Prevalence of ocular surface dysfunction in patients presenting for cataract surgery evaluation

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Purpose: To report the prevalence of ocular surface dysfunction in patients presenting for cataract surgery evaluation.


Design: Prospective case series.

Methods: Consecutive patients presenting for cataract surgery evaluation were identified. Patient information including demographics, medical history, slitlamp findings, tear osmolarity, and tear matrix metalloproteinase-9 (MMP-9) levels were recorded. Patients were considered to have ocular surface dysfunction if any of the following outcomes were present: visually significant abnormal corneal surface examination, positive MMP-9 test, or abnormal osmolarity values (>307 mOsm/L or >7 mOsm/L intereye difference). Patient symptoms were recorded using the ocular surface disease index (OSDI) or Symptom Assessment in Dry Eye questionnaires.

Results: There were 120 patients (69% women), mean age 69.5 years ± 8.4 (SD). Abnormal osmolarity was found in 68 patients (56.7%), and abnormal MMP-9 in 76 patients (63.3%). Clinical findings showed that 47 patients (39.2%) had positive corneal staining on presentation, 9 patients (7.5%) had epithelial basement membrane dystrophy, and 2 patients (1.6%) had Salzmann nodules. Questionnaire data showed 54 (54.0%) of 100 patients reported symptoms suggestive of ocular surface dysfunction. In the asymptomatic group of 46 patients, 39 (85%) had at least 1 abnormal tear test (osmolarity or MMP-9) and 22 (48%) had both tests abnormal. Overall, 96 (80%) of 120 patients had at least 1 abnormal tear test result suggestive of ocular surface dysfunction and 48 patients (40%) had 2 abnormal results.

Conclusions: Objective ocular surface dysfunction findings were common among patients presenting for cataract surgery, yet many presented undiagnosed. Clinicians should be aware of this high prevalence and consider screening with tear testing before surgery.

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Ocular surface dysfunction includes a spectrum of diseases that impair the ocular surface leading to a constellation of clinical signs and patient symptoms. Dry-eye disease is likely the most common subtype of ocular surface dysfunction; however, many others can be present along with dry-eye disease or masqueraded as dry-eye disease. These include blepharitis, epithelial basement dystrophy, Salzmann nodular degeneration, allergic conjunctivitis, conjunctivochalasis, floppy eyelid syndrome, and others. The prevalence of dry-eye disease varies in the literature but has been reported to be as high as 35% in some populations.1–4

Cataract surgery is one of the most common procedures performed in the United States with a growing annual incidence.5 The typical age of patients having cataract surgery is over 50 years. Dry-eye disease and meibomian gland dysfunction are very common diseases, and prevalence significantly increases with age.6 In the setting of preoperative cataract surgery planning, dry-eye disease and meibomian gland dysfunction can impair critical refractive
measures such as keratometry values worsening surgical outcomes. In addition, ocular surface dysfunction has been reported to increase after cataract surgery. One study found that up to 62% of patients presenting for cataract surgery had a tear breakup time (TBUT) of less than 5 seconds, and 76% had corneal staining. Another study showed worsening of corneal fluorescein staining patterns for up to 3 months after cataract surgery. In addition, TBUT was found to be significantly reduced postoperatively compared with presurgery baseline for up to 1 month after cataract surgery. Dry-eye disease has also been found to increase postoperatively, especially in patients having femtosecond laser–assisted cataract surgery compared with manual phacoemulsification. The altered tear film caused by dry-eye disease can impair important aspects of visual quality and function, which might further affect the patient’s perceived surgical outcome.

It is well known that there is a poor association between the signs and symptoms of ocular surface dysfunction, making it difficult to accurately diagnose. Common tools used to diagnose ocular surface dysfunction, and specifically dry-eye disease, in addition to slitlamp evaluation include traditional tests (fluorescein staining, TBUT, Schirmer test) and validated questionnaires (eg, ocular surface disease index [OSDI] and Symptom Assessment in Dry Eye [SANDE]). Some traditional tests such as invasive TBUT and Schirmer test have been shown to have a low sensitivity and specificity and can be subject to error in interpretation; however, newer point-of-care diagnostics such as tear osmolarity and matrix metalloprotease-9 (MMP-9) testing have been shown to have a high sensitivity and specificity in diagnosing ocular surface dysfunction.

