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Preview Version

The effect of COVID-19 on visual outcome and dry eye after SMILE

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ABSTRACT

Purposes: To evaluate the impact of coronavirus disease 2019 (COVID-19) on postoperative visual acuity, optical quality, and severity of dry eye disease in patients after small incision lenticule extraction (SMILE).

Methods: This is a retrospective, comparative study. Patients who underwent SMILE were included and divided into two groups according to the period at the eye center of the Second Affiliated Hospital of Zhejiang University. The first group included patients who underwent SMILE before the large-scale COVID-19 pandemic in China (Group 1). The second group comprised patients who underwent SMILE during the pandemic with a confirmed infection of COVID-19 (Group 2). The visual acuity, the severity of dry eye, ocular surface disease index (OSDI), oculus keratography analysis, and individual Zernike coefficients were evaluated and compared between the 2 groups.

Results: A total of 43 eyes of 23 patients and 45 eyes of 26 patients were included in Groups 1 and 2, respectively. The OSDI score in Group 2 was significantly higher than Group 1 ($P < 0.01$). The corrected distance visual acuity (CDVA, logMAR) at 3 months postoperatively in Group 1 was better than in Group 2 ($P < 0.001$). Despite the improvement over 1 month after the COVID-19 infection, the OSDI score was still higher in Group 2 than in Group 1 ($P < 0.01$). The bulbar and limbal redness were significantly higher in Group 2 than in Group 1 at both 1 month and 3 months ($P < 0.05$), while no significant differences were found in tear breakup time or tear meniscus height. Spherical aberration (SA) at the 4 mm zone was significantly higher in Group 2 than in Group 1 both at 1 month and 3 months ($P < 0.001$), while no significant changes were observed in corneal total higher-order aberrations. No significant correlation was found between the bulbar/limbal redness index and SA.

Conclusions: COVID-19 infection impaired visual outcomes and aggravated dry eye severity among postoperative SMILE patients.

1. Introduction

Currently, numerous studies have shown that femtosecond-assisted laser in situ keratomileusis and small incision lenticule extraction (SMILE) are safe and effective refractive surgeries for correcting myopia.[1,2] During the pandemic of coronavirus disease 2019 (COVID-19), ocular transmission was possible by detection of SARS-CoV-2 on the ocular surface.[3,4] Ocular manifestations mainly involve the conjunctiva, cornea, sclera, anterior chamber, pupil, retina, optic nerve and visual cortex, extraocular muscles and their cranial innervation, orbit, and lacrimal organ system. Anterior segment manifestations include conjunctivitis, ocular pain, discharge, and redness.[5] Depression, anxiety, and sleep disturbance were reported closely related to the severity of dry eye, especially during COVID-19.[6,7] Systemic biomarkers such as serum D-dimer and ferritin levels, were shown closely related to visual acuity among ophthalmic patients who had a recent history of COVID-19 or those with positive COVID-19 antibody status.[8] Ophthalmic manifestations may develop during or following COVID-19 infection.[9] Dry eye patients who have been infected with COVID-19 tend to have a more severe dry eye condition and parameters such as lower lipid layer thickness, worse papillae grading, shorter non-invasive tear breakup time, and meibomian gland dysfunction.[10] Patients undergoing refractive surgeries, such as SMILE, may also experience prolonged dry eye symptoms lasting up to 6 months post-operation.[11,12] However, the effect of a recent infection of COVID-19 on visual acuity, optical quality, and severity of dry eye disease among SMILE patients has not yet been investigated.

In China, the infection rate of COVID-19 is quite low due to stringent pandemic control and large-scale nucleic acid testing before November

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2022. Due to the relaxation of anti-COVID-19 measures in early December 2022, the COVID-19 infection rate in China reached its peak with an estimated 82.4% as of February 7, 2023.[13,14] We noticed that patients with a recent history of COVID-19 after corneal refractive surgery frequently complained of dry eye, foreign body sensation, redness, and blurred vision. Since dry eye severity differs between femtosecond assisted laser in situ keratomileusis group and SMILE group, SMILE patients were included in this study to control confounding factors.

We conducted a retrospective study of patients who underwent SMILE from January to February 2023 with a recent history of COVID-19 infection. The control group comprised patients who underwent SMILE from January to February 2022 with complete medical records. The ocular surface disease index (OSDI) was used to assess the self-reported severity of dry eye through teleconsultation. All medical records with subjective dry eye parameters and visual outcomes post-refractive surgery were analyzed to evaluate the impact of COVID-19.

2. Materials and methods

This study is a retrospective, comparative analysis of patients who underwent SMILE at the eye center of the Second Affiliated Hospital of Zhejiang University. We included Patients aged over 18 years with uneventful SMILE surgery conducted before (January 1, 2022, to February 28, 2022) and during (January 1, 2023, to February 28, 2023) the period of the large-scale COVID-19 infection in China with complete clinical data. We consider a simulation study to compare tear break-up time (TBUT) between two groups that aims to have 90% power to detect a standard deviation of 2 and a minimal meaningful difference of 2 at $\alpha = 0.05$ significance level. The required sample size for each group is $n = 42$ with 50% dropout. All the procedures in this study were approved by the Ethics Committee of the Second Affiliated Hospital, School of Medicine, Zhejiang University (No.2023-0664). Written informed consent was given from every patient.

2.1. Patients

The patients were divided into two groups based on the time of their SMILE and the post-operative follow-up. All of the SMILE patients from January 1, 2022, to February 28, 2022, and January 1, 2023, to February 28, 2023 were screened. All of the SMILE patients who had one visit during the period with complete 3 months' medical records were assessed for eligibility. Group 1 included SMILE patients who underwent SMILE before the large-scale infection of COVID-19 in China (January 1, 2022, to February 28, 2022). Group 2 included patients who underwent SMILE during the large-scale infection of COVID-19 in China (January 1, 2023, to February 28, 2023).

