The prediction of right atrial pressure using electrocardiogram: a novel approach

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Abstract

Aims Pulmonary hypertension (PH) is a serious disorder that can complicate pulmonary and cardiovascular diseases. Right atrial (RA) pressure is a robust predictor of the pulmonary hypertension severity, which is measured via right heart catheterization. Limited studies have been carried out to assess the association between electrocardiogram data and the RA pressure as a prognostic factor of PH. In this study, the relation between P wave and PR segment changes with RA pressure was evaluated.

Methods and results In this study, 94 patients in PH groups of 1, 3, and 4, based on the World Health Organization classification, were entered. RA pressure was measured using the right heart catheterization. PR segment and P wave morphology in leads II and V1 were evaluated in patient’s electrocardiogram. The median age of the patients was 35.5 years old in which 64.9% of them were female. The distribution of patients in groups 1, 3, and 4 PH were 77.7%, 5.3%, and 17%, respectively. Among the studied P wave and PR segment changes, PR segment depression in lead II and pulmonary P wave in lead V1 had significant relation with the RA pressure (P-value < 0.001). The sensitivity, specificity, and negative predictive values of PR segment depression for detection of patients with high RA pressure (RA pressure > 14 mmHg) were 80%, 84%, and 94%. The specificity and negative predictive values of pulmonary P wave in lead V1 were determined 89% and 88%.

Conclusions It was found that the PR segment depression in lead II and pulmonary P wave in lead V1 associate with the RA pressure in patients with precapillary PH. PR segment depression had useful sensitivity, specificity, and negative predictive values, and the pulmonary P wave in lead V1 had acceptable specificity and negative predictive values for detection of patients with high RA pressure. Therefore, the electrocardiogram can be used as a screening tool for determination of pulmonary hypertension severity.

Keywords Pulmonary hypertension; Electrocardiogram; P wave; PR segment; Right heart catheterization; Right atrial pressure

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Introduction

Pulmonary hypertension (PH) is a fatal disease which can complicate respiratory and cardiovascular diseases.1 Early treatment of PH can improve patient survival. PH symptoms progress gradually; hence, patients with PH have mild symptoms until advanced stages of the disease. Therefore, regular evaluation of patients is necessary.2-4 Several methods are available for evaluation of the PH patients,1 and it has been tried to find new techniques for this aim as well.5 It is well-known that the haemodynamic study via the right heart catheterization (RHC) is the best method of the PH assessment.5,6 Among the RHC data, the only chamber pressure, which is directly used for the PH severity evaluation, is the right atrial (RA) pressure.1 Measurement of the RA pressure using RHC is expensive and invasive. Electrocardiogram (ECG) is an inexpensive, widely accessible, and non-invasive diagnostic method in cardiology. Development of a relationship between ECG and RA pressure can provide a PH severity prognostic factor using the ECG data. Several studies have described the association between RA dimension and ECG data, such as P wave height in lead II and V1, as a PH severity...
prognostic factor when the RA dimension has been measured using echocardiography and magnetic resonance imaging. This is while findings related to the association between RA pressure and P wave are very limited. Furthermore, PR segment, which is induced by atrial repolarization, conduction through atrioventricular node and ventricular conduction system, has not been well evaluated. This paper aims to determine the association between P wave and PR segment with the RA pressure as a prognostic factor in patients with PH.

Methods

This trial was a descriptive-analytical study that was performed on patients in groups 1, 3, and 4 PH based on the World Health Organization (WHO) classification,11 (precapillary PH patients), in a referral centre of PH, over a period of 5 years.

Patients with systemic hypertension, diabetes mellitus, coronary artery disease, electrolyte abnormality, ejection fraction <45%, congenital heart disease, and valvular heart disease (except tricuspid and pulmonary regurgitation) were excluded due to their confounding ECG changes. Patients with uninterpretable ECG and non-sinus rhythm ECG, due to lack of P wave and PR segment, were also excluded from the analysis. Finally, 94 patients were included in our study. 12-lead ECG was carried out in supine and standard patients’ position with paper speed of 25 mm per second and voltage lead of 10 mm per millivolt, within maximum 3 days of RHC. RHC was carried out via different accesses (femoral, jugular, subclavian, and brachial vein) with guide of fluoroscopy. Pressure of RA was measured at the end of expiration.

