060
I	0 (0.0)	6 (3.9)	
11	l (30.5)	56 (36.6)	
111	8 (45.8)	65 (42.5)	
IV	3 (23.7)	26 (17.0)	
Blood pressure	( ),		
SBP, mmHg	110.7 ± 17.1	118.9 $\pm$ 16.9	0.108
DBP, mmHg	$71.2 \pm 13.3$	$75.1\pm13.2$	0.326
Blood test results			
Cr, μmol/L	$\textbf{99.9} \pm \textbf{28.7}$	$86.5\pm24.5$	0.073
BUN, μmol/L	$8.2\pm1.9$	$7.1\pm2.3$	0.101
NT-proBNP, fmol/mL	2443 (1742.3–3970.4)	1078.7 (574.7-2061.6)	0.001
cTnl	0.05 (0.0115–0.115)	0.05 (0.0335–0.05)	0.733
ECG test results	,	· · · · · · · · · · · · · · · · · · ·	
QRS duration, ms	$155.8 \pm 32.318.4$	$123.8\pm32.6$	<0.001
LBBB	0 (0.0)	53 (34.6)	0.014
AF	(8.3)	8 (5.2)	0.648
Echocardiography results			
LVEF, %	31.8±9.3	$34.8\pm8.9$	0.260
LVEDD, mm	$69.4\pm8.5$	65.1 $\pm$ 8.5	0.093
RV, mm	24.1 $\pm$ 4.4	$21.7 \pm 3.9$	0.046
LA, mm	$\textbf{46.1} \pm \textbf{8.7}$	$\textbf{42.9} \pm \textbf{7.9}$	0.188

Table 2. Patient characteristics categorized according to RBBB.

Data are expressed as mean  $\pm$  standard deviation, median (interquartile range), or n (%); *p* values were calculated from independent-samples t-tests or  $\gamma^2$  tests for categorical data. Bold data indicate *p* < 0.05.

Five patients lacked LVEDD data, 16 lacked RV data, 7 lacked LA data, 4 lacked LVEF data, 33 lacked NT-pro-BNP data, 7 lacked Cr data, 8 lacked BUN data, and 103 lacked cTnl data.

NYHA, New York Heart Association; SBP, systolic blood pressure; DBP, diastolic blood pressure; Cr, creatinine; BUN, blood urea nitrogen; NT-pro BNP, N-terminal fragment pro-brain natriuretic peptide; cTnI, cardiac troponin; RBBB, right bundle branch block; LBBB, left bundle branch block; AF, atrial fibrillation; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; RV, right ventricle; LA, left atrium.

RBBB is generally considered a benign finding that does not imply increased risk when found in asymptomatic healthy individuals.<sup>8,15–17</sup> A recent study indicated that a reduced LVEF was not associated with an increased likelihood of RBBB, and RBBB did not affect the prognosis among patients with RBBB without evidence of heart disease.<sup>18</sup> However, among patients with heart failure, the presence of RBBB has been associated with a poor prognosis.<sup>19,20</sup> The present study indicated that patients with IDCM with RBBB had enlarged RV dimensions (Table 2) and that RBBB was an independent predictor of a poor prognosis in patients with IDCM. Keller et al.<sup>21</sup>



**Figure 1.** Kaplan–Meier curves demonstrating differences in groups divided according to the presence of RBBB. Cum, cumulative; RBBB, right bundle branch block.



**Figure 2.** Receiver operating characteristic curve of LVEDD and QRS duration. LVEDD, left ventricular end-diastolic dimension.

revealed significant associations between RBBB and RV dysfunction and cardiac injury in their multivariable regression, and a recent study showed that RV dysfunction is being increasingly recognized in patients with heart failure and is an independent predictor of adverse outcomes in such patients.<sup>22</sup> These studies indicate that RBBB may reflect the RV dimensions or RV dysfunction as well as the possibility that the prognostic impact of RBBB is related to the prognostic impact of RV dysfunction. This should be assessed in future explorations. Other researchers have stated that **RBBB** is associated with an increased risk of myocardial infarction and pacemaker insertion and that the prognosis of patients with acute myocardial infarction and RBBB at admission remains poor compared with patients who do not have bundle branch block.<sup>8,23,24</sup> Additionally, in China, Li et al.<sup>25</sup> reported that the presence of RBBB, but not LBBB or the QRS duration, was an independent predictor of all-cause mortality in patients with DCM; this is consistent with the findings of our study.

