Original Article

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TANAFFOS

Simple Screening of Pulmonary Artery Hypertension Using Standard Chest X Ray: An Old Technique, New Landmark

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Background: Pulmonary artery hypertension (PAH) is difficult to diagnose because of its nonspecific symptoms. Although echocardiography can reliably and rapidly recognize the presence of pulmonary hypertension, chest X ray (CXR) is more widely used because of its availability. The objective of this study was to find a parameter, which, by changing the scale of CXR, is still useful for detection of PAH.

Materials and Methods: This case control prospective study included 100 subjects with a clinical finding of dyspnea. Additionally, thirty healthy volunteers (control group) were included in this study. Systolic pulmonary artery pressure (SPAP) was determined by echocardiography. Widening of pulmonary hilum, projection of the right side of the heart border (PRHB) and the ratio of these parameters to the chest diameter were compared to SPAP using the regression method. A cut-off point was determined for parameters that showed significant correlation.

Results: The most prevalent disease in the dyspnea group was COPD (28%). Average SPAP was 41.8±17.3 (ranging from 10 to 87 mmHg). Multivariate analysis of the covariance revealed significant correlation between SPAP, age, sex and hilar widening (r=0.44, P=0.0001) that was higher than PRHB and hilar widening + PRHB (r= 0.374. and r= 0.438, respectively). The ROC curve showed that the area under the curve was not significantly different for all parameters and the best cut-off point with sensitivity of more than 80% was as follows: hilar size more than 112 mm, PRHB more than 44 and hilum/chest ratio more than 0.44.

Conclusion: Hilum/chest ratio is the proper substitution for the hilar size in case of changing the scale of the chest X ray. Evaluation of hilar widening and PRHB could lead to identifying more subjects suffering from undiagnosed PAH.

Key words: Pulmonary artery pressure, Pulmonary artery hypertension, Echocardiography, Chest X ray, Chest roentgenogram

INTRODUCTION

Dyspnea is a common chief complaint in the outpatient department (1). Pulmonary arterial hypertension (PAH) is a rare cause of dyspnea, but it should be considered in dyspneic subjects with a normal physical exam of the chest, pulmonary function test and chest roentgenogram. Evaluation of pulmonary artery pressure requires echocardiography in routine practice (2). The American College of Chest Physicians has recommended obtaining a chest X ray (CXR) in patients who are suspected of having PAH, in order to reveal features supportive of a diagnosis of PAH (2). Matthay et al. (3) reported criteria for diagnosing patients suspected of having PAH in CXR. These criteria consist of: 1) More than 16 mm of the right descending pulmonary artery in the postero-anterior view, and 2) More than 18 mm of the left descending artery of the left lung in the lateral view. However, these criteria are problematic for patients whose descending artery cannot be visualized in CXR. For this reason we need more generalized criteria to screen suspected patients with PAH in routine CXR. New digital techniques enable the radiologists to change the scale of CXR and in these cases evaluation of the descending pulmonary artery with the aforementioned criteria is not decisive. Matthay et al. (3) reported that a close relationship did not exist between the subjective assessment of pulmonary hilum widening and pulmonary arterial pressure (PAP) (3). This idea is in contrary to a previous report which indicated that the summed horizontal measurement of the pulmonary artery from the midline to its first division is divided by the transverse chest diameter, wherein it is more than 0.38 in favor of PAP more than 45 mmHg (4). This parameter considers the age, body growth and the changing of the CXR scale to better estimate hilar enlargement. In this study we evaluated the accuracy of traditional and some new landmarks in the routine chest X ray method, which helps physicians in diagnosing and screening PAH.

MATERIALS AND METHODS

PATIENTS

One hundred consecutive subjects complaining of dyspnea referred to a subspecialty clinic of lung disease and 30 normal volunteers as the control group were entered this prospective study. All subjects with a poor echocardiographic window, infiltrative or mass lesion that obscured the landmark of hilum were excluded from this study. Additionally, the indication of CXR and echocardiography was discussed with all patients and each patient signed an informed consent form. The Ethics Committee of our university approved the study.

TECHNIQUES AND PROTOCOL

This study followed the recommendations of the Standards for Reporting of Diagnostic Accuracy (STARD) statement. A questionnaire was designed for respiratory symptoms and then completed by the subjects. A lung physical exam was carried out, which showed normal to scattered wheeze or rales. All subjects performed a baseline spirometry and lung volume pulmonary function test. CXR was taken in the postero-anterior view and standing position when the patient was in near deep inspiration.

