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ORIGINAL ARTICLE

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 V_1 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 V_1 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 V_1 were determined 89% and 88%.

Conclusions It was found that the PR segment depression in lead II and pulmonary P wave in lead V_1 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 V_1 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 assesment.[1,6] 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 V_1, as a PH severity

prognostic factor when the RA dimension has been measured using echocardiography and magnetic resonance imaging.[7–9] 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,[10] 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 V_1, and pulmonary P wave in lead V_1 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 V_1 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*).[10]

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 V_1 was greater than that of with pulmonary P wave criterion. Forty-one (43.6%) of patients had mitral P wave in lead V_1, and nineteen (20.2%) of patients had pulmonary P wave in lead V_1.

Figure 1 Normal and depressed PR segment.

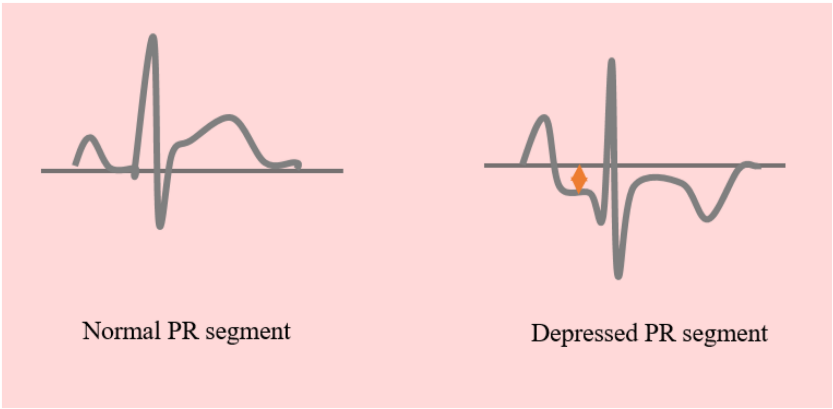

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Figure 2 The morphology of normal, pulmonary, and mitral P waves in lead V_1.

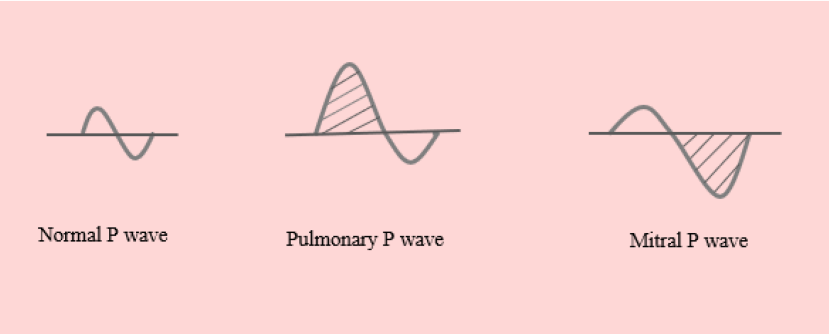

Table 1 Demographic, haemodynamic, and ECG characteristics

Characteristics and variables	Value[a]	Interquartile range
Age	35.5 (17–84)	32–45.5
Sex		
Female	64.9% (61)	-
Male	35.1% (33)	-
PH groups		
Group 1 PH	77.7% (73)	-
Group 3 PH	5.3% (5)	-
Group 4 PH	17% (16)	-
PR segment duration (mS) in lead II	60 (0–140)	40–80
P wave duration in lead II (mS)	100 (20–200)	80–105
P wave amplitude in lead II (mV)	0.15 (0.05–0.40)	0.10–0.25
Mitral P wave in lead V_1	43.6% (41)	-
Pulmonary P wave in lead V_1	20.2% (19)	-
PR depression more than 1 mm in lead II	29.8% (28)	-
RA pressure (mmHg)	10 (3–24)	7–12

[a]The age, PR segment duration in lead II, P wave duration in lead II, P wave amplitude in lead II, and RA pressure are expressed as median (maximum–minimum). Sex, PH groups, mitral P wave in lead V_1, and pulmonary P wave in lead V_1 are reported as percentage. mS, millisecond; mmHg, millimetre Hg; mV, millivolt; PH, pulmonary hypertension.

