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A Survey of Ophthalmologists Regarding Practice Patterns for Dry Eye and Sjogren's Syndrome

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Abstract

OBJECTIVE—To survey ophthalmologists about current practice patterns regarding the evaluation of dry eye patients and referrals for a Sjogren's syndrome (SS) work-up.

METHODS—An online survey was sent to ophthalmologists affiliated with the Scheie Eye Institute or Wills Eye Hospital using REDCap in August 2015. Descriptive statistics were used to summarize the data.

RESULTS—474 survey invitations were sent out and 101 (21%) ophthalmologists completed the survey. The most common traditional dry eye test performed was corneal fluorescein staining (62%) and the most common newer dry eye test performed was tear osmolarity (18%).

Half of respondents (51%) refer fewer than 5% of their dry eye patients for SS work-ups, with 18% reporting that they never refer any patients. The most common reasons for referrals included positive review of systems (60%), severe dry eye symptoms (51%) or ocular signs (47%), or dry eye that is refractory to treatment (42%). The majority (83%) felt that there is a need for an evidence-based standardized screening tool for dry eye patients to decide who should be referred for evaluation for SS.

CONCLUSIONS—Ophthalmologists continue to prefer the use of traditional dry eye tests in practice, with the most common test being corneal fluorescein staining. There is an under-referral of dry eye patients for SS work-ups, which is contributing to the continued underdiagnosis of the

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disease. The majority of respondents felt that there was a need for an evidence-based standardized screening tool to decide which dry eye patients should be referred for SS evaluations.

Keywords

survey; dry eye practice patterns; dry eye disease; Sjogren's syndrome

Dry eye disease (DED) is a multifactorial disease of the ocular surface characterized by loss of homeostasis of the tear film that results in symptoms of discomfort, pain and visual disturbances that significantly affect quality of life^{1, 2}. Tear film instability, hyperosmolarity, ocular surface inflammation, and neurosensory abnormalities play etiological roles in DED.² It is highly prevalent, and is one of the most common reasons that patients seek care from an ophthalmologist³, affecting up to 50% of adults.⁴

There currently is no gold standard test for diagnosing DED, and as a result a variety of diagnostic tests are utilized. Traditional tests include ocular surface staining with a variety of vital dyes, tear break-up time, and Schirmer testing.⁵ In recent years, newer tests have become available including tear osmolarity testing, MMP-9 testing, and various methods to image the tear film and meibomian glands^{5, 6}. However, it is unknown how the introduction of these new testing modalities has influenced the way ophthalmologists evaluate DED patients.

In addition, a subset of DED patients have underlying Sjogren's syndrome (SS), a chronic, debilitating, and potentially deadly autoimmune disease which is characterized by irreversible damage to the lacrimal glands and salivary glands with a loss of tear and saliva production, leading to a significant reduction in quality of life.⁷⁻⁹ The disease is also associated with autoantibody production, systemic complications, and an almost 20-fold higher risk of lymphoma that increases with disease duration.¹⁰ Lacrimal gland involvement in SS often leads to aqueous deficient dry eye, which is classically associated with a marked decrease in tear production and severe ocular surface inflammation.¹¹ SS is estimated to affect between 2 to 4 million Americans, with half of SS patients remaining undiagnosed due to the nonspecific nature of early clinical manifestations and an average delay in diagnosis of up to 7 years from the onset of symptoms¹¹⁻¹³.

The diagnosis of SS is complex and requires collaboration among multiple subspecialists including ophthalmology, rheumatology, and oral medicine. Several different sets of classification criteria for SS have been proposed. One of the more commonly used classification criteria sets is the American European Consensus Group (AECG) criteria. The AECG set of criteria includes both symptoms and signs of DED (Schirmer without anesthesia of 5 mm/5 min or vital dye staining of the ocular surface 4 van Bijsterveld scoring system).⁸ In 2012, the American College of Rheumatology (ACR)/Sjogren's International Collaborative Clinical Alliance (SICCA) criteria were proposed that no longer included subjective symptoms and only included objective signs.¹⁴ Finally, more recently, the ACR-EULAR criteria were proposed which contains elements of both the AECG and ACR/SICCA criteria.¹⁵

Because SS patients often have DED, they frequently first seek care from an ophthalmologist, who is in a position to facilitate early referrals for work-ups for SS. However, it is unclear which symptoms and signs ophthalmologists currently use when deciding whether or not to refer a dry eye patient for a SS work-up, or how often dry eye patients are being referred for evaluations. Early diagnosis and management are essential for the optimal management of SS to improve quality of life and to monitor patients for the development of systemic complications such as lymphoma¹¹.

