


The Accuracy of Combined Electrocardiogram Criteria to Diagnose Right Atrial Enlargement in Adults With Uncorrected Secundum Atrial Septal Defect

Clinical Medicine Insights: Cardiology
Volume 13: 1–7
© The Author(s) 2019
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/1179546819869948



Purwati Pole Rio, Hariadi Hariawan, Dyah Wulan Anggrahini, Anggoro Budi Hartopo  and Lucia Kris Dinarti

Department of Cardiology and Vascular Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada and Dr Sardjito Hospital, Yogyakarta, Indonesia.

ABSTRACT

BACKGROUND: Right atrium (RA) enlargement in uncorrected atrial septal defect (ASD) is due to chronic volume overload. Several electrocardiogram (ECG) criteria had been proposed for screening RA enlargement. This study aimed to compare the accuracy of ECG criteria in detecting RA enlargement in adults with uncorrected ASD.

METHODS: This was a cross-sectional study involving 120 adults with uncorrected secundum ASD. The subjects underwent ECG examination, transthoracic echocardiography, and right heart catheterization. An RA enlargement was determined with RA volume index by transthoracic echocardiography. Various ECG and combined ECG criteria were evaluated. Statistical analysis was performed to analyze the sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV).

RESULTS: An RA enlargement was detected in 64.2% subjects. The P wave height > 2.5 mm in lead II criterion had the best specificity (100%) and PPV (100%), but low sensitivity (19%) and accuracy (48%). The combined 2 ECG criteria (QRS axis > 90°, R/S ratio > 1 in V1) had 82% sensitivity, 56% specificity, 73% accuracy, 77% PPV, and 63% NPV. The combined 3 ECG criteria (QRS axis > 90°, R/S ratio > 1 in V1, and P wave height > 1.5 mm in V2) had 35% sensitivity, 86% specificity, 53% accuracy, 82% PPV, and 43% NPV.

CONCLUSIONS: The combined 2 ECG criteria (QRS axis > 90° and R/S ratio > 1 in V1) had increased sensitivity, better accuracy, and more balance of PPV and NPV as compared with P wave > 2.5 mm in II criterion and combined 3 ECG criteria to diagnose RA enlargement in adults with uncorrected ASD.

KEYWORDS: Secundum atrial septal defect, right atrial enlargement, right atrial volume index, electrocardiogram, combined ECG criteria

RECEIVED: March 15, 2019. **ACCEPTED:** July 23, 2019.

TYPE: Original Research

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CORRESPONDING AUTHORS: Anggoro Budi Hartopo, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada and Dr Sardjito Hospital, Jl. Kesehatan No. 1, Yogyakarta 55281, Indonesia. Email: a_bhartopo@ugm.ac.id

Lucia Kris Dinarti, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada and Dr Sardjito Hospital, Jl. Kesehatan No. 1, Yogyakarta 55281, Indonesia. Email: kris_dinarti@ugm.ac.id

Introduction

Atrial septal defect (ASD) is one of the most common congenital heart diseases (CHDs), with a prevalence of 3 to 6 in 10 000 live births.¹ Patients with uncorrected ASD are often asymptomatic, until they reach adulthood when complications, such as pulmonary artery hypertension, right heart failure, and Eisenmenger syndrome, occur. The physical examinations of patients with ASD are usually unremarkable, and therefore electrocardiogram (ECG) can be used as an initial screening and diagnostic tool.¹ An ECG can detect the evidence of an enlarged right heart chamber when ASD diagnosis is suspected before referring to a cardiologist for echocardiographic examination.¹

Enlargement of the right atrium (RA) in patients with uncorrected ASD is a consequence of chronic volume overload. Several ECG criteria have emerged to indicate RA enlargement. The most widely accepted ECG criterion is a high P wave, peaking mainly in leads II, III, and aVF with the deviation of the P wave axis on the frontal view. However, several

studies have shown that this ECG criterion is limited only to obstructive pulmonary disease and is found in neither pulmonary hypertension, interstitial lung disease, nor RA volume overload (such as in patients with ASD).^{2–4} Kaplan et al⁵ found that a high P wave criterion was only detected in 6% of patients with RA enlargement. According to a previous study, the best predictors of RA enlargement were as follows: QRS axis > 90°, P wave height in V2 > 1.5 mm, and R/S ratio in V1 > 1 without right bundle branch block (RBBB), with all combined 3 criteria having 100% specificity and 49% sensitivity.⁵

