Assessment of the development of primary open-angle glaucoma and diabetic retinopathy using digital medicine

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Abstract. The leading place in the structure of blindness and low vision is occupied by two diseases: primary open-angle glaucoma and diabetic retinopathy. The combination of two diseases in one eye gives an even more severe prognosis for vision. Modern diagnostic equipment helps in accurate and early diagnosis of the disease by analyzing digital data of the optic nerve head and macular area of the retina according to the results of an optical coherence tomograph. A mathematical model for predicting the development of diabetic retinopathy and primary open-angle glaucoma according to the proposed mathematical criteria has been developed. The criteria represent the ratio of the integral area of the neuroretinal rim to the integral volume of the neuroretinal rim; the retinal thickness criterion and criterion of the primary open-angle glaucoma and diabetic retinopathy are calculated. A computer program has been developed. The algorithm of the program, which includes windows for entering digital data of the macular zone and parameters of the optic nerve head, is presented. The result of the program is the statement of the risk of developing combined pathology of the fundus in a particular patient.

1 Introduction

1.1. The problem of vision disability in diabetic retinopathy and open-angle glaucoma

Glaucoma and diabetic retinopathy have a dominant position in the structure of blindness and low vision. If the two above-mentioned diseases are combined, degeneration of the nerve fiber layer occurs, namely, the damage of the complex of retinal ganglion cells and the peripapillary layer of retinal nerve fibers [1–6].

The relationship between glaucoma and diabetic retinopathy has been studied for several decades and is confirmed by the common pathogenetic mechanisms: damage to the inner layers of the retina as a result of oxidative stress, activation of vascular endothelial growth factor, mechanical compression of axons in the optic nerve head [7–10].

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1.2. The state of the retina in the comorbid pathology of the fundus

With comorbid pathology it is difficult for a practicing ophthalmologist to determine the disease that causes vision loss: glaucoma or diabetic retinopathy. With ophtalmoscopy, the changes in the optic nerve head are noticed only at the late stages of glaucoma. Severe retinal edema with hemorrhages and traction syndrome also occurs at the late stages of diabetic retinopathy [11–14].

1.3. Methods for diagnosing two diseases

Invaluable assistance in diagnosing fundus pathology is provided by modern ophthalmic diagnostic devices [15–17].

Optical coherence tomography makes it possible for diabetic retinopathy to assess the structure of the retina layer by layer and make a diagnosis at the morphological level, taking into account the cytoarchitectonics and morphology of the retina. The tomograph gives the opportunity to study in detail the structure of the optic nerve head at the early stages of glaucoma. The earliest changes in the optic nerve head are not detected ophthalmoscopically [18–21].

1.4. Digital medicine in ophthalmology

Diagnostic equipment helps the doctor to make a diagnosis, but at the same time provides a huge amount of digital material. Only using interdisciplinary knowledge and directions, such as mathematical modeling and programming, it is possible to analyze large amounts of digital data and to predict the course of diseases [22–25].

Digital methods are used not only in ophthalmology, but also in other fields of science and technology [26–30].

2 Problem

To develop a mathematical model and a computer program for predicting comorbid diseases, namely, diabetic retinopathy and primary open-angle glaucoma, based on a comprehensive analysis of data from an optical coherence tomograph (thickness of sectors in the macular zone, parameters of the optic nerve head and neuroretinal rim).

3 Materials and methods

A mathematical model for processing digital data of an optical coherence tomograph is proposed. To optimize the work of a doctor with a patient with type 2 diabetes mellitus and minimize the time required to predict the progression of primary open-angle glaucoma and diabetic retinopathy, criteria that allow for a quantitative assessment of the patient's fundus structures have been developed.

To assess the prognosis of primary open-angle glaucoma and diabetic retinopathy, it was proposed to use the following criteria: the thickness of the macular zone in 9 areas using an optical coherence tomograph, the integral volume and integral area of the neuroretinal rim and the area of the optic disc excavation.