The inclusion criteria were postoperative myopia patients (Group 1 patients were confirmed with no history of COVID-19 confirmed by negative COVID-19 nucleic acid testing or antigen testing before February 28, 2022; Group 2 patients had a previous history of asymptomatic or mild COVID-19 infection within 3 months confirmed by positive COVID-19 nucleic acid testing or antigen testing). All patients finished postoperative visits at the out-patient clinic at 1 month and 3 months with complete medical records including visual acuity, corneal topography, and Oculus Keratography analysis. The exclusion criteria included moderate to severe COVID-19 infection, previous ocular surgery, severe dry eyes, keratoconus, topographic suspicion of keratoconus, ocular trauma, surgical complications, cataract, glaucoma, uveitis, retinopathy, pregnancy, breastfeeding, and systematic disease that could be accompanied by severe dry eyes, such as diabetes mellitus and connective tissue disorders. Soft contact lens or rigid gas permeable contact lens users were excluded. The study design flowchart was shown in Fig. 1.

2.2. Collection and analysis of higher-order aberrations (HOAs) and dry eye paremeters

Medical records and dry eye parameters including age, gender, surgery records, intraocular pressure, spherical equivalence, corrected

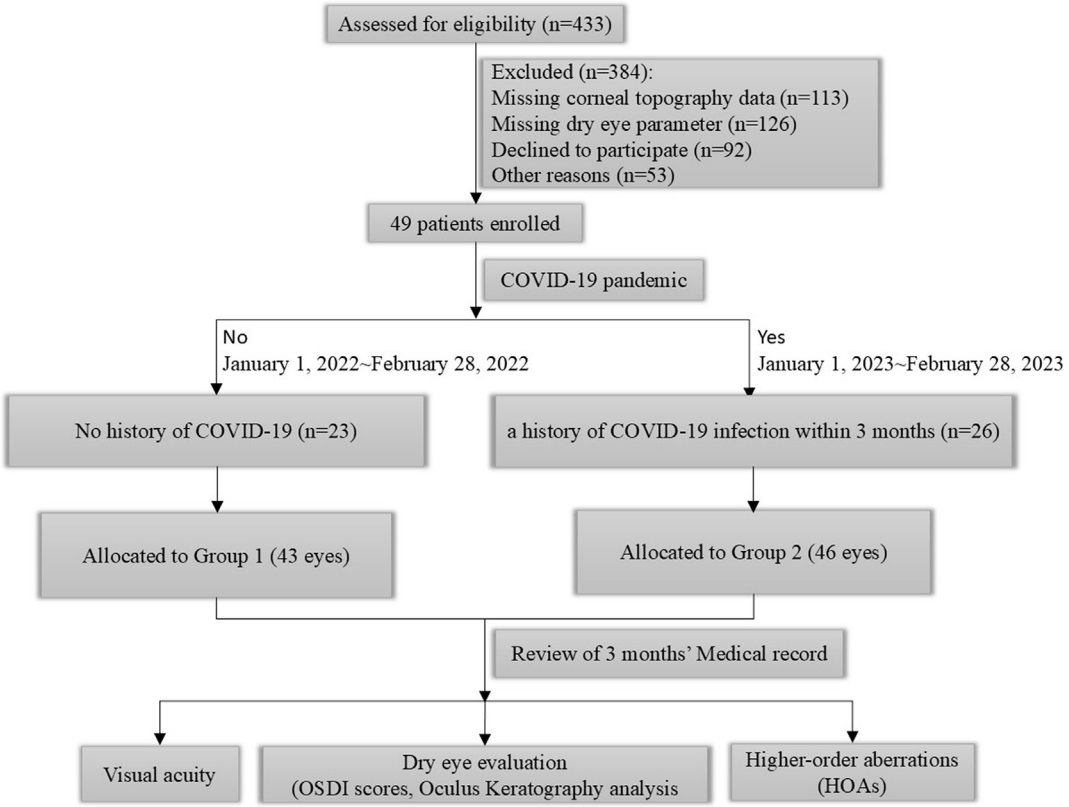

Fig. 1. Flow chart of the study.

visual acuity (CDVA, LogMAR) measured with logarithmic visual acuity chart, automatic tear meniscus height (TMH), first and mean non-invasive breakup time (NIBUT), bulbar redness, and limbal redness were collected (Oculus Keratography, Oculus Optikgeräte GmbH). Individual Zernike coefficients of 3rd-to 6th-order HOAs were exported from corneal topography (Pentacam HR, Oculus Optikgeräte GmbH). The OSDI scores were collected through teleconsultation in 3 subscales: typical symptom (3 questions), vision function (6 questions), and environmental triggers (3 questions). Participants were classified into 4 different categories of the dry eye based on total OSDI score: normal (score 0–12), mild (score 13–22), moderate (score 23–32), and severe (score 33–100).[15]

2.3. Statistical analysis

Statistical analysis was performed using SPSS (version 21.0, IBM Corp.). Quantitative data was presented by mean ± standard deviation, and the categorical data was presented by percentage. The Kolmogorov–Smirnov test was used for the normality of the data. For quantitative data, the difference among the three groups was evaluated by one-way ANOVA, and the student's t-test was used to calculate the difference between the 2 groups. For categorical data, the chi-square test or the fisher's exact test was used. Pearson's correlation test was used for correlation analysis between corneal HOA changes and dry eye parameters.

