3 = trichiasis involving more than half of the lid margin.

11. Mucocutaneous junction involvement. The severity of mucocutaneous junction involvement was scored from 0 - 3, where 0 = normal mucocutaneous junction and 1, 2, and 3 are mild-, moderate-, and severe irregularity of the mucocutaneous junction (Fig. 2). Fluorescein staining of the conjunctiva was helpful to evaluate the involvement of the mucocutaneous junction. Normal mucocutaneous junction showed the linear staining at the end of the conjunctiva, and either mild-, moderate-, or severe irregularity of this line was observed in the eyes with mucocutaneous junction involvement. In eyes where significant keratinization of the lid margin or extensive symblepharon formation made it difficult to evaluate mucocutaneous junction involvement, a score of 3 was assigned.

12. Meibomian gland involvement. The severity of meibomian gland involvement was determined clinically by the nature of the meibomian gland secretion expressed manually at the center of the upper lid, and scored from 0 - 3, where 0 = clear oily fluid expressed, 1 = yellowish-white oily fluid expressed, 2 = thick cheesy material expressed, and 3 = inability to express any fluid from the meibomian glands.

13. Punctal involvement. Punctal damage and occlusion were graded from 0 - 3, where 0 =normal patent puncta, 1 = iatrogenic punctal occlusion (e.g., punctal plugs or suture), 2 = either superior or inferior puncta occluded by scarring, and 3 = both superior and inferior puncta occluded by scarring.

Overall total score

Each eye was evaluated and graded by at least 2 trained corneal specialists. When the scores varied from one corneal specialist to another, the scores were averaged or determined after a discussion. The results were then added together to give an overall score from 0 to 39, with 39 representing the most severely affected eyes.

Visual acuity

We categorized the 138 eyes from the 73 patients according to their visual acuity. In group 1 (n=28 eyes) visual acuity was 20/20 or better, in group 2 (n=36 eyes) it was worse than 20/20 and up to and including 20/200, in group 3 (n=32 eyes) it was worse than 20/200 and up to and including 20/2000, and in group 4 (n=42 eyes) it was worse than 20/2000.

Eye complications independent of ocular surface disorders

Cataract, glaucoma, retinal diseases, or other eye diseases independent of ocular surface disorders were also evaluated and their presence, absence, or the inability to diagnosis due to ocular surface abnormality was recorded.

Statistical analysis

Spearman correlation coefficients (two-tailed) were used to evaluate whether the scores of the 13 components were correlated with logarithm of the minimum angle of resolution (LogMAR) visual acuity. The correlation between the total score and logMAR and the correlations between the subtotal scores of 3 problem categories and the total score were also evaluated. Using a logistic regression model, the scores for each of the 13 components in eyes with better visual acuity (20/200 or better; i.e., groups 1 and 2) were compared with the scores obtained for eyes with poorer visual

acuity (worse than 20/200; i.e., groups 3 and 4). The statistical model for predicting logMAR visual acuity was calculated using a linear model with stepwise variable selection (multivariable regression analysis). In multivariable regression analysis, cataract and glaucoma were graded as follows: with cataract, 1; without cataract or lens invisible, 0; with glaucoma, 1; and without glaucoma or unable to diagnosis glaucoma, 0. All statistical tests were conducted at a 5% level of significance.

RESULTS

A total of 138 eyes of 73 patients from the 3 institutions were included in this study. There were 33 males and 40 females. Their age ranged from 10 to 83 years (47.9 ± 18.5, mean ± SD). At disease onset, the patients' age ranged from 2 to 69 years (mean 28.4 ± 18.2 years), and the duration of the illness prior to seeking consultation at our centers ranged from 1 to 54 years (18.8 ± 15.5). Drugs were the most commonly associated etiologic factor in 47 patients (64.4%). Because 14 of these patients used 2 or 3 types of drugs simultaneously it was difficult to identify the drug(s) implicated in disease-onset, therefore, we considered all their drugs causative. The causative drugs were antibiotics in 21 patients, cold remedies in 18, non-steroidal anti-inflammatory drugs (NSAIDs) in 10, anticonvulsants in 6, and other in 4 patients. The precise history regarding the use of drugs was unclear in 20 patients because of the long interval between disease-onset and this study.

Corneal complications

A detailed summary of the 7 evaluated components comprising corneal complications is shown in Table 1. Among the 138 eyes examined, 114 (82.6%) manifested a total loss of POV (grade 3). Moderate to severe (grade 2 or 3) corneal SPK was present in 93 eyes (67.4%), neovascularization in 83 (60.1%), and conjunctivalization in 82 (59.4%).