This study aimed to compare the accuracy of various ECG criteria and combined ECG criteria in detecting RA enlargement in adult patients with uncorrected ASD. As a refinement from previous study using similar ECG criteria,⁵ this study used more homogeneous subjects, which were adult patients with uncorrected ASD, where RA enlargement could be caused by chronic volume and pressure overload. This study evaluated which ECG criteria could be best applied. Therefore, for better



screening adults with uncorrected ASD, the ECG criteria for RA enlargement with more sensitive and more accurate properties are needed. In addition, this study used the right atrial volume index (RAVI) measured with transthoracic echocardiography to diagnose RA enlargement, in accordance with recommendations from current guidelines.⁶

Methods

This research was an observational study with a cross-sectional design. This research was performed from November 2017 to March 2018 in Dr Sardjito Hospital, Jogjakarta, Indonesia, a national referral hospital for CHD in the region. The subjects were adult patients with uncorrected secundum ASD who were registered in the COngenital HeArt Disease in adult and Pulmonary Hypertension (COHARD-PH) registry. The COHARD-PH registry is a hospital-based single-center registry of adult patients with CHDs in Dr Sardjito Hospital, Jogjakarta, Indonesia which has been conducted since 2012 and continues to date.⁷ For this study, the inclusion criteria were as follows: (1) uncorrected secundum ASD; (2) complete clinical data, 12-lead ECG recording, and transthoracic echocardiogram taken within 1 month of this study; and (3) having sinus rhythm during ECG recording. The exclusion criteria in this study were as follows: (1) having other congenital abnormalities, (2) having left ventricular ejection fraction < 50%, (3) having significant valve abnormalities (ie, mitral stenosis, aortic stenosis, pulmonary stenosis, and aortic regurgitation), (4) having other respiratory system or lung disease, (5) having a history of acute myocardial infarction, and (6) having atrioventricular and bundle branch blocks.

The subjects underwent thorough anamnesis and physical examination as part of the registry protocol. The 12-lead ECG examination was performed with the standard procedure and technique. The echocardiographic parameters of RA volume were taken from the transthoracic echocardiography database in the echo-lab of Dr Sardjito Hospital. The hemodynamic assessment by right heart catheterization was performed in accordance with standard procedures via non-sedated, femoral access and guided with fluoroscopy in the cath-lab of Dr Sardjito Hospital. The mean pulmonary artery pressure (mPAP) was directly measured and pulmonary vascular resistance (PVR) was calculated based on the indirect Fick method formula. Informed consent was obtained from each of the subjects participating in the study. The study protocol was approved by the Medical and Health Research Ethic Committee of Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Jogjakarta, Indonesia.

The results of the 12-lead ECG examinations were assessed by 2 examiners who were competent in reading ECGs (cardiology residents) and were blinded to the subject's transthoracic echocardiographic results. The 2 examiners had acceptable interobserver agreement based on Kappa assessment (90% agreement). The ECG results were analyzed to detect the

various ECG criteria, as follows: QRS axis > 90°, P wave height > 1.5 mm in lead V2, R/S ratio > 1 in lead V1 without RBBB, QRS height < 6 mm in lead V1, QRS height in lead V2/V1 > 3, P wave initial force (PIF) > 0.06 mm in lead V2, PIF > 0.06 mm in lead V1, presence of Q wave in lead V1, and P wave height > 2.5 mm in lead II. Based on a previous study,⁵ we analyzed the combined 2 ECG criteria (QRS axis > 90° and R/S ratio > 1 in lead V1) and 3 ECG criteria (QRS > 90°, R/S ratio > 1 in lead V1, and P wave height > 1.5 mm in lead V2). The measurement of numerical parameters from ECG was performed with the ImageJ software (National Institutes of Health [NIH], USA).