Given that ocular surface dysfunction has been shown to have an adverse impact on visual function and can worsen after surgery, it is critical to identify and address any tear film and ocular surface abnormalities before cataract surgery. Little has been reported about the prevalence of tear film and ocular surface abnormalities using modern diagnostic tests preoperatively in patients having cataract surgery. The purpose of this study is to report the prevalence of visually significant ocular surface dysfunction as evidenced by either an abnormal tear-film parameter (elevated MMP-9 or abnormal osmolarity), or corneal surface slitlamp evaluation findings in patients presenting for cataract surgery assessment.

PATIENTS AND METHODS

Consecutive patients presenting for cataract surgery evaluation were included in the study. Patients were recruited from 2 physician’s practices (P.K.G., C.E.S.) at the Duke University Eye Center and Weill Cornell Medicine, respectively. Institutional Review Board approval was obtained at both institutions; all research was conducted in accordance with this approval, was U.S. Health Insurance Portability and Accountability Act compliant, and adhered to the tenets of the Declaration of Helsinki. Inclusion criteria included age 18 years or older and presentation to the ophthalmology clinic for cataract surgery evaluation. Patients who had ophthalmic surgery in the last 3 months or those who were receiving either topical or systemic corticosteroids were excluded from the study. The following parameters were recorded from the clinical record: demographic and clinical information including sex, age, medical and surgical history, slitlamp evaluation findings of the corneal surface, OSDI, or SANDE questionnaire score, tear osmolarity, and tear MMP-9 test results.

The SANDE questionnaire consists of 2 questions and a visual analog scale to quantify ocular discomfort or irritation. The first question asks: “How often do your eyes feel dry and/or irritated?” The second question asks: “How severe do you feel your symptoms of dryness and/or irritation are?” For each question, the patient is presented with a 100 mm horizontal line and asked to rate each question. Multiplying scores from the frequency question and the severity question, and then obtaining its square root yields the final SANDE score. For the purpose of disease stratification, the SANDE scores were graded as “normal” if less than 20, mild dry-eye disease if 20 to 39, moderate dry-eye disease if 40 to 59, and severe dry-eye disease if the score was more than 59.

The OSDI questionnaire is a validated questionnaire composed of 3 subscales: vision-related function, ocular symptoms, and environmental triggers. The questionnaire is 1 page and patients have the option to abstain from answering certain questions in the ocular symptom and environmental trigger subsections. Each subscore is summed and then the index score is calculated by multiplying the total score by 25 and dividing by the number of questions answered. The OSDI is assessed on a scale of 0 to 100. Scores of 0 to 12 are considered normal; abnormal scores range from mild dry-eye disease, moderate dry-eye disease, or severe dry-eye disease (33 to 100).

Tear osmolarity was measured using the Tearlab Osmolarity System (Tearlab Corp.). The test was performed before the instillation of eyedrops or other testing. Patients were unable to have osmolarity testing if they had used artificial tears within 2 hours before testing. The system was calibrated as per manufacturer’s instructions. Osmolarity samples were collected from the tear meniscus near the lateral canthus from both eyes. An osmolarity value of more than 307 mOsm/L in either eye or an intereye difference greater than 7 mOsm/L, and/or presence of elevated MMP-9 levels on the ocular surface was measured using Immulonadry (Rapid Pathogen Screening, Inc.). The test was administered before the instillation of eyedrops. Testing was conducted in accordance with provided manufacturer instructions; the sampling strip was placed on the palpebral conjunctiva and dabbed in multiple locations until saturated. This test is considered positive if the concentration of MMP-9 measured in the assay is higher than 40 ng/mL. A positive/abnormal test was defined as the appearance of a red indicator line adjacent to the blue control line, read and interpreted at least 10 minutes after completion of the sample collection.

