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Article

Efficacy of Strip Meniscometry for Detecting Lacrimal Obstructive Diseases Among Patients With Epiphora

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Purpose: Strip meniscometry (SM) is a new technique for evaluating tear film volume. The aim of the present study was to evaluate the efficacy of SM in detecting lacrimal obstructive diseases (LODs) in patients with epiphora retrospectively.

Methods: One-hundred sixty-six patients (53 men, 113 women; mean age: 72.4 ± 8.0 years) who were referred to Saitama Medical University Hospital with epiphora as their chief complaint were enrolled; finally, 72 patients with and 89 patients without LOD were examined. We assessed tear volume using SM, tear meniscus height (TMH), tear meniscus area (TMA), and Schirmer-1 test values. Patients with LOD underwent lacrimal intubation surgery to treat their epiphora; their SM scores were assessed before and 8 weeks after surgery.

Results: SM, TMH, TMA, and Schirmer-1 values were significantly higher in the LOD group (10.80 ± 3.63 mm, 0.49 ± 0.24 mm, 0.06 ± 0.06 mm^2, 18.46 ± 8.00 mm, respectively) than in the non-LOD group (5.44 ± 3.20 mm, 0.30 ± 0.18 mm, 0.03 ± 0.04 mm^2, 11.84 ± 7.16 mm). The area under the receiver operating characteristic curve (AUC) for SM was 0.88, the sensitivity and specificity were 82% and 84%. The AUC was significantly larger for SM than for the Schirmer-1 test and TMA. The SM scores significantly improved after surgery (5.30 ± 2.20 mm) compared with those before (10.69 ± 3.20 mm).

Conclusions: SM was significantly better than the Schirmer-1 test, TMH, and TMA for detecting LOD and evaluating the effect of lacrimal surgery.

Translational Relevance: SM, widely used for dry eye, is also useful for using epiphora.

Introduction

Epiphora is one of the commonest complaints of patients visiting the ophthalmology outpatient clinic. The causes of epiphora include ocular surface disorders, such as dry eye, infectious and noninfectious inflammation, anatomic anomalies in eyelid structure, and/or obstruction of the tear outflow tract. Although epiphora is not a vision-threatening disorder, it can negatively affect the patients' quality of life.[1] In particular, it causes discomfort and interferes with daily activities, such as reading, driving, working on a computer, and watching television.[2] Therefore, the effective management of epiphora can markedly improve the patients' quality of life. However, few studies have investigated the causes of epiphora, probably because it is a complex condition that can have multiple causes, and patients may have a history of eye drop treatment for other diseases. Furthermore, epiphora examinations can only be performed by a specialist. In essence, epiphora is an imbalance between the production and drainage of tears through the lacrimal drainage pathway.

To determine whether a patient has lacrimal obstructive disease (LOD), the tear volume and tear meniscus on the conjunctival sac must be measured. The tear meniscus can be measured using optical coherence tomography (OCT).[3] In this regard, tear meniscus height (TMH) and tear meniscus area (TMA) are greater in patients with LOD than in individuals without LOD,[4] and both parameters improve following lacrimal surgery.[5] One study that

compared healthy subjects and epiphora patients revealed that the sensitivity and specificity of TMH are 92% and 96%, respectively, whereas those of TMA are 97% and 99%, respectively.[5]

The fluorescein disappearance test (FDT) can be used to distinguish between epiphora patients with LOD and individuals without LOD. We previously reported that the sensitivity of FDT in detecting lacrimal obstruction was 100%, and that its specificity was 91%.[6] However, although FDT is simple and effective, it cannot quantitatively measure tear volume.

Strip meniscometry (SM), which was introduced by Dogru et al.,[7] is a new technique for evaluating tear film volume; it uses meniscometry strips designed to absorb the tear meniscus without touching the conjunctiva. The polyethylene terephthalate SM strip has a central ditch composed of a urethane-based material and contains a natural blue dye.[7] When the strip is applied to the lateral, lower-lid tear meniscus for 5 seconds, tears are absorbed toward the central ditch, which is then stained. The SM score is thus determined by the length of the stained tear column. As such, SM is a semiquantitative assessment and therefore an improvement over qualitative measurements provided by FDT. However, although the efficacy of SM has been reported in patients with dry eye,[8] it has not been reported in patients with epiphora.

In the present study, we prospectively investigated the efficacy of SM in detecting LOD among patients with epiphora.

Methods

This retrospective study was approved by the ethics committee of Saitama Medical University Hospital (19008.01) and was conducted according to the Declaration of Helsinki. The need for informed consent was waived by the ethical committee because the study had a retrospective design.

We enrolled 166 patients (53 men, 113 women) who were referred to Saitama Medical University Hospital between October 2017 and November 2018 with lacrimation as the chief complaint. All patients with a history of wearing contact lenses, previous lacrimal surgery, eyelid trauma, ectropion, entropion, exotropia, or esotropia were excluded.

