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Original Article

Clinical characteristics of dilated cardiomyopathy with pulmonary hypertension

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Abstract: Objective: The goal of this study was to evaluate the clinical characteristics of patients with dilated cardiomyopathy (DCM) with pulmonary hypertension (PH), to explore risk factors of patients with PH secondary to DCM. Methods: Two hundred and fifty DCM patients were retrospectively analyzed. The characteristics of basic clinical data, ultrasound index, biochemical index, RDW, and PDW were analyzed. Correlation between the above indexes and PASP or LVEF was investigated. Risk factors of PH secondary to DCM were analyzed by logistic regression analysis. Results: Length of medical history of the DCM-PH group (DCM with PH) was higher than that of the DCM group (DCM without PH), the percentage of patients with symptoms and signs of right heart failure of the DCM-PH group was higher than that of the DCM group ($p<0.01$). PASP was positively correlated with LAD, LVDd, RVDd, NT-proBNP, UA, Cr, and CYC, length of medical history, RAD, TBIL, RDW-SD, RDW-CV, PDW, P-LCR, MPV, were negatively correlated with LVEF and PA. LVEF was positively correlated with PA, negatively correlated with PASP, NT-proBNP, lengths of medical history, LAD, LVDd, RAD, RVDd, TBIL, UA, Cr, CYC, RDW-CV, and P-LCR. Conclusion: With increased PASP and decreased LVEF, the abnormality of ultrasound indexes, biochemical indexes, and RDW and PDW were more significant. Therefore, this study provides the basis of prevention, clinical diagnosis, and treatment for the occurrence of PH in patients with DCM.

Keywords: Dilated cardiomyopathy, pulmonary hypertension, pulmonary artery systolic pressure

Introduction

Dilated cardiomyopathy (DCM) is a cardiomyopathy with no definite cause, its clinical features are cardiac enlargement, decreased ejection fraction, arrhythmia, and embolism. DCM has a high mortality rate and is thought to be associated with viral infection, autoimmune, and genetic factors [1]. PH is a pulmonary vascular disease that causes pulmonary arterioles to contract, vascular remodeling, and *in situ* thrombosis, resulting in increased pulmonary circulation resistance due to various reasons, progressive increase in pulmonary vascular resistance eventually leads to right heart failure and death [2].

Left heart disease (LHD) is the most common cause of pulmonary hypertension (PH) in clinical practice [3]. According to 2015 ESC/ERS guidelines, PH-LHD was classified as the second category of PH [2]. Heart failure caused by dilated cardiomyopathy (DCM) is the commonest left heart disease that leads to PH [2]. PH develops in LHD in response to a passive backward transmission of filling pressures, mainly driven by LV diastolic function, enhanced by exercise-induced mitral regurgitation, and a loss of LA compliance [4]. In some patients, these purely mechanical components of venous congestion may trigger a superimposed component, combining pulmonary vasoconstriction, decreased NO availability, increased endothelin expression, and desensitization to natriuretic peptide - induced vasodilation and vascular remodeling [4-6]. However, it is not clear whether PH-LHD caused by different reasons has different clinical and hemodynamic characteristics. PH is an independent risk factor for increased cardiac mortality in DCM patients

[7]. Other research found that the mortality of 79% patients with secondary PH due to heart failure is twice as high as in patients without PH [8]. In the current study, the clinical characteristics of DCM with PH were evaluated and the risk factors associated with secondary PH in DCM were analyzed in order to provide the basis of prevention, clinical diagnosis, and treatment for the occurrence of PH in patients with DCM.

