# REPUBLIC OF AZERBAIJAN

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#### **ABSTRACT**

of the dissertation for the degree of Doctor of Philosophy

# ASSESSING THE IMPROVEMENT OF INITIAL DIAGNOSTIC CRITERIA AND MONITORING PATHOLOGY OF THE ORGAN OF VISION IN CONSCRIPTION AGE YOUTH

Specialty: 3219.01 – eye diseases

Field of science: Medicine

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# GENERAL CHARACTERISTICS OF THE RESEARCH

# The research relevance and development degree

Improving the quality of life and health of the population is among the priority problems of state policy. Currently, visual pathologies are expanding among the world's population day by day. According to the latest studies, about 43.3 million of the growing world population suffer from blindness, and 295 million - moderate to severe vision impairment<sup>1,2</sup>. The increasing use of computers and mobile devices in the near distance and reducing time spent outdoors with a sedentary lifestyle allow for supposing that these figures will increase by 1,5-2 times by 2050<sup>3</sup>. Such a wide spread of vision pathologies and plans to combat blindness require extensive analysis in different populations and age groups.

The identification of visual pathologies among conscription-age young men and statistical research of the main diseases causing unfitness for military service (MS) is extremely important to ensure the health of youth serving in the army. In the Republic of Azerbaijan, military service is mandatory for young men who have reached conscription age. MS requires high health criteria for recruits and soldiers. Herewith, these criteria include adequate visual acuity as part of the standards<sup>4</sup>. Visual

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<sup>&</sup>lt;sup>1</sup> Bourne RRA. Magnitude, temporal trends, and projections of the global prevalence of blindness and distance and near vision impairment: a systematic review and meta-analysis / Bourne R.R.A., Flaxman S.R., Braithwaite T. [et al.] // The Lancet Global Health, – 2017, 5(9), – e888-e97.

<sup>&</sup>lt;sup>2</sup> GBD 2019 Blindness and Vision Impairment Collaborators; Vision Loss Expert Group of the Global Burden of Disease Study. Trends in prevalence of blindness and distance and near vision impairment over 30 years: an analysis for the Global Burden of Disease Study. // Lancet Glob Health., – 2021, 9(2), – e130-e143.

<sup>&</sup>lt;sup>3</sup> Holden, B.A. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050 / B.A.Holden, T.R.Fricke [et al.] // Ophthalmology, –2016, 123(5), –p.1036-1042.

<sup>&</sup>lt;sup>4</sup> Regulation on military-medical expertise // Resolution No. 59 of the Cabinet of Ministers of the Republic of Azerbaijan dated February 29, 2008. – Baku: Legislative Collection of the Republic of Azerbaijan, - 2008, - p.177.

pathologies are widespread among the population of the Republic of Azerbaijan, like in all other parts of the world. It should be particularly noted that the prevalence of visual pathologies among the young age group during the last ten years has been considered in several studies<sup>5,6,7</sup>. Their results explained the trend of expanding eye diseases among the young age group and the need for taking appropriate measures for early diagnosis and prevention of their rapid progression.

The prevalence of ocular pathologies among military staff manifests itself differently in different geographical countries. The studies performed among American conscripts showed refractive errors in 22-34% of candidates<sup>8</sup>. In Asian countries with widespread refractive errors, myopia is identified in 86.1% of conscripts.

In general, very few studies show the role of various eye diseases in unfitness for military service. Thus, in Poland, a long-term 12-year analysis of the prevalence of various eye diseases and cases of unfitness for military service among conscripts and military staff was performed. In a similar study performed in Great Britain, Dignan et al. also published the occurrence of myopia among refractive defects causing unfitness for military service 10. Among the most recent studies, the results of the extensive research performed among the conscription-age youth in Turkey have shown that 40,1% of young men, unfit for MS due to visual

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 $<sup>^5</sup>$  Агаева Р.Б.Заболеваемость вследствие болезней глаза и его придаточного аппарата лиц молодого возраста от 18 до 29 лет в Республике Азербайджан // Oftalmologiya, —Bakı: — 2013.-N3,-s.59-63.

<sup>&</sup>lt;sup>6</sup> Rüstəmova, N.M. Əhalinin əlilləşməsində göz xəstəliklərinin rolunun müqayisəsi / N.M.Rüstəmova // Oftalmologiya, − Bakı: 2016. №1(20), − s.30-34.

<sup>&</sup>lt;sup>7</sup> Агаева Р.Б.Исследование близорукости на фоне общей заболеваемости болезней глаза и его придаточного аппарата у подростков в возрасте от 14 до 17 лет в Азербайджанской Республике. // Oftalmologiya, Bakı: – 2013. – N.2, – s.18-21.

 $<sup>^8</sup>$  Buckingham RS, Cornforth LL, Whitwell KJ& Lee RB. Visual acuity, optical and eye health readiness in the military // J. Mil Med. -2003. - N 168, -p. 194–198

Michal S. Nowak, Piotr Jurowski, Roman Gos and Janusz Smigielski. Ocular findings among young men: a 12-year prevalence study of military service in Poland //ActaOphthalmol. - 2010. - N 88,-p. 535–540.

<sup>&</sup>lt;sup>10</sup> Dignan AP. A decade of experience of examining candidates for entry to the army. // J. R. Army Med Corps. 1992. - N 138, -p. 19–22.

pathology, had refractive errors<sup>11,12</sup>.

Among eye diseases, early identification of some progressive diseases in young men is particularly important. Thus, the diagnosis of keratoconus (KC) related to ectatic corneal diseases occurring in this age group is one of the relevant issues. The use of modern diagnostic equipment in the last ten years has created wide opportunities for early diagnosis of ectasia<sup>13</sup>.

The screening of KC at earlier stages allows for maintaining higher visual functions. Herewith, it is important to identify this disease before military service. Thus, failure to timely identify the disease causes progressive visual deterioration during the service period and leads to the discharge of young men from military service. Therefore, it is extremely important to identify KC in young men first registered for and sent to military service and study its clinical and tomographic specificity <sup>14,15</sup>.

