Egyptian Journal of Chest Diseases and Tuberculosis (2014) **63**, 419–422

The Egyptian Society of Chest Diseases and Tuberculosis

Egyptian Journal of Chest Diseases and Tuberculosis

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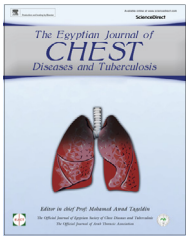

ORIGINAL ARTICLE

Echocardiography versus right heart catheterization in class I pulmonary hypertension

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Received 10 September 2013; accepted 9 December 2013
Available online 2 January 2014

KEYWORDS

Pulmonary arterial hypertension;
Echocardiography;
Swan-Ganz catheter

Abstract It has been agreed that pulmonary hypertension should be determined by right heart catheterization. However, being invasive and refused by many patients, echocardiography was thought to be a reasonable substitute to determine a solid diagnosis of pulmonary arterial hypertension. So fourteen patients with pulmonary arterial hypertension (class I) were studied by estimating pulmonary artery systolic pressure by both transthoracic echocardiography and right heart catheterization using Swan-Ganz catheter. The patients were 4 males and 10 females with mean ages about 46.25 ± 23.33 in males and 36.8 ± 11.63 in females (total mean age was about 39.5 ± 15.46 years). Mean value of the Echo SPAP: 82.79 + 34.25 mmHg, however in the RHC SPAP 76.21 + 24.97.

Comparing both clinical procedures via the Altman and Bland statistical method showed discrepancy between both procedures. Results showed that the 6MWD (mean + SD 262.64 ± 85.98) is significantly correlated with the mean pulmonary arterial pressure only.

Conclusion: Echocardiography cannot be reliable alone in the proper decision making of diagnosis and management of pulmonary arterial hypertension.

Introduction

Pulmonary hypertension is an hemodynamic and pathophysiologic state that can be found in multiple clinical conditions [1]. Definitive diagnosis of pulmonary hypertension (PH) requires an elevated mean pulmonary arterial pressure of 25 mmHg at rest measured by right heart catheterization (RHC) [2]. Pulmonary hypertension was classified into five classes according to the ESC/ERS 2009 [2], based on the Dana point classification 2008 [3]. Class1; pulmonary arterial hypertension, included the following entities, (Idiopathic, Heritable (Bone morphogenic protein receptor 2, activin receptor like Kinase 1, endoglin, Unknown), drugs and toxins induced, associated with (APAH) (Connective tissue diseases, human immunodeficiency virus infection, portal hypertension,

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

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congenital heart disease, schistosomiasis, chronic hemolytic anemia), persistent pulmonary hypertension of the newborn).

In class 1 PAH, the core of the medical problem is the pulmonary artery itself [4], where the different entities shared the hemodynamic profile of pre-capillary pulmonary hypertension but presented a completely distinct clinical course [5]. Moreover, class 1 PAH could be treated by specific drug therapy targeting the pulmonary circulation with different drugs that were approved for use worldwide [6]. However, PAH was considered a rare disorder, with an estimated prevalence of 15–50 patients per 1 million of the population in Europe [7], because the clinical picture was subtle [4]. This group was thought to be under recognized and under diagnosed [8].

According to the definition of the ESC/ERS guidelines 2009, right heart catheterization was needed for accurate diagnosis of the pulmonary artery pressure [3]. Although RHC is now a relatively safe procedure, it is invasive and impractical to perform in patients for whom it is not clearly indicated. Consequently there is a clear need for noninvasive procedures that aid diagnosis and allow identification of patients for whom diagnostic RHC is warranted, because of a high likelihood of the existence of PH [9].

Transthoracic echocardiography (TTE) is one such tool and is widely available and safe. By using transthoracic echocardiography, assessment of pulmonary artery systolic pressure could be done by measuring maximum tricuspid regurgitation velocity and applying modified Bernoulli equation to convert these values into pressure values; PASP = $(Vmax^2 \times 4)$ + RAP [10].

Rationale

The study at hand aimed at evaluation of whether echocardiography can be considered alone as a reliable tool for diagnosis and follow up of pulmonary arterial hypertension without the need for performing right heart catheterization.

Methodology

Twenty-five patients were provisionally diagnosed as pulmonary hypertension class I according to the ESC/ERS 2009, for proof by performing right heart catheterization. However fourteen patients only consented for performing right heart catheter, so the actual study population was 14 subjects.