Materials and methods

Patients

Two hundred and fifty DCM patients hospitalized in Jinan 6th people's Hospital from October 2012 to November 2017 were retrospectively analyzed. DCM was diagnosed based on 2015 ESC/ERS guidelines [2]. The patients were included when they met the following criteria: left ventricular end-diastolic diameter (LVEDd) >5.0 cm (female), LVEDd >5.5 cm (male); left ventricular ejection fraction (LVEF) <45% and (or) Left ventricular fraction shortening rate (FS) <25%; mean pulmonary artery pressure (MPAP) >25 mmHg (1 mmHg=0.133 kPa) measured at sea level and resting state, or more than 30 mmHg after activity [9]. The criteria for estimating PH by echocardiography is PASP ≥50 mmHg. The patients were excluded if PH was caused by COPD, interstitial lung disease, pulmonary disease, and hypoxemia caused by sleep apnea, idiopathic, familial, related factors (collagen, portal hypertension, infection, drugs/toxins), chronic thrombosis, and embolism or PH was caused by other diseases, such as sarcoidosis, histiocytosis, etc., or if patients had coronary heart disease, acute myocardial infarction, severe arrhythmia, hypertrophic cardiomyopathy, restrictive cardiomyopathy, valvular heart disease, constrictive pericarditis, congenital heart disease, diabetic cardiomyopathy, hypertensive cardiopathy, cardiogenic shock with insufficient blood volume or vasodilator, supine systolic pressure <90 mmHg or >180 mmHg, pulmonary vascular malformation, cerebrovascular accident, malignant tumor, severe liver failure (elevated transaminase exceeding the normal limit by 3 times), renal failure, serious infectious diseases, uncontrolled thyroid disease, hematological disease, medium and severe anemia, a history of bleeding in the last six months or disease of immune system or they live on the plateau all year round.

Among them, 143 cases of DCM patients with PH were clarified into DCM-PH group and 107 cases of DCM patients without PH were clarified into DCM group. Patients in DCM group with PH were divided into three groups (A, B, C) according to the severity of PH. Moreover, 250 patients were divided into four groups (I, II, III, IV) according to the severity of LVEF reduction. The study was approved by the Ethics Committee of Jinan 6th people's Hospital.

Observation index

Clinical data: General clinical data included age, gender, length of medical history, history of drinking, history of smoking, symptoms and signs of right heart failure.

Echocardiography: Ultrasonic instrument with Philips xMATRIX iU2 type and GE LOGIQ-E9 type color Doppler ultrasound, equipped with S51 heart two-dimensional probe, frequency of 1~5 MHz, frame frequency 60-90 frame/S. M axial echocardiography was used to measure LAD, LVDd, RAD, RVDd and LVEF. PASP was measured by tricuspid valve regurgitation estimation, PASP equals right ventricular systolic pressure (RVSP). According to the modified formula of Bernoulli (RVSP = 4 $Vmax^2$ + RAP), Vmax is the maximum reflux velocity of tricuspid valve (m/s), RAP is right atrial pressure. The RAP can be estimated based on the size of the right atrium and the extent of the tricuspid valve regurgitation. Right atrium diameter was normal, mild tricuspid regurgitation, RAP was about 5 mmHg, the right atrium was slightly enlarged, moderately tricuspid regurgitation, and the RAP was about 10 mmHg. The right atrium was enlarged markedly, with a severe tricuspid regurgitation, and the RAP was about 15 mmHg.

Electrocardiogram (ECG): ECG and/or 24 hours dynamic ECG of patients was analyzed. Arrhythmias such as auricular fibrillation or atrial flutter occurs, premature ventricular contraction were recorded.

Detection of NT-proBNP: The blood of the elbow vein was collected, collected in the EDTA anticoagulant vacuum tube, after resting 30 minutes, 3000 turn/min serum was separated with

Table 1. Comparison of general clinical characteristics between the DCM- PH group and the DCM group

Project	DCM with PH (n=143)	DCM without PH (n=107)	P
Age (years)	56.33 ± 10.52	54.17 ± 11.72	0.127
Male (cases) %	117 (81.82)	87 (81.31)	0.918
Auricular fibrillation or Atrial flutter (cases) %	59 (41.26)	32 (29.91)	0.065
Premature ventricular contraction (cases) %	6 (4.20)	4 (3.74)	0.856
History of drinking (cases) %	51 (35.66)	47 (43.93)	0.905
History of smoking (cases) %	75 (52.4)	45 (42.06)	0.130
Months of medical history (months)	57.27 ± 45.96	19.70 ± 25.39	P<0.01
Symptoms and signs of right heart failure (cases) %	70 (48.95)	31 (28.97)	0.001

