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Optimization of approaches to early phenotypic diagnosis and an algorithm for differentiated management of patients with chronic obstructive pulmonary disease

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Abstract. The practice of managing patients with COPD is determined not only by the approaches of early diagnosis, but also to a greater extent by the number of exacerbations, the number of exacerbations requiring hospitalization, and the assessment of the impact of the disease on the patient's daily life and health. For the most part, these indicators are subjective, and the clinical features of the course of respiratory pathology do not always allow us to focus on the likelihood of respiratory exacerbation and the reason for hospitalization from exacerbation.

The results of our research have shown that the number of exacerbations and the number of exacerbations requiring hospitalization in patients with COPD correlates with a morphological marker - a violation of mucociliary clearance and the depth of its violations. When assessing the relationships, a positive relationship of the average strength between the time of elimination of the agent with the number of exacerbations ($r = 0.37$) and the number of hospitalizations ($r = 0.45$) was noted.

Keywords. COPD, patients, hospitalizations.

Introduction. Today in the world there is a pronounced and significant level of underdiagnosis of the disease, its steady progression. The damage caused to the health of the population due to COPD requires scientific researchers to develop, implement and substantiate the possibilities of using screening methods for early diagnosis of COPD for a wide range of population in the regions [1; p.13-20].

The extremely low use of screening tests, including the use of validated questionnaires and screening functional tests - 6-second test, Stange's test and Genche's test, allowing to suspect an obstructive component, remains the main "gap" in the early diagnosis of COPD.

To overcome the problems of underdiagnostics in primary health care, it is necessary to conduct large-scale population screening studies in various regions [4; p.47-52].

The aim of this study was to optimize approaches to early phenotypic diagnosis and differential management of patients with chronic obstructive pulmonary disease.

Material and research methods. 375 patients with COPD were examined.

The research practice is based on approaches that determine the level of validation of the diagnostic significance of the COPD questionnaire for general practitioners (Chronic Airways Diseases A Guide for Primary Care Physicians, 2005),

screening functional tests (6-second test, Stange's test and Genche's test) in relation to the severity of obstructive disorders, assessment of mucociliary clearance (saccharin test according to the Amelly method) in relation to the history of exacerbations (number and need for hospitalization of the patient), assessment of the degree of influence of chronic obstructive pulmonary disease on the patient's daily life and health (CAT test), and also the ratio of the obtained estimates to the nature of the disease phenotype (A, B, C, D) in accordance with the recommendations of GOLD (2017).

Research results. We studied the sensitivity, specificity and diagnostic value of the COPD questionnaire for general practitioners (Chronic Airways Diseases A Guide for Primary Care Physicians, 2005), which allows translating the patient's answers into quantitative characteristics and correlating them with the presumptive diagnosis of COPD, and functional impairment of the FVD. within the framework of the "gold standard", which is presented in Table 1. The diagnostic value of the questionnaire under consideration, calculated by the ratios of the parameters (A + D) / (A + B + D + C), was 95.8%.

Table 1

Sensitivity, specificity and diagnostic value of the COPD screening questionnaire for general practitioners

	COPD disease according to the criteria of the "gold standard" FEV_1 / FZHEL ≤70% and FEV_1≤80%		
	есть	нет	
COPD diagnostic threshold at 17 or more points	358 A	25 B	Diagnostic sensitivity - the proportion of a truly positive test among patients A / (A + C) - 95.5%
Diagnostic threshold for the likelihood of COPD at 16 or less points	17 C	600 D	Diagnostic specificity - the proportion of a truly negative test among healthy D / (B + D) - 96.0%

Considering the frequency of occurrence of positive results of the questionnaire to the degree of obstructive disorders, its high diagnostic value was noted, which makes it possible to diagnose COPD in the early stages of the disease (Table 2).

Table 2

The ratio of the diagnostic threshold to functional indicators

	Functional class of COPD disease			
	FEV_1	50%< FEV_1	30%< FEV_1	FEV_1

	≥80%, n=34	<80%, n=53	<50%, n=153	<30%, n=135
COPD diagnostic threshold> 95% (17 or more points)	25(73,5%)	48(90,5%)	150(98,0%)	135(100%)
COPD diagnostic threshold <95% (16 or less points)	9(26,5%)	5(9,5%)	3(9,5%)	-

The practice of using tests to measure the duration of the forced expiration, the test with the maximum breath-hold during inspiration and the test with the maximum breath-hold on the expiration in the provision of medical services at the primary care level can significantly improve the quality of diagnosis of obstructive disorders. It was noted that with the severity of the obstruction, the frequency of positive screening tests increases: from 76.5% to 100% for the Stange test, from 85.3% to 100% for the Gench test and from 94.1% to 100% for 6 second sample. Evaluation of the ratio of the criterion of the "gold" standard of obstructive disorders with the number of positive functional screening tests showed a high frequency of three positive test samples in confirming obstruction and the degree of its aggravation from 88.2% to 100%.