In all subjects, we first assessed tear volume using anterior-segment OCT. To this end, we used the CASIA2 (TOMEY, Nagoya, Japan), which is currently the newest commercially available swept-source OCT system. The TMH was manually measured from the cornea–meniscus junction to the lower eyelid–meniscus junction along the vertical line from the apex of the cornea. TMA was measured as the area of tears surrounding the cornea and lower eyelids along the line of TMH. Anterior swept-source OCT was performed under natural blink conditions (Fig. 1). Next, the Schirmer-1 test was performed without topical anesthesia. After 30 or more minutes, we performed SM using SMTube (Echo Electricity Fukushima, Japan). The SM strip was applied to the lateral lower-lid tear meniscus for 5 seconds without touching the ocular surface (Fig. 1).

Thereafter, all patients underwent a complete ophthalmologic examination, including slit-lamp examination and dry eye testing. We assessed lid position anomalies, eyelash anomalies, blepharitis, allergic conjunctivitis, infectious conjunctivitis, conjunctivochalasis, facial palsy, and punctal stenosis or obstruction in all patients. Conjunctivochalasis was graded as follows: grade 0, no fold; grade 1, single, small fold; grade 2, more than two folds, not higher than the tear meniscus; and grade 3, multiple folds, higher than the tear meniscus.[2] Only eyes of grade 2 or 3 were regarded as having conjunctivochalasis.

Subsequently, the lacrimal pathway was washed to determine whether it was obstructed. To this end, we used a 23-G, single-size, Nakamura's lacrimal washing needle (Inami, Tokyo, Japan) filled with saline. We checked whether there was resistance to passage of the lacrimal cannula and there was reflux of fluid from the same or opposite punctum. A patient was diagnosed with non-LOD when the saline reached their nasal cavity with no resistance and there was no reflux of fluid. When there was reflex of fluid or saline did not reach the nasal cavity, we probed the lacrimal pathway. If there were soft stops in the canaliculus, we diagnosed LOD. In cases where LOD was difficult to distinguish, Jones dye testing was also used.[9] One drop of 1% fluorescein solution is instilled in the conjunctival sac. A small cotton was introduced into the meatus of the nose at intervals from 1 to 5 minutes. If the cotton came out stained with the dye, it was not LOD. Next, we syringed lacrimal pathway with saline. If the cotton was stained with dye, we diagnosed functional LOD. When the cotton was not stained, we diagnosed LOD. In LOD patients, we detected the obstructive location of lacrimal pathway using the lacrimal endoscope (Fibertech, Chiba, Japan). All ophthalmologic examinations, irrigation tests, and Jones dye tests were performed by the same examiner (SI).

