Al-Azhar Med. J. *July, 2015, 191-199*
DOI: 10.12816/0018612 ***Issues_title_English:*** 2015 Vol.44 Issue 2-3

ROLE OF ECHOCARDIOGRAPHY IN ASSESSMENT OF PULMONARY HYPERTENSION SECONDARY TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE

By

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ABSTRACT

Background: Echocardiography is readily available noninvasive technique that can be used to asses pulmonary artery pressure in chronic obstructive pulmonary disease (COPD).

Objective: Evaluation of the role of echocardiography in diagnosis and assessment of pulmonary hypertension (PH) in COPD patients in different stages of severity, stable condition and in exacerbation.

Patients and methods: This study included 80 patients with COPD admitted in chest department of Al-Azhar University Hospital (Damietta), during the period from June 2011 to June 2013. Patients were divided into four equal groups. The first group included those with stable COPD; the second group included patients with COPD exacerbation; the third group included cigarette smokers without manifestations of COPD; and the fourth group included healthy non-smokers. All subjects of the present work were exposed to full history taking, detailed clinical examination and laboratory investigations (arterial blood gases, chest X-ray, electrocardiogram, pulmonary function tests, spirometry (FEV1, FVC, FEV1/ FVC%) and Doppler echocardiography.

Results: No significant difference between groups as regard to age, while there was significant increase of smoking in COPD cases when compared to healthy controls. There were significant increase of smoking in both groups A and B when compared to group C. In addition, there were significant increase of peak tricuspid jet velocity; intermediate tricuspid jet velocity and right atrium pressure in group B and group (A) when compared to group C and group D. Similarly, there were significant increase of calculated pulmonary arterial pressure in groups B and A when compared to groups C and D. The overall prevalence of pulmonary arterial pressure (PAP) in COPD cases was 65.0% with significant increase of both prevalence and severity of PAP in group B when compared to group A. There were significant, inverse correlations between pulmonary artery pressure on one side and both SaO2, PaO2, and FEV1/FVC the other side. On the other hand, there was significant positive correlations between PAP from one side, and PaCO2, hemoglobin concentration, WBCs, peak intermediate tricuspid jet velocity and right atrium pressure on the other side.

Conclusion: The results of the present study showed an association of pulmonary hypertension in 65% of COPD cases, and this reflected impact of clinical, physiologic and pathologic changes of the disease on PAP. It is advisable to screen all COPD patients for pulmonary hypertension (PH) using ECHO and to control pulmonary artery pressure in those cases as a line of treatment of COPD itself.

Keywords: Echocardiography; pulmonary hypertension; chronic obstructive pulmonary disease.

INTRODUCTION

Mild to moderate pulmonary hypertension is a common complication of chronic obstructive pulmonary disease (COPD) and is associated with increased risk of exacerbation and decreased survival **(Chaouat et al., 2008 and Fossati et al.,**

2014). Pulmonary hypertension with COPD usually worsens during exercise, sleep and exacerbation **(Kessler et al., 2008).**

Pulmonary vascular remodeling in COPD is the main cause of increase in pulmonary artery pressure and is thought to results from the combined effects of hypoxia, inflammation and loss of capillaries in severe emphysema **(Barbera and Blanco, 2009).** Echocardiography is readily available noninvasive technique that can be used to asses pulmonary artery pressure in COPD **(Fayngersh et al., 2011).** Echocardiography is an important modality in noninvasive assessment of pulmonary hypertension and has been used to screen for the disease, determine right and left heart structure and function, and assess response to therapy in persons with pulmonary hypertension **(Simonneau et al., 2009).** Current guidelines recommend echocardiography to estimate pulmonary artery pressure and to assess right atrial enlargement, right ventricular enlargement, pericardial effusion, left ventricular systolic or diastolic dysfunction, left atrial or ventricular enlargement and valvular heart disease as part of initial evaluation of a patient suspected of having PH **(McGoon et al., 2010).** Echocardiography is particularly helpful in the assessment and long-term management of patients with pulmonary hypertension **(Fisher et al., 2009).**

The aim of this study was to evaluate the role of echocardiography in diagnosis and assessment of PH in COPD patients in different stages of severity, stable condition and in exacerbation, and to evaluate the relationship between PH and clinical, spirometric and demographic data.

SUBJECTS AND METHODS

This study included 80 patients with chronic obstructive pulmonary diseases admitted in chest department of Al-Azhar University Hospital (Damietta); during the period from June 2011 to June 2013. Patients were divided into four equal groups; ***The first group*** included those with stable COPD; ***the second group*** included patients with COPD exacerbation; the third group included ***cigarette smokers*** without manifestations of COPD; and the fourth group included healthy non-smokers normal persons.

