Titolo rivista/libro: European journal of ophthalmology

Titolo articolo/sezione: Noninvasive screening of ocular surface disease in otherwise healthy patients scheduled for cataract surgery

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ISSN: 1120-6721

DOI: 10.1177/11206721241228621

Anno: 2024

Volume: 34

Fascicolo: 5

Editore:

Pag. iniziale: 1475

Pag. finale: 1480

Original research article

EJO European Journal of Ophthalmology

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European Journal of Ophthalmology
2024, Vol. 34(5) 1475–1480

DOI: 10.1177/11206721241228621
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Abstract

Purpose: To evaluate prevalence and characteristics of pathological ocular surface findings in healthy patients undergoing cataract surgery using a noninvasive ocular surface workup and a validated questionnaire.

Design: Prospective single-centre study (sub-analysis clinical trial no. NCT05754437).

Methods: Healthy patients undergoing senile cataract surgery were screened preoperatively by Oculus Keratograph (K5 M; Oculus GmbH, Wetzlar, Germany) for the evaluation of tear meniscus height (TMH), non-invasive keratograph break-up time (NIKBUT), and meibomian gland dropout. Ocular discomfort symptoms were scored by ocular surface disease index (OSDI) questionnaire.

Results: 120 eyes of 120 patients (62 females, 58 males; mean age 73.85 years, range 47–91 years) were included. All patients had at least 1 abnormal finding, while 19 (15.8%; 95% CI [0.09–0.22]) had alterations of all parameters. In detail, 39 patients (32.5%; 95% CI [0.24–0.41]) had pathological TMH (mean 0,15 mm [0.03 SD]), 102 (85%; 95% CI [0.79–0.91]) had pathological NIKBUT (mean 3.64 s [2.63 SD]), 117 (97.5%; 95% CI [0.95–1]) had some degree of gland dropout (mean 1.62 [0.70 SD]), 78 patients (65%; 95% CI [0.56–0.74]) had pathological OSDI scores (mean 28.63 [15.08 SD]). Using TFOS DEWS II criteria, 66 patients (55%; 95% CI [0.42–0.60]) resulted affected by dry eye.

Conclusions: This quick noninvasive screening documented the high prevalence of pathological ocular surface parameters in patients without risk factors or previous diagnosis of dry eye who are scheduled for cataract surgery.

Keywords

Ocular surface disease, dry eye, cataract surgery, preoperative screening, Keratograph

Date received: 31 October 2023; accepted: 10 January 2024

Introduction

Cataract surgery is among the most frequently performed procedures worldwide. It is cost effective and has a substantial socioeconomic effect, increasing patients' economic productivity, social autonomy, and quality of life.[1,2] However, it is not a risk-free procedure, and undesired effects or iatrogenic conditions may occur, even after uneventful surgery. The most frequent postoperative complaints are related to ocular surface disturbances characterized by a wide range of symptoms including foreign body sensation, photophobia, fluctuating

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vision and epiphora.[3] This finding is not surprising since the majority of surgical procedures are performed on olders, a population with a higher incidence of ocular surface disease (OSD) or dry eye disease (DED).[3] Pre-existing OSD or DED represent a major risk factor for postoperative DED, along with a variety of surgery-related parameters, such as the use of a traumatic lid speculum, the prolonged exposure of the operating microscope light, the corneal incisions and the toxicity from perioperative topical therapies, among others.[4,5] Moreover, pre-existing ocular surface abnormalities may negatively impact preoperative evaluations (e.g., intraocular lens power calculation) in patients presenting for cataract surgery, thus determining suboptimal postoperative visual outcomes.[6]

Signs and symptoms of ocular surface dysfunction are often poorly correlated, therefore patient-reported symptoms or history cannot be used to accurately assess the ocular surface status. Furthermore, many patients, especially older ones with severe vision impairment due to cataract, may not feel compelled to report ocular surface discomfort symptoms (not directly linked to their underlying condition) during routine preoperative evaluation. To overcome this drawback, easy, quick, and noninvasive diagnostic tools could be employed in addition to conventional subjective questionnaires to screen patients undergoing surgery.

Moreover, because of pre-existing ocular surface abnormalities may have a detrimental impact on postoperative outcomes, and may further worsen after cataract surgery causing disabling symptoms, it is critical to define the prevalence of such alterations, especially in patients without frank signs/symptoms, more likely to go unnoticed during a standard preoperative assessment (e.g., patients with no ocular comorbidity or previous surgery, who do not present systemic diseases and do not assume medications). This could allow the identification of both subjects at-risk and patients with alterations of the ocular surface status who require more in-depth evaluations and possibly preoperative management of OSD.

