Original Article

ISSN: 1735-0344 *Tanaffos 2022; 21(1):78-84*

TANAFFOS

Correlation of Echocardiographic and Right Heart Catheterization Estimations of Pulmonary Artery Systolic Pressure

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Received: 23 November 2020
Accepted: 3 August 2021

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Background: Pulmonary artery pressure (PAP) is one of the most important and valuable markers in cardiovascular disease, measured by right heart catheterization (RHC) as the gold standard diagnostic modality. However, due to several limitations, such as invasiveness, lack of repeatability, and high health costs, echocardiographic estimation of PAP has been used to substitute RHC for diagnosis and monitoring of this disease. This study aimed to evaluate the correlation of echocardiographic and RHC estimations of systolic PAP.

Materials and Methods: In this study, patients, who were referred to Masih Daneshvari Hospital in Tehran, Iran, evaluated by RHC and echocardiography, were selected. The median PAP (mPAP) and systolic PAP (sPAP) for each modality, time interval between the two modalities, sex, and age were extracted from the patients' records. The RHC mPAP data was used for categorization of patients as pulmonary hypertension, while the sPAP data of two modalities was used to assess correlations and define a cut-off point by the ROC analysis. Data analysis was performed using SPSS version 24, and the level of statistical significance was less than 0.05.

Results: Seventy-six patients, including 31 males (40.8%) and 45 females (59.2%) with the mean age of 45±14 years, were evaluated in this study. The mean sPAP was 71.98±30.22 mmHg when measured by RHC and 69.75±26.03 mmHg when measured by echocardiography (correlation coefficient=0.805; P<0.001). Agreement between the two measurements was 97%, and the accuracy of echocardiography was 43%. By considering 40 mmHg as the cutoff point, the sensitivity and specificity of echocardiography were estimated at 89.2% and 42.8%, respectively. Based on the ROC analysis, the highest sensitivity (86.7%) and specificity (87.5%) were achieved with an estimated sPAP of 57.5 mmHg.

Conclusion: Echocardiography showed a good correlation and agreement with RHC in estimating sPAP; therefore, it is appropriate for screening of patients because of high sensitivity. However, for diagnosis confirmation, monitoring, and follow-up of pulmonary hypertension via echocardiography, high specificity is needed, which can be achieved by considering sPAP of 57.5 mmHg as the cutoff value for pulmonary hypertension.

Key words: Echocardiography; Right heart catheterization; Pulmonary artery pressure; Pulmonary hypertension; Screening

INTRODUCTION

Pulmonary arterial hypertension (PAH) persistently increases the pulmonary artery pressure (PAP) above 25 mmHg. It is also defined as an estimated systolic PAP (sPAP) above 36 mmHg at rest (1). It can occur in sporadic/idiopathic or familial forms and is associated with pharmacological and toxic agents, scleroderma, schistosomiasis, acquired human immunodeficiency virus (HIV) infection, portal hypertension, muscular dysfunction, left-sided heart failure, pulmonary disorders, chronic thromboembolic pulmonary hypertension, hematologic disorders (e.g., hemolytic anemia), and metabolic disorders.

PAH can increase the risk of right-sided heart enlargement, heart failure, arrhythmia, bleeding into the lungs, hemodynamic instability, and repeated hospitalization and leads to an increase in diagnostic and therapeutic costs. The one-, three-, and five-year survival rates of PAH have been estimated at 68%, 47%, and 37%, respectively. The concurrent occurrence of right-sided heart failure with PAH can increase the mortality rate considerably (2-7).

Right heart catheterization (RHC) is the gold diagnostic modality for measuring PAP, especially in patients with PAH. However, RHC has several limitations, such as invasiveness, lack of repeatability, and high health costs (8, 9). Doppler echocardiography, as a non-invasive diagnostic method, can estimate PAP, left atrial pressure, cardiac output, and pulmonary vascular resistance in a wide range of cardiovascular and pulmonary diseases (8-10). Several studies have reported that non-invasive diagnostic modalities can detect PAP elevations in the initial stages and show no significant differences with RHC.

This study aimed to evaluate the reliability and accuracy of PAP measurements by echocardiography, as a non-invasive alternative, and to compare RHC with echocardiography.