3. Results

A total of 43 eyes of 23 patients and 45 eyes of 26 patients were included in Group 1 and Group 2, respectively. The preoperative baseline characteristics of 2 groups were comparable (Table 1). The pre-operative dry eye severity assessed by TMH, first NIBUT, and the mean NIBUT, did not significantly differ between the 2 groups (Table 1, $P = 0.619$, $P = 0.577$, $P = 0.791$, respectively). Furthermore, there was no significant difference in corneal topography parameters, including flat keratometry, steep keratometry, and astigmatism magnitude between the 2 groups (Table 1, $P = 0.926$, $P = 0.987$, and $P = 0.587$, respectively).

3.1. Visual acuity and refractive outcomes

The percentage of CDVA equal to or better than 20/20 showed no significant difference between groups both at 1 month (Fig. 2A, Table 2, $P = 0.584$) and 3 months (Fig. 2C–Table 2, $P = 0.326$). Similarly, the percentage of spherical equivalent refraction (SER) within ±0.50 D showed no significant difference between groups both at 1 month (Fig. 2B–Table 2, $P = 0.085$) and 3 months (Fig. 2D–Table 2, $P = 0.326$). However, the CDVA (logMAR) at 3 months postoperatively in Group 1 was significantly higher than in Group 2 (0.011 ± 0.027 vs. -0.001 ± 0.007, $P < 0.001$) (Fig. 2C–Table 2).

Table 1
Pre-operative baseline characteristic of included patients.

	Group 1	Group 2	P value
Number	43 eyes (23 patients)	45 eyes (26 patients)	–
Age	27.2 ± 6.2	29.4 ± 5.7	0.117
Sex	4 males (17.4%)	5 males (19.2%)	0.868
MRSE	−4.86 ± 1.57	−4.76 ± 1.48	0.744
CCT	537.77 ± 19.19	542.61 ± 20.22	0.251
IOP	14.83 ± 2.17	14.42 ± 2.52	0.411
Kf	42.74 ± 1.22	42.76 ± 1.38	0.926
Ks	43.87 ± 1.24	43.86 ± 1.36	0.987
Astig	1.14 ± 0.52	1.07 ± 0.68	0.587
TMH	0.20 ± 0.05	0.19 ± 0.05	0.619
First NIBUT	6.45 ± 2.80	6.09 ± 3.32	0.577
Mean NIBUT	7.71 ± 2.41	7.86 ± 2.75	0.791

MRSE - mean refractive spherical equivalent, CCT - central corneal thickness, IOP - intraocular pressure, Kf - flat keratometry, Ks - steep keratometry, Astig - Astigmatism magnitude, TMH - tear meniscus height, NIBUT - non-invasive break-up time.

3.2. OSDI scores after COVID-19 infection

The OSDI scores were collected by telephone from all included patients. In Group 2, we further divided patients into two categories based on the time interval between COVID-19 infection and SMILE as within 1 month (n = 13) and more than 1 month (n = 13). ANOVA revealed a significant difference among the three groups ($P < 0.01$). The OSDI score was significantly higher for patients in Group 2 than in Group 1 (Fig. 3, 18.3 ± 10.0 vs. 5.3 ± 3.9, $P < 0.001$). Patients who underwent SMILE within 1 month after COVID-19 infection showed significantly higher OSDI scores than those who operated more than 1 month after infection (Figs. 3 and 23.0 ± 8.3 vs. 13.6 ± 9.6, $P < 0.001$). Notably, even after 1 month, patients in Group 2 still had a mild dry eye with significantly higher OSDI scores than Group 1 (Figs. 3 and 13.6 ± 9.6 vs. 5.3 ± 3.9, $P < 0.001$). The higher OSDI score in Group 2 indicated COVID-19 infection exacerbated the severity of dry eye after SMILE, and may persist for more than one month.

3.3. Oculus keratography analysis

The preoperative baseline characteristics of corneal topography (flat keratometry, steep keratometry, and astigmatism) and dry eye severity (TMH, first NIBUT, and mean NIBUT) were comparable between the 2 groups (Table 1).

The post-operative TMH, first NIBUT, and mean NIBUT were comparable between the 2 groups both at 1 month and 3 months (Table 3). Limbal and bulbar redness classification was also one of the measurements to evaluate dry eye disease.[16] Evaluation of limbal and bulbar redness using the oculus keratography analysis indicated significantly higher redness indices in Group 2 compared to Group 1 at 1 month (Table 3, $P < 0.05$ for total bulbar, nasal bulbar, and temporal limbal; $P < 0.01$ for nasal limbal) and at 3 months (Table 3, $P < 0.01$ for total bulbar, nasal bulbar, temporal bulbar, nasal limbal, and temporal limbal). However, no significant difference was observed in TMH, NIBUT, and redness index in both groups between 1 month and 3 months.

In our study, no patients reported conjunctivitis, ocular pain, or discharge. Although TMH and NIBUT were not affected, the higher bulbar and limbal redness indices in Group 2 indicated more severe dry eye or conjunctival congestion as signs of inflammation related to ocular manifestation developed during or after COVID-19 infection.

3.4. Corneal HOAs changes

There was no significant difference in central corneal thickness, anterior corneal flat keratometry, and steep keratometry between the 2 groups at 3 months, which indicated no obvious edema or thickening of the cornea (Table 4). We further analyzed the corneal HOAs between 2 Groups. Preoperative corneal HOAs were comparable between 2 groups (Table 4). Significant changes were found in Z (4, 0) (spherical aberration, SA) of the 4 mm zone at 1 month and 3 months, and Z (4, 0) of the 6 mm zone at 3 months (Table 4). However, further Pearson's correlation analysis between Z (4, 0) of the 4 mm zone with redness showed no statistically significant correlations (Table 5).

