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RS time: A novel electrocardiographic parameter for diagnosis of pulmonary embolism

A.S.Mahmoud, H.K.Rashid, S.A.Moustafa and S.I.Farag
Cardiovascular medicine,Dept., Faculty of Medicine, Benha Univ., Benha, Egypt
E-mail:Drahmedsaeed201490@gmail.com

Abstract

Background: Pulmonary embolism [PE] is one of the leading causes of cardiovascular mortality worldwide. PE which presents itself with various symptoms and clinical severities, sometimes is detected incidentally, while other times may cause sudden death. The heterogeneous clinical presentation of PE may lead to difficulties in recognition, and thus delays in the initiation of life-saving treatments. In order to overcome these difficulties, several risk scoring systems and diagrams have been developed, based on history, physical examination, and laboratory findings, to assess the clinical probability of PE. The aim of our study was to assess the relationship between diagnosis of acute PE with QRS duration and prolonged RS time measured from the inferolateral leads in surface ECG. Methods: Our study had a prospective and retrospective design that was conducted on multi-centres. This study was conducted on 140 patients presented to Benha university hospitals, Dar-Elshefaa hospital and International medical center with suspected pulmonary embolism, in the period from January 2019 till November 2020. Patients of the study were classified into two groups; Group A with confirmed PE and group B excluded from PE. Patients with confirmed PE were subdivided into 2 groups [massive and sub massive PE] according to the distribution of the filling defect in CT pulmonary angiography and hemodynamic instability . RS time was calculated and compared between the 2 groups. Results: The normal and confirmed PE patients were compared according to risk factors and we found that diabetes mellitus and hypertension were with significant importance [p value 0.017 for both]. Patients with history of malignancy or history of recent surgery were more in confirmed patients with PE than normal group but without significant value. Also in confirmed PE patients. In the current study, Geneva score [REV] was estimated to all patients. Geneva score [REV] was significantly higher among patients with confirmed PE . P value [< 0.001]. In the current study, Patients with confirmed PE had significant elevation in Troponin and D-dimer . In the current study, RS time and QRS duration in ECG were obtained from all patients and comparison between patients with confirmed PE and normal was done. Patients with confirmed PE had significant prolongation in mean RS time [63.5 ± 3.9 SD]. In our study the confirmed group with diagnosis of PE were reclassified into massive and sub massive PE .RS time was compared between the 2 groups. RS time in surface ECG was more prolonged in patients with massive PE than submassive PE. Also in the current study S1Q3T3 pattern , sinus tachycardia and incomplete RBBB were compared between the 2 groups. S1Q3T3 pattern and sinus tachycardia were more obvious and significant in patients with confirmed PE. Conclusion: ECG is a fast non invasive easily accessible in-expensive diagnostic tool . Early detection of specific ECG changes could help in early diagnosis of PE . There is a difficulty in diagnosis of PE through a single ECG parameter .Our study doesn't hypothesize that prolonged RS time alone is enough to diagnose PE . However , our findings indicate prolonged RS time on surface ECG is a novel and effective parameter that can be very beneficial [with other parameters and in correlation with clinical data] for predicting the diagnosis of acute PE in the ER.

Key words: electrocardiographic parameter, RS time, diagnosis, pulmonary embolism.

1. Introduction

Pulmonary embolism [PE] is one of the leading causes of cardiovascular mortality worldwide**.** PE which presents itself with various symptoms and clinical severities sometimes is detected incidentally, while other times may cause sudden death **[1] .**

The heterogeneous clinical presentation of PE may lead to difficulties in recognition, and thus delays in the initiation of life-saving treatments. In order to overcome these difficulties, several risk scoring systems and diagrams have been developed, based on history, physical examination, and laboratory findings, to assess the clinical probability of PE **[2].**