Systolic pulmonary artery pressure (SPAP) was determined by an echocardiography instrument in the parasternal, apical, and subcostal views. SPAP was estimated by two echocardiographic methods: 1) measuring the peak systolic velocity of the tricuspid regurgitation (TR) jet with a continuous-wave spectral Doppler and adding an estimation of RA pressure (RAP) to the gradient (SPAP=[(TR Velocity)^2 × 4] + estimated right atrial pressure) (5,6). Right atrial pressure estimation was based on the degree of inferior vena cava collapse during spontaneous respiration (7). 2) Measuring the time of onset of ejection to peak systolic velocity across the RV outflow tract and pulmonary valve (5). This technique was used when there was an insufficient TR jet signal. According to a previous report, PAH was considered when SPAP was more than 35 mmHg (8).

According to individualized conditions, other complementary diagnostic tests such as the high resolution computed tomography (HRCT), methacholine challenge test, lung perfusion scan and bronchoscopy were done to confirm the final diagnosis.

MEASUREMENTS

CXR was reviewed by a radiologist and a pulmonologist who were blinded to groups and SPAP and means of measurements were used in the analysis. In the CXR of all subjects, four measurements were done: 1) Measuring the widening of hilum from the most lateral visible border of hilum to the other lateral border (Figure 1). 2) Projection of the right heart border (PRHB) that consists of the distance from the right visible border of the right side of the heart up to the midline of the thorax. 3) Ratio of hilar widening to the chest widening that consists of widening of the interior chest cage in the level of hilum (hilum / chest ratio). 4) Addition of PRHB to hilum (Hilum + PRHB). All measurements were performed in a day or two days after echocardiography.

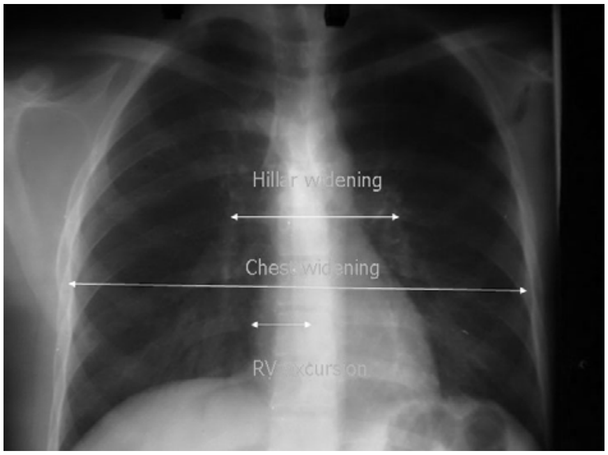

Figure 1. Outline of radiological parameters used to evaluate pulmonary artery hypertension (PRHB= Projection of right side of heart border)

STATISTICS

According to the prevalence of pulmonary artery hypertension in our region, with an alpha risk of 0.05 and power of 80%, 130 subjects were selected.

Only thirty normal volunteers agreed to enter the study and perform CXR and echocardiography; therefore, due to unequal number of case and control groups, number of cases was adjusted to obtain adequate potency as mentioned above. Normal distribution of data was checked using the Kolmogorov Smirnov test. For comparing quantitative values, the unpaired *t* test was used. Comparison of SPAP and imaging parameters between the case and control groups was done using the student *t* test. Correlations of new parameters in CXR with SPAP were tested using least square regression. SPAP was used as a gold standard for measuring the cut-off point of new radiological parameters to determine PAH. The STARD guideline was followed when designing and performing the study. EPI INFO 2003 and SPSS 14 software were used for statistical analysis. Significance was accepted at $P<0.05$.

RESULTS

Demographic Characteristics

The mean age of all subjects was 61.5±15.6 years and the male to female ratio was 5/7. The mean age in the case group (patients suffering from dyspnea) was 63.6±13.9 years, which was significantly higher than the control group (53±19.2 years) (t=2.9, P=0.004). The most prevalent diseases in the dyspnea group were COPD (28%) and bronchiectasis (15%) in the chronic lung disease group and congestive heart failure (12%) in the heart disease group. Other less common ailments included IPF, lung abscess, pulmonary thromboembolism, silicosis and tuberculosis.

Baseline Values

Average SPAP for the case and control groups was 41.8±17.3 mmHg (range 10 to 87). The comparison of mean hilar widening, PRHB and chest diameter showed that PRHB and hilar widening + PRHB diameter were significantly different between the case and control groups (Table 1).