Conjunctival and eyelid complications

Among the 6 evaluated components that comprise conjunctival and eyelid complications, the meibomian glands were most frequently and most severely involved; 102 of the 138 eyes (73.9%) manifested grade 3 meibomian gland involvement (Table 2). The scores for punctal damage and mucocutaneous involvement were also high; grade 2 or 3 punctal damage was assigned to 93 eyes (67.4%), and grade 2 or 3 mucocutaneous involvement to 71 eyes (51.4%).

Eye complications independent of ocular surface disorders

Cataract was observed in 11 eyes out of 138 eyes. Glaucoma was diagnosed in 4 eyes, none of which had central loss of visual fields. There were no other eye complications independent of ocular surface disorders.

Visual acuity

The number of eyes in each of the 4 groups was fairly evenly distributed (Table 3). Of the 138 eyes examined, 74 (53.6%) had visual acuity worse than 20/200 (group 3, n=32; group 4, n=42). Only 28 eyes (20.3%) had visual acuity equal to or better than 20/20.

Correlation between visual acuity and grade of complications

When we compared eyes with better (20/200 or better) and worse (worse than 20/200) visual acuity with respect to the scores obtained for each of the 13 components, we found that with the exception of epithelial defect, the scores differed significantly (Table 4).

We estimated the correlation coefficient between the visual acuity of the 138 eyes and the severity grade, scored from 0 - 3, of each of the 13 evaluated components in the 3 categories of complications. We found that all 13 components were significantly correlated with logMAR; the correlation coefficient (R) ranged from 0.359 to 0.810 ($p<0.0001$); for corneal epithelial defects R was 0.169 ($p=0.0473$) (Table 5). Of all the scores, corneal neovascularization, opacification, and conjunctivalization were most highly correlated with poor vision ($R= 0.810$, $p<0.0001$; $R= 0.784$, $p<0.0001$; and $R= 0.726$, $p<0.0001$, respectively).

The statistical model for predicting logMAR was calculated using a linear model with stepwise variable selection as follows: logMAR = -0.2573 + cataract* 0.4153 + POV* 0.2814 + SPK* 0.08551 + epithelial defect* 0.3018 + neovascularization* 0.3471 + opacification* 0.3202 + keratinization* 0.1347. This multivariable regression analysis showed that corneal neovascularization, opacification, keratinization, and cataract had a significant effect on logMAR (Table 6). The predicted logMAR was significantly correlated with the actual logMAR visual acuity measured ($R=0.960$, $p<0.0001$).

Overall total score

The mean overall total score for the 13 components was 19.3 ± 9.5 (range 0 to 35). As shown in Tables 3 and 4 and Fig. 2, eyes with a higher total score had poorer vision. The averaged scores for the 4 visual acuity groups were: group 1, 5.86 (range 0-19), group 2, 16.64 (range 2-28), group 3, 23.31 (range 15-33), and group 4, 27.45 (range 18-35). Pearson's analysis clearly demonstrated that the total score was significantly correlated with logMAR visual acuity ($R=0.806$, $p<0.0001$) (Fig. 3). The subtotal scores of 3 problem categories correlated with the overall total score (Fig. 4).

DISCUSSION

Severe ocular surface disease arising from SJS or TEN is associated with significant visual morbidity.[1-4] The evaluation of ocular complications in these patients is extremely important as ocular involvement often represents the only long-term complication of SJS. There is currently no established method for evaluating the spectrum of ocular manifestations arising from these diseases. In this study, we detailed the characteristic ocular complications in the chronic stage of SJS, and developed a grading system to assess more objectively the extent and severity of 13 components of these ocular complications. To the best of our knowledge, this is the first study that specifically attempted to improve and standardize the evaluation of ocular complications in SJS.

As we set out to develop a grading system that could be used easily by ophthalmologists, we identified complications that were important and could be easily evaluated by simple slit lamp examination. After several pilot studies, we eventually settled on 13 components of 3 categories of complications that we considered important for the assessment of severe or cicatricial ocular surface disorders. We used a simple

method for grading the severity of these complications, the components were assigned scores that reflected whether involvement was mild, moderate, or severe. This grading system was judged easy and convenient at the 3 participating ophthalmology centers that evaluated 138 eyes from 73 SJS patients. The results obtained at the 3 centers were consistent and comparable. Ours is one of few prospective studies on the ocular complications of SJS, and each patient was carefully evaluated by at least 2 ophthalmologists. To the best of our knowledge, this is the largest study reported to date.

