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Correlation between spirometry values and pulmonary artery pressure in young healthy subjects

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Contribution of authors

Alon Grossman- Writing of manuscript, data analysis

Ofra Kalter-Leibovici and Michal Benderly- Statistical analysis

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Abstract:

Background: Pulmonary hypertension (PH) is frequently associated with parenchymal lung disease.

Objectives: To evaluate the association between spirometric values and pulmonary artery systolic pressure (PASP) in young subjects without overt lung disease

Methods: Applicants to the Israeli air force undergo routine evaluation that includes resting spirometry and echocardiography. Applicants with evidence of overt lung disease were excluded from the study. All echocardiographic studies performed in the years 1994-2010 (N=7042) were retrieved. Medical files in which PASP was measured and spirometric values were available were reviewed. The association between PASP and forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), FEV1/FVC ratio, peak expiratory flow rate (PEFR) and forced expiratory flow $_{25-75}$ (FEF $_{25-75}$) was evaluated.

Results: We identified 646 air force applicants who underwent echocardiography in which PASP was measurable and had a record of spirometry. Applicants were mostly male (607 applicants, 94% of study population) and their average age was 18.2±0.7 years. Mean PASP was 26.4±5.2 mmHg (range 10-41 mmHg). None of the spirometric variables were found to be in correlation with PASP.

Conclusions: PASP in young healthy subjects is not associated to a significant degree with spirometric variables. Lung mechanics probably do not contribute significantly to PASP in this population.

Key words: spirometry, pulmonary hypertension, screening

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Introduction

The factors contributing to pulmonary hypertension (PH) are various and include an increase in pulmonary vascular resistance, intrathoracic pressure swings due to severe airway obstruction, alveolar hypoxia and structural changes in the pulmonary vasculature [1-4]. These factors are probably more prominent in subjects with overt lung disease, but the factors determining pulmonary artery systolic pressure (PASP) in healthy subjects are less well characterized. In addition, the association between lung volumes and flow rates and PASP in young healthy subjects has not been previously reported. This study was performed in order to evaluate the association between lung volumes and flow rates and PASP and to evaluate whether healthy subjects with higher PASP have higher lung volumes and flow rates compared with those with lower PASP.

Methods

Study population:

The study was approved by the ethics committee of the Medical Corps of the Israel Defense Force (IDF). All applicants to the Israeli air force (IAF) undergo preliminary evaluation at the IDF recruitment center and only those without any significant underlying medical conditions are referred for further evaluation at the IAF aeromedical center (AMC). This evaluation includes thorough history taking and physical examination, resting ECG and resting spirometry. Applicants with a history of bronchial asthma (active in the 5 years preceding the evaluation), other parenchymal lung disease or a history of spontaneous pneumothorax are not referred for evaluation at the IAF AMC and thus were excluded from the study. Applicants who were diagnosed with obstructive or restrictive lung disease during the screening process based on basic spirometric and more extensive evaluation, if required, were

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disqualified from the selection process and were thus excluded from the study. Applicants evaluated at the IAF AMC in the years 1994-2010 who had measurable PASP in the presence of tricuspid regurgitation (TR) and had a record of spirometry in their medical file were included in the study.

***Spirometry*:**

Spirometry was performed using standardized equipment and technique, as defined by the ATS/ERS task force [5]. All applicants performed 3 attempts and the best of 3 measurements was recorded. The following variables were recorded: 1) forced vital capacity (FVC)- defined as the maximal volume of air exhaled with maximally forced effort from a maximal inspiration, i.e. vital capacity performed with a maximally forced expiratory effort, expressed in liters at body temperature and ambient pressure saturated with water vapor (BTPS) 2) forced expiratory volume in 1 second (FEV_1)- defined as the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration, expressed in liters at BTPS. 3) peak expiratory flow rate (PEFR)- defined as the maximum expiratory flow achieved from a maximum forced expiration, starting without hesitation from the point of maximal lung inflation, expressed in L/s-1 4) FEV_1/FVC ratio 5) forced expiratory flow (FEF_{25-75}) defined as the mean forced expiratory flow between 25% and 75% of the FVC. All spirometric variables were corrected for height, weight age and gender.

***Echocardiography*:**

We reviewed all routine echocardiographic studies of aircrew applicants performed at the AMC between January 1994 and January 2010. All echocardiographic studies were obtained with one of three devices (HP 500 SONOS, ATL 5000HDI, PHILIPS HD 11 XE). 2nd generation devices (HP 500 SONOS and ATL 5000HDI) were used from 1994-2008. A 3rd generation device (PHILIPS HD 11 XE) was used from 2008

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onward. All studies were performed by one of three experienced sonographers and interpreted by one of two cardiologists specialized in echocardiography. TTE included two-dimension, M-mode and Doppler studies according to standard American Society for Echocardiography guidelines for obtaining images, quantification of chamber dimensions and assessment of valvular regurgitation [6-8]. All studies performed at the IAF aero medical center are performed in four windows- left and right parasternal long axis views, parasternal short axis view and apical four-chamber view. In cases where elevated PASP or tricuspid regurgitation is suspected based on these four windows, a subcostal window is added. All TR gradients were measured during the inspiratory phase. Measurements were corrected for body surface area (BSA). The right ventricular (RV) systolic pressure is equivalent to the PASP. The pressure gradient across the tricuspid valve was derived from tricuspid systolic regurgitant flow velocity, measured by continuous-wave Doppler, using the simplified Bernoulli equation [9]. Right atrial pressure was estimated as 5mmHg [10]. Thus, the RV systolic pressure estimation equaled the tricuspid pressure gradient + 5mmHg.

