EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 4
24-31
Year: 2020

PAAT/RVET PULMONARY ARTERY ACCELERATION TIME IN DIAGNOSIS OF PULMONARY HYPERTENSION BY PULSED WAVE SPECTRAL DOPPLER TECHNIQUE

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Article Received on 27/01/2020 **Article Revised on 18/02/2020** **Article Accepted on 08/03/2020**

ABSTRACT
Pulmonary hypertension is a pathophysiological, hemodynamic condition defined as an increase in mean pulmonary arterial pressure ≥ 25 mmHg at rest, assessed by right heart catheterization which is the gold standard investigation despite its own inherent risks. Transthoracic echocardiographic estimates pulmonary artery pressure conventionally calculated from the maximal velocity of the tricuspid regurgitation jet (traditional method). Pulmonary artery acceleration time is an accurate parameter reflecting pulmonary artery Systolic pressure independently of tricuspid regurgitation. This study aimed to assess echocardiographic pulmonary artery acceleration time in the diagnosis of PHT when compared with TR jet using pulsed wave doppler spectral technique in suspected patients with pulmonary hypertension. This is a multicenter cross-sectional study performed in Baghdad/ Iraq from June 2017 to May 2018 on 245 referred patients with unexplained shortness of breathing. Each patient was subjected to transthoracic echocardiogram using Pulsed-wave Doppler measuring pulmonary artery acceleration time, while the Continuous-wave Doppler was used to measure the peak velocity of TR, in addition to find the correlation between that Pulmonary Artery Acceleration Time and Pulmonary Artery Systolic Pressure. The patients were divided into 2 groups; 183 With no PHT & 62 with PHT. There was a significant correlation between Pulmonary Artery Systolic Pressure and Peak velocity of TR, Pulmonary Artery Systolic Pressure and Pulmonary Artery Acceleration Time /RV Ejection Time. Pulmonary Artery Acceleration Time was an excellent prediction of PHT, with (93.6% sensitivity), (95.1% specificity), it can be concluded that pulmonary artery acceleration time is a useful, valuable, easily obtainable and accurate Echo parameter when compared with Peak velocity of TR in the assessment of Pulmonary Artery Systolic.

KEYWORDS: Pulmonary artery acceleration time, Pulmonary hypertension, Pulsed wave spectral doppler technique.

INTRODUCTION
Pulmonary hypertension (PHT) is a pathophysiological, hemodynamic disorder defined as an increase in mean pulmonary arterial pressure (mPAP) ≥ 25mmHg at rest, assessed by right heart catheterization that is a gold standard investigation.[1] Pulmonary hypertension could be a complication of cardiac or pulmonary disease or a primary disorder of small pulmonary arteries.[2] In people aged over 50 years, PHT is the third most frequent cardiovascular problem after coronary artery disease and systemic hypertension.[3,4,5]

PHT is classified into five groups according to the 2015 ESC / ERS Guidelines Group 1- Pulmonary Arterial hypertension (PAH), Group 2-Pulmonary hypertension owing to left heart disease (LHD), Group 3- Pulmonary hypertension owing to lung disease / hypoxia, Group4- Chronic thromboembolic pulmonary hypertension (CTEPH) and Group 5- Pulmonary hypertension with multifactorial mechanisms.[6]

The diagnosis of PHT requires a clinical suspicion based on symptoms & physical examination and investigations.[7,8,9] including clinical presentation, cardiogram (ECG), chest radiograph, pulmonary function tests & arterial blood gases, CT and pulmonary angiography, cardiac magnetic resonance imaging, abdominal ultrasound scan and RT heart catheterization.

Doppler technique examines the flow of blood direction, velocity and pattern of blood flow through the heart & great vessels; Rely on a more parallel alignment between the beam and the flow of blood.; misalignment of the interrogating beam will lead to underestimation or overestimation of true velocity.[10,11]

Spectral Doppler imaging (Flow wave Form is a way of measuring blood flow[12]; this measurement can be carried out and represented in various ways & it is a complementary to the two dimension imaging (2D) & there are five types of Doppler techniques: Continuous wave Doppler (CW), Pulsed wave Doppler (PW), Color flow imaging, Duplex Doppler and Tissue Doppler.

Pulse Doppler is a short intermittent waves so the pulsed Doppler instrument "listen" only at a fixed and very brief time interval after transmission of the pulse, and this permits returning signals from one specific distance from the transducer to be selectively received and analyzed, a process by adjusting the time between transmission and reception.