The initial ocular pathologic process in SJS, inflammation and necrosis of the conjunctiva, is often accompanied by the destruction of goblet cells.[4,13,14] The production of mucin by these cells is vital for maintaining an adequate tear film essential for corneal clarity. Dry eye secondary to goblet cell destruction is the most common long-term ocular complication in patients with various ocular surface diseases.[4,13,14] Cicatricial lid- and conjunctival complications include symblepharon formation, forniceal shortening, keratinization, lid malposition (e.g., entropion), and misdirected eyelashes (trichiasis).[4,13,15-22] Limbal stem cell destruction, evidenced by loss of the POV, may also occur at disease onset and be accompanied by severe inflammation. The combination of these complications may result in recurrent corneal erosion, ulceration, vascularization, stromal scarring, conjunctivalization of the corneal surface, and progressive corneal melting and perforation.[4,13,15-22]

In our study, drugs were the most commonly identified etiologic factor; in 47 patients (64.4%) antibiotics (n=21 patients) cold remedies (n=18 patients), or NSAIDs (n=10) were the causative agents. These findings are consistent with previous reports.[15,16,19,23]

Of all the complications, severe (grade 3) meibomian gland involvement and loss of the POV (102 and 114 eyes, respectively) were the most common ocular complications of SJS. We found that the total score for each eye was significantly correlated with its visual acuity; consistently, eyes with higher overall scores had poorer vision. We categorized the complications as those involving predominantly the cornea, the conjunctiva, and the eyelid. As expected, corneal complications were most likely to have a detrimental effect on vision. In particular, corneal neovascularization and opacification were highly correlated with post-treatment visual acuity in the chronic stage. Conjunctivalization, a sequela of limbal stem cell deficiency, was also correlated with poor vision in our series.

In our study, there was a high rate of lid complications in chronic SJS. Of the eyelid complications, meibomian gland involvement was moderate or severe (grade 2 or 3) in 111 of the 138 eyes (80.4%). We found that eyes without apparent corneal complications also manifested cicatricial eyelid changes. As such, the meibomian glands appear to be susceptible to the injury following SJS. As the meibomian glands play a critical role in the stabilisation of the tear film, this is likely to contribute to the disruption of the tear film and severe dry eye condition experienced in patients in the chronic stage of SJS.

The use of a standardized method for grading the extent and severity of ocular complications in SJS patients offers significant advantages. The grading system introduced here can be used in the initial evaluation and the follow-up and monitoring of ocular complications in SJS patients. As documented here, the lid margin is a commonly affected site in the disease process. However, because attention often focuses

on the ocular surface, changes in the lid margin may be overlooked. Our grading system ensures that important ocular complications are detected by corneal specialists as well as non-specialized ophthalmologists.

Ocular surface reconstructive procedures such as limbal- and cultivated epithelial stem cell transplantation have been used to treat severe ocular manifestations in SJS patients.[8-11,24] However, as many of the reported studies are non-randomized case series without control arms and as there is currently no standardized method for grading ocular complications in SJS patients in the acute and chronic stage, it is difficult to compare the treatment outcomes of these studies. Our grading system also provides a standardized method for evaluating patients prior to corneal and ocular surface transplantation procedures. The use of an objective method of grading the severity of the patient's preoperative condition may ultimately help in prognosticating the long-term clinical outcome of these eyes following surgery.

This is the first study that describes a method for classifying and grading the severity of ocular involvement in SJS patients. Our findings have important clinical implications and facilitate the objective evaluation of patients with ocular complications from of SJS. The method presented here may be adapted for use in patients with cicatricial ocular surface diseases arising from other causes such as ocular cicatricial pemphigoid and chemical injury. It also provides a common platform for the discussion and management of patients with ocular surface disorders and may be useful for predicting treatment outcomes. Our method also enables ophthalmologists to monitor more objectively the progression of complications during the follow-up of these patients.

Table 1. Summary of corneal complications

Complications	Grade 0	Grade 1	Grade 2	Grade 3
	No. (%)	No. (%)	No. (%)	No. (%)
Superficial punctuate keratopathy (SPK)	22(15.9)	23(16.7)	18(13.0)	75(54.3)
Epithelial defect	135(97.8)	2(1.4)	1(0.7)	0(0)
The loss of palisades of Vogt (POV)	21(15.2)	3(2.1)	0(0)	114(82.6)
Conjunctivalization	41(29.7)	15(10.9)	10(7.2)	72(52.2)
Neovascularization	35(25.4)	20(14.5)	22(15.9)	61(44.2)
Opacification	43(31.2)	41(29.7)	28(20.3)	26(18.8)
Keratinization	105(76.1)	10(7.2)	5(3.6)	18(13.0)

