

ANNOTATION

Dissertation work for the degree of Doctor of Philosophy (PhD)
in the educational program "8D10102 - Medicine"

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on the topic: "Diagnostic potential of optical coherence tomography of retina and choroid in patients with chronic obstructive pulmonary disease"

Relevance of the problem

Chronic obstructive pulmonary disease (COPD) remains a leading cause of global morbidity and mortality. According to the World Health Organization, COPD causes approximately 3.5 million deaths annually (approximately 5% of all deaths globally). In Kazakhstan, the prevalence of the disease among people over 40 years of age reaches 5.9%, reflecting a significant burden on the healthcare system and indicating a likely underestimation of the true incidence. One of the systemic manifestations of COPD is vascular-hypoxic changes in the visual organ, affecting the retina and choroid—tissues with high metabolic activity and sensitivity to oxygen deficiency.

Optical coherence tomography (OCT) is a highly accurate and noninvasive method for layer-by-layer fundus imaging, allowing for objective assessment of structural changes in systemic diseases. However, the international and domestic literature lacks data on the comprehensive analysis of retinal-choroidal changes in patients with COPD, particularly depending on the stage of the disease.

Objective: to determine changes in the parameters of retina and choroid using optical coherence tomography of the eye in patients with COPD.

Tasks:

1. To study the use of optical coherence tomography of retina and choroid in patients with chronic obstructive pulmonary disease worldwide and in Kazakhstan using a systematic review;
2. To identify associations between changes in retinal and choroidal parameters based on optical coherence tomography data in patients with COPD;
3. To conduct a comparative analysis of retinal and choroidal parameters in patients with COPD using optical coherence tomography, taking into account the stage;
4. To develop diagnostic criteria for changes in retina and choroid based on optical coherence tomography data in patients with COPD..

Brief description of the study

This dissertation study was conducted between May 16, 2020, and September 27, 2021, at the Almaty Ophthalmology Center. Participants included patients with a history of COPD who presented to the Ophthalmology Center, as well as those invited through social media advertisements and at medical organizations. The study was approved by the Local Ethics Committee of the Faculty of Medicine and

Healthcare of Al-Farabi Kazakh National University (Protocol No. IRB-A415, October 23, 2019).

The study included patients with a confirmed diagnosis of COPD established by a pulmonologist and documented in the outpatient chart. In all patients, COPD was verified by spirometry with bronchodilation in accordance with generally accepted quality criteria. A total of 51 patients with COPD (50.9% men, 49.1% women; mean age 57.2 ± 6.2 years) and 51 participants without COPD, selected according to the inclusion criteria, participated. All patients with COPD were divided into two groups depending on the severity of the disease and the GOLD classification: patients with COPD stages A and B (GOLD A-B) and patients with COPD stages C and D (GOLD C-D). The GOLD A-B group included 17 (50%) men and 17 (50%) women; mean age 56.0 ± 7.2 years. The GOLD C-D group included 7 men (41.7%) and 10 women (58.3%); mean age was 63.6 ± 3.5 years. OCT was used to measure the retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), and subfoveal choroidal thickness (SFT).

The obtained data (all variables) were tested for normality using the Kolmogorov-Smirnov test. All parameters are presented as mean \pm standard deviation. To determine the difference between two independent groups, the t-test or Mann-Whitney U-test was used. For more than two independent groups, one-way analysis of variance (ANOVA) with a least significant difference (LSD) post-hoc test was used. The Kruskal-Wallis test was used for groups in which the parametric test assumptions were not met. When comparing categorical variables, the chi-square test was used. Spearman's correlation coefficients (ρ) were calculated to assess associations between variables. A p value of < 0.01 was considered statistically significant. All statistical processing was performed using SPSS Statistics 26.0 (IBM, USA).

Correlations between OCT parameters and the degree of respiratory failure, disease duration, and COPD stage were analyzed. In patients with COPD, the mean subfoveal choroidal thickness (SCT) progressively decreased with increasing COPD severity ($p < 0.001$). Ganglion cell layer thickness (GCT) in all quadrants differed between the Global Initiative for Chronic Obstructive Lung Disease (GOLD) C-D group and the control group ($p < 0.01$), as well as between the GOLD A-B and GOLD C-D groups ($p < 0.01$). Retinal nerve fiber layer thickness (RNFL) differed between the control group and the GOLD C-D group ($p < 0.01$), as well as between the GOLD A-B (mild, moderate) and GOLD C-D (severe, very severe) groups ($p < 0.01$).

