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FREQUENCY AND RISK FACTORS OF COMPLICATIONS OF SURGICAL TREATMENT OF CORNEAL DISEASES

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112 patients (80 men, 32 women; 89 and 39 eyes, respectively) aged from 20 to 48 years with various corneal pathologies were retrospectively examined. The patients were operated using the following types of operations: intrastromal implantation of the corneal segment; crosslinking of corneal collagen using ultraviolet radiation and riboflavin; combined use of these methods in various variants with and without photorefractive and phototherapeutic keratectomy. Intraoperative complications were observed mainly during implantation of the intrastromal segments of the cornea. 10 % of various types of intraoperative complications accounted for 100 such operations. The combined use of corneal collagen crosslinking with both photorefractive keratectomy and phototherapy keratectomy is associated with the same risk of postoperative complications. The risk of postoperative complications is relatively high in patients aged 30 years and older, with a preoperative level of visual acuity without correction of less than 0.2 and with a central corneal thickness of 470 microns.

Key words: keratoconus, corneal rings, combined operations, frequency, complications, stitching

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ЧАСТОТА І ЧИННИКИ РИЗИКУ УСКЛАДНЕНЬ ОПЕРАТИВНОГО ЛІКУВАННЯ ХВОРОБ РОГІВКИ

Під ретроспективним спостереженням знаходилися 112 пацієнтів (80 чоловіків, 32 жінок; відповідно 89 і 39 очей) віком 20–48 років з різними патологіями рогівки. Пацієнти були оперовані із застосуванням таких видів операцій: інтрастромальна імплантація рогівкового сегмента; перехресне зв'язування рогівкового колагену з використанням ультрафіолету випромінювання і рібофлавіну; комбіноване застосування цих методів в різних варіантах з і без фоторефрактивному і фототерапевтичної кератоектомією. Інтраопераційні ускладнення спостерігалися в основному при імплантації інтрастромальних рогівкових сегментів. В цілому на 100 таких операцій припадає 10 % інтраопераційних ускладнень різного типу. Комбіноване використання кросслінкінг рогівкового колагену з фоторефракціонной кератоектомією і фототерапевтичною кератоектомією пов'язано з однаковим ризиком післяопераційних ускладнень. Частота ускладнень при перехресному зв'язуванні рогівкового колагену з використанням УФ-випромінювання і рибофлавіну була порівняно більше. Ризик післяопераційних ускладнень порівняно високий у пацієнтів у віці 30 років і старше, з доопераційним рівнем гостроти зору без корекції менш 0,2 і при центральній товщині рогівки <470 мкм.

Ключові слова: кератоконус, рогівкові кільця, поєднані операції, ускладнення, кросслінкінг

This work is the fragment of a doctoral dissertation: "Prevalence and nosological structure, corneal diseases in Azerbaijan and ways to optimize surgical treatment".

In the world, more than 32 million people are considered blind (visual acuity < 3/0); m□r□th□□190 million people have visual acuity < 6/18. Of these, 2.7 and 22,176 million live in Central and Western Europe, respectively. In the world, 3.09 %, in Europe, 2.35–3.54 % of cases of blindness are associated with corneal pathologies [6]. The prevalence of corneal diseases and blindness due to these pathologies in India was 3.7 and 0.12 %, respectively [7]. In China, according to the study of corneal samples collected during corneal surgery (1854), infectious keratitis was detected in 74.16 % of cases, corneal tumors and keratoconus in 3.18 % of cases, for other pathologies it was 13.86 % [9]. This indicates an increasing role of surgical activity in the treatment of not only dystrophic, but also inflammatory diseases of the cornea. Corneal transplantation, ultraviolet suturing and implantation of intrastromal corneal segments, Bowman layer transplantation, keratoplasty and deep anterior layered keratoplasty are widely used [5]. The concept of component corneal surgery has been developed – the use of one donor cornea for the treatment of three recipients [10]. Corneal surgery, like all operative medicine, is not without the risk of complications. In component corneal surgery, complications in the form of perforation of the descemet membrane (4–20 %), pseudo-anterior chamber (1 %), Urrets-Zavaly syndrome, inconsistencies between the size of the donor and recipient cornea, epithelial and stromal rejection (3–15 %) and others are described [10]. An effective method of surgical treatment of purulent corneal ulcers developing against the background of neuroparalytic keratitis has been developed [3]. With long-term follow-up (up to 8 years), a recurrence of the ulcer was noted in 2 patients, an increase in tear production in 2 patients. Showing the safety and effectiveness of femtosecond implantation of intrastromal corneal segments in the treatment of keratoconus, the authors note the areactive course of the postoperative period and the absence of subjective