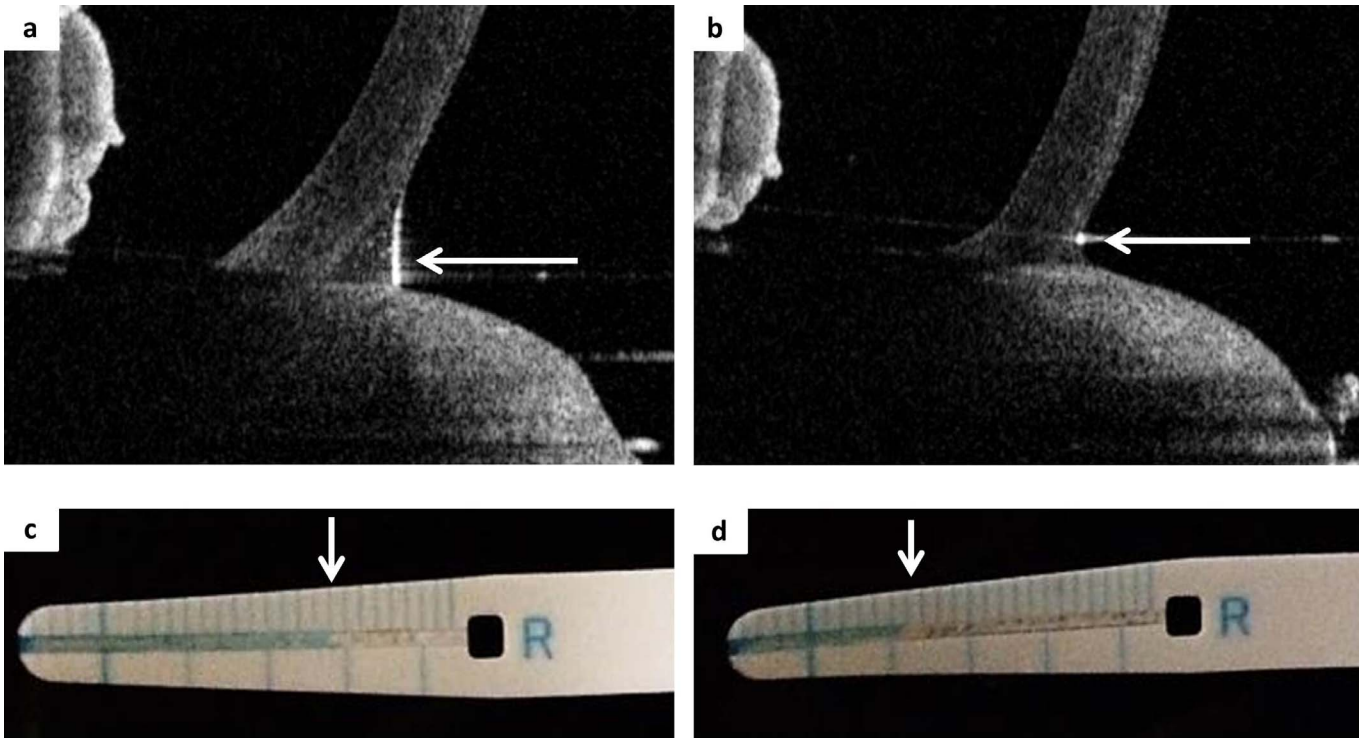

Figure 1. Representative results of a 70-year-old woman with right nasolacrimal obstructive disease. (a) Anterior-segment OCT image showing the tear meniscus (*white arrow*) preoperatively. (b) Postoperative anterior segment OCT image. (c) Tear meniscus improved (*white arrow*). Preoperative SM tube result. The SM value of the right eye was 19 mm. (d) The SM value of the right eye improved to 11 mm after surgery.

The severity of epiphora symptoms was scored as follows: Munk score 0, no eye watering; Munk score 1, occasional watering requiring dabbing less than twice a day; Munk score 2, watering requiring dabbing two to four times a day; Munk score 3, watering requiring dabbing five to 10 times a day; and Munk score 4, watering requiring dabbing more than 10 times a day, or constant watering.[10]

In all patients with LOD who underwent lacrimal surgery, we pierced the obstructed site using a lacrimal endoscope (Fibertech, Chiba, Japan) and intubated the lacrimal pathway. To this end, we used LACRIFAST (Kaneka Medical Products, Osaka, Japan) with a lacrimal tube. After the surgery, we washed the lacrimal pathway every 2 weeks to prevent occlusion and infection. After 8 weeks, we removed the lacrimal tube. The patients with LOD who underwent lacrimal surgery were assessed by SM, the Schirmer-1 test, and TMH and TMA measurement before and 8 weeks after surgery. By syringing, we checked that there was no resistance to the passage of the lacrimal cannula at this time.

Statistical Analysis

All statistical analyses were performed using JMP version 11 (SAS Institute, Tokyo, Japan) and STATA (version 14; StataCorp LP, College Station, TX) software. All data were expressed as mean ± SD. The Mann-Whitney U test was used to compare the Schirmer-1 test, SM, TMH, and TMA data between the LOD and non-LOD groups. Diagnostic variables for LOD were analyzed using receiver operating characteristic (ROC) curves. Sensitivity and specificity were calculated from these curves. The optimal cutoff values for the Schirmer-1 test, SM, TMH, and TMA values were calculated using Youden's Index. The Wilcoxon test was used to compare the Schirmer-1 test, SM, TMH, and TMA values before and after surgery. The Spearman's rank correlation coefficient was used for the correlation between SM and Schirmer-1, TMH, and TMA. The χ^2 test was used to compare symptoms with the SM and Schirmer-1 test values. Statistical significance was set at $P < 0.05$, and P values $<$ 0.001 were listed as $P < 0.001$.

Table 1. Profile of LOD and Non-LOD Group

	LOD Group ($n = 72$)	Non-LOD Group ($n = 89$)	P Value
Age	71.7 ± 8.5	72.9 ± 7.5	0.91[a]
Male/female	21/51	32/67	0.72[b]
SM, mm	10.80 ± 3.63	5.44 ± 3.20	<0.001[c]
Schirmer test, mm	18.46 ± 7.97	11.84 ± 7.16	0.008[c]
TMH, mm	0.49 ± 0.24	0.30 ± 0.18	0.08[c]
TMA, mm^2	0.06 ± 0.06	0.03 ± 0.04	0.19[c]
Diagnosis	52 Nasolacrimal obstruction	79 Conjunctivochalasis (47/79 complications dry eye)	
	18 Common canaliculus obstruction	7 Allergic conjunctivitis	
	2 Superior canaliculus obstruction	3 Trichiasis	

[a] *t*-test.
[b] χ^2.
[c] Mann-Whitney *U* test.

Results

In total, 166 patients were enrolled. Of these, five were excluded, three underwent previous lacrimal surgery and two wore contact lenses. Thus, 72 patients with LOD and 89 patients without LOD were eligible for analysis. There was no patient with functional LOD. The mean ages of the study participants were 71.7 ± 8.5 and 72.9 ± 7.5 years in the LOD and non-LOD groups, respectively. Neither mean age nor sex ratio differed significantly between the groups. The causes of epiphora in patients with LOD were nasolacrimal obstruction (52 patients; 72%), common canaliculus obstruction (18 patients; 25%), and superior canaliculus obstruction in (two patients; 3%). The causes of epiphora in patients without LOD was conjunctivochalasis (79 patients; 89%), allergic conjunctivitis (7 patients; 8%), and trichiasis (3 patients; 3%). Forty-seven patients with conjunctivochalasis had dry eye as a complication.