Table 2. Comparison of ultrasonic index and test index between the DCM group and the PH group

Project	DCM with PH (n=143)	DCM without PH (n=107)	P
LAD (mm)	50.77 ± 6.31	42.71 ± 5.29	P<0.01
LVDd (mm)	68.82 ± 7.09	60.81 ± 4.86	P<0.01
RAD (mm)	50.69 ± 5.75	43.62 ± 7.41	P<0.01
RVDd (mm)	29.28 ± 4.31	25.21 ± 3.11	P<0.01
LVEF (%)	25.37 ± 5.79	36.13 ± 6.71	P<0.01
PASP (mmHg)	61.70 ± 7.05	38.26 ± 7.28	P<0.01
NT-proBNP (pg/ml)	6410.24 ± 3592.49	2788.17 ± 2318.66	P<0.01
TBIL (umol/L)	32.12 ± 13.73	18.90 ± 5.01	P<0.01
PA (mg/L)	161.77 ± 44.27	232.44 ± 53.87	P<0.01
UA (umol/L)	546.04 ± 103.43	397.47 ± 85.76	P<0.01
Cr (umol/L)	100.19 ± 14.23	82.73 ± 16.89	P<0.01
CYC (mg/L)	1.41 ± 0.36	0.97 ± 0.23	P<0.01
RDW-SD (fl)	45.14 ± 3.63	42.53 ± 2.65	P<0.01
RDW-CV (%)	14.80 ± 1.65	13.63 ± 1.31	P<0.01
MPV (fl)	13.66 ± 1.96	12.52 ± 2.29	P<0.01
PDW (fl)	17.40 ± 1.73	15.86 ± 2.28	P<0.01
P-LCR (%)	39.47 ± 2.97	36.92 ± 4.27	P<0.01

centrifuge. Plasma NT-proBNP was determined by chemiluminescence immunoassay.

Detection of biochemical indicators: The biochemical indicators of the first fasting venous blood test in all subjects were recorded: Uric acid (UA), Creatinine (Cr), Cystatin C (CYC), Total bilirubin (TBIL), Pre-albumin (PA), etc.

Blood routine test: Platelet parameters including platelet (PLT), mean platelet volume (MPV), platelet distribution width (PDW), platelet-large cell ratio (P-LCR). The red blood cell (RBC) parameters include the RBC distribution width coefficient of variation (RDW-CV) and RBC distribution width standard deviation (RDW-SD).

Statistical analysis

Statistical analysis software package SPSS22.0 was used for data analysis. The measurement data are expressed as mean ± standard deviation and enumeration data are described using constituent ratios. Chi square test was used to analyze the data among different groups, student t test was used to analyze two independent samples. Correlation study was analyzed using Pearson correlation analysis, the correlation coefficients were represented by R values. Regression analysis was performed by multiple logistic regression analysis. $p<0.05$ was considered as statistically significant difference.

Results

Patient characteristics

There were a total of 204 male patients and 46 female patients, aged 22-82 years, with an average age of 50 (40 ± 11). There were 143 cases of DCM patients with PH were clarified into the DCM-PH group and 107 cases of DCM patients without PH were clarified into the DCM group.

The average age of the DCM-PH group was 56.33 ± 10.52 years, and the average age of the DCM group was 54.17 ± 11.72 years (p= 0.127). There were 117 male patients (81.82%) in the DCM-PH group and 87 male patients (81.31%) in the DCM group (p=0.918). There

Table 3. Correlation between PASP and age, length of medical history, ultrasonic index, test index

Project	R	P
Age	0.087	0.168
Length of medical history	0.519	P<0.01
LAD	0.655	P<0.01
LVDd	0.656	P<0.01
RAD	0.586	P<0.01
RVDd	0.609	P<0.01
LVEF	-0.744	P<0.01
NT-proBNP	0.632	P<0.01
TBIL	0.539	P<0.01
PA	-0.699	P<0.01
UA	0.657	P<0.01
Cr	0.642	P<0.01
CYC	0.661	P<0.01
RDW-SD	0.448	P<0.01
RDW-CV	0.485	P<0.01
MPV	0.344	P<0.01
PDW	0.424	P<0.01
P-LCR	0.458	P<0.01

Pearson correlation 0.8-1 extremely strong correlation; 0.6-0.8 strong correlation; 0.4-0.6 medium correlation; 0.2-0.4 weak correlation; 0.0-0.2 very weakly correlated or not correlated.