N=138

Table 2. Summary of conjunctival and eyelid complications

Complications	Grade 0	Grade 1	Grade 2	Grade 3
	No. (%)	No. (%)	No. (%)	No. (%)
Conjunctival complications				
Hyperemia	46(33.3)	61(44.2)	15(10.9)	16(11.6)
Symblepharon formation	40(29.0)	54(39.1)	21(15.2)	23(16.7)
Eyelid complications				
Trichiasis	42(30.4)	41(29.7)	44(31.9)	11(8.0)
Mucocutaneous junction involvement	16(11.6)	51(37.0)	34(24.6)	37(26.8)
Meibomian gland involvement	13(9.4)	14(10.1)	9(6.5)	102(73.9)
Punctal damage	36(26.1)	9(6.5)	15(10.9)	78(56.5)

N=138

Table 3. Ocular complications and visual acuity of SJS patients

	Visual acuity			
Complications	Group 1 VA equal or better than 20/20 Average grade	Group 2 VA 20/20 to 20/200 Average grade	Group 3 VA 20/200 to 20/2000 Average grade	Group 4 VA worse than 20/2000 Average grade
No. of eyes	28	36	32	42
Corneal complications				
SPK	0.82	1.92	2.40	2.78
Epithelial defect	0	0	0.03	0.07
The loss of POV	0.82	2.78	3.00	3.00
Conjunctivalization	0.11	1.36	2.59	2.76
Neovascularization	0.25	1.11	2.38	2.90
Opacification	0.11	0.61	1.66	2.31
Keratinization	0.04	0.11	0.50	1.26
Conjunctival complications				
Hyperemia	0.36	0.89	1.19	1.40
Symblepharon formation	0.18	0.97	1.19	2.07
Eyelid complications				
Trichiasis	0.57	1.08	1.38	1.50
Mucocutaneous junction involvement	0.79	1.56	1.91	2.10
Meibomian gland involvement	1.32	2.50	2.69	2.90
Punctal damage	0.50	1.78	2.65	2.58
Total score	5.86	16.64	23.31	27.45

Table 4. Comparison between ocular complications and visual acuity

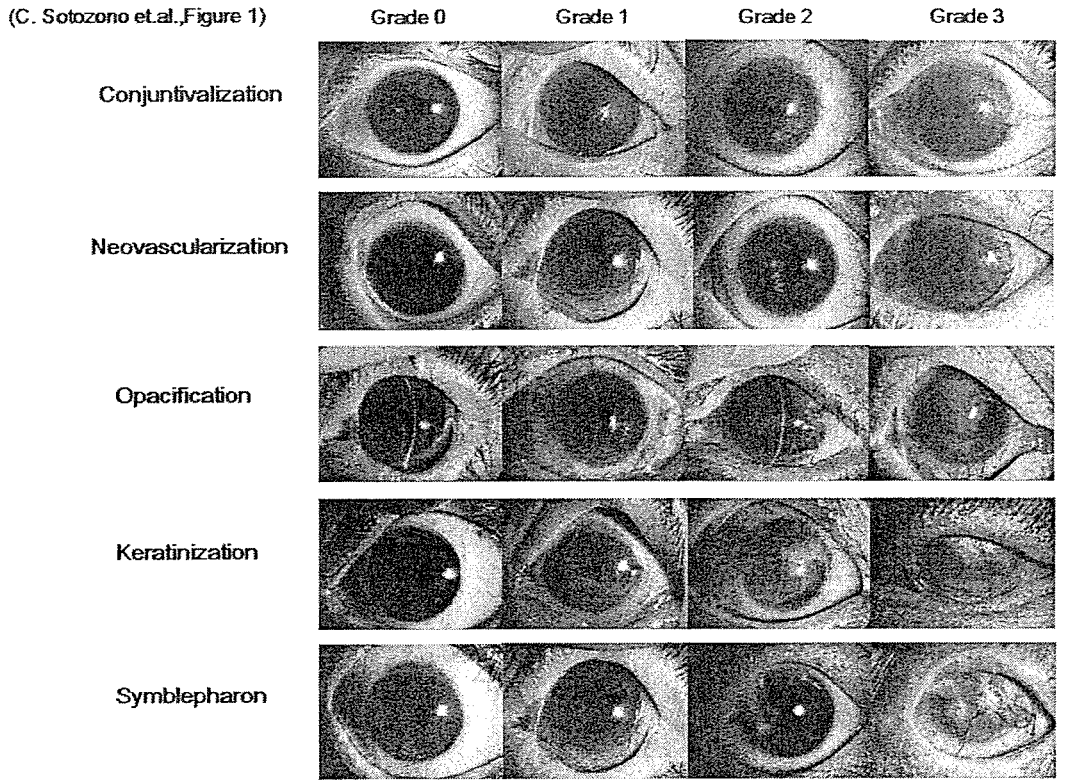
Complications	VA of 20/200 or better - average grade	VA worse than 20/200 - average grade	P value
No. of eyes	64	74	
Corneal complications			
SPK	1.44	2.62	<0.0001
Epithelial defect	0	0.05	0.1208
The loss of POV	1.92	3.00	<0.0001
Conjunctivalization	0.81	2.69	<0.0001
Neovascularization	0.73	2.68	<0.0001
Opacification	0.39	2.03	<0.0001
Keratinization	0.08	0.93	<0.0001
Conjunctival complications			
Hyperemia	0.66	1.31	<0.0001
Symblepharon formation	0.63	1.69	<0.0001
Eyelid complications			
Trichiasis	0.86	1.45	0.0002
Mucocutaneous junction involvement	1.23	2.01	<0.0001
Meibomian gland involvement	2.02	2.81	<0.0001
Punctal damage	1.26	2.61	<0.0001
Total score	11.86	25.66	