The SM scores in the LOD group (10.80 ± 3.63 mm) were significantly higher than those in the non-LOD group (5.44 ± 3.20 mm; $P < 0.001$ by Mann-Whitney *U* test). Although the Schirmer-1 values in the LOD group (18.46 ± 8.00 mm) were significantly higher than those in the non-LOD group (11.84 ± 7.16 mm), the TMH and TMA values were not significantly different between the LOD group (0.49 ± 0.24 mm, 0.06 ± 0.06 mm^2, respectively) and non-LOD group (0.30 ± 0.18 mm, 0.03 ± 0.04 mm^2, respectively; Table 1).

We calculated the area under the curve (AUC) of the ROC curve for SM; the AUC of the SM values was 0.88, and the optimal cutoff value for SM was more than 8 mm, which yielded a sensitivity of 82% and specificity of 84% for detecting LOD. The AUCs of the Schirmer-1 test, TMH, and TMA values were 0.73, 0.79, and 0.71, respectively. The sensitivities of the Schirmer-1 test, TMH, and TMA at the optimal cutoff values were 83%, 93%, and 59%, and the specificities were 57%, 60%, and 77%, respectively (Fig. 2, Table 2). The AUC of the SM values was significantly larger than that of the Schirmer-1 test ($P < 0.001$) and TMA ($P = 0.002$), but not of TMH ($P = 0.078$). The SM values showed positive correlation with Schirmer-1 test values ($r = 0.430$, $P < 0.001$), TMH ($r = 0.437$, $P < 0.001$), and TMA ($r = 0.355$, $P < 0.001$) (Fig. 3).

Figure 4 shows the SM, Schirmer-1, TMH, and TMA values before and 8 weeks after surgery. The SM values significantly improved 8 weeks after surgery compared with those before surgery (5.30 ± 2.20 vs. 10.69 ± 3.20 mm; $P < 0.001$). The values of the Schirmer-1 test, TMH, and TMA also significantly improved after surgery (12.82 ± 7.14 mm, 0.33 ± 0.17 mm, and 0.03 ± 0.02 mm^2, respectively) compared with those before surgery (18.64 ± 7.94 mm, 0.50 ± 0.25 mm, and 0.06 ± 0.7 mm^2, respectively; Table 3). The severity of epiphora (Munk score) also improved after surgery (0.33 ± 0.82) compared with that before surgery (3.62 ± 1.47). In all postoperative patients, the lacrimal syringe passed through the nasal cavity without resistance at 8 weeks after surgery.

During the examination of SM, 98 of 161 patients (61%) felt a touch sensation, 15 (9%) felt a foreign-body sensation, and 48 (30%) felt nothing. In

