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Regular Article

Accuracy of chest radiography in predicting pulmonary hypertension: A case-control study

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ABSTRACT

Objective: To assess the accuracy of chest radiography (CXR) in predicting pulmonary hypertension (PH).
Methods: We studied 108 consecutive patients with suspected PH who underwent right heart catheterization (RHC). All were PH treatment naives. Hemodynamic criteria included a mean pulmonary artery pressure >25 mmHg at rest, and a mean pulmonary wedge pressure <15 mmHg. Postero-anterior and lateral CXR were obtained shortly before RHC. To avoid a selection bias which could be introduced by examining only patients with suspected PH, we included in the analysis the CXR of 454 additional patients with different diagnosis: 57 with left heart failure (LHF) and pulmonary venous hypertension at RHC, 197 with chronic obstructive pulmonary disease, and 200 non-obstructed controls. CXR were examined independently by 4 raters, who were blinded to clinical, hemodynamic, and spirometric data. The diagnosis of PH was made if a prominent main pulmonary artery was associated with anyone of: isolated enlargement of right ventricle, right descending pulmonary artery >16 mm in diameter, pruning of peripheral pulmonary vessels.
Results: Eighty-two patients had PH confirmed at RHC. Weighted sensitivity of CXR was 96.9% (95% confidence interval, 94.9 to 98.2%), and weighted specificity 99.8% (95% confidence interval, 99.6 to 99.9%). By considering the 165 patients who underwent RHC, weighted sensitivity of CXR was unchanged, and weighted specificity decreased to 99.1%. None of the patients with PH were misclassified as having LHF, and vice versa.
Conclusions: CXR is accurate in predicting PH. It may aid clinicians in selecting patients with suspected PH for hemodynamic ascertainment.

Introduction

Pulmonary hypertension (PH), in its "pre-capillary" form, is a rare but devastating disorder that carries high morbidity, and mortality [1,2]. Clinical symptoms and signs are nonspecific, and the definitive diagnosis rests on the hemodynamic documentation of a mean pulmonary artery pressure exceeding 25 mmHg at rest with a normal pulmonary artery wedge pressure [1,2].

The suspicion of the disease is often raised by the incidental finding of elevated pulmonary artery systolic pressure at Doppler echocardiography (DE). Even though DE is a valuable screening method, estimates of pulmonary artery pressure are frequently inaccurate [3,4].

Chest radiography is still ubiquitous in clinical practice, and will likely remain so for quite some time for it is inexpensive and minimally invasive in terms of radiation exposure [5]. The radiologic abnormalities associated with PH have been described [6–10], but very few studies investigated on the predictive accuracy of chest radiography [11–13].

The present study was designed to assess the sensitivity and specificity of chest radiography in the diagnosis of pre-capillary PH. We examined postero-anterior and lateral chest radiographs of 108 consecutive patients with clinically suspected PH who underwent right heart catheterization (RHC). To avoid a selection bias, we included in the analysis the chest radiographs of 454 additional individuals: 57 with chronic left heart failure and pulmonary venous hypertension, 197 with chronic obstructive pulmonary disease, and 200 with normal lung function.

Materials and Methods

Ethics Statement

The study was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki), and was approved by the institutional review board (Comitato Etico, Azienda

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Ospedaliero Universitaria Pisana). Before entering the study, the patients provided an informed written consent.

Sample

The sample comprised 108 consecutive patients with suspected PH, who were referred to the CNR Institute of Clinical Physiology and Tuscany Foundation "G. Monasterio", Pisa, Italy, between January 1, 2006 and December 31, 2011. The above institutions serve as referral center for the diagnosis and treatment of PH. The suspicion of the disease had been raised by the referring physicians on the basis of relevant presenting symptoms (primarily unexplained dyspnea on exertion), risk factor assessment, or elevated pulmonary artery systolic pressure at DE. None of the patients was receiving any medication for PH at the time of study entry.

To avoid a selection bias which could be introduced by examining only the chest radiographs of patients with suspected PH, we included in the analysis the chest radiographs of 454 additional subjects from two distinct groups.

The first consisted of 57 patients with left heart failure (LHF) who were evaluated at the above institutions between January 1, 2002 and December 31, 2008. The diagnosis of LHF was based on the Framingham criteria [14], and the finding of a left ventricular ejection fraction ≤40% at echocardiography. The 57 patients underwent RHC as part of their clinical evaluation.