For all, history taking, clinical examination, 6 min walk distance, arterial blood gases, pulmonary function test (spirometry) and transthoracic echocardiography were done. Pulmonary artery systolic pressure was measured by both echocardiography and right heart catheter. Plain chest X-ray was done post catheterization to detect any complications.

Right heart catheterization was performed by using the Swan-Ganz catheter, multilumen, balloon tipped, 110 cm long, done under complete aseptic precautions. The route of entry was via the right internal jugular vein.

Putting in consideration, the exclusion criteria for performing that right heart catheter: Tricuspid or pulmonary valve mechanical prosthesis, right heart mass (thrombus and/or tumor) and tricuspid or pulmonary valve endocarditis [11].

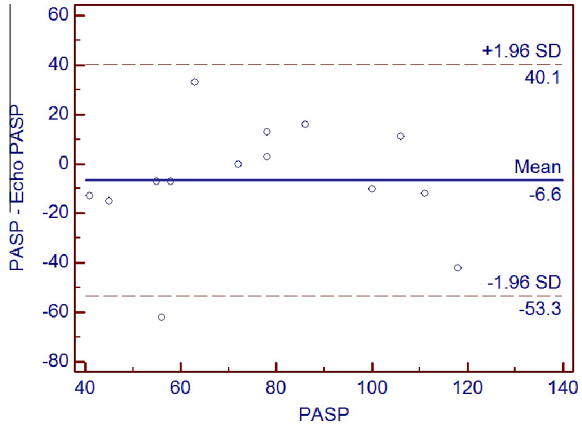

Figure 1 Comparison of the difference in pulmonary artery systolic pressure estimated by RHC and Doppler echocardiography against the mean of the two values "method of Altman and Bland".

Results

The study population included 14 patients, 4 males and 10 females, with mean age 39.5 ± 15.46 years.

Study population echocardiographic mean EF: 69.79 ± 4.32, no clinical manifestations of left side heart failure.

Right heart catheterization parameters

Mean value of the mean PAP: 46.21 ± 14.65 mmHg.

PCWP: less than 12 mmHg in all cases except 5 cases with the diagnosis of bilharzial PAH and pulmonary aneurysmal dilatation, where the wedging procedure failed.

Mean 6 MWD: 262.64 ± 85.98 (< 300 m), 10 patients below 300 m, and 4 patients above 300 m.

The plot showed that 1 case (7%) was out of standard deviation, and 6 cases (43%), showed difference more than 10 mmHg between both procedures (see Fig. 1 and Table 4).

Discussion

This study included 25 patients provisionally diagnosed as having pulmonary hypertension class 1 according to the ESC/ERS, 2009 [2], waiting for confirmation by performing right heart catheter. However, 11 patients refused performing the RHC, thus the study population was actually 14 sub-classified as idiopathic, familial, and associated (Table 1). Starting the drug therapy for those who refused performing the RHC was an issue of debate, which raises the question of reliability on echocardiography in determining the need to start specific drug therapy.

The study population was 14 divided into 4 males and 10 females, a ratio that was almost known all over the world, twice in females than males [12]. The reason for the higher female prevalence in PAH was never clarified: some hypotheses

Table 1 Subclasses of the cases.

Diagnosis	Idiopathic	Associated	Familial
Number	5	8 (3 SLE and 5 Bilharzial)	1

Table 2 Comparison between the study subjects divided according to gender in the other parameters.

	Males (n = 4)	Females (n = 10)	Independent samples t test	
			t	p
Age	46.25 ± 23.33	36.8 ± 11.63	−1.04	0.32
Echo E.F	69.25 ± 0.96	70 ± 5.14	0.28	0.78
Echo PASP	76.75 ± 22.41	85.2 ± 38.78	0.40	0.69
RHC PASP	79.75 ± 18.84	74.8 ± 27.84	−0.32	0.75
mPAP	49.5 ± 15	44.9 ± 15.11	−0.52	0.62
6 MWD	305 ± 78.73	245.7 ± 86.57	−1.18	0.26
PaO2	69.5 ± 7.59	47.4 ± 13.66	−3.01	0.011**
SaO_2	93.75 ± 2.63	78.1 ± 16.59	−1.83	0.092

E.F, ejection fraction; PASP, pulmonary artery systolic pressure; RHC, right heart catheter; mPAP, mean pulmonary artery pressure as calculated from RHC; 6 MWD, 6 min walk distance; PaO_2, arterial oxygen tension; SaO_2, oxygen saturation.
** Significant difference at $p < 0.5$.

involve the role of sex hormones (estrogens), autoimmunity, or an X-linked locus in disease predisposition [13].

