International Journal of Research Studies in Medical and Health Sciences
Volume 4, Issue 11, 2019, PP 03-10
ISSN : 2456-6373

Determining Right Atrial Pressure Assessed by Echocardiography as Compared to Cardiac Catheterization in Patients with Pulmonary Hypertension and Left Sided Heart Failure

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ABSTRACT

Background: *No standard noninvasive diagnostic method is introduced to estimate right atrial pressure (RAP), especially in those with pulmonary hypertension (PH). Due to necessity for accurate noninvasively assessment of pulmonary artery pressure (PAP), we attempted to find out more accurate echocardiographic parameters in comparison with cardiac catheterization for estimation of RAP in patients with PH who had heart failure (HF).*

Methods: *This cross-sectional study was performed on 41 patients with PH who had HF referred to our general teaching hospital in 2016. All subjects were indicated for right heart catheterization (RHC) due to suspicion of PH and left sided heart failure based on transthoracic echocardiography (TTE) findings.*

Results: *The highest correlation was revealed between RAP and some parameters determined by echocardiography including maximum inferior vena cava (IVC) size ($r = 0.75$, $p < 0.001$), maximum right atrial volume index (RAVI) ($r = 0.62$, $P<0.001$), minimum RAVI ($r = 0.61$, $P<0.001$), and right atrial (RA) area ($r = 0.59$, $p < 0.001$). When applying cutoff value of 1.95 for maximum IVC Size, we identified patients with RAP above 8 mmHg with sensitivity of 80% and specificity of 88% (Area Under Curve=0.89, $p<0.0001$).Using the multivariate linear regression analysis, maximum IVC size (beta = 5.5, $p < 0.001$, CI=3.24-7.32), maximum RAVI (beta = 0.07, $p < 0.001$,CI=1.66-4.39), and peak systolic velocity of tricuspid annulus by pulsed wave Doppler tissue imaging (TAS') (beta = -0.57, $p = 0.022$,CI= -0.90- -1.06) were main predictors of RAP. According to the results of pointed multivariate model, RAP could be measured by the following formula:*

RAP =2.04+ 5.5 Maximum IVC size + 0.07 Maximum RAVI - 0.57 TAS' ($r=0.8$, $r2=0.66$).

Conclusion: *In summary, of all diametric and functional cardiovascular parameters assessed by echocardiography, a formulaic combination of maximum IVC size, maximum RAVI and TAS' can effectively use to assess RAP in patients with HF and PH.*

Keywords: *Pulmonary Artery Pressure, Right Atrial Pressure, Echocardiography, Right Heart Catheterization, pulmonary Hypertension, Heart Failure.*

INTRODUCTION

Pulmonary Hypertension (PH) is defined as an increase in mean pulmonary arterial pressure (mPAP)>25 mmHg at rest as assessed by right heart catheterization (RHC)(1).

As the gold standard, cardiac catheterization can obtain accurate measures of right atrial pressure (RAP), however this method is limited because of its invasive nature as well as requiring hospitalization cost and side effects, thus introducing an accurate and reliable method as an acceptable tool for replacing catheterization has been under investigated within recent studies(2, 3).

There is currently controversy over whether echocardiography provides reliable estimations of pulmonary pressure .One of the most important cause of this discrepancy is difference between RAP estimation in Echocardiography and RHC(4, 5).

The main cause of inaccurate estimation of RAP in echocardiography compared to catheterization include inaccuracy of assessing RAP based on the finding of inferior vena cava(IVC),and lack of tricuspid regurgitation and thus inability to measurement of tricuspid regurgitation gradient(TRG)(4, 6).

On the basis of publications reporting, correlations with invasive measurement data, Doppler echocardiography is still recommended as the primary tool for early screening and assessment of patients with clinical suspicion of PH(7-9).

Due to necessity for accurate noninvasively assessment of PAP, we attempted to find out more accurate echocardiographic parameters in comparison with cardiac catheterization for estimation of RAP in patients with PH and HF.