Patients were considered to have signs of visually significant ocular surface dysfunction if any of the following were present: positive MMP-9 test, osmolarity values above 307 mOsm/L or an intereye difference greater than 7 mOsm/L, and/or presence of corneal surface examination findings indicative of visually significant ocular surface dysfunction (eg, punctate epithelial erosions, epithelial basement membrane dystrophy, Salzmann nodules, pterygium). The number of patients with at least 1 positive test suggestive of ocular surface dysfunction was determined and the prevalence of ocular surface dysfunction in the study population presenting for cataract surgery evaluation was calculated by summing the patients who had had at least 1 abnormal objective test for ocular surface dysfunction (ie, abnormal osmolarity or MMP-9 or corneal surface examination findings) divided by the total number of patients in the study. Symptoms of ocular surface dysfunction in this population were assessed using the questionnaire results. The OSDI scores higher than 12 and SANDE score higher than 19 were considered abnormal results suggestive of ocular surface dysfunction. Descriptive statistics were computed.
for all variables, and SAS software (version 9.4, SAS Institute, Inc.) was used for analysis.

RESULTS
Table 1 shows the patient demographics and clinical history. Among the 120 patients included in the study, 83 (69%) were women and 37 (31%) were men. The mean patient age at the time of cataract evaluation was 69.5 years ± 8.4 (SD) (range 44 to 91 years). Other relevant demographic information included previous refractive surgery in 25 patients (20.8%), previous autoimmune disease in 14 (11.7%), and a history of diabetes mellitus in 18 (15.0%). Out of all patients, 52 (43.3%) had a preexisting diagnosis of ocular surface dysfunction at the time of cataract evaluation, and the remaining 68 (56.7%) had no history of ocular surface dysfunction. There was no statistically significant difference in age or other demographic variables, except sex ($P = .01$), between those with no history of ocular surface dysfunction and those with a history of ocular surface dysfunction.

Tables 2 and 3 display the point-of-care testing results in the study population. Among the entire study population ($n = 120$), all patients had both osmolarity and MMP-9 testing. The majority (44 [57.9%]) of the 76 patients who had abnormal MMP-9 levels were patients who had no previous ocular surface dysfunction. By contrast, there was also a small subset of patients who exhibited a normal osmolarity but had a positive MMP-9 ($n = 28$), suggesting the presence of non-dry-eye disease, ocular surface dysfunction, or dry-eye disease masquerader. Twenty-three patients (19.2%) in the study population displayed at least 1 positive tear film test with no other abnormal signs or symptoms; 17 (73.9%) of the 23 patients did not have a history of ocular surface dysfunction. Similarly, chi-square testing showed that the proportion of patients with abnormal osmolality values who also had a history of ocular surface dysfunction was similar to that in the group with no history of ocular surface dysfunction ($\chi^2 = 0.325; P = .57$). Similar proportions were also observed when comparing MMP-9 positivity ($\chi^2 = 0.127; P = .72$).

Slitlamp evaluation findings showed 47 (39.2%) of 120 patients had corneal staining indicative of ocular surface dysfunction, 9 patients (7.5%) presented with epithelial basement membrane dystrophy, and 2 patients (1.6%) had Salzmann nodules. When looking at both tear osmolarity and MMP-9 outcomes, 96 patients (80.0%) had at least 1 abnormal point-of-care test suggestive of ocular surface dysfunction, and 48 patients (40.0%) had both abnormal test results.