The assessment of the sensitivity, specificity and diagnostic value of screening functional tests is compared with the results of functional disorders within the framework of the "gold standard" of COPD diagnosis, presented in Table 3.

Table 3

Sensitivity, specificity and diagnostic value of screening functional tests for the diagnosis of COPD,%

	Positive Screening Functional Tests		
	6 second test	Stange test	Genche test
Diagnostic sensitivity	94,7	92,8	89,3
Diagnostic specificity	96,0	94,4	91,2
Diagnostic value	94,5	93,8	90,5

Based on the above results, a scoring scale was developed for assessing the results of functional screening tests, reflecting their diagnostic threshold in the diagnosis of obstructive syndrome (Table 4).

The use of this scale makes it possible to objectify the degree of functional disorders in screening programs for the diagnosis of obstructive diseases.

Table 4

Scale of point assessment of indicators of functional screening tests in the diagnosis of obstructive disorders

Points	Diagnostic screening tests		
	6 seconds, sec	Stange test, sec	Genche test, sec
0	Less than 6	Over 40	Over 30
1	7-9	39-30	29-25
2	10-11	29-25	24-20
3	12-13	24-20	19-15
4	More than 14	Less than 19	Less than 14

The summarized quantitative assessment of the results of the validated questionnaire and the scoring of functional screening tests, reflecting the severity of obstructive disorders and correlating with the parameters of the "gold standard", emphasizes its high diagnostic accuracy (Table 5), where, with a total of 17-20 points, mild obstructive disorders were found; at 21-23 points - moderate obstructive disorders; at 24-26 points - pronounced and more than 27 points - pronounced obstructive disorders.

Table 5

Diagnostic value of screening test approaches in the diagnosis of obstructive disorders

Options	quantifying the results of the validated questionnaire and functional screening tests			
	18-20 points	21-23 points	24-26 points	More than 27 points
FEV_1, % from due	79,6±3,3	59,1±4,9	41,8±3,4	25,6±4,1
FEV_1/ FZHEL	66,6±2,7	63,9±4,7	60,6±3,7	60,1±5,7

The practice of managing patients with COPD is determined not only by the approaches of early diagnosis, but also to a greater extent by the number of exacerbations, the number of exacerbations requiring hospitalization, and the assessment of the impact of the disease on the patient's daily life and health. For the most part, these indicators are subjective, and the clinical features of the course of respiratory pathology do not always allow us to focus on the likelihood of respiratory exacerbation and the reason for hospitalization from exacerbation.

The results of our research have shown that the number of exacerbations and the number of exacerbations requiring hospitalizations in COPD patients correlates with a morphological marker - a violation of mucociliary clearance and the depth of its violations. When assessing the relationships, a positive relationship of the average strength between the time of elimination of the agent with the number of exacerbations ($r = 0.37$) and the number of hospitalizations ($r = 0.45$) was noted.

Comparing the frequency of exacerbations and hospitalizations, the diagnostic threshold for the saccharin test of more than 25 minutes was determined, which correlated with the frequency of exacerbations more than 2 times a year and the number of required hospitalizations, and was also determined by the level of

quantitative assessment of the validated questionnaire and functional screening tests characterizing the severity of respiratory obstructive disease. (Table 6).

Table 6

Characteristics of indicators of the state of mucociliary clearance at different levels of the diagnostic threshold of obstructive disorders

Options	quantifying the results of the validated questionnaire and functional screening tests			
	18-20 points	21-23 points	24-26 points	More than 27 points
MCC, min	14,6±1,1	24,4±0,8	29,7±1,2	36,9±0,9

We calculated the diagnostic value of a parameter that determines the ratio of the result of the diagnostic scale, including the total assessment for the diagnosis of COPD to the result of the scale for assessing the impact of the disease on the patient's life (CAT) and characterizing a certain status of the patient through the prism of clinical manifestations of the severity of the disease to assessing the degree of influence of the disease on the life of the patient (Ind - Рд / Рсат). The ratio was used to determine indices Ind> 1.2 - clinical manifestations of the disease prevailing over the parameter of the effect of the disease on the patient's life (phenotype A and C according to GOLD), which had a positive correlation with MRC (r = 0.52) and an inverse correlation according to the results CAT test (r = -0.43) of medium strength of connection and Ind≤1.2 - a pronounced effect on the patient's life (phenotype B and D according to GOLD), who had a positive correlation with CAT (r = 0.75) of strong strength communication.

