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Original Research

Quality of life and patient satisfaction after submandibular gland transplantation in patients with severe dry eye disease

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ABSTRACT

Purpose: Submandibular gland (SMG) transplantation improves the tear film and other ocular-surface features for patients with severe dry eye disease (DED). Using the dry eye-related quality of life (QOL) questionnaire, we aimed to evaluate whether DED patients' QOL would benefit from SMG transplantation and determine whether preoperative ophthalmologic and QOL measurements could predict which patients would be most satisfied with this surgery.

Methods: This prospective study included DED patients with successful SMG transplantation. Using the Chinese version of the Dry Eye Related Quality of Life (CDERQOL) instrument, QOL was measured before and 1-year after surgery.

Results: The QOL data of 51 consecutive patients were analyzed. Before surgery, all the patients had a poor QOL. One year after surgery, all five QOL domains (Dry Eye Symptom Bother, Impact on Daily Activities, Emotional Impact, Impact on Work, and Satisfaction with Treatment) showed significant improvement ($P < 0.01$). Unsuccessful treatment experience with cyclosporin eyedrops as well as pre-surgical low scores of visual acuity and all five QOL domains (except for "Satisfaction with Treatment") were found to significantly increase the post-surgical QOL scores ($P < 0.01$); however, pre-surgical Schirmer's test, break-up times of tear-film, and corneal fluorescein staining measurements showed no effects or contradictory correlations with post-surgical QOL scores.

Conclusion: The life quality and satisfaction of DED patients showed significant improvement after SMG transplantation. Patients with severe and refractory DED could reap the benefits of surgery. A subjective QOL questionnaire is very valuable for predicting and evaluating the treatment effect.

1. Introduction

Dry eye is a relatively common disease of the tear film and ocular surface that presents as discomfort, visual disturbances, and tear-film instability, with potential damage to ocular surfaces [1]. Patients with mild-to-moderate dry eye disease (DED) generally benefit from pharmaceutical tear substitutes, cyclosporin eyedrops, or occlusion of tear drainage. However, for those with severe DED, these conventional therapeutic options are insufficient [2]. In recent years, ophthalmologists in conjunction with oral and maxillofacial surgeons have successfully transferred patients' submandibular gland (SMG) to the temporal region with the Wharton's duct passing through a subcutaneously prepared tunnel and opening in the eye. Using basal secretions of transplanted SMGs, this procedure provides a continuous, endogenous source of ocular lubrication as a tear substitute. Reports from different centers proved that the secretions from all viable transplanted SMGs maintain stable function for at least 5–10 years [3–7], and patient's post-surgical tear film and other ocular-surface features improved significantly as validated by break-up times of tear-film (BUT) and corneal fluorescein staining (FL) and rose Bengal staining

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tests [2,4,6–14]. SMG transplantation, which was recommended by the international dry eye workshop in 2007[15], offers an alternative and promising treatment for patients with severe DED.

DED is a symptom-based disorder and the symptoms severely affect patients' quality of life (QOL) [16]. One of the foremost objectives in caring for DED patients is the symptom remission and QOL improvement. Owing to the multifactorial etiology and the variability of symptoms, most clinical studies fail to demonstrate a significant correlation between symptoms and clinical test values [15]. Therefore, evaluation of the treatment efficacy for DED should depend not only on objective clinical tests but also on assessments of patient's symptoms and their impact on patients' QOL [17,18]. Questionnaires for QOL have been widely used for the evaluation of treatment effect for mild-to-moderate DED [19,20]. To our best knowledge, the reports of SMG transplantation for severe DED have mainly only focused on the improvement of objective clinical tests [2–4,6,7,9,10]. It is essential to provide data on patients' QOL to evaluate the value of SMG transplantation for severe DED.

Previously, we developed the Chinese version of Dry Eye Related Quality of Life (CDERQOL) Scale and proved that the CDERQOL scale was a reliable and valid instrument for evaluating Chinese patients with dry eye syndrome and could be used as a measure of treatment efficacy [21]. In the current study, using the CDERQOL scale, we prospectively evaluated the QOL for patients with severe DED before and 1 year after SMG transplantation. This study aimed to evaluate whether SMG transplantation could improve the QOL for severe DED patients. Besides, we aimed to determine whether preoperative ophthalmologic and QOL measurements could predict which patients would be most satisfied with this surgery.