Of the 68 patients who had no previous diagnosis of ocular surface dysfunction, 41 (60%) were women and 27 (40%) were men. Figure 1 shows the breakdown of normal and abnormal ocular surface dysfunction test results for this subgroup. Osmolarity and MMP-9 testing was performed in all 68 patients. In the population of 68 patients with no previous diagnosis of ocular surface dysfunction, 55 patients (81%) demonstrated at least 1 positive tear film test for ocular surface dysfunction (either abnormal osmolarity or abnormal MMP-9); however, only 21 of these patients (31%) with no history of ocular surface dysfunction demonstrated positive corneal staining on slitlamp evaluation. The OSDI or SANDE questionnaires were completed by 56 of the 68 patients in this group of whom 30 (54%) were found to be normal and 10 (18%) had mild, 7 (12%) had moderate, and 9 (16%) had severe ocular surface symptoms. Of note, when examining the 30 patients who scored “normal” on the questionnaire, 24 (83%) had either an abnormal osmolarity or abnormal MMP-9 test, whereas 14 (47%) had abnormal results on both tests.

There were 100 patients in the study population who completed either the OSDI or SANDE questionnaires and each was categorized from normal to severe. There were 46 patients (46%) who were graded as normal and 19 (19%) had mild, 12 (12%) had moderate, and 23 (23%) had severe ocular surface symptoms based on the validated questionnaires. In the cohort of 46 patients who scored “normal” on the questionnaire, 14 (30%) had positive corneal staining on slitlamp evaluation. Furthermore, 26 (56.5%) of these patients had an abnormal osmolarity test, and 35 patients (76%) demonstrated a positive MMP-9 test. Overall, although displaying no clinical symptoms based on questionnaire results, 39 of these patients

<table>
<thead>
<tr>
<th>Table 2. Distribution of point-of-care testing and questionnaire values in the study population.</th>
<th>History of OSD</th>
<th>No History of OSD</th>
<th>All Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
<td>Osmolarity</td>
<td>MMP-9</td>
<td>Questionnaire data</td>
</tr>
<tr>
<td>Total (n)</td>
<td>52</td>
<td>68</td>
<td>120</td>
</tr>
<tr>
<td>Abnormal, n (%)</td>
<td>52 (59.7%)</td>
<td>68 (56.7%)</td>
<td>76 (63.3%)</td>
</tr>
<tr>
<td>Total (n)</td>
<td>31</td>
<td>37 (54.4%)</td>
<td>68 (56.7%)</td>
</tr>
<tr>
<td>Abnormal, n (%)</td>
<td>31 (61.5%)</td>
<td>44 (64.7%)</td>
<td>76 (63.3%)</td>
</tr>
<tr>
<td>Total (n)</td>
<td>44</td>
<td>56</td>
<td>100</td>
</tr>
<tr>
<td>Abnormal, n (%)</td>
<td>44 (63.6%)</td>
<td>26 (46.4%)</td>
<td>54 (54%)</td>
</tr>
<tr>
<td>Mild DED, n (%)</td>
<td>28 (80.6%)</td>
<td>10 (26.3%)</td>
<td>19 (19%)</td>
</tr>
<tr>
<td>Moderate DED, n (%)</td>
<td>9 (20.5%)</td>
<td>7 (12.5%)</td>
<td>12 (12%)</td>
</tr>
<tr>
<td>Severe DED, n (%)</td>
<td>5 (11.4%)</td>
<td>9 (16.1%)</td>
<td>23 (23%)</td>
</tr>
</tbody>
</table>

OSD = ocular surface dysfunction; DED = dry-eye disease; OSDI = ocular surface dysfunction; MMP-9 = matrix metalloproteinase-9

*P = .01
had at least 1 objective sign of ocular surface dysfunction based on an abnormal tear test (osmolarity or MMP-9), and 22 (48%) had both abnormal osmolarity and abnormal MMP-9. Table 3 further highlights the objective testing results of all patients who completed questionnaires.

The r-squared analysis demonstrated very little correlation between tear osmolarity and questionnaire scores. For the entire study population, each value recorded from the SANDE questionnaire was compared with the respective osmolarity value in the right eye (r^2 \leq 0.01), the left eye (r^2 = 0.003), and the difference in osmolarity between eyes (r^2 < 0.001; difference between eyes, r^2 = 0.004).