The diagnosis of SS is hampered by significant limitations of sensitivity and specificity of traditional autoantibodies with an established link to SS^{16, 17}. While Sjogren's Syndrome A (SSA/Ro) and Sjogren's Syndrome B (SSB/La) antibodies are traditionally described as the hallmark antibodies of SS and are included in the diagnostic criteria for SS, they are only found in 60–70% of SS patients presenting to rheumatology clinics¹⁸. Recently, new candidate SS antibodies were described in a mouse model for SS¹⁹ and are commercially available in the "Sjo" finger stick kit performed in the office or as a blood draw (Bausch & Lomb, Rochester, NY). However, it is unclear how many ophthalmologists are currently aware of this kit and how many are using it in their practice or are ordering this blood test.

Currently there is no standardized approach to DED patients regarding ophthalmologic evaluation or referral of patients for a SS work-up. Therefore, our goal was to survey ophthalmologists to assess current practice patterns regarding the evaluation of DED patients and referrals for SS work-ups.

Methods

In August 2015, we conducted an online survey of ophthalmologists using [REDCap.com](https://www.researchprotocols.org/2015/1/e10000.html), a secure web application that can be used to build and manage online survey and databases²⁰. The survey invitation was sent to 474 ophthalmologists from across the country who are or were affiliated with the Scheie Eye Institute or Wills Eye Hospital. The questionnaire created for this study was designed to assess each ophthalmologist's practice patterns regarding dry eye patients and referrals for evaluations for SS and has not previously been validated (see Supplemental Digital Content). The survey included questions regarding the ophthalmologists' specialties, practice setting, and dry eye patient populations. Ophthalmologists were also asked about their knowledge and preferences regarding dry eye testing in their offices, as well as about the use of standardized dry eye grading scales. The surveyed ophthalmologists were asked to rank their top 3 traditional dry eye tests from the following tests: fluorescein staining of the cornea, tear break-up time, lissamine green staining of the conjunctiva, rose bengal staining of the conjunctiva, and Schirmer test (unanesthetized or anesthetized). Similarly, they were asked to rank their top 3 newer dry eye tests from the following tests: tear osmolarity assessment, MMP-9 testing with InflammDry® (RPS Diagnostics, Sarasota, FL), Lipiview® (TearScience, Morrisville, NC), optical coherence tomography of tear film, and meibography. The survey also included questions regarding their general knowledge about SS, the Sjo test (Bausch & Lomb, Rochester, NY), as well as referral patterns and testing of dry eye patients with suspected SS. Ophthalmologists were asked to respond the survey questions through the [Redcap.com](https://www.researchprotocols.org/2015/1/e10000.html) web application.

Statistical Analysis

We performed descriptive analyses of this survey data by calculating the percentage of respondents with a response in a particular category. We compared survey responses between ophthalmologists in academic practices vs. non-academic practices, and between cornea specialists vs. non-cornea specialists using the Fisher exact test. All the statistical analyses were performed using SAS v9.4 (SAS Institute Inc., NC, Cary).

Results

Of the 474 survey invitations sent out, 101 (21.3%) ophthalmologists responded and completed the survey. The characteristics of survey respondents are shown in Table 1. The majority of the respondents were cornea specialists (42.6%), followed by comprehensive ophthalmologists (20.8%). Over half of respondents were in full-time private practice (56.4%), with about one-third practicing full-time in an academic institution (35.6%). Overall, there were no statistically significant differences in the responses of physicians in academic versus non-academic settings (all $p>0.11$). The majority (78.2%) of respondents had been in practice for more than 5 years. Overall, more than half (60.4%) of the participants reported that dry eye patients make up about 20–60% of their practice, and that they spent on average 5 minutes or less performing a dry eye examination in the office.