PATIENTS AND METHODS

This cross-sectional multi-center study was carried out in three hospitals in Baghdad/Iraq (Baghdad Teaching hospital, Iraqi Center for cardiac surgery and Al-Yarmouk teaching hospital) from June 2017 to May 2018 on 245 Patients of both sexes who were referred to Echo department, complaining from shortness of breathing with exertion for echocardiography evaluation. Each patient was subjected to full echo examination assessment including a Pulsed-wave Doppler study for measurement of pulmonary artery pressure, including detailed study of the RV & Pulmonary Artery Pressure assessment and right ventricular ejection time (RVET), in addition to Continuous-wave Doppler to measure the peak velocity of Tricuspid Regurgitation (TRVmax). The pulmonary Artery Systolic Pressure (PASP) was calculated as [4 X(TRVmax)2 + right atrial pressure] according to Bernoulli Equation; Accordingly, the relationship between PAAT, and PASP. Patients with congenital heart disease including PS, patients with atrial fibrillation, patients with heart rate <60 and >100 and patients with poor image quality were excluded from our study.

Data were collected through a questionnaire form including personal data (Age, Gender) history of Pulmonary disease; hypertension, diabetes mellitus, Coronary artery disease and Connective tissue disease. ECG was performed for all patients.

Echocardiography including 2D/ M-mode echocardiography, Conventional Doppler Echocardiography and Pulsed wave tissue Doppler imaging were done to the patients as well as Transthoracic echocardiographic examination using the General Electric Vivid E9 equipped with a phase array transducer of 3.5 MHZ frequency and the subject in the left lateral decubitus position. Echocardiographic parameters were obtained from the mean of 3 to 6 cardiac cycles.

Measurements were performed according to the recommendation of the American Society of Echocardiography and European Society of Cardiology.

Statistical analysis

Data were analyzed by using the (SPSS) version 22 program, and discrete variables presented using their number and percentage, chi square test used to analyze the discrete variable (or Fisher exact test when chi square is not valid; due to low sample size <20 and if 2 or more with expected frequency less than 5).

RESULTS

This study included 62 PAH patients and 183 controls. Table (1) showed that there was a highly significant association between PAH patients and RV dilation ($p<0.001$). Mean based diameter was significantly higher among PAH patients ($p<0.001$), while mean TAPSE was significantly lower among PAH patients ($p<0.001$). No significant differences were observed between PAH patients and controls regarding RVH ($p=0.5$). Mean RVOT was significantly higher among PAH patients ($p<0.001$). Mean RA size was significantly higher among PAH patients ($p<0.001$). Mean RV systolic function S' was significantly lower among PAH patients ($p<0.001$). Mean E/E' TR was significantly higher among PAH patients ($p=0.001$). A significant association was observed between PAH patients and RV diastolic dysfunction ($p<0.001$). There was a highly significant association between positive TR and PAH patients ($p<0.001$). A highly significant association was observed between PAH patients and severe TR ($p<0.001$). Mean velocity of TR was significantly higher among PAH patients ($p<0.001$).

Table (1): Distribution of RV function measures according to PAH patients and controls.

Variable	Control		PAH		P
	No.	%	No.	%	
RV					
Normal	173	94.5	29	46.8	**<0.001*** S
Dilated	10	5.5	33	53.2	
Based diameter					
Mean±SD	34.8±7.2		45±11		**<0.001**** S
TAPSE					
Mean±SD	22.3±2.7		18.2±4.9		**<0.001**** S
RVH					
Mean±SD	4.7±5.3		4.1±0.9		0.5** NS
RVOT					
Mean±SD	24.9±5.5		33.6±9.1		**<0.001**** S
RA size					
Mean±SD	29.3±5.5		39.3±10.4		**<0.001**** S
RV systolic function S'					
Mean±SD	11.8±0.9		10.6±2.1		**<0.001**** S
E/E' TR					
Mean±SD	4.3±1.1		5.2±1.8		**0.001**** S
RV diastolic function					
Normal	107	96.4	25	67.6	**<0.001***** S
Abnormal	4	3.6	12	32.4	
TR					
Negative	88	48.1	0	-	**<0.001*** S
Positive	95	51.9	62	100.0	
Severity of TR					
Trivial	60	58.3	8	12.9	**<0.001***** S
Mild	41	39.8	26	41.9	
Moderate	2	1.9	24	38.7	
Severe	0	-	4	6.5	
Velocity of TR					
Mean±SD	1.3±1.9		3.2±0.5		**<0.001**** S

***Chi square test, **Independent sample t-test, *** Fishers exact test, S=Significant, NS=Not significant.**

There was a highly significant association between PAH patients and dilated IVC (p<0.001). A highly significant association was observed between PAH patients and not collapse IVC (p<0.001). Mean PASP was significantly higher among PAH patients (p<0.001) and mean PADP was significantly higher among PAH patients (p<0.001). No significant differences were observed between PAH patients and controls regarding MPAP and PR. Mean size of pulmonary trunk was significantly higher among PAH patients (p<0.001). There was a significant association between moderate PR and PAH patients (p=0.05). All these findings were shown in table 2.