Table 5. Correlation analyses between 13 complications and logMAR visual acuity

Complications	Coefficient	P value
Neovascularization	0.810	<0.0001
Opacification	0.784	<0.0001
Conjunctivalization	0.726	<0.0001
Symblepharon formation	0.649	<0.0001
SPK	0.601	<0.0001
The loss of POV	0.550	<0.0001
Punctal damage	0.518	<0.0001
Mucocutaneous junction involvement	0.488	<0.0001
Keratinization	0.477	<0.0001
Meibomian gland involvement	0.453	<0.0001
Hyperemia	0.383	<0.0001
Trichiasis	0.359	<0.0001
Epithelial defect	0.169	0.0473

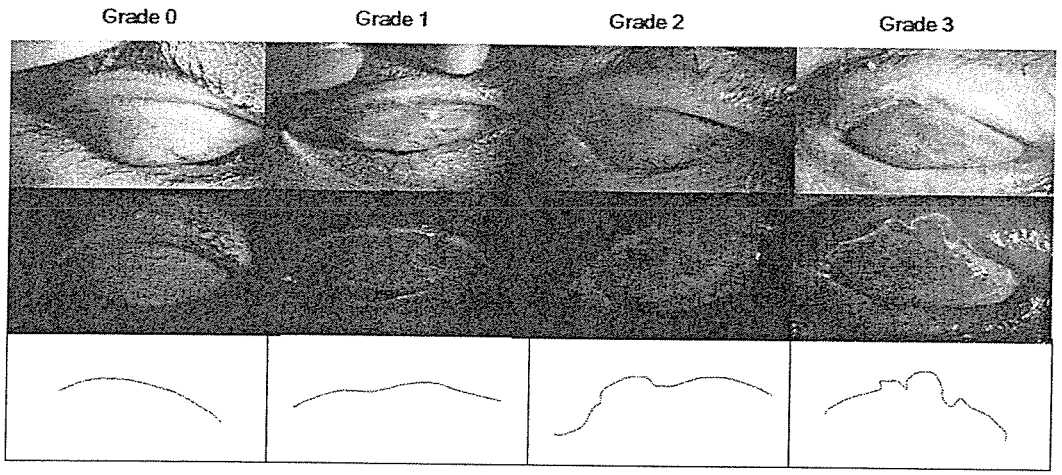
Table 6. Multivariable regression analysis

Variables	Coefficient	95% Confidence Intervals	P values
Intercept	-0.2573	-0.5449-0.0303	0.0786
Neovascularization	0.3471	0.2113-0.4849	<.0001
Opacification	0.3203	0.1734-0.4672	<.0001
Keratinization	0.1347	0.0281-0.2413	0.0142
Cataract	0.4153	0.0249-0.8057	0.0375
The loss of POV	0.2814	-0.0784-0.6412	0.1228
SPK	0.0855	-0.0296-0.2006	0.1423
Epithelial defect	0.3018	-0.1057-0.7093	0.1434