Materials and Methods

This cross-sectional study was performed on 41 patients with PH and HF who referred to our general teaching hospital in 2016. All subjects were indicated for RHC due to suspicion of PH based on transthoracic echocardiography (TTE) findings. The exclusion criteria were non-sinus rhythms (atrial fibrillation, atrial flutter, or complete cardiac blocks), pulmonary valve stenosis, tricuspid stenosis, and tricuspid or pulmonary valves replacement. All patients gave written informed consent after explaining the details of study before participation. The echocardiography assessment was done on left lateral decubitus and supine position using a GE vividS5 instrument and standard echocardiographic views including parasternal, apical 4-chamber (A4C), subcostal and suprasternal views. Some cardiac cycles in each view with the flow velocity sweep speed of 100mm/s were recorded. In this study, right ventricular (RV) systolic function was assessed using Doppler TissueImaging (DTI), M-Mode, and two dimensional(2D) techniques to determine the functional parameters of peak systolic velocity of tricuspid annulus by pulsed wave DTI (TAS') ,Tricuspid annular plane systolic excursion (TAPSE), and fractional area change (FAC). TAPSE was acquired by placing an M-mode cursor through the tricuspid annulus in the A4C view and measuring the amount of longitudinal motion of the annulus at peak systole. FAC was obtained from the A4C view by tracing the RV area both in systole and diastole, RV FAC = RV end diastolic area − RV end systolic area/RV end diastolic area(10).RVdiastolic function was also assessed by measurements of the peak early (E wave) and late (A wave) diastolic filling velocities of tricuspid inflow, deceleration time of E wave (DT), tricuspid lateral annularearly diastolic velocity by DTI (e'), tricuspid lateral annular late diastolic velocity by DTI(a')and the ratio of early diastolic TV inflow to tricuspid lateral annular early velocity by DTI(tricuspid E/e'). RV diastolic function was classified as normal or impaired relaxation (E/A ratio < 0.8), pseudo normal filling (E/A ratio of 0.8 to 2.1with an E/e'ratio > 6or diastolic flow predominance in the hepatic veins) and restrictive filling (E/A ratio> 2.1 with deceleration time < 120 ms) patterns(10). The systolic function of left ventricle (LV) was assessed by determining LV ejection fraction (LVEF) using the modified Simpson rule. LV systolic function was also assessed and classified as mild, moderate, and severe dysfunction. The maximum size of IVC was also assessed in subcostal view, and viewed in its long axis, measurements should be made with the patient lying supine, because left lateral position may underestimate the maximal IVC diameter (11, 12). The maximum and minimum IVC diameters were determined after inspiration to assess IVC collapsibility index (IVCCI): ([IVC max-IVCmin]/IVC max). IVC Index (Maximum IVC size/ BSA) is also measured. Other measured parameters including hepatic vein systolic velocity (HVS), hepatic vein diastolic velocity (HVD), hepatic vein systolic velocity time integral (HVS-VTI), hepatic vein diastolic velocity time integral (HVD-VTI), Hepatic vein systolic filling fraction (SFF), which is the ratio of VTIs(HVS VTI/[HVS VTI+HVD VTI]), hepatic vein systolic reversal velocity (HVS r), hepatic vein diastolic reversal velocity (HVDr), hepatic vein systolic reversal velocity time integral (HVSr VTI), hepatic vein diastolic reversal velocity time integral (HVDr VTI). In echocardiography assessment of pulmonary artery, the parameters of PAP, TRG, and acceleration time of the pulmonary valve (PVAT) were assessed. The maximum right atrium Volume (RAV) was assessed at end-systolic time (when tricuspid was closed) and the minimum RAV was also assessed when RA was contracted at end-diastolic time in apical four chamber view and RAV was finally indexed (RAVI) to body surface area (BSA) and recorded using modified Simpson methods. Measurement of right atrial (RA) area was done in standard A4Cview.TR is graded into mild, moderate, and severe. Severe TR is defined quantitatively as an effective regurgitant orifice area (EROA) of ≥40 mm2 and a regurgitant volume of ≥45 ml according to both the European Association of Cardiovascular Imaging (EACVI) and American Society of Echocardiography (ASE) recommendations (13, 14). All subjects were assessed by cardiac catheterization immediately, within 30 minutes after echocardiography assessment. In catheterization lab, pulmonary artery systolic and diastolic pressures, RV systolic and diastolic pressures, pulmonary capillary wedge pressure(PCWP) and mean RAP were obtained and compared with the values which assessed by the echocardiography. All study protocols were approved by the research and ethical committee at Tehran University of Medical Sciences.