2. Patients and methods

2.1. Study population

This study was approved by the Institutional Review Board of the Peking University Health Science Center and was conducted in accordance with the Declaration of Helsinki guidelines for human research. All patients provided informed consent prior to participation. Between October 2013 and March 2018, consecutive patients with severe DED who were referred to our center for SMG transplantation were recruited. The diagnosis was made by an ophthalmologist using the indications including persistently pronounced symptoms of dry eye and failure of other previous ophthalmologic treatments, along with a Schirmer's test value of < 2 mm, a BUT value of < 5 s, and positive FL test during ophthalmologic evaluation [7].

2.2. Surgical procedures

SMG transplantation was performed as described previously [10]. In brief, under general anesthesia, the SMG including the facial artery, facial vein, and Wharton's duct was harvested from the submandibular triangle and then transferred to the temporal region. The facial artery and facial vein were anastomosed with the superficial temporal artery and vein, respectively. Wharton's duct was passed through a tunnel prepared subcutaneously to the upper lateral conjunctival fornix. The distal end of Wharton's duct was sutured to form an opening in the upper lateral conjunctival fold.

2.3. Data collection

QOL was evaluated using the CDERQOL, a newly developed, standardized, and validated quality-of-life questionnaire, which is also the first Chinese version dry eye-specific QOL scale [21]. It contains 45 items classified into five domains: Dry eye symptom bother (12 items), Impact on daily activities (7 items), Emotional impact (10 items), Impact on work (7 items), and Satisfaction with treatment (9 items). Each item was measured using a 5-point Likert-type scale, which ranged from "completely disagree" (1 point) to "completely agree" (5 points) [21].

Before and 1 year after surgery, patients were asked to complete the questionnaire independently. For patients with too poor vision to read, the items were read aloud by a non-related person (i.e., by someone other than the doctor or the patient's relatives). Meanwhile, the patients underwent ophthalmologic examinations including Schirmer's test, BUT, FL, and best-corrected visual acuity (BCVA).

Before the ophthalmologic examinations, the room temperature was set to 23 °C to avoid the influence of local hyperthermia and physical activity on secretion of transplanted SMGs, and patients rested without any physical activity or glandular stimulation. BCVA was tested firstly, followed by FL and BUT, and the Schirmer's test was tested at last. BCVA measurement was performed with spectacle or contact lens correction. The standard logarithmic visual acuity chart (National Standard of the People's Republic of China GB11533-2011, a tumbling E-chart) was used. Test chart background luminance was ≥ 200 cd/m^2. The measurement was conducted at a distance of 5 m from the chart, with each eye tested independently, beginning with the right eye. Patients were asked to indicate which direction each "E" was facing, starting with large rows and continuing to smaller rows until the optotypes couldn't be reliably identified any more. The reading was recorded as the decimal corresponding to the smallest row of which the patient could read more than ½ of the optotypes. If patients couldn't see any optotypes at 5 m, visual acuity was measured at 4 m, 3 m, 2 m, and 1 m and was calculated by the formula: visual acuity = 0.1 × distance/5. Schirmer's test was performed for 5 min using Whatman No. 41 paper strips (35 × 5 mm. Tianjin Jingming New Technological Development Co., Ltd) without topical anesthesia, and the length of the moistened paper strips was recorded as the Schirmer's test scores. For the FL test, a fluorescein strip was wetted with two drops of sterile unpreserved saline, which then touched the inferior palpebral conjunctiva. Patients were asked to blink three times, and the staining was evaluated using a slit lamp. The corneal surface was divided into four quadrants—upper nasal, lower nasal, upper temporal, and lower temporal. Punctate staining was recorded using a standardized grading system of 0–3 for each of the four areas, and the sum of the four quadrants was taken as the FL scores. For the BUT test, a fluorescein strip was wetted with two drops of sterile unpreserved saline before touching the inferior palpebral conjunctiva. Patients were asked to blink three times before opening their eyes. The time from opening of the eyes to the appearance of the first dry spot was measured three times using a slit lamp, and the mean value was recorded as the BUT score.

2.4. Statistical methods

The baseline characteristics of our study participants is presented separately based on gender. Then, we compared the clinical measurements and quality of life scores before and after the surgical treatment by using Wilcoxon signed ranks tests for skewed and ordinal clinical data, and paired-samples *t*-tests for normally distributed data (e.g., domain-specific QOL scores).