A system of criteria that describes the prognosis of comorbid diseases of primary open-angle glaucoma and diabetic retinopathy in patients with type 2 diabetes mellitus is presented:

$$\left\{ \begin{array}{l} R_1 = \frac{\sum_1^9 (h_i - h_{min})}{(h_{max} - h_{min}) \cdot m} \\ \frac{S_b}{V_b} \\ R_{GDR} = \frac{S_b \cdot \sqrt{S_e}}{V_b \cdot R_1} \end{array} \right. . \quad (1)$$

where

R_{GDR} – criterion of the primary open-angle Glaucoma and Diabetic Retinopathy;

$\frac{S_b}{V_b}$ – inverse value of the mean value of the width of the neuroretinal belt, m^{-1} ;

V_b – integral volume of the neuroretinal rim, m^3 ;

S_b – integral area of the neuroretinal rim, m^2 ;

S_e – optic disc excavation area, m^2 ;

R_1 – retinal thickness criterion;

m – number of retinal scan sectors ($m = 9$);

h_i – thickness of retinal sectors (in each sector of the macular zone), μm ;

h_{max} – maximum retinal thickness of the macular zone, μm ;

h_{min} – retinal thickness in one of the scanning sectors of the macular zone, excluding the central and extreme sectors, μm .

The table that shows the correspondence between the shown criteria and the prognosis of primary open-angle glaucoma and diabetic retinopathy in patients with type 2 diabetes mellitus is developed (table 1).

Table 1. The prognosis of the disease depending on the criterion R_{GDR} and the relation $\frac{S_b}{V_b}$.

R_{GDR}	$\frac{S_b}{V_b}$	Disease diagnosis	Risk of progression	Disease prognosis
$3 \leq R_{GDR} < 5.5$	$\frac{S_b}{V_b} < 3.5$	Stage 1 glaucoma	Low	Good prognosis for vision
$5.5 \leq R_{GDR} < 10$	$3.5 \leq \frac{S_b}{V_b} < 5$	Stage 2 glaucoma	High	Good prognosis for vision
$R_{GDR} \geq 10$	$\frac{S_b}{V_b} \geq 5$	Stage 3 glaucoma	High	Bad prognosis for vision

4 Results and discussion

4.1. Algorithm for the automated formulation of the prognosis of the development of primary open-angle glaucoma and diabetic retinopathy

Based on the digital data of an optical coherence tomograph related to the thickness of the macular zone in nine sectors of the retina, the parameters of the neuroretinal rim and the optic nerve head, a computer program that automatically determines the prognosis of the disease was created. The program is a module for inputting initial data, a calculation module and a module for outputting data (setting a forecast for the development of a disease).

The data entry module contains the data of the optical coherence tomograph on the thickness of the retina in nine scanning sectors, the absence or presence of edema in each of the sectors of the macular zone, the integral volume, the integral area of the neuroretinal rim and the excavation area of the optic nerve head.

The program provides an input of initial data for an optical coherence tomograph in the form of retinal thicknesses in 9 sectors of the macular zone, information on the presence or absence of edema in each sector of the macular zone, as well as parameters of the neuroretinal rim and optic nerve head. For the convenience of a practitioner, the color scheme of the program repeats the interface of an optical coherence tomograph.

The calculation module implements algorithms for logical operations and mathematical operations.

Logical operations represent an exception from the calculation of the criterion R_1 for areas of the macular zone where there is no retinal edema. The algorithm of mathematical operations is a sequential calculation of retinal thickness criterion R_1 and criterion of the primary open-angle glaucoma and diabetic retinopathy R_{GDR} , as well as the ratio $\frac{S_b}{V_b}$. After

the calculation, a logical operation is performed to compare the obtained criterion value R_{GDR} as well as the ratio $\frac{S_b}{V_b}$ with the prognosis of the disease.

The data output module displays data on the prognosis of the development of primary open-angle glaucoma and diabetic retinopathy on the computer screen in the form of a text message.

The algorithm of the program for setting the prognosis of diabetic retinopathy and primary open-angle glaucoma is illustrated in Figure 1.

Fig. 1. Algorithm of the program for setting the prognosis of the development of diabetic retinopathy and primary open-angle glaucoma.

4.2. Automatic disease prognosis

To debug the program, the data of a specific patient were used: a patient M, 68 years old with a diagnosis of type 2 diabetes mellitus, HbA1c 9 %, non-proliferative diabetic retinopathy, diabetic macular edema, open-angle primary stage III glaucoma.

The program included data on the thickness of the macular zone, the integral volume of the neuroretinal rim, as well as the area of excavation of the optic nerve head and the neuroretinal rim of the patient under study.

The windows for entering data into a computer program for an optical coherence tomograph (figure 2) and parameters of the optic nerve head (figure 3) are presented.

