

Original article

Reprint

Effect of patient adherence to treatment on the efficacy of penetrating keratoplasty

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Abstract:

Objective: to determine the relationship between adherence to treatment in patients who underwent penetrating keratoplasty (PKP) and corneal graft survival during 12 months of follow-up.

Materials and methods. A retrospective analysis of treatment outcomes was performed in 56 patients who underwent high-risk PKP. Depending on the degree of adherence (full or partial), the patients were divided into two groups. The group of patients with full adherence included those who attended more than 90% of visits during the first year after the intervention, while the group of patients with partial adherence included those who missed more than 10% of medical visits.

Results. The group of patients with full adherence was characterized by the following features: a higher proportion of women ($p=0.033$); on average, 7 years younger age of patients ($p=0.021$); and a predominance of higher education ($p=0.014$). A year after PKP, a favorable outcome was more often noted among patients with full adherence (74%) vs. partial adherence (48%) ($p=0.046$). Calculation of the odds ratio (OR 3.52; confidence interval [CI]: 1.1362–10.88; $p=0.045$) indicated a statistically significant role of treatment adherence as a factor in the effectiveness of keratoplasty. In the group of patients with full adherence, visual acuity was achieved on average by two lines higher to the top of the Golovin–Sivtsev table at the end of 12 months of observation ($p=0.003$).

Conclusion. Adherence to treatment after PKP has a significant impact on corneal graft survival and clinical outcome. The development and implementation of a set of measures to increase adherence can significantly improve the level of safety and effectiveness of high-tech patient care in disabling corneal pathology.

Keywords: keratoplasty, penetrating keratoplasty, corneal opacity, patient compliance, patient adherence, transplantology

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Introduction

Corneal diseases are among the leading causes of poor visual acuity and visual disability in Russia. They affect approximately 4.5 million people worldwide [1, 2]. In many forms of corneal blindness, visual functions can be successfully restored by corneal transplantation. Despite the rapid development of layer-by-layer transplantation technology, penetrating keratoplasty (PKP) remains the most popular technique [3, 4]. Unlike rehabilitation after cataract surgery or keratorefractive surgery, patients after PKP are in need of continuous use of eye drops, multiple visits to the attending physician, and delayed removal of sutures [5, 6]. During this period, the rates of important postoperative complications such as persistent erosion, infection, and graft rejection are high [7, 8]. This specification defines a close association between remote clinical outcomes of PKP and adherence to treatment regimens. Individual treatment adherence is a measure of patient compliance with physician recommendations regarding (a) lifestyle changes, (b) taking medications, (c) undergoing medical procedures and interventions, and (d) medical visits [9, 10]. Poor adherence

to treatment is a serious problem in PKP, as well as in other types of organ transplantation or tissue grafting, leading to elevated medical complications and mortality, along with increased healthcare costs [11].

According to the World Health Organization, adherence to treatment is determined by various factors that can be associated with the patient, disease, treatment regimen, physician and healthcare system, as well as socioeconomic realities [10]. Studying the role of patient adherence in the short-term clinical outcome of PKP is a relevant task in contemporary clinical ophthalmology, healthcare management and medical sociology.

Objective: to determine the relationship between patient adherence to treatment after PKP and corneal graft survival during 12 months of follow-up.

Materials and methods

We conducted a retrospective study at the Division for Ophthalmology of the Volga District Medical Center of the Federal Medical and Biological Agency (VDMC FMBA),

Nizhny Novgorod, Russia. We also performed a sequential analysis of digital medical records of patients observed in the division in 2015-2022. The inclusion criteria for the study were as follows: referral for treatment with the PKP method on one or both eyes, postoperative observation in the Division for Ophthalmology, VDMC FMBA, and medical examination at 12±2 months after surgery. The exclusion criterion was keratoconus as an underlying disease. Patients with keratoconus belong to the low-risk patient group of patients, and are characterized by young age and high odds of a favorable outcome, which determines their clinical and sociodemographic heterogeneity as opposed to high-risk patients. That is why this study examined treatment outcomes of a high-risk patient group. According to current concepts of risk factors for graft disease, the latter patients had underlying keratitis and keratouveitis outcomes, Fuchs endothelial corneal dystrophy, and complications of open globe injury [12].

Depending on the attendance of postoperative visits, patients were classified into two groups. Treatment adherence was considered full if over 90% of appointments were attended during the first year of postoperative observation, and partial if more than 10% of medical visits were missed. The criterion of 90% adherence to the treatment strategy was selected based on published studies [13, 14]. The follow-up duration was identified by the fact that in the case of uncomplicated postoperative period, 12 months after PKP, the patient was weaned off steroids and the corneal sutures were removed, allowing for minimizing pharmacotherapy and frequency of follow-up visits. During the first year, postoperative examinations were routinely performed at 1, 2, and 4 weeks, followed up by examinations at 2, 3, 4, 6, 9, and 12 months after PKP. Graft transparency at the end of the observation period was considered a favorable outcome, while the corneal graft rejection or opacity was considered an unfavorable outcome.

