AUTHOR'S TRANSLATION

ORIGINAL RESEARCH

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Gas exchange abnormalities impact on quality of life parameters in chronic obstructive pulmonary disease patient

Preamble

Chronic obstructive pulmonary disease (COPD) – one of the most important medical and social problems both in Ukraine and in the world. Its relevance is due to high rates of prevalence, morbidity, mortality and growing economic losses. The problems of COPD is insufficient emphasis on prevention, late diagnosis and lack of adequate treatment (Feshchenko Y.I., 2009; 2011).

Gas exchange abnormalities are the part of the pathophysiology of COPD. In the Global Initiative for Chronic Obstructive Lung Disease (GOLD) summarized that gas exchange abnormalities – a reduction of ventilation and ventilation drive, worsening respiratory muscle function due to high work of breathing in severe obstruction and hyperinflation, ventilation-perfusion disturbances that the amount resulting in hypoxemia and hypercapnia (Rodriguez Roisin R. et al., 2011). The main complications of COPD is pulmonary insufficiency and chronic pulmonary heart disease. Pulmonary failure – a failure to provide normal pulmonary arterial blood gas composition at rest or during moderate exercise. This syndrome combines symptoms such as dyspnea, cyanosis , decreased level of physical activity and quality of life. Chronic pulmonary heart disease is considered as a syndrome of circulatory failure with peripheral edema development that complicates the course of many diseases with damage only lung structure or function. Major importance in the development of peripheral edema has hypercapnia – increase of CO_2 in the blood, which is a potent vasodilator (Gavrysiuk V.K., 2011).

An integral part of current medical science is the study of health related quality of life, HRQL. This theme is relevant and in relation to chronic obstructive lung disease (COPD), in that experts GOLD (Global Initiative for Chronic Obstructive Lung Disease) in 2011, noted that within the same GOLD spirometry classification category in COPD patients may take place any state of health – from relatively good to very bad. Therefore, assessment of quality of life in patients with COPD is needed (Rodriguez Roisin R. et al., 2011). The most often used definition of quality of life is a balance between what person want to achieve in life and what has already been achieved or achievable, but that definition is too abstract for practical use (Jones P.W., Wijkstra P.J., 2006). The World Health Organization has defined quality of life as "an individual's perception of their position

in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, and their relationship to salient features of their environment (WHOQOL Group, 1993).

Scientists need to measure the impact of the disease on quality of life, which would be allowed this option to compare among different patients, and in the context of the results of the treatment. For this purpose, measurement of health disorders should be standardized, so that each patient was examined the same, and questionnaires were suitable for all patients with a particular nosology. All items questionnaires should be acceptable, at least potentially, for each patient (Rodriguez Roisin R. et al., 2011). The study of quality of life in patients with COPD is an important part of their health care, and at end-stage COPD can be used to predict the life expectancy of the patient (Habraken J.M. et al., 2011).

St George's respiratory questionnaire (SGRQ) examines the health problems of patients with asthma, COPD, bronchiectasis, kyphoscoliosis, sarcoidosis, and contains two parts. . The first part examines the symptoms – Symptoms Score – the patient's respiratory problems from the previous period (from 1 month to 1 year), their frequency and severity. The second part concerns the limitation of physical activity due to dyspnea at the moment (Activity Score) and the influence of psychosocial problems caused by breathing problems (Impacts Score). Also deducted the total account is Total Score – impact diseases on general health. Account 100 points represents the worst possible health, 0 points is the best possible state of health (Jones P.W., Forde Y., 2008).

High level points of the questionnaire is associated with mortality, repeated hospitalizations, the high cost of medical care. The scientific issue when evaluating the results of the questionnaire is to determine the level of change, which would be considered to be significant. Minimal clinically significant difference is the smallest difference points of the questionnaire, in which the patient feels better, and which comes in the absence of adverse events and excessive increase of the cost of treatment. For SGRQ this difference is 4 points (Kocks J.W.H. et al., 2006).

Means (95% confidence intervals) for SGRQ scores in normal subjects with no history of respiratory disease are given in table 1.