and objective signs of negative consequences [1]. During such operations, Korean scientists observed the development of herpetic keratitis (12.5 %), delayed wound healing (5 %), bacterial keratitis (12.5 %) and epithelial ingrowth (25 %) [8]. Combined treatment of keratoconus with the use of intrastromal corneal segments and corneal cross-linking showed an improvement in the main parameters of the visual organ and the authors do not describe any intra– and post-operative complications [11]. Based on the generalization of literature data on the use of intrastromal implantation of corneal segments, their high efficiency is shown and the most common complications are identified: segment decentralization, insufficient tunnel depth and segment asymmetry, corneal neovascularization, ring segment displacement, segment migration, infectious keratitis [12]. Complications during and after corneal operations depend on many factors, including the experience of doctors, the availability of an ophthalmological institution, and the adequacy of treatment tactics, which have regional characteristics. Therefore, monitoring the outcomes of these operations is an urgent task.

The purpose of the study was to distinguish the frequency and risk factors of complications in various variants of surgical treatment of corneal diseases.

Materials and methods. The retrospective observation included 112 patients (80 men, 32 women; 89 and 39 eyes, respectively) aged from 20 to 48 years (mean age 29.5±0.8 years) with various corneal pathologies. Before admission to the National Center of Ophthalmology named after Academician Zarifa Aliyeva of the Ministry of Health of the Republic of Azerbaijan (Baku city), patients were observed in the polyclinic department of the center. The follow-up period ranged from 5 to 12 years. The observation included patients with corneal pathologies who were operated on for the first time at the Center using the following types of operations: intrastromal implantation of the corneal segment (PVC); cross-linking of corneal collagen using UV radiation and riboflavin (CROSSLINKING); combined use: PVC + CROSSLINKING; CROSSLINKING + photorefractive keratectomy (FRK); CROSSLINKING + phototherapeutic keratectomy (FTK). The operations were performed by different surgeons during 2016–2018, the postoperative follow – up lasted 12 months. The indication for the use of ICRS was keratoconus in stage II–III. CXL in various variants was used for the following indications: keratoectasia; corneal dystrophy; keratitis and corneal ulcers. The number of ICRS, CXL, ICRS + CXL, CXL + FRK, CXL + FTK operations, respectively, was: 48; 32; 21; 16; 11 (128 eye). Before the operation, all patients were examined comprehensively, visual acuity with and without correction, refractive error (using an automatic keratorefractometer), keratometric indicators (Kmin, Kmax, Kaverage) obtained by topography (Wavelight, Oculyzer – "Alcon", Germany) were evaluated; corneal thickness data measured using optical coherent topography (Cirrus in HD-October-5000, Karl Zeiss, Germany), endothelial cell density (endothelial microscope Tomei E. M. –3000, Japan). All the complications documented during the operation and within 12 months after the operation were taken into account when assessing the frequency of complications. The patients were grouped according to the methods of operations (ICRS, CXL, ICRS + CXL, CXL + FRK, CXL + FTK), by gender (men and women), age (up to 30 years; 30 years and older), by visual acuity before surgery (<0.20; ≥0.20<0.40 w□th□ut □□rr□□t□□□), □□□□rding to the spherical (from –1.0 to –9.0; from –1.0 to +1.5 dptr) and cylindrical (from –2.0 to –8.0; from–2.0 to +1.0 dptr) component of refraction, average, maximum and minimum keratometry (less than the median and more than the median), the central thickness of the cornea (less than the median and more than the median). The frequency of complications was determined in these subgroups.

Statistical processing of the materials was carried out using the Excel –10 program using the data analysis package. The confidence interval (95 % was calculated at t equal to 1.96. The statistical error of the indicators was determined by the formula for fractions [4]. The shifted reliability of the difference in the frequency of complications between the subgroups was determined by the criterion $\chi 2$ [4].

Results of the study and their discussion. Demographic and clinical characteristics of patients before surgery showed that men predominate among patients (69.5±4.1 % P<0.05), the proportion of persons under the age of 30, 30 years and older (51.6±4.4 and 48.4±4.4 %, with visual acuity without correction of <0.20 and ≥0.20 <0.40 (54.7±4.4 and 45.3±4.4 % did not differ significantly from each other. The central thickness of the cornea before the operation is ICRS, CXL, ICRS + CXL, CXL + FRK, CXL + FTK, respectively, in 47.9±7.2; 56.3±8.8; 42.9±10.8; 62.5±12.1; 54.5±15.0; and 51.6±4.4 % of patients was more than 470 microns. Average keratometry in 52.1±7.2; 56.3±8.8; 37,3±10,3; 31,3±11,6; 72,7±13,4 and 49.2±4.4 % of patients in these groups had more than 46 dptr. The median of the spherical and cylindrical components of refraction, keratometry indicators and corneal thickness distributed the aggregate into parts, the proportion of which also did not differ significantly from each other. The distribution of patients according to these characteristics, depending on the types of surgical interventions,

had a similar characteristic. The frequency of preoperative and postoperative complications in various types of operations is shown in table 1.