The ratio of the estimates obtained with the nature of the disease phenotype (A, B, C, D) in accordance with the GOLD recommendations (2017), taking into account the parameters of the state of mucociliary clearance and integrated indicators of clinical manifestations of the disease to the assessment of the effect of the disease on the patient, made it possible to generalize the patient's status by the phenotype of the disease. where:

A - persons with COPD with clinical manifestations of the disease, which have an unexpressed effect of the disease on the patient's life (Ind> 1.2) and without a pronounced violation of the morphological marker of mucociliary clearance (MCC less than 25 min), which determines the absence of exacerbation or its exacerbation no more than 1 time in year;

B - persons with COPD with clinical manifestations of the disease, which have a pronounced effect of the disease on the patient's life (Ind≤1.2) and without a pronounced violation of the morphological marker of mucociliary clearance (MCC less than 25 min), which determines the absence of exacerbation or its exacerbation no more than 1 time per year ;

C - persons with COPD with clinical manifestations of the disease that have an unexpressed effect of the disease on the patient's life (Ind> 1.2) and with a

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pronounced violation of the morphological marker of mucociliary clearance (MCC for more than 25 min), which determines exacerbations 2 or more times a year, as well as more than 1 hospitalization per year.

D - persons with COPD with clinical manifestations of the disease, which have a pronounced effect of the disease on the patient's life (Ind≤1.2) and with a pronounced violation of the morphological marker (MCC for more than 25 minutes), which determines exacerbations 2 or more times a year, as well as more than 1 hospitalization per year.

Determination of the phenotype of the disease in relation to the clinical manifestations of the disease, its impact on the patient's life and the severity of the morphological marker was compared with the phenotypes recommended by GOLD (2017). It was noted that out of 112 patients with phenotype D according to GOLD, in 110 patients (98.2%) phenotype D was verified according to the diagnostics modified by us; out of 98 patients with phenotype C, 100 patients (102%). For phenotypes B and A according to GOLD, there was a 100% coincidence of diagnostic significance.

Conducting a questionnaire survey and assessing the CAT test, screening functional tests (6-second test, Stange's test and Genche's test) and a test for the state of mucocystic clearance allows forming a group of COPD patients with varying degrees of severity of obstructive ventilation disorders in specialists, determining the effect of the disease on the patient's health and, according to the ratio of quantitative assessments, divide patients into phenotypic types of the disease that coincide with the GOLD recommendations (2017), choose the right therapy for each individual based on the GOLD recommendations, and prevent unreasonable high-cost medical services (Table 7).

Considering the provision on medical effectiveness, which is assessed by the formula:

$$\mathbf{Km} = \frac{\textbf{The number of cases of achieved medical results}}{\textbf{Number of cases evaluated}}$$

we can state that the indicator of medical efficiency is 0.98-1.0.

In summary, the assessment of the results obtained reflects that the diagnostic value of the questionnaire in question was 95.8%, functional screening test approaches in the diagnosis of obstructive disorders from 90.5-94.5% and in the presence of 3 positive functional screening test approaches increases to 93, nine%.

Table 7

Treatment regimens by disease phenotype

	Therapy: DDACP and acetylcysteine	*Therapy: DDACP + ICS / LABA and acetylcysteine / antibiotic*
	C-persons of COPD, with clinical manifestations of the disease, having an unexpressed effect of the disease on the	D - persons with COPD, with clinical manifestations of the disease, which have a pronounced effect of the disease on the

MCC more than 25 minutes	patient's life (Ind> 1.2) and with a pronounced violation of the morphological marker that determines exacerbations 2 or more times a year, as well as more than 1 hospitalizations per year (100 patients)	patient's life (Ind≤1.2) and with a pronounced violation of the morphological marker that determines exacerbations 2 or more times a year, as well as more than 1 hospitalization per year (110 patients)
MCC less than 25min	A-persons of COPD, with clinical manifestations of the disease, which have an unexpressed effect of the disease on the patient's life (Ind> 1.2) and without a pronounced violation of the morphological marker, which determines the absence of exacerbation or its exacerbation no more than 1 time in year (75 patients)	B - persons with COPD, with clinical manifestations of the disease, which have a pronounced effect of the disease on the patient's life (Ind≤1.2) and without a pronounced violation of the morphological marker, which determines the absence of exacerbation or its exacerbation no more than 1 time per year (90 patients)
	Ind >1,2	Ind ≤1,2
	Therapy: KDBA or KDAHP	*LABA or DDAHP therapy*

Conclusions: The developed and proposed algorithm for managing COPD patients at the level of primary health care institutions, including approaches for screening diagnosis of chronic obstructive pulmonary disease, identification of obstructive and morphological disorders, as well as assessing the degree of influence of chronic obstructive pulmonary disease on the patient's daily life and health, is aimed at early diagnosis, determination of management of chronic obstructive pulmonary disease, strategies for the prevention of disease progression, which will prevent expensive medical costs.

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