Table (2): Distribution of RV function measures according to PAH patients and controls.

Variable	Control		PAH		P
	No.	%	No.	%	
IVC size					
Normal	175	96.2	28	45.2	**<0.001*** S
Dilated	7	3.8	34	54.8	
IVC collapse					
Not collapse	12	6.6	35	56.5	**<0.001*** S
Collapse	169	93.4	27	43.5	
PASp					
Mean±SD	12.7±14.9		54.6±18.5		**<0.001**** S
PADP					
Mean±SD	1.1±4.4		5.3±14.2		**<0.001**** S
MPAP					0.4** NS

Mean±SD	0.7±3.2		1.8±7.9		
Size of pulmonary trunk					**<0.001**** S
Mean±SD	25.5±4.7		34.5±9.8		
PR					
Negative	154	84.2	47	77.0	0.2* NS
Positive	29	15.8	14	23.0	
Severity of PR					
Trace	29	78.4	4	28.6	
Mild	8	21.6	6	42.9	**0.05***** S
Moderate	0	-	4	28.6	
Severe	0	-	0	-	

***Chi square test, **Independent sample t-test, *** Fishers exact test, S=Significant, NS=Not significant.**

There was a significant association between PAH patients and positive PAAT (p=0.004). Mean PAAT time was significantly shorter for PAH patients (p<0.001). A highly significant association was observed between PAH patients and severe PAAT (p<0.001). Mean RVET was significantly lower among PAH patients (p=0.04). Mean PAAT/RVET ratio was significantly lower among PAH patients (p<0.001). There was a significant association between pericardium effusion and PAH patients (p=0.02). A highly significant association was observed between PAH patients and pulmonary vascular resistance (p<0.001). All these findings were shown in table 3.

Table (3): Distribution of pulmonary artery acceleration characteristics according to PAH patients and controls.

Variable	Control		PAH		P
	No.	%	No.	%	
PAAT					
Negative	172	95.6	3	4.8	**0.004*** S
Positive	8	4.4	59	95.2	
Time (PAAT)					**<0.001**** S
Mean±SD	123.8±20		79.9±16.2		
PAAT severity					
Normal	63	34.4	2	3.2	
Borderline	111	60.7	4	6.5	**<0.001***** S
Mild	5	2.7	26	41.9	
Severe	4	2.2	30	48.4	
RVET					**0.04**** S
Mean±SD	300.9±46.2		287.1±49.8		
PAAT/RVET					**<0.001**** S
Mean±SD	0.41±0.08		0.28±0.07		
Pericardium effusion					
Negative	166	91.2	50	80.6	**0.02***** S
Positive	16	8.8	12	19.4	
PVR					
Normal	99	95.2	17	27.4	**<0.001***** S
Abnormal (≥3 WU)	5	4.8	45	72.6	

Fishers exact test, **Independent sample t-test, * Chi square test, S=Significant, NS=Not significant**

There was a significant association between PAH patients with abnormal PVR and dilated RV (p=0.02). No significant differences were observed between PAH patients with normal PVR and those with abnormal PVR regarding based diameter, RVH, RVOT, RV systolic function S', E/E' TR, RV diastolic function and TR. Mean TAPSE was significantly lower among PAH patients with abnormal PVR (p=0.05). Mean RA size was significantly higher among PAH patients with abnormal PVR (p=0.01). A significant association was observed between PAH patients with abnormal PVR and severe TR (p=0.006). Mean velocity of TR was significantly higher among PAH patients with abnormal PVR (p<0.001). All these findings were shown in table 4.

There are inverse significant correlation between PAAT with TRV $_{max}$, PASP, and ratio of PAAT/RVET as noted in table (4), Figure 1.