Dry Eye Tests

The results of the ranking of top 3 traditional dry eye tests and top 3 newer dry eye tests are shown in Table 2. The majority of participants reported that they more frequently used traditional dry eye tests compared to newer tests in the office. The most common traditional dry eye tests performed were corneal fluorescein staining (ranked as most common by 62%), tear break-up time (49%) and anesthetized Schirmer's test (32%). Among the newer diagnostic tests, tear osmolarity assessment was the most frequently test used, with 18% ranking this as most commonly used newer test used.

Dry Eye Grading Scales

The majority of the respondents (82.2%) reported that they do not routinely use a standard DED severity grading scale. About half of the respondents (51.5%) were familiar with the Dry Eye Workshop (DEWS) dry eye severity grading scale¹; however among those familiar with the scale, only 19% (n=10) use it routinely in their offices. Most (57.1%) of those who do not routinely use the scale feel it takes too long to use in the office. Only a quarter of respondents (25.7%) were familiar with the Sjogren's International Collaborative Clinical Alliance (SICCA) Ocular Staining Score (OSS) grading scale²¹ and among those who were familiar, only about a quarter (23%, n=6) use it routinely in their offices. Those who do not use the OSS grading routinely felt it either takes too long (42.1%) or is not clinically useful (47.4%)

Sjogren's Syndrome

Table 3 summarizes the responses to questions about SS. Half of respondents (50.5%) reported that they refer fewer than 5% of their dry eye patients for SS work-ups, with 18% reporting that they never refer any patients. The most common reasons for referrals included

positive review of systems (60.4%) (most common extraocular symptom: dry mouth), severe dry eye symptoms (50.5%) or signs (46.5%), or dry eye that is refractory to treatment (41.6%). The most common ocular signs that would cause referral for SS workup were severe corneal staining (59.4%), unanesthetized Schirmer's score of <5mm (37.6%) and severe conjunctival lissamine green staining (28.7%). Approximately two-thirds (67%) of respondents were not familiar with either one of the two current sets of classification criteria for SS available at the time of the survey, specifically the American-European Consensus Group Criteria (AECG)⁸ and the American College of Rheumatology/Sjogren's International Collaborative Clinical Alliance Criteria (ACR/SICCA)¹⁴.

Over half of respondents (53.5%) had never heard of the Sjo test. Of those who were familiar with it, only 7% of ophthalmologists were routinely checking this test on their dry eye patients. 93% of respondents were unsure how the Sjo test results would guide their management of patients. The overwhelming majority of respondents (83%) felt that there was a need for an evidence-based standardized screening tool for dry eye patients to decide who should be referred for evaluation for SS.

When comparing referral patterns for SS workups and between cornea and non-cornea specialists (Table 4), cornea specialists reported referring patients more often to a rheumatologist (100% vs. 66.7% for referring at least 5%, $p < 0.0001$, Fisher exact test) or ordering blood work for SS antibodies (79.1% vs. 40.7% for ordering at least 5%, $p < 0.0001$, Fisher exact test) compared to non-cornea specialists. Cornea specialists were also more commonly familiar with the DEWS dry eye severity grading scale than non-cornea specialists (43.9% vs. 17.0%, $p = 0.006$, Fisher exact test).

Discussion

Our study survey provides insight into how ophthalmologists currently approach patients with DED. Our results can be compared to a survey done in 2000 by Korb in which he surveyed 36 optometrists and 41 ophthalmologists nationally and internationally with a background in dry eye about their preferred test²². In contrast to that study, our survey included 101 ophthalmologists in the United States who are comprehensive ophthalmologists and subspecialists. Similar to the study conducted by Korb²² fifteen years ago, we found that ophthalmologists in our survey still prefer using traditional dry eye tests despite the increased availability of newer in-office DED tests. However, in contrast to Korb's study in which there was no clear top choice of DED test, our study found over half of ophthalmologists reported that corneal staining with fluorescein as the most common test for the evaluation of DED patients. Also consistent with previous reports, conjunctival staining with lissamine green is not frequently used in DED evaluations, despite the fact that conjunctival staining with lissamine green is an integral part of the DEWS severity grading scale and the OSS scale that is part of the ocular classification criteria for SS. Therefore, it is critical that ophthalmologists perform conjunctival staining with lissamine green, in addition to corneal staining with fluorescein.