Table 4. Correlation between LVEF and age, length of medical history, ultrasonic index, and the test index

Project	R	P
Age	0.007	0.903
Length of medical history	-0.508	P<0.01
LAD	-0.557	P<0.01
LVDd	-0.535	P<0.01
RAD	-0.508	P<0.01
RVDd	-0.480	P<0.01
PASP	-0.744	P<0.01
NT-proBNP	-0.741	P<0.01
TBIL	-0.426	P<0.01
PA	0.530	P<0.01
UA	-0.545	P<0.01
Cr	-0.512	P<0.01
CYC	-0.494	P<0.01
RDW-SD	-0.391	P<0.01
RDW-CV	-0.519	P<0.01
MPV	-0.342	P<0.01
PDW	-0.382	P<0.01
P-LCR	-0.445	P<0.01

Pearson correlation 0.8-1 extremely strong correlation; 0.6-0.8 strong correlation; 0.4-0.6 medium correlation; 0.2-0.4 weak correlation; 0.0-0.2 very weakly correlated or not correlated.

were no statistically significant differences between the two groups (p>0.05) of the percentage of patients with auricular fibrillation or atrial flutter, the percentage of patients with premature ventricular contraction, or the percentage of patients who had the history of drinking or smoking. The length of medical history and the percentage of patients with symptoms and signs of right heart failure of the DCM-PH group was higher than that of the DCM group (p<0.01) (**Table 1**).

Comparison of ultrasonic index between DCM-PH group and DCM group

LAD, LVDd, RAD, RVDd, PASP of the DCM-PH group were significantly higher than those of the DCM group (p<0.01). NT-proBNP, TBIL, PA, UA, Cr, CYC, RDW-SD, RDW-CV, MPV, PDW, P-LCR of the DCM-PH group were higher than those of the DCM group (p<0.01) (**Table 2**).

Correlation between PASP and clinical characteristics and ultrasonic index

In DCM-PH group, PASP was not correlated with age, but strongly positive correlated with LAD, LVDd, RVDd, NT-proBNP, UA, Cr, and CYC, medium positive correlated with length of medical history, RAD, TBIL, RDW-SD, RDW-CV, PDW, P-LCR, weakly correlated correlation with MPV, strongly negative correlated with LVEF and PA (**Table 3**).

Correlation between LVEF and clinical characteristics and ultrasonic index

Among 250 patients, LVEF was not correlated with age, medium positive correlated with PA, strongly negative correlated with PASP and NT-proBNP, medium negative correlated with length of medical history, LAD, LVDd, RAD, RVDd, TBIL, UA, Cr, CYC, RDW-CV and P-LCR, weakly correlated with RDW-SD, MPV, PDW (**Table 4**).

Comparison of clinical indexes between DCM with different degree of PH

Length of medical history, LAD, LVDd, RVDd, NT-proBNP, CYC of group B were significantly higher than those of group A (p<0.01). Length of medical history, LAD, LVDd, RAD, RVDd, NT-proBNP, TBIL, Cr, CYC, RDW- SD, RDW-CV,

Table 5. Comparison of age, length of medical history, ultrasonic index, and the test index between DCM with different degree of PH