Table (4): Correlation between TR and pulmonary artery measurements in PHT patients

	PAAT	
	R	**p-value**
$TR_{V\ max}$	-0.365	0.004 [S]
PASP	-0.408	0.001 [S]
RVET	-0.002	0.988
ratio of PAAT/RVET (m/sec^2)	-0.447	<0.001 [S]

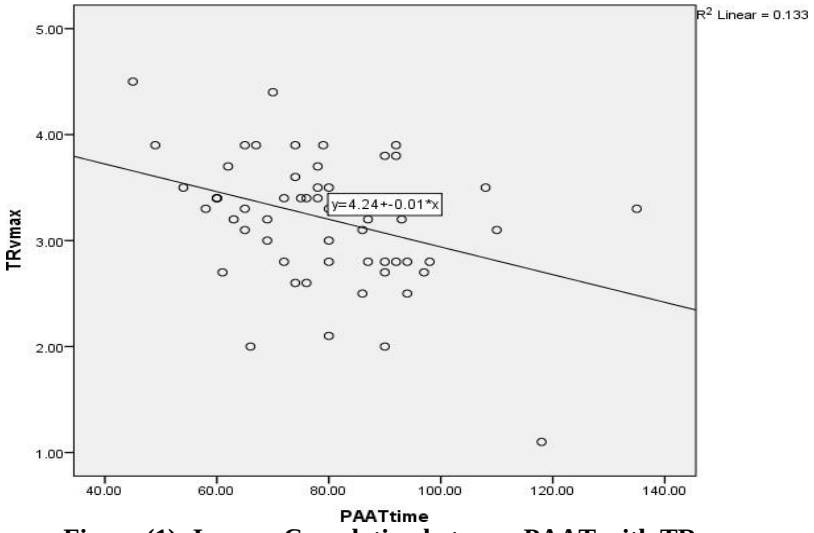

Figure (1): Inverse Correlation between PAAT with TR $_{V\ max}$

PAAT has the excellent ability as predictor of PHT better than $TR_{V\ max}$ and ratio PAAT/RVET, as illustrated in tables 5,6; Figures 2,3,4.

Table (5): diagnostic validity of various parameters as predictor of PHT by AUC

Variables	AUC	Interpretation	p-value
$TR_{V\ max}$	0.887	Good	<0.001
PAAT	0.957	Excellent	<0.001
ratio of PAAT/RVET	0.879	Good	<0.001

(AUC: Area under curve)

Table (6): diagnostic validity of various parameters as predictor of PHT by Cut point.

Variables	Cut point	SN	SP	PPV	NPV
$TR_{V\ max}$	>2.7	82.5%	85.4%	77.6%	88.9%
PAAT	≤98	93.6%	95.1%	86.6%	97.8%
ratio of PAAT/RVET	≤0.308	71.0%	96.2%	86.3%	90.7%

SN: sensitivity, SP: specificity. PPV: positive predictive value, NPV: negative predictive value

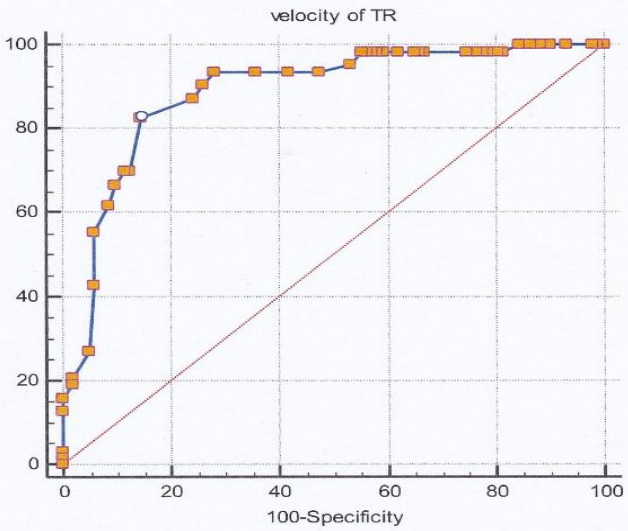

Figure 2 : ROC (Receiver operator curve) curve analysis of $TR_{V\ max}$ as predictor of PHT

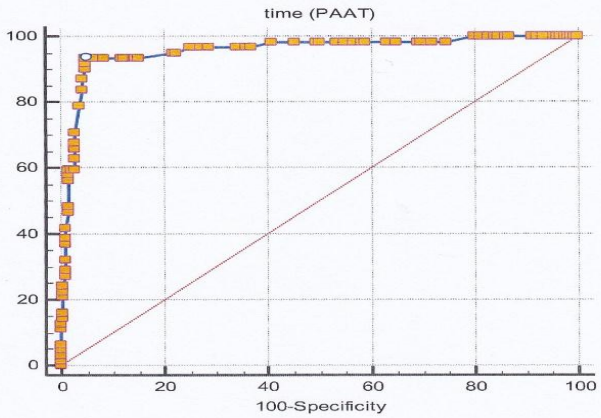

Figure 3 : ROC (Receiver operator curve) curve analysis of PAAT as predictor of PHT