The study plays a great role for the state and the military service system in the proper assessment of visual impairments and ensuring the health of youth serving in the army. Thus, in the time of wide opportunities provided by refractive surgery, the correction of refractive errors allowed for improving the visual acuity of military staff serving in the army. According to the results of some studies, the type of laser vision correction surgery to be performed for young men remains a

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Kocak, N. The prevalence of disorders causing disability in young adult males in Turkey between 2009-2011 / N.Kocak, T.Turker, I.Aydin [et al.] // Pak J Med Sci., - 2013. 29(5),- p.1240-124.

Gundogan FC, Kocak N, Akyildiz R, Yolcu U, Ilhan A, Aydin I, et al. The prevalence and causes of visual impairment in young Turkis men. Pak J Med Sci. – 2015. - N31(4), –p.837-842

<sup>&</sup>lt;sup>13</sup> Global Keratoconus Foundation: [Electronic resource] / Keratoconus. – December 26, 2012. URL: <a href="http://kcglobal.org/content/view/14/26/">http://kcglobal.org/content/view/14/26/</a>.

<sup>&</sup>lt;sup>14</sup> Godefrooij DA. Age-specific incidence and prevalence of keratoconus: a nationwide registration study / DA Godefrooij, GA de Wit, CS Uiterwaal [et al.] // Am J Ophthalmol. – 2017, 175, – p.169–72.

Ambrósio, R.Jr. Paradigms, paradoxes, and controversies on keratoconus and corneal ectatic diseases / R.Jr.Ambrósio, F-C.Silva, I.Lopes // Int J Keratoconus Ectatic Corneal Dis., – 2018, 7(15), – p.35-49.

relevant problem<sup>16</sup>.

Research performed among US military staff has shown the high efficiency of the Wavefront-Guided Femto Lasik surgery. Another study showed the superiority of surface ablation in excimer laser correction among American army servants, and just different surface ablation types were analyzed <sup>17,18</sup>.

Another study, performed in China, showed that young military servants who had undergone Lasik surgery had more severe complications after receiving eye injuries during their service. Therefore, researchers have recommended the exemption of those who have undergone Lasik surgery from military service<sup>19</sup>.

Considering all the aforementioned, the examination of young men who have undergone keratorefractive surgery in Azerbaijan before military service should be improved.

Herewith, in some cases, it is particularly important to perform an advanced examination with the implementation of modern diagnostic techniques to diagnose retina and optic nerve pathologies and identify malingering in young men passing the physical evaluation board. In the identification of pathological changes or cases of simulation, developing the advanced examination procedure plays an important role<sup>20</sup>.

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<sup>&</sup>lt;sup>16</sup> Tanzer D.J.<sup>1</sup>, Brunstetter T., Zeber R., Hofmeister E., Kaupp S., Kelly N., Mirzaoff M., Sray W., Brown M., Schallhorn S. Laser in situ keratomileusis in United States Naval aviators. // J Cataract Refract Surg. 2013. - N39. -p. 1047-58.

<sup>&</sup>lt;sup>17</sup> Denise S. Ryan. Wavefront-Guided Versus Wavefront-Optimized Photorefractive Keratectomy: Visual and Military Task Performance / Denise S. Ryan, MS, Rose K. Sia, MD, Richard D. Stutzman, MC USA (Ret.) [et al.] // Military Medicine, - 2017.- 182(1-2), -p.1636–1644.

 $<sup>^{18}</sup>$  Sia RK, Ryan DS , Edwards JD, Stutzman RD, Bower KS. The U.S. Army Surface Ablation Study: comparison of PRK, MMC-PRK, and LASEK in moderate to high myopia. J Refract Surg.  $-\,2014.\,$  Apr; -  $30(4).-p.256-64.\,$ 

<sup>&</sup>lt;sup>19</sup> Xiao JH, Zhang MN, Jiang CH, Zhang Y, Qiu HY. Laser in situ keratomileusis surgery is not safe for military personnel. // Chin J Traumatol. – 2012. – N 15(2), – p. 77-80.

<sup>&</sup>lt;sup>20</sup> Soares, T.S. Pattern-reversal visual evoked potentials as a diagnostic tool for ocular malingering / T.S.Soares, P.Y.Sacai, A.Berezovsky [et.al.] //Arquivos Brasileiros de Oftalmologia, – 2016. 79(5), – p.303-307.

Considering all these points, the early identification of some ocular diseases in young men with the implementation of the advanced examination before the MS, statistical research of eye characteristics making them unfit for military service, timely application treatment procedures, and improvement of visual acuity will contribute to the state health and military system.

# Object and Subject of the Research

20,049 young men who passed the Military Medical Examination Board (MMEB) in 2016-2018 in the National Ophthalmology Center named after academician Zarifa Aliyeva were involved in the study. The data have been analyzed for different groups of young men involved in the advanced examination. The inclusion criteria were conscription age young men registered for military service, and the exclusion criteria were women and non-conscription age men.

The purpose of the study. Assess the implementation of advanced examination techniques in the diagnosis and monitoring of ocular pathologies in conscription age youth.

#### The Research Tasks:

- 1. Study the incidence of ocular pathologies in young men aged 17-35, improve the initial diagnostics using modern diagnostic methods, and analyze pathologies causing unfitness for MS;
- 2. Study the incidence of corneal ectasia in young men in Azerbaijan and assess the diagnostic significance of Scheimpflug Tomography (ST) in its early identification. Analyze the sensitivity and specificity of tomographic parameters in the subclinical and early clinical stages of the disease, build a model consisting of discriminative parameters, and demonstrate the diagnostic significance of the instrument;
- 3. Analyze diagnostic characteristics in evaluating young men according to the criteria for fitness for MS in connection with the wide application of keratorefractive surgery. Assess the diagnostic significance of the advanced examination of these young men using ST;
- 4. Herewith, assess the implementation of some modern diagnostic techniques while performing various tests in the vision function ocular malingering cases. Demonstrate the diagnostic significance of electrophysiological examination techniques in the evaluation of func-

tional vision conditions and optical coherence tomography in the evaluation of structural conditions of visual organs;

5. Develop and prepare examination algorithms for the justified implementation of advanced, complex diagnostic techniques by military physicians and physical evaluation boards.