The purpose of this study was to evaluate the prevalence and the characteristics of pathological ocular surface findings in otherwise healthy patients undergoing senile cataract surgery using a noninvasive screening that combined a widely used diagnostic tool with a validated subjective questionnaire. Since noninvasive screening tools may not be available in every ophthalmology clinic, a further outcome was to evaluate whether objective data correlate to patient-reported symptoms.

Methods

This prospective single-centre study is a sub-analysis conducted between April and November 2022 of a clinical trial performed at the University Magna Graecia of Catanzaro (Italy) (NCT05754437). The study was approved by the local Ethics Committee (Comitato Etico Regione Calabria – Sezione Area Centro) and was performed in accordance with relevant guidelines and regulations. Before any procedure, all participants signed a written informed consent form.

Consecutive patients scheduled for senile cataract surgery were evaluated for the inclusion in the study. Exclusion criteria were: pre-existing diagnosis of OSD or DED, chronic and regular use of therapies for OSD or DED (topical, instrumental, or oral), any other ocular comorbidity, previous ocular surgery (in both eyes), use of systemic drugs with a known or suspected link to DED (e.g., diuretics, antidepressants, antihistamines, hormone replacement therapy), systemic diseases known to impair ocular surface status (e.g., autoimmune diseases and diabetes).[3]

All patients were assessed 7 ± 2 days before the scheduled surgery. Demographic information was collected along with medical and ocular history. Noninvasive ocular surface examination was carried out in the eye to be operated by means of Oculus Keratograph 5 M (K5 M; Oculus GmbH, Wetzlar, Germany) by an experienced examiner (C.R.). All the measurements were taken between 9:00 a.m. and 11:00 a.m. in a dimly lit room with controlled temperature (21–24 °C) and humidity (30–60%). The instrument allowed the evaluation of tear meniscus height (TMH), noninvasive Keratograph break-up time (NIKBUT), infrared meibography of the lower eye lid for the calculation of meibomian glands dropout. Briefly, TMH images were captured with infrared illumination and a built-in ruler was used to its fine measurement in millimetres (mm) along the centre of the lid margin. The cut-off provided by the instrument (0.20 mm) was used to distinguish between normal ($\geq$) or pathological values ($<$). NIKBUT used Placido rings that were reflected on the corneal surface: the interval time between the last complete blinking and the first distortion the 22 concentric rings reflected on the corneal surface was defined as "NIKBUT FIRST"; the average time of all tear film break-ups occurring in the measured period of up to 24.98 s (s) (time limit set by the device's software) was also measured and defined as "NIKBUT AVG". Values $<$ 10 s were considered pathological by the instrument for both parameters. Finally, a tear stability level of severity ("NIKBUT CLASS") was calculated by the instrument according to the following classification incorporated in the instrument: class $0 > 10$ s (normal), class I 6–10 s, class II 3–6 s, class III < 3 s.

Meibomian gland dropout was evaluated using infrared transillumination of the lower eyelid. The degree of its deficiency was classified according to the Meiboscore using a 0 to 3 scale: grade 0 = no gland loss (normal); grade 1 = area of gland loss up to 33% of the total gland area; grade 2 = area of gland loss between 33 and 66%; and grade 3 = area of gland loss of 67% or more.[7]

Besides the above-mentioned diagnostic work-up, ocular discomfort symptoms were also investigated by means of Ocular Surface Disease Index (OSDI) questionnaire. The OSDI questionnaire is a reliable 12-item questionnaire composed of 3 subscales: vision-related function, ocular symptoms, and environmental triggers noticed during the past week.[8,9] Patients rate the frequency of their symptoms from 0 to 4 with 0 indicating "none of the time" and 4 corresponding to "all of the time". Each response is given score from 0 to 4. The sum of all values will give the OSDI score that ranges from 0 to 100. A score of 13 or more is suggestive of DED. The severity was further calculated as follows: mild = 13–22, moderate = 23–32, severe > 32. Dry eye diagnosis was obtained using the following Tear Film & Ocular Surface Society (TFOS) Dry Eye WorkShop (DEWS) II criteria: positive symptom score (OSDI score ≥ 13) plus non-invasive break-up time < 10 s.[10]

Statistical analysis was performed with GraphPad Prism 8.2.1 (GraphPad Software, Inc., San Diego, CA). Prevalence and confidence intervals (CI) were calculated for all parameters. Descriptive statistics including mean and standard deviation (SD) are reported for all variables. Correlation analysis between OSDI scores and the other continuous objective variables was performed using Pearson's correlation coefficient. A P value < 0.05 was considered statistically significant.

Results

During the study period a total of 754 patients scheduled for senile cataract surgery were screened for enrolment. Of these, 120 patients (62 females and 58 males; mean age 73.9 years, range 47–91 years) satisfied study criteria and were included in the analysis. Mean values and standard deviations (SD) for each parameter investigated before surgery are shown in Table 1.