The ECGs of patients were analysed manually by an expert cardiologist who had no information about patient’s characteristic and their RHC data. PR segment depression more than 1 mm in lead II (Figure 1), PR segment duration in lead II, P wave duration in lead II, P wave amplitude in lead II, mitral P wave in lead V1, and pulmonary P wave in lead V1 were measured. The isoelectric point was defined at the line between the end of T wave and the beginning of next P wave. Each variable was evaluated in three beats, and the mean of these measurements was considered in the analysis. In this study, mitral and pulmonary P wave in lead V1 refers to negative portion of P wave area more than 0.04 mm-s and positive portion of P wave area more than 0.06 mm-s (Figure 2).

Statistical analysis was performed using SPSS software. Numerical variables are reported as minimum, maximum, median and interquartile range and categorical variables are presented as percentage. Multilinear regression analysis with stepwise and backward elimination technique were used for evaluation of relationship between ECG data and RA pressure. The significant level of P-value was <0.05. Cohen’s $f^2$ was calculated and used as an effect size.

Results

Ninety-four patients were entered in the analysis and their characteristics are summarized in Table 1. Minimum, maximum, and median age of these patients were 17, 84, and 35.5 years old, respectively; 64.9% of the patients were female (61 of 94). Patients were categorized based on WHO classification of PH into different groups: 77.7% (73) in group 1 PH, 5.3% (5) in group 3 PH, and 17% (16) in group 4 PH. The RA pressure range was 3 to 24 mmHg with median of 10 mmHg. The number of patients with criterion of mitral P wave in lead V1 was greater than that of with pulmonary P wave criterion. Forty-one (43.6%) of patients had mitral P wave in lead V1, and nineteen (20.2%) of patients had pulmonary P wave in lead V1.

Figure 1 Normal and depressed PR segment.
By using multiple linear regression analysis and stepwise method, PR segment depression and pulmonary P wave in lead V1 were found as significant predictors of RA pressure ($P$-value < 0.001) (Table 2). In this analysis, Cohen’s $f^2$ is 0.63, which means that the effect size is large. Therefore, PR segment depression and pulmonary P wave in lead V1 can be relatively strong predictors of the RA pressure. Backward elimination technique was also used for the regression analysis, and the $P$-value of 0.084 was found for the P wave amplitude in lead II.

Patients were divided into two groups of severe and non-severe RA pressure, based on their RA pressure (>14 mmHg and ≤14 mmHg). Twenty of patients (21.28%) had severe RA pressure while 78.72% had non-severe RA pressure. Sensitivity, specificity, positive predictive value, and negative predictive value of PR segment depression and pulmonary P wave in lead V1 were evaluated.

The sensitivity and specificity of PR segment depression were 80%, 84% and those of pulmonary P wave in lead V1 were 55%, 89%. The positive and negative predictive values of PR segment depression were 57%, 94% and those of pulmonary P wave in lead V1 were 58%, 88% (Table 3).

**Discussion**

Initiation of PH results in electrocardiogram changes which can also develop during the disease progression. Some studies have evaluated the ECG changes in PH patients such as
Tonelli study where they showed that the heart rate, PR interval, R/S ratio in lead V₁, QRS duration, and QT interval increase from the beginning to the end stage of PH and all patients with PH had abnormal ECG at the time of death. Therefore, the ECG can be used as an available and low cost method for disease evaluation. For example, a decrease in the P wave amplitude and duration in lead II and R wave amplitude in lead V₁ are used as criteria of response to treatment. In addition, ECG variables of right ventricular abnormality can be used for deciding time of lung transplantation listing.

Right atrial pressure measured using right heart catheterization is a robust prognostic factor of PH. Based on PH guidelines, the RA pressure more than 14 mmHg is an indicator of PH mortality more than 10% in a year. RA pressure rise may lead to ECG changes especially in P wave and PR segment which are the result of atrial depolarization and repolarization. In the current study, we tried to discover the relation between the P wave morphology and PR segment changes with RA pressure in the precapillary PH patients. In the previous studies, the association between ECG parameters and RA size has been evaluated. Despite the importance of RA pressure in the determination of PH prognosis, a limited number of studies have been carried out on this topic. Furthermore, most of these studies have considered only the P wave morphology. In this study, the PR segment was considered as well which has not been assessed in patients with PH so far.