Project	Group A PASP50-59 mmHg (n=52)	Group B PASP60-69 mmHg (n=63)	Group C PASP≥70 mmHg (n=28)
Age (years)	56.08 ± 12.00	56.81 ± 9.90	55.71 ± 9.17
Length of medical history	41.44 ± 36.13▲,※	65.22 ± 40.71▲	68.75 ± 63.83※
LAD (mm)	48.62 ± 5.08▲,※	51.60 ± 6.54▲	52.89 ± 6.87※
LVDd (mm)	65.12 ± 5.48▲,※	70.14 ± 7.84▲	72.71 ± 4.45※
RAD (mm)	49.29 ± 6.26※	50.56 ± 5.25★	53.57 ± 4.92★,※
RVDd (mm)	27.19 ± 3.71▲,※	29.43 ± 4.20▲,★	32.82 ± 3.13★,※
LVEF (%)	27.37 ± 4.87▲,※	25.24 ± 6.29▲,★	21.96 ± 4.58★,※
NT-proBNP (pg/ml)	4772.46 ± 2497.98▲,※	6751.08 ± 3631.17▲,★	8684.93 ± 3874.13★,※
TBIL (umol/L)	29.38 ± 12.46※	31.53 ± 12.38★	38.54 ± 16.97★,※
PA (mg/L)	175.23 ± 43.59※	165.08 ± 37.87★	129.30 ± 44.22★,※
UA (umol/L)	531.19 ± 117.81	548.81 ± 88.44	567.39 ± 105.70
Cr (umol/L)	97.76 ± 11.29※	98.09 ± 15.17★	109.42 ± 13.63★,※
CYC (mg/L)	1.26 ± 0.30▲,※	1.48 ± 0.33▲	1.55 ± 0.43※
RDW-SD (fl)	44.59 ± 3.16※	45.09 ± 3.91	46.61 ± 3.89※
RDW-CV (%)	14.39 ± 1.40※	14.71 ± 1.63★	15.76 ± 1.77★,※
MPV (fl)	13.45 ± 2.09※	13.52 ± 2.02★	14.36 ± 1.39★,※
PDW (fl)	17.08 ± 1.82※	17.32 ± 1.74	18.00 ± 1.48※
P-LCR (%)	38.60 ± 4.15※	39.76 ± 1.90	40.42 ± 1.76※

▲Group A was compared with group B, P<0.05; ★Group B was compared with group C, P<0.05; ※Group A was compared with group C, P<0.05.

MPV, PDW, and P-LCR of group C were significantly higher than those of group A (p<0.01). RAD, RVDd, NT-proBNP, TBIL, Cr, RDW-CV, and MPV of group C were significantly higher than those of group B (p<0.01). LVEF of group B was significantly lower than that of group A, LVEF and PA of group C were significantly lower than those of group A, LVEF and PA of group C were significantly lower than those of group B (p<0.01) (**Table 5**).

Comparison of clinical indexes between DCM with LVEF decline in different degrees

Months of medical history, LAD, LVDd, RAD, RVDd, PASP, NT-proBNP, TBIL, UA, Cr, CYC, RDW-SD, RDW-CV, and P-LCR of group II were significantly higher than those of group I (p<0.01). Length of medical history, LAD, LVDd, RAD, RVDd, PASP, NT-proBNP, TBIL, UA, Cr, CYC, RDW-SD, RDW-CV, MPV, PDW, and P-LCR of group III were significantly higher than those of group II (p<0.01). Length of medical history, LAD, LVDd, RVDd, PASP, NT-proBNP, RDW-SD, RDW-CV, PDW, and P-LCR of group IV were significantly higher than those of group III (p<0.01). PA of group II was significantly lower than that of group I, PA of group III was significantly lower than that of group II, PA of group IV was significantly lower than that of group III (p<0.01) (**Table 6**).

Multivariate logistic regression analysis

The patients' general clinical index, ultrasonic index, and test index were included in the multiple factor Logistic regression analysis, the results showed that length of medical history, symptoms and signs of right heart failure, LAD, RVDd, LVEF, NT-proBNP, TBIL, PA, UA, CYC, RDW-SD, RDW-CV, and PDW were associated with PH in patients with DCM (**Tables 7-10**).

