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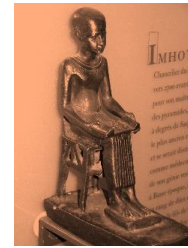
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Original Article

Diagnostic and Prognostic Value of Right Ventricular Strain Analysis in Pulmonary Embolism Patients

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ABSTRACT

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Background: Conventional echocardiographic parameters lack sensitivity for identifying pulmonary embolism (PE) patients.

Aim of the Study: This study aims to assess the diagnostic and prognostic value of right ventricular free wall strain (RV FWS) in PE.

Patients and Methods: This cross-sectional controlled study included 32 suspected PE patients who attended the outpatient clinic at Al-Azhar University. A control group of 30 healthy subjects without a history of cardiac or respiratory diseases was also enrolled. PE was confirmed by computed tomography pulmonary angiography (CTPA). Based on CTPA results, patients were classified into two groups: PE-negative patients (group I) and PE-positive patients (group II).

Results: There was no significant difference in clinical parameters between suspected PE patients with positive CT findings and those with negative findings. Contrary to conventional echo parameters, which showed no statistically significant difference between the PE-confirmed group, control group, and suspected patients with negative results, right ventricle longitudinal strain (RVLS) was significantly lower in the PE-confirmed group. All patients had a favorable prognostic outcome.

Conclusion: The use of RV FWS in identifying PE patients may have a significant impact on diagnostic accuracy, appropriateness of treatment, and quality of patient monitoring and follow-up.

Keywords: Pulmonary embolism; RV longitudinal strain; Speckle tracking echocardiography.



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INTRODUCTION

Recent increments in pulmonary embolism-associated mortality are recorded ^[1]. Severe PE of sudden onset with hemodynamic compromise is accompanied by 30% fatality within 90 days if left untreated ^[2].

The utilization of transthoracic echocardiogram [TTE] can provide significant data in cases where there is a suspicion of PE. Furthermore, TTE is currently considered a routine investigation in patients who have already been diagnosed with PE as it may affect management strategies ^[3]. However, the sensitivity of routine right ventricular [RV] function indices to exclude PE is diminished especially in low-risk cases ^[4].

The utilization of speckle-tracking echocardiography [STE] has become prevalent in clinical settings due to its ability to measure myocardial deformation. This echocardiographic technique incorporates strain imaging parameters, which are increasingly being integrated into routine clinical practice. The utilization of RVLS has been proposed as a contemporary parameter for assessing RV function ^[5].

We aimed to assess the diagnostic and prognostic value of RV-free wall strain analysis in PE patients.

PATIENTS AND METHODS

This study cross-sectional-controlled study included 32 suspected PE patients who attended at Al-Azhar University outpatient clinic. Another group of 30 healthy subjects without a history of cardiac or respiratory diseases was enrolled as a control group. PE was confirmed by CTPA, and according to its results, the patients were classified into PE-negative patients [group I], and PE-positive patients [group II]. Our study guided the declaration principles of Helsinki. Ethical approval was obtained from our institution [Al-Azhar University]. Informed written consent was obtained from every patient at the time of recruitment.

Patients with a history of PE, high-risk PE, chronic pulmonary hypertension, significant valvular lesion, ischemia, left ventricular systolic or diastolic dysfunction, significant arrhythmia [atrial fibrillation, AV block, and intraventricular conduction delay], chronic obstructive pulmonary disease and chronic heart disease were excluded from the study.

Data collection: Patient clinical data were collected such as history, clinical examination, clinical probability assessment via simplified Well's score, risk stratification of pulmonary embolism confirmed patients using simplified pulmonary embolism severity index [PESI] score, and major adverse cardiovascular events during the hospital stay and after 6 months. [Death, major bleeding events, PE recurrence, and rehospitalization].

The following investigations were done for every patient; 12 leads electrocardiogram, conventional RV echocardiography [RVLS and CTPA].

Conventional RV Echo

The 2D TTE procedure was conducted using a "Philips iE33 X Matrix" ultrasound machine. The TTE examination utilized "S5-1" matrix array transducers [manufactured by Philips Medical Systems, Andover, USA] that were equipped with strain rate imaging [STE] technology. The transducers operated at a range of frequencies from 1 to 5 MHz.

We typically use ECG gating to aid with image collection and processing. American Society of Echocardiography and European Association of Cardiovascular Imaging guidelines were followed to examine the left and right heart chambers for chamber quantification ^[6]. RV fractional area change [RVFAC] was determined by measuring the proximal RV outflow diameter in the parasternal long axis view [RVPLAX], as well as the RV basal, mid, and length diameters in the apical four-chamber view.

