



# Evaluation of the Clinical Findings of Patients with Penetrating Keratoplasty Followed by Telephone Due to the COVID-19 Pandemic

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## Abstract

**Objectives:** To evaluate changes in the clinical findings of keratoplasty patients who could not be examined face-to-face and were followed up by telephone during the coronavirus disease 2019 (COVID-19) pandemic.

**Materials and Methods:** Patients with penetrating keratoplasty who presented to the cornea department between March 2020 and February 2021 were grouped according to whether they showed clinical deterioration (Group 1: no deterioration, Group 2: deterioration). The patients' last visit prior to the COVID-19 pandemic and their first visit after the pandemic-related lockdown ended were evaluated. The demographic data, follow-up period, and ophthalmological examination findings of all patients were recorded and the data were compared between the groups.

**Results:** Thirty-five eyes of 35 patients were included in the study. Signs of deterioration were detected in 8 (22.8%) of the patients (Group 1), while no deterioration was detected in 27 (77.2%) of the patients (Group 2). In the last follow-up visit prior to the COVID-19 pandemic, mean best corrected visual acuity (BCVA) was  $1.26 \pm 0.43$  LogMAR (range: 0.52-1.80) in Group 1 and  $1.41 \pm 1.02$  LogMAR (range: 0-3.1) in Group 2 ( $p=0.692$ ). Mean BCVA in the first control during the pandemic was  $2.07 \pm 0.86$  LogMAR (range: 1.3-3.1) in Group 1 and  $1.49 \pm 1.08$  LogMAR (range: 0-3.1) in Group 2 ( $p=0.08$ ). At the first visit during the COVID-19 pandemic, the mean intraocular pressure of Group 1 was  $16.38 \pm 8.58$  mmHg (range: 0-31), and Group 2 was  $17.11 \pm 3.7$  mmHg (range: 11-26) ( $p=0.984$ ).

**Conclusion:** The continuation of treatment initiated prior to the pandemic was probably the most important reason why deterioration was not observed in keratoplasty patients. In situations such as pandemics where face-to-face visits with patients may be disrupted, it may be possible to follow the patients safely with telemedicine visits until the difficult circumstances resolve.

**Keywords:** COVID-19, penetrating keratoplasty, telemedicine

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## Introduction

Coronavirus disease 2019 (COVID-19) is caused by a member of the coronavirus family called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>1</sup> SARS-CoV-2 first appeared in Wuhan, China in 2019 and spread from person to person.<sup>1</sup> COVID-19 was declared a pandemic by the World Health Organization on March 11, 2020.<sup>2</sup>

The COVID-19 pandemic brought about radical changes in many areas of life, including reshaping patient follow-up.<sup>3</sup> The Centers for Disease Control and Prevention recommended telemedicine instead of face-to-face clinic visits in order to maximize social distancing.<sup>4</sup> Virtual patient visits were reported to increase by 257% to 700% because of the pandemic.<sup>5</sup> In accordance with this recommendation, ophthalmology clinics also triaged patients and scheduled face-to-face examinations only for emergency cases. For patients classified as non-urgent, telemedicine followed up was initiated.<sup>6</sup>

Corneal blindness is the third most common cause of blindness in the world.<sup>7</sup> Corneal transplantation is essential in the treatment of end-stage corneal decompensation and is the most commonly performed tissue transplantation in the world.<sup>8</sup> Because of the avascular structure of the cornea, corneal transplantation has more successful outcomes compared to other organ transplants.<sup>9</sup> During the COVID-19 pandemic, the number of keratoplasty surgeries decreased while emergency surgeries such as tectonic keratoplasty continued to be performed.<sup>10</sup>

This study aimed to evaluate changes in the clinical findings of corneal transplant patients who were unable to have face-to-face visits during the COVID-19 pandemic and were followed up by telephone.