Table 1

The normal level of the results of the questionnaire of St George's Hospital (Jones P.W., Forde Y., 2008)

Symptoms score	Activity score	Impacts score	Total score
12 (9-15)	9 (7-12)	2 (1-3)	6 (5-7)

In 1987 EuroQoL Group was created, international multidisciplinary network of specialists in the study of the health status participants of which developed the EQ-5D questionnaire, that found wide application in clinical research and practical medicine. The questionnaire is simple to use, available to understand by patients regardless of their level of education. Narrative of the questionnaire contains 5 questions, taking into account such vital spheres: mobility, self-care, the usual everyday activities (such as work, study, housework, family or leisure activities), pain (discomfort), anxiety (depression). Every single issue can have one of three responses that meet the absence of problems, moderate or extreme problems. Visual-analog scale in EQ-5D designed to reflect the patient's own health assessment on the segment, one final point of which marked as "100" represents the best possible state of health that can imagine the patient, and the other marked "0" – the worst (Rabin R. et al., 2011).

Object and methods of research

We study the of quality of life features in COPD patients with gas exchange abnormalities. This study aimed to improve the diagnosis of gas exchange abnormalities in COPD patients with the attention to quality of life parameters. To achieve the goal we resolved the following tasks:

- to evaluate the quality of life of COPD patients with SGRQ and EQ-5D;
- to explore the relationship between quality of life and the results of capnometry in COPD patients;
- to study the effect of hypercapnia on quality of life of COPD patients.

This work was financed from the state budget of Ukraine.

The study was coordinated with the local Medical Ethics Committee of the NIPhP NAMS, participants were familiarized with the study protocol and signed an informed consent form to participate in the study.

Patients with COPD were divided into three groups depending on the stage of the disease, which have the following names in further text:

- stage II COPD patients;
- stage III COPD patients;
- stage IV COPD patients.

To study the quality of life patients filled the questionnairies: SGRQ (Jones P.W., Forde Y., 2008) and the EQ-5D (Rabin R. et al., 2011).

The patient is instructing before filling out the questionnaire SGRQ, the investigator ask him to answer each question as he feels his disease. The patient fill out the questionnaire at the table in a quiet room without being distracted and without affecting the family, friends or health care workers.

After filling SGRQ the doctor checks the questionnaire regarding the lack of spaces and asks the patient to answer skipped questions. The results are calculated with the use a special calculator based on Excel. Each item of the questionnaire has empirically counted up weight variation and responses: Yes/No or true/false (Incalzi R.A. et al., 2009). The results of the compute answers questionnaire SGRQ are grouped in 4 domains – due to the symptoms (symptoms score), limitation of activity (activity score), limitation of activity (impacts score) total score (total score). The greater is the points of the questionnaire is worse quality of life.

Before the filling out the questionnaire EQ-5D the researcher instruct the patient to off one answer for each question, taking into account the health state at the time of the survey. The results are calculated with the use a special "key" questionnaire and is expressed in the form of an index. The questionnaire also contains the EQ-5D visual-analog scale, all of which had their own displays the evaluation of patient's health (Rabin R. et al., 2011).

Capnometry was conducted for all participants on a set for the study of the cardiorespiratory system "Oxycon Pro", "Cardinal Health" (Germany), the following parameters were evaluated:

- fractional concentration of carbon dioxide in exhaled air, % ($FECO_2$, %);
- end-tidal fractional concentration of carbon dioxide in exhaled air,% ($FETCO_2$,%).

Data collection and mathematical processing carried out by licensing software products included in the package Microsoft Office Professional 2007 license Russian Academic OPEN No Level № 43437596. Statistical analysis was performed using mathematical and statistical features MS Excel (Lapach S.N. et al., 2000). The parameters studied in this work were evaluated by determining the mean (M), the mean error (m), reliability (t), the level of significance (p) followed by comparison using t Student-test. Correlation analysis was carried out using the parametric Pearson correlation with subsequent authenticated results using Student's criterion.

Results and discussion

The study involved 100 participants (74 men and 26 women) aged 38 to 84 years, mean age (61,0 ± 1,0) years.

A group of stage II COPD patients amounted to 30 patients (23 men and 7 women) with a mean age (57,5 ± 2,1) years and the average forced expiratory volume at timed interval of 1,0. second (FEV_1) (64,3 ± 1,5) %.

A group of stage III COPD patients consists of 45 patients (30 men and 15 women) with a mean age (59,0 ±1,8) years and the average FEV_1 (41,0 ± 0,8) %.

A group of stage IV COPD patients consists of 25 patients (21 men and 4 women) with a mean age (65,6 ± 1,8) years and the average FEV_1 (26,4 ± 0,6) %.

Analysis of the results obtained from SGRQ and EQ-5D demonstrated that the quality of life of patients, on average, by groups of observations with the progression of COPD gets worse (see table 2).