Results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Normality of data was analyzed using the Kolmogorov-Smirnov test. Categorical variables were compared using chi-square test. Quantitative variables were also compared with T- test or Mann- Whitney U test. The association between the parameters assessed by the two diagnostic modalities, the Pearson's or Spearman's correlation test was used. The multivariable linear regression modeling was applied to determine main determinants of RAP. For defining cutoff value of IVC, receiver operating characteristic (ROC)curve analysis was used. Statistical analysis was done by the statistical software SPSS version 16.0 for windows (SPSS Inc., Chicago, IL). P values of 0.05 or less were considered statistically significant.

RESULTS

In total, 41 consecutive patients were assessed using both modalities of echocardiography and catheterization to determine and compare RAP. The mean age of participants was 47.7±13.9years (minimum16 years, maximum 73 years) and thirty patients (73%) were male. The demographic, echocardiographic and cardiac catheterization parameters assessed in the subjects are presented in Tables 1 and 2. The main indication for RHC was Left sided heart failure in candidates for heart transplantation. The highest correlation was revealed between RHC-RAP and some parameters determined by echocardiography, including maximum IVC size ($r = 0.75$, $p < 0.001$), maximum RAVI ($r = 0.62$, $P<0.001$), minimum RAVI ($r = 0.61$, $P<0.001$), and RA area ($r = 0.59$, $p < 0.001$). When applying cutoff value of 1.95 for maximum IVC Size, we identified patients with RAP above 8 mmHg with sensitivity of 80% and specificity of 88% (Area under Curve=0.89, $p<0.0001$, Fig.1). Using the multivariate linear regression analysis, maximum IVC size (beta = 5.5, $p < 0.001$, CI=3.24-7.32), maximum RAVI (beta = 0.07, $p < 0.001$,CI=1.66-4.39), and TAS' (beta = -0.57, $p = 0.022$,CI= -0.90- -1.06) were main predictors of RAP among all variables in Table 1. According to the results of pointed multivariate model, RAP could be measured by the following formula:

RAP =2.04+ 5.5 maximum IVC Size + 0.07 maximum RAVI - 0.57 TAS' ($r=0.8$, $r2=0.66$).

Fourteen patients (34%) had severe TR. In these patients some parameters including Maximum IVC size($r=0.75$,$p=0.002$),HVS ($r=-0.56$, $p=0.03$), RV diameter($r=0.53$,$p=0.04$), minimum RAVI ($r=0.54$, $p=0.04$), and RAA($r=0.60$,$p=0.02$) had significant correlation with RAP.

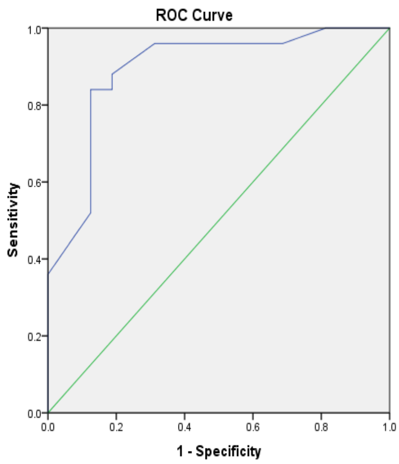

Figure1. *Sensivity and specificity of IVC for predicting RAP elevation*

Table1. *Echocardiographic data of study subjects and its correlation with RHC- RAP*