We also assessed the potential moderating effects of demographic characteristics, treatment history, pre-surgical clinical, and QOL status on the effectiveness of treatment. Multi-level linear regression models were used by considering domain-specific scores of the CDERQOL scale as dependent variables. The random effects model for subject-level intercepts were used to account for person-specific differences in the quality of life outcomes. Fixed effects included time variable (0 = pre-surgery, 1 = post-surgery) and a potential moderator, with further adjustment for age and sex. Interactions between time and potential moderators were tested separately to determine the moderating effects for each domain score.

Statistical analysis was performed using SPSS software version 20 (SPSS Inc., Chicago, IL, USA). Where applicable, a P value of less than 0.05 was considered statistically significant. Because we tested the QOL

Table 1
Demographic characteristics and treatment history of the study population (N = 51).

Characteristics	Gender, n (%)		χ [2] value	*P* value
	Male (n = 25)	Female (n = 26)		
Age group, years			0.017	0.895
< 30	12 (48.0)	12 (46.2)		
≥30	13 (52.0)	14 (53.8)		
Side			0.017	0.895
Left	12 (48.0)	12 (46.2)		
Right	13 (52.0)	14 (53.8)		
Treatment history				
Pharmaceutical tear substitutes	25 (100.0)	26 (100.0)	–	–
Occlusion of tear drainage	19 (76.0)	16 (61.5)	1.238	0.266
Cyclosporin eyedrops	15 (60.0)	20 (76.9)	1.695	0.193

improvements and potential moderating factors in each of the five domains separately, we applied Bonferroni correction to adjust for multiple testing in corresponding analyses, where *P* value < 0.01 (i.e., 0.05/5) was used as the significance threshold.

3. Results

3.1. Study population demographics

Fifty-six consecutive severe DED patients completed the questionnaire before surgery. The transplantation surgery failed in two patients owing to venous thrombosis, and follow-up data was missing for three patients. Therefore, a final total of 51 patients were included in the analysis. The demographic characteristics and treatment history of participants are presented in Table 1. Twenty-five patients (49%) were male, and 26 (51%) were female, with a mean age of 31 (25–40) years at enrolment. Steven–Johnson's syndrome (34 patients) was the primary etiology of dry eye, followed by acute conjunctivitis (6 patients). Etiology for 11 patients was not clear. All patients had undergone unsuccessful ophthalmologic treatments in the past: 51 cases (100%) of pharmaceutical tear substitutes, 35 (68.6%) of occlusion of tear drainage, and 35 (68.6%) of cyclosporin eyedrops. Results of chi-square tests showed that the distributions of demographics and treatment history did not differ statistically by sex (*P* > 0.05, Table 1).

3.2. Effects of surgical treatment on clinical outcomes

Ophthalmologic examinations showed significant improvements 1 year after the operation (*P* < 0.001). Median Schirmer's test values increased from a preoperative level of 0 mm–19 mm. Median BUT scores improved from 0 to 2. Median FL scores reduced from 12 to 8 (Table 2). Postoperative BCVA improved in 26 (51%) eyes and showed significant improvement over preoperative values (*P* < 0.05; Fig. 1, Table 3).

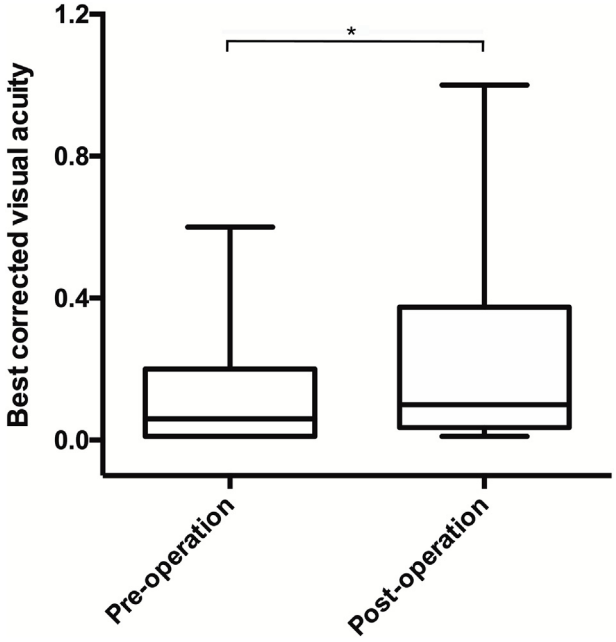

Fig. 1. Pre- and post-operative best-corrected visual acuity.
Best-corrected visual acuity improved significantly from 0.06 (interquartile range: 0.19) to 0.1 (interquartile range: 0.34). *P* = 0.0171, Mann–Whitney test. *$P < 0.05$.