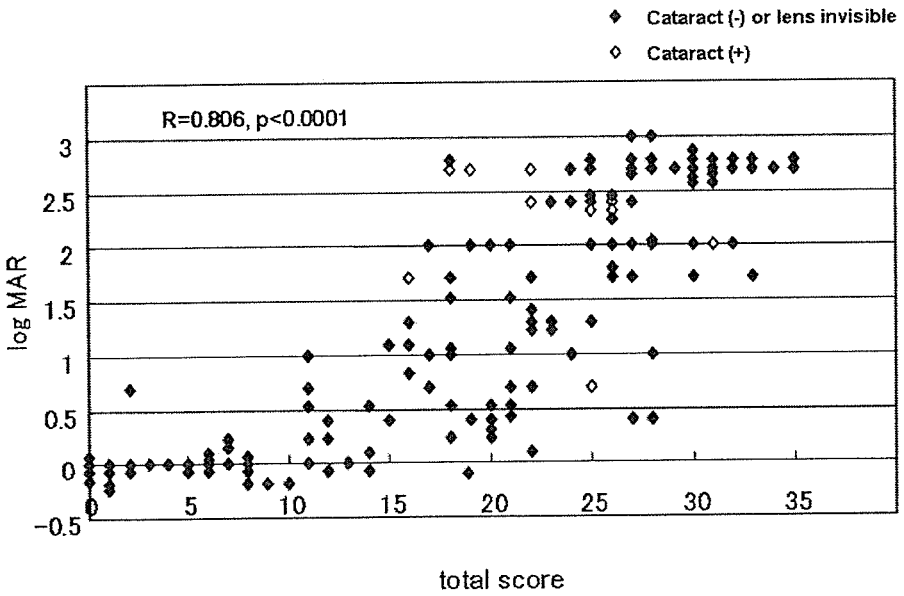

(C. Sotozono et.al.,Figure 1)
Grade 0
Grade 1
Grade 2
Grade 3
Conjuntivalization
Neovascularization
Opacification
Keratinization
Symblepharon

A new way to grade ocular manifestations in Stevens-Johnson syndrome

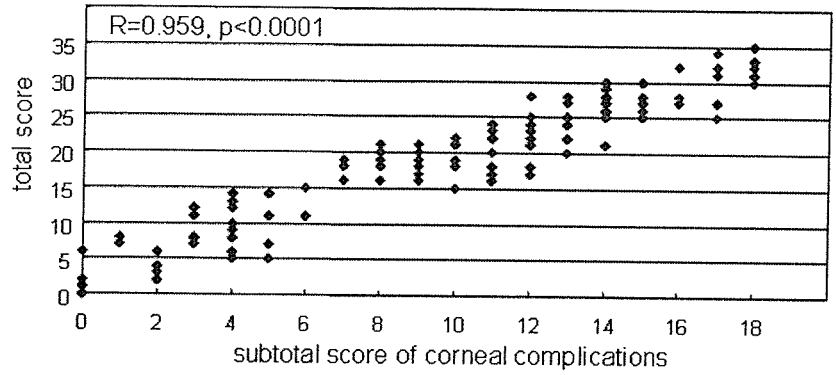
(C. Sotozono et.al.,Figure 2)

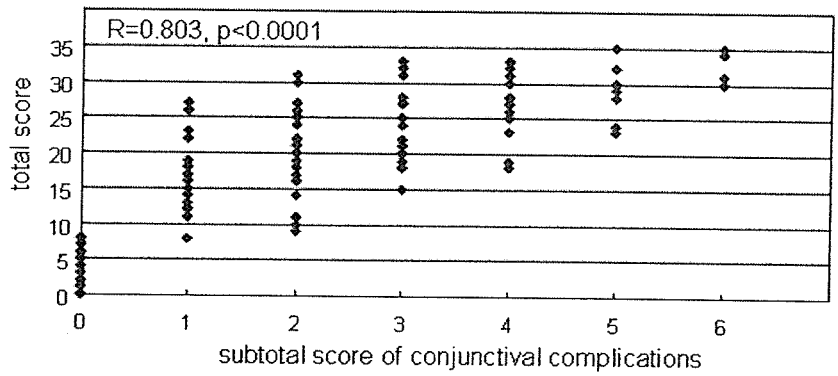


(C. Sotozono et.al.,Figure 3)



(C. Sotozono et.al.,Figure 4)





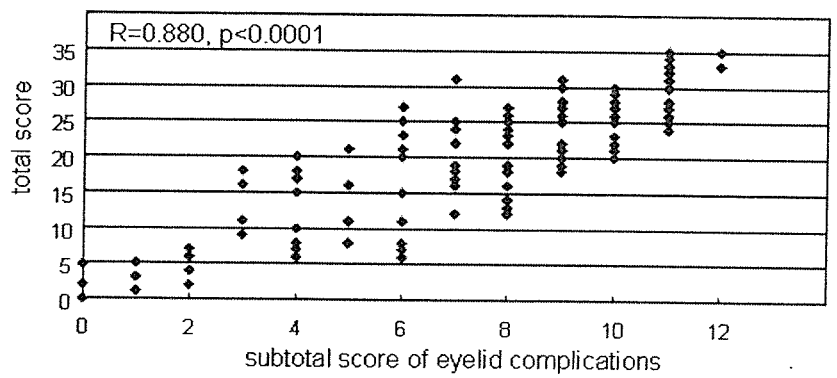


Figure Legends

Figure 1. Grading scores of corneal and conjunctival complications

Figure 2. Grading scores of mucocutaneous junction involvement
A score of grade 1 was assigned for normal mucocutaneous junction, and grades 1, 2, and 3 for mild-, moderate-, and severe irregularity of the mucocutaneous junction, respectively (upper). Fluorescein staining of the conjunctiva was helpful to evaluate the severity of the involvement of mucocutaneous junction (middle and lower).