The overall prevalence of ocular surface dysfunction based on the use of objective tests in patients having cataract surgery evaluation was found to be 80%. This value was calculated by summing the patients who had had at least 1 abnormal test for ocular surface dysfunction (ie, abnormal osmolarity or MMP-9, or corneal surface examination findings indicative of ocular surface dysfunction), divided by the total number of patients in the study (96 of 120 = 80%).

DISCUSSION

Ocular surface dysfunction can be symptomatic or asymptomatic and can affect a wide demographic of patients. Dry-eye disease is one of the more common forms of ocular surface dysfunction that alters the tear film and overall integrity of the ocular surface. In the setting of patients having cataract surgery, in particular for those who have a specific refractive visual goal or are having a multifocal or toric intraocular lens (IOL), it is critical to identify signs of ocular surface dysfunction before surgery, even in the absence of significant symptoms. An abnormal tear film and/or corneal surface impacts keratometric and topographic measurements taken during the preoperative workup, and thus can lead to IOL calculation errors and can impair visual function and quality.16,18

Previous studies have shown that patient symptoms do not correlate well with objective measures and signs of ocular surface dysfunction; however, patient-reported symptoms are the most common trigger to a clinician to further assess the ocular surface and obtain point-of-care testing.20,31 The recent introduction of point-of-care tear film testing allows for rapid objective assessment of the ocular surface, which might allow the clinician to diagnose and treat ocular surface dysfunction in otherwise asymptomatic patients before cataract extraction is performed.

### Table 3. Cross-tabulation of objective testing and questionnaire results.*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Questionnaire (+)</th>
<th>Questionnaire (–)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmolarity (+)</td>
<td>21</td>
<td>22</td>
<td>43</td>
</tr>
<tr>
<td>MMP-9 (+)</td>
<td>10</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>26</td>
<td>57</td>
</tr>
<tr>
<td>Osmolarity (–)</td>
<td>11</td>
<td>13</td>
<td>24</td>
</tr>
<tr>
<td>MMP-9 (–)</td>
<td>12</td>
<td>7</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>20</td>
<td>43</td>
</tr>
<tr>
<td>MMP-9 (+)</td>
<td>32</td>
<td>35</td>
<td>67</td>
</tr>
<tr>
<td>MMP-9 (–)</td>
<td>22</td>
<td>11</td>
<td>33</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>46</td>
<td>100</td>
</tr>
</tbody>
</table>

*(+) = abnormal result; MMP-9 = matrix metalloproteinase-9

*Only the 100 patients who completed a questionnaire were included in this analysis.
A small subset of patients in this study had normal tear osmolarity and abnormally elevated MMP-9 levels (n = 28). Although it is possible that mild dry-eye disease is still present in this scenario, clinicians should be alerted to other forms of ocular surface dysfunction that can raise MMP-9 levels, such as epithelial basement membrane dystrophy, allergic conjunctivitis, pterygium, and conjunctivochalasis. Similar to dry-eye disease, these disorders can have a significant adverse impact on cataract surgical planning and postoperative outcomes, especially if the precorneal tear film is altered by them. A study by Trattler et al. assessed corneal staining and TBUT in patients having cataract surgery, making the case that many patients exhibit clinical signs of dry eye in the cataract surgery population.

The present study focuses on point-of-care testing of the tear film as an objective way to assess the ocular surface for dysfunction. Using these tests and clinical corneal examinations, we found an even higher prevalence of ocular surface dysfunction, suggesting that there are even more patients who go undiagnosed with traditional tests. The present study also supports the concept that objective nonsymptom-based preoperative ocular surface dysfunction screening is of value because many patients with potentially visually significant signs of ocular surface dysfunction will be asymptomatic. In fact, in this study population, a higher percentage of patients had either 1 or both abnormal tear tests in the asymptomatic group compared with the entire study population, further highlighting the disconnect between the signs and symptoms of ocular surface dysfunction. This is consistent with previous studies that have shown less than 60% of ocular surface dysfunction to be symptomatic and that early or mild disease might not present with subjective symptoms. Specifically, we found that 80% of patients presenting for cataract evaluation had objective signs of ocular surface dysfunction on preoperative point-of-care testing and clinical examination. Of particular note, the majority of patients (57%) who presented for preoperative evaluation had no previous diagnosis of ocular surface dysfunction, yet 81% of that cohort was found to have at least 1 abnormal tear film test, suggesting that ocular surface dysfunction is often overlooked or underdiagnosed in this population. Because of the similar proportions of patients with abnormal tear testing between those with and without a history of ocular surface dysfunction, testing patients based only on previous diagnosis might miss patients who have objective signs of ocular surface dysfunction.