## Materials and Methods

Thirty-five eyes of 35 patients who presented to our cornea unit and underwent corneal transplantation between March 2020 and February 2021 were included in the study. The patients' demographic data, follow-up period, and complete ophthalmologic examination findings including best corrected visual acuity (BCVA), intraocular pressure (IOP) measurements, and anterior and posterior segment examinations at their last visit prior to the COVID-19 pandemic and their first in-person visit during the COVID-19 pandemic were recorded. The medications used by the patients and any changes in these medications were noted. Patients were grouped as having clinical deterioration (Group 1) and not having deterioration (Group 2). Clinical deterioration was defined as signs of graft failure or graft rejection and recurrence of keratitis in patients with

keratitis etiologies. The patients' treatment and complaints were managed by telephone visits during the interim period when they patients could not attend in-person follow-up visits because of the pandemic.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ege University Ethics Committee (decision number: 21-5T/4).

### Statistical Analysis

Statistical analysis was performed using SPSS version 26 (IBM Corp, Armonk, NY, USA) software package. The Wilcoxon test was used to compare data from before and during the pandemic data. The Mann-Whitney U test was used to compare data between the groups with and without clinical deterioration. P values <0.05 were accepted as statistically significant.

## Results

Thirty-five eyes of 35 patients, 14 (40%) women and 21 (60%) men, were included in the study. The patients' mean age was  $63.40 \pm 13.43$  years (range: 28-86) and the mean follow-up time was  $45.22 \pm 51.23$  months (range: 5-280). The mean time without follow-up was  $5.03 \pm 2.20$  months (range: 2-11) (Table 1). Twenty-seven (77.1%) of the patients had received their first corneal transplant, 7 (20%) had their second, and 1 (2.9%) had received a third corneal transplant.

The patients' mean BCVA was  $1.38 \pm 0.92$  LogMAR (range: 0-3.1) at last follow-up before the COVID-19 pandemic and  $1.62 \pm 1.05$  LogMAR (range: 0-3.1) at the first visit during the COVID-19 pandemic. There was a statistically significant decrease in BCVA ( $p=0.009$ , Wilcoxon test).

Mean IOP values at last follow-up visit before the COVID-19 pandemic and at the first visit during the pandemic were  $16.14 \pm 3.30$  mmHg (range: 8-22) and  $16.94 \pm 5.07$  mmHg (range: 0-31) ( $p=0.128$ , Wilcoxon test) (Table 2).

**Table 1. Demographic data of the patients included in the study**

Sex	n (%)
Female	14 (40)
Male	21 (60)
Total	35 (100)
	<b>Mean ± SD (range)</b>
Age (years)	$63.40 \pm 13.43$ (28-86)
Follow-up time (months)	$45.22 \pm 51.23$ (5-280)
Time without follow-up (months)	$5.03 \pm 2.20$ (2-11)
SD: Standard deviation	

**Table 2. Clinical findings of the patients before and during the pandemic**

	Pre-pandemic Mean ± SD (range)	First visit during pandemic Mean ± SD (range)	p value
BCVA (LogMAR)	$1.38 \pm 0.92$ (0-3.1)	$1.62 \pm 1.05$ (0-3.1)	0.009
IOP (mmHg)	$16.14 \pm 3.30$ (8-22)	$16.94 \pm 5.07$ (0-31)	0.128
BCVA: Best corrected visual acuity, IOP: Intraocular pressure, SD: Standard deviation			