Figure 3. Correlation between the total score and logMAR visual acuity
The overall total score of 13 components (0-39) versus logMAR showed a significant positive correlation (Spearman, $R=0.806$, $P<0.0001$).

Figure 4. Correlations between subtotal score of 3 categories and overall total score
Subtotal scores of corneal, conjunctival, and eyelid complications versus the total score all showed a significant positive correlation (Spearman, $R=0.959$, $P<0.0001$, $R=0.803$, $P<0.0001$, $R=0.880$, $P<0.0001$, respectively).

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Midterm Results on Ocular Surface Reconstruction Using Cultivated Autologous Oral Mucosal Epithelial Transplantation

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• PURPOSE: To perform a midterm assessment of the integrity and reproducibility of cultivated autologous oral mucosal epithelial sheets, and to evaluate the clinical efficacy of their transplantation in ocular surface.

• DESIGN: Observational case series.

• METHODS: Cultivated autologous oral mucosal epithelial sheets were created using amniotic membrane and buccal mucosal epithelium from 12 patients with Stevens-Johnson syndrome, chemical and thermal injury, pseudo-ocular cicatricial pemphigoid, and idiopathic ocular surface disorder. They were transplanted onto 15 eyes from these patients who were then followed up for a mean of 20 months; with the longest follow-up being 34 months. We assessed their clinical outcomes with special reference to neovascularization.

• RESULTS: Cultivated autologous oral mucosal epithelial sheets could be generated from all patients. On the second postoperative day, 14 of 15 sheets transplanted demonstrated total re-epithelialization on the cornea. During the follow-up, the ocular surface was stable and transparent without any major complications in 10 of 15 eyes (67%), and the transplanted epithelium survived for at least 34 months. There were five eyes (33%) with small but long-standing epithelial defects, three of these healed spontaneously, and two (13%) required reoperation. In 10 eyes, postoperative visual acuity was improved by more than 2 lines. All eyes manifested some peripheral corneal vascularization.

• CONCLUSIONS: We established a successful tissue-engineering technique to generate cultivated autologous oral mucosal epithelial sheets and succeeded in reconstructing the ocular surface. We suggest that this surgical modality may be both safe and useful, especially in younger patients with the most severe ocular surface disorders. (Am J Ophthalmol 2006;141:267–275. © 2006 by Elsevier Inc. All rights reserved.)

See accompanying Editorial on page 356.

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THE COMPLETE LOSS OF CORNEAL EPITHELIAL STEM cells attributable to acute or chronic ocular surface disorders leads to limbal deficiency that results in the conjunctivalization of the corneal surface, that is, conjunctival epithelial invasion with superficial vascularization and subepithelial scarring. Various degrees of pathologic keratinization, symblepharon, and entropion also occur, resulting in serious visual loss. Surgical approaches to ocular surface diseases such as Stevens-Johnson syndrome (SJS), ocular cicatricial pemphigoid, and chemical injury include limbal transplantation[1] and amniotic membrane (AM) transplantation.[2] These approaches were both developed in the 1990s and have produced some positive therapeutic results.

The more recently developed and improved surgical modality that uses cultivated corneal epithelial stem cell sheets has already been implemented widely.[3–7] The primary concept and cultivation technique for epithelium is an extension of the method first introduced in the 1970s by Rheinwald and Green[8] that employed tissue-engineered epidermal sheets to treat thermal skin injuries.

Despite a number of failures, in part attributable to a lack of knowledge regarding stem cells, in 1997 Pellegrini and associates[9] successfully restored damaged human corneal surfaces by transplanting autologous cultivated corneal epithelium. Subsequently, patients with unilateral damage received transplants of cultivated corneal epithelial stem cells obtained from the healthy contralateral eye. This has become an established, successful approach.[3,10,11] Patients with bilateral eye damage required the transplantation of cultivated corneal epithelial stem cells from

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TABLE 1. Baseline Data of Patients Receiving an Oral Mucosal Epithelial Culture Reconstruction