The enlargement of RA was measured using RAVI based on transthoracic echocardiography. On the 4-chamber view, the endocardial area of RA was thoroughly traced but did not include the atrial appendage, vena cava, and pulmonary veins. Right atrial volume was calculated using Simpson methods and then indexed against the body surface area to obtain RAVI. The current guidelines recommend that the normal RAVI values are 25 ± 7 mL/m² in men and 21 ± 6 mL/m² in women.⁵ The RAVI value was increased if its value was greater than 1.96 above the standard deviation, which was ≥ 39 mL/m² in men and ≥ 33 mL/m² in women.⁵ Right ventricle (RV) diameter and cut-off for enlarged RV were in accordance with the current guidelines.⁶ Experienced sonographers performed the transthoracic echocardiography. A senior cardiology consultant interpreted the RAVI results. The ECG and transthoracic echocardiographic measurements were performed within 1 month apart.

For statistics analysis, the subjects were divided into 2 groups, ie, subjects with enlarged RA (increased RAVI) and those without (no increased RAVI). The comparison of various and combined ECG criteria between groups was performed with chi-square or Fisher exact test, whichever was applicable. Comparison of continuous data was conducted by Student *t* test. The various and combined ECG criteria which had significant statistical difference to indicate enlarged RA were further analyzed for their diagnostic performance. As a note, Bonferroni correction was not performed in the statistics analysis. The diagnostic performance of various and combined ECG criteria toward enlarged RA was assessed by the analysis of accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The *P* value < .05 was considered statistically significant.

Results

For this study, 120 subjects fulfilled the study criteria and were enrolled for the analysis. Most of the subjects (89%) were female. The mean age of the subjects was 37.00 ± 10.82 years. From the ECG examination, 79.2% of the subjects met the criteria of the QRS axis > 90°, 33.3% met the criteria of P wave height > 1.5 mm in V2, 75% met the criteria of R/S ratio > 1 in lead V1 without RBBB, 68.3% met the criteria of the

Table 1. The demography, ECG criteria, transthoracic echocardiogram, and hemodynamic characteristics of adults with uncorrected secundum ASD.

| CHARACTERISTICS | VALUE (N = 120) |
|--|---------------------|
| Sex—female, n (%) | 107 (89.2) |
| Age (years), mean \pm SD | 37.00 \pm 10.82 |
| BMI (kg/m ²), median (Q1-Q3) | 19.03 (16.44-22.19) |
| ECG criteria, n (%) | |
| QRS axis $>$ 90° | 95 (79.2) |
| P wave height $>$ 1.5 mm in lead V2 | 40 (33.3) |
| R/S ratio $>$ 1 in lead V1 without RBBB | 90 (75.0) |
| P wave height $>$ 2.5 mm in lead II | 15 (12.5) |
| Combined 2 criteria (QRS axis $>$ 90° and R/S ratio $>$ 1 in V1) | 82 (68.3) |
| Combined 3 criteria (QRS $>$ 90°, R/S ratio $>$ 1 in V1, and P $>$ 1.5 mm in V2) | 33 (27.5) |
| Transthoracic echocardiographic results | |
| Defect diameter (cm), median (Q1-Q3) | 2.35 (2.0-2.80) |
| RAVI (mL/m ²), mean \pm SD | 44.28 \pm 21.13 |
| Increase in RAVI, n (%) | 77 (64.2) |
| Right ventricular diameter (cm), median (Q1-Q3) | 4.32 (1.90-6.60) |
| Enlarged right ventricle, n (%) | 86 (71.7) |
| TAPSE (mm), mean \pm SD | 25.88 \pm 4.90 |
| Severity of TR, n (%) | |
| Mild TR | 45 (37.8) |
| Moderate TR | 44 (37.0) |
| Severe TR | 30 (25.2) |
| Hemodynamic parameters by RHC | |
| MPAP (mm Hg), median (Q1-Q3) | 40.5 (24.00-58.00) |
| MPAP \geq 25 (mm Hg), n (%) | 86 (71.7) |
| PVR (Woods unit), median (Q1-Q3) | 4.08 (1.70-14.60) |