MATERIALS AND METHODS

Patient selection and study protocol

This retrospective, analytical, descriptive study was approved by the Review Board of Shahid Beheshti University of Medical Sciences (SBUM), Tehran, Iran. Patients who were assessed by both echocardiography and RHC in an interval of <1 month were selected for analysis (a two-year assessment). Census sampling method was applied, and patients with incomplete medical records were removed. There were no acute events or therapeutic changes in the two modalities. The study sample, according to the formula for correlation studies, was measured to be 76. The M-mode echocardiography and RHC were carried out by a team of four cardiologists in the pulmonary hypertension clinic of Masih Daneshvari Hospital.

Data, including age, gender, disease category, PAP measured by Doppler echocardiography, PAP measured by RHC (median PAP [mPAP] and sPAP), and time interval between the two diagnostic modalities, were extracted from the patients' files. For categorization of patients, pulmonary hypertension (PH) was defined as mPAP>25 mmHg. However, to assess agreement and correlation of two modalities, sPAP was estimated. Patients were divided into four categories: PAH, PH due to left heart disease, PH due to chronic lung disease, and PH associated with chronic thromboembolism.

Statistical analysis

Parametric data are expressed as mean and standard deviation (SD). Qualitative and classified data are presented as number and percentage. The average values were compared by paired t-test, and their correlations were evaluated by Pearson's correlation coefficient test. The Bland-Altman analysis was also performed to assess the agreement of two modalities. Moreover, the receiver operating characteristic (ROC) curve analysis was carried out to determine a new cutoff point with the highest sensitivity and specificity. Data were analyzed in SPSS

version 24 (IBM Inc., IL, USA). P-value less than 0.05 was considered statistically significant.

RESULTS

Descriptive data:

Seventy-six patients with the mean age of 45±14 years were evaluated in this study, including 31 men (40.8%). The youngest patient was 15 years old, and the oldest one was 76 years old. Based on RHC, 14 (18.4%) patients had no PH. Other patients were categorized into the following groups: 28 (36.8%) patients in group 1 with PAH; 9 (11.8%) patients in group 2 with left heart disease; 7 (9.2%) patients in group 3 with chronic pulmonary disease; and 18 (23.6%) patients in group 4 with chronic thromboemboli. No patient was categorized in group 5 (multifactorial). The mean time interval between RHC and echocardiography was 23±51 days.

Correlation and agreement of two modalities:

There was no significant difference in the mean sPAP measured by RHC and echocardiography (71.98±30.22 and 69.75±26.03 mmHg, respectively; P=0.42). The correlation coefficient between the two modalities was 0.805 (P<0.001) (Figure 1). The correlation coefficient was 0.77 for patients older than 35 years and 0.86 for patients younger than 35 years. As shown in the Bland-Altman plot in Figure 1, 97% of measurements were between two SD lines, which represents a significant agreement between echocardiography and RHC in measuring sPAP. Also, in 44 (57%) patients, the difference between the two measurements was more than 10 mmHg, which indicates an accuracy of 43%. Overestimation and underestimation were up to 32.9 and 37.7 mmHg, respectively, and the mean measurement difference was 2.4 mmHg.

Sensitivity, specificity, and optimal cutoff points:

The sensitivity and specificity of echocardiography were 89.2% and 42.8%, respectively. Therefore, it is a suitable modality for screening, but not for follow-up and monitoring of patients. It must be considered that categorization of patients into PH subgroups by the gold standard test (RHC) was based on the measured mPAP >25 mmHg, while in echocardiography, it was based on the estimated sPAP >36 mmHg. However, to substitute RHC with echocardiography for PH confirmation, high specificity is required. The best sPAP cutoff point for defining PH was determined by the ROC analysis. This analysis was carried out for all patients with PH and for some subgroups. Figures 1, 2 and table 1 present the newly defined cutoff points.