By using multiple linear regression analysis and stepwise method, PR segment depression and pulmonary P wave in lead V_1 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 V_1 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.

Table 2 The relation between right atrial pressure severity and electrocardiogram variables

Variables	*P* value
PR segment duration in lead II	0.866
PR segment depression	0.000
Pulmonary P wave in lead II	0.084
Mitral P wave in lead II	0.777
Pulmonary P wave in lead V_1	0.000
Mitral P wave in lead V_1	0.332

The analysis was carried out using multiple linear regression and stepwise method.

Patients were divided into two groups of severe and non-severe RA pressure, based on their RA pressure ($>$14 mmHg and $\leq$14 mmHg).[1] 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 V_1 for prediction of severe RA pressure were evaluated.

The sensitivity and specificity of PR segment depression were 80%, 84% and those of pulmonary P wave in lead V_1 were 55%, 89%. The positive and negative predictive values of PR segment depression were 57%, 94% and those of pulmonary P wave in lead V_1 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

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Table 3 Accuracy of PR segment depression and pulmonary P wave in lead V_1 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				
With PR segment depression	12	16	80%	84%	57%	94%
Without Pulmonary P wave in lead V_1	66	9				
With Pulmonary P wave in lead V_1	8	11	55%	89%	58%	88%

Tonelli study where they showed that the heart rate, PR interval, R/S ratio in lead V_1, 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.[12] 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 V_1 are used as criteria of response to treatment.[13,14] In addition, ECG variables of right ventricular abnormality can be used for deciding time of lung transplantation listing.[15]

Right atrial pressure measured using right heart catheterzation 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.[1] 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.[7–9,16] 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.[12] 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.[17] 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 V_1 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 enlargment.[7,9,16,18] 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.[19] Unlike pulmonary P wave in lead II, pulmonary P wave in lead V_1 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 V_1 was found as a valuable marker of RA enlargment.[7,9] However, Kaplan *et al*. found that pulmonary P wave in lead V_1 had low power of prediction for RA enlargment.[8]

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.[20] 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.[21] In addition, this may be used as a predictor of heart block in inferior MI.[22] 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 V_1 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 V_1, 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 V_1 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.

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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 V_1 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 more than 1 mm in lead II and pulmonary P wave in lead V_1 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.