Eight (22.8%) of the patients included in the study showed signs of deterioration, while the other 27 (77.2%) were clinically stable. The mean age was 66.25±12.94 years (range: 47-86) in Group 1 and 62.56±13.7 years (range: 28-78) in Group 2. There was no significant age difference between the groups (p=0.798, Mann-Whitney U test). Patients in Group 1 went without follow-up for a mean of 5.76±2.3 months (range: 4-11), while those in Group 2 went without follow-up for 4.81±2.16 months (range: 2-11). The time without follow-up was similar in both groups (p=0.08, Mann-Whitney U test). The mean time since corneal transplantation was 49.75±36.77 months (range: 1-131) in Group 1 and 36.77±54.57 months (range: 0-274) in Group 2 (p=0.265, Mann-Whitney U test). BCVA at last follow-up before the COVID-19 pandemic was 1.26±0.43 LogMAR (range: 0.52-1.80) in Group 1 and 1.41±1.02 LogMAR (range: 0-3.1) in Group 2 (p=0.692, Mann-Whitney U test). BCVA at first follow-up during the COVID-19 pandemic was 2.07±0.86 LogMAR (range: 1.3-3.1) in Group 1 and 1.49±1.08 LogMAR (range: 0-3.1) in Group 2 (p=0.08, Mann-Whitney U test). The mean IOP before the COVID-19 pandemic was 17.13±1.55 mmHg (range: 14-19) Group 1 and 15.85±3.64 mmHg (range: 8-22) in Group 2 (p=0.312, Mann-Whitney U test). During the COVID-19 pandemic, the mean IOP values in Group 1 and Group 2 were 16.38±8.58 mmHg (range: 0-31) and 17.11±3.7 mmHg (range: 11-26), respectively (p=0.984, Mann-Whitney U test) (Table 3).

In Group 1, there was a significantly decrease in BCVA during the pandemic compared to pre-pandemic values (p=0.027, Wilcoxon test). BCVA in Group 2 did not show a significant decrease during the pandemic (p=0.309, Wilcoxon test).

No significant change in pre-pandemic IOP was observed during the pandemic in Group 1 (p=0.931, Wilcoxon test) or Group 2 (p=0.055, Wilcoxon test).

In Group 1, 5 patients had graft failure, 2 had loosening of sutures, and 1 had recurrence of herpes.

The most common causes of corneal transplantation in the patients included in the study were pseudophakic bullous keratopathy (n=13), herpetic keratitis (n=7), keratoconus (n=4), and perforated corneal ulcer (n=3). Indications for keratoplasty in Group 1 were herpetic keratitis (n=4), keratoconus (n=1), pseudophakic bullous keratopathy (n=1), perforated corneal ulcer (n=1), and gelatinous drop-like dystrophy (n=1).

Corneal sutures were still present in 54.3% (n=19) of the patients, while 45.7% (n=16) of the patients no longer had corneal sutures. There was no statistically significant relationship between suture presence and clinical deterioration (p=0.782, chi-square test).

At the last follow-up visit before the COVID-19 pandemic, all patients used artificial tears, 88.5% used topical cyclosporine, 34.2% (n=12) used topical dexamethasone, 34.2% (n=12) used topical fluorometholone, and 20% (n=7) used loteprednol. Of the patients who could not come for in-person follow-up due to the pandemic, 91.4% (n=32) continued the same treatment, 2 patients were switched from topical dexamethasone to topical fluorometholone at other centers, and 1 patient used dexamethasone instead of fluorometholone.

The most common ocular comorbidities were herpetic keratitis (50%, n=4) and glaucoma (37.5%, n=3) in Group 1 and glaucoma (55.5%, n=15) and herpetic keratitis (11.1%, n=3) in Group 2. None of the patients in Group 1 had systemic disease, while 3.7% (n=1) of the patients in Group 2 had hypertension and 3.7% (n=1) had diabetes mellitus.

### Discussion

In this study we analyzed changes in the clinical findings of penetrating keratoplasty patients who had telephone follow-up

**Table 3. Comparison of clinical findings in patients with clinical deterioration (Group 1) and without clinical deterioration (Group 2)**

	Group 1 Mean ± SD (range)	Group 2 Mean ± SD (range)	p value
Age (years)	66.25±12.94 (47-86)	62.56±13.7 (28-78)	0.798
Time without follow-up (months)	5.76±2.3 (4-11)	4.81±2.16 (2-11)	0.08
Time since corneal transplantation (months)	49.75±36.77 (1-131)	36.77±54.57 (0-274)	0.265
BCVA before pandemic (LogMAR)	1.26±0.43 (0.52-1.80)	1.41±1.02 (0-3.1)	0.692
BCVA at first visit during pandemic (LogMAR)	2.07±0.86 (1.3-3.1)	1.49±1.08 (0-3.1)	0.080
IOP before pandemic (mmHg)	17.13±1.55 (14-19)	15.85±3.64 (8-22)	0.312
IOP at first visit during pandemic (mmHg)	16.38±8.58 (0-31)	17.11±3.7 (11-26)	0.984