The Research Methods: In the study, retrospective and prospective data were obtained using selective methods and generalized according to volume. Clinical examinations included visual acuity test, refractometry, retinoscopy, biomicroscopy, biometry, perimetry, tonometry, ST of the cornea, electrophysiological examination techniques electroretinography (ERG) and visual evoked potential (VEP) test. Optical coherence tomography (OCT) was used to evaluate the changes in the retinal structure and the optic disc condition. Statistical studies were performed using MS EXCEL and SPSS 23 software.

The Applicant's Individual Contribution to the Research. In all clinical cases included in the thesis, diagnostic procedures and data collection, statistical processing, and analysis have been totally performed by the author.

# The Scientific Novelty of the Research:

- 1. For the first time in Azerbaijan, complex studies were performed using modern diagnostic equipment on conscription age youth, which improved the diagnosis, early screening, and monitoring of some ocular pathologies;
- 2. Studying the prevalence of various ocular pathologies in conscription age youth with visual impairments in Azerbaijan allowed for assessing the main pathologies reflecting discharge from MS;
- 3. An artificial intelligence-based machine learning model was built based on the determination of the diagnostic significance and accuracy of ST in the early identification of KC in young men in Azerbaijan, especially in those who are suspicious of corneal ectasia and have high visual acuity;
- 4. Criteria for fitness for military service were determined based on the analysis of corneal parameters using ST along with general examinations of conscripts who have undergone refractive surgery and have high visual acuity;
  - 5. The significance of implementing a possible combination of

the visual evoked potential test, electroretinography and some diagnostic tests in the identification of ocular malingering cases was shown, and an effective diagnostic algorithm has been developed for this purpose.

# The Practical Significance of the Research:

- As a result of the research, methods of screening and monitoring some eye diseases in conscription age young men registered for military service using advanced diagnostic techniques will significantly improving the vigilance of polyclinic ophthalmologists who are members of the physical evaluation board and the quality of medical care provided to young men sent to MS.
- The sensitivity and specificity of ST at the early and subclinical corneal ectasia stages were defined, and the diagnostic significance of the instrument in the young population of Azerbaijan was shown. This, in turn, will contribute to the practice of refractive surgeons.
- The criteria for fitness of young men with refractive errors and those who underwent keratorefractive surgery for MS were assessed based on the analysis of visual acuity, ophthalmoscopic condition of the eye and corneal parameters using ST, which, in turn, emphasizes the importance of the practical implementation of this method in the examination of conscripts by physical evaluation boards.
- The analysis of the results of the advanced examination performed using electrophysiological techniques when assessing visual acuity in simulation cases has shown the practical significance of this diagnostic method and will allow physical evaluation boards to identify the facts of simulation.

## The Key Points to be Defended:

- In some cases, during the initial examination by MMEBs, young men should pass an advanced diagnostic examination.
- In cases of suspicion of corneal ectasia, even in cases of high visual acuity, ST should be performed mandatorily due to its high diagnostic efficiency at an early stage of the disease.
- The advanced ST examination of conscripts who have undergone refractive surgery plays an important role in their proper medical

assessment and in preventing some complications that may occur during the service. Herewith, excimer laser correction of refractive errors eliminates restrictions associated with refractive errors and makes young men fit for MS without such restrictions.

- Implementing electrophysiological examination techniques along with some diagnostic tests in cases of suspicion of simulation allows for identifying ocular malingering. Electroretinography should mandatorily be performed in cases of complaints of impaired dark adaptation where a normal eye fundus is observed. In some cases, the OCT examination identifies structural changes in the retina and optic nerve.

# The Approbation and Practical Application of the Research.

The study results are implemented in the practice of the Military Physician and Health Evaluation Boards of the National Ophthalmology Centre, named after academician Zarifa Aliyeva.

The Dissertation Approbation. The dissertation materials were discussed at the following scientific meetings: the Conference of Young Ophthalmologists (Baku, 2014), the Scientific-Practical Conference dedicated to the 92nd anniversary of acad. Z.Aliyeva (Baku, 2015), the Scientific-Practical Conference dedicated to the Dear Memory of acad. Z.Aliyeva (Baku, 2016), International Scientific Conference dedicated to the 95th anniversary of acad. Z.Aliyeva (Baku, 2018), 35th Conference of the European Society of Cataract and Refractive Surgery (Lisbon, Portugal, 2017), International Ophthalmology Conference held at the joint initiative of the Turkish Ophthalmology Association and Azerbaijan Society of Ophthalmologists (Baku, 2022), and International Scientific-Practical Conference dedicated to the 100th anniversary of Acad. Z.Aliyeva (Baku, 2023). The preliminary discussion of the research was held at the scientific meeting attended by employees of the National Ophthalmology Center named after acad. Z. Aliyeva (06.06.2022, protocol No.1) and the discussion of the scientific seminar was held at the meeting of the FD 1.03 Dissertation Council at the National Ophthalmology Center named after acad. Z. Aliyeva (07.06.2023, protocol No.1).

**Publications.** There were 32 scientific publications on the dissertation topic (19 papers, 11 theses, and 2 methodical resources).

Name of the organization where the dissertation work was conducted. The dissertation was performed was implemented on the basis of the Medical Expertise department at the National Ophthalmology Center named after academician Zarifa Aliyeva. The work is a part of the scientific plan (2016-2020) of the National Center of Ophthalmology named after academician Zarifa Aliyeva "Assessment of the prevalence of myopia, myopic astigmatism, and keratoectasia, effectiveness of diagnostic and treatment methods".

The dissertation scope and structure. The dissertation comprises 179 computer pages (258,588 characters). The main content of the dissertation is divided into 6 chapters and includes a literature overview, a description of the study object and the examination techniques, the 4th Chapter reflecting the independent study results, conclusions, practical recommendations, and a reference list. 225 literary sources were used in the writing of the dissertation, of which 58 were by Azerbaijani, 6 - by Russian, and 161 - by other foreign scientists. The dissertation comprises 30 tables and 52 figures.