In the current study, it was shown that the PR segment duration had no significant association with the RA pressure. Tonelli et al. analysis showed that the PR interval increased during PH progression. However, the PR interval is summation of PR segment and P wave duration, and the increase in the PR interval may be resulted from an increase in the P wave duration. The results of this study showed that there is no relation between P wave duration in lead II and RA pressure.

Likewise, P wave amplitude in lead II and mitral P wave in lead V₁ had no association with the RA pressure. However, in many studies, P wave amplitude in limb leads and pulmonary P wave in lead II were used to predict the RA enlargement. Rio et al. found almost similar result to the findings of this research about the P wave amplitude in lead II, but their study was carried out on patients with PH due to atrial septal defect. Unlike pulmonary P wave in lead II, pulmonary P wave in lead V₁ was correlated with RA pressure and can predict its severity (RA pressure more than 14 mmHg) with 55% sensitivity, 89% specificity and 58% positive predictive value and 88% negative predictive value. In a number of previous studies, pulmonary P wave in lead V₁ was found as a valuable marker of RA enlargement. However, Kaplan et al. found that pulmonary P wave in lead V₁ had low power of prediction for RA enlargement.

The other finding of this study was the association between the PR segment depression more than 1 mm in lead II with the RA pressure. The PR segment has received more attention in pericarditis which present with diffuse PR segment depression. In a few studies, the PR segment was evaluated in acute myocardial infarction (MI) which showed PR segment depression may be seen in circumflex artery occlusion. In addition, this may be used as a predictor of heart block in inferior MI. The PR segment was not evaluated in the patients with PH in the previous studies. PR segment depression more than 1 mm in lead II can predict severe RA pressure (RA pressure more than 14 mmHg) with 80% sensitivity, 84% specificity, 57% positive predictive value, and 94% negative predictive value. Therefore, the PR segment depression more than 1 mm in lead II can be used as a predictor of RA pressure severity with high sensitivity, specificity, and negative predictive value.

According to the findings of the current study, morphology of P wave in lead II and V₁ has been changed in patients with precapillary PH. The PH does not only result in pulmonary P wave but also can lead to mitral P wave morphology even mitral P wave in lead V₁, which is more common than pulmonary P wave in this lead. Furthermore, PR segment depression in lead II is relatively common in patients with precapillary PH patients. Among P wave and PR segment changes, pulmonary P wave in lead V₁ and PR segment depression more than 1 mm have a significant relation with RA pressure as a robust predictor of PH severity. Therefore, these variables can be used as available and inexpensive prognostic factors of PH.

In the current study, most of patients were in group 1 PH, and the number of patients in group 3 were limited (five cases). As the results may be different in each group of PH, it is recommended that another study will be performed with large number of cases in each PH group.

Table 3  Accuracy of PR segment depression and pulmonary P wave in lead V₁ for prediction of RA pressure

|                  | Non-severe RA pressure (n) | Severe RA pressure (n) | Sensitivity (%) | Specificity (%) | Positive predictive value (%) | Negative predictive value (%) |
|------------------|----------------------------|------------------------|----------------|----------------|-----------------------------|-----------------------------|
| Without PR segment depression | 62                         | 4                      | 80%            | 84%            | 57%                         | 94%                         |
| With PR segment depression | 12                         | 16                     | 80%            | 84%            | 57%                         | 94%                         |
| Without Pulmonary P wave in lead V₁ | 66                         | 9                      | 55%            | 89%            | 58%                         | 88%                         |
| With Pulmonary P wave in lead V₁ | 8                          | 11                     | 55%            | 89%            | 58%                         | 88%                         |

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Conclusion

Based on the results of this study, it can be concluded that the PR segment depression more than 1 mm in lead II and pulmonary P wave in lead V1 associate with RA pressure in patients with precapillary PH, with useful specificity and negative predictive value. Sensitivity was excellent for PR segment depression. Despite the fact that the P-value of P wave amplitude in lead II (0.084) is not statistically significant, further evaluations are required to investigate its association with the RA pressure. Therefore, the PR segment depression can be used as a screening tool for determination of pulmonary hypertension severity and reference of patients to specialized centers.

Conflict of interest

The authors declare that there is no conflict of interest.

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