Electrocardiogram signs of right ventricular hypertrophy may help identify pulmonary hypertension in patients with dilated cardiomyopathy

Chengzhi Chen a,1, Jingyan Liu a,1, Zhiyong Liu a, Xin He a, Xuming Yuan a, Xiufen Ouyang a, Lei Wang a, Xiaoping Li b,*

a Department of Cardiology, Liuyang People Hospital, Liuyang 410300, China
b Department of Cardiology, Sichuan Academy of Medical Sciences and Sichuan Provincial People’s Hospital, Chengdu, Sichuan 610072, China

ARTICLE INFO

Article history:
Received 25 June 2018
Received in revised form 15 December 2018
Accepted 17 December 2018
Available online xxxx

Keywords:
Dilated cardiomyopathy
Pulmonary hypertension
Right ventricular hypertrophy
EGC

ABSTRACT

Objective: To the authors’ knowledge, limited data are available regarding the association between Electrocardiogram (ECG) signs of right ventricular hypertrophy (RVH) and pulmonary hypertension (PH) in patients with dilated cardiomyopathy (DCM). We aimed to assess the accuracy of the recommended ECG criteria of RVH for predicting PH in patients with DCM.

Methods: According to the definition of PH (mPAP ≥ 25 mm Hg), 35 patients with DCM were divided into 2 groups: DCM with PH (n = 22) and DCM without PH (n = 13). Right heart catheterization was performed in all patients. Seventeen parameters of RVH recommended by the AHA/ACCF/HRS for diagnosis of RVH on ECG were determined.

Results: The following parameters were correlated with mPAP: RV1 > 6 mm, SV5 > 10 mm, RSV6 < 0.4, RV1 + SV5 or VS > 10.5 mm and Pn amplitude. The following parameters were significantly different between DCM patients with and without PH: S in V1 (SV5) > 10 mm, S in V6 (SV6) > 3 mm, R:S ratio in V5 (R:SV5) < 0.75, RV1 + SV5 or VS > 10.5 mm, S > R inf, S > R inf and R:S v1 > R: v3, although results were no longer significant after correcting for multiple comparisons. High specificity (92.3–100%), low sensitivity (31.8–50%), high positive predictive value, and low negative predictive value of established parameters of RVH were noted for predicting PH in patients with DCM.

Conclusion: Several ECG signs of RVH may be useful for the diagnosis of PH in patients with DCM.

© 2018 Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

In the six World Symposium on Pulmonary Hypertension (PH), five groups of disorders that cause PH were identified, PH due to left heart disease (LHD) is the most common form of PH [1,2]. The presence and context of PH due to LHD is a well-established prognostic factor of morbidity or mortality in patients with DCM, and the incidence of cardiac death in patients with DCM with PH was >11-fold that in DCM patients without PH [3,4].

Transthoracic echocardiography is recommended as a screening test in the evaluation of suspected PH, and this will provide essential information regarding concomitant left-sided valvular or ventricular dysfunction, although echocardiography could underestimate the pulmonary artery systolic pressure (PASP) by previous study [5]. Right heart catheterization (RHC) is the gold standard for diagnosis of pulmonary hypertension (PH) and also for differential diagnosis between pre-capillary PH and post-capillary PH, which is essential or therapeutic decisions [1,6,7]. RHC and echocardiography in patients with PH can be technically demanding and often involves significant cost, RHC has been associated with a few complications. Thus, this invasive diagnostic procedure should be performed in expert centers [6]. Simple, non-invasive tools are needed to assist clinicians in the evaluation of patients with possible PH and help clinicians decide whether to proceed with additional further tests. An ECG is a simple diagnostic tool. ECG signs of PH are represented by surrogate parameters of RVH due to right
ventricular pressure overload and the importance of ECG in the diagnosis of PH has already been established reported [8].

The underlying pathogenesis of PH due to LHD is not fully understood and is likely to be multifactorial [2,7,9]. The first organ directly affected by LHD is the lung. In response to physical and biological stressors, remodeling of the pulmonary circulation and parenchyma are responsible for contributing to the development of PH. Initially, right ventricular adaptation with hypertrophy and increased contrac-
tility compensate for the increase in pulmonary vascular resistance. Ultimately, right ventricular uncoupling to the demands of the pulmonary circulation leads to RV failure [10]. The previous study has suggested that an increase in RV mass in DCM not only associated with a
dilated LV cavity in the absence of coronary artery stenosis (Simpson’s technique) and a dilated LV cavity in the absence of coronary
artery disease, arterial hypertension, and secondary cardiac muscle disease attributable to any known systemic condition [12].