4. Discussion

COVID-19 infection affected multiple organs, including the eyes.[17] The eye transmission route speculations involved the conjunctiva angiotensin-enzyme II binding mode or the tears-nasolacrimal duct route.[18] The incidence of ocular manifestations in COVID-19 patients has been reported as high as 30%,[19] including conjunctivitis (86.4%), ocular pain (34.4%), dry eye (33.3%), and floaters (6.7%).[20] At the beginning of the pandemic, a lot of physicians described eye redness, irritation, or

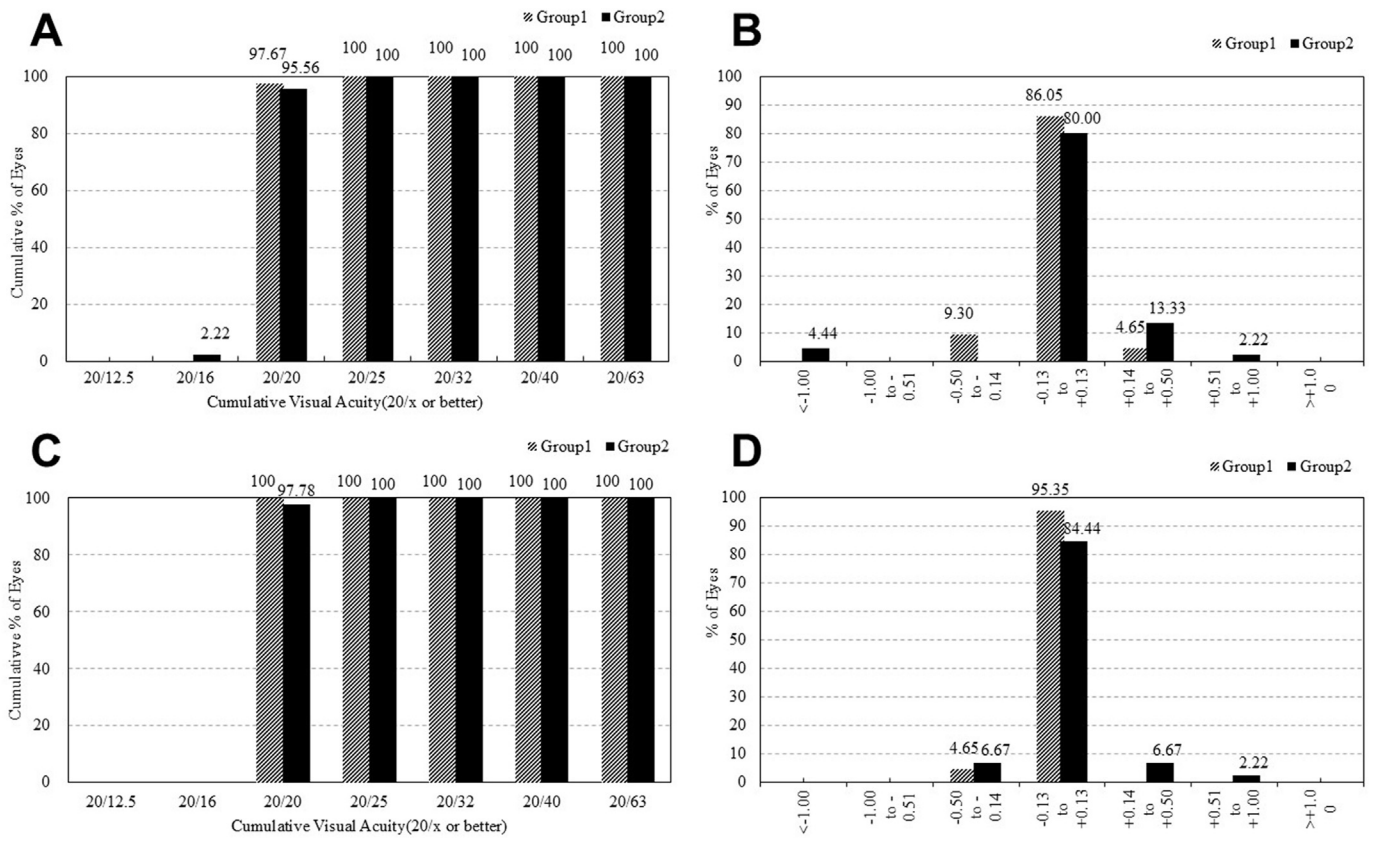

Fig. 2. Visual acuity and refractive outcomes after SMILE in 2 groups. Cumulative postoperative corrected distance visual acuity (CDVA) for SMILE at 1 month (A: 97.67% of Group 1 and 95.56% of Group 2 achieved CDVA equal to or better than 20/20) and 3 months (C: 100% of Group 1 and 97.78% of Group 2 achieved CDVA equal to or better than 20/20). Spherical equivalent refraction (SER) after SMILE at 1 month (B: 100% of Group 1 and 93.34% of Group 2 achieved SER within ±0.50 D) and 3 months (D: 100% of Group 1 and 97.78% of Group 2 achieved SER within ±0.50 D).

"conjunctival congestion" among patients in Wuhan, China. A cross-sectional study identified acute conjunctivitis in approximately 11.6% of COVID-19 cases.[21] In our study, we found significant differences in OSDI scores, bulbar redness, and limbal redness rather than in TMH or NIBUT. Though the secretion of tears has not been significantly affected, the higher OSDI scores and redness indices indicated more severe dry eye disease after COVID-19 infection.[22] Regarding the ocular manifestations, we observed among postoperative patients of refractive surgery, a conventional treatment may not be sufficient to alleviate symptoms and prevent possible complications. An optimized treatment strategy may need more attention and further study.