# MATERIALS AND METHODS OF THE RESEARCH

20,049 young men examined in 2016-2018 by the MMEB of the National Ophthalmology Centre named after academician Zarifa Aliyeva were involved in the study; the data on 930 of them were analyzed in the general part of the research. Also, the data on young men involved in the advanced examination were collected and analyzed by pathologies. The data on 638 young men with corneal ectasia, involved in the Scheimpflug tomography examination, were analyzed in a keratoconus group; to assess the instrument's diagnostic efficiency at the early stage of the disease, the data on 186 of them have been extensively analyzed. The data on 340 young men who underwent keratorefractive surgery over the research period was analyzed in the excimer laser group, and 207 of them were involved in the advanced examination, and the data of these patients has been extensively analyzed.

During the research period, 561 young men were involved in electrophysiological tests. 289 of them passed the VEP examination to identify the simulation of visual acuity, amblyopia, and optic pathway pathology. To demonstrate the instrument's diagnostic significance in

cases of amblyopia and simulation based on the received results, the parameters obtained in the VEP examination of 63 young men were analyzed. To check dark adaptation in 272 young men, the ERG examination was performed, and the data on 42 of them were taken, where pathology was identified; the ERG data of 15 young men were extensively analyzed.

The data of 60 young men involved in the OCT examination to diagnose optic nerve and retinal pathology was analyzed in the OCT group. The parameters of the OCT examination of 38 of them were extensively analyzed in the optic neuropathy group, and in other cases, clinically significant OCT results were shown as clinical cases.

Upon application, all young men passed a complex examination: refractometry (TOMEY RC-5000, Japan); definition of visual acuity visometry (Projector Huvitz CCP-3100, Korea); biomicroscopy (Slit Lamp TOMEY TSL-5000, Japan); tonometry (TOMEY FT-1000, Japan, contactless with pneumatic tonometer or contact with Goldmann tonometer); ophthalmoscopy (Slit Lamp TOMEY TSL-5000, Japan) with 78.0 D fundus lens (VOLK, USA). Where appropriate, young men were involved in the following advanced examinations: biometry (IOL Master 500, Germany), B-scan ocular examination (Ultrascan Bscan Alcon, USA); perimetry (Humphrey Field Analyzer II, USA); accurate corneal analysis with Scheimpflug tomography WaveLight® ALLEGRO Oculyzer (Alcon, USA), and structural changes in optic fibers and retina with Spectral OCT (Cirrus HD-OCT 5000; Carl Zeiss Meditec) using Disc Cube 200×200 and Macular Cube 512×128 software, respectively. To identify the functional vision impairment and simulation and assess the visual pathway condition and the functional condition of the outer retinal layers, visual evoked potential (VEP) tests and the ERG (electroretinogram) examination (ROLAND CON-SULT – Super Color-Ganzfeld 0450 S (Germany)) were performed.

Statistical studies were performed using MS EXCEL and SPSS (IBM SPSS Statistics 23.0, IBM Corp., USA) software. The number of young men involved in the general part of the research was calculated according to the population with a 95% confidence interval and a 5% margin of error. Statistical calculations were performed by variance and

discriminant methods. In the statistical processing of the received results, the mean (M) and standard deviation ( $\pm$  SD), t-Student, Wilcoxon and Mann-Whitney U-test, and Pearson's goodness criterion -  $\chi^2$  (Chisquare Pearson) were used. The ROC curve (Receiver operating characteristic curve) was used to assess the diagnostic efficiency of the ST to identify eyes with keratoectasia. The results value p<0.05 was considered statistically significant.

#### THE RESEARCH RESULTS AND THEIR DISCUSSION

In the general part of the research, the incidence of different vision pathologies in 930 young men and the diseases causing restrictions or unfitness for military service due to their visual impairment were analyzed. The average age of the young men involved in the study was 22,13±4,8. Young men were divided into 4 groups by age: 334 (35,9%), 360 (38,7%), 140 (15,1%), and 96 (10,3%) young men in the 17-20, 21-25, 26-29, and 30-35 age groups were examined, respectively.

In general, 648 ( $69\pm1,5\%$ ) of the visually impaired young men who passed the examination had different refractive errors, and 288 ( $31\pm1,1\%$ ) had other ocular pathologies.

Among the young men examined for refractive errors, myopia, and myopic astigmatism were observed in  $61,1\pm2,4\%$  of cases, hyperopia and hyperopic astigmatism in  $23,8\pm1,6\%$  of cases, and mixed astigmatism in  $15,1\pm1,4\%$  of cases. According to the obtained results, myopia incidence prevailed. Meanwhile, high-degree myopia accounted for 47% of total myopia, where  $\leq$  -10,0 D cases made up 15%. Anterior and posterior segment pathologies were observed in, respectively,  $11,1\pm1,1\%$  and  $6,6\pm0,8\%$  of cases. Diseases associated with various types of eye injury were grouped separately, including injury to both the anterior and posterior eye segments and the eye-protective lacrimal apparatus. The cases of such diseases accounted for  $6,6\pm0,8\%$  of young men in general. The pathology of the oculomotor system accounted for  $5,4\pm0,7\%$  of cases and the protective lacrimal apparatus  $1,3\pm0,4\%$  of cases.

The analysis of the burden of visual pathologies causing unfitness for military service showed that refractive errors accounted for 51%, anterior segment pathologies 17,5%, posterior segment pathologies 10,4%, pathologies caused by injury and its complications 10,4%, oculomotor system pathologies 8,7%, and protective lacrimal apparatus pathologies 2,0% of cases. The results are shown in Table 1.

Table1
The general structure of the ocular pathologies causing unfitness for MS

Diagnosis	n	%	
Posterior segment pathologies	61	10,4	
Anterior segment pathologies	102	17,5	
Ocular pathologies associated with	61	10,4	
trauma	01	10,4	
Ocular alignment disorders	51	8,7	
Pathology of the protective and lacrimal	12.	2,0	
apparatus of the eye	12		
Refractive errors	301	51,0	
Total	588	100	

Herewith, the obtained results showed that 67 (7,2%) young men were recognized as unfit for MS in both peacetime and wartime according to the provisions of the Regulation on the Military Medical Examination (RMME). The analysis of visual pathologies responsible for this showed that refractive errors accounted for 40,3%, retinal pathologies 28,4%, corneal pathologies 12%, lens pathologies 11,9 %, optic nerve and pathway pathologies 6%, and glaucoma 1,5% of cases.