Table 3
Best-corrected visual acuity comparison between pre-operation and one year after operation.

	< 0.05	0.05–0.1	0.12–0.3	0.4–0.6	0.8–1.0
	1	2	3	4	5
Pre-operation	25	9	9	8	0
Post-operation	12	15	11	9	4

Note: Wilcoxon signed ranks test was used. Z value = -4.874. *P* < 0.001.

3.3. Effects of surgical treatment on QOL

Results of paired-samples *t* tests showed that scores of all 5 QOL domains (Dry Eye Symptom Bother, Impact on Daily Activities, Emotional Impact, Impact on Work, and Satisfaction with Treatment) were significantly improved after surgical treatment (*P* < 0.001, Table 2). All observed improvements remained significant after

Table 2
Comparisons of clinical measurements and quality of life scores pre- and post-surgical treatment.

Outcomes	Pre-surgery	Post-surgery	*t* or *Z* value*	*P* value
Clinical outcomes, median (IQR)				
Schirmer's test (mm)	0 (1)	19 (15)	−6.216*	< 0.001
BUT (s)	0 (0)	2 (4)	−4.727*	< 0.001
FL	12 (2)	8 (2)	6.145*	< 0.001
Level of best-corrected visual acuity	2 (2)	2 (2)	−4.874*	< 0.001
Domains of quality of life, mean (SD)				
Dry eye symptom bother (range: 12–60)	45.3 (8.6)	25.3 (4.7)	19.027	< 0.001
Impact on daily activities (range: 7–35)	27.9 (4.3)	20.1 (4.2)	13.801	< 0.001
Emotional impact (range: 10–50)	36.5 (9.7)	24.7 (7.0)	9.388	< 0.001
Impact on work (range: 7–35)	27.4 (6.4)	19.5 (4.7)	10.641	< 0.001
Satisfaction with treatment (range: 9–45)	17.5 (1.4)	33.0 (4.7)	−22.940	< 0.001

Note: *Wilcoxon signed ranks test was used for skewed and ordinal data. IQR = interquartile range; SD = standard deviation.

Table 4
Moderating effects of demographics and treatment history on quality of life improvements.

Variables	Domains of quality of life scale, β (SE)				
	Symptom Bother	Daily Activities	Emotional Impact	Impact on Work	Satisfaction with Treatment
Age	−0.00 (0.08)	0.01 (0.05)	0.01 (0.09)	0.06 (0.06)	−0.00 (0.04)
Time	−23.85 (2.85)**	−8.05 (1.55)**	−8.07 (3.44)*	−7.57 (2.04)**	15.89 (1.87)**
Age * Time	0.12 (0.08)	0.01 (0.04)	−0.12 (0.10)	−0.01 (0.06)	−0.01 (0.05)
Male	−0.55 (1.98)	0.40 (1.22)	1.20 (2.42)	−1.55 (1.59)	0.44 (1.00)
Time	−21.04 (1.48)**	−8.38 (0.79)**	−11.19 (1.79)**	−7.58 (1.05)**	15.58 (0.96)**
Male * Time	1.96 (2.11)	1.26 (1.12)	−1.41 (2.55)	−0.62 (1.49)	−0.02 (1.37)
Occlusion of tear drainage	1.21 (2.15)	−1.74 (1.32)	−2.95 (2.62)	0.85 (1.71)	1.73 (1.07)
Time	−19.71 (1.28)**	−8.63 (0.65)**	−12.80 (1.53)**	−8.43 (0.89)**	15.97 (0.82)**
Occlusion of tear drainage * Time	1.16 (2.29)	−2.75 (1.16)*	−2.93 (2.72)	−1.74 (1.59)	1.28 (1.47)
Cyclosporin eyedrops	1.36 (2.10)	−1.65 (1.31)	−3.29 (2.61)	−0.52 (1.71)	3.18 (1.03)**
Time	−21.09 (1.26)**	−8.86 (0.63)**	−12.40 (1.54)**	−8.83 (0.87)**	16.69 (0.78)**
Cyclosporin eyedrops * Time	−3.21 (2.25)	−3.48 (1.12)**	−1.65 (2.75)	−3.02 (1.55)	3.56 (1.39)**

Note: Multi-level linear regressions were adjusted for age and gender; moderating effects were tested by adding an interaction term. β = regression coefficient; SE = standard error. *$P < 0.05$; **$P < 0.01$ (the significance level after Bonferroni correction).