Though most patients recovered from COVID-19 within a few weeks, many experienced long-lasting problems or symptoms,[23] especially those with autoimmune diseases.[24] A study assessing 6-month consequences of COVID-19 in patients discharged from the hospital reported common symptoms such as fatigue or muscle weakness (52%), sleep difficulties (26%), anxiety or depression (23%).[25] In a meta-analysis, the prevalence was even higher with 45% of depression, 47% of anxiety, and 34% of sleeping disturbances, respectively.[26] Sleep disorders correlated significantly with the severity of dry eye.[27] Sleep deprivation or circadian rhythms disturbances led to shortened TBUT, reduced tear secretion, and disrupted the levels of circulating or tear film secretion and composition, further resulting in health issues including insulin resistance, poor glycemic control, and obesity.[7] Other mechanisms linking sleep disorders to dry eye included disorders in hormone metabolism[28] and physiological emotion.[29] Overall, tear alterations may be a potential factor linking sleep disturbance and dry eye. COVID-19 infection involves manifestations including fatigue, emotional change, and ocular ingestion or infection, which may result in reduced sleep duration and circadian rhythm disturbances, thus aggravating dry eye severity. Though the incidence of dry eye increased after COVID-19, no significant difference in preoperative dry-eye parameters was found in this study. These may be due to the appropriate treatment in the condition of abnormal dry-eye parameters or severe dry-eye symptoms before SMILE. In our previous practice, patients without obvious respiratory symptoms or dry-eye symptoms were allowed to undergo SMILE. However, in this study, we found higher OSDI scores among those who underwent SMILE within 1 month after COVID-19 infection than uninfected group and more than 1 month group. We supposed that dry eye was easily triggered and exacerbated by SMILE surgery, even if appropriate treatment alleviated symptoms within a month of COVID-19 infection. Our results demonstrated that an optimized and prolonged dry-eye treatment may be needed for COVID-19 infected patients before refractive surgery.

Visual impairment has been reported in approximately 16% of COVID-19 patients.[17] The possible sight-threaten ocular complications after COVID-19 infection included: uveitis, cotton wool spots, retinal hemorrhages, retinal artery/vein occlusion, ophthalmic artery occlusion, and central serous retinopathy.[30,31] COVID-19 was confirmed to exacerbate dry eye.[20] Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on the ocular surface epithelial cells and glands may cause a microenvironment alteration, instability of the tear film, and ocular inflammation indicated by bulbar or limbal redness.[32] Worse scores of OSDI and shorter TBUT were associated with worse visual acuity and contrast sensitivity, respectively.[33] There was also a significantly negative correlation between TBUT and the HOA progression index, and a significantly positive correlation between OSDI scores and the HOA progression index.[34] In our study, the COVID-19 infected group exhibited higher OSDI scores, higher bulbar/limbal redness, and higher HOAs. Thereby, worse dry eye parameters probably contributed to worse HOAs, thus resulting the reduced CDVA in the COVID-19 infected group.

Table 2
Visual acuity and refractive outcomes after SMILE in 2 groups.

		Group 1	Group 2
CDVA at 1 month (logMAR)	≥20/12.5	0	0
	≥20/16	0	1 (2.22%)
	≥20/20	42 (97.67%)	43 (95.56%)
	≥20/25	43 (100%)	45 (100%)
	≥20/32	43 (100%)	45 (100%)
	≥20/40	43 (100%)	45 (100%)
	≥20/63	43 (100%)	45 (100%)
	total	0.006 ± 0.037	0.003 ± 0.018
CDVA at 3 months (logMAR)	≥20/12.5	0	0
	≥20/16	0	0
	≥20/20	43 (100%)	44 (97.78%)
	≥20/25	43 (100%)	45 (100%)
	≥20/32	43 (100%)	45 (100%)
	≥20/40	43 (100%)	45 (100%)
	≥20/63	43 (100%)	45 (100%)
	total	0.011 ± 0.027	−0.001 ± 0.007**
SER at 1 month (D)	<-1.00	0	2 (4.44%)
	−1.00 to −0.51	0	0
	−0.50 to −0.14	4 (9.30%)	0
	−0.13 to +0.13	37 (86.04%)	36 (80.00%)
	+0.14 to +0.50	2 (4.65%)	6 (13.33%)
	+0.51 to +1.00	0	1 (2.22%)
	>+1.00	0	0
SER at 3 months (D)	<-1.00	0	0
	−1.00 to −0.51	0	0
	−0.50 to −0.14	2 (4.65%)	3 (6.67%)
	−0.13 to +0.13	41 (95.35%)	38 (84.44%)
	+0.14 to +0.50	0	3 (6.67%)
	+0.51 to +1.00	0	1 (2.22%)
	>+1.00	0	0

CDVA - corrected distance visual acuity, SER - Spherical equivalent refraction. **: test significant at $P < 0.01$ compared to Group1.