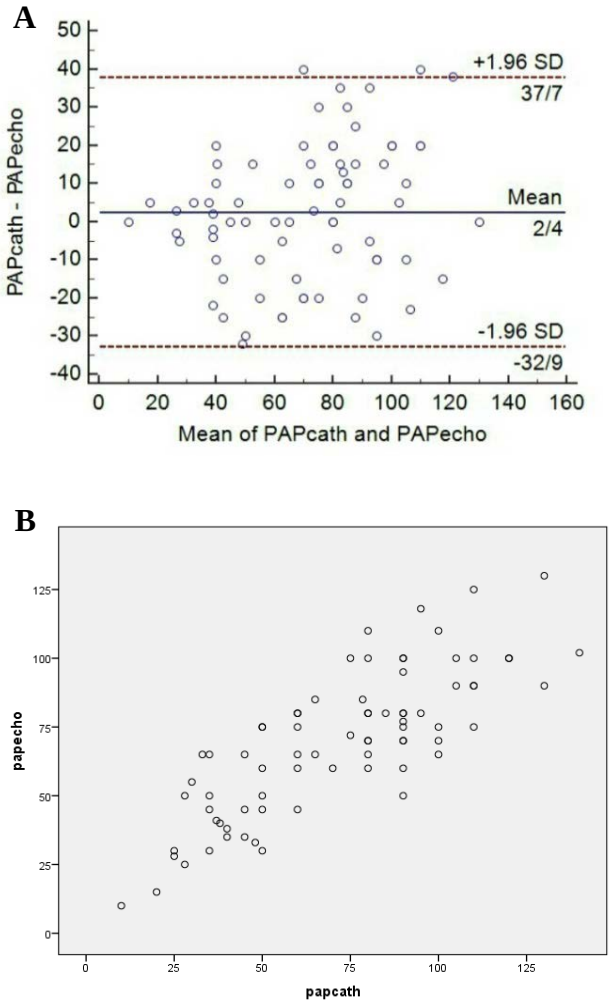

Figure 1. Linear correlation (A) and agreement (Bland-Altman representation) (B) between Doppler echocardiographic and RHC methods for systolic PAP evaluation.

Table 1. Sensitivity and specificity for defined cut off of patients' subgroups

Group	AUC	Sensitivity (%)	Specificity (%)	Cut off
All (p=0.000)	0.927	100	25	29
		86.7	87.5	57.5
Age<35(p=0.00)	0.978	100	33.3	36.5
		93	100	60
Age≥35(p=0.00)	0.890	100	100	29
		88.9	70	47.5
CTEPH(p=0.00)	0.979	100	50	32.5
		92.9	100	52.5

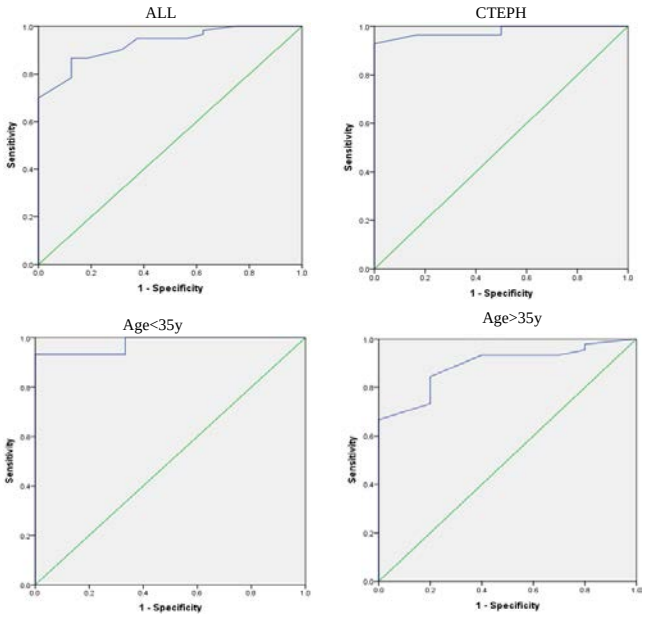

Figure 2. ROC analysis of all patients and subgroups of them

DISCUSSION

The main finding of this study is that echocardiography has a good correlation and agreement with RHC in estimating sPAP; therefore, it is suitable for screening because of its high sensitivity. However, for diagnosis confirmation, monitoring and follow-up of PH with high-specificity echocardiography is needed. The ROC analysis showed that in this study, a concentration of 57.5 mmHg was a more efficacious sPAP cutoff point than 36 mmHg.

Table 2 presents the results of several studies. In our study, the correlation coefficient of two modality measurements was 0.86. The correlation of mean measurements was 72.6 in several studies (range: 0.62-0.89). The present study reported the highest correlation of all studies, except for a study by Sohrabi et al. which indicated the high homogeneity of cases (all cases had mitral stenosis) (11). Bias, defined as the difference in the mean sPAP measured by the two modalities, was -2.4 mmHg, which represents adequate accuracy and overall overestimation. In other studies, the mean values of overestimation and underestimation were 2.16 mmHg and 5.56 mmHg, respectively, and the mean of bias was 3.6 (Table 2, 3). The Bland-Altman analysis showed 97% agreement of measurements by the two modalities, which is higher than that reported by Sohrabi et al. (11).