Tests in which cardiac abnormalities were identified (with the exception of tricuspid regurgitation or elevated PASP) or absence of measurable regurgitant tricuspid flow were excluded from the study.

Statistical analysis:

Demographic spirometric and echocardiographic characteristics are presented as frequencies (%) or means± standard deviation as applicable. The association between TR peak and spirometric findings was assessed by spearman correlation.

Results

A total of 6598 subjects underwent routine echocardiography which was interpreted as normal at the IAF AMC during the years 1994-2010. Nineteen hundred studies

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(29%) demonstrated tricuspid regurgitation enabling measurement of PASP. Spirometric parameters were available in 647 applicants (34%). Applicants were young (average age 18.16±0.73) and without any significant underlying medical condition. The demographic, spirometric and echocardiographic variables of study population are presented in table 1. Mean systolic pulmonary artery pressure in the entire cohort was 26.2±4.5 mmHg, and in those in whom spirometry was available in the medical record was 26.4±5.2 mmHg. None of the spirometric variables was correlated with PASP as is presented for FVC and FEV1 in figure 1 and 2, respectively. When comparing subjects with PASP that was lower than 17 mmHg and those with PASP that was higher than 26 mmHg, no significant difference in all spirometric values was noted.

Discussion

The association between intrinsic lung pathology and PASP is well recognized and obstructive lung disease is one of the most common causes of pulmonary hypertension in adults. Whether PASP elevation in these patients is secondary to the lung pathology or both share a common pathogenic mechanism is unclear. Performance of spirometry and echocardiography in young, healthy subjects in an attempt to determine the association between spirometric values within the normal range and PASP is important as it may provide preliminary evidence for the pathogenesis of PH in structural lung disease. The population studied in this cohort was extremely healthy, as the screening process disqualifies all subjects with significant disease from entering the screening process at the IAF AMC. Although there are no reference values for spirometry specifically based on Israeli cohorts, the values of our cohort are similar to those reported in a large cohort from Central Europe [12].

PASP in young subjects was previously found to be correlated with left atrial diameter, left ventricular end diastolic and systolic diameters and left ventricular mass [13]. These parameters all probably reflect that PASP in this population is primarily

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determined by increased blood volume, but it is difficult to determine the contribution of the lung to PASP in this population. This study failed to show any significant correlation between spirometric variables and PASP in young, healthy subjects. It is thus possible that PH is a late consequence of pulmonary disease and thus is not associated with normal spirometric variables in asymptomatic individuals.

One of the major purposes of pre-participation screening of athletes and military recruits is to exclude obstructive lung disease, particularly because elite athletes may be at an increased risk for the development of airway injury [14]. Exercise-induced asthma, a particular concern in athletes and military recruits, is a relatively common condition, which may present initially during military service or participation in active sports [15]. Military aviation may place at-risk individuals at a particularly high-risk for the development of airway disease because breathing cold dry air causes epithelial injury and the hyperpnea performed during military aviation exposes the airway epithelium to increased shear stress and transmural pressure gradients [16, 17]. Yet, the need for screening for exercise-induced bronchospasm is debatable considering its relatively low yield [18]. Thus, it would seem that additional tools are required for the diagnosis of exercise induced bronchospasm or other forms of occult lung disease among athletes and military applicants. Because PASP in young healthy subjects is predominantly determined by increased blood flow through the pulmonary vasculature [13], lung pathology probably contributes little, if at all, to PASP.

This study has several limitations. First, it was performed in a retrospective manner and no follow up was performed. Thus, the true prevalence of future development of clinically evident lung disease is unknown. Second, only 34% of the medical records contained both echocardiography and spirometry, thus representing a relatively small cohort. Third, the cohort included mostly males as flight academy is voluntary and most applicants are male. It is known that the prevalence PH is different in females

and males [18] and thus the results are probably applicable only to males. Because many of air force academy applicants are disqualified for non-medical reasons, most applicants evaluated in the study could not be followed-up. The fact that the study was performed retrospectively certainly limits the ability to evaluate the rate of development of lung pathology in the cohort and to evaluate whether the applicants with the higher values on admission had a greater chance of developing overt lung disease. Because echocardiography and spirometry were performed during the screening process for flight academy, it is possible that the anxiety associated with this, may have led to increased heart rate and blood pressure and may have influenced the results. Yet, there is no reason to believe that those with higher PASP values had a different physiologic response than those with lower values and thus the association between the two should have remained persistent. Because we did not have reliable information regarding the prevalence of tobacco consumption in the study cohort, we could not compare smoking to non smoking individuals. This is a limitation due to the fact that smoking certainly affects spirometry values [20], but there is no reason to believe that smoking prevalence will differ between those with different values of PASP.