The RVSP was calculated from the peak tricuspid regurgitation [TR] jet velocity using the simplified Bernoulli equation, and the RA pressure was calculated from the diameter and collapsibility of the inferior vena cava [IVC] using data from subcostal ultrasound images as a guide ^[6].

The measurement of tricuspid annular plane systolic excursion [TAPSE] was conducted using M-mode echocardiography, with the cursor being aligned optimally along the direction of the tricuspid lateral annulus in the apical four-chamber view. Furthermore, the RV-centric perspective was employed, utilizing a tissue Doppler cursor positioned at the designated area of interest located at the lateral aspect of the tricuspid annulus, which was captured at a significantly elevated frame rate. The velocity S' was observed to be the maximum systolic velocity.

To prevent underestimation of velocity, the Doppler cursor was aligned with both the basal segment and the annulus. The acquisition of RIMP was accomplished through the utilization of Tissue Doppler imaging. The formula for right ventricular index of myocardial performance [RIMP] is derived by dividing the sum of isovolumic relaxation time [IVRT] and isovolumic contraction time [IVCT] by ejection time [ET].

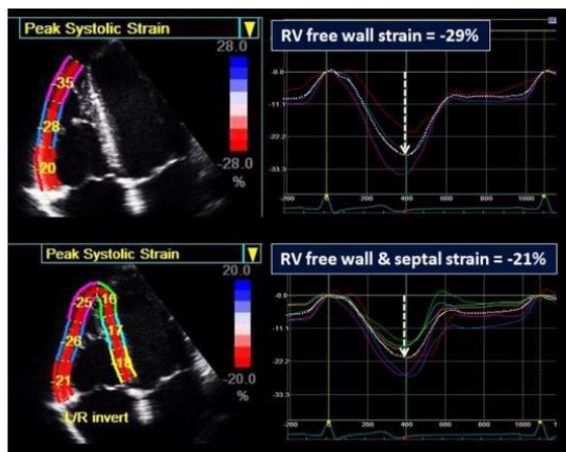


Figure [1]: Measurement of RV systolic strain by 2D STE [6].

RV free wall longitudinal strain

The calculation of RV-free wall longitudinal strain was performed offline using the Qlab 9 software package [cardiac motion quantification [CMQ]; Phillips Medical Systems] on digitally stored images.

The measurement of longitudinal strain for all segments of the right ventricle was conducted using the RV-focused view. Automated border tracking was performed during end-diastole, followed by manual correction to ensure the inclusion of both the endocardial and epicardial borders in the calculation. The peak strain for the segment was determined as the maximum negative value observed on the time strain curve throughout the entirety of the cardiac cycle.

The study involved the measurement of peak longitudinal strain in six distinct myocardial regions, consisting of three septal segments and three free wall segments. Subsequently, the septum was excluded from the analysis to estimate the global longitudinal strain of the free wall.

CT pulmonary angiography: The thoracic images were acquired in a caudal-cranial direction using a 16-MDCT scanner. An 18-gauge catheter was employed to establish intravenous access

via the antecubital vein. The resulting images were observed on a Picture Archiving and Communication System [PACS] monitor utilizing IMPAX version 4.1. The images were presented using three distinct grayscale settings to facilitate the interpretation of lung window, mediastinal, and pulmonary embolism-specific features.

Statistical analysis: The data were subjected to analysis using the Statistical Program for Social Science [SPSS] version 22. The quantitative data were represented as the mean plus or minus the standard deviation [SD]. The Shapiro test was used to determine the normality of the data. The qualitative data were represented in terms of frequency and percentage. A one-way ANOVA was used when comparing more than two quantitative means. The chi-square test was used when comparing categorical data. A P-value < 0.05 was considered significant.

RESULTS

Table [1] shows the clinical and demographic characteristics of the studied subjects. Twenty-one individuals were confirmed to have PE [PE-positive group] with a mean age of 47 ± 9 years, and 11 suspected individuals were deemed free of PE [PE negative] patients' mean age was 50 ± 13 years [$n = 11$]. Regarding control, the mean age was 49 ± 11 years, [$n = 30$] with no significant difference in the three groups regarding the demographic data.