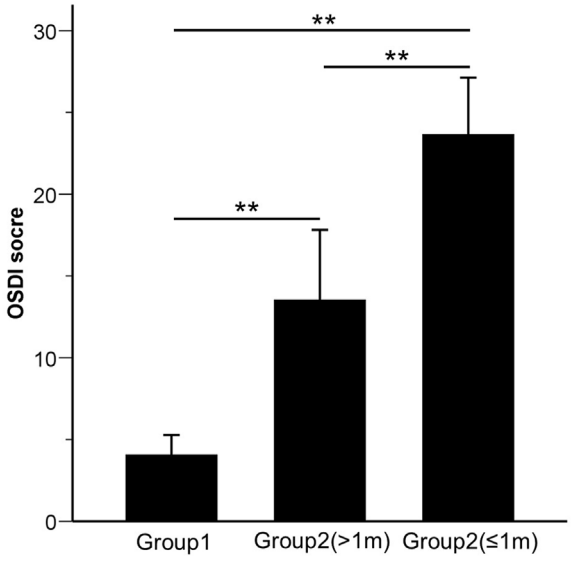

Fig. 3. OSDI scores after SMILE in 2 groups. OSDI scores were 5.3 ± 3.9, 13.6 ± 9.6, 23.0 ± 8.3 in Group 1, Group 2 (>1m) and Group 2 (≤1m), respectively. Group 1: no COVID-19 infection. Group 2 (>1m): the time between COVID-19 infection and SMILE as more than 1 month in Group 2; Group 2 (≤1m): the time between COVID-19 infection and SMILE as within 1 month in Group 2. **: test significant at P < 0.01.

However, the mechanism and corresponding treatment strategies may need further study.

The ocular manifestations played an important role at different stages of COVID-19, potentially offering early warnings for adjusting therapeutic strategies.[35] Timely ophthalmic care was essential for patients who experienced significant vision loss, as delays in outpatient

Table 3
Post-operative Oculus Keratography parameters.

	Group 1	Group 2	*P* value
TMH, 1m	0.18 ± 0.05	0.20 ± 0.06	0.296
First NIBUT, 1m	5.95 ± 2.79	6.42 ± 2.95	0.441
Mean NIBUT, 1m	7.97 ± 2.13	8.43 ± 2.53	0.357
Total bulbar redness, 1m	0.70 ± 0.41	0.89 ± 0.33	0.021*
Nasal bulbar redness, 1m	0.69 ± 0.50	0.91 ± 0.38	0.026*
Temporal bulbar redness, 1m	0.76 ± 0.40	0.93 ± 0.42	0.051
Nasal limbal redness, 1m	0.35 ± 0.28	0.53 ± 0.35	0.009**
Temporal limbal redness, 1m	0.38 ± 0.35	0.57 ± 0.42	0.022*
TMH, 3m	0.19 ± 0.04	0.19 ± 0.05	0.577
First NIBUT, 3m	6.85 ± 3.30	6.58 ± 3.48	0.700
Mean NIBUT, 3m	8.65 ± 2.53	7.88 ± 3.12	0.210
Total bulbar redness, 3m	0.68 ± 0.35	0.96 ± 0.29	0.000**
Nasal bulbar redness, 3m	0.67 ± 0.42	1.03 ± 0.48	0.000**
Temporal bulbar redness, 3m	0.73 ± 0.39	1.00 ± 0.39	0.001**
Nasal limbal redness, 3m	0.31 ± 0.22	0.67 ± 0.37	0.000**
Temporal limbal redness, 3m	0.34 ± 0.29	0.63 ± 0.35	0.000**

TMH - tear meniscus height, NIBUT - non-invasive break up time. *: test significant at $P < 0.05$ compared to Group1; **: test significant at $P < 0.01$ compared to Group1.

Table 4
Comparison of corneal HOAs changes.

		Group 1	Group 2	P value
Corneal topography (3 month)	CCT	440.60 ± 26.44	453.11 ± 22.39	0.018*
	Kf	38.72 ± 1.52	38.72 ± 1.78	0.997
	Ks	39.48 ± 1.66	39.51 ± 1.89	0.952
	Astig	0.79 ± 0.37	0.78 ± 0.44	0.907
4 mm zone	tHOAs pre	0.111 ± 0.037	0.104 ± 0.037	0.424
	tHOAs 1m	0.154 ± 0.056	0.145 ± 0.046	0.420
	tHOAs 3m	0.162 ± 0.058	0.152 ± 0.050	0.420
	Z (4, 0) pre	0.044 ± 0.020	0.037 ± 0.019	0.114
	Z (4, 0) 1m	0.003 ± 0.033	0.028 ± 0.029	0.000**
	Z (4, 0) 3m	−0.009 ± 0.042	0.019 ± 0.025	0.000**
6 mm zone	tHOAs pre	0.389 ± 0.075	0.360 ± 0.075	0.073
	tHOAs 1m	0.619 ± 0.158	0.563 ± 0.148	0.088
	tHOAs 3m	0.617 ± 0.160	0.576 ± 0.156	0.219
	Z (4, 0) pre	0.240 ± 0.065	0.233 ± 0.071	0.652
	Z (4, 0) 1m	0.306 ± 0.109	0.342 ± 0.116	0.136
	Z (4, 0) 3m	0.283 ± 0.102	0.334 ± 0.109	0.026*

CCT - central corneal thickness, Kf - flat keratometry, Ks - steep keratometry, Astig- Astigmatism magnitude, tHOAs - total higher−order aberrations. *: test significant at $P < 0.05$. **: test significant at $P < 0.01$.

Table 5
Pearson's correlation coefficient between Z (4, 0) of 4 mm zone and redness.

	Z (4, 0) 1m	Z (4, 0) 3m
Total bulbar redness	−0.058	−0.047
Nasal bulbar redness	−0.024	−0.037
Temporal bulbar redness	−0.065	−0.034
Nasal limbal redness	−0.003	0.005
Temporal limbal redness	0.124	0.127

ophthalmic care may result in worse visual prognoses.[36] This study contributed insights into outpatient ophthalmic care for patients after corneal refractive surgery during and after the COVID-19 pandemic.