Correlation of SPAP with radiological parameters

The regression model revealed a significant correlation between SPAP and hilar widening (r=0.336, P<0.001) that was higher than PRHB and hilar widening + PRHB (r= 0.274. and r= 0.239, respectively) (Table 2 and Figure 2). Multivariate analysis of co-variance showed that adding age and sex to the formula could improve the regression model (Table 2); again hilar widening affected by age and sex showed the best correlation with SPAP (r=0.44, P<0.001). Based on this result, a formula for calculating SPAP according to the hilar size was determined:

SPAP [Female] = -7.15 + (0.29 × hilar size) + (0.21 × age)

SPAP [Male] = -12.5 + (0.29 × hilar size) + (0.21 × age)

Accuracy of hilar widening and hilum/chest ratio for diagnosing pulmonary artery hypertension

The ROC curve was used to determine the accuracy of four evaluated radiological parameters (Figure 3). The area under the curve for all of the radiological parameters was not significantly different. The PRHB area under the curve was 0.622 (95% CI= 0.456-0.787), which was the largest followed by the hilum/chest ratio, which was 0.605 (95% CI= 0.414-0.796).

Table 3 shows the best accuracy of radiological parameters according to the cut-off point adopted from the ROC curve. Hilar widening and the hilum/chest ratio showed that the best results and the best cut-off points for them were 112 mm and 0.44 respectively. With this cut-off point PAH could be diagnosed in 82-86% of subjects.

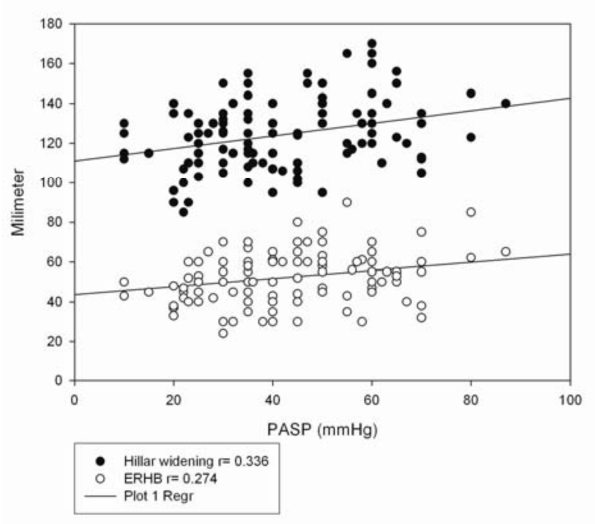

Figure 2. Regression model to evaluate the correlation between SPAP and hilar widening and the projection of the right side of the heart border (PRHB)

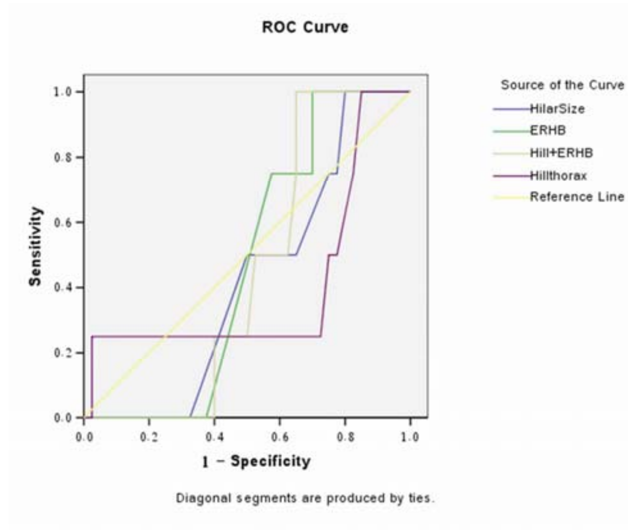

Figure 3. ROC to evaluate the accuracy of hilar widening and the projection of the right side of the heart border (PRHB) using chest X ray

Table 1. Comparison of mean and standard deviation of SPAP, hilar widening, PRHB and chest diameter in subjects suffering from dyspnea and the control group

	Dyspnea group	Control group	T test	P value
SPAP (mmHg)	47.7 ± 14.7	21.6 ± 7.7	9.14	0.0001
Hilar widening (mm)	125.6 ± 17.9	119 ± 17.5	1.7	0.08
PRHB (mm)	53.7 ± 12.7	46.2 ± 8.3	2.9	0.004
Chest widening (mm)	249.6 ± 24.6	264 ± 29.7	-1.5	0.13
Hilum/chest ratio	0.48 ± 0.04	0.46 ± 0.06	0.96	0.34
Hilum + PRHB (mm)	179 ± 26	164 ± 22.3	2.7	0.008