Table 2. Summary of several new studies on using ECHO to assess PAP

Author, year	N	Mean age (y)	Correlation	Bias (mmHg)
Lindqvist et al. 2011 (9)	30	62	0.85	6.1
Fisher et al. 2009 (22)	65	54	0.66	-0.6
Hammerstingl et al. 2012(10)	155	70.5	0.83	
Sohrabi et al. 2015 (11)	300	49.9	0.89	-1.8
Testani et al. 2010 (12)	618		0.52	10
Sun et al. 2011 (13)	102	31		6.7
Hellenkamp et al. 2018 (14)	90	64.8	0.73	
Lafitte et al. 2013 (17)	310	64.8	0.8	4
Rich et al. 2011(18)	160	53.4	0.68	2.2
El-Korashy et al. 2014 (19)	14	39.5	0.7	-6.6
Greiner et al. 2014 (20)	1695	63	0.78	-2
van Riel et al. 2017 (21)	65	62	0.62	-2.9
Ahmed et al. 2016 (23)	51	45.2	0.72	4.4
Amsallem et al. 2016 (24)	307	49.5	0.84	-0.2
D'Alto et al. 2013 (25)	152	56	0.67	-0.5

Table 3. summary of several new meta-analyses on using ECHO to assess PAP

Author, year, country	Time interval	N0. of articles	No. of total patients	Correlation	Sensitivity	Specificity
Janda,2011 Canada (15)	1984-2009	29	1998	0.7	83	72
Taleb,2013 USA (16)	1984-2009	9	929		88	56
Zhang, 2010 China (26)	2000-2009	6	736		82	68
Finkelhor,2015 USA (27)	to 2011	32	2604	0.68		

A meta-analysis by Janda et al. on 28 studies showed an overall sensitivity and specificity of 83% and 72%, respectively (15). Also, the meta-analysis by Taleb et al. on nine studies showed an overall sensitivity and specificity of 88% and 56%, respectively (16). The sensitivity and specificity of echocardiography were 89.2% and 36.3% in our study, respectively. Therefore, echocardiography had higher sensitivity, but lower specificity. To monitor, follow-up, and manage PH patients, a higher specificity is needed. Accordingly, we used the ROC analysis to define a cutoff point for the estimated sPAP (sPAP=57.5 mmHg) instead of 36 mmHg to achieve the highest specificity. This analysis suggested defining an estimated sPAP cutoff point in low-bias studies in the future.

It must be noted that categorization of patients into PH subgroups by the gold standard test (RHC) was based on the measured mPAP>25 mmHg, while in echocardiography, it was based on the estimated sPAP>36 mmHg. However, for agreement and correlation assessment of the two modalities and the ROC analysis, the sPAP data was used. Some studies suggest that echocardiography is appropriate for screening, although it cannot substitute RHC or the management decision (13,17-19). Also, some studies suggest that echocardiography is suitable for sPAP estimations (9,11,20). A third group of studies concluded that echocardiography can substitute neither RHC nor sPAP estimations (21-25).

The meta-analysis by Janda et al. in 2011 concluded that echocardiography is appropriate for functional and structural heart diseases, but not for diagnosis or monitoring of treatment (15). Moreover, the meta-analyses by Taleb et al. (16) and Zhang et al. (26) concluded that echocardiography is appropriate for PH screening, but not for definite diagnosis of PAP. Also, a meta-analysis by Finkelhor et al. concluded that echocardiography is suitable for PH assessment only for subgroup 2 (with heart disease) (27). Our study showed that by considering an sPAP cutoff point of 57.5 mmHg for PH definition, echocardiography is appropriate for both screening and substitution of RHC.

The limitations of this study include the use of multiple echocardiographic instruments, low generalizability due to the heterogeneity of patients' diseases, and selection bias in the referral pulmonary disease center. Therefore, the results of this study apply to the setting of Masih Daneshvari Hospital, and it is suggested to conduct multicenter studies with more homogeneity of the participants in the future.

CONCLUSION

Echocardiography has a good correlation and agreement with RHC in estimating sPAP; therefore, it is suitable for screening because of its high sensitivity. However, for diagnosis confirmation, monitoring and follow-up of PH via echocardiography with high specificity is needed. The ROC analysis showed that a cutoff sPAP of 57.5 mmHg is more efficacious than 36 mmHg to achieve this goal.

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