Discussion

In LHDs, and more specifically in left heart failure, PH can easily be suspected by a stepwise approach, combining clinical presentation, specific echocardiographic features and other modalities such as ECG and other imaging techniques. Although no single variable can dif-

Table 6. Comparison of age, length of medical history, ultrasonic index, and the test index between DCM with LVEF decline in different degrees

Project	Group I LVEF40-44% (n=53)	Group II LVEF30-39% (n=71)	Group III LVEF 20-29% (n=106)	Group IV LVEF<20% (n=20)
Age (years)	55.11 ± 12.37	56.68 ± 11.67	54.92 ± 10.51	54.20 ± 8.26
Length of medical history	9.73 ± 16.40▲	35.66 ± 33.20★	51.22 ± 36.54※	91.00 ± 75.57
LAD (mm)	40.74 ± 5.41▲	46.89 ± 5.32★	49.71 ± 6.39※	53.65 ± 7.55
LVDd (mm)	59.17 ± 4.04▲	63.65 ± 5.62★	68.34 ± 7.45※	72.45 ± 4.99
RAD (mm)	40.85 ± 6.14▲	47.59 ± 6.37★	50.14 ± 6.76	52.80 ± 4.19
RVDd (mm)	24.26 ± 2.53▲	26.76 ± 3.50★	28.93 ± 4.40※	31.55 ± 4.15
PASP (mmHg)	35.28 ± 9.82▲	48.89 ± 9.64★	58.46 ± 9.14※	68.95 ± 4.42
NT-proBNP (pg/ml)	1387.56 ± 621.82▲	3869.92 ± 2463.72★	6043.18 ± 2771.75※	11305.80 ± 3740.15
TBIL (umol/L)	18.93 ± 6.97▲	24.07 ± 9.30★	30.21 ± 13.58	35.08 ± 17.50
PA (mg/L)	247.76 ± 63.21▲	193.60 ± 49.69★	172.81 ± 44.97※	140.47 ± 46.74
UA (umol/L)	367.58 ± 88.50▲	468.83 ± 93.82★	535.14 ± 113.12	555.95 ± 94.04
Cr (umol/L)	76.25 ± 15.48▲	91.74 ± 16.54★	99.63 ± 14.63	103.17 ± 10.03
CYC (mg/L)	0.94 ± 0.28▲	1.16 ± 0.31★	1.36 ± 0.38	1.48 ± 0.33
RDW-SD (fl)	42.02 ± 2.50▲	43.63 ± 3.18★	44.80 ± 3.51※	46.61 ± 3.80
RDW-CV (%)	13.02 ± 0.81▲	14.13 ± 1.23★	14.66 ± 1.58※	16.36 ± 1.82
MPV (fl)	12.14 ± 2.28	12.83 ± 2.10★	13.73 ± 1.99	14.13 ± 1.90
PDW (fl)	15.72 ± 2.27	16.31 ± 2.10★	17.22 ± 1.83※	18.38 ± 1.51
P-LCR (%)	36.00 ± 4.90▲	37.76 ± 4.12★	39.55 ± 2.16※	40.71 ± 2.06

▲Group I was compared with group II, P<0.05; ★Group II was compared with group III, P<0.05; ※Group III was compared with group IV, P<0.05.

Table 7. Logistics regression analysis of the dependent variable of PH

Variable	B	S.E.	Walds	df	P	Exp (B)	95% CI	
							Lower Bound	Upper Bound
Age	-0.001	0.014	0.008	1	0.927	0.999	0.972	1.027
Sex	-0.222	0.415	0.285	1	0.593	0.801	0.355	1.807
History of drinking	0.214	0.180	1.418	1	0.234	1.239	0.871	1.761
History of smoking	-0.437	0.332	1.726	1	0.189	0.646	0.337	1.240
Months of medical history	-0.039	0.006	37.838	1	<0.001	0.962	0.950	0.974
Symptoms and signs of right heart failure	-0.774	0.315	6.059	1	0.014	0.461	0.249	0.854
Intercept	1.778	0.905	3.865	1	0.049			

ferentiate PH-LHD from pre-capillary PH, the presence of multiple risk factors and findings should raise suspicion for PH-LHD [2].