Variable	Mean	P-value	Pearson correlation
BSA(cm^2)	1.74±0.23	0.030	0.03
FAC (%)	30.1±11.6	0.022	-0.36
TAPSE (mm)	15.6±4.1	0.009	-0.40
TAS' (cm/sec)	7.1±2.2	0.017	-0.37
E TV(m/s)	0.52±0.15	0.461	0.12
A TV(m/s)	0.44±0.13	0.032	-0.35
E TV DT (msec)	171.0±57.1	0.183	-0.22
e' (cm/s)	6.8±2.9	0.944	0.01
a' (cm/s)	6.8±4.1	0.029	-0.35
E/e' TV	8.5±4.3	0.859	-0.03
IVC size (cm)	1.96±0.62	<0.001	0.75
IVC Index	1.13±0.38	<0.001	0.58
IVCCI(%)	29.7±13.2	0.017	-0.37
Hepatic vein systolic velocity(cm/s)	0.46±0.31	0.400	-0.14
Hepatic vein diastolic velocity(cm/s)	0.44±0.22	0.961	0.01
Hepatic vein systolic VTI (cm)	8.46±6.9	0.184	-0.21
Hepatic vein diastolic VTI (cm)	8.0±6.0	0.661	-0.07
Hepatic vein systolic reversal velocity (cm/s)	0.27±0.20	0.584	-0.09
Hepatic vein diastolic reversal velocity (cm/s)	0.33±0.22	0.209	0.20
Hepatic vein systolic reversal VTI (cm)	3.2±3.5	0.749	-0.05
Hepatic vein diastolic reversal VTI (cm)	4.4±4.5	0.636	0.08
Systolic filling fraction (%)	46.0±25.6	0.614	-0.08
Mean PAP (mmHg)	29.5±9.8	0.486	0.18
PAP (mmHg)	60.5±14	0.370	0.14
TRG (mmHg)	49.2±13.8	0.898	-0.02
LVEF (%)	30.7±17.4	0.032	-0.34
RV diameter (cm)	3.4±0.6	0.001	0.50
Minimum RA volume index (ml/m^2)	30.6±15.7	<0.001	0.61
Maximum RA volume index (ml/m^2)	41.2±19.5	<0.001	0.62
PV AT (msec)	97.2±25.7	0.293	-0.18
RA Area (cm^2)	22.0±7.1	<0.001	0.59
RVOT VTI (cm)	9.6±4.1	0.060	-0.30
RV diastolic function			
Normal	2 (4.9%)		
Impaired relaxation	13 (31.7%)		
Pseudo normal filling	19 (46.3%)		
Restrictive filling	7 (17.1%)		
TR severity			
Mild	3 (7.3%)		
Mild to moderate	12 (29.3%)		
Moderate	12 (29.3%)		
Severe	14 (34.1%)		
PA Doppler Notching	17 (41.5%)		

RHC, right heart catheterization ;RAP, right atrial pressure; BSA, body surface area ;FAC, fractional area change; TAPSE, Tricuspid annular plane systolic excursion;TAS' ,peak systolic velocity of tricuspid annulus by pulsed wave DTI ; E TV,peak early diastolic filling velocity of tricuspid valve; A TV , late diastolic filling velocity of tricuspid valve;E TV DT,deceleration time of E wave; e',Tricuspid lateral annular early diastolic velocity by DTI ; a', Tricuspid lateral annular late diastolic velocity by DTI; IVC, inferior vena cava; IVCCI, inferior vena cava collapsibility index; VTI, velocity time integral; PAP, pulmonary artery pressure; TRG, tricuspid regurgitation gradient; LVEF, left ventricle ejection fraction; RV, right ventricle; RA, right atrium; PVAT, pulmonary valve acceleration time; RVOT VTI, right ventricular outflow tract velocity time integral, TR, tricuspid regurgitation; PA, pulmonary artery.

Table2. *The results of RHC*

Characteristic	Value (n=41)
RA pressure (mmHg)	11.7±6.0
RV systolic pressure(mmHg)	58.0±19.9
Minimum RV diastolic pressure(mmHg)	1.73±4.8
Maximum RV diastolic pressure (mmHg)	14.2±7.1

PA systolic pressure (mmHg)	58.1±19.8
PA diastolic pressure (mmHg)	26.2±9.8
PCWP (mmHg)	24.0±8.6

RHC, right heart catheterization; RA, right atrium; RV, right ventricle;PA, pulmonary artery;PCWP, pulmonary capillary wedge pressure

Discussion

Estimation of RAP and PAP in patients with PH especially in follow up using echocardiography as noninvasive method is still a matter of debate, because of the imperfect correlation between the measurements of echocardiography and RHC(15).Increased RAP have prognostic implications for both morbidity and mortality, making the accurate assessment of RAP a determining factor in patient assessment, management, and outcomes(16-20).

In our study, we evaluated the value of different indices of echocardiography for predicting of RAP in patients with PH and HF.

In our study we try to find out more accurate echocardiographic estimation of RAP (Echo-RAP). In this regard, some echocardiography parameters including maximum IVC size, maximum RAVI and TAS' could be significantly associated with RHC-RAP and thus can be the main indicators for predicting raised RAP. In the present study, in addition to demonstrating the pointed association, we achieve a new equation for estimating Echo-RAP through three pointed echocardiographic indicators.