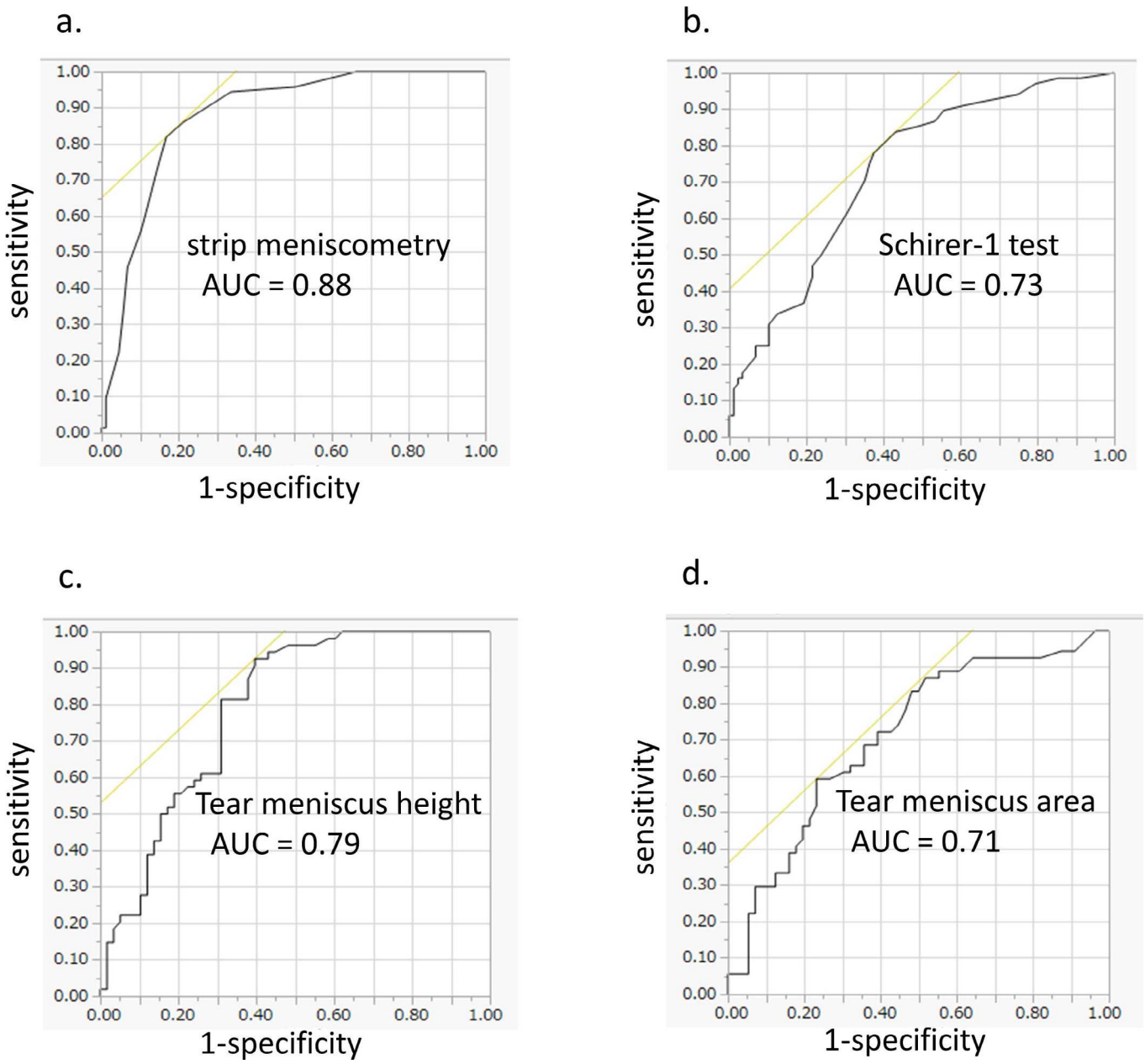

Figure 2. (a) ROC curve for the sensitivity and specificity of SM in detecting LOD. The area under the ROC curve was 0.88. The optimal cutoff value of SM for determining LOD was more than 8 mm, with a sensitivity of 82% and a specificity of 84%. (b) ROC curve for determining the sensitivity and specificity of the Schirmer-1 test in detecting LOD. The area under the ROC curve was 0.73. The optimal cutoff value was more than 12 mm, which yielded a sensitivity of 83% and a specificity of 57%. (c) ROC curve for determining the sensitivity and specificity of the TMH test, as measured using anterior-segment OCT, in detecting LOD. The area under the ROC curve was 0.79. The optimal cutoff value was more than 0.28 mm, which yielded a sensitivity of 93% and a specificity of 60%. (d) ROC curve for determining the sensitivity and specificity of the TMA test, as measured using anterior-segment OCT, in detecting LOD. The area under the ROC curve was 0.71. The optimal cutoff value was more than 0.073 mm^2, which yielded a sensitivity of 59% and a specificity of 77%.

Table 2. Sensitivity and Specificity in SM, Schirmer-1 Test, TMH, and TMA

	AUC	*P* Value	Sensitivity, %	Specificity, %	Cut-Off Value
SM	0.88	Ref.	82	84	8 mm
Schirmer-1 test	0.73	0.002	83	57	12 mm
TMH	0.79	0.078	93	60	0.28 mm
TMA	0.71	<0.001	59	77	0.073 mm^2

contrast, during the Schirmer-1 test, all of the patients felt something, 41 (25%) felt a touch sensation and 120 (75%) felt a foreign-body sensation or pain.

Discussion

In the present study, we demonstrated that SM was significantly better than the Schirmer-1 test, TMH, and TMA in detecting LOD in patients with epiphora, showing higher sensitivity and specificity. SM was also useful for evaluating the effects of lacrimal surgery.

Recently developed epiphora detection methods include TMH and TMA measurements using anterior-segment OCT.[3–5,11] In the present study, the sensitivity and specificity of TMH and TMA in