Electrocardiography **[ECG]** is known to provide useful information for diagnosis of acute PE, as well as several ischemic, inflammatory and arrhythmic heart diseases**.** Electrocardiography **[ECG]** is commonly used for prognosis of APE patients because it is accessible, dynamic, and relatively easy to evaluate **[3]**. The most common electrocardiographic changes known to be associated with the prognosis of APE are sinus tachycardia, right bundle branch block [RBBB], ST/T changes, right axis deviation, S1Q3T3, QRS fragmentation, and atrial arrhythmias **[4].**

An ECG parameter that directly measures this delay has not been demonstrated yet. The delay in electrical conductivity exhibits itself in stretching the S-wave in inferolateral leads, causing an increase in the elapsed time from the beginning of QRS to the peak of the S-wave [RS time]. The prolongation of RS time due to conduction delay in the right ventricle caused by a sudden pressure overload in the right ventricle is also used in the diagnosis of APE **[4].**

The aim of this work is to assess the relationship between diagnosis of acute PE with QRS duration and prolonged RS time measured from the inferolateral leads in ECG.

2. Patients and Methods

2.1. Study design

It is a multi-centre prospective and retrospective cross sectional observational study that was conducted at cardiology department at Benha university hospitals , Dar Elshefaa hospital in Cairo and international medical center .

2.2. Patients

Our study included 140 patients admitted to cardiovascular department at Benha university hospital , Dar Elshefaa hospital and international medical center with suspected pulmonary embolism from the period of January 2019 to November 2020 .

2.3. Inclusion criteria

All patients admitted to cardiovascular department with suspicious of PE were subsequently referred to the computerized tomographic pulmonary angiography [CTPA] for confirmation of PE . PE was confirmed as partial and/or complete endoluminal filling defect in the pulmonary artery system in at least two consecutive computed tomography [CT] sections .

2.3. Exclusion criteria

- Patients with LBBB .
- Patients with complete RBBB
- Patients with baseline ECG abnormalities .
- Rhythm other than sinus rhythm .
- Morbid obesity with technical difficulty to perform CT pulmonary angiography .
- Patients with inconclusive results of multi-slice CT angiography
- Patients with contraindication to contrast .

2.4Methodology

Ethical consideration

The protocol was approved by the ethical committee of department of cardiology Benha university .

All patients with suspected were subjected to :

Full history taking :

With special focus on Sex, Age, Smoking, Diabetes Mellitus, Hypertension, history of malignancy or recent surgery or bone fracture .

General Examination

With special emphasis on blood pressure, heart Rate, respiratory rate, lower limb edema, oxygen saturation under non-invasive monitoring .

Local Examination:

Heart sounds, heart murmurs, galloping sounds, chest examination .

Laboratory investigations

Venous samples were drawn from all patients on admission before starting medications and the followings were done :

- **Serum creatinine level** Normal level was 0.3 – 1.3 mg/dl.
- **Troponin-I**
- **D-dimer [** normal level is less than 0.50 µg/ml. A positive D-Dimer is 0.50 µg/ml or greater**].**

Electrocardiography

Digital 12-lead standard ECG with a paper speed of 25 mm/s and 10 mm/mV was done for all patients in our study group to detect rate, rhythm , axis , any conduction abnormalities , mainly RBBB , S1Q3T3 pattern T wave inversion in anterior leads QRS duration and RS time duration . QRS duration was defined as the time from the start of the QRS complex to the J-point and was measured from the lead with the longest duration. RS time which is a part of QRS was defined as the time from the beginning of the QRS complex to the nadir of the S wave**.** RS time was measured from the infero-lateral leads with the longest duration as shown in figure [1] .

The ROC curve analyses revealed that the cut-off value of RS time for predicting acute PE was 64.20 ms with a sensitivity of 85.3% and a specificity of 79.4% [4] **.**

All measurements were recorded in milliseconds [msec]. The ECG records obtained from the patients' files were scanned with a scanner and examined with digital processing software.

Fig. (1) ECG shows prolonged RS time in a patient with acute pulmonary embolism [4].