Additionally, we assessed various demographic and ophthalmological parameters, and social determinants of health. The patient groups were compared by their gender- and age-based structure, presence of higher education in patients, and geographic distance. The latter parameter was measured in kilometers from the patient's actual location to the medical institution using the Yandex Maps app. Patients were categorized in those living at a distance of more than 50 km and less than 50 km. Patient disability was one of the assessed social determinants of health. Also, the maximum values of visual acuity of the operated eye before and after the surgery were taken into account.

Statistical analyses were performed using the SPSS 22.0 statistical software (IBM, USA). Continuous variables are presented as $M \pm SD$, where M is the arithmetic mean and SD is the standard deviation. Normality of the data distribution was assessed by quantile graphs and the Shapiro-Wilk criterion. In case of normal distribution of samples, Student's t -test was performed to assess the significance of differences between groups. For non-normal data, we used Mann-Whitney U test to compare two independent samples. To compare binary categorical variables, χ^2 criterion and Fisher criterion were employed. The relationship between patient adherence and the clinical outcome was measured using binary logistic regression with odds ratio (OR) and confidence interval (CI) assessment. Kaplan-Meier survival

analysis was used to compare the probability of maintaining a favorable outcome of PKP for 12 months after phacoemulsification in patient groups. The statistical significance was assumed at $p < 0.05$.

Results

According to the specified inclusion criteria, we initially selected 84 patients who underwent PKP for data collection. Of these, 28 cases of keratoconus were excluded. As a result, we analyzed data of 56 patients operated by the PKP method from 2015 to 2021 and followed up in 2015-2022. The group of patients with full adherence included 27 patients (48%), while 29 patients exhibited partial adherence to treatment.

The observation period ranged from 1 to 68 months with the mean duration of 18±9 months. The total number of prescribed medical appointments was 781, of which 112 (14.3%) were missed by patients. The mean age of patients was 67.0±11.2 (35–82) years. In a comparative analysis, the group of patients with full adherence was characterized by a predominance of women ($p=0.033$), 7 years younger age of patients ($p=0.021$) and a predominant presence of higher education ($p=0.014$) (Table). The visual acuity did not differ between groups before the PKP surgery ($p=0.787$). Same was true about the proportion of patients with established disability ($p=0.432$) and the distance from the patient's residence to the medical institution ($p=0.358$).

One year after the PKP, we registered a favorable outcome in 34 (60.7%) patients: more often among patients with full (74%) than partial (48%) adherence ($p=0.046$). In the full adherence group, on average, the visual acuity of patients based on Golovin-Sivtsev table was two lines higher to the top at the end of 12 months of follow up in full adherence group ($p=0.003$) (Table). OR values indicated a statistically significant role of patient adherence to treatment as a factor in keratoplasty effectiveness (OR 3.52; CI: 1.1362-10.88; $p=0.045$). Using the Mantel-Cox log-rank test, statistically significant differences were identified confirming higher probability of a favorable outcome after PKP in the full adherence group ($p=0.045$) (Figure).

Discussion

The presented study demonstrated for the first time a statistically significant effect of patient adherence to treatment on corneal graft survival. For the analysis, we used one of the most unbiased and simple methods of retrospective quantitative assessment of treatment adherence based on the analysis of patient visits to the attending physician. Missed appointments cause a number of multidirectional problems and, therefore, increase the burden on the patient, the physician, and the healthcare system. Studies on organ transplantation convincingly prove that unplanned interruptions in treatment increase the risk of complications [15]. The absence of live contact with the physician increases the risk of nonadherence to pharmacotherapy, which leads to poor graft survival. Full adherence in our sample was 48%, that is slightly lower than in the study demonstrating full adherence in 68.5% of New Zealand patients [14]. In part, this difference can be explained by the criteria for forming the cohort, one of which excluded patients with keratoconus in our study. However, both results confirm lower adherence to treatment in patients

after PKP compared with recipients of donor organs. In a multicenter study on kidney transplantation, the prevalence of full adherence to postoperative monitoring ranged from 76% to 100% [15]. Low adherence to the postoperative monitoring regimen was observed in patients after liver transplantation (53%). However, it is necessary to take into account the proportion of marginalization among patients with liver pathology [16]. At the same time, the lack of uniform criteria for both full and partial adherence limits the possibility to adequately compare the results of various studies [17].