Bonferroni correction.

3.4. Moderating factors for surgical treatment effects on QOL

3.4.1. Moderating effects of demographics and treatment history

Results of multi-level linear regressions indicated that age and sex did not modify the surgical treatment effects on any of the five QOL domains ($P > 0.05$, Table 4). The treatment history of "use of occlusion of tear drainage" was found to increase the treatment effects on "Dry Eye Impact on Daily Activities" ($P = 0.022$), which was not significant after Bonferroni correction. The treatment history of "use of cyclosporin eyedrops" was shown to increase the treatment effects on "Dry Eye Impact on Daily Activities" and "Satisfaction with Treatment" ($P < 0.01$, Table 4).

3.4.2. Moderating effects of pre-surgical clinical measurements

Pre-surgical low-level BCVA was shown to increase improvements in "Symptom Bother" and "Satisfaction with Treatment" after surgery ($P < 0.01$, Table 5). Pre-surgical low-level of BUT was shown to increase improvements in "Satisfaction with Treatment" after surgery ($P = 0.046$), which lost significance after Bonferroni correction; while no moderating effects were found for Schirmer's test. In contrast, pre-surgical low-score of FL was shown to increase the improvement of "Satisfaction with Treatment" after surgery ($P < 0.01$, Table 5).

3.4.3. Moderating effects of pre-surgical QOL status

Pre-surgical measurements of low-quality in all five domains were found to increase the treatment effect on all corresponding domain scores ($P < 0.01$), except for "Satisfaction with Treatment" (Table 6). Pre-surgical low-quality in "Symptom Bother," "Impact on Daily Activities," and "Impact on Work" were found to increase the score in the domain of "Satisfaction with Treatment" after surgery ($P < 0.01$) (Table 6). The results implied that the more severe (lower life quality) the patient was, the higher benefits he/she could achieve from surgical treatment.

3.5. Correlations between post-surgical clinical measurements and QOL scores

Spearman correlation analysis revealed that better post-surgical BCVA was related with higher quality in post-surgical "Dry Eye Impact on Daily Activities" ($P < 0.01$). Exploratory analysis showed that patients with post-surgical Schirmer's test score ≥25 had significantly lower treatment satisfaction than those with lower test score ($t = 4.062$, $P < 0.01$); all patients with the score ≥25 reported "agree" and "completely agree" for the item "too much tear after physical activity".

4. Discussion

Several clinical studies have provided evidence for the improvement of ophthalmologic examination results in severe DED patients after SMG transplantation [2–4,6,8–10]. However, QOL data, which are as important as objective examination results in evaluating the outcome of

Table 5
Moderating effects of pre-surgical clinical measurements on quality of life improvements.

Variables	Domains of quality of life scale, β (SE)				
	Symptom Bother	Daily Activities	Emotional Impact	Impact on Work	Satisfaction with Treatment
Schirmer's test	−0.06 (2.18)	−1.94 (1.35)	−2.08 (2.69)	2.13 (1.73)	1.15 (1.11)
Time	−19.03 (1.22)**	−7.11 (0.64)**	−10.65 (1.46)**	−7.51 (0.87)**	15.30 (0.80)**
Schirmer's test * Time	−3.83 (2.33)	−2.39 (1.23)	−4.49 (2.79)	−1.34 (1.67)	0.99 (1.53)
BUT	−2.49 (1.94)	−2.48 (1.14)*	−1.58 (2.43)	−1.94 (1.53)	−1.66 (0.99)
Time	−20.50 (1.15)**	−8.13 (0.61)**	−12.27 (1.39)**	−8.48 (0.79)**	16.15 (0.72)**
BUT * Time	1.97 (2.12)	1.70 (1.12)	1.80 (2.56)	2.75 (1.45)	−2.71 (1.32)*
FL	0.46 (0.71)	1.15 (0.43)**	1.81 (0.86)*	−0.61 (0.55)	−1.58 (0.33)**
Time	−36.84 (8.42)**	−19.26 (4.37)**	−30.51 (10.16)**	−18.82 (5.95)**	33.95 (4.98)**
FL * Time	1.50 (0.75)	1.03 (0.39)*	1.66 (0.90)	0.98 (0.53)	−1.64 (0.44)**
Best-corrected visual acuity	−5.63 (4.72)	−7.71 (2.82)**	1.69 (6.42)	−3.58 (4.06)	−9.70 (2.50)**
Time	−22.72 (1.21)**	−8.81 (0.68)**	−13.77 (1.57)**	−9.29 (0.90)**	17.10 (0.80)**
Best-corrected visual acuity * Time	17.97 (5.12)**	7.12 (2.88)*	12.86 (6.62)	9.56 (3.78)*	−10.43 (3.37)**