Exclusion criteria: Patients with one or more of the following conditions were excluded: Ischemic heart diseases, valvular heart diseases, left ventricular heart failure, venous thromboembolic diseases, primary pulmonary hypertension, chronic pulmonary diseases other than COPD, e.g. pulmonary fibrosis, bronchiectasis and poor echocardiographic visualization.

All subjects of the present work were exposed to full history taking, detailed clinical examination and laboratory investigations (arterial blood gases, chest X-ray, electrocardiogram, pulmonary function tests, spirometry (FEV1, FVC, FEV1/ FVC%), and Doppler echocardiography.

Criteria for diagnosing pulmonary hypertension included a) Peak tricuspid jet velocity was <2.8 m/s; ‘‘unlikely’’; >3.4 m/s, and the diagnosis of PH ‘‘likely’’; (2.8–3.4 m/s) ‘‘possible’’. These were determined from the equation (Modified Bernoulli equation: RVSP = 4

(TR velocity)^2 – (PRA). Classification of the severity of pulmonary hypertension was done based on the American Society of Echocardiography guidelines for classification of severity of pulmonary hypertension **(Cheitlin et al., 2003)** into: 1) mild PH: PAP was 30-39 mmHg; 2) moderate: PH PAP was 40-79 mmHg; and 3) severe PH: PAP was 80 mmHg or more.

Data management: Data were collected, revised, coded, tabulated, and introduced to a PC using Statistical Package for Social Science (SPSS 15.0.1 for windows; SPSS Inc, Chicago, IL, 2001). Quantitative data were presented as arithmetic mean and standard deviation; while qualitative data were presented as relative frequency and percent distribution. One way analysis of variance (ANOVA; F) test was used for comparison between means, and Chi Square was used for comparison between relative frequencies. P value < 0.05 was considered significant.

RESULTS

Age in the study group ranged from 59 to 70 years; and there was no statistically significant difference between studied groups (the mean age was 64.10±2.46, 63.95±2.16, 63.75±1.94, and 64.50±2.25 years, in groups A, B, C and D respectively). Smoking (pack/year) showed ranged from 20 to 54 packs, and there were significant increase in both groups A and B when compared to group C (31.90±7.22, 34.80±7.91 vs 28.30±3.45 respectively). Smoking was reported in control group as much as stable COPD group. The GOLD classification of COPD was grade II in 50% and 30% in groups A and B respectively; grade III was reported in 35% and 50.0% in groups A and B respectively and finally grade IV reported in 15% and 20% of groups A and B respectively (Table 1).

Echocardiographic findings in studied groups showed significant increase of peak tricuspid jet velocity; intermediate tricuspid jet velocity and right atrium pressure in group B (COPD exacerbation) (3.36±0.51, 2.90±0.21, and 6.97±1.02 respectively) and group (A) (3.05±0.60, 2.74±0.25, and 6.34±1.22 with the same order) when compared to group C (2.93±0.62, 2.71±0.26, and 6.11±1.24 respectively), and group D (2.59±0.52, 2.44±0.22, and 5.43±1.04 with the same order). Similarly, there were significant increase of calculated pulmonary arterial pressure in groups B and A (44.40±18.79, 33.40±9.01) when compared to groups C and D (24.10±2.95, 20.65±2.47 respectively) (Table 2).

Secondary pulmonary hypertension in studied groups showed no cases were in groups C and D; while the PAP was 40.0%, 30.0% and 5.0% (mild, moderate and severe respectively) in group B; compared to 40.0%, 15.0% and 0.0% (mild, moderate and severe respectively) in group A; with significant increase of both prevalence and severity of PAP in group B when compared to group A (Table 3).

There were significant inverse correlations between pulmonary artery pressure on one side and SaO_2, PaO_2, and FEV_1/FVC on the other side. On the other hand, there was significant, positive correlation between PAP from one side and, $PaCO_2$, hemoglobin concentration, WBCs, peak & intermediate tricuspid jet velocity and right atrium pressure (Table 4).

Table (1): General characteristics of studied cases

Groups / Parameters		Group A (stable COPD)	Group B (COPD exacerbations)	Group C (cigarette smokers)	Group D (control group)	t-test	P value
Age (mean±SD)		64.10±2.46	63.95±2.16	63.75±1.94	64.50±2.25	0.41	0.74(NS)
Smoking(packs/year)		31.90±7.22	34.80±7.91	28.30±3.45	31.63±6.78	3.69	0.031*
GOLD, COPD classification	II	10(50.0%)	6(30.0%)			1.67	0.43(NS)
	III	7(35.0%)	10 (50.0%)				
	IV	3(15.0%)	4(20.0%)				