Conclusions

PASP in young healthy subjects is not associated to a significant degree by spirometric variables. Lung mechanics probably do not contribute significantly to PASP in this population, in which increased blood flow through the pulmonary vasculature is probably the major determinant of this variable.

Conflict of interest: none

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Figure 1: Correlation between TR peak and FEV1

Figure 2: Correlation between TR peak and FVC

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Table 1: Demographic, spirometric and echocardiograph variables in study population

Age, years	18.16±0.73
Males (% of cohort)	607(94%)
Body surface area, m^2	2.1±0.1
Systolic blood pressure, mmHg	128.3±11.9
Diastolic blood pressure, mmHg	70.7±8.8
Forced vital capacity, liters	4.58±0.7
Forced expiratory volume in 1 second, liters	4.04±0.5
Forced expiratory volume in 1 second/ Forced vital capacity, %	88.8±5.9
Peak expiratory flow rate, liters/minute	7.96±1.5
Forced expiratory flow rate $_{25-75}$, liters/minute	4.6±0.9
Pulmonary artery systolic pressure, mmHg	26.4±5.2
Aortic root, millimeters	28.3±2.4
Left atrium, millimeters	33.6±3.7
Posterior wall, millimeters	8.8±0.8
Interventricular septum, milimeters	9.0±0.8

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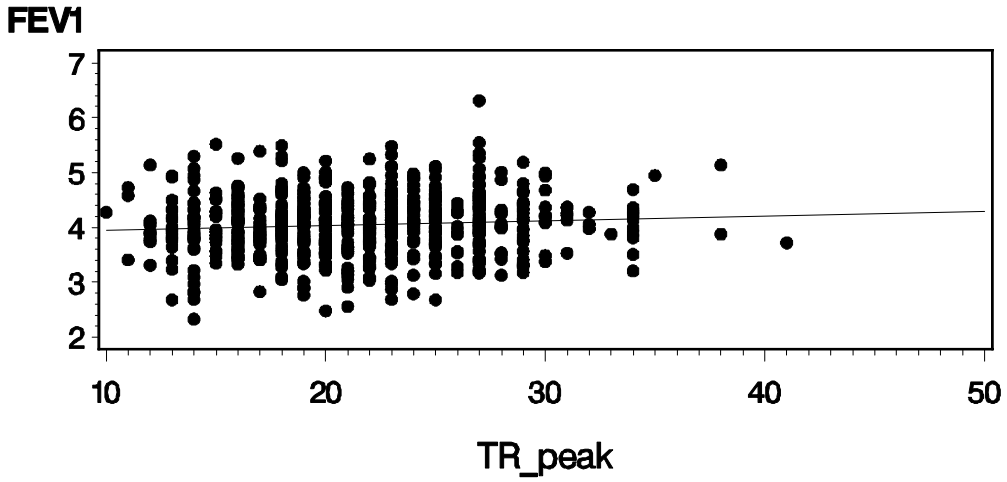
----- Correlation between TR_peak and FEV1 -----



Regression Equation:
FEV1 = 3.867731 + 0.008513* TR_PEAK

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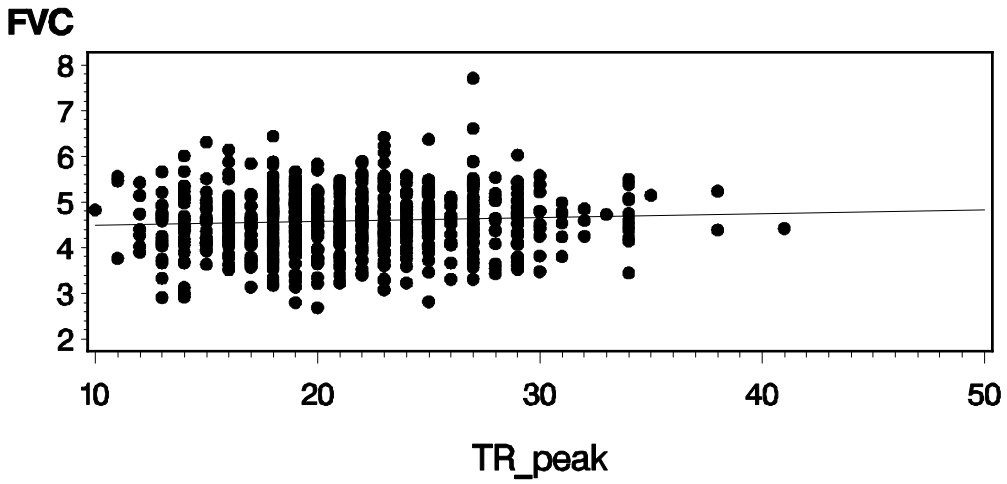
----- Correlation between TR_peak and FVC -----



Regression Equation:
FVC = 4.398043 + 0.008419* TR_PEAK