BCVA: Best corrected visual acuity, IOP: Intraocular pressure, SD: Standard deviation

instead of face-to-face visits because of the COVID-19 pandemic, and we found no clinical deterioration except for a statistically significant decrease in BCVA. When the patients were grouped according to whether or not they showed clinical deterioration, there were no significant differences in ophthalmological findings between the groups.

The indication for penetrating keratoplasty is an important factor affecting post-keratoplasty graft survival. Keratoconus and pseudophakic bullous keratopathy are the pathologies with the best prognosis for keratoplasty.<sup>11,12,13</sup> Approximately half (48.5%) of the cases in our study were keratoconus and pseudophakic bullous keratopathy, which we believe is one of the reasons the patients' prognosis was not markedly affected by pandemic-related disruptions in follow-up examinations.

Nearly all (91.4%) of the patients continued medical treatment as initiated before the pandemic. We consider this to be the main factor contributing to the low rate of clinical deterioration despite the interruption in face-to-face visits. In addition, the use of topical cyclosporine or steroids by most patients reduces the likelihood of graft rejection by reducing inflammation. This is supported by studies showing that inflammation is an important risk factor for graft rejection.<sup>14,15</sup>

Of the patients included in the study, 22.9% had a history of recurrent keratoplasty. In their study including 377 patients, Yu et al.<sup>16</sup> reported that repeated penetrating keratoplasty was an important risk factor for graft failure. Consistent with their findings, the low percentage of patients with recurrent keratoplasty in our study may also be a reason for the low rate of deterioration.

The long time since corneal transplantation in the groups with and without deterioration (mean, 49.75 and 36.77 months, respectively) and the fact that these patients were clinically stable during this period significantly reduced the likelihood that their condition would deteriorate. In addition, the short time without face-to-face follow-up (mean, 5.76 and 4.81 months for Groups 1 and 2, respectively) is likely responsible for the low rate of deterioration and comparable outcomes in the groups.

When all patients in the study were analyzed together, we observed a significant decrease in BCVA during the pandemic compared with pre-pandemic BCVA values. However, when the patients were grouped according to whether they showed deterioration, there was no significant difference between BCVA values before and during the pandemic. This may be a result of the decrease in BCVA in the group without deterioration, which could be related to ophthalmological problems unrelated to corneal transplantation, such as the development of cataract in phakic patients and posterior capsular opacification in pseudophakic patients.

The presence of corneal sutures triggers inflammation and is an important risk factor for neovascularization.<sup>17</sup> Although sutures were present in over half of our patients (54.3%), there was no relationship between the presence of sutures and clinical deterioration. This can be attributed to the regular continuation of anti-inflammatory therapy.

## Conclusion

The implementation of movement restrictions and the potentially fatal prognosis of COVID-19 resulted in dramatic reductions in admissions to health institutions. This in turn led to disruptions in patient follow-up. As in many surgical interventions, postoperative follow-up after corneal transplantation is important. The main reason the patients in our study did not exhibit deterioration was that they continued their treatment after their last face-to-face examination. Emphasizing this during phone visits with patients also played an important role. In situations such as pandemics where face-to-face visits with patients may be disrupted, it may be possible to follow up patients safely with telemedicine visits until the unfavorable circumstances are resolved.

## Ethics

**Ethics Committee Approval:** Ege University Medical Research Ethics Committee (decision no: 21-5T/4, date: 06.05.2021).

**Informed Consent:** Obtained.

**Peer-review:** Externally peer reviewed.

## Authorship Contributions

Concept: M.P., Design: M.P., Data Collection or Processing: S.Y., Ö.B.S., Analysis or Interpretation: S.Y., Ö.B.S., M.P., Literature Search: S.Y., Writing: S.Y., Ö.B.S., M.P.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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