Echocardiography:

Echocardiographic examination of the patients included in the study was performed with a Vivid S6 Pro ultrasound system [GE Vingmed Ultrasound AS N-3190, Horten,Norway] using the standard imaging techniques recommended by the European Association of Cardiovascular Imaging [5] .

Routine Digital gray scale 2D measurements were obtained, including mid left ventricular short axis views at the level of the papillary muscle and standard apical views [4-chamber, 2-chamber, and long axis]. All parameters were averaged over three heart cycles [five cycles for arrhythmia]. [5].

Each patient laid in supine and left lateral positions; the following echocardiographic variables were measured :-

Assessment of the left side of the heart: [according to recommendations of the European Association Cardiovascular Imaging [5].

The value of TAPSE was obtained using M-mode echocardiography. It is the difference between end systolic and end diastolic distance from the tricuspid annulus to the apex. TAPSE is usually acquired by placing an M-mode cursor through the tricuspid annulus and measuring the amount of longitudinal motion of the annulus at peak systole figure [3] [9].

In total, there have been more than 40 studies with over 2000 normal subjects evaluating the utility of TAPSE with a lower reference value for impaired RV systolic function of 16 mm [7].

A.Assessment of right ventricular function

Global assessment of right ventricular systolic function

Fractional Area Change of the Right Ventricle

RV FAC was obtained from a four-chamber view by tracing the RV endocardium both in systole and diastole from the annulus, along the free wall to the apex, and then back to the annulus, along the interventricular septum as shown in **figure [2] .** Then the RVFAC is calculated as follows :

End-Diastolic Area [Cm2] - End Systolic Area [Cm2]/ End Diastolic Area] [Cm2] .

Its main limitation is related to the need of good endocardial border delineation, which can be difficult to achieve in the highly trabeculated RV [6]. Lower reference value for normal RV systolic function is of 35% [7].

Tricuspid annular plane systolic excursion [TAPSE]

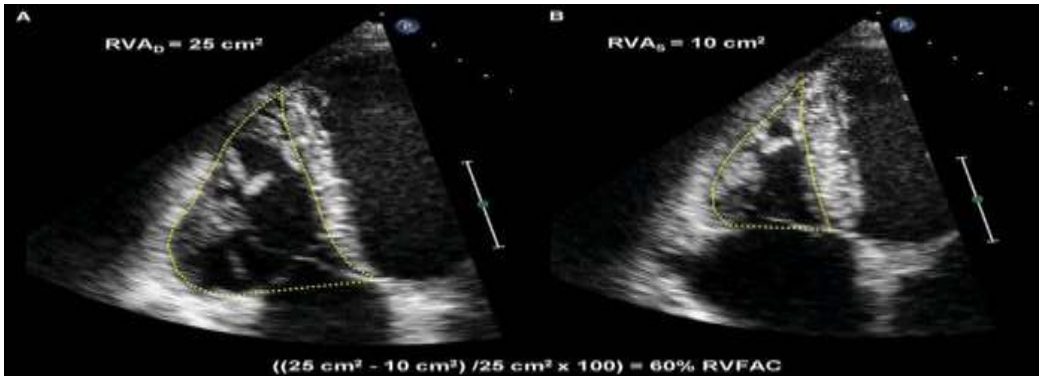
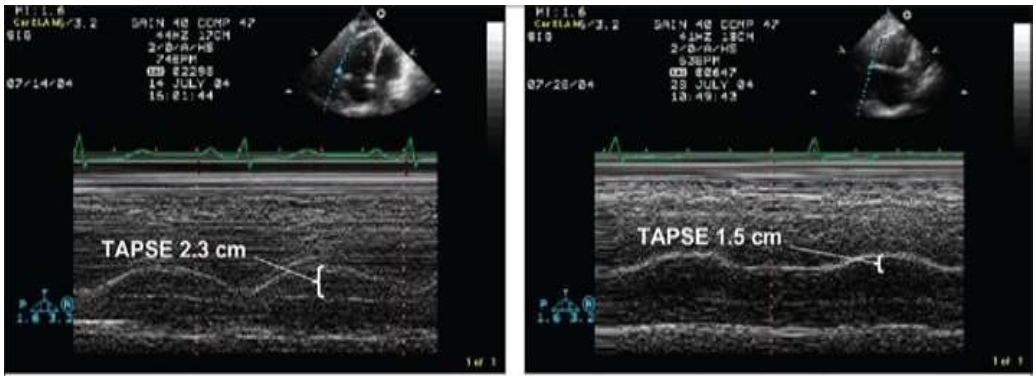