Table 2

Indicators of the quality of life of patients surveyed, (M ± m)

Indicators	Stage II COPD patients (n = 30)	Stage III COPD patients (n = 45)	Stage IV COPD patients (n = 25)
Index EQ-5D	0,64 ± 0,05	0,59 ± 0,04	0,41 ± 0,06$^{*\#}$
Mean EQ-5D visual analogue scale indication	61,0 ± 2,9	56,2 ± 2,5	36,7 ± 3,9$^{\#\wedge}$
Symptoms score	49,6 ± 3,3	68,3 ± 3,0$^{\&}$	76,4 ± 3,6$^{\#}$
Activity score	51,2 ± 4,1	62,3 ± 3,3	78,2 ± 4,1$^{\#\wedge}$
Impacts score	32,1 ± 3,4	47,8 ± 2,9$^{\&}$	63,4 ± 4,5$^{\#\wedge}$
Total score	40,8 ± 3,2	55,6 ± 2,7$^{\&}$	70,0 ± 3,9$^{\#\wedge}$

Notes:

* – statistically significant difference between stages III COPD patients and stage IV COPD patients, $p < 0.05$;

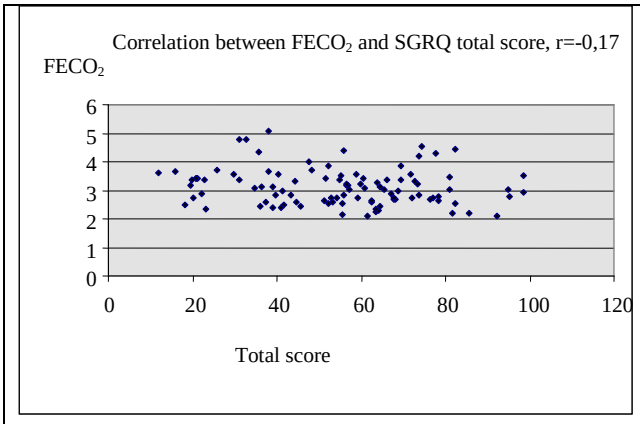
– statistically significant difference between stages II COPD patients and stage IV COPD patients, $p < 0,01$;

^ – statistically significant difference between stages III COPD patients and stage IV COPD patients, $p < 0,01$;

& – statistically significant difference between stages II COPD patients and stage III COPD patients, $p < 0,01$.

What is more the quality of life worsening is not only clinically meaningful for SGRQ (with a difference of 4 points), and statistically credible with all domains of questionnaire with $p < 0.01$.

The GOLD guideline demonstrated that the quality of life in COPD patients does not depend on the magnitude of the FEV1 with a coefficient of correlation r =-0.23 (Rodriguez Roisin R. et al., 2011). We conducted a correlation analysis for capnometry parameters ($FECO_2$ and $FETCO_2$) and total score of the questionnaire SGRQ and got similar results (Figure 1).



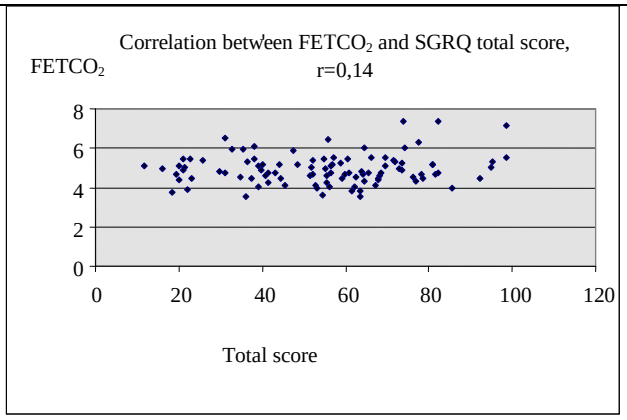


Figure 1. The results of correlation analysis capnometry parameters ($FETCO_2$ and $FECO_2$) and and total score of the questionnaire SGRQ in the general population of patients

When searching the relationship between a SGRQ total score with the $FECO_2$ the correlation coefficient was-0.71, and the correlation analysis of $FETCO_2$ – 0.14, respectively. Thus, as in the case with the forced expiratory volume at timed interval of 1,0. second, the quality of life of patients with COPD in general does not depend on parameters of capnometry in the general population of patients with COPD.