The second group included 397 subjects of whom 197 had chronic obstructive pulmonary disease (COPD), and 200 were non-obstructed controls. They were evaluated at the CNR Institute of Clinical Physiology from November 1, 2001 through October 31, 2003 as part of a larger cohort enrolled in a European case-control study aimed at assessing genetic susceptibility to the development of COPD [15]. The criteria for case recruitment were: (a) firm clinical diagnosis of stable COPD; (b) airflow obstruction as indicated by a post-bronchodilator ratio of forced expiratory volume in one second over forced vital capacity (FEV_1/FVC) <0.7 and FEV_1 ≤70% of the predicted value; (c) smoking history ≥20 pack-years. Patients were excluded if they had a diagnosis of asthma, chronic lung disorders other than COPD, active lung cancer, or if they had had a clinically confirmed acute exacerbation in the 4 weeks preceding the study entry. By design, the controls were recruited to match the COPD patients on age, gender, and smoking history. The criteria for control recruitment were: (a) FEV_1/FVC ratio >0.7; (b) both FVC and FEV_1 >80% of predicted value; (c) no history of chronic lung disease, and no acute respiratory infection in the 4 weeks preceding the study entry. Postero-anterior and lateral chest radiographs were taken on the day of recruitment. The 397 individuals were followed up for a median time of 9.9 years (interquartile range, 8.6 to 10.7 years), and none of them developed PH. This comes of no surprise given that PH is a very rare disorder.

Table 1
Reading table for chest radiographs.

1. Heart
Prominence of the main pulmonary artery
Yes
No
Enlargement of the right ventricle
Yes
No
Enlargement of the left ventricle
Yes
No
2. Pulmonary vessels
Right descending pulmonary artery >16 mm in diameter
Yes
No
Pruning of the peripheral vessels
Yes
No
Dilated upper lobe vessels
Yes
No
3. Lung parenchyma and pleura
Interstitial edema
Yes
No
Emphysema
Yes
No
Fibrosis
Yes
No
Pleural effusion
Yes
No

Table 2
Baseline characteristics of 108 patients with suspected pulmonary hypertension.

Characteristic	PH (n = 82)		No PH (n = 26)	
Age, years	66	(57-74)	72	(68-75)
Male sex	32	(39)	9	(35)
MRAP, mmHg	4	(2-7)	2	(2-4)
MPAP, mmHg	41	(33-49)	17	(13-21)
MPWP, mmHg	6	(4-9)	6	(5-8)
CI, L/min/m^2	2.6	(2.2-3.1)	3.0	(2.6-3.5)
PVR, mmHg/L/min/m^2	12.5	(9.6-16.2)	3.1	(2.3-4.4)

Data are numbers (%), or medians (interquartile range).
PH = pulmonary hypertension (pre-capillary).
MRAP = mean right atrial pressure.
MPAP = mean pulmonary artery pressure.
MPWP = mean pulmonary wedge pressure.
CI = cardiac index (cardiac output/body surface area).
PVR = pulmonary vascular resistance = MPAP-MPWP/CI.

Study Protocol

Right Heart Catheterization

RHC was performed by experienced physicians (BF, CM) with the patient at rest and without sedation. End-expiratory pressure measurements were taken at the level of the right atrium, right ventricle, and pulmonary artery over at least five cardiac cycles. Cardiac output was measured in triplicate by the thermodilution method, and the average value calculated. PH was diagnosed if the mean pulmonary artery pressure (MPAP) at rest was >25 mmHg, and the mean pulmonary wedge pressure (MPWP) <15 mmHg [1,2]. Oxymetry was used to detect left-to-right shunting.

Chest Radiography

Postero-anterior and lateral digital chest radiographs were obtained at a standard 2-m focus-to-detector distance with the patients upright,

Table 3
Baseline characteristics of 57 patients with left heart failure.

Age, years	67	(57-73)
Male sex	43	(75)
COPD comorbidity	17	(30)
MRAP, mmHg	7	(5-10)
MPAP, mmHg	33	(31-40)
MPWP, mmHg	20	(18-23)
CI, L/min/m^2	2.4	(2.0-2.9)
PVR, mmHg/L/min/m^2	5.8	(4.3-7.9)

Data are numbers (%), or medians (interquartile range).
COPD = chronic obstructive pulmonary disease.
For other abbreviations, see Table 2.