Table. Comparative characteristics of patients with complete and partial adherence to visiting a doctor after penetrating keratoplasty

Parameter	Group of patients based on their adherence to treatment		P
	Partial (n=29)	Full (n=27)	
Age, years	70.38±8.06	63.4±13.1	0.021*
Gender (n male/female)	20/9	11/16	0.033*
Higher education, n (%)	11 (38%)	19 (70%)	0.014*
Disability, n (%)	17 (59%)	13 (48%)	0.432
Visual acuity prior to surgery	0.034±0.058	0.029±0.062	0.787
Distance more than 50 km, n (%)	12 (41%)	8 (30%)	0.358
Visual acuity after surgery	0.173±0.204	0.354±0.235	0.003*
Favorable outcome, n (%)	14 (48%)	20 (74%)	0.046*

*, significance level $p < 0.05$.

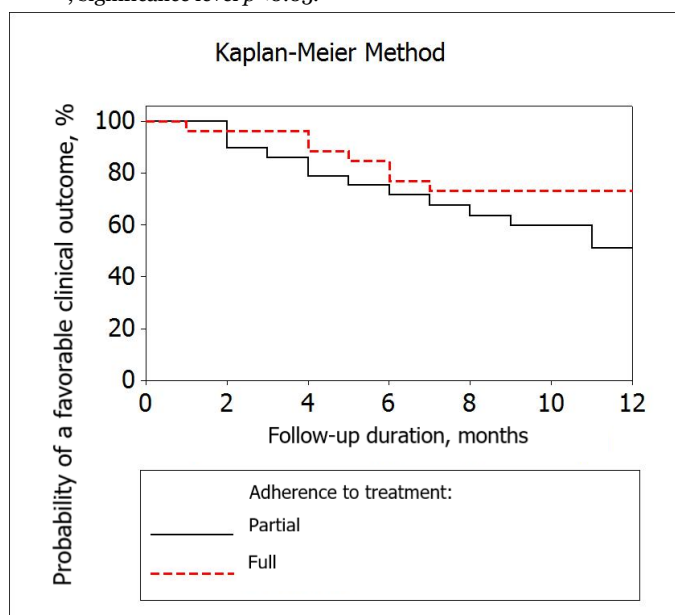


Figure. Kaplan-Meier analysis of corneal graft survival in the study patient groups. Patients with full adherence to treatment demonstrate a higher probability of a favorable clinical outcome after 12 months of follow-up ($p = 0.045$, Mantel-Cox log-rank test).

The results of our comparative study helped identify some social determinants of health in patients with full and partial adherence to treatment after PKP. In the first case, this is a 63-year-old woman with higher education, while in the second case, this is a 70-year-old man without higher education and with a disability. The education level, gender and age are significant factors affecting adherence to treatment for many chronic noncommunicable diseases [18, 19]. The adherence of glaucoma patients to outpatient visits has shown an association with the education level, income size, bad habits, and the presence of a family [20]. Given the predominantly elderly age of patients with disabling corneal pathology, it is of particular interest for further research to identify the role and attitudes of relatives, as well as the patients' assessment of the attending physician personality, in the formation of adherence to treatment [19].

Irregularity of medical visits requires more time and effort from the physician to coordinate treatment. A significant proportion of planned but missed appointments creates a financial problem of forced downtime for medical institutions with limited resources of time, finances, and specialists. Our results demonstrate the complex nature of the problem, which includes, in addition to clinical, also social aspects affecting the rehabilitation success of patients with disabling corneal pathology. High costs of surgical treatment and early rehabilitation of the patient, associated with the high cost of material for corneal restoration and a long hospital stay, are certainly justified by the favorable treatment outcome. At the same time, partial adherence to recommendations at the outpatient stage nullifies the previously achieved success, which determines the high value of each postoperative appointment for all participants in the surgical rehabilitation process: the patient, his relatives, doctors, and the medical institution.

The absence of statistically significant differences between the patient groups regarding the incidence of disability and remoteness of the place of residence can be explained by the lower power of nonparametric analysis methods in conditions of a small sample size. In addition to the sample size, the retrospective nature of our study can be considered a limitation. The strengths of our study are its comparative design and an integrated approach to the analysis of demographic, social and clinical aspects of the considered problem. Further examination of the topic requires identifying the causes of follow-up interruption on the part of a patient and elucidating the associations between quality of life, patient satisfaction, and treatment adherence. Also, our data imply the need to develop methods for targeted impact on the patient adherence to treatment after PKP.

Conclusion

Our study revealed a statistically significant effect of adherence to treatment after PKP on corneal graft survival and clinical outcome. We established that high-risk patients were characterized by a poor adherence to attending postoperative medical examinations within 12 months after PKP. Patients who attended all scheduled appointments were younger and had higher education. Development and implementation of a set of measures to improve treatment adherence can significantly improve the safety and effectiveness of high-tech patient care in disabling corneal pathology.

Respecting patient rights. The study does not contain identifying information about patients.

Author contributions: the authors contributed equally to the preparation of the manuscript.

Conflict of interest: none declared by the authors.

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