During the next stage of questionnaries' results analysis, we compared the quality of life of patients with COPD without hypercapnia and with hypercapnia – with a high (more than 5,6 %) the concentration of CO_2 at the end of exhalation. According to J. Pointer the highest normal $FETCO_2$ level is 5.6% (Pointer J., 2011). In patients with hypercapnia there is statistically significant worse quality of life regarding questionnaire data from the results of EQ-5D. As for the SGRQ, the difference of the quality of life depends on its domain. The symptoms score was almost the same in both groups, impact score was much worse (but not significantly) in patients with hypercapnia, total score is greater (clinically significant) in a group of patients with hypercapnia. Activity score, which due to the questionnaire concerns the limitation of physical activity to dyspnea at the moment (Jones P.W., Forde Y., 2008), in this domain, the quality of life of patients with hypercapnia is much worse than in patients without hypercapnia, with statistically reliable difference (Figure 2).

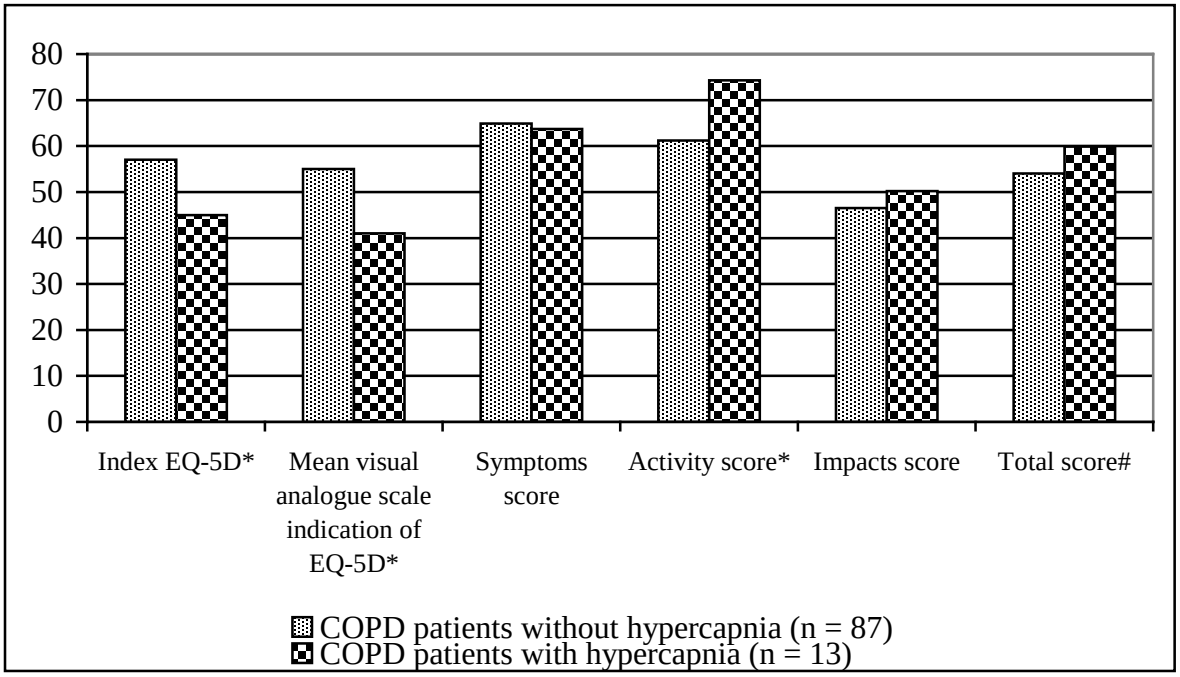


Figure 2. Indicators of the quality of life of COPD patients with and without hypercapnia.

Notes:

* – statistically reliable difference of indicators between groups, $p < 0,05$;

– clinically significant difference between groups.

We decided to follow as the result of the correlation analysis between indicators of quality of life and the results of the capnometry will be changed if the group of observation will involve only the patients with hypercapnia (Figure 3).