Tomograph data				
Type the results of measuring retinal thickness				
№	Retinal zones	Macular area scanning sector	Retinal thickness, microns	Edema (yes/no)
1	2	3	4	5
1	Fovea centralis	Centre	419	yes
2		Tempo	484	yes
3	ParaFovea	Superior	463	yes
4		Nasal	466	yes
5	PeriFovea	Inferior	404	yes
6		Tempo	451	yes
7		Superior	429	yes
8		Nasal	402	yes
9		Inferior	350	yes

Fig. 2. Data input of layer thickness in the macular zone for an optical coherence tomograph with indication of sectors with macular edema.

Measurement data of the optic nerve disc			
Type the results of the measurement of the optic nerve disc			
№	Tomograph data	Value	Dimension
1	2	3	4
1	Integral area of the neuroretinal belt	1.732	mm2
2	Integral volume of the neuroretinal belt	0.253	mm3
3	Excavation area of the optic nerve disc	1.242	mm2

Fig. 3. Entering the parameters of the optic nerve head and the neuroretinal rim. Entering the parameters of the optic nerve head and the neuroretinal rim.

The result of the program is the statement of the risk of progression and prognosis of the disease. A window for outputting data from a computer program with a prognosis of a disease for a patient under study with primary open-angle glaucoma and diabetic retinopathy in type 2 diabetes mellitus is presented (figure 4).

Diagnosis

Open-angle glaucoma step III in combination with diabetic retinopathy

Prognosis

High risk of progression with bad vision prognosis

Fig. 4. Computer program data entry window with setting a prognosis of the risk of disease development for a patient with primary open-angle glaucoma and diabetic retinopathy in type II diabetes mellitus.

As a result of calculation of the program, the following diagnosis was set: stage III glaucoma, a high risk of disease progression and a poor prognosis for vision. The results of mathematical modeling coincide with the clinical diagnosis of the doctor.

An alternative way to predict the development of glaucoma is a clinical analysis of the optic nerve head according to the result of ophthalmoscopy. Thus, the doctor examining the patient evaluates the width of the neuroretinal rim, which is located between the edge of the optic nerve head and the edge of the excavation. The analysis of the neuroretinal rim is carried out according to the ISNT rule: the largest from below, less from above, less from the nose, less from the temple. It is obvious that the proposed computer analysis of the digital parameters of the optic nerve head based on the results of an optical coherence tomograph is more accurate.

5 Conclusion

An effective mathematical model for predicting the development of comorbid pathology of primary open-angle glaucoma and diabetic retinopathy has been developed. The

mathematical model is based on the proposed criteria: criterion of the primary open-angle glaucoma and diabetic retinopathy R_{GDR} , retinal thickness criterion R_1 as well as ratios $\frac{S_b}{V_b}$

The result of the work is the creation of the program. The program interface fully corresponds to the interface of the optical coherence tomograph repeating its color scale: green - normal, yellow - warning, red - pathology.

The first data entry window is the input of digital data on the materials of the "macula" protocol for nine sectors of the macular zone (Fovea – 1 zone, ParaFovea – 4 zones, PeriFovea – 4 zones). The program table records information about the presence or absence of edema in nine sectors of the macula. It is determined that there is edema if it is shown by the tomogram accordingly and the retinal area is in red light. If any areas of the macula are green, they are marked in the program table as there is no retinal edema.

Digital parameters of the optic nerve head are further entered into the program: integral volume of the neuroretinal rim, integral area of the neuroretinal rim, optic disc excavation area. The program analyzes the entered data according to the developed formulas. The logical operation of the program gives the opportunity to exclude areas of the retina without edema.

Then a mathematical calculation using a tomogram of the optic nerve head is carried out. The ratio of the integral area of the neuroretinal rim to the integral volume of the neuroretinal rim is taken into account, the retinal thickness criterion and criterion of the primary open-angle glaucoma and diabetic retinopathy are calculated.

On the basis of the statistical studies, the intervals of values of the criteria characteristic of stage I glaucoma, stage II glaucoma, stage III glaucoma in combination with diabetic retinopathy were developed. These glaucoma stage intervals are included in the program. Further, according to the program, logical operations are performed: the ratio of the calculated criteria with intervals according to the stages of glaucoma in combination with diabetic retinopathy.

The result of the program is the data output window "forecast of the risk of developing comorbid pathology of the fundus". The monitor screen displays the printed conclusion that in a particular patient diagnosed with comorbid glaucoma and diabetic retinopathy the risk of disease development may be either "high risk of developing disease" or "low risk of developing disease".

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