Abbreviations: ASD, atrial septal defect; BMI, body mass index; ECG, electrocardiogram; MPAP, mean pulmonary artery pressure; PVR, pulmonary vascular resistance; RAVI, right atrial volume index; RBBB, right bundle branch block; RHC, right heart catheterization; TAPSE, tricuspid annular peak systolic excursion; TR, tricuspid regurgitation.

combined 2 ECG criteria, and 27.5% of the subjects met the criteria of the combined 3 ECG criteria. The P wave height $>$ 2.5 mm in lead II was only found in 12.5% of the subjects (Table 1).

From transthoracic echocardiographic examination, the median (interquartile range) of septal defect diameter was 2.35 (2.0-2.80) cm. The mean RAVI value was 44.28 \pm 21.13 mL/m² and RAVI enlargement was obtained in 77 (64%) subjects. Right ventricle enlargement was found in 71.7% of the subjects. The RV function, assessed with tricuspid annular peak

systolic excursion (TAPSE), was still normal for all subjects. The degree of tricuspid regurgitation indicated that most subjects had mild to moderate tricuspid regurgitation (37.8% and 37.0%, respectively). From hemodynamic parameters by right heart catheterization, most subjects (71.7%) had developed pulmonary hypertension (mPAP \geq 25 mm Hg) with the median (interquartile range) of mPAP at 40.5 (24.00-58.00) mm Hg (Table 1).

From the ECG analysis, as shown in Table 2, there were significant differences between subjects who experienced

Table 2. The analysis of various and combined ECG criteria in detecting RA enlargement in adults with uncorrected secundum ASD.

| ECG CRITERIA | INCREASED RAVI (N = 77), N (%) | NO INCREASED RAVI (N = 43), N (%) | P VALUE | OR (95% CI) |
|---|-----------------------------------|--------------------------------------|---------|--------------------|
| QRS axis > 90° | 72 (93.5) | 23 (53.5) | 0.000 | 12.52 (4.22-37.12) |
| P wave height > 1.5 mm in V2 | 32 (41.5) | 8 (18.6) | 0.011 | 3.11 (1.28-7.59) |
| R/S ratio > 1 in V1 | 66 (85.7) | 24 (55.8) | 0.000 | 4.75 (1.98-11.42) |
| QRS < 6 mm in V1 | 42 (54.5) | 31 (72.1) | 0.059 | 0.47 (0.21-1.04) |
| Q wave in V1 | 48 (62.3) | 16 (37.2) | 0.008 | 2.79 (1.30-6.04) |
| PIF > 0.06 mm in V2 | 31 (40.3) | 7 (16.3) | 0.007 | 3.47 (1.37-8.78) |
| QRS height in V2/V1 > 3 | 13 (16.9) | 9 (20.9) | 0.583 | 0.77 (0.30-1.98) |
| PIF > 0.06 mm in V1 | 6 (7.8) | 3 (7.0) | 0.871 | 1.13 (0.27-4.75) |
| P wave height > 2.5 mm in II | 15 (19.5) | 0 (0) | 0.002 | 1.70 (1.49-1.99) |
| Combined 2 criteria (QRS axis > 90° and R/S ratio > 1 in V1) | 63 (81.8) | 19 (44.2) | 0.000 | 5.68 (2.47-13.10) |
| Combined 3 criteria (QRS > 90°, R/S ratio > 1 in V1 and P > 1.5 mm in V2) | 27 (35.1) | 6 (13.9) | 0.013 | 3.33 (1.25-8.89) |

Abbreviations: ASD, atrial septal defect; CI, confidence interval; ECG, electrocardiogram; OR, odds ratio; PIF, P wave initial force; RA, right atrium; RAVI, right atrial volume index.