Several researches have evaluated the correlation between RAP and different IVC parameters (21-31).

The American Society of Echocardiography (ASE) in 2015 recommended using maximal IVC diameter 1 to 2 cm from the junction of the RA and the IVCCI to give an estimate of RAP (32).

Most, but not all,(11, 22) studies have showed good correlations between the IVCCI and RAP ($0.57 < r < 0.76$)(21, 24, 28, 31).The validity of adjusting the evaluation of IVC index is controversial. Data correlating IVC size indexed mainly to BSA are inconsistent and limited to only a few studies (22, 24, 30, 33, 34).Mintz et al found a correlation between IVC index and RAP. In our study we found significant correlation between Maximum IVC size, IVC index and IVCCI with RAP, maximum IVC size also is predictor value of RAP.

Nagueh et al showed correlation between SSF and RAP. SFF< 55% was found to be the most sensitive (86%) and specific (90%) sign of RAP > 8 mm Hg(28). Beigel et al showed that the best model for the prediction of mean RAP was 21.6 - 24 HVSFF (16). Ommen et al showed the correlation between the HVSFF and atrial reversal velocity and RAP was inverse ($r2=0.32$; $P=.002$)(29). In our study we did not found any significant correlation between HVSFF, HVS, HVD, HVS VTI, HVD VTI, HVSr VTI, HVDr VTI, HVSr velocity, HVDr velocity and RAP in PH patients. They also did not have any predictor role.

Nagueh et al found a strong correlation between RAP and thetricuspid E/e' ratio ($r = 0.75$).They found that a high E velocity combined with a low e', resulting in an E/e' ratio> 6, signals an RAP > 10 mm Hg(35).Sade et al reproduced these findings, showing a good correlation between E/e' ratio and RAP ($r = 0.7$), giving the formulation of RAP = 1.62 E/e' + 2.13, which was also applicable and a good indicator of RAP in mechanically ventilated patients (36).

In our study we could not find any significant correlation between tricuspid E/e' ratio and RAP in PH patients, but TV A velocity and TV a', had significant correlation.

We could not confirm the predictive role of some other parameters such as TV Evelocity, TV Avelocity, DT, or tricuspidE/e' ratio that were expected to be strong predictors for RAP in PH patients. A study by Patelet al in patients with heart failure did not find a good correlation between RAP and E/e' ratio either (37). The patients in our study had heart failure(HF) and were candidate for heart transplantation, we might hypothesized this index has not good correlation in HF patients with PH.Michaux et al did not found a correlation between the E/e' ratio and RA pressure in anesthetized, paralyzed, and mechanically ventilated patients either. ($r = -0.11$, $p = 0.48$) (38).

Patel et al assessed the utility of 3DE for evaluation of increased RAP, However, RA volume by 3DE was found to correlate with RAP ($r = 0.51$, $P < .001$) in patients with heart failure, in their study 3DRAVi in conjunction with IVC parameters had a high accuracy for detection of elevated RAP (37).In our study maximum RAVI and minimum RAVI significantly correlate with RAP and maximum RAVI had predictive role to RAP estimation. Nagueh et al found that qualitative and 2D echocardiographic measures of the RA (both size and volume) do not significantly correlate with RAP(28).Further advances in non-invasive methods of estimating RAP are expected, especially because 3D echocardiography offers now the possibility of estimating RA volume more precisely than previously.

Conclusion

In summary, of all diametric and functional cardiovascular parameters assessed by echocardiography, a formulaic combination of maximum IVC size, maximum RAVI and TAS' can effectively use to assess RAP in PH patients. Further assessment should be considered to validate these parameters specially by applying advanced echocardiography methods

Study Limitation

The limited number of patients was the main limitation of this study. Most of the patients in our study had severe LV systolic dysfunction that might affect our results.

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Citation: *Roya Sattarzadeh Badkoubeh et.al., "Determining Right Atrial Pressure Assessed by Echocardiography as Compared to Cardiac Catheterization in Patients with Pulmonary Hypertension and Left Sided Heart Failure", International Journal of Research Studies in Medical and Health Sciences. 2019; 4(11): 03-10.*