Note: Multi-level linear regressions were adjusted for age and gender; moderating effects were tested by adding an interaction term. β = regression coefficient; SE = standard error. *$P < 0.05$; **$P < 0.01$ (the significance level after Bonferroni correction).

Table 6
Moderating effects of pre-surgical quality of life status on domain-specific quality of life improvements.

Pre-surgical quality of life domains	Domains of quality of life scale, β (SE)				
	Symptom Bother	Daily Activities	Emotional Impact	Impact on Work	Satisfaction with Treatment
Symptom Bother	0.27 (0.05)**				0.20 (0.06)**
Time	13.16 (3.14)**				6.25 (3.45)
Symptom Bother * Time	−0.73 (0.07)**				0.21 (0.07)**
Daily Activities		0.53 (0.08)**			0.36 (0.11)**
Time		5.37 (3.23)			4.40 (4.22)
Daily Activities * Time		−0.47 (0.11)**			0.40 (0.15)**
Emotional Impact			0.33 (0.07)**		0.06 (0.05)
Time			12.74 (3.44)**		12.97 (2.66)**
Emotional Impact * Time			−0.67 (0.09)**		0.07 (0.07)
Impact on Work				0.42 (0.06)**	0.44 (0.06)**
Time				7.81 (2.37)**	3.02 (2.40)
Impact on Work * Time				−0.57 (0.08)**	0.46 (0.09)**
Satisfaction with Treatment					0.21 (0.35)
Time					29.23 (8.59)**
Satisfaction with Treatment * Time					−0.78 (0.49)

Note: Multi-level linear regressions were adjusted for age and gender; moderating effects were tested by adding an interaction term. β = regression coefficient; SE = standard error. *$P < 0.05$; **$P < 0.01$ (the significance level after Bonferroni correction).

SMG transplantation, are typically lacking in literature reports. Our results showed that the scores of all five QOL domains of included patients were significantly improved. The mean scores of “Dry Eye Symptom Bother” showed the best improvement from 45.3 to 25.3 (maximum score = 60), followed by “Impact on Daily Activities” from 27.9 to 20.1 (maximum score = 35), “Impact on Work” from 27.4 to 19.5 (maximum score = 35), and “Emotional Impact” from 36.5 to 24.7 (maximum score = 50). Meanwhile, “Satisfaction with Treatment” increased from 17.5 to 33 (maximum score = 45). To our best knowledge, this study proved for the first time that besides the objective ophthalmologic examination results, DED patients' life quality also had significant improvement after SMG transplantation.

All of the included patients had experienced ophthalmologic treatment attempts including pharmaceutical tear substitutes, occlusion of tear drainage, or cyclosporin eyedrops before the SMG transplantation. However, our study showed that the results of both the clinical examination and patients' QOL were poor after these ophthalmologic treatments. As for these refractory DED cases, SMG transplantation showed promising treatment effect and should hence be a recommended treatment option for patients with advanced DED. It should be pointed out that the mean scores of “Dry Eye Symptom Bother” that showed the best improvement, were only reduced to 25 out of 60 score points. Therefore, this surgery cannot completely reverse or cure DED and it had to be emphasized to every patient before surgery.