increased RAVI compared with those who did not experience increased RAVI on various and combined ECG criteria. The combined 2 ECG criteria and 3 ECG criteria were significantly higher in subjects with increased RAVI. All subjects with ECG P wave height > 2.5 mm in lead II criterion had increased RAVI, with a mean \pm SD value of 60.47 ± 16.51 mL/m². The mean RAVI in subjects with ECG P wave height \leq 2.5 mm in lead II criterion was also increased, but it was significantly lower as compared with subjects with ECG P wave height > 2.5 mm in lead II (mean \pm SD: 41.98 ± 20.86 mL/m², $P = .01$). Subjects with positive combined 2 ECG criteria had significantly higher mean RAVI as compared with those without combined 2 ECG criteria (mean \pm SD: 48.91 ± 21.40 mL/m² vs 34.50 ± 17.31 mL/m², $P < .001$).

Table 3 shows the diagnostic values of various and combined ECG criteria, which include sensitivity, specificity, accuracy, PPV, and NPV. The ECG criteria of QRS axis > 90° had the best sensitivity, which was 94%, followed by the R/S ratio > 1 in lead V1 with 86% sensitivity and the combined 2 ECG criteria with 82% sensitivity. The P wave height > 1.5 mm in V2 only had 42% sensitivity. The widely accepted P wave height > 2.5 mm in lead II criterion had the lowest sensitivity (19%). The criterion of QRS axis > 90° had the best odds ratio (OR) in predicting RA enlargement, but the specificity of this criterion was only 47%. The criterion for RA enlargement by P wave height > 2.5 mm in lead II criteria had the best specificity and PPV of 100%;

however, the sensitivity and accuracy were low (19% and 48%, respectively). The combined 2 ECG criteria had an OR of 5.68, a sensitivity of 82%, a specificity of 56%, and an accuracy of 73% to diagnose RA enlargement. They had 77% PPV and 63% NPV, which were balanced values. The combined 3 ECG criteria (QRS axis > 90°, R/S ratio > 1 in V1, and P wave height > 1.5 mm in V2) had a sensitivity of 35%, a specificity of 86%, and an accuracy of 53% to diagnose RA enlargement. They had higher PPV (82%) but low NPV (43%). When compared with a widely accepted P wave height > 2.5 mm in lead II criterion, the combined 2 ECG criteria had a higher sensitivity, a better accuracy, and a balanced predictive value for diagnosing RA enlargement in adults with uncorrected secundum ASD.

Discussion

In this study, the widely accepted ECG criterion of P wave height > 2.5 mm in lead II only had a low sensitivity of 19% and a PPV of 48% for diagnosing RA enlargement in adults with uncorrected secundum ASD. Despite its 100% specificity and 100% NPV, the low sensitivity and inadequate PPV made the criterion not eligible for the screening purpose to detect RA enlargement in individuals with uncorrected secundum ASD. Better performance was achieved using combined 2 ECG criteria, ie, QRS axis > 90° and R/S ratio > 1 in V1. The combined 2 ECG criteria had increased sensitivity, better accuracy, and higher PPV and NPV for diagnosing RA enlargement in adults with uncorrected secundum

Table 3. The various and combined ECG criterion diagnostic values in detecting RA enlargement in adults with uncorrected secundum ASD.

| ECG CRITERIA | SENSITIVITY (%) | SPECIFICITY (%) | ACCURACY (%) | PPV (%) | NPV (%) | OR |
|--|-----------------|-----------------|--------------|---------|---------|-------|
| QRS axis > 90° | 94 | 47 | 77 | 76 | 80 | 12.52 |
| P wave height > 1.5 mm in V2 | 42 | 81 | 56 | 80 | 44 | 3.11 |
| R/S ratio > 1 in V1 | 86 | 44 | 71 | 73 | 63 | 4.75 |
| PIF > 0.06 mm in V2 | 40 | 84 | 56 | 82 | 44 | 3.47 |
| Q wave in V1 | 62 | 63 | 63 | 75 | 48 | 2.79 |
| P wave height > 2.5 mm in II | 19 | 100 | 48 | 100 | 41 | 1.70 |
| QRS axis > 90° and R/S ratio > 1 in V1 (combined 2 criteria) | 82 | 56 | 73 | 77 | 63 | 5.68 |
| QRS > 90°, R/S ratio > 1 in V1, and P > 1.5 mm in V2 (combined 3 criteria) | 35 | 86 | 53 | 82 | 43 | 3.33 |

Abbreviations: ASD, atrial septal defect; ECG, electrocardiogram; OR, odds ratio; NPV, negative predictive value; PPV, positive predictive value; PIF, P wave initial force; RA, right atrium.