Regarding respiratory rate, it was significantly higher in group II [24 ± 4.7] than the control [14 ± 4.8] and group I [20 ± 3.9], also the O₂ saturation was significantly lower in group II [94 ± 2.9] compared to both the negative [96 ± 1.3] and the control groups [96 ± 2.7] with no significant difference between the control and group I. In addition, the simplified wells score, was significantly higher in both groups compared to the control group [0] and was significantly higher in group II [$2.2 \pm .6$] compared to group I [$1.27 \pm .47$]. There was no incidence of death, major bleeding, and PE recurrence in all the groups during the hospital stay and after 6 months.

The echocardiographic parameters of patients and controls are illustrated in Table 3. PE patients were more likely to have lower RV function. As RVFAC, Tie index, and S wave were significantly lower in PE patients [however still within the normal range], TAPSE showed no significant difference between the three groups. The estimated pulmonary artery systolic pressure

and RV mid-diameter were significantly higher in the PE group.

As regards the RV-free wall, longitudinal strain was significantly lower in negative and positive groups compared to the control group. Moreover, it was significantly lower in the

positive group compared to the negative group. In addition, considering the cut-off value from the ROC table, it was -20.0 , which revealed an area under the curve of 0.98 exhibiting 98% sensitivity, and 73% specificity positive predictive value was 0.88 and the negative predictive value was 0.99 .

Table [1]: Descriptive statistics of demographic data

Variables		Group I [PE-negative; n = 11]	Group II [PE-positive; n = 21]	Control [n = 30]	P-value
Age [Years], Mean \pm SD		50.7 \pm 13	47.8 \pm 9	49.4 \pm 11	P= 0.395 ^a P1 = 0.18 P2 = 0.51 P3 = 0.09
Sex	Male	5 [45%]	12 [57.1%]	15 [50%]	0.819 ^b
	Female	7 [55%]	7 [42.8%]	15 [50%]	
Comorbidities	DM	7 [63.6%]	17 [81%]	17 [56.6%]	0.301 ^b
	HTN	8 [72.7%]	16 [76.1%]	13 [43.3%]	0.592 ^b

Table [2]: Descriptive statistics of clinical data

	Group I [PE-negative; n = 11]	Group II [PE-positive; n = 21]	Control [n = 30]	P-value
Wells Score, Mean \pm SD	1.27 \pm .47	2.2 \pm .6	0 \pm 0	P1 = 0.001 P2= 0.001 P3= 0.001
Respiratory rate, Mean \pm SD	20 \pm 3.9	24 \pm 4.7	14 \pm 4.8	P1 = .17 P2= 0.05 P3= 0.04
Saturation, Mean \pm SD	96 \pm 1.3	94 \pm 2.9	96 \pm 2.7	P1 = .17 P2= 0.02 P3= 0.02

Table [3]: Descriptive statistics and results of echocardiographic measures for comparison between the three groups

Variables	Group I [PE-negative; n = 11]	Group II [PE-positive; n = 21]	Control [n = 30]	P-value
TAPSE	22 \pm 5.4	19.28 \pm 4.4	22.6 \pm 2.8	P1= 0.2 P2= 0.4 P3= 0.6
esPAP	33.1 \pm 15.1	38.67 \pm 15.8	14.9 \pm 1.56	P1= 0.001 P2= 0.04 P3= 0.001
Tie index	0.5 \pm 0.11	0.4 \pm 0.1	0.44 \pm 0.07	P1= 0.002 P2= 0.5 P3= 0.05
RVAC	40.1 \pm 4.8	37.4 \pm 10.5	50.5 \pm 4.8	P1= 0.001 P2= 0.3 P3= 0.001
S wave	13.1 \pm 3.4	11.8 \pm 2.9	16.4 \pm 2.2	P1= 0.001 P2= 0.7 P3= 0.001
Basal RV	32.09 \pm 6.02	37.8 \pm 4.7	35.4 \pm 4.7	P1= 0.06 P2= 0.009 P3= 0.12
Mid RV	24.9 \pm 2.9	31.05 \pm 5.2	26.4 \pm 3.4	P1= 0.001 P2= 0.001 P3= 0.27
Longitudinal RV	52.45 \pm 6.6	55.45 \pm 7.4	50.8 \pm 5.8	P1= 0.3 P2= 0.1 P3= 0.9
RVFWS	-18.8 \pm 2	-14.2 \pm	-23.3 \pm 2.8	P1= 0.001 P2= 0.001 P3= 0.001

P1: comparison of the control group and the negative group. P2: comparison of the control group and the positive, P3: comparison of the positive group and the negative group: Significant at $P \leq 0.05$.