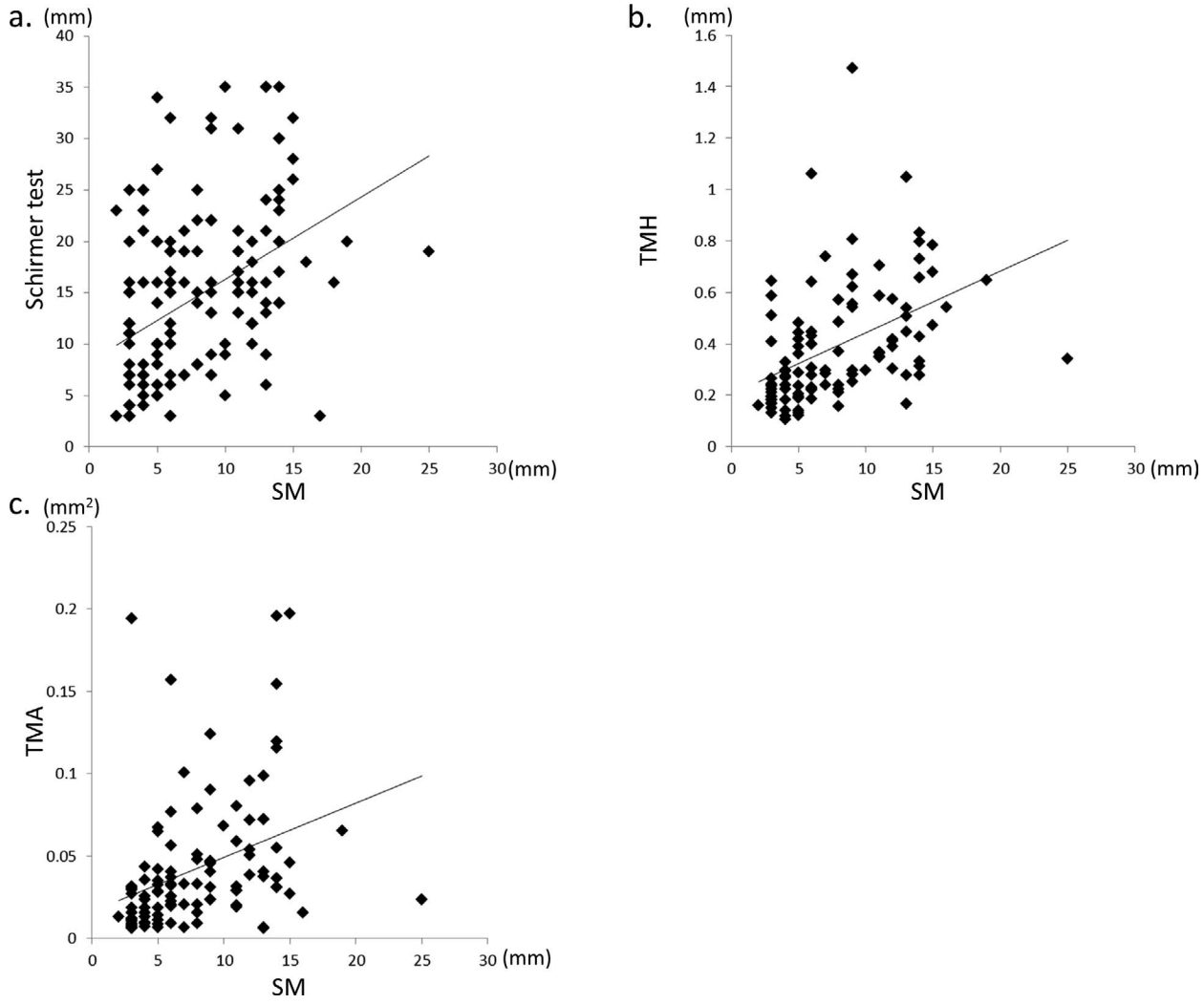

Figure 3. (a) Scatter plot of SM values and Schirmer-1. SM values correlates positively with Schirmer-1 test value ($r = 0.430$, $P < 0.001$). (b) Scatter plot of SM and TMH. SM values correlates positively with TMH ($r = 0.437$, $P < 0.001$). (c) Scatter plot of SM and TMA. SM values correlates positively with TMA ($r = 0.355$, $P < 0.001$).