The mean age of study population was 39.5 ± 15.46 which was congruent to the findings in different studies; 36.4 ± 15 years [14] and 37 years [15] While others stated that the mean age was 53 ± 14 years [13,16].

The mean ejection fraction for the cases was within the normal range 69.79 ± 4.32. The known normal ranges 55–70% and might even reach up to 77% [17].

The results showed that the mean 6 MWD of the study population was <300 m, which signified poor prognosis [2] and indicated that most of the patients present in late stages of the disease; a finding that was also mentioned in other studies [12].

Although there was no statistical significance between the age difference in males and females, yet the mean age for affected males was 46.25 ± 23.33 years while that for females was 36.8 ± 11.63 years (Table 2). It was assumed that females with pulmonary hypertension were of younger age at presentation than males due to the fact that testosterone actually has pulmonary vasodilatory effect, thus offering a less severe form of disease in men [18]. Some studies, demonstrated that estrogen exerts beneficial effects on the pulmonary vasculature especially on treatment response [12]. However, it seems to contradict the female predominance that is observed in PAH. Thus, estrogen can be accused of being a cornerstone in the pathobiology of the PAH, what is called ''estrogen paradox'' [19]; especially if estrogen was used as a replacement therapy

Table 3 Correlation between different subjects' parameters (n = 14).

		m PAP	6 MWD
Echo E.F	P. correlation	0.118	0.268
	Sig. (2-tailed)	0.689	0.354
Echo PASP	P. correlation	0.726**	−0.488
	Sig. (2-tailed)	0.003**	0.077
RHC PASP	P. correlation	0.836**	−0.407
	Sig. (2-tailed)	0.0001**	0.149
mPAP	P. correlation	–	−0.58*
	Sig. (2-tailed)	–	0.029*

* Significant correlation at $p < 0.05$.
** Significant correlation at $p < 0.01$.

Table 4 Correlation between Echo PASP and right heart catheterization PASP in the study subjects (n = 14).

Echo PASP	RHC PASP	Pearson correlation test	
		Pearson correlation	p value
82.79 ± 34.25	76.21 ± 24.97	0.718268	0.003809**

** Significant correlation at $p < 0.01$.

[20]. The hemodynamic changes that occur during gestation, labor and delivery, are poorly tolerated by PAH patients: this may be reflected in earlier clinical deterioration [12]. Tofovic hypothesized that unbalanced estradiol metabolism (i.e., a shift toward the 16-hydroxylation pathway and/or reduced activity of the 2-hydroxylation pathway, corresponding to elevated estradiol and decreased methodroxy estradiol levels) may be of influence in increasing the risk of PAH and/or exacerbates the progression of disease [21].

The Altman and Bland statistical method was performed to evaluate the agreement between RHC and echocardiography measurements of PASP, which showed disagreement in 43% of the cases, with pressure difference more than 10 mmHg, despite the presence of positive correlation between them (r 0.7, p 0.003). These findings were in concordant with Rich and Coworkers, who found that echocardiography estimates of PASP were determined to be inaccurate in 50.6% of patients despite the presence of moderate correlation between echocardiography and RHC measurements of PASP (r 0.71, $p < .01$) [22].

6 MWD was found to have a high statistical significant correlation with mPAP and not with PASP whether by echo or by RHC (Table 3). 6 MWD is used in the follow up of PAH patients and considered to be an important prognostic determinant [23]. It is used as a form of submaximal exercise testing that is simple, reproducible, safe, inexpensive, and applicable to everyday activities, sensitive to therapeutic interventions and of prognostic relevance [24]. The PaO_2 was found to be significantly lower in females than males (Table 2), which is mostly due to the earlier clinical deterioration [12]. Oxygen tension affection had been regarded as a cause rather than a result in the pathophysiology of pulmonary arterial hypertension, mainly due to the hypoxic vasoconstriction response that appears in pulmonary vasculature [25]. However from the results in the study at hand, hypoxia and pulmonary arterial

hypertension showed a mutual affection that might be related to the changes in pulmonary artery endothelium [26].

Conclusion

RHC is a procedure for diagnosis and follow up of the cases of PAP, while echo is a simple non-invasive way for screening of suspected patients. Thus, one cannot rely on echo alone for the start of specific drug therapy for PAH.

Conflict of interest

None.

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