All patients (100%; 95% CI [1.0–1.0]) had at least 1 abnormal result, while 19 patients (15.8%; 95% CI [0.09–0.22]) had alterations of all parameters investigated. In detail, 39 individuals (32.5% of the total; 95% CI [0.24–0.41]) had pathological TMH (mean value of 0,15 mm [0.03 SD]). One hundred and two (85%; 95% CI [0.79–0.91]) had abnormal NIKBUT FIRST values (mean value of 3.64 s [2.63 SD]), while 65 (54.2%; 95% CI [0.45–0.63]) had pathological NIKBUT AVG values (mean value of 3.89 s [3.38 SD]). According to the NIKBUT CLASS for severity staging, 82 patients (68.3% 95% CI [0.60–0.77]) were scored as pathological: of these, 29 patients (24.2%; 95% CI [0.16–0.32]) were graded as class I, 32 (26.7%; 95% CI [0.19–0.35]) as class II and 21 (17.5%; 95% CI [0.11–0.24]) as class III.

Concerning meibomian glands status, 117 patients (97.5%; 95% CI [0.95–1]) had some degree of glands dropout (mean value of 1.62 [0.70 SD]). Of these, 59 patients (49.2%; 95% CI [0.40–0.58]) as grade 1, 43 (35.8%; 95% CI [0.27–0.44]) as grade 2, 15 (12.5%; 95% CI [0.07–0.18]) as grade 3.

Table 1 Overall mean and standard deviation (SD) of analyzed parameters ($n = 120$ eyes).

Value	TMH (mm)	NIKBUT FIRST (s)	NIKBUT AVG (s)	OSDI SCORE
Mean	0.3	5.5	9.7	20.8
SD	0.2	5.4	7.3	16.3

NIKBUT First = Noninvasive Keratograph Breakup time first, NIKBUT AVG = Average Noninvasive Keratograph Breakup OSDI SCORE = Ocular Surface Disease Index questionnaire score. TMH = Tear meniscus height

Seventy-eight patients (65%; 95% CI [0.56–0.74]) had pathological OSDI scores (mean value 28.63 [15.08 SD]). Figure 1 shows the distribution of OSDI scores for each severity class.

Sixty-six patients (55%; 95% CI [0.42–0.60]) were diagnosed as affected by DED using the TFOS DEWS II criteria, since they pathological values of both OSDI score and NIKBUT first.

Coexisting pathological values of TMH, NIKBUT, meibomian gland dropout and OSDI score are shown in Figure 2.

Pearson's correlation coefficient was used to evaluate whether OSDI scores paralleled other objective variables. A weak degree of correlation was found only between OSDI score and TMH ($r = -0.22$; 95% CI −0,39 to −0,04; $p = 0.01$).

Discussion

In the present study, a preoperative screening including a combination of symptoms' questionnaire and noninvasive diagnostic workup by means of a widely used device was able to detect at least one pathological parameter in the totality of patients scheduled for senile cataract surgery. Moreover, in more than 15% of these patients, all parameters investigated fell in the pathological range. The parameter that was found most commonly altered was meibomian gland dropout followed by NIKBUT FIRST, NIKBUT CLASS, OSDI score, NIKBUT AVG and TMH. Employing the diagnostic criteria proposed in the DEWS II diagnostic methodology report, we identified that 55% of the study participants were indeed affected by an undiagnosed DED. Notably, since we investigated patients with cataract considered "otherwise healthy" (i.e., without previous diagnosis of DED or established risk factors), more than half of them would have not received a preoperative diagnosis and management of DED if not screened using noninvasive ocular surface workup and validated questionnaire. Confirming the poor/null agreement between signs and symptoms, ocular

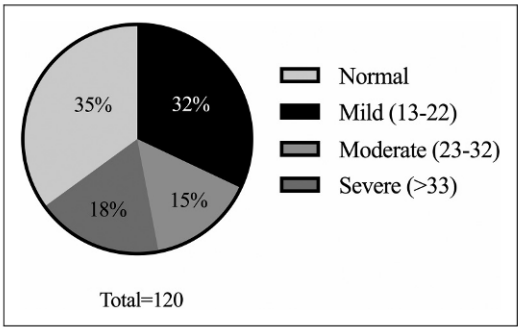

Figure 1 Pie chart showing the distribution of severity classes of dry eye disease according to ocular surface disease index score.