# Prevalence and Screening of Corneal Ectasia

For the research period in 2016, 2017, and 2018, the prevalence of KC was 3,2±0.2%, 2,95±0.2%, and 3,4±0.3%, respectively ( $\chi^2$  = 8,81; p< 0,05). In general, over three years under study, the prevalence of KC was 3,18±0,2%, which showed that it was not among the rare diseases of the male population in Azerbaijan.

If we consider that the age of 15-30 is an important period for

youth from the standpoint of education, personal development, integration into the social environment, and military service of young men, this is also the time when the development and progress of ectasia are observed at their peak. According to our study results,  $5.8\pm0.9\%$  of young men diagnosed with KC have stage III in both eyes and  $0.8\pm0.4\%$  of them have KC stage III in one eye and KC stage IV in another eye.  $0.6\pm0.3\%$  were diagnosed with KC stage IV in both eyes, and corneal transplantation was indicated for most of them.

According to the study results, 17,1% of young men were diagnosed with KC at the early stage and 17,6% - with KC stage I. As a result, timely monitoring and the choosing of proper treatment tactics (corneal collagen crosslinking (CCL), combined Photorefractive keratectomy (PRK) +CCL, or intracorneal ring implantation (ICRI)) will prevent the progressive development of the disease and preserve visual function. Thus, 359 of the research subjects were diagnosed with KC during the examination by MMEB and were attracted to further examination and treatment after informing them of the disease. During the initial examination, retinoscopy was one of the diagnostic criteria giving the ground for referring candidates suspected of ectasia to tomography.

Based on the study results, the most sensitive ST parameters at the subclinical and early stages of the disease in young men in Azerbaijan have been defined. As a result, the most sensitive ST parameters in the identification of the early clinical KC were, consecutively, D parameter, anterior and posterior elevation indices (AE, PE), progressive pachymetry indices (PPİ<sub>avg</sub>, PPİ<sub>max</sub>), and from the topometric map, index of surface variance (ISV), keratoconus index (KI), and index of height decentration (IHD) (Table 2). Although the diagnostic significance of single parameters is low from a sensitivity and specificity standpoint, their combination and the joint analysis of the obtained results raise the suspicion of the early clinical stage of the disease to 98% (Figure 1). As can be seen from Table 2. the parameters such as D, AE, PE, PPI<sub>avg</sub> and PPImax showed 90 % maximum sensitivity and specificity in determining subclinical KC (Figure 1). The most sensitive parameters in the thin cornea have higher cut-off values in confirming the diagnosis of the disease compared to normal and thick corneas. Thus, for parameter D, this value was calculated as >2.33 for subclinical KC and >2.57 for clinical KC.

According to the study results, in cases of suspected corneal ectasia, the initial ophthalmological examination of young men registered for and sent to military service should be performed according to the algorithmic sequence shown in Figure 2.

During tomographic examination of the cornea, candidates suspected of corneal ectasia should be dynamically monitored with suspicion of KC or early-stage KC according to the algorithm in Figure 3.

Table 2
Cut-off points, sensitivity and specificity of the main effective
ST parameters derived from ROC curve analysis

	Subclinical KC			Clinical KC		
Parameters	Sensitivity	Specificity	Cut-off points	Sensitivity	Specificity	Cut-off points
D	0,969	0,958	>1,42	0,967	0,990	>1,55
PE	0,800	0,792	>6,5	0,967	0,994	>10,5
AE	0,933	0,875	>4,0	0,967	0,969	>5,0
PPIavg	0,867	0,750	>1,04	0,867	0,948	>1,07
PP max	0,900	0,708	>1,34	0,967	0,938	>1,49
IVA	0,833	0,750	>0,17	0,967	0,990	>0,18
KI	0,867	0,667	>1,03	0,933	0,979	>1,03
IHD	0,900	0,750	>0,011	0,967	0,969	>0,013

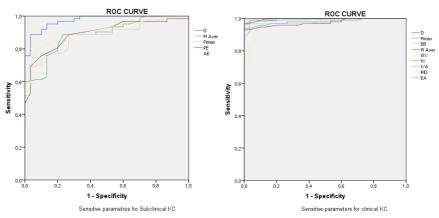


Figure 1. Receiver operating characteristic curves of main effective ST parameters to detect subclinical and clinical KC.

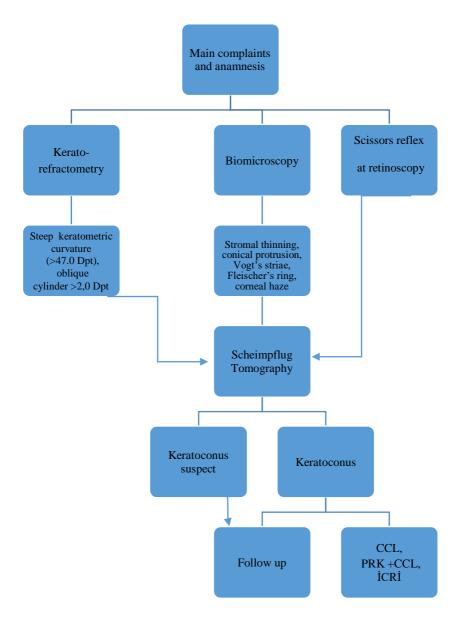


Figure 2. Main reasons of referral suspected candidates for keratoectasia for ST examination and next follow-up.