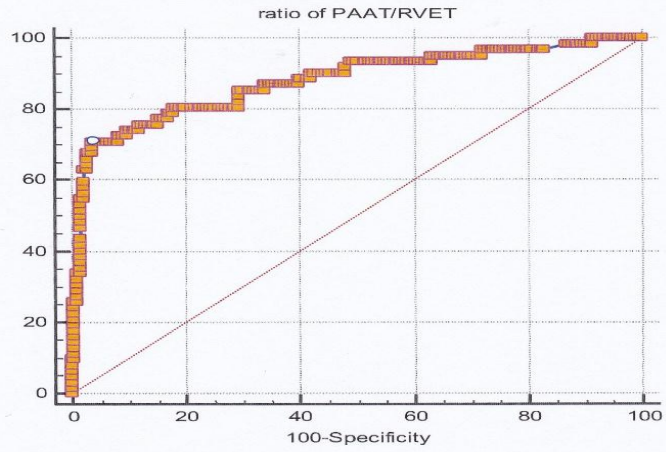

Figure 4: ROC (Receiver operator curve) curve analysis of ratio of PAAT/RVET as predictor of PHT

DISCUSSION

The traditional and most widely accepted transthoracic method for the estimation of pulmonary artery pressures[13,14] relies on the measurement of Peak Velocity of TRV[13,14] and in mild or sever TR there is no clear cut-point in the TR jet contour or envelope[17] this point; Another one in sever TR there is low velocity (< 2.8) m/s; this give underestimation of PASP; Lastly there

are a lot of errors in calculating TR max by the Bernoulli equation where there is a modified form of the equation and in calculate the RAP is often overestimated if IVC measurement is used, leading to overestimation of PASP.

Alternative techniques have been developed to assess pulmonary hemodynamics so in this study A strong, inverse correlation between PAAT and PASP. Quantification of this relationship by linear regression led to the derivation of an equation by which PAAT can be used to provide PASP values comparable with those obtained using TRV max; MPAP = 90 - (0.6 X PAAT).

Thus, TR-independent PASP that appears to perform well across a wide range of pulmonary artery pressures in a significant number of patients have mild TR or less or sever TR, rendering the reliance on TRV max for the measurement of PASP; So the PAAT for the PASP has the potential to significantly increase the overall percentage of patients. Kitabatake et al[17] showed that PAAT correlates well with MPAP as determined by cardiac catheterization. They further demonstrated that PAAT corrected for REVET, slightly strengthened the correlation between PAAT and MPAP.
In a subsequent study, Dabestani et al[18] described that same relationship as one that observed the following equation: In the current study we found similar equation to estimate mPAP in PHT Patients as.
MPAP = 90 - (0.6 X PAAT).

In contrast, Kitabatake et al[19] found that neither the MPAP nor the correction for RVET improved the accuracy of estimating the MPAP using PAAT. Together, these studies established the capacity of Doppler derived measurements of pulmonary arterial flow to provide accurate estimates of MPAP Despite these important publications, the use of PAAT in clinical practice has remained relatively limited. This is largely because the vast majority of echocardiographic reports estimate the pulmonary artery pressure relied on Peak Velocity of TRV-derived PASP.

There was a significant association between PAH patients and positive PAAT (p=0.004). Mean PAAT time was significantly shorter for PAH patients (p<0.001). A highly significant association was observed between PAH patients and PAAT (p<0.001); Mean PAAT/RVET ratio was significantly lower among PAH patients (p<0.001); A highly significant association was observed between PAH patients and pulmonary vascular resistance (p<0.001).

There was a highly significant association between PAH patients and RV & RA dilation[20,21] (p<0.001); while mean TAPSE & RV Systolic Function (S) were significantly lower among PAH patients (p<0.001). No significant differences were observed between PAH patients and controls regarding RVH (p=0.5). Mean RVOT was significantly higher among PAH patients (p<0.001); Mean E/E' TR was significantly higher among PAH patients (p=0.001). A significant association was observed between PAH patients and RV diastolic dysfunction[22] (p<0.001). There was a highly significant association between positive TR and PAH patients (p<0.001). A highly significant association was observed between PAH patients and severe TR (p<0.001). Mean velocity of TR was significantly higher among PAH patients (p<0.001). All these findings were shown in table 9A.

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