Serum CA-125 Level in Patients with Chronic Obstructive Pulmonary Disease with and without Pulmonary Hypertension

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a progressive and debilitating disease and is going to be the 3rd most common cause of death worldwide. Pulmonary hypertension (PH) has severely bad influence on prognosis in COPD patients. Hence, early diagnosis of it is important for appropriate therapy. Echocardiography is used for this purpose, which requires cardiologist and expensive equipment which may not be available anywhere. CA-125, a biomarker of ovarian cancer, has shown to be associated with left ventricular failure. We aimed to show the relationship between CA-125 levels and PH in patients with COPD.

Methods: Ninety patients with stable COPD were enrolled into the study. Levels of CA-125 were measured from venous blood, and in the same day systolic pulmonary artery pressure (sPAP) was measured by transthoracic echocardiography.

Results: Of 90 Patients 51 had PH and 39 had not. Patients with PH had significantly higher CA-125 levels compared with controls (mean 39.15 U/ml vs. 24.22 U/ml, P < 0.04). Levels of CA-125 were correlated with sPAP (r = 0.17, P = 0.01).

Conclusions: The CA-125 biomarker can be used to identify COPD patients with pulmonary hypertension. Since it is cheap and easily available it can help in centers with less access to echocardiography.

Keywords: CA-125, chronic obstructive pulmonary disease, pulmonary hypertension

Rezumat

Nivelul seric de CA-125 la pacienții cu bronhopneumopatie obstructivă cronică cu și fără hipertensiune pulmonară

Introducere: Boala pulmonară obstructivă cronică (BPOC) este o boală progresivă și debilitantă și va fi la 3-a cauza de deces la nivel mondial. Hipertensiunea pulmonară (HP) are o influență negativă severă asupra prognosticului la pacienții cu BPOC. Prin urmare, diagnosticul precoce este important pentru un tratament adecvat. Ecocardiografia este folosită în acest scop, dar necesită cardiolog și echipamente costioase care nu sunt disponibile oriunde. CA-125, un biomarker de cancer ovarian, a fost asociat cu insuficiența ventriculară stângă. În acest studiu ne-am propus să arătăm relația dintre nivelul CA-125 și HP la pacienții cu BPOC.

Metodă: Douăzeci și patru de pacienți cu BPOC stabili au fost înrolați în studiu. Nivelurile de CA-125 au fost măsurate din sânge venos, și în aceeași zi a fost măsurată presiunea sistolică arterială pulmonară (sPAP) prin ecocardiografie tranzstoracică.

Rezultate: Din 90 de pacienți, 51 au avut HP și 39 nu au avut. Pacienții cu HP au avut nivel de CA-125 semnificativ mai mare comparativ cu lotul control (media 39,15 U/ml față de 24,22 U/ml, p < 0,04). Nivelurile de CA-125 au fost correlate cu sPAP (r = 0,17, p = 0,01).

Concluzii: Biomarkerul CA-125 poate fi utilizat pentru identificarea pacienților cu BPOC cu hipertensiune pulmonară. Având în vedere că este ieftin și ușor accesibil poate ajuta în centre cu acces mai redus la ecocardiografie.

Cuvinte-cheie: CA-125, bronhopneumopatie obstructivă cronică, hipertensiune pulmonară

Introduction

Chronic obstructive pulmonary disease (COPD) is a common disease and is estimated to be the 3rd or 4th most common cause of death worldwide. It is a progressive disease and some patients may develop pulmonary artery hypertension and cor pulmonale, which worsens the prognosis. Echocardiographic examination of the heart is used for diagnosis and confirmation of presence of pulmonary hypertension and/or cor pulmonale. However, there are some limitations for echocardiographic examination, such as requirement for cardiologist and relatively expensive equipment that may not be available in anywhere and/or anytime, and transfer of severely ill patients during acute exacerbation from wards or ICUs to echocardiography unites may have some risks. In addition, maximum tricuspid regurgitation velocity cannot be evaluated in one-third of COPD patients due to the low echogenicity of emphysematous lungs.

Cancer antigen-125 (CA-125) is a tumor marker of ovarian cancer, however it is nonspecific and its level increases in various malignant and nonmalignant disease. In pulmonary disease, increased CA-125 level is reported in tuberculosis and non-tuberculosis mycobacterial disease, idiopathic pulmonary fibrosis, bronchiectasis, pneumonia and malignant disease in lung and pleura. Also, there are reports of increase of CA-125 level in patients with congestive heart failure. In a study CA-125 level was correlated with pulmonary artery pressure (PASP) in patients with right ventricular dysfunction. The aim of this study was to evaluate association of CA-125 level with severity of COPD and pulmonary hypertension in patients with COPD.

Methods

Our study consisted of 90 patients with stable COPD who were referred for echocardiography. There were selected patients whose spirometry were compatible with ATS guide-
lines and were measured with only one spirometer (Spirolab II, Mir Italy). Patients were assigned to mild, moderate, and severe COPD according to GOLD classification of COPD1.