** = significant ; NS = non-significant*

Table (2): Echocardiographic findings and calculated PAP in studied cases

Groups / Parameters	Group A (stable COPD)	Group B (COPD exacerbations)	Group C (cigarette smokers)	Group D (control group)	t-test	P value
Peak tricuspid jet velocity (msc)	3.05±0.60	3.36±0.51	2.93±0.62	2.59±0.52	6.25	<0.001*
Intermediate tricuspid jet velocity (msc)	2.74±0.25	2.90±0.21	2.71±0.26	2.44±0.22	12.68	<0.001*
Right atrium pressure (cm H_2O)	6.34±1.22	6.97±1.02	6.11±1.24	5.43±1.04	6.25	<0.001*
Calculated PAP (mmHg)	33.40±9.01	44.40±18.79	24.10±2.95	20.65±2.47	16.12	<0.001*

Table (3): Prevalence of secondary pulmonary hypertension in studied groups

Groups / Parameters	Group A (stable COPD)	Group B (COPD exacerbations)	Group C (cigarette smokers)	Group D (control group)
Mild	8(40.0%)	8(40.0%)	0(0.0%)	0(0.0%)
Moderate	3(15.0%)	6(30.0%)	0(0.0%)	0(0.0%)
Severe	0(0.0%)	1(5.0%)	0(0.0%)	0(0.0%)
Statistics	$X^2 = 25.87$, $p < 0.001$*			

Table (4): Correlation between pulmonary artery pressure and respiratory functions, hemoglobin, Peak and intermediate tricuspid jet velocity, and right atrium pressure

Variables	PAP	
	r	P
SaO_2	-0.612	<0.001*
PaO_2	0.51	<0.001*
$PaCO_2$	0.47	<0.001*
FEV1/FVC	-0.307	0.006*
Hemoglobin	0.320	0.004*
WBCs	0.330	0.004*
Peak tricuspid jet velocity	0.691	<0.001*
Intermediate tricuspid jet velocity	0.765	<0.001*
Right atrium pressure	0.691	<0.001*

DISCUSSION

Chronic obstructive pulmonary disease (COPD) is a leading cause of mortality and morbidity worldwide. It is characterized by progressive airflow limitation, and COPD severity is assessed using (FEV_1); However, FEV_1 is poorly correlated with clinical manifestations of the disease and standardized measurement of patient related outcomes has been proposed for more comprehensive assessment of disease severity **(Burge et al., 2013).**

COPD causes pulmonary hypertension in some patients and leads to right ventricular hypertrophy and enlargement and eventually right heart dysfunction. Pulmonary hypertension is associated with decreased functional capacity and increased mortality. Therefore, early and accurate diagnosis of significant pulmonary hypertension is crucial **(Leuchte et al., 2006).** The evaluation of right ventricular (RV) function is clinically useful in patients with chronic obstructive pulmonary disease (COPD) because the presence of RV failure has prognostic implications **(Burgess et al., 2002).**

The present study was designed to assess pulmonary hypertension (PH) in COPD patients in different stages of severity in stable condition and in exacerbation, and to evaluate the relationship between pH, spirometry and demographic data. In the first three groups (smoking groups), smoking packs per year ranged from 20 to 54 pack with a mean of 31.63±6.78 pack and there was significant increase of packs in COPD exacerbation group and stable COPD group in comparison to non COPD smokers group. These results were comparable to that reported by **Guvenc et al. (2013)** who reported that, the mean smoking packs per year was 28.00±17.78 packs/year

In the present study, FEV1/FVC ranged from 39 to 99 with a mean of 70.57±19.13, and there was statistically significant variance between studied groups as regard FEV1 and FEV1/FVC (healthy controls followed by non COPD smokers had the better functions, while COPD exacerbation and stable COPD groups had the worst respectively). These results were better than those reported by **Vitarelli et al. (2006)** who reported that the mean FEV1/FVC was 58.9±19.3, and these lower levels are logic as they included COPD patients only in their study. Similar results were reported by **Wells et al. (2015)**. On the other hand, **Sabit et al. (2010)** reported that respiratory functions significantly reduced in COPD patients in comparison to non COPD patients and these results are in accordance with those of the present study.

Pulmonary artery pressure showed significant differences between studied groups. The highest pressure was observed in COPD exacerbation group, followed by stable COPD group, then non COPD smokers and finally non-smokers non COPD group. These results were in agreement with that reported by **Uz et al. (2011)**. The present study revealed an increased PAP in 26 COPD patients (65%) and there was significant, inverse correlation between pulmonary artery pressure from one side and both SaO_2 and FEV_1/FVC from the other side. On the other hand, there were significant, positive correlation between PAP and hemoglobin

concentration, peak and intermediate tricuspid jet velocity and right atrium pressure in group A and B. In addition, there was significant increase of peak and intermediate Tr Jet velocity, and right atrium pressure, and decrease of oxygen saturation in cases with elevated PAP in comparison to cases with normal PAP. On the other hand, there was no difference between both groups as regard age, smoking packs per year and BMI. These results are in agreement with **Andersen et al. (2012)**. In addition, **Melek et al. (2006)** reported that there was no difference between cases with normal and elevated pulmonary artery pressure as regard age, and decrease of respiratory function tests.