One previous research found that patients in the DCM with PH were younger than those without PH [10]. In the current study, DCM patients with secondary PH were more likely to develop complete heart failure. The longer the history of DCM, the greater the likelihood of secondary PH was found to be. LAD, LVDd, RAD, RVDd, PASP of the DCM-PH group were higher than those of the DCM group, and LVEF of the DCM-PH group was lower than that of the DCM group. Chemla et al. [11] reported that increased pressure in the left atrium and left ventricle led to a passive rise in pulmonary venous pressure, trans-pulmonary pressure and capillary wedge pressure, which could lead to an increase in pulmonary artery pressure.

Previous studies have found that the risk of atrial arrhythmias and ventricular tachycardia in patients with DCM-PH was increased. The increased incidence of arrhythmias may be related to left atrial structural remodeling and electrical remodeling result in the occurrence of a reentry, micro-inflammation, oxidative str-

Table 8. Logistics regression analysis of the dependent variable of PH

Variable	B	S.E.	Walds	df	P	Exp (B)	95% CI	
							Lower Bound	Upper Bound
LAD	-0.179	0.052	11.982	1	0.001	0.836	0.756	0.925
LVDd	-0.068	0.038	3.311	1	0.069	0.934	0.867	1.005
RAD	0.039	0.040	0.941	1	0.332	1.039	0.961	1.124
RVDd	-0.128	0.058	4.910	1	0.027	0.880	0.785	0.985
LVEF	0.170	0.032	27.494	1	<0.001	1.185	1.112	1.263
Intercept	8.985	3.013	8.893	1	0.003			

Table 9. Logistics regression analysis of the dependent variable of PH

Variable	B	S.E.	Walds	df	P	Exp (B)	95% CI	
							Lower Bound	Upper Bound
NT-proBNP	0.000	0.000	9.961	1	0.002	1.000	1.000	1.000
TBIL	-0.144	0.039	13.933	1	<0.001	0.866	0.803	0.934
PA	0.015	0.006	6.521	1	0.011	1.015	1.004	1.027
UA	-0.011	0.003	11.458	1	0.001	0.989	0.982	0.995
Cr	0.025	0.020	1.627	1	0.202	1.025	0.987	1.065
CYC	-3.169	0.934	11.499	1	0.001	0.042	0.007	0.263
Intercept	8.348	2.496	11.158	1	0.001			

Table 10. Logistics regression analysis of the dependent variable of PH

Variable	B	S.E.	Walds	df	P	Exp (B)	95% CI	
							Lower Bound	Upper Bound
RDW-SD	-0.191	0.062	9.477	1	0.002	0.826	0.732	0.933
RDW-CV	-0.467	0.112	17.317	1	<0.001	0.627	0.503	0.781
MPV	0.134	0.116	1.320	1	0.251	1.143	0.910	1.435
PDW	-0.296	0.130	5.220	1	0.022	0.744	0.577	0.959
P-LCR	-0.028	0.063	0.202	1	0.653	0.972	0.860	1.099
Intercept	18.932	2.941	41.443	1	<0.001			

ess and metabolic abnormalities in patients with DCM, abnormal liver and kidney function lead to accumulation of various pro-inflammatory factors and metabolites in the body for a long time, which can damage the myocardium [12-14].

Serum bilirubin has been reported to be associated with the progression of cardiac insufficiency [15]. Right ventricular afterload was increased after PH in patients with DCM, which causes right ventricular dilatation and failure, in turn increases right atrial pressure and central venous pressure, leading to liver congestion and insufficient perfusion. Congestion damage not only affects the normal function of liver cells, moreover, swollen hepatocytes also compress the intrahepatic bile duct and lead to increased serum bilirubin. Serum bilirubin level was closely related to the deterioration of cardiac function and the increase of right atrial pressure, and it was an independent risk factor for evaluating the prognosis of patients with PH [16].