PH due to lung or chronic thromboembolic disease was excluded. Clinical assessment, laboratory examination, echocardiography and coronary angiography were routinely performed. According to the definition of PH (mPAP ≥ 25 mm Hg) [1], 35 patients with DCM were divided into 2 groups: DCM with PH (n = 22) and DCM without PH (n = 13).

2.2. ECG

Standard 12 lead ECGs in the supine position (paper speed 25 mm/s, sensitivity 1 mV = 10 mm) were obtained. The ECGs were analysed by 2 independent observers blinded to the study result. Discrepancies were resolved by consensus. The current guidelines had list 24 ECG criteria for diagnosis of RVH [13]. All ECG criteria were checked in 35 patients, apart from the R:SV1, R:SV3, R: SV1 > R:SV4, ventricular activation time, and R:SV5 to R:SV1, which were checked in 34 patients because no R wave was present in lead V1 in one patient. Because 10 patients had atrial fibrillation, Pn amplitude was checked in the other 25 patients. A retrospective analysis of the ECGs was performed.

2.3. Echocardiography

Patients were imaged in the left lateral decubitus position using a commercially available Philips IE-33 system equipped with a 3.5 MHz transducer. Two-dimensional grey-scale, pulsed, continuous, and color Doppler data were acquired on the same day before right heart catheterization. Left ventricular end diastolic Diameter (LVEDD), right ventricle end diastolic diameter (RVEDD) and left ventricular ejection fraction (LVEF) were determined according to the recommendations [14].

2.4. Right heart catheterization

Right heart catheterization had been performed in all patients inserted from a jugular approach by use of a 6F Swan-Ganz catheter (Edwards life sciences, USA). Cardiac output was estimated using direct Fick principle. PH was defined as mPAP ≥ 25 mm Hg during measurements at rest, without inhalation of nitric oxide and oxygen. Pulmonary arterial hypertension is defined by a mean PAOP > 25 mm Hg at rest, by a PAOP-15 mm Hg and by PVR > 3 mm Hg/l/min (Wood units). PH due to left heart disease was defined as mPAP ≥ 25 mm Hg and PAOP > 15 mm Hg. Transpulmonary pressure gradient (TPG) was calculated by subtracting PAOP from mPAP. Pulmonary vascular resistance (PVR) was calculated by dividing TPG by cardiac output. The patient subgroup with no PH was defined as mPAP-25 mm Hg [4,6,7]. World Health Organization (WHO) Groups 1, 3, 4 PAH has been excluded [2].

2.5. Statistical analysis

Statistical analysis was performed with SPSS software (version 13.0, Chicago, Illinois). Continuous variables are expressed as the mean ± SD or as medians and interquartile ranges, normal distribution of variables were analyzed by Kolmogorov- Smirnov test. Independent sample t-test were used for comparison of the prevalence of individual RVH parameters between groups with PH and without PH. Statistical differences in categorical variables were evaluated by the chi-square test or Fisher’s exact test. The sensitivity, specificity, and positive and negative predictive values (PPV and NPV) of the individual parameters showing statistically significant difference in frequency between groups were calculated. The relationship between ECG parameters of RVH and PH was estimated by Pearson or Spearman correlation tests. Adjusted P values were evaluated by Bonferroni correction. P value < 0.05 was considered statistical significance.

Table 1 Comparison of the baseline characteristics between groups with PH and without PH.

<table>
<thead>
<tr>
<th>With PH (n = 22)</th>
<th>Without PH (n = 13)</th>
<th>K-S* P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>44.6 ± 11.6</td>
<td>53.6 ± 12.0</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>4 (18.2)</td>
<td>7 (53.8)</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>5.49 ± 4.96</td>
<td>4.54 ± 5.82</td>
</tr>
<tr>
<td>History</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation, n (%)</td>
<td>8 (36.4)</td>
<td>2 (15.4)</td>
</tr>
<tr>
<td>NYHA class III, n (%)</td>
<td>9 (40.9)</td>
<td>9 (69.2)</td>
</tr>
<tr>
<td>NYHA class IV, n (%)</td>
<td>13 (59.1)</td>
<td>4 (31.8)</td>
</tr>
<tr>
<td>Admission vital signs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>105.9 ± 16.9</td>
<td>111.0 ± 11.7</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>68.6 ± 12.0</td>
<td>68.5 ± 7.47</td>
</tr>
<tr>
<td>Heart rate, beat/min</td>
<td>82.5 ± 14.7</td>
<td>78.7 ± 16.2</td>
</tr>
<tr>
<td>Laboratory values at admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>95.1 ± 48.0</td>
<td>104.1 ± 31.7</td>
</tr>
<tr>
<td>BUN (μmol/L)</td>
<td>7.56 ± 3.59</td>
<td>9.11 ± 3.04</td>
</tr>
<tr>
<td>NT-ProBNP (pmol/mL)</td>
<td>3606.65 ± 1312.5</td>
<td>1928.9 ± 1432.4</td>
</tr>
</tbody>
</table>