Fig. (2) RVFAC measured at end-diastole [A] and end-systole [B]. Both images are optimized by decreasing the depth or using the zoom function. The RVFAC is calculated as [25 cm2 - 10 cm2]/25 cm2 X 100 = 60% [normal]. RVAD, RV area at end-diastole; RVAS, RV area at end- systole. [8].



A **B**

Fig. (3) Representative M-mode recordings through the lateral tricuspid valve annulus for the purpose of measuring the tricuspid annular plane systolic excursion. Tracings were taken from two separate patients: [a] one with relative preservation of right ventricular function and the other [b] from a patient with significant right ventricular dysfunction. [10].

B.Assessment of pulmonary artery pressure

Tricuspid valve regurgitant velocity [TRV] represents the pressure difference between the right atrium and the RV and can be measured from continuous wave doppler of the tricuspid regurgitant jet from the apical four chamber view or from the parasternal RV inflow view if the regurgitant jet is eccentric. When pulmonary stenosis is absent, the RV systolic pressure [RVSP] is assumed to be equivalent to the systolic pulmonary artery pressure [SPAP] and can be calculated from the TRV using the simplified Bernoulli equation. The simplified Bernoulli equation [$P = 4[TRmax]^2$] is used to calculate this pressure difference using peak TR velocity. This method correlates well with PASP on right heart catheterization . The normal cutoff value for invasively measured mean PA pressure is 25 mmHg. In the echocardiography SPAP is more commonly measured and reported. Normal resting values are usually defined as a peak TR gradient of 2.8 to 2.9 m/s or a peak systolic pressure of 35 or 36 mm Hg, assuming an RA pressure of 3 to 5 mm Hg , a value of 2.9 – 3.4 m/s indicates intermediate probability, and a value > 3.4 m/s suggests a high probability for pulmonary hypertension . This value may increase with age and increasing body surface area .The American College of Cardiology Foundation and American Heart Association expert consensus document on PH recommends further evaluation ofpatients with dyspnea with estimated RVSP > 40 mm Hg [7]

2.5.Statistical analysis

The collected data were tabulated and analyzed using SPSS version 16 soft ware [SpssInc, Chicago, ILL Company]. Categorical data were presented as number and percentages, Chi square [χ^2] and Fisher's exact tests were used to analyze them. Quantitative data were tested for normality using Shapiro-Wilks test assuming normality at $P > 0.05$. Normally distributed variables were expressed as mean ± standard deviation and analyzed by student "t' test for 2 independent groups. Non parametric data were presented as median and inter-quartile range [IQR], and analyzed by Mann Whitney U [Z_{MWU}] test for 2 independent groups. Correlations were assessed by Person's [r] and spearman's coefficients [rho] for parametric and non parametric variables respectively. Univariate and multivariate binary logistic regression analysis was run to detect the significant predictors of PE. ROC curve was constructed to detect cutoff value of RS time with optimum sensitivity and specificity in prediction of PE. P value ≤ 0.05 was considered significant [12].