Each patient underwent a 2-dimensional Doppler transthoracic echocardiographic examination (kontron) with use of a 2.5-MHz transducer. Right ventricular enlargement was classified to mild, moderate, and severe enlargement after measuring right ventricular end-diastolic and end-systolic dimension. Patients with COPD were divided into 2 groups: with or without pulmonary hypertension. Pulmonary hyper tension was defined as pulmonary artery systolic pressure greater than 35 mm Hg. After echocardiography, venous blood sample were taken from peripheral vein and freezed. The echo cardiologist was blind to results of CA-125. All CA-125 samples were measure by ELISA method using of commercially available kit (Accu-Bind ELISA Microwells Monobind Inc Lake Forest, CA 92630, USA).

Statistical analysis

SPSS version 19 (IBM corporation) is used for statistical analysis. Nominal variables were compared with x2 test and the continuous ones with Student’s t-test. All results were expressed as the percentage for Nominal variables, continuous variables as mean ± standard deviation, and correlations were examined by Pearson’s test. P value of less than 0.05 was considered statistically significant.

Results

Of 90 patients, 51 patients (56.7%) had PH and 39 (43.3%) didn’t have PH. The comparison of two groups is presented in Table 1. The two groups did not differ significantly for age, sex, and current smoking, so they cannot act as confounders. Patients with pulmonary hypertension had significantly higher CA-125 levels than those without hypertension (p value=0.003). There was a positive correlation of systolic pulmonary artery pressure and CA-125 with Pearson coefficient r =0.17 and p value=0.01 (Figure 1).

Discussion

In the current study there was correlation between serum CA-125 level and PASP, which is in agreement with Uz et al11; they measured CA-125 levels of 52 patients with COPD and found that patients with PASH had significantly higher CA-125 levels than those without PASH. In another study, among 40 patients with COPD, CA-125 level was correlated with right heart dilatation and positively correlated with PASP (r = 0.550, p < 0.001)12. Ordu et al13, measured proBNP and CA-125 in 102 patients with congestive heart failure and concluded that: “baseline NT-proBNP and CA-125 levels are comparably reliable as heart-failure markers”, and suggested that CA-125 can be used for prognosis prediction in heart failure. In a study by Bulut et al14 among 52 patients with COPD, those with cor pulmonale had significantly higher mean serum levels of CA-125, CEA, and CA 19.9 with p < 0.05. Brain natriuretic peptide (BNP) and CA-125 were significantly higher in patients with congestive heart failure than in those without congestive heart failure. Elevated CA-125 and BNP may be more valuable than separately detection of CA-125 or BNP for diagnosis and evaluation of treatment in congestive heart failure15.

However, little is known about the patho-physiologic mechanism of elevation of CA-125 level in non-neoplastic conditions. Neoplastic cells do not secret CA-125 by them-selves16; it is produced by peritoneal mesothelial cells which are activated directly or indirectly by mediators such as interleukin-6. In non-malignant conditions, it is hypothe- sized that serosal irritation due to inflammation, mechani- cal stress or fluid congestion stimulates mesothelial cells to release CA-12517. Huang et al18, in a study of 109 patients with congestive heart failure showed that patients with serous cavity effusion demonstrated higher serum CA-125

| Table 1 Comparison of COPD patients with and without systolic pulmonary artery hypertension |
|---------------------------------|---------------------------------|----------------|-----------------|-----------------|
| PH n=51 (56,7) | No PH n=39 (43,3) | Total n=90 | P value |
| Sex | | | | |
| Male n (%) | 31 (60,8) | 26 (66,7) | 57 (63,3) | 0,56 |
| Female n (%) | 20 (39,2) | 13 (33,3) | 33 (33,3) |
| Age mean ± SD | 63,39±8,90 | 65,31±11,2 | 65,22 ± 9,92 | 0,61 |
| Smoking | | | | |
| Yes n (%) | 37 (72,5) | 31 (79,5) | 68 (75,6) | 0,44 |
| No n (%) | 14 (27,5) | 8 (20,5) | 22 (24,4) |
| FEV1 (percent of predicted) mean ± SD | 32,42±13,05 | 43,56±18,23 | 37,30 ± 16,41 | 0,001 |
| SPAP value (mm Hg) mean ± SD | 53,52+14,18 | 32,30+5,60 | 44,33 ± 15,43 | 0,000 |
| CA-125 level (U/ml) mean ± SD | 41,28+41,46 | 19,52+15,92 | 31,85 ± 34,51 | 0,003 |
| Elevated Ca-125 | | | | |
| Yes n (%) | 24 (47,1) | 5 (12,8) | 29 (32,2) | 0,001 |
| No n (%) | 27 (52,9) | 34 (87,2) | 61 (67,8) |

PH: Pulmonary hypertension
than patients without effusion (82.91 vs. 44.98 U/ml). They conclude that mechanical excitation of mesothelial cells from serous fluid effusion plays an important role in increased CA-125 secretion.

The limitation of this study is that, sPAP estimated by Doppler echocardiography may overestimate or underestimate the values comparing to those obtained by right heart catheterization. However, as in both group of patients (with and without sPAP/PH) sPAP was measured by the same method this limitation cannot have significant effect on results.

**Conclusion**

In conclusion, serum levels of CA-125 appear to be useful to identify patients with PH. Since it is both cheap and easy, it could be used as a valuable blood test for the screening of PH in patients with COPD.

### References