Statistical differences in categorical variables were evaluated by the chi-square test or Fisher’s exact test. Sensitivity, specificity, and positive and negative predictive values (PPV and NPV) of the individual parameters showing statistically significant difference in frequency between groups were calculated. The relationship between ECG parameters of RVH and PH was estimated by Pearson or Spearman correlation tests. Adjusted P values were evaluated by Bonferroni correction. P value < 0.05 was considered statistical significance.
3. Results

3.1. Characteristics of the study population

The cohort consisted of 35 patients with DCM of which 11 (31.4%) women and 24 (68.6%) men. 2 patients fulfilled criteria of right bundle branch block. 3 patients had incomplete right bundle branch block. 3 patients fulfilled criteria of left bundle branch block. 6 patients had intraventricular conduction delays. 10 patients had atrial fibrillation. Table 1 summarizes the baseline characteristics of the cohort. The prevalence of individual parameters was compared between groups with PH and without PH. Patients with PH had a younger age, higher NT-ProBNP levels, larger RVEDD, larger LAD (left atrial diameter), higher mPAP, higher PAWP, higher TPG, higher PVR, and lower CO than patients without PH. There were no significant differences between the two groups in sex ratio, disease duration, prevalence of atrial fibrillation, blood pressure, heart rate, creatinine level, blood urea nitrogen level, LVEDD, and LVEF.

3.2. Prevalence of RVH in two groups according to ECG criteria

The ECG signs of right ventricular hypertrophy in DCM with PH was clearly evident (Fig. 1). The comparison of the prevalence of RVH between the groups with or without PH was given in Table 2. The following parameters were significantly more common in the DCM with PH group than in the DCM without PH group: SV5 > 10 mm, SV6 > 3 mm.

---

**Table 1**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>PH Group</th>
<th>Non-PH Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Younger</td>
<td>Older</td>
</tr>
<tr>
<td>NT-ProBNP</td>
<td>Higher</td>
<td>Lower</td>
</tr>
<tr>
<td>RVEDD</td>
<td>Larger</td>
<td>Smaller</td>
</tr>
<tr>
<td>LAD</td>
<td>Larger</td>
<td>Smaller</td>
</tr>
<tr>
<td>mPAP</td>
<td>Higher</td>
<td>Lower</td>
</tr>
<tr>
<td>PAWP</td>
<td>Higher</td>
<td>Lower</td>
</tr>
<tr>
<td>TPG</td>
<td>Higher</td>
<td>Lower</td>
</tr>
<tr>
<td>PVR</td>
<td>Higher</td>
<td>Lower</td>
</tr>
<tr>
<td>CO</td>
<td>Lower</td>
<td>Higher</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>PH Group</th>
<th>Non-PH Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV5</td>
<td>&gt; 10 mm</td>
<td>&lt; 10 mm</td>
</tr>
<tr>
<td>SV6</td>
<td>&gt; 3 mm</td>
<td>&lt; 3 mm</td>
</tr>
</tbody>
</table>

---

**Fig. 1.** Electrocardiogram signs of right ventricular hypertrophy in 3 case(1–3) of DCM with PH and 3 case(4–6) of DCM without PH.
There were no significant differences in the prevalence of the following parameters between the two groups: RV1 > 6 mm, R:SV1 > 1, R:SV5 < 0.75, R:SV6 > 3 mm, S > R in I, S > R in II, R:SV1 > R:SV3. 

Fig. 1 (continued).
3.3. Relationship between ECG criteria of RVH and mPAP

Though results were no longer significant after correcting for multiple comparisons.