Our study still have several limitations. Firstly, we mainly focused on the dry eye parameters and visual acuity of post-SMILE patients with COVID-19 infection, whereas some other ocular conditions like conjunctivitis, ocular pain, floaters, and fundus complications were not evaluated comprehensively. Secondly, as a retrospective study, dry eye parameters including limbal redness and HOAs were not routinely conducted in all post-SMILE surgery, thus the comprehensiveness of qualified participants might be limited to some extension. Moreover, the influence of medications during COVID-19 infection was commonly used from 1 to 3 days in this study, which could be a potential confounding factor. It's challenging to predict a pandemic of COVID-19 and design a prospective study in advance. Nevertheless, our study sugguests that the appropriate treatment to alleviate the relevant ocular symptoms and complications is beneficial to secure a better outcome of surgery.

5. Conclusions

In conclusion, COVID-19 infection impaired visual acuity, optical quality and aggravated dry eye severity among postoperative SMILE patients compared to control group.

Study approval

The authors confirm that any aspect of the work covered in this manuscript that involved human patients or animals was conducted with the ethical approval of all relevant bodies and the study was performed in accordance with the Declaration of Helsinki,and the protocol was approved by the Ethics Committee of the Second Affiliated Hospital, School of Medicine, Zhejiang University (approval number: 2023-0664).

Author contributions

The authors confirm contribution to the paper as follows: Conception and design of study: W Han, Z Fang; Data collection: Y Li, DJ Song, XY He; Analysis and interpretation of results: Y Li, K Zhang, TP Zhu, Z Fang; Drafting the manuscript: W Han, Z Fang; All authors reviewed the results and approved the final version of the manuscript.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

COVID-19	Coronavirus disease 2019
SMILE	Small incision lenticule extraction
OSDI	Ocular surface disease index
CDVA	Corrected distance visual acuity
SA	Spherical aberration
TMH	Tear meniscus height
NIBUT	Non-invasive break up time
HOA	Higher-order aberrations
SER	Spherical equivalent refraction

References

1. Li M, Li M, Chen Y, et al. Five-year results of small incision lenticule extraction (SMILE) and femtosecond laser LASIK (FS-LASIK) for myopia. *Acta Ophthalmol*. 2019; 97(3):e373–e380. https://doi.org/10.1111/aos.14017.
2. Zhao PF, Hu YB, Wang Y, et al. Comparison of correcting myopia and astigmatism with SMILE or FS-LASIK and postoperative higher-order aberrations. *Int J Ophthalmol*. 2021;14(4):523–528. https://doi.org/10.18240/ijo.2021.04.07.
3. Li M, Yang Y, He T, et al. Detection of SARS-CoV-2 in the ocular surface in different phases of COVID-19 patients in Shanghai, China. *Ann Transl Med*. 2021;9(2):100. https://doi.org/10.21037/atm-20-6026.
4. Rodriguez-Ares T, Lamas-Francis D, Trevino M, et al. SARS-CoV-2 in conjunctiva and tears and ocular symptoms of patients with COVID-19. *Vision*. 2021;5(4). https://doi.org/10.3390/vision5040051.
5. Dong J, Chen R, Zhao H, et al. COVID-19 and ocular complications: a review of ocular manifestations, diagnostic tools, and prevention strategies. *Adv Ophthalmol Pract Res*. 2023;3(1):33–38. https://doi.org/10.1016/j.aopr.2022.11.001.
6. He Q, Chen Z, Xie C, et al. The association between dry eye disease with depression, anxiety and sleep disturbance during COVID-19. *Front Psychiatry*. 2021;12:802302. https://doi.org/10.3389/fpsyt.2021.802302.
7. Li A, Zhang X, Guo Y, et al. The association between dry eye and sleep disorders: the evidence and possible mechanisms. *Nat Sci Sleep*. 2022;14:2203–2212. https://doi.org/10.2147/NSS.S378751.
8. Sanjay S, Bhakti Mistra S, Patro SK, et al. Systemic markers in ophthalmic manifestations of post corona virus disease-19 (COVID-19). *Ocul Immunol Inflamm*. 2023;31(2):410–415. https://doi.org/10.1080/09273948.2021.2025253.
9. Sen M, Honavar SG, Sharma N, et al. COVID-19 and eye: a review of ophthalmic manifestations of COVID-19. *Indian J Ophthalmol*. 2021;69(3):488–509. https://doi.org/10.4103/ijo.IJO_297_21.
10. Liao X, Wong ACC, Wong JOY, et al. Investigating the impact of COVID-19 infection on dry eye parameters. *Diagnostics*. 2023;13(9). https://doi.org/10.3390/diagnostics13091524.
11. Shen Z, Zhu Y, Song X, et al. Dry eye after small incision lenticule extraction (SMILE) versus femtosecond laser-assisted in situ keratomileusis (FS-LASIK) for myopia: a meta-analysis. *PLoS One*. 2016;11(12):e0168081. https://doi.org/10.1371/journal.pone.0168081.
12. Kobashi H, Kamiya K, Shimizu K. Dry eye after small incision lenticule extraction and femtosecond laser-assisted LASIK: meta-analysis. *Cornea*. 2017;36(1):85–91. https://doi.org/10.1097/ICO.0000000000000999.
13. Fu D, He G, Li H, et al. Effectiveness of COVID-19 vaccination against SARS-CoV-2 omicron variant infection and symptoms - China, december 2022-february 2023. *China CDC Wkly*. 2023;5(17):369–373. https://doi.org/10.46234/ccdcw2023.070.
14. Bai Y, Peng Z, Wei F, et al. Study on the COVID-19 epidemic in mainland China between November 2022 and January 2023, with prediction of its tendency. *J Biosaf Biosecur*. 2023;5(1):39–44. https://doi.org/10.1016/j.jobb.2023.03.001.
15. Schiffman RM, Christianson MD, Jacobsen G, et al. Reliability and validity of the ocular surface disease index. *Arch Ophthalmol*. 2000;118(5):615–621. https://doi.org/10.1001/archopht.118.5.615.
16. Sanchez-Gonzalez MC, Capote-Puente R, Garcia-Romera MC, et al. Dry eye disease and tear film assessment through a novel non-invasive ocular surface analyzer: the OSA protocol. *Front Med*. 2022;9:938484. https://doi.org/10.3389/fmed.2022.938484.
17. Ripa M, Motta L, Schipa C, et al. "Vision loss" and COVID-19 infection: a systematic review and meta-analysis. *Vision*. 2022;6(4). https://doi.org/10.3390/vision6040060.
18. Armstrong L, Collin J, Mostafa I, et al. In the eye of the storm: SARS-CoV-2 infection and replication at the ocular surface? *Stem cells translational medicine*. 2021;10(7): 976–986. https://doi.org/10.1002/sctm.20-0543.
19. Wu P, Duan F, Luo C, et al. Characteristics of ocular findings of patients with coronavirus disease 2019 (COVID-19) in hubei Province, China. *JAMA ophthalmology*. 2020;138(5):575–578. https://doi.org/10.1001/jamaophthalmol.2020.1291.
20. Inomata T, Kitazawa K, Kuno T, et al. Clinical and prodromal ocular symptoms in coronavirus disease: a systematic review and meta-analysis. *Invest Ophthalmol Vis Sci*. 2020;61(10):29. https://doi.org/10.1167/iovs.61.10.29.
21. Guemes-Villahoz N, Burgos-Blasco B, Garcia-Feijoo J, et al. Conjunctivitis in COVID-19 patients: frequency and clinical presentation. *Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie*. 2020;258(11):2501–2507. https://doi.org/10.1007/s00417-020-04916-0.
22. Schulze MM, Ng A, Yang M, et al. Bulbar redness and dry eye disease: comparison of a validated subjective grading scale and an objective automated method. *Optom Vis Sci : official publication of the American Academy of Optometry*. 2021;98(2):113–120. https://doi.org/10.1097/OPX.0000000000001638.
23. Yan Z, Yang M, Lai CL. Long COVID-19 syndrome: a comprehensive review of its effect on various organ systems and recommendation on rehabilitation plans. *Biomedicines*. 2021;9(8). https://doi.org/10.3390/biomedicines9080966.
24. Brito-Zeron P, Acar-Denizli N, Romao VC, et al. Post-COVID-19 syndrome in patients with primary Sjogren's syndrome after acute SARS-CoV-2 infection. *Clin Exp*