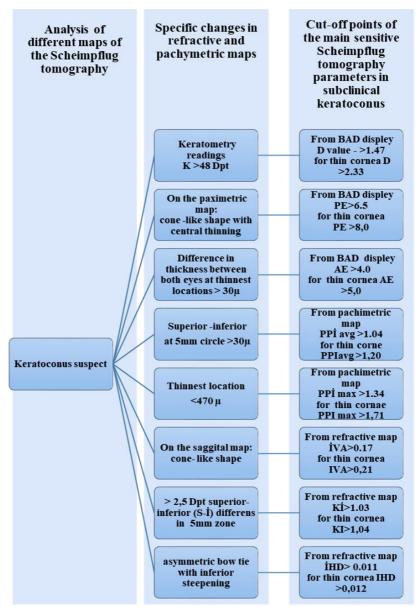


Figure 3. Algorithm for characteristic changes in ST and cut-off points for effective parameters in the early diagnosis of KC.

# Assessment of outcomes of youth eligible for MS after Excimer laser surgery

In the time of wide opportunities provided by refractive surgery, the correction of refractive errors allowed for improving the visual acuity of military staff serving in the army. Based on the results of the research on young men with high visual acuity, who had keratorefractive surgery, to prevent any complications that might arise during MS, more detailed examinations were performed for them and were assessed subjective and objective surgery outcomes.

Based on advanced examination results and the analysis of the surgery outcomes shown by the young men, 155 of them were recognized as fit for military service without any restrictions. All young men were examined by the MMEB at least 6 months  $(8,1\pm1,7)$  after the surgery. Table 3 shows the pre-and post-surgery average refraction in young men with different refractive errors, fit for MS.

Table 3
Preoperative and postoperative average spherical equivalent of refraction

Refractive error	Preoperative refractive	Postoperative refractive		
	data	data		
Myopia	-4,5±1,3	-0,5±1,3		
Hyperopia	$5,07 \pm 1,55$	0,75±1,4		
Mix Astigmatism	-2,5 ± 1,51	-0,3±0,87		

Qeyd:  $\chi^2 = 28,53$ ; p<0,001

The key surgery outcome was the high uncorrected visual acuity identified during the visual acuity examination. In  $92\pm2.5\%$  (143) of the examined young men, uncorrected visual acuity was 0,9-1,0 (decimal) in both eyes, while in  $8.0\pm1.1\%$  (12), it was between 0,5-0,7 (decimal) (p<0,05).

The correction efficiency index EI (the ratio of the mean uncorrected visual acuity 6 months after surgery to the mean corrected visual acuity before surgery) and the safety index SI (the ratio of the mean corrected visual acuity 6 months after surgery to the mean

corrected visual acuity before surgery) were calculated.

Figure 4 shows the safety and efficiency indices calculated for the correction of various ametropia in young men, which proves the efficiency of the procedures with a generally high outcome.

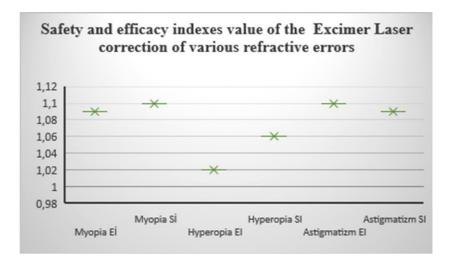


Figure 4. Safety and efficacy indexes Excimer Laser correction of various refractive errors

In general, when examining young men with various refractive errors, who underwent Excimer Laser correction, for fitness to MS, the key factors causing restrictions for military service were related to the high preoperative refractive error, refractive amblyopia, some complications during and after the surgery, and their negative impact on visual acuity and quality. The implementation of ST allowed for correctly assessing the health status of young men who underwent keratorefractive surgery by determining the laser correction complications and stromal thinning in the cornea as a result of high preoperative ametropia. ST identified  $\leq 430~\mu m$  stromal thinning in the cornea due to high preoperative refraction in 127 (37,4%), iatrogenic ectasia in 4 (1,2%), decentralized ablation area in 3 (0.9%) young men and an increase in related high-order aberrations. Also, in biomicroscopy, vario-

us degrees of subepithelial haze were observed in 9 (2.6%) and epithelial ingrowth after LASIK was observed in 3 (0.9%) young men. Funduscopy identified various peripheral retinal dystrophies in 64 (18,8%) cases and the retinal condition after peripheral laser photocoagulation in 14 (4,1%), young men. Based on the study analysis, MMEBs are recommended to implement the algorithm in Fig. 5 when examining conscripts who have undergone keratorefractive surgery.

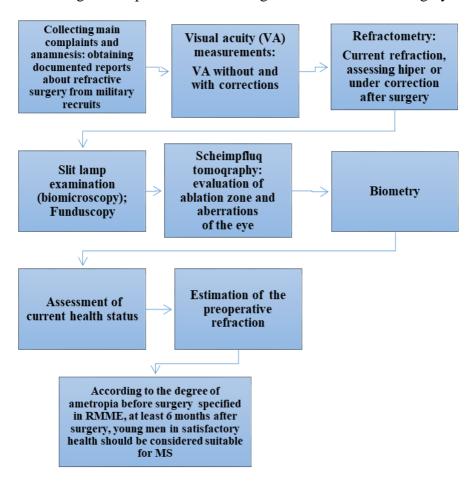


Figure 5. An improved screening algorithm for young people undergoing keratorefractive surgery

# Rules for implementing advanced examination techniques in cases of suspicion of ocular malingering.

In this part of the study, the significance of the P100 component in the VEP examination for the prognostic determination of visual acuity in the diagnosis of amblyopia and ocular malingering cases was analyzed. Of the amblyopic eyes involved in the study, 19 young men had dysbinocular, 4 central, and 24 refractive amblyopia. In 17 young men, ocular malingering was confirmed by VEP examination, and the obtained results were analyzed in the simulation group.