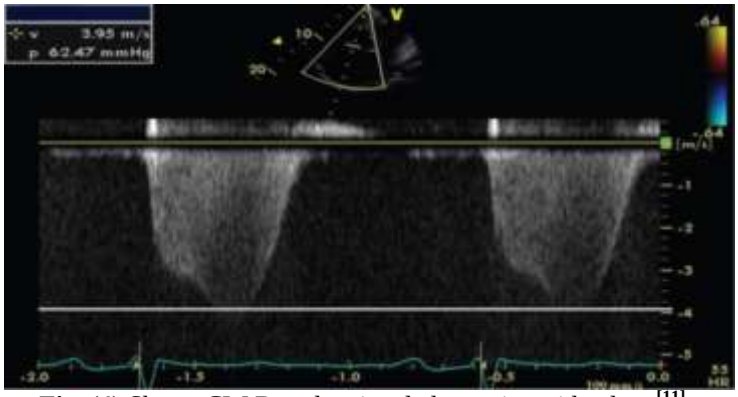


Fig. (4) Shows CW Doppler signal along tricuspid valve. [11] .

3. Results

Our patients were predominantly males 69 (57.4%) and 51 were females (42.5%). The mean age was 58 ± 10.2 years, the youngest was 27 years old and the oldest was 76 years old. **(Table 1)**.

Table (1) Distribution of the studied cases as regards demographic data and risk factors.

Diabetes mellitus was the most prevalent risk factor among the patients (64.1%) followed by hypertension (63.3%), smoking (60.8%) & whereas patients with recent surgery or fracture or with malignancy were found in (30%, 4.1% respectively).

Variable			Suspected patients of PE (n=120)	
			No	%
Personal data	Age (years)	Mean±SD	58.0±10.2	
		Range	27-76	
	Gender	Female	51	42.5
		Male	69	57.5
Risk factors	Smoking	Yes	73	60.8
	DM	Yes	77	64.1
	Hypertension	Yes	76	63.3
	History of malignancy	Yes	5	4.1
	History of recent surgery or fracture	Yes	36	30

5.Discussion

History and physical examination, ECG Echocardiography and CT pulmonary angiography were performed on all patients.

There were 79 (56.4 percent) men and 61 (43.6 percent) women among our patients, according to the demographics and risk variables we tracked. The average age was 58.2 years, with the youngest being 29 and the oldest being 78.

Diabetes mellitus was the most common risk factor among the patients [55 percent], followed by hypertension [54 percent], smoking [52.1 percent], and patients with recent surgery or fracture or cancer [25.7 percent, 3.6 percent] correspondingly.

With age, the prevalence of VTE rises from less than five per 100,000 children to more than four times that number for the elderly. The risk of VTE is three times greater in those over 65 than in those between the ages of 45 and 54 [13].

Raskob et al. [14] showed that this age-related rise in VTE incidence is mostly due to a disproportionate increase in the burden of PE. According to many research, men are more likely to suffer from venous thromboembolism (VTE) than women.

Although the statistics on male sex and pulmonary embolism are inconsistent, a study of national mortality data indicated that males died at a rate 20-30 percent greater than women from pulmonary embolism [15].

Males are more likely than females in the elderly, according to Alotaibi et al. [16], who conducted their research in this area. PE is more common in women younger than 55 years of age. DVT, 48 occurrences per 100,000, and PE, 69 cases per 100,000 persons, account for the entire yearly incidence of venous thromboembolism in the general population.

Cox proportional-hazards regression models were used in the research of Chung et al. [17] to determine the risk of DVT and PE. Patients with type 2 diabetes (T2DM) had a greater overall incidence of VTE than those without the disease [12.0 versus 7.51 per 10,000 person-years]. Compared to the control group, T2DM patients had a 1.44-fold increased risk of developing a VTE. T2DM patients had a higher risk of developing DVT and PE than those without the disease. Patients with type 2 diabetes (T2DM) had a significantly increased risk of developing DVT and PE than those without the condition. As a result of the long-term national cohort research, T2DM patients had a higher risk of VTE than the general population, according to the findings.

This study indicated that of the 105 individuals investigated, 85 had proven pulmonary embolism and 55 had not. They showed that the diagnostic accuracy for PE detection is continually rising with reported sensitivity and specificity values above 90% with speedy correct exclusion and PE diagnosis.

An analysis by Abdellatif and colleagues found that of the 182 individuals studied, 108 developed pulmonary embolism (PE) in a meta-analysis of seven trials that included a total of 182 patients. There were 889.9 percent and 94.6 percent sensitivity and specificity in the pooled study.