Table 1

Complications of operations in corneal pathologies

Name of operations	N	Types of complications during operations	n	%	Types of postoperative complications	n	%
Implantation of intrastromal corneal segments	40	Incomplete formation of channel	2	4.2±2.8	Migration of segment	2	4,.±2,.8
		Endothelial perforation	1	2.1±2.1	Corneal melting	1	2,.1±2,.1
		Vacuum loss	1	2.1±2.1	Corneal infection	3	6.3±3,.5
		Edema around segment	1	2.1±2.1	All	6	12.5±4.7
		All	5	10..4±4.4			
Corneal collagen crosslinking method (CXL)	32				Infectious keratitis	2	6.3±4.3
					Corneal edema	4	12.5±5.8
					Corneal opacity	1	3,.1±3.1
					Sterile infiltrates	1	3.1±3.1
					All	8	25.0±7.6
Corneal collagen crosslinking method in combination with ICRS	21	Incomplete formation of channel	1	4.8±4.6	Migration of segment	2	9.5 ±6.4
		Vacuum loss	1	4.8±4,.6	Infectious keratitis	1	4.8±4.6
		All	2	9.5±6.4	Stroma edema	2	9.5±6.4
					Corneal opacity	1	4.8±4.6
					All	6	28.6±9.8
Corneal collagen crosslinking method with photorefractive keratectomy	16				Corneal opacity	2	12.5±8.2
					Infectious keratitis	1	6.3±6.1
					Stroma edema	1	6..3±6.1
					Dry eyes	1	6..3±6.1
					All	5	31.3±11.5
Corneal collagen crosslinking method with phototherapy keratectomy	11				Corneal opacity	1	9.1±8.6
					Stroma edema	1	9.1±8.6
					Infectious keratitis	1	9.1±8.6
					Total	3	27.3±13.4
Total	128		8	6.3±2.1		28	21.9±3.6
(N is the number of operated eyes, n is the number of complications)							

Intraoperative complications were observed mainly during implantation of intrastromal corneal segments without (4.2±2.8 % incomplete canal formation, 2.1±2.1 % vacuum loss, 2.1±2.1 % endothelial perforation, 2.1±2.1 % edema around the segment, only 10.4±4.4 %) and with a combination with CXL (4.8±4.6 % incomplete canal formation, 4.8±4.6 % vacuum loss, only 9.5±6.4 %). In total, 10 % of various types of intraoperative complications accounted for 100 such operations. Complications after corneal collagen crosslinking (CXL) – infectious keratitis was observed in 6.3±4.3 % of cases, corneal edema in 12.5±5.8 % of cases, corneal opacity in 3.1±3.1 % of cases, sterile infiltrates in 3.1±3.1 % of cases. Complications after the method of corneal collagen crosslinking with photorefractive keratectomy — corneal opacity in 12.5±8.2 % of cases, infectious keratitis in 6.3±6.1 % of cases, dry eye in 6.3±6.1 % of cases. Complications after the method of corneal collagen crosslinking with phototherapy keratectomy – corneal opacity, stroma edema, infectious keratitis in 9.1±8.6 % of cases.

In case of incomplete formation of the canal and corneal perforation, repeated surgery was postponed for 3 months and after complete restoration of the corneal defect, repeated surgical intervention was performed. Complications in the form of edema, infections and corneal opacities were amenable to appropriate medical treatment and we achieved the expected result.

The frequency of total cases of complications of corneal surgery for various demographic and clinical characteristics of patients is shown in table 2. The frequency of complications in men prevailed over women out of 89 in 27 women, out of 89 in 9 cases in men.

Table 2

The frequency of complications in corneal surgery, depending on the demographic and clinical characteristics of patients

Signs	Variants of signs	Number of operations	Number of complications	Frequency of complications per 100 operations P	P
Gender	Men	89	27	30.3±4.8	>0.05
	Women	89	9	23.1±6.7	
Age, years	<30	66	10	15.1±4.4	<0.05
	≥30	62	26	41.9±6.2•	
Visual acuity without correction	<0.20	70	25	35.7±5.7•	<0.05
	≥0.20 <0.40	58	11	18.9±5.1	
Spherical equivalent, dptr	(–9.0)–(–1.0)	60	17	28.3±5.8	>0.05
	(–1.0)– (+1.5)	68	19	27.9±5.4	
The cylindrical equivalent, dptr	(–8.0)–(–2.0)	65	18	27.7±5.5	>0.05
	(–2.0)–(+1.0)	63	18	28.6±5.7	
Medium keratometria, dptr	<46.0	63	17	27.0±5.6	>0.05
	≥46.0	65	19	29.2±5.6	
Maximum keratometria, dptr	<50	66	20	30.3±5.6	>0.05
	≥50	62	16	25.8±5.5	
Minimal keratometria, dptr	<43	60	17	28.3±5.8	>0.05
	≥43	68	19	27.9±5.4	
Central corneal thickness, microns	<470	66	24	36.4±5.9•	<0.05
	≥470	62	12	19.4±5.0	
Operation time	2016	25	11	28.1±4.0	<0.05
	2017	39	13	44.0±9.9•	
	2018	64	12	33.3±7.5	
Total		128	36	28.1±4.0	