Case	Age/Gender	Disease	Condition of Oral Cavity	Feeder Cell Condition	Culture Serum	Density of Cell Seeding (Cell/Well)	Days Reach Confluence	Integrity of Culture Sheet
1	33/M	Chemical	Good	Good	FBS	1.0×10^5	5	Excellent
2	33/M	Chemical	Good	Good	FBS	1.0×10^5	5	Excellent
3	27/M	Chemical	Good	Good	FBS	1.0×10^5	6	Excellent
4	24/M	SJS	Moderate	Good	FBS	0.9×10^5	6	Excellent
5	14/F	SJS	Moderate	Good	FBS	0.7×10^5	6	Excellent
6	24/M	SJS	Moderate	Good	FBS	1.1×10^5	8	Excellent
7	65/F	SJS	Moderate	Good	FBS	0.7×10^5	6	Fair
8	61/F	OSD	Good	Moderate	FBS	1.0×10^5	7	Excellent
9	69/M	Chemical	Good	Good	FBS	1.0×10^5	6	Excellent
10	65/F	SJS	Moderate	Good	AS	1.5×10^5	7	Excellent
11	70/M	SJS	Moderate	Good	AS	1.3×10^5	6	Excellent
12	67/F	SJS	Moderate	Good	AS	1.5×10^5	6	Excellent
13	29/M	Thermal	Moderate	Good	AS	1.0×10^5	5	Excellent
14	81/F	pOCP	Good	Good	AS	1.5×10^5	6	Excellent
15	64/M	Chemical	Moderate	Good	AS	1.5×10^5	7	Excellent

AS = autologous serum; Chemical = chemical injury; FBS = fetal bovine serum; OSD = idiopathic ocular surface disorder; pOCP = pseudo-ocular cicatricial pemphigoid; SJS = Stevens-Johnson syndrome; Thermal = thermal injury.

cadaver donors or a living-related eye. While this method also yielded some success,[4,12] immunologic rejection and microbial infection as a result of immunosuppressive therapy after allogeneic transplantation continue to present challenges.

In the context of regenerative medicine, the transplantation of cultivated mucosal epithelial stem cell sheets created from autologous cell sources presents a viable alternative in cases with bilateral eye damage that vitiates the use of autologous corneal epithelial stem cells. Oral mucosal epithelium has attracted attention as a cell source, and favorable results have been obtained in animal- and preliminary human pilot studies.[13–16]

Here we present midterm clinical data on 15 eyes grafted with cultivated autologous oral mucosal epithelial transplants. The corneal surface in 13 of our 15 eyes was stable and remained fairly transparent despite some peripheral corneal neovascularization.

METHODS

THIS STUDY WAS APPROVED BY THE INSTITUTIONAL REview Board for Human Studies of Kyoto Prefectural University of Medicine; prior informed consent was obtained from all patients. We report on 15 eyes from 12 patients with bilateral total limbal deficiency; their ages ranged from 14 to 81 years. The preoperative diagnosis was SJS in five patients, chemical injury in four, and thermal injury, pseudo-ocular cicatricial pemphigoid, and idiopathic ocular surface disorder of unknown etiology in one patient each. Preoperatively, all 15 eyes manifested severe destruction of the ocular surface with limbal deficiency, but also reasonable reflex tearing with some meniscus height.

The 12 patients presented displayed total limbal deficiency in either the acute or chronic phase. This was diagnosed by the complete absence of the palisades of Vogt. The four eyes in the acute phase had sustained chemical (n = 3) or thermal injury (n = 1) and manifested persistent epithelial defects involving the entire cornea, complete limbal deficiency, and sustained conjunctival inflammation. The injury to these four eyes was of grade IIIb or IV according to the grading system we proposed elsewhere.[17] The 11 eyes in the chronic phase included seven with SJS, two with chemical injuries, and one each with pseudo-ocular cicatricial pemphigoid and idiopathic ocular surface disorder. All 11 eyes manifested total conjunctivalization on the cornea with conjunctival cicatrization. Of the 15 eyes, seven had received previous treatment consisting of AM transplantation alone (n = 2), limbal transplantation with AM transplantation (n = 1), keratoepithelioplasty with AM transplantation (n = 1), and penetrating keratoplasty (n = 1); both eyes in one patient had been grafted with cultivated allogeneic corneal epithelial sheets in the acute phase. The mean follow-up period in our midterm study was 20 months; the longest follow-up was 34 months.

• PROCEDURE FOR THE TISSUE-ENGINEERING OF AUTOLOGOUS ORAL MUCOSAL EPITHELIAL SHEETS: After obtaining informed consent in accordance with the tenets of the Declaration of Helsinki for research involving human subjects, we harvested human AM at the time of elective Cesarean section. Under sterile conditions, the membranes were deprived of their amniotic epithelium by