Lissamine green staining of the conjunctiva is included in both the DEWS severity scale and OSS scale. Dry eye severity scales help stratify and categorize patients' dry eye disease, and

can be useful in monitoring treatment response. However, our study found a low level of familiarity with the use of these grading scales, and the majority of our respondents felt that these scales either took too long or were not clinically useful. Our study found that only a quarter of respondents were familiar with the SICCA OSS grading scale²¹ and among those who were familiar, only about a quarter (23%, n=6) use it routinely in their offices. The OSS scale was proposed by the SICCA group to develop a standardized method for evaluating for ocular involvement in Sjogren's syndrome²¹, and is a part of the American College of Rheumatology (ACR)/SICCA criteria and also the more recently approved ACR/European League Against Rheumatism (EULAR) classification criteria for SS.¹⁵ The OSS scale is composed of scores from corneal staining with fluorescein as well as conjunctival staining with lissamine green. The OSS score is calculated by the summation of the fluorescein score for the cornea and the lissamine green scores for the nasal and temporal bulbar conjunctiva; with additional points given for the presence of central corneal staining, confluence, or the presence of filaments²¹. Therefore, in order to assess patients for the ocular classification criteria for SS, the ocular surface must be assessed using the OSS grading scale. Increased awareness and utilization of the OSS grading scale is needed so that dry eye patients can be properly evaluated for possible SS.

In our study, we found that the most common reasons for SS referrals included positive review of systems (most common extraocular symptom: dry mouth) and the presence of severe corneal staining. Overall there was a low referral rate of dry eye patients for SS evaluations with half of respondents reporting that they refer less than 5% of their dry eye patients for SS work-ups, and about 1 in 5 reporting that they never refer any patients. There appear to be several contributing factors to this low referral rate. Approximately two-thirds of respondents were not familiar with either one of the two current sets of classification criteria for SS available at the time of the survey. We found that the majority of ophthalmologists in our survey felt that there is a need for a standardized approach to dry eye evaluation and tools for screening those who warrant referral for SS workups. An increased awareness and familiarity with the SS classification criteria and the OSS grading scale, as well as the development of a standardized screening tool could increase referrals of dry eye patients for SS evaluations.

Over half of respondents had never heard of the Sjo test, and of those who were familiar with the test, the majority were unsure how the results affect their management. Further studies regarding the interpretation and clinical meaning of the Sjo test results would be helpful and may increase use of this test by ophthalmologists.

Finally, we found that many ophthalmologists have been slow to adopt newer dry eye tests into practice and most continue to rely on traditional in-office dry eye examinations. Newer diagnostic modalities in dry eye, such as tear osmolarity assessment, determination of surface inflammatory markers (e.g. matrix metalloproteinase 9) by using in-office rapid screening kits, Lipiview® and meibography, are available adjunctive tests for the evaluation of DED. It is possible that the hesitation to implement these tests in the office is due to the lack of evidence that show an additional benefit to the evaluation of DED patients over traditional tests.²³

Our study had certain limitations. For example, our survey did not include questions about all possible biomarkers for SS such as HLA-DR or cytokines. However, because the Sjo kit is currently available and marketed to ophthalmologists we chose to focus on assessing knowledge about those antibody tests. Future surveys that include other SS biomarkers would be helpful. In addition, our sample size was limited in that 101 ophthalmologists responded to the survey. However, this response rate is similar or higher than that of other previously published survey studies^{24, 25}, and a strength of our study was that it included cornea specialists as well as non-cornea specialists. Finally, our study was only sent to ophthalmologists and did not include other eye care providers such as optometrists. In the future, we plan to survey a broader range of eye care providers to increase the generalizability of our findings.