In the groups of male and female patients, the total frequency of intra and postoperative complications was 30.3±4.8 and 23.1±6.7 %, respectively, and did not differ significantly from each other (p>0.05). In groups of patients with the size of the average, minimum and maximum keratometry, as well as the central thickness of the cornea, more and less than their medians, a comparative assessment of the total level of intra and postoperative complications confirms the validity of the null hypothesis (p>0.05). A statistically significant difference in the frequency of complications was noted when comparing the subgroups by age (30 and ≥30 years, respectively, 15.1±4.4 and 41.9±6.2 %), by visual acuity before surgery (0.20 and ≥0.20 0.40, respectively, 35.7±5.7 and 18.9±5.1 %) and by the years of surgery (in 2016, 44.0±9.9 % and in 2018, 18.8±4.9 %), and also in terms of the size of the central thickness of the cornea (470 microns and 470 microns, respectively, 36.4±5.9 and 19.4±5.0 %), the change in the total level of intra and postoperative complications in dynamics for 2016–2018 can be attributed to an increase in the skills of using surgical methods of keratoconus treatment. The high risk of intra and postoperative complications in the group of patients older than 30 years should be taken into account when planning treatment tactics and performing intervention at a young age. The size of the relative risk of intra and postoperative complications was 2.77 due to age, 1.88 due to the initial level of visual acuity, 1.87 depending on the thickness of the cornea and 2.34 due to organizational factors. The value of the attributive risk of intra and postoperative complications was 26.8 % due to age, 16.8 % due to the initial level of visual acuity, 17.0 % depending on the thickness of the cornea and 25.2 % due to organizational factors. Thus, the choice of surgical methods and their combination options for the treatment of keratoconus primarily depends on the clinical situation, rather than on the risk of complications during operations.

Kim and co-authors [8] note that with ICRS, CXL and a combination of ICRS with CXL, the complication rate was 12.5, 5.0 and 37.5 %. In our observation, the frequency of postoperative complications during these operations was 12.5±4.7, 25.0±7.6 and 28.6±9.8 %, respectively. It is obvious that in our observation, the frequency of complications in CXL was higher, and in other types of interventions, there was no noticeable difference in indices. Vasileva I. V. and co-authors [2] report on the effectiveness of implantation of intrastromal corneal segments, but do not provide statistical confirmation of reliability due to the small number of operated patients. Studeny P and co-authors [11] present the results of combined implantation of intrastromal corneal segments with cross-linking of corneal collagen using UV radiation and riboflavin, which are consistent with the results of our observation.

The structure of postoperative complications in the combination of ICRS with CXL in the observations of Kim and co-authors was dominated by epithelial ingrowth (25 %), and in our observation, stroma edema and segment migration (9.5 % each). Izmailova S. B. and co-authors [2] observed complications during implantation of corneal segments in 8.7 % of cases with manual, 1.8 % of cases with vacuum fixation. The overall level of complications in our work (12.5±4.7 %) is close to the data of these authors. There is a similarity in the structure of postoperative complications. In both cases, the frequency of segment migration was similar (2.5 and 4.2±2.8 %). In our observation, the significance of a decrease in the frequency of complications in the dynamics for 2016-2019 was confirmed, which is associated with an increase in the experience of surgeons. In addition, the dependence of the risk of complications on the age of patients, on the central thickness of the cornea and on the preoperative level of visual acuity is shown.

Conclusions

1. The frequency of complications after implantation of intrastromal segments, corneal collagen crosslinking and a combination of these operations (12.5±4.7; 25.0±7.6 and 28.6±9.8 %) differs significantly from each other.

2. The combined use of corneal collagen crosslinking with both photorefractive keratectomy and phototherapeutic keratectomy is associated with the same risk of postoperative complications (31.3±11.5 and 27.3±13.4 %).

3. The risk of postoperative complications is relatively high in patients aged 30 years and older, with a preoperative level of visual acuity without correction of less than 0.2 and with a central corneal thickness of 470 microns.

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