Table 2. Correlation of SPAP and radiological parameters on chest X- ray

	Correlation of SPAP and radiological parameters			Correlation of SPAP and radiological parameters + age + sex		
	R	R^2	P value	R	R^2	P value
Hilar widening (mm)	0.336	0.113	0.0001	0.44	0.194	0.0001
PRHB (mm)	0.274	0.075	0.002	0.374	0.14	0.002
Hilum/chest ratio	0.16	0.026	0.29	0.42	0.182	0.09
Hilum + PRHB (mm)	0.239	0.057	0.008	0.438	0.192	0.0001

Table 3. Accuracy of the new cut-off point for radiological parameters to evaluate PAH according to the SPAP gold standard

	Hilum size = 112 mm	Hilum/chest ratio= 0.44	PRHB=44 mm	Hilum +PRHB=158 mm
Sensitivity	82%	86%	75%	82%
Specificity	31%	44%	42%	31%
PPV	78%	85%	40%	78%
NPV	38%	33%	75%	38%

PPV= positive predicted value, NPV= negative predicted value

DISCUSSION

In this study the diameter of pulmonary hilum (hilar widening), right ventricular projection and the ratio of these parameters to the chest diameter were compared to SPAP. Overall results of this study show that pulmonary hilar widening is the best parameter to predict pulmonary artery hypertension. The cut-off point for diagnosing pulmonary artery hypertension was 112 mm for hilar widening and 0.44 for the hilum / chest ratio. Hence, the hilum / chest ratio is the preferred parameter to be used in case of changing the scale of CXR or for children. Moreover, age and sex increase the value of this parameter and so we could calculate the SPAP by the previously mentioned formula.

Chest radiography is a simple and cheap diagnostic method that is available globally and thus this technique is considered a useful tool to screen patients with elevated pulmonary arterial hypertension (9). Efficacy and accuracy of this method have been evaluated in a study done on pulmonary artery hypertension by measuring the right and left descending pulmonary artery (RDPA and LDPA respectively) diameter (3). In another study, the quality of chest radiographs decreased the accuracy of the parameter by 64% (10). However, the diameter of hilum is always obvious unless it is covered by opacity. Matthay et al. (3) quantitatively classified the enlargement of the main pulmonary artery into three stages in COPD patients and they did not find a close relationship between the subjective main pulmonary enlargement and absolute mean pulmonary pressure. The sensitivity, specificity and overall accuracy of the main pulmonary enlargement in this study were 72%, 93% and 77%, respectively. The author concluded that the accuracy of this method is lower than measuring RDPA and LDPA. Chetty et al. (11) repeated this study one year later in COPD patients. They evaluated one new index: hilar thoracic index and the hilar width with the quantitative measurement. This study showed that the Hilar Thoracic Index had the best correlation with pulmonary artery pressure; sensitivity and specificity of this index with a cut-off point of 0.36 was 95% and 100%, respectively. On the other hand, the sensitivity and specificity of RDPA with a cut-off point of 20 mm were 95% and 79%, respectively. Recently, Lin et al. evaluated the RDPA parameter in PAH, but their study did not find any satisfactory RDPA cut-off point for predicting PAH (12).

In our study, the case group consisted of a heterogeneous group of patients complaining of dyspnea. Final diagnosis varied from chronic heart failure or chronic lung disease to leukemia. The sample size was larger, a control group was considered and new statistical methods were used. Therefore, this study is more generalized than the study by Matthay et al. (3) and Chetty et al. (10).

Regression coefficient between the SPAP and hilar diameter was significant, but admixing sex and age by the multiple analysis of the co-variance method improved the model insomuch that a formula to calculate SPAP from hilar size was created, although the main aim of this article was not to measure SPAP from CXR. The most important application of this study is directed at subjects suffering from pulmonary vascular disorders, who have been referred for primary medical care. If the physical exam and initial evaluation such as spirometry and chest X ray abnormalities are not conclusive, radiological parameters discussed in this study such as hilar size more than 112 mm, PRHB more than 44 mm and hilum / chest ratio more than 0.44 could help the physician in deciding to order echocardiography (the number is easy to memorize). Although hilar size alone has shown the best result, using the hilum / chest ratio is the best method intended for controlling the effect of age, sex, ethnicity and minimizing the CXR. Generally these parameters have shown similar results and one of them (according to the findings in CXR) is sufficient for decision making. These parameters may help in the early detection of subjects suffering from primary pulmonary hypertension in the asymptomatic stage, when treatment is more effective. Evaluations of these parameters are so easy that the inter-observer variation would be negligible.

In conclusion, the results of the present study have shown that the evaluation of hilar widening, hilum / chest ratio and the projection of the right heart border in CXR are valuable parameters to diagnose and screen PAH.

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