The indications for SMG transplantation vary in literature reports [2,9,10]. In our department, based on the patient's medical history, dry eye symptoms, previous treatment experience, and ophthalmologic examinations, we listed out detailed indications for SMG transplantation. Although all patients showed obvious improvement in some ophthalmologic examination results, especially that of the Schirmer's test, some patients were still dissatisfied with the surgery results. According to this study, patients who had experienced unsuccessful treatment of cyclosporin eyedrops had higher post-surgical QOL score improvements. Worse results of pre-surgical BCVA and all five QOL domains (except for “Satisfaction with Treatment”) were found to increase the post-operative QOL score improvements. Considering that all patients had undergone unsuccessful ophthalmologic treatments, it was not surprising that they obtained low scores in preoperative “Satisfaction with Treatment.” Hence, the scores of preoperative “Satisfaction with Treatment” were unnecessary to indicate the severity of the disease and did not show correlation with postoperative “Satisfaction with treatment.” Pre-surgical low-level of BCVA, low-quality in “Symptom Bother,” “Impact on Daily Activities,” and “Impact on Work” showed strong correlation with high post-operative QOL scores. Hence, the QOL questionnaire should also be used for pre-operative evaluation to choose eligible patients for SMG transplantation, and it should be included in the priority list when making the indications. This study implied that the more severe the DED was, the more QOL improvement the patients could have from this surgery. However, once irreversible corneal damage occurred in the most severe DED patients, the visual acuity improvement could not always be expected after SMG transplantation. Therefore, the indications for SMG transplantation should be based on a comprehensive analysis.

Pre-surgical low-level BCVA increased improvements in “Symptom Bother” and “Satisfaction with Treatment,” and FL increased the improvement of “Satisfaction with Treatment” after surgery. However, the pre-surgical Schirmer's test or BUT values showed no effect on post-operative QOL scores. Theoretically, pre-surgical ophthalmologic tests values, which reflected the severity of the disease, should show correlations with post-operative QOL scores. Nevertheless, in the present stusy, transplantation was indicated only for end-stage DED. Pre-surgical Schirmer's test and BUT values showed distributions concentrated on only two or three points (0 mm or 1 mm in Schirmer's test and 0 s, 1 s, or 2 s in BUT) and did not present enough variability to make statistical correlations with postoperative QOL scores. Besides, for the DED patients, most clinical studies fail to demonstrate significant correlation between symptoms and clinical test values [15]. This indicates that pre-surgical evaluation with only objective ophthalmologic examination is not enough for predicting the patients' QOL after SMG transplantation. Thus, combination with subjective QOL is necessary.

Regarding the correlation between post-surgical ophthalmologic evaluation and the patients' QOL after SMG transplantation, our results showed that better post-surgical BCVA was related with higher quality in post-surgical “Impact on Daily Activities”. The values of post-surgical Schirmer's test varied from 8 mm to 44 mm. The patients' QOL and satisfaction were different according to the values of Schirmer's test. Improvement of Schirmer's test from a median of 0 mm before the operation to 18 mm after, indicated that the transplanted SMG provided sufficient lubrication for the eyes and significantly improved patients' QOL and satisfaction. However, when over-secretion of transplanted SMG (Schirmer's test values ≥ 25 mm) occurred, the patients' QOL and satisfaction became lower. The patients reported “agree” and “completely agree” for the item “too much tear after physical activity.” The low osmolality of secretions from transplanted SMGs compared to natural tears may result in corneal epithelial microcystic edema in patients with epiphora [4,7]. Severe epiphora was founded to be related to decreased visual acuity in patients after SMG transplantation [7]. It would also lead to social awkwardness. Therefore, prevention of

epiphora by modified surgical modality and timely management of severe epiphora are critical for improvement of patients' QOL and satisfaction [8,22].

Dry eye was caused by Steven–Johnson's syndrome in most of the patients (34/51). However, the etiology of dry eye in many of our patients were not precise enough. There were two reasons for this problem. Firstly, the mean preoperative medical history of our patient cohort was 10.7 years. Many of the patients couldn't recall all the details of the onset of the disease now. Secondly, the educational level of the patients and the local medical services in rural and remote areas of China were in poor conditions many years ago. It is impossible to get any firsthand objective medical records of the disease now, and patients' descriptions about the onset and diagnosis of their diseases were always vague or paradoxical. To avoid misjudgement, we didn't give specific etiology of the dry eye in some of our patients. This was one of the shortcomings of this research.

5. Conclusions

This study proved that DED patients' QOL (based on Dry Eye Symptom Bother, Impact on Daily Activities, Emotional Impact, Impact on Work, and Satisfaction with Treatment) showed significant improvements after SMG transplantation. Subjective QOL questionnaire, as one part of the comprehensive system, is valuable for predicting and evaluating the treatment effect of SMG transplantation and other therapies for severe DED.

Conflicts of interest

The authors declare no conflict of interest.

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