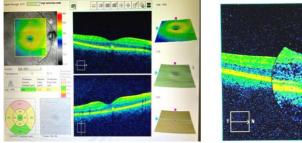
The obtained results showed that although in the amblyopia group, the P100 component latency was normal in the 60' stimulus, it was prolonged in the 15' stimulus, and its amplitude was reduced in both stimuli. It should be noted that in the amblyopia group, the average visual acuity was  $0.073\pm0.015$  (according to the Snellen (decimal) scale). The obtained results showed that although the P100 component latency in the amblyopia group in the 60' stimulus was normal,  $108.2\pm5.4$  and  $110\pm8.5$  in the reference and amblyopia groups, respectively (p=0,405), it was prolonged in the 15' stimulus and made up  $112.1\pm5.1$  and  $121.6\pm11.6$  in the reference and amblyopia groups, respectively (p<0,001). The amplitude was reduced in both stimuli; thus, 1N75P 60 was  $13.7\pm3.03$  and  $7.8\pm2.7$  in the reference and amblyopia groups, respectively, and 1N75P 15 was  $8.7\pm3.15$  and  $5.6\pm2.8$  in the reference and amblyopia groups, respectively (p<0,001).

Of those involved in the ERG examination, retinitis pigmentosa was confirmed in 27, congenital stationary night blindness (CSNB) in 7, and cone-rod dystrophy in 8 young men. In 6 of them, pathological changes were not detected in the eye fundus during ophthalmoscopy, but ERG showed severe pathological changes in the function of the rods; these young men were diagnosed with CSNB and recognized as unfit for military service. The obtained results show that, along with modern diagnostic examination techniques, the ERG examination plays the role of the gold standard in the identification of this pathology and its clinical manifestations.

The OCT examination, which plays the role of an important diagnostic tool in the pathologies of the optic nerve and afferent optic pathways, allows for directly analyzing quantitative indicators of the nerve fibers and

ganglion cell layer. OCT confirmed optic neuropathy in 38 young men. In the diagnosis of optic neuropathy, the retinal nerve fiber layer (RNFL), the thickness between the ganglion cell and inner limitation layers, the central thickness of the retina, and the thickness of the RNFL quadrants showed a statistically significant difference between the groups. In particular, although the lower indicators for RNFL and its quadrants were mostly observed in the temporal and nasal parts, compared to the reference group, they were statistically significantly different in the upper, nasal and lower quadrants (p< 0,001). Although the central thickness of the retina did not differ between the groups, the volume indicators differed sharply. A statistically significant difference was also observed in the thickness between the ganglion cell and inner plexiform layers (p<0,001). This, in turn, shows the indispensable role of OCT examination in evaluating the structural changes of the retina and optic nerve and the follow-up and treatment of some neuro-ophthalmological diseases.

In the OCT examination, the analysis of structural retinal changes has also played the role of the most informative tool in some clinical cases. Also, in 22 young people, the OCT scan examination was the most informative tool for assessing degenerative changes in the structural layers of the retina and monitoring structural alteration in the foveolar morphology that can directly affect visual acuity (Figure 6).



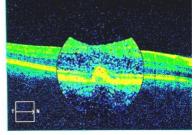


Figure 6. OCT image of the destructive changes in the fovea affecting visual acuity after injury.

The analysis results show that performing examinations by physical evaluation boards according to the improved algorithm developed by us in cases of suspicion of simulation allows for properly assessing the health status (Figure 7).

Rules for conducting ophthalmological examinations in cases of suspected ocular malingering

- · Examination of visual acuity, color and binocular vision
- Conducting fogging and confusing tests

#### Examination of the eyeball and ocular movement apparatus

- Slit lamp biomicroscopy and funduscopy
- · Assessment of phoria and deviations

#### Electrophysiological examination methods

- Evaluation of amblyopia or pathology of the visual pathways
  - visual evoked potential examination (VEP)
- Evaluation of night vision electroretinogram (ERQ)

Structural and quantitative assessment of central retinal zone and optic nerve fibers and ganglion cell layer and visual field assessment

- Optic Coherent tomography
- Perimetry

Cases of negative simulation after Excimer Laser Surgery and assessment of anterior and posterior segment of the eye and aberrations that may affect visual acuity

• Schempflug Tomography

Providing final health status assessment, based on the results of the final examinations with repeated visual acuity measurements, confusing and fogging tests.

Figure 7. The improved screening algorithm for conscripts in ocular malingering cases

### **CONCLUSIONS**

- 1. A large-scale study has shown that among young men, refractive errors rank first in eye pathology with 69%. Among the young men examined for refractive errors, myopia, and myopic astigmatism were observed in 61,1±2,4% of cases, hyperopia and hyperopic astigmatism in 23,8±1,6% of cases, and mixed astigmatism in 15,1±1,4% of cases. High-degree myopia accounted for 47% of total myopia. Anterior and posterior segment pathologies were observed in, respectively, 11,1±1,1% and 6,6±0,8% of cases. The cases of diseases associated with various types of eye injury accounted for 6,6±0,8% of young men in general. The pathology of the oculomotor system accounted for 5,4±0,7% of cases and the protective and lacrimal apparatus 1,3±0,4% of cases [1, 2, 10, 19, 32].
- 2. The analysis of the burden of ocular pathologies causing unfitness for MS showed that refractive errors accounted for 51%, anterior segment pathologies 17,5%, posterior segment pathologies 10,4%, pathologies caused by injury and its complications 10,4%, oculomotor system pathologies 8,7%, and protective and lacrimal apparatus pathologies 2,0% of cases.
- 3. In young men with visual impairments involved in the advanced examination, the prevalence of KC was 3,18±0,2%. In general, 359 young men were first diagnosed with KC during the examination by MMEB. Since the studied population mostly consisted of young men and due to earlier screening by involving in an advanced examination, the number of those diagnosed with KC at an early stage in both eyes was significantly high; thus, 17,1% of the young men were diagnosed with the subclinical or early stage of KC and 17,6% of stage I KC [26, 27].