Conclusions

Despite the introduction of several new diagnostic dry eye tests in recent years, we found that ophthalmologists continue to prefer the use of traditional dry eye tests in practice, with the most common test being corneal fluorescein staining. There continues to be an under-referral of dry eye patients for SS work-ups, which is contributing to the continued under-diagnosis of the disease. This under-referral could partly be due to a lack of familiarity with the OSS grading scale used to evaluate patients for the ocular criteria for SS. The overwhelming majority of ophthalmologists in our study felt that there is a need for an evidence-based standardized screening tool for dry eye patients to decide who should be referred for SS evaluation. An increased knowledge of the SS classification criteria and the development of improved standardized screening tools could help in the optimization of timely evaluations for SS, leading to earlier diagnosis and better outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of survey respondents (n=101)

Characteristics of survey respondents	n (%)
<i>Sub-specialty</i>	
Cornea	43 (42.6%)
Glaucoma	5 (5.0%)
Neuro-ophthalmology	4 (4.0%)
Oculoplastics	4 (4.0%)
Pediatric ophthalmology	10 (9.9%)
Retina	14 (13.9%)
No subspecialty listed	21 (20.8%)
<i>Setting of practice</i>	
Academic	36 (35.6%)
Equal time in academic and private practice	7 (6.9%)
Private practice	57 (56.4%)
Unknown	1 (1.0%)
<i>Years in practice</i>	
2 years or less	10 (9.9%)
2–5 years	12 (11.9%)
5–10 years	21 (20.8%)
10–20 years	24 (23.8%)
20 years or more	28 (27.7%)
Unknown	6 (5.9%)
<i>Percent of patients in practice with dry eye</i>	
0–20%	25 (24.8%)
20–40%	38 (37.6%)
40–60%	23 (22.8%)
60–80%	10 (9.9%)
>80%	3 (3.0%)
Not applicable	2 (2.0%)
<i>Length of time typically spent performing dry eye examination in the office</i>	
30 seconds or less	13 (12.9%)
30–60 seconds	20 (19.8%)
1–3 minutes	23 (22.8%)
3–5 minutes	23 (22.8%)
More than 5 minutes	19 (18.8%)
Not applicable	3 (3.0%)

Table 2

Top 3 most commonly used traditional and newer dry eye tests done in the office as rated by survey respondents. Respondents ranked their top 3 choices from each list.

	Percent selected as top 1, 2, 3 for each dry eye test			
Traditional dry eye tests	Top 1	Top 2	Top 3	Top 1, 2, 3 combined
Fluorescein staining of the cornea	63 (62.4%)	21 (20.8%)	6 (5.9%)	90 (89.1%)
Tear break-up time (TBUT)	19 (18.8%)	49 (48.5%)	11 (10.9%)	79 (78.2%)
Lissamine green staining of the conjunctiva	6 (5.9%)	7 (6.9%)	12 (11.9%)	25 (24.8%)
Rose bengal staining of the conjunctiva	2 (2.0%)	3 (3.0%)	8 (7.9%)	13 (12.9%)
Schirmer test - unanesthetized	4 (4.0%)	7 (6.9%)	11 (10.9%)	22 (21.8%)
Schirmer test - anesthetized	5 (5.0%)	14 (13.9%)	32 (31.7%)	51 (50.5%)
Newer dry eye tests				
Tear osmolarity	18 (17.8%)	2 (2.0%)	3 (3.0%)	23 (22.8%)
InflammaDry® (MMP-9)	6 (5.9%)	8 (7.9%)	3 (3.0%)	17 (16.8%)
Lipiview®	3 (3.0%)	8 (7.9%)	2 (2.0%)	13 (12.9%)
Optical coherence tomography of tear film	4 (4.0%)	0 (0.0%)	2 (2.0%)	6 (5.8%)
Meibography	2 (2.0%)	1 (1.0%)	2 (2.0%)	5 (4.9%)

TBUT =Tear Break up; MMP-9=Matrix Metalloproteinase 9

Table 3

Ophthalmologist responses regarding Sjogren's syndrome (SS) management and referral patterns