ASD. Therefore, the screening for RA enlargement in uncorrected secundum ASD patients was better if performed by the combined 2 ECG criteria.

Kaplan et al⁵ indicated that the P wave height > 2.5 mm in lead II criterion was very specific (100% specificity) to detect RA enlargement, but the sensitivity was very low. A study by Tsao et al⁸ which evaluated RA enlargement by cardiac magnetic resonance imaging (MRI) using ECG criteria found that the P wave height criterion in inferior leads > 2.5 mm had very low sensitivity and accuracy, despite 100% specificity. In a similar study, the P wave height criterion in V1 > 1.5 mm only had low accuracy and sensitivity to detect RA enlargement.⁸ Baranchuk and Bayés de Luna⁹ showed that the P wave criterion (high voltage, amplitude ≥ 0.25 mV) was very specific but less sensitive to detect enlargement of RA. Reeves¹⁰ also found that the peaked P wave criterion had very low PPV.

A recent study by Allison et al¹¹ which used RAVI measurements with 2-dimensional (2D) transthoracic echocardiography to identify RA enlargement found that P wave criteria (P wave height ≥ 2 mm in lead II, P wave height > 1 mm in lead V1, or both) had an adequate PPV for predicting RA enlargement in both men and women. However, the P wave criterion had a low sensitivity.¹¹ An earlier study by Caird and Wilcken¹² found only a small correlation between P wave criteria and anatomical anomalies from RA. Different results were shown by another study, which found that RA enlargement or increased RA pressure was an important factor that influenced P wave changes in patients with cor pulmonale.¹³

The study by Maeda et al³ showed that peaked P wave criteria were poorly associated with pulmonary hypertension. There was only a small correlation between peaked P wave criteria and RA overload.³ Vertical elongation of RA was an important factor in affecting the peaked P wave ECG pattern in chronic obstructive pulmonary disease rather than the

hemodynamic effects on RA of impaired pulmonary function.³ The study was corroborated by our study in adult patients with uncorrected secundum ASD, in whom chronic RA and RV volume overload and pulmonary artery hypertension occurred, which resulted in the P wave height > 2.5 mm in lead II that is only detected in 19% of the subjects, the P wave height > 1.5 mm in V2 was found in 41% of the subjects, and P wave height > 1.5 mm in V1 was only found in 7% of the subjects who had RA enlargement from transthoracic echocardiogram.

A hemodynamic study in patients with ASD showed that left-to-right shunts occurred most frequently in the late phase of ventricular systole and the early phase of ventricular diastole.¹⁴ It can be assumed that in these phases there are increases in RA and RV volumes which chronically cause enlargements of RA and RV. In patients with ASD, left-to-right shunts which mostly take place in the early diastolic phase occur because RV has good compliance. This left-to-right shunt will reverse when right heart failure occurs, without necessarily increasing pressure on RA. The results of this study showed that in patients with ASD the RV dilates prior to the dilatation of RA.¹⁴ This hemodynamic phenomenon explains why in this study the 2 best criteria for predicting RA enlargement were the QRS axis > 90° and the R/S ratio in lead V1 > 1 and the combination of the 2 criteria which are widely known as ECG criteria for RV enlargement.