ST showed high diagnostic efficiency in the KC diagnosis. The most sensitive ST parameters in the identification of the subclinical and early clinical KC were, consecutively, the D parameter, AE, PE, PPİ<sub>avg</sub>, PPİ<sub>max</sub>, İVA, ISV, KI, and IHD parameters. Although the diagnostic significance of individual parameters is low from a sensitivity and specificity standpoint, the early clinical stage of the disease was identified with a 98% accuracy based on the model built as a result of their combination. Based on the obtained results, an examination

- algorithm for the early screening of corneal ectasias in the population and an algorithm consisting of the effective parameters of the ST for early screening were developed [3, 5, 7, 11-18, 21].
- 4. According to the study results, the correction of refractive errors in young men by Excimer Laser showed high efficiency. 155 young men were recognized as fit for military service without any restrictions 6 months  $(8,1\pm1,7)$  after the surgery. According to the obtained results, the safety and efficiency indices for keratorefractive surgeries performed on young men were high [6].
  - When examining young men with various refractive errors, who underwent Excimer Laser correction, for fitness to military service, the key factors causing restrictions for military service were related to the high preoperative refractive error, refractive amblyopia, some complications during and after the surgery, and their negative impact on visual acuity and quality. ST identified  $\leq 430~\mu m$  stromal thinning in the cornea due to high preoperative refraction in 127 (37,4%), iatrogenic ectasia in 4 (1,2%), decentralized ablation area in 3 (0,9%) young men, and an increase in related high-order aberrations [9].
- 5. The examination of young men by the MMEB according to an algorithm developed based on advanced complex diagnostic examinations allowed for identifying cases of ocular malingering. The P100 component amplitude in µV, measured in the visual evoked potential test included in the examination algorithm allowed for assessing visual acuity based on objective parameters. The obtained results showed that the P100 component latency in the 60' stimulus was 108,2±5,4 μV and 110±8,5 μV in the reference and amblyopia groups, respectively, without statistically significant difference between the groups (p=0,405), it was prolonged in the 15' stimulus and made up 112.1±5.1 µV and 121.6±11.6 µV in the normal control and amblyopia groups, respectively (p<0.001). The P100 component amplitude in the 60' stimulus was 13,7±3,03 μV and 7,8±2,7 μV in the reference and amblyopia groups, respectively, and in the 15' stimulus it was  $8.7\pm3.15 \,\mu\text{V}$  and  $5.6\pm2.8 \,\mu\text{V}$  in the reference and amblyopia groups, respectively (p<0.001) [21, 29].

- 6. The obtained results show that, along with modern diagnostic examination techniques, the ERG examination plays the role of the gold standard in the identification of hereditary retinal pathology and its clinical manifestations. Of those involved in the ERG examination, retinitis pigmentosa was confirmed in 27, CSNB in 7, and cone-rod dystrophy in 8 young men. Although CSNB belongs to rare diseases, the ERG examination identified the diversity of its clinical manifestations and the specifics of its differentiation from other hereditary retinal pathologies [10, 23].
- 7. The OCT examination included in the advanced examination algorithm created wide opportunities for analyzing the structural retinal changes and the quantitative indicators of the nerve fibers and the ganglion cell layer. OCT confirmed optic neuropathy in 38 young men; the comparison of the obtained results with the reference group showed a clear statistical difference. In young people diagnosed with optic neuropathy, the retinal nerve fiber layer and its thickness indicators by quadrants, the thickness between the ganglion cell and inner limitation layers, and the central thickness of the retina were statistically significantly different from the control group (p< 0,001) [25, 29, 31].

#### PRACTICAL RECOMMENDATIONS

- 1. Based on statistically significant results, the major ocular pathology causing unfitness for MS is refractive errors, where the trend of myopia is currently growing. Therefore, prophylactic medical examination and timely treatment of children and adolescents are of great importance to timely correct refractive errors and prevent the progression of myopia.
- 2. Early diagnosis of corneal ectasia and timely treatment measures such as CCL, PRK+CCL, or ICRI will reduce the need for corneal transplantation by preserving the visual functions of young people and thus reduce the share of disability related to corneal pathology. Tomographic examination of the cornea of candidates with suspected corneal ectasia in specialized centers according to established algorithms is extremely important.

- 3. When analyzing the ST results, it is recommended to prove the diagnosis of early stage ectasia according to the calculated machine learning models. The obtained results are of particular importance for refractive surgeons when choosing patients for Excimer Laser surgery to prevent iatrogenic ectasia that may occur after the surgery. Thus, the model obtained as a result of the complex analysis of the most discriminative ST parameters and their cut-off values gives this opportunity to refractive surgeons when diagnosing the subclinical and early stages of corneal ectasia in young men.
- 4. It is recommended to perform a detailed examination of young men, who have undergone keratorefractive surgery for fitness for military service in specialized centers. The surgeon who performs the surgery should consider that the young man will pass military service after the surgery, and it is recommended to represent a comprehensive and detailed extract showing the preoperative degree of refractive errors to properly certify him for the service. Herewith, in these young men, it is recommended to give preference to mostly wavefront-based, superficial ablation techniques according to the program covering a wide ablation zone. This should be considered to reduce high-order aberrations that will negatively affect the visual function of these young men during military service and minimize any complications that may arise.
- 5. Ocular malingering cases should be identified by initially performing as many confusing and obfuscating tests as possible, which in turn will save time and reduce the burden of additional advanced diagnostic examinations. When assessing the functional condition of vision, the VEP test is an informative tool for evaluating the state of visual pathways or the presence of amblyopia.
- 6. In the case of complaints of impaired and rapidly deteriorated dark adaptation, an electroretinography examination should be performed due to the suspicion of stationary night blindness, even when funduscopy did not identify severe pathological changes.

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#### LIST OF ABBREVIATIONS AND TERMS

**MMEB** – Military Medical Examination Board

MS – Military Service

**OCT** – Optic Coherent Tomography

**RNFL** – Retinal nerve fiber layer

**KC** – Keratoconus

**CNSB** – Congenital Stationary Night Blindness

**VEP** – Visual Evoked Potential

**ERG** – Electroretinography

CCL – Corneal Collagen Crosslinking
iCRi – Intracorneal Ring Implantation

PRK – Photorefractive KeratectomyST – Scheimpflug Tomography

D value from Belin/Ambrosio Enhanced Ectasia
 Display

**AE** – anterior elevation **PE** – posterior elevation

PPİ<sub>avg</sub> – averege progressive pachymetry index
 PPİ<sub>max</sub> – maximal progressive pachymetry index

iVA – index of vertical asymmetryiSV – index of surface variance

**Kİ** – keratoconus index

**İHD** – index of height decentration

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