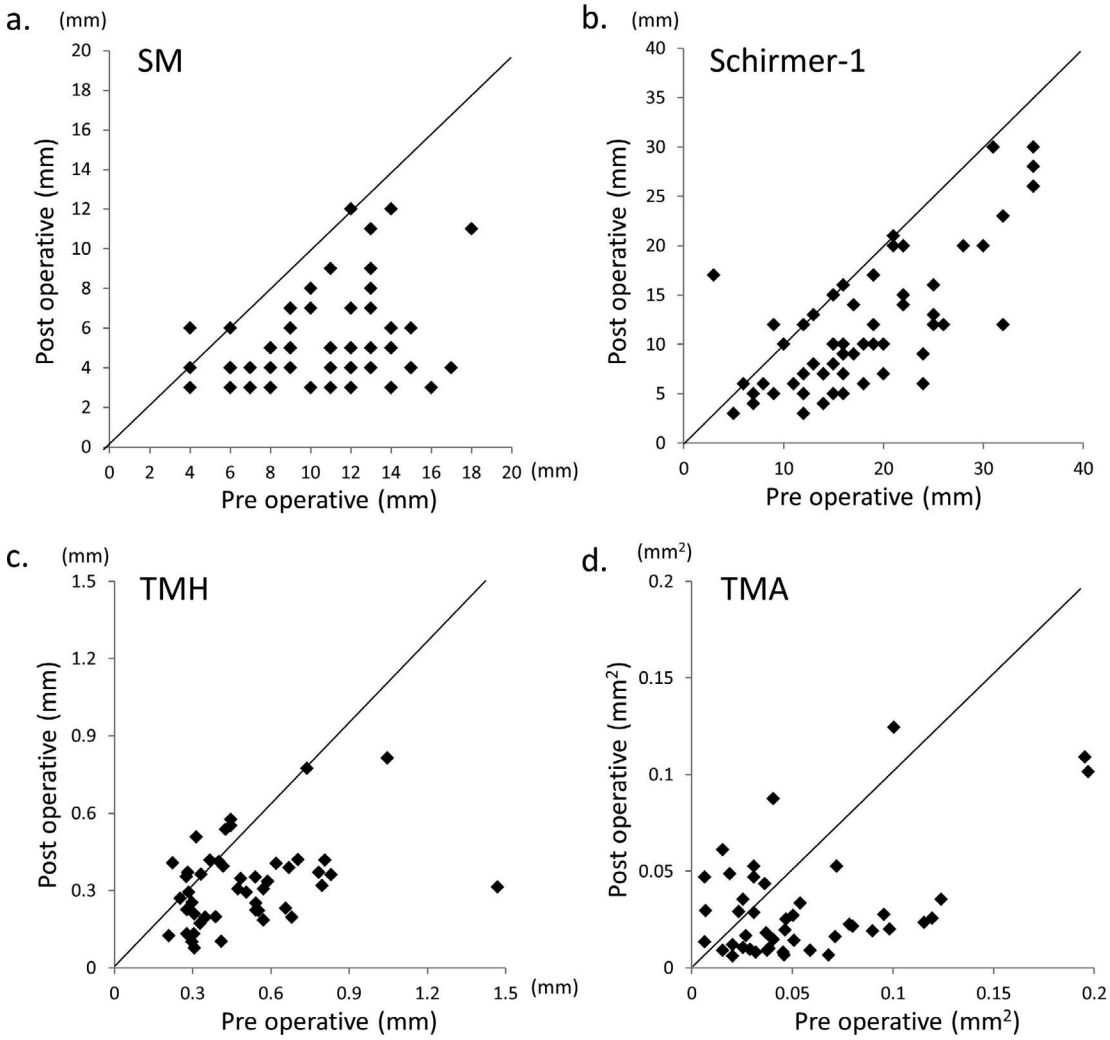

Figure 4. (a) Scatter plot of SM values before and after surgery in patients with LOD who underwent lacrimal surgery. SM values were significantly improved 8 weeks after surgery (5.30 ± 2.20 mm) compared with those before surgery (10.69 ± 3.20 mm, $P < 0.001$). (b) Scatter plot of the Schirmer-1 test values before and after surgery. The values of the Schirmer-1 test significantly improved after surgery (12.82 ± 7.14 mm) compared with those before surgery (18.64 ± 7.94 mm, $p < 0.001$). (c) Scatter plot of TMH before and after surgery. The values of TMH significantly improved after surgery (0.33 ± 0.17 mm) compared with those before surgery (0.50 ± 0.25 mm, $P < 0.001$). (d) Scatter plot of TMA before and after surgery. The TMA values significantly improved after surgery (0.03 ± 0.02 mm^2) compared with those before surgery (0.06 ± 0.7 mm^2, $P < 0.001$).

Table 3. Changes in SM, Schirmer-1 Test, TMH, TMA, and Munk Score

	Preoperative	Postoperative	*P* Value[a]
SM, mm	10.69 ± 3.20	5.30 ± 2.20	<0.001
Schirmer test, mm	18.64 ± 7.94	12.82 ± 7.14	<0.001
TMH, mm	0.50 ± 0.25	0.33 ± 0.17	<0.001
TMA, mm^2	0.06 ± 0.07	0.03 ± 0.02	<0.001
Munk score	3.62 ± 1.47	0.33 ± 0.82	<0.001

[a] Wilcoxon test.

detecting LOD were inferior to those reported in previous studies.[3–5] However, in those studies, the range of TMH in patients with LOD was 0.23 to 0.40 mm, whereas that of TMA was 0.02 to 0.05 mm^2. These were similar to the values obtained in the present study. This may have occurred because previous studies[4,11] compared patients with epiphora to individuals without epiphora, whereas we compared patients with LOD complaining of epiphora to those without LOD but who had the same complaint. It is reported that external dacryocystorhinostomy (DCR) improved TMH and TMA from 0.707 to 0.278 mm and from 0.197 to 0.025 mm^2, after 2

months in LOD patients.[5] The degree of improvement of TMH and TMA were less in this study than in previous studies. We thought the difference was derived from surgical differences. Furthermore, OCT-based measurements of the tear meniscus are influenced by trichiasis, entropion, ectropion, eye position, and particularly by conjunctivochalasis or conjunctival folds parallel to the lid.[12] In one study, the tear meniscus areas at the nasal, center, and temporal locations differed significantly in patients with conjunctivochalasis.[13] In the present study, we evaluated the tear meniscus from the cornea–meniscus junction to the lower eyelid–meniscus junction along the vertical line from the apex of the cornea. Thus, the OCT tear meniscus may not have reflected the total tear volume in the present study. Conversely, SM absorbs tears via capillary action, and thus may not be markedly affected by tear irregularity of the kind present in conjunctivochalasis.