The data obtained demonstrate that even in the early stages of COPD, significant changes in individual layers of the retina and choroid are detected, and the severity of structural abnormalities increases as the disease progresses. It has been proven that decreased choroidal thickness, as well as thinning of the inner and outer retinal layers, can be considered markers of chronic hypoxia and microcirculatory disorders.

Scientific novelty

1. For the first time, the characteristics of changes in retinal and choroidal parameters using OCT data in patients with COPD of varying severity were comprehensively characterized.
2. Statistically significant correlations were established between COPD severity and retinal and choroidal morphometric data obtained using OCT.
3. Diagnostically significant OCT parameters were identified that allow for differentiation of COPD stages and detection of early signs of systemic hypoxia (Appendix A).
4. An algorithm for applying OCT changes was developed, enabling the use of this method in interdisciplinary clinical practice (Appendix B).

Practical significance

1. The obtained data expand the potential for early detection of systemic COPD complications by incorporating ophthalmologic monitoring into a comprehensive diagnostic package (certificate of entry of information into the state register of rights to objects protected by copyright No. 64067 (Appendix B));
2. The study results substantiate the use of posterior segment OCT as a method for detecting initial hypoxic disturbances preceding the development of severe clinical symptoms;
3. The obtained results have practical value for implementation in ophthalmologic and pulmonologic services and can be used within the framework of interdisciplinary monitoring of patients with COPD..

The main provisions submitted for defense

1. Patients with COPD exhibit characteristic structural changes in the retina and choroid, determined by OCT and intensifying as respiratory failure progresses against the background of the underlying disease.
2. A statistical association exists between OCT parameters and clinical and functional indicators of COPD, reflecting the impact of systemic hypoxia on the visual organ.
3. Structural indicators of the retina and choroid can serve as early markers of vascular-hypoxic disorders in COPD.
4. The developed diagnostic criteria for OCT changes allow for improved early detection of systemic COPD complications.

Conclusions

1. COPD is accompanied by significant morphological changes in the retina and choroid associated with chronic hypoxia and microcirculation disorders.
2. Changes in the parameters of the retina and choroid, determined by the OCT method, correlate with the stage of COPD, which confirms their diagnostic significance: with an increase in the stage of the disease to COPD GOLD C-D, there is a statistically significant depletion of CTX ($p=0.00001$), RNFL ($p=0.00001$) and SGC ($p<0.01$).

3. OCT of the retina and choroid is an informative method for early detection of systemic manifestations of COPD and can be included in interdisciplinary diagnostic algorithms.
4. The developed diagnostic criteria allow the use of OCT of the eye as an additional tool for monitoring the condition of patients, contributing to the improvement of the quality of diagnosis and observation..

Dissertation approval

The main provisions of the work were presented in the form of a scientific abstract at an international conference and published in the collection “Abstracts of the IX Annual International Scientific-Practical Conference “Medicine Pressing Questions”, May 6-8, 2020, Baku, Azerbaijan”, topic of the report: “The influence of the course of COPD on changes in the parameters of the retinal nerve fiber layer thickness, the thickness of the macular and the ganglion cell complex”.

Publications

On the topic of the dissertation, 4 works have been published, including 3 works in journals recommended by the Committee for Quality Assurance in Science and Higher Education of the Ministry of Science and Higher Education of the Republic of Kazakhstan, 1 article in a journal of the international citation database Scopus (Medical Journal of Malaysia, Q3, 46th percentile): “Changes in fundus by optical coherence tomography in patients with chronic obstructive pulmonary disease: A systematic review”, Medical Journal of Malaysia ISSN: 03005283 Volume: 80 Issue: 5 Pages: 635 – 641 Review 2025 EID: 2-s2.0-105017415392 <https://pubmed.ncbi.nlm.nih.gov/41016006/>, 1 publication in the materials of foreign conferences.

Implementation of research results

Integration as a mandatory element of diagnostics of the retina and choroid using OCT in patients with COPD was introduced into the work of Focus Ophthalmology Center LLC (Appendix G).

Volume and structure of the dissertation

The dissertation is presented on 94 pages of computer-typeset Microsoft Word text editor and consists of an introduction, main body, conclusion, and a list of references. The dissertation has four appendices. The bibliography includes 131 sources in Russian and English. The work is illustrated with 12 tables and 14 figures.