The results of the present study proved that pulmonary hypertension was correlated with echocardiographic parameters of the right atrium; and thus it can be used for diagnosis of pulmonary hypertension in COPD patients as it is noninvasive, inexpensive and can be used in outpatients settings.

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خلفية البحث: يعتبر مرض السدة الرئوية المزمنة مشكلة صحية كبيرة نظرا لزيادة معدلات انتشاره وخطورته، وهو أحد الأسباب المؤدية للعجز والوفاة. ويتوقع أن يصبح ثالث سبب للوفاة في العالم بحلول عام 2020،ويعرف مرض السدة الرئوية المزمنة بأنه حالة مرضية تتصف بإعاقة تدفق الهواء في الشعب الهوائية، وهذه الإعاقة ترتبط بحدوث التهابات في الرئة نتيجة تعرضها للغازات والجزيئات المهيجة مثل السجائر. ويعد إرتفاع ضغط الدم فى الشريان الرئوي من أخطر مضاعفات المرض لأنه يضاعف من احتمالات الوفاة، و قد وجد أن حوالي 2.25% من المرضى مصابون بارتفاع شديد في ضغط الدم في الشريان الرئوي، وأن حوالي62.50% مصابون بارتفاع متوسط في ضغط الدم في الشريان الرئوي.

الهدف من البحث: تقييم دور الموجات فوق الصوتية على القلب فى قياس وتشخيص إرتفاع ضغط الدم فى الشريان الرئوى فى مرضى السدة الرئوية المزمنة وتحديد العلاقة بين مستوى إرتفاع ضغط الدم فى الشريان الرئوى ووظائف التنفس وبعض الصفات السريرية والديموجرافية للمرضى ومقارنتها بالأصحاء والمدخنين

المرضي وطرق البحث: شملت الدراسة ثمانين من مرضى السدة الرئوية المزمنة تم أخذهم من قسم الصدر بمستشفى جامعة الأزهر (بدمياط)، وقد تم تقسيم المرضى إلى أربعة مجموعات متساوية: المجموعة الأولى: مرضى السدة الرئوية المزمنة وحالتهم مستقرة، والمجموعة الثانية: مرضى السدة الرئوية المزمنة، وحالتهم متفاقمة، والمجموعة الثالثة:عشرين مريضا مدخنا ولا يعانون من مرض السدة الرئوية المزمنة، والمجموعة الرابعة:عشرين مريضا غير مدخنين ولا يعانون من مرض السدة الرئوية المزمنة. وقد خضع جميع المرضى إلى الآتى: تاريخ مرضى كامل، وفحص طبى شامل، وجميع

الفحوصات و الأبحاث المعملية الروتينية، ونسب الغازات بالدم، وأشعة عادية على الصدر، وظائف التنفس، ورسم قلب، وموجات فوق صوتية على القلب.

النتائج: خلصت الدراسة إلى حدوث ارتفاع طفيف في ضغط الشريان الرئوي في 31.2٪، وارتفاع متوسط في 16.2٪ وارتفاع شديد في 1.25٪ من الحالات. – وقد ارتبط إرتفاع ضغط الدم فى الشريان الرئوي فى مرضى السدة الرئوية المزمنة بعلاقة عكسية مع وظائف التنفس ودرجة تشبع الهيموجلوبين بالأوكسجين. وقد وجدت علاقة إيجابية بين ارتفاع ضغط الدم فى الشريان الرئوى فى مرضى السدة الرئوية وتركيز الهيموجلوبين، وذروة سرعة تدفق الدم فى الصمام ثلاثي الشرفات والأذين الأيمن.وقد أثبتت الدراسة الأهمية القصوى للموجات فوق الصوتية فى الكشف المبكر عن إرتفاع ضغط الشريان الرئوى فى مرضى السدة الرئوية المزمنة. وقد أوصت الدراسة بضرورة عمل مسح شامل أولى لمرضى السدة الرئوية بإستخدام الفحص بالموجات فوق الصوتية للكشف المبكر عن مضاعفات المرض على القلب ومنها تشخيص إرتفاع ضغط الشريان الرئوي وكذلك أوصت الدراسة بضرورة متابعة المرضى الذين تم تشخيص إرتفاع ضغط الشريان الرئوى لديهم بالموجات فوق الصوتية.