Pre-test likelihood of pulmonary embolism [PE] may be estimated using the Geneva score, which is a clinical decision criteria. In 2001, the Geneva University Hospital's clinical staff released the initial criteria, which were amended and streamlined in 2006 [20].

Each patient's Geneva score [REV] was calculated as part of our research investigation. Patients with a verified PE P value (p 0.001) had a substantially higher Geneva score.

Troponin and D-dimer levels were significantly elevated in patients with verified PE in our research.

Using a high-sensitivity technique, Lankeit et al. [21] investigated the function of cardiac troponin T in assessing the risk of acute PE in normotensive individuals. Their TnT threshold [14 pg/ml] showed a 100% sensitivity and negative predictive value for the 30-day risk of death or significant sequelae.

Many research have examined the link between D-dimer levels and the extent of PE as measured by CT angiography, however the relationship between troponin and D-dimer levels remains ambiguous.

Patients with acute PE and hs-cTnI levels >0.1 ng/ml had substantially higher D-dimer concentrations in the research by Walter et al. [23]. D-dimer serum levels were considerably greater in individuals with symptoms of cardiac damage owing to acute PE.

Patients with acute pulmonary embolism (PE) showed greater D-dimer and troponin-I levels and worse oxygen saturation than those without PE, according to a research by Rencuzogullari et al. [4]. When it came to age and gender, there was no statistical difference between the two groups. Acute PE patients had a median revised Geneva score of 3.0 [3.0-4.5] compared to 3.5 [1.0-6.0] for those without PE, but there was no statistical difference in the Wells score between the two groups. Despite the fact that more individuals with PE had had surgery or had been immobilised during the preceding four weeks; had more symptoms of deep vein thrombosis; and had a history of hypertension than those without PE, these differences did not have statistical significance.

Stretching the S-wave in inferolateral leads is caused by a delay in electrical conductivity that results in an increase in the time it takes to reach the peak of the S-wave [RS time]. In order to aid in the diagnosis of PE, the RS time might be measured. All patients in our research had RS time and QRS length recorded on their ECGs, and the results were compared between those with verified PE and those who were otherwise healthy. The mean RS duration was significantly longer in patients with verified PE (63.5% 3.9% SD).

Similarly to our findings, the research of Rencuzogullari et al. [4] found that PE patients had a higher RS time and a longer QRS length compared to those without the condition [69.657.63 vs. 59.726.35; p=0.001].

According to Gümüşda et al. [24], RS time extension was shown to be an independent predictor of death in their multivariate analysis as well. In acute pulmonary

embolism, RS time > 64.8 msec accurately predicted one-month death with a sensitivity of 68% and a specificity of 73%, according to ROC analysis. RS time, a new ECG parameter, should be assessed in each patient with an acute pulmonary embolism, according to the researchers. The one-month death rate of individuals with acute pulmonary embolism may be better predicted if the RS time is extended.

Both groups were also compared in terms of the S1Q3T3 pattern, sinus tachycardia, and R-RBBB. Patients with a confirmed PE had a more pronounced S1Q3T3 pattern and sinus tachycardia. According to Qaddoura et al., [3], Gümüşda et al., [24], Stein et al., [25], and et al., [26], these findings are in line with previous studies. There was a consensus among the authors that RBBB, T wave inversion, ST depression, and QRS fragmentation are the most often seen ECG alterations for the diagnosis and prognosis of APE.

5. Conclusion

The electrocardiogram (ECG) is a quick, painless, and inexpensive diagnostic tool. The early observation of particular ECG alterations may aid in the early diagnosis of PE.. Diagnosing PE using a single ECG measure is tricky. Our data did not suggest that longer RS duration is sufficient to diagnose PE.. As a result, our results show that extended surface ECG QRS time may be a unique and useful indicator for predicting the diagnosis of acute PE [in conjunction with other measures and in combination with clinical data].

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