3.4. Predictive values of ECG signs of RVH in diagnosing PH in patients with DCM

In the present study, we first evaluated the value of ECG of RVH to detect PH in DCM patients. The chief findings of the present study were that: 1) Group with PH had a younger age, higher NT-ProBNP levels, larger RVEDD, larger LA, higher mPAP, higher TPG, higher PVR, and lower CO than Group without PH; 2) The ECG parameters $S_{V5} > 10$ mm, $S_{V6} > 3$ mm, $R_{V1} + S_{V5} or V6 > 10.5$ mm, $S > R$ inf, and $R > S$ inf and $R_{V1} > R_{V5}$ had a low sensitivity (31.8–50%), but a high specificity (92.3–100%) in identifying DCM patients with PH.

4. Discussion

In the present study, we first evaluated the value of ECG of RVH to detect PH in DCM patients. The chief findings of the present study were that: 1) Group with PH had a younger age, higher NT-ProBNP levels, larger RVEDD, larger LA, higher mPAP, higher TPG, higher PVR, and lower CO than Group without PH; 2) The ECG parameters $S_{V5} > 10$ mm, $S_{V6} > 3$ mm, $R_{V1} + S_{V5} or V6 > 10.5$ mm, $S > R$ inf, and $R > S$ inf and $R_{V1} > R_{V5}$ had a low sensitivity (31.8–50%), but a high specificity (92.3–100%) in identifying DCM patients with PH.

3.3. Relationship between ECG criteria of RVH and mPAP

The relationship between ECG criteria of RVH and mPAP and RV diameter were shown in Table 3. $R_{SV1}$, $S_{SV5}$, $R_{SV5}$, $R_{V1} + S_{V5}$ or $V6$, and $P_a$ amplitude were correlated with mPAP.

3.4. Predictive values of ECG signs of RVH in diagnosing PH in patients with DCM

Table 4. Predictive values of ECG signs of RVH in diagnosing PH in patients with DCM.
outcome is a picture of biventricular and bialtrial enlargement in patients with ischaemic or non-ischaemic cardiomyopathy [20]. For unknown reasons, ventricular dilation causes the QRS vector to shift towards the transverse plane and away from the frontal plane, resulting in differential effects on QRS voltages in the chest and the limb leads described by Goldberger [21]. So-called Goldberger’s triad consists of: 1) High precordial QRS voltages, defined as \((S_v + S_v^2) ≥ 3.5 \text{ mV}\); 2). Relatively low limb lead QRS voltages, defined as total QRS amplitude (i.e. \(R + S\)) ≤ 0.8 mV in each of the limb leads; and 3). Poor R wave progression in the precordial leads V1 to V3 or V4 [22,23].

4.1. Limitation

The present study has several limitations. This was a retrospective study in a single center with a relatively small sample size. Our findings should be considered preliminary, and should be verified by larger population sample defined according to these specific criteria. Moreover, it should be noted that only a few of the recommended ECG criteria proved to be useful in the diagnosis of RVH in previous study [24], and most of the ECG criteria for RVH have high positive and low negative predictive value which means that a significant proportion of patients with RVH will be underdiagnosed using the ECG criteria [18]. So that, it may lead to low sensitivity of ECG signs of RVH in diagnosing PH in patients with DCM. Finally, in the present study, the ECG analysis included only assessment of RV hypertrophy criteria, biventricular hypertrophy was not assessed using cardiac magnetic resonance imaging and may influence some of our findings.

In summary, DCM patients with PH had worse clinical and hemodynamic parameters than those without PH. RH ≥ 6 mm, SV5 ≥ 10 mm, R:Sv6 < 0.4, Rh1 + Sv5 or Sv6 > 10.5 mm were correlated with mPAP. The recommended ECG criteria based on the S wave amplitude in ECG lead V5 \((S_v ≥ 10 \text{ mm}, R:Sv5 < 0.75, Rh1 + Sv5 or Sv6 > 10.5 \text{ mm}), S concentrating in V6, the ratio of R wave amplitude to S in II, the ratio of R wave amplitude to S in I, the ratio of R wave amplitude to S in II and R:Sv6 > R:Sv2 were useful for predicting were useful for in the diagnosis PH in patients with DCM.

Authors' contributions

CC and JL carried out the patient enrollment, data collection. ZL, XH, XY, OX and LW participated in the data collection and performed the statistical analyses. CC, JL and XL conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Acknowledgments

This study was supported in part by grants from Medical Scientific Research Foundation of Hunan Province (no. C2014-046) and the National Natural Science Foundation of China (no. 81470521).

References