It is well established that the signs and symptoms of ocular surface dysfunction increase after cataract surgery and this can lead to patient dissatisfaction, frustration, and concern for complications. Patients are more accepting of their diagnosis and treatment of ocular surface dysfunction when they are made aware of it before surgery. Given the very high prevalence of abnormal tear film parameters in patients presenting for cataract evaluation, clinicians should be more cognizant of screening presurgical candidates for dry-eye disease and other forms of ocular surface dysfunction. Noninvasive point-of-care tests such as osmolarity, MMP-9, noninvasive TBUT, meibography, and other tests can be easily integrated into clinical practice and technician-performed work-up protocols.

Although the primary goal of our study was not to assess differences between diagnostic tests, it is important to note that tear film tests such as osmolarity and MMP-9 were more sensitive in diagnosing ocular surface dysfunction than either questionnaire because 83% of those who had no history of ocular surface dysfunction and scored “normal” on the questionnaire had at least 1 abnormal tear film test. This poor association between tear testing and patient symptoms suggests that symptomatology alone might miss many patients with significant ocular surface dysfunction.

We suspect that the relatively high prevalence of ocular surface dysfunction in our study population is related in part to the age of the study population as well as the high percentage of women included in the study. In the literature, ocular surface dysfunction and dry-eye disease have been associated with increasing age as well as with female sex. Demographics of patients who seek cataract surgery show a similar pattern, with increased incidence in older female patients.

A limitation of this study is that the patients were recruited from 2 academic centers, which might potentially alter generalizability of our data. Another limitation of our study is that patients were tested at 1 point in time and the ocular surface and associated disorders can be dynamic with fluctuations that might be missed on a single test. Future studies with serial observations of the tear film and ocular surface might potentially allow a more precise diagnosis of ocular surface dysfunction. In practice, clinicians have a variety of screening tests available and the present study shows that there are multiple viable options for screening patients for ocular surface dysfunction. Future studies might be considered to compare the various clinical tools we have available to determine whether there is a single best screening tool in this patient population.

In summary, the present study using objective testing techniques, suggests that ocular surface dysfunction has a high prevalence and is underdiagnosed among patients who present for cataract surgery evaluation. Thus, all cataract surgeons might consider screening patients preoperatively for ocular surface dysfunction to achieve the highest visual outcomes and patient satisfaction postoperatively. The signs and symptoms of ocular surface dysfunction are often poorly correlated, and this study also supports a similarly poor correlation between patient-reported symptoms and diagnostic tear testing results. Ocular surface dysfunction of any severity level can lead to suboptimal visual outcomes in cataract surgery and our study demonstrates the importance of careful screening for ocular surface dysfunction and other ocular surface disorders in this patient population.
WHAT WAS KNOWN

- Ocular surface dysfunction in preoperative cataract surgery patients can lead to suboptimal postoperative visual outcomes.
- Signs and symptoms of ocular surface dysfunction are often poorly correlated and patient-reported symptoms alone cannot be used to accurately assess the ocular surface.

WHAT THIS PAPER ADDS

- There was a high prevalence of ocular surface dysfunction among patients presenting for cataract surgery as measured by point-of-care objective tear tests.
- Because better visual quality might be achieved if ocular surface dysfunction is treated before surgery, it is worth considering preoperative tear testing in patients presenting for cataract surgery.

REFERENCES


Neither of the other authors has a financial or proprietary interest in any material or method mentioned.

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