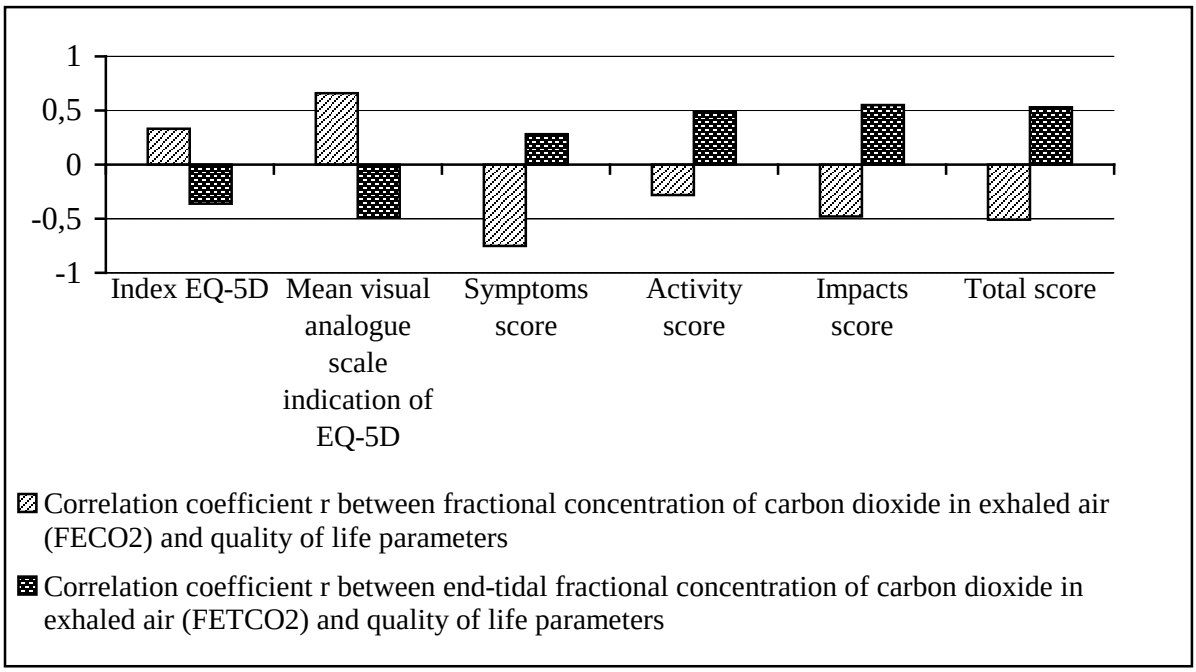


Figure 3. The results of correlation analysis for capnometry parameters ($FECO_2$ and $FETCO_2$) and quality of life in patients with hypercapnia

If the quality of life in general population does not depend from the results of the capnometry, in patients with hypercapnia the presence of such correlation take place. The lower the concentration of CO_2 in the air during exhalation and the higher at the end of the exhalation, the worse is the quality of life.

In our previously published paper showing that in patients COPD the reducing of the CO_2 concentration in the exhaled air testifies to the violation of balance of ventilation and perfusion in the lungs and especially this apply for $FECO_2$, reducing the level of which is the marker of lung hyperinflation (Ishchuk S.G., 2013). And really, this figure shows that with a decrease $FECO_2$ the quality of life indicators worsen. Dropping the index and the average mark of visual-analog scale of EQ-5D (r is equal to 0,66 and 0,33, respectively) and increases the points all 4 domains of quality of life questionnaire SGRQ, because ventilation-perfusion imbalance in patients progressing. The most vulnerable category is the symptoms score – r =-0,77.

The dependence of the concentration of carbon dioxide at the end of exhalation and indicators of quality of life has the reverse character: indicators of quality of life EQ-5D deteriorate and all 4 domains of quality of life questionnaire SGRQ increases with increasing $FETCO_2$ that takes place in hypercapnia. Wherein the most vulnerable category is impact score – r = 0.55.

Thus, in patients with gas exchange abnormalities and hypercapnia formed a different pattern and more serious character disorders quality of life than in the general population of patients with COPD.

Conclusions:

1. the patients' quality of life affected with disease progression from (40,8 ± 3,2) points in the II stage to (70,0 ± 3,9) total score points SGRQ in IV stage COPD, $p < 0.01$;
2. indicators of quality of life does not depend on the results of the capnometry in the general population of patients with COPD;
3. in patients with hypercapnia takes place more severe limitation of activity – (30,9 ± 5,4) points activity score than in patients without hypercapnia – (61,2 ± 2,6) points, with the statistically reliable difference, $p < 0,05$. At hypercapnia among other indicators of quality of life the impact score is the category that gets worse in the largest extent.

Thus, diagnosis and correction of hypercapnia are clinically relevant task because such complication significantly affects the quality of life of patients. We consider it important perspectives in a non-invasive, with the use of capnometry, determination of concentration CO_2 in the exhaled air, which will serve as an additional diagnostic tool in the management of patients with COPD. The timely detection of hypercapnia and the signs of the imbalance of ventilation and perfusion in the lungs will allow prescribe adequate treatment and to maintain and improve the quality of life of patients.

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