References

1. Galiè N, Humbert M, Vachiery J-L, Gibbs S, Lang I, Torbicki A, Simonneau G, Peacock, Vonk Noordegraaf A, Beghetti M, Ghofrani A. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Respir J* 2015; **46**: 903.
2. Galie N, Hoeper MM, Humbert M, Torbicki A, Vachiery JL, Barbera JA, Beghetti M, Corris P, Gaine S, Gibbs JS, Gomez-Sanchez MA. Guidelines for the diagnosis and treatment of pulmonary hypertension: the task force for the diagnosis and treatment of pulmonary hypertension of the european Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT). *Eur Heart J* 2009;**30**: 2493-2537.
3. Galiè N, Ghofrani HA, Torbicki A, Barst RJ, Rubin LJ, Badesch D, Fleming T, Parpia T, Burgess G, Branzi A, Grimminger F, Kurzyna M, Simonneau G. Sildenafil citrate therapy for pulmonary arterial hypertension. *N Engl J Med* 2005; **353**: 2148–2157.
4. Kim NH. Diagnosis and evaluation of the patient with pulmonary hypertension. *Cardiol Clin.* 2004; **22**: 367–373 v-vi.
5. Mirtajaddini M, Amin A, Naderi N, Taghavi S. The correlation between uric acid level and right heart catheterization findings in pulmonary hypertension. *Multidiscip Cardio Annal*. 2019; **10**: e97040.
6. Humbert M, Sitbon O, Yaïci A, Montani D, O'callaghan DS, Jaïs X, Parent F, Savale L, Natali D, Günther S, Chaouat A. Survival in incident and prevalent cohorts of patients with pulmonary arterial hypertension. *Eur Respir J* 2010;**36**: 549.
7. Allison JD, Macedo FY, Hamzeh IR, Birnbaum Y. Correlation of right atrial enlargement on ECG to right atrial volume by echocardiography in patients with pulmonary hypertension. *J Electrocardiol* 2017; **50**: 555–560.
8. Kaplan JD, Evans GT Jr, Foster E, Lim D, Schiller NB. Evaluation of electrocardiographic criteria for right atrial enlargement by quantitative two-dimensional echocardiography. *J Am Coll Cardiol* 1994; **23**: 747–752.
9. Tsao CW, Josephson ME, Hauser TH, O'Halloran TD, Agarwal A, Manning WJ, Yeon SB. Accuracy of electrocardiographic criteria for atrial enlargement: validation with cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 2008;**10**: 7.
10. Zipes DP, Libby P, Bonow RO, Mann DL, Tomaselli GF. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. Elsevier; 2019.
11. Galiè N, McLaughlin VV, Rubin LJ, Simonneau G. An overview of the 6th World Symposium on Pulmonary Hypertension. *Eur Resp J*. 2019; **53**: 1802148.
12. Tonelli AR, Baumgartner M, Alkukhun L, Minai OA, Dweik RA. Electrocardiography at diagnosis and close to the time of death in pulmonary arterial hypertension. *Ann Noninvasive Electrocardiol* 2014; **19**: 258–265.
13. Waligóra M, Tyrka A, Podolec P, Kopec G. ECG markers of hemodynamic improvement in patients with pulmonary hypertension. *Biomed Res Int* 2018; **2018**: 4606053.
14. Pilka M, Darocha S, Banaszkiewicz M, M Wieteska-Miłek, Mańczak M, Mańczak R, Kędzierski P, Florczyk M, Dobosiewicz A, Torbicki A, Kurzyna M. Assessment of electrocardiographic markers of acute and long-term hemodynamic improvement in patients with pulmonary hypertension. *Ann Noninvasive Electrocardiol* 2020;**25**: e12758.
15. Bossone E, Paciocco G, Iarussi D, Agretto A, Iacono A, Gillespie BW, Rubenfire M. The prognostic role of the ECG in primary pulmonary hypertension. *Chest* 2002; **121**:513–518.
16. Reeves WC. ECG criteria for right atrial enlargement. *Arch Intern Med* 1983; **143**: 2155–2156.
17. Bandorski D, Bogossian H, Ecke A, Wiedenroth C, Gruenig E, Benjamin N, Arlt M, Seeger W, Mayer E, Ghofrani A, Hoeltgen R, Gall H. Evaluation of the prognostic value of electrocardiography parameters and heart rhythm in patients with pulmonary hypertension. *Cardiol J* 2016; **23**: 465–472.
18. Cheng XL, He JG, Liu ZH, Gu Q, Ni XH, Zhao ZH, Luo Q, Xiong CM. The value of the electrocardiogram for evaluating prognosis in patients with idiopathic pulmonary arterial hypertension. *Lung* 2017; **195**: 139–146.
19. Rio PP, Hariawan H, Anggrahini DW, Hartopo AB, Dinarti LK. The accuracy of combined electrocardiogram criteria to diagnose right atrial enlargement in adults with uncorrected secundum atrial septal defect. *Clin Med Insights Cardiol.* 2019; **13**:1179546819869948–1179546819869948.
20. McNamara N, Ibrahim A, Satti Z, Ibrahim M, Kiernan TJ. Acute pericarditis: a review of current diagnostic and management guidelines. *Future Cardiol* 2019; **15**: 119–126.
21. Zhan ZQ, Nikus K, Birnbaum Y. PR depression with multilead ST elevation and ST depression in aVR by left circumflex artery occlusion: How to differentiate from acute pericarditis. *Ann Noninvasive Electrocardiol* 2020; **25**: e12752.
22. Jim MH, Siu CW, Chan AO, Chan RH, Lee SW, Lau CP. Prognostic implications of PR-segment depression in inferior leads in acute inferior myocardial infarction. *Clin Cardiol* 2006; **29**: 363–368.