Variable	Univariate analysis		Multivariate analysis	
	Unadjusted HR (95% CI)	þ value	Adjusted HR (95% CI)	þ value
Age	1.031 (1.008–1.056)	0.009	1.021 (0.995-1.048)	0.118
Sex	1.031 (0.608–1.751)	0.909	_	_
NYHA class	1.486 (1.062–2.081)	0.021	1.295 (0.812-2.066)	0.278
Syncope	1.168 (0.423–3.229)	0.765		_
Smoking	1.179 (0.703–1.976)	0.533	_	_
SBP	0.992 (0.977–1.007)	0.299	_	_
DBP	0.974 (0.953–0.995)	0.016	0.977 (0.952-1.002)	0.075
RBBB	2.987 (1.411–6.323)	0.004	2.898 (1.201–6.995)	0.018
LBBB	0.902 (0.522–1.558)	0.711	/	_
QRS > 115	1.626 (0.932–2.838)	0.087	_	_
AF	0.477 (0.204–1.114)	0.087	_	_
LVEDD	1.029 (1.001–1.057)	0.042	1.034 (1.004–1.066)	0.029
LVEF	0.979 (0.949–1.009)	0.169		_
RA diameter	2.208 (1.037-4.702)	0.040	1.848 (0.800-4.270)	0.151
NT-pro-BNP	1.000 (1.000–1.000)	0.398	1.000 (1.000–1.000)	0.661
FBG	1.131 (0.982–1.303)	0.087	_	_
Cr	1.007 (0.998-1.017)	0.143	_	_
cTnl	1.071 (0.909–1.263)	0.413	_	_
PH	1.104 (0.393–3.105)	0.851		

Table 3. All-cause mortality in univariate and multivariable analyses.

NYHA, New York Heart Association; SBP, systolic blood pressure; DBP, diastolic blood pressure; RBBB, right bundle branch block; LBBB, left bundle branch block; QRS, QRS duration; AF, atrial fibrillation; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; RA, right atrial; NT-pro BNP, N-terminal fragment pro-brain natriuretic peptide; FBG, fasting blood glucose; Cr, creatinine; cTnl, cardiac troponin; PH, pulmonary hypertension. Bold data indicate p < 0.05.



**Figure 3.** Relationship between RBBB + increased LVEDD ( $\geq$ 63 mm) and survival. Cum, cumulative; RBBB, right bundle branch block; LVEDD, left ventricular end-diastolic dimension.

The effect of left ventricular function on the outcome of patients with heart failure has been well documented.<sup>26-28</sup> However, LVEDD, an indicator of left ventricular systolic dysfunction, was a contradictory predictor of prognosis in patients with DCM. Previous studies have shown that a higher LVEDD is significantly related to an unfavorable outcome in patients with IDCM.<sup>29,30</sup> Other studies have shown that the prognosis of patients with DCM with a mildly dilated left ventricle was similar to that of patients with a moderately to severely dilated left ventricle.<sup>31–33</sup> In the present study, the LVEDD was an independent predictor of a poor prognosis in patients with IDCM, and the combination of the LVEDD and RBBB provides more clinically relevant information than RBBB alone for assessing the risk of all-cause mortality in patients with IDCM.

### Study limitations

This study has several limitations. First, this was a single-center study performed in Fuwai Hospital in Beijing; therefore, the data described herein cannot be extrapolated to the entire population of patients with IDCM. Second, because all-cause mortality was the primary endpoint, we did not obtain complete data on the incidence of cardiac death, heart failure rehospitalization, and lethal ventricular arrhythmias. Such data could have provided more compelling and conclusive results than those of all-cause mortality alone. In addition, because the present study was a retrospective analysis, we did not collect precise information about medical therapy in patients with IDCM; thus, we did not include medication as an evaluation index in this study, which may have influenced the all-cause mortality.

### **Authors' contributions**

Xiaoping Li and Li Lai contributed to the conception of the study. Rong Luo and Chao Yan contributed significantly to the data analysis and manuscript preparation. Wei Fang and Rong Jiang performed the data analyses and wrote the manuscript. Yibin Tang and Wei Hua helped perform the analysis with constructive discussions.

### **Declaration of conflicting interest**

The authors declare that there is no conflict of interest.

### Funding

This work was supported by National Natural Science Foundation of China (No.81500297, No.81470521 and No.81770379).

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