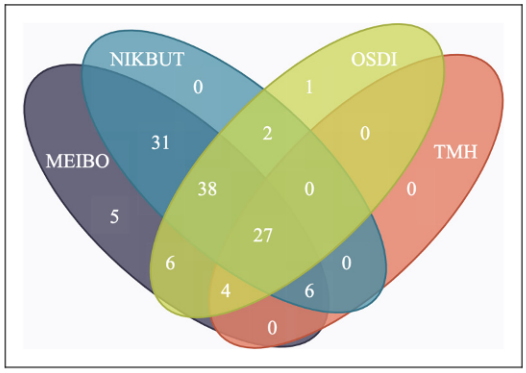

Figure 2 Venn diagram of pathological meibomian gland loss (MEIBO), Noninvasive Keratograph Breakup time (NIKBUT) considering at least one pathological value among NIKBUT first, AVG, and class, Ocular Surface Disease Index questionnaire (OSDI) and tear meniscus height (TMH).

discomfort symptoms were present in our population even in the absence of frank alterations of ocular surface parameters, and were found to be weakly correlated only with TMH. The abnormalities of the ocular surface status detected in the present study are even more impressive considering that only patients without a definite diagnosis of OSD/DED or established risk factors - except for age - were included. It is already known from large epidemiological studies (e.g., Physician's Health Study) that DED prevalence increases every 5 years after the age of 50.[11] Age-related DED is a well-recognized condition whose alterations affect various structures of the ocular surface system, from lacrimal and meibomian glands to the eyelid.[12] Recently, it has become more apparent that, similar to autoimmune DED, age-related one is characterized by a significant inflammation involving a complex immune response responsible for the profound alterations of the ocular surface.[13] Being the totality of patients undergoing senile cataract surgery older adults, this procedure is performed on a population that deserves preoperative assessment.

To our knowledge, this is the first study employing a combination of subjective questionnaire and noninvasive diagnostic tool to screen the ocular surface status of patients that are candidate to cataract surgery. Although it is difficult to directly compare our results with those reported in other studies, it should be pointed out that in all of them an impairment of various parameters of the ocular surface was reported using different combinations of tests. In particular, in the PHACO study despite upwards of 60% of routine patients screened for cataract surgery were asymptomatic, 50% of them had central corneal fluorescein staining[14]; in another study, the prevalence of OSD in patients presenting for cataract surgery was higher than 80%, and more than 50% of asymptomatic patients had an abnormal tear osmolarity or matrix metalloproteinase-9 level.[15] Furthermore, it has been reported that 52% of patients undergoing cataract surgery have clinical signs of meibomian gland dysfunction (MGD), the most common type of DED.[16] More recently, a Norwegian study employing DWES II criteria to ascertain the prevalence of DED in patients scheduled for cataract surgery found the same percentage of our study (55%); the authors highlighted that DED was associated with female sex, while, in agreement with our study, they have not found a correlation between signs and symptoms of DED.[17]

Although modern cataract surgery has been recognized as one of the most promising surgical procedures, studies have reported that postoperative outcomes are negatively affected by DED onset or worsening.[18] Despite a variety of surgery-related factors have been associated with the development of iatrogenic DED, preoperative ocular surface impairment represents the most common causative factor that can be modifiable if promptly diagnosed and treated. However, an educational gap still exists between the awareness of DED impact on cataract surgery outcomes and the efforts made by ophthalmologists to address this issue in the routine clinical practice. A recent annual ASCRS clinical survey reported that despite more than 90% of respondents felt mild-to-moderate DED affected patient satisfaction after cataract surgery, only 10% of them were using diagnostic testing in their routine preoperative assessments.[19] The most reasonable explanation is the common perception that preoperative ocular surface evaluation may be cumbersome, increasing work-up time for the surgeon. The recent rapid rise in commercially available noninvasive diagnostic tools for DED opens up a new perspective in the screening of patients undergoing cataract surgery.[20] We believe that integrating the noninvasive ocular surface diagnostics in the routine preoperative practice as a minimal workup for screening the eventual presence of pre-existing DED has little appreciable effect on patient turnover and doctor workload, while aiding in a rapid and reliable examination of the ocular surface status. Furthermore, this diagnostic tool does not require a direct contact with the eye, having little/no effect on subsequent ocular surface tests,

thus making this examination feasible by different figures of trained medical personnel (not necessarily ophthalmologists). In case of pathological results of the screening or in patients with a known DED, a variety of additional tests should be performed before surgery in order to identify DED subtype and severity, such as corneal and conjunctival staining, Schirmer's test, break-up time, meibum expression testing, corneal sensitivity and point-of-care tests such as matrix metalloproteinase 9 and tear osmolarity.[21]

The present study suffers from some limitations that deserve mentioning. Firstly, we did not complement the noninvasive work-up with the conventional tests like ocular surface staining, as recommended by the TFOS DEWS II diagnostic battery and the American Society of Cataract and Refractive Surgery (ASCRS) preoperative OSD algorithm.[10,19] Secondly, meibography was conducted on lower eyelids only. This was finalized to avoid upper lid manipulation and induced tearing