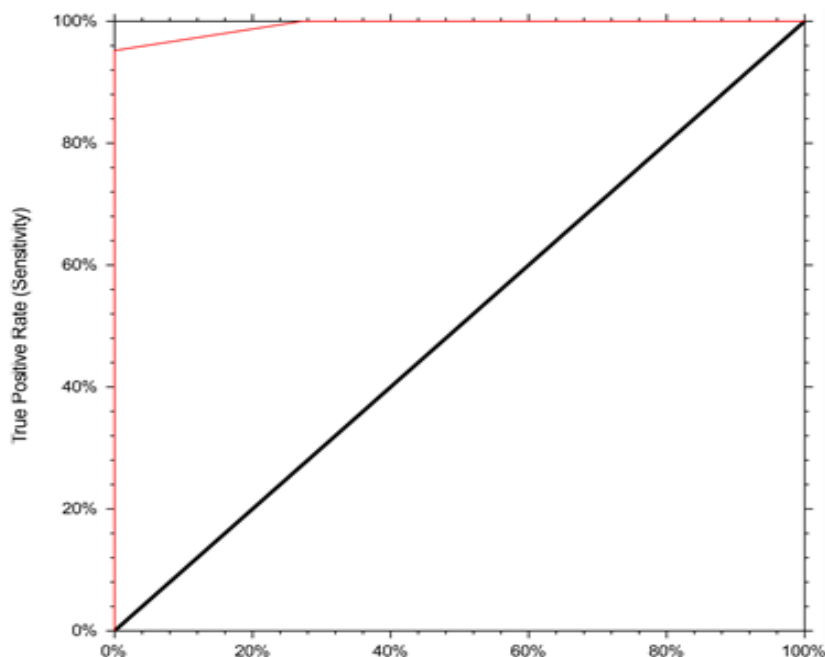


Figure [2]: RV FWS Roc curve

DISCUSSION

The primary focus of this study involved the assessment of the impact of calculating RV FWS on the enhancement of both sensitivity and specificity in the diagnosis of PE.

While previous studies have provided evidence in favor of using qualitative measures to assess RV function in cases of acute PE [7], these subjective methods are dependent on individual experiences. In cases where there is uncertainty regarding the diagnosis of PE, a computed tomography pulmonary angiography/ventilation-perfusion [CTPA/VQ] scan is typically necessary. However, it is worth noting that RV FWS can offer supplementary information in situations where the diagnosis is borderline.

In regional healthcare facilities lacking CT or nuclear imaging capabilities, strain echocardiography may serve as a viable alternative for identifying patients who require transfer to facilities equipped with advanced imaging modalities and therapeutic interventions.

Strain analysis has a unique advantage over traditional RV parameters as it can assess intrinsic myocardial performance and can discriminate between active motion and passive motion. Longitudinal strain, which can be detected using by speckle tracking, is a credible and precise way to quantify RV systolic function, and has been thoroughly validated [8].

In contrast to the measurements of TAPSE and RV S' velocity, the assessment of RV FWS evaluates the function of the free wall of the RV. This approach offers a theoretical advantage by avoiding the sampling of solely basal segmental function [9]. It enables the detection of subclinical RV damage in various diseases, including cardiomyopathies, cardiac amyloidosis, cancer, and pulmonary arterial hypertension even when conventional parameters of RV systolic function are in the normal range [10].

A recent meta-analysis identified a total of 22 studies that investigated the test performance characteristics of TTE in individuals suspected of having PE and concluded that the standard TTE metrics for RV size and function are insufficiently sensitive to exclude the presence of PE [5].

In accordance with Ballas and colleagues' study which concluded that The most sensitive Echo parameter was RV FWS [44/73; $p < 0.001$, for all other echo indices] as it was reduced in PE patients, our study found that RV FWS was 98% sensitive for PE, suggesting that it may have advantages over more conventional evaluations of RV function [11].

Also, it was noticed in a study by **Trivedi et al.** [12], that RV FWS was an accurate detector of PE. RV FWS produced an accurate classifier [AUC 0.966, SE 0.013, $p < 0.022$] with significantly higher performance than the model

without RV FWS. hence, we conclude that it may be useful at the point of care or in diagnostic algorithms when PE is suspected.

Our study is limited by the low number of patients and lack of local Ventilation-perfusion scan availability.

Conclusion: Our results imply that RV FWS is the most useful echocardiographic marker for differentiating PE patients from controls and that including RV FWS with established measures of RV size and function greatly increases diagnostic accuracy.

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