Questions regarding Sjogren's Syndrome (SS)	n (%)
<i>Percent of dry eye patients referred to a rheumatologist for a SS work-up</i>	
None	18 (17.8%)
<5%	51 (50.5%)
5–10%	18 (17.8%)
>10%	10 (10.0%)
Unknown	4 (4.0%)
<i>Common reasons for referral of dry eye patients for SS work-up (check all that apply)</i>	
Positive review of systems	61 (60.4%)
Severe dry eye symptoms	51 (50.5%)
Ocular signs consistent with severe dry eye	47 (46.5%)
Refractory to dry eye treatment	42 (41.6%)
Other disease	5 (5.0%)
None of the above	4 (4.0%)
Not applicable	12 (11.9%)
<i>Extra-ocular symptoms routinely asked about when trying to decide when to refer a dry eye patient for a SS work-up (check all that apply)</i>	
Dry mouth	82 (81.2%)
Frequent dental problems/cavities	25 (24.8%)
Dry nose	16 (15.8%)
Joint pain	53 (52.5%)
Joint swelling	37 (36.6%)
Dry skin	24 (23.8%)
Constipation	3 (3.0%)
Vaginal dryness	13 (12.9%)
Rash	11 (10.9%)
Other	1 (1.0%)
Not applicable	13 (12.9%)
<i>Ocular signs that would cause referral of dry eye patients for SS work-up (check all that apply)</i>	
Moderate corneal fluorescein staining	7 (6.9%)
Severe corneal fluorescein staining	60 (59.4%)
Moderate lissamine green staining of conjunctiva	16 (15.8%)
Severe lissamine green staining of conjunctiva	29 (28.7%)
Schirmer test <8 mm/min	6 (5.9%)
Schirmer test <5 mm/min	38 (37.6%)
Other	3 (3.0%)
None of the above	9 (8.9%)
Not applicable	14 (13.9%)

Questions regarding Sjogren's Syndrome (SS)	n (%)
<i>Do you think there is a need for an evidence-based standardized screening tool for dry eye patients to decide who should be referred to a rheumatologist for a SS work-up?</i>	
No	14 (13.9%)
Yes	84 (83.2%)
Unknown	3 (3.0%)
<i>Have you heard of Sjo test?</i>	
No	54 (53.5%)
Yes	41 (40.6%)
Unknown	6 (5.9%)

SS= Sjogren's syndrome

Table 4

Comparison of survey responses between cornea and non-cornea specialists

	Non-cornea specialists (n=58)	Cornea specialists (n=43)	Fisher exact P-value
<i>Percent of dry eye patients referred to a rheumatologist for a SS work-up</i>			<0.0001
None	18 (33.3%)	0 (0.0%)	
<5%	32 (59.3%)	19 (44.2%)	
5%	4 (7.5%)	24 (55.8%)	
<i>Do you think there is a need for an evidence-based standardized screening tool for dry eye patients to decide who should be referred to a rheumatologist for a SS work-up?</i>			1.00
No	8 (14.6%)	6 (14.0%)	
Yes	47 (85.5%)	37 (86.1%)	
<i>Percent of dry eye patients in whom you order blood-work for traditional antibodies looking for SS</i>			<0.0001
None	32 (59.3%)	9 (20.9%)	
<5%	16 (29.6%)	13 (30.2%)	
5%	6 (11.1%)	21 (48.8%)	
<i>Are you familiar with the 2 current sets of diagnostic criteria for Sjogren's syndrome (AECG and ACR/SICCA criteria)?</i>			0.006
No	44 (83.0%)	23 (56.1%)	
Yes	9 (17.0%)	18 (43.9%)	
<i>Have you heard of the Sjo test?</i>			<0.0001
No	40 (75.5%)	14 (33.3%)	
Yes	13 (24.5%)	28 (66.7%)	
<i>Are you familiar with Dry Eye WorkShop (DEWS) severity grading scale?</i>			<0.0001
No	41 (75.9%)	2 (4.9%)	
Yes	13 (24.1%)	39 (95.1%)	
<i>Are you familiar with the Ocular Staining Score (OSS)?</i>			0.002
No	46 (85.2%)	23 (56.1%)	
Yes	8 (14.8%)	18 (43.9%)	