The level of serum PA in CHF patients was lower than that in patients with CHF because of autoimmune response. This study found that UA, Cr, and CYC were higher than those of the DCM group. In the DCM-PH group, PASP has strongly positive correlation with UA, Cr, and CYC. The meta-analysis of Smith et al. [17] shows that 63% of patients with CHF combined with at least mild renal impairment, 20% had moderate or even more severe renal impairment. For every 10 percent drop in glomerular filtration rate (GFR), the mortality rate increased by seven percent. Therefore, renal function is an important index to evaluate the severity and prognosis of heart failure [17]. Increased incidence of cardiogenic death in patients with DCM-PH is independently correlated with serum uric acid levels [7]. Zharikov et al. [18] has reported that UA inhibits vasodilation caused by acetylcholine, the higher the UA level, the less nitric oxide (NO) and cyclic guanosine monophosphate (cGMP) produced by pulmonary artery endothelial cells. Endogenous NO has the effects of relaxing pulmonary vascular smooth muscle, decreasing smooth muscle proliferation, inhibiting platelet aggregation, reducing leukocyte adhesion, mediating nerve signal

transduction and apoptosis. UA may be involved in the formation of PH by reducing the formation of NO, and the higher the UA concentration, the faster the PH was formed [18]. UA can stimulate the increase of arginase activity in endothelial cells, local arginine decreased resulting in a reduction in NO production [18, 19].

Platelet related indicators can predict patient mortality, the more severe heart failure was, the greater the degree of platelet activation was [20]. High MPV levels in patients with idiopathic cardiomyopathy tend to suggest left ventricular ejection dysfunction [21]. The reason may be that ventricular dilatation and decreased ventricular contractility often lead to blood siltation, which leads to the increase of MPV and activation of platelets. Another study suggests that MPV is an independent predictor of coronary flow reserve attenuation in patients with idiopathic DCM. When MPV >8.3 fl, the attenuation of coronary artery flow reserve was severe, the sensitivity was 95% and the specificity was 82% [22]. PDW has the advantages of low cost, convenient inspection and simple operation. It can help physicians assess the risk level of patients with heart failure and make a simple prediction, and intervene and treat high-risk patients as early as possible, so as to reduce the mortality of patients [23].

RDW-SD, RDW-CV, MPV, PDW, P-LCR of the DCM-PH group were higher than those of the DCM group. In patients with DCM, the RAAS was activated and erythropoietin activity decreased, which resulted in the increase of ineffective erythropoiesis and the increase of RDW level [24]. RDW is closely related to the inflammatory state [25, 26]. The decrease of cardiac function in patients with DCM leads to low perfusion and hypoxia, producing a series of inflammatory factors such as interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor receptor (TNFR), pre-albumin and hs-CRP, etc, causing the level of RDW to rise [27]. Oxidative stress in patients with DCM can affect the survival rate of erythrocytes and lead to the increase of RDW level [28]. The volume load of patients with heart failure was overloaded, and the ratio of early mitral inflow and early diastolic mitral annulus velocity (E/E') increased, which induces and exacerbates heart failure and leads to the increase of RDW level [29]. DCM patients had low nutritional status. This is due to the decrease of vitamin B12 and folic acid intake, the increase of erythropoietin, the decrease of serum iron and total iron binding capacity, and the decrease of the ability of storing and using iron in human body, which results in high RDW level [30, 31].

There are also some limitations in this study. First, right cardiac catheterization is considered to be the golden standard for the diagnosis of PAH, but it is difficult to perform because of poor compliance and high cost. In this study, echocardiography was used to quantitatively estimate pulmonary artery pressure, which has the advantages of convenience, economy, repeatability and noninvasiveness. Second, the cases of DCM in this study include not only idiopathic DCM, but also some alcoholic cardiomyopathy. The clinical characteristics of different types of DCM can be investigated in the future. Third, as a retrospective study, this study did not assess the impact of the above indicators on the prognosis of DCM patients. This study is a single-center study, and further multicenter, prospective, large-sample studies are needed to confirm the results.

In conclusion, our study shows that the length of medical history, symptoms, and signs of right heart failure, LAD, RVDd, LVEF, NT-pro BNP, TBIL, PA, UA, CYC, RDW-SD, RDW-CV, and PDW could be used as the predictors of secondary PH in patients with DCM.

Disclosure of conflict of interest

None.

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