Rheumatol. 2021;39(Suppl 133):57–65. https://doi.org/10.55563/clinexprheumatol/0anatx (6).
25. Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet*. 2023;401(10393):e21–e33. https://doi.org/10.1016/S0140-6736(23)00810-3.
26. Deng J, Zhou F, Hou W, et al. The prevalence of depression, anxiety, and sleep disturbances in COVID-19 patients: a meta-analysis. *Ann N Y Acad Sci*. 2021;1486(1):90–111. https://doi.org/10.1111/nyas.14506.
27. Magno MS, Utheim TP, Snieder H, et al. The relationship between dry eye and sleep quality. *Ocul Surf*. 2021;20:13–19. https://doi.org/10.1016/j.jtos.2020.12.009.
28. Thompson KI, Chau M, Lorenzetti MS, et al. Acute sleep deprivation disrupts emotion, cognition, inflammation, and cortisol in young healthy adults. *Front Behav Neurosci*. 2022;16:945661. https://doi.org/10.3389/fnbeh.2022.945661.
29. Kastelan S, Bakija I, Bogadi M, et al. Mental disorders as influencing factors for discordances in the signs and symptoms of dry eye disease. *Psychiatr Danub*. 2021;33(Suppl 4):588–595.
30. Zhang Y, Stewart JM. Retinal and choroidal manifestations of COVID-19. *Curr Opin Ophthalmol*. 2021;32(6):536–540. https://doi.org/10.1097/ICU.0000000000000801.
31. Sen S, Kannan NB, Kumar J, et al. Retinal manifestations in patients with SARS-CoV-2 infection and pathogenetic implications: a systematic review. *Int Ophthalmol*. 2022;42(1):323–336. https://doi.org/10.1007/s10792-021-01996-7.
32. Meduri A, Oliverio GW, Mancuso G, et al. Ocular surface manifestation of COVID-19 and tear film analysis. *Sci Rep*. 2020;10(1):20178. https://doi.org/10.1038/s41598-020-77194-9.
33. Szczotka-Flynn LB, Maguire MG, Ying GS, et al. Impact of dry eye on visual acuity and contrast sensitivity: dry eye assessment and management study. *Optom Vis Sci : official publication of the American Academy of Optometry*. 2019;96(6):387–396. https://doi.org/10.1097/OPX.0000000000001387.
34. Denoyer A, Rabut G, Baudouin C. Tear film aberration dynamics and vision-related quality of life in patients with dry eye disease. *Ophthalmology*. 2012;119(9):1811–1818. https://doi.org/10.1016/j.ophtha.2012.03.004.
35. Sun S, Su W, Lin CQ, et al. COVID-19: the novel coronavirus disease and its manifestations and management in ophthalmology. *Discov Med*. 2020;29(158):145–157.
36. Leung EH, Fan J, Flynn Jr HW, et al. Ocular and systemic complications of COVID-19: impact on patients and healthcare. *Clin Ophthalmol*. 2022;16:1–13. https://doi.org/10.2147/OPTH.S336963.