SM offers four major advantages in terms of detecting LOD. First, tear volume measurement by SM takes only 5 seconds. Second, the SM strip does not touch the ocular surface or eyelids during examination and therefore causes minimal eye pain and discomfort. In fact, in the present study, 9% of patients felt a foreign-body sensation, but none experienced irritation during SM. In contrast, 75% of patients felt a foreign-body sensation or pain during the Schirmer-1 test ($P < 0.001$ by χ^2 test). Third, it is easy to measure tear volume in patients with epiphora using SM, whereas in patients with dry eye, particularly those with conjunctivochalasis, it is difficult to absorb tears using SM and measure tear volume without touching the conjunctiva. In patients with epiphora, even those with conjunctivochalasis, it is relatively easy to absorb the tears without touching the conjunctiva because there is a high tear volume. Finally, SM is less costly and requires less space than anterior-segment OCT. Thus, we think that SM is a good screening test for LOD and enables detailed examination and irrigation testing of the lacrimal pathway.

FDT is a useful method for screening LOD. According to Zappia and Milder,[9] the positivity rate of FDT in detecting lacrimal diseases is 95%. However, in our previous study, 14 of 48 (29%) patients with non-LOD conjunctivochalasis had a false-positive FDT result.[14]

The cotton thread test is similar to SM; it is minimally invasive and stimulates little reflex tearing.[15] However, it does not correlate with the tear meniscus curvature, probably because, according to Yokoi et al.,[16] the cotton thread used in the test is composed of a collection of longitudinally aligned threads, so its capillarity may be lost as it absorbs water. The Schirmer strip, with its more rigid, mesh-like structure, is more stable for measuring tear volume than the cotton thread test. The structure of the SM strip is similar to that of the Schirmer strip, and thus, SM may be more suitable than the cotton thread test.

Silicone tube intubation was first introduced by Keith[17] to treat patients with nasolacrimal duct obstruction as an alternative to DCR, which is the treatment of choice for primary acquired nasolacrimal duct obstruction cases. However, silicone lacrimal intubation has become an established alternative treatment and is a less invasive procedure than DCR. The reported success rate of silicone tube intubation in patients with nasolacrimal duct stenosis ranges from 40% to 75%.[18–22] In the present study, all patients with LOD underwent tube intubation surgery; we removed the tube 8 weeks after surgery. Previously, the reported timing of tube removal varied from 1 week to several years, with 2 to 6 months postintubation being the most common.[22–24] We evaluated the SM, Schirmer-1, TMH, and TMA values after removing the tube. No patient showed re-obstruction at this point; their symptoms, SM, Schirmer-1, TMH, and TMA values had all improved.

The present study had several limitations. First, we did not confirm the reproducibility of SM in patients with epiphora. In healthy subjects, as well as in those with dry eye, our previous study verified the reproducibility of SM, showing little difference in SM findings among six examiners in in vivo and in vitro reproducibility tests.[7] Hence, in the present study, we performed statistical analysis using non-parametric tests. Second, we did not verify the reproducibility of SM in patients with conjunctivochalasis. Dogru et al.[7] reported that SM may not be useful in determining tear meniscus volume in eyes with conjunctivochalasis, in disorders of lid margin congruity, or in ocular surface–lid apposition. Perhaps tears cannot be adequately absorbed if the meniscus is divided because of conjunctivochalasis; this might constitute a bias in the present study. Third, we could not evaluate the reflex tearing changes of the ocular surface. Reflex tearing may occur when if Schirmer strip touches the conjunctiva. The friction caused by blinking may also induce reflex tearing in conjunctivochalasis and patients with dry eyes. We performed SM at 30 minutes or more after

the Schirmer-1 test to prevent irritation to the conjunctiva. Moreover, we performed SM carefully to avoid touching the conjunctiva in patients with conjunctivochalasis. However, it is difficult to completely eliminate the effects of reflex tearing.

Fourth, the sample size of patients without LOD was small, and we could not perform separate analyses for each disease. Further studies with larger samples are necessary. Finally, we considered only the short-term, and not the long-term, postoperative period in the present study. We compared SM before surgery with that on the day of silicone tube removal. Thus, we did not evaluate long-term changes and differences in recurrence. Further studies are necessary to investigate this.

Conclusions

We demonstrated that SM, with high sensitivity and specificity, was superior to other methods in detecting LOD. Furthermore, our findings indicate that SM was useful for evaluating the effect of lacrimal surgery. SM is an easy method that can rapidly (within 5 seconds) evaluate tear volume.

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