In this study, the RV enlargement ECG criteria to detect an increase in RAVI had a sensitivity of 82%, a specificity of 56%, and a PPV of 77%. This finding was supported by the study of Kaplan et al⁵ which showed that RV enlargement often accompanied RA enlargement. Another study found an enlarged RA area showing 100% sensitivity and specificity in diagnosing RV enlargement and hypertrophy.¹⁵ In the Kaplan et al⁵ study, 2 of the 3 most powerful criteria for predicting RA enlargement

were the criteria often associated with RV enlargement and hypertrophy, ie, the R/S ratio in V1 > 1 and the QRS axis > 90°. This study showed that RV enlargement was found in all patients who also had RA enlargement.

The ECG criteria of R/S ratio > 1 in lead V1 occurs because lead V1 is directly facing RV and will show a high R wave in V1 as the end result of accumulation of the depolarization direction.¹⁶ In this study, it was found that the R/S ratio > 1 in V1 had a good sensitivity (86%) and 44% specificity in detecting increased RAVI. Right axis deviation as indicated by the QRS > 90° in this study is the best criterion to predict RA enlargement, with a sensitivity of 94%, a specificity of 47%, an accuracy of 77%, and a PPV of 80%. These results are in line with the previous study on subjects with idiopathic pulmonary artery hypertension and pulmonary hypertension due to collagen diseases which found that the ECG criterion of QRS axis > 100° was highly predictive of RV enlargement.¹⁷

This study had a clinical implication that by examining 2 combined ECG criteria which had increased sensitivity and accuracy for RA enlargement, the doctors, especially those working in primary health care services and general practitioners, were aware that the right heart chambers were dilated. When combined by physical examination, this simple and ubiquitous examination can lead to the suspicion of ASD. In developing countries, the screening in population by ECG for CHD has not been applied as health policy, and therefore the prevalence of adult patients with CHD is increasing due to lack of diagnosis and proper treatment during childhood. Our registry indicates that ASD patients, who remain asymptomatic for decades and have obscured physical finding, seek medical treatment after they develop pulmonary hypertension or right heart failure.⁷ Therefore, the ECG with more sensitive and accurate criteria for detecting RA enlargement can assist the screening and early finding which will lead to further examination, such as transthoracic echocardiography, to confirm the diagnosis of ASD.

Study limitations

This study has several limitations: (1) This study was conducted with a cross-sectional design so that the measurements of echocardiography and ECG were not done at the same time, but within the 30-day limit. Various factors can affect the patient's hemodynamic condition which can affect the ECG measurement. (2) The ECG data were obtained from case report forms of the COHARD-PH registry, so there were limitations in identifying several extracardiac factors that could affect the P wave voltage on ECG during recording. (3) The gold standard used to identify RA enlargement in this study is 2D transthoracic echocardiography. Although this method is the simplest and most affordable measurement, some previous studies mentioned that the measurement of RA volume using this method is often underestimated compared with MRI,

multislice computed tomography (MSCT), or 3-dimensional (3D) echocardiography. (4) The measurement of RA wall thickness was not performed to detect the presence of RA hypertrophy. (5) The ECG criteria in this study were previously described markers with fixed thresholds. The study did not explore the potential of different markers and/or variation of thresholds.

Conclusions

The ECG criterion of P wave height > 2.5 mm in lead II had low sensitivity and low PPV for diagnosing RA enlargement in adults with uncorrected secundum ASD. The combined 2 ECG criteria, ie, QRS axis > 90° and R/S ratio > 1 in lead V1, had higher sensitivity, better accuracy, and balance of PPV and NPV for diagnosing RA enlargement in adults with uncorrected secundum ASD. The combined 2 ECG criteria were powerful for screening of RA enlargement which will lead to confirmed diagnosis of ASD.

Acknowledgements

The authors express their gratitude to the COHARD-PH research assistants who maintain the database for the research. The authors are indebted to sonographers in the echo-lab of Dr Sardjito Hospital who performed the transthoracic echocardiography. The authors also express their gratitude to Klinik Bahasa (Office of Research and Publication, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada) for English language and grammar editing of the manuscript.

Author Contributions

All authors made major contributions for this manuscript: protocol design (PPR, HH, LKD), data acquisition (PPR, DWA, ABH, LKD), data analysis and statistics (PPR, HH, ABH, LKD), preparation and writing of the final version (PPR, DWA, ABH), and accept of final version (PPR, HH, DWA, ABH, LKD).

ORCID iD

Anggoro Budi Hartopo  <https://orcid.org/0000-0002-6373-1033>

REFERENCES

1. Arrington CB, Tani LY, Minich LL, Bradley DJ. An assessment of the electrocardiogram as a screening test for large atrial septal defects in children. *J Electrocardiol.* 2017;40:484-488. doi:10.1016/j.jelectrocard.2007.06.001.
2. Caird FI, Wilcken DE, Williams RS. The electrocardiogram in diffuse interstitial disease of the lung and its relation pulmonary function. *Am J Cardiol.* 1962;10:14-19. doi:10.1016/0002-9149(62)90261-8.
3. Maeda S, Katsura H, Chida K. Lack of correlation between P pulmonale and right atrial overload in chronic obstructive airways disease. *Br Heart J.* 1991;65:132-136. doi:10.1136/hrt.65.3.132.
4. Shmock CL, Mitchell RS, Pomerantz B, Pryor R, Maisch JC. The electrocardiogram in chronic airways obstruction. *Chest.* 1971;60:335-340. doi:10.1378/chest.60.4.335.
5. 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. doi:10.1016/0735-1097(94)90763-3.
6. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr.* 2015;28:1-39. doi:10.1016/j.echo.2014.10.003.
 7. Krisdinarti L, Hartopo AB, Anggrahini DW, Sadewa AH, Wahab AS, Setianto BY. Clinical characteristics of adult uncorrected secundum atrial septal defect: a pilot study. *J Med Sci.* 2016;48:89-97. doi:10.19106/JMedSci004802201603.
 8. Tsao CW, Josephson ME, Hauser TH, et al. Accuracy of electrocardiographic criteria for atrial enlargement: validation with cardiovascular magnetic resonance. *J Cardiovasc Magn Reson.* 2008;10:7. doi:10.1186/1532-429X-10-7.
 9. Baranchuk A, Bayés de Luna A. The P-wave morphology: what does it tell us. *Herzschrittmacherther Elektrophysiol.* 2015;26:192-199. doi:10.1007/s00399-015-0385-3.
 10. Reeves WC. ECG criteria for right atrial enlargement. *Arch Intern Med.* 1983;143:2155-2156. doi:10.1001/archinte.1983.00350110141029.
 11. 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. doi:10.1016/j.jelectrocard.2017.04.012.
 12. Caird FI, Wilcken DE. The electrocardiogram in chronic bronchitis with generalized obstructive lung disease: its relation to ventilatory function. *Am J Cardiol.* 1962;10:5-13. doi:10.1016/0002-9149(62)90260-6.
 13. Saha NC. Study of the P wave in normal and obstructive lung disease in Delhi. *Am Heart J.* 1970;80:154-161. doi:10.1016/0002-8703(70)90162-6.
 14. Levin AR, Spach MS, Boineau JP, Canent RV, Capp MP, Jewett PH. Atrial pressure-flow dynamics in atrial septal defect (secundum type). *Circulation.* 1968;37:476-488. doi:10.1161/01.CIR.37.4.476.
 15. Cacho A, Prakash R, Sarma R, Kaushik VS. Usefulness of two dimensional echocardiography in diagnosing right ventricular hypertrophy. *Chest.* 1983;84:154-157. doi:10.1378/chest.84.2.154.
 16. Mattu A, Brady WJ, Perron AD, Robinson DA. Prominent R wave in lead V1: electrocardiographic differential diagnosis. *Am J Emerg Med.* 2001;19:504-513. doi:10.1053/ajem.2001.25776.
 17. Ahearn GS, Tapson VF, Rebeiz A, Greenfield JC Jr. Electrocardiography to define clinical status in primary pulmonary hypertension and pulmonary arterial hypertension secondary to collagen vascular disease. *Chest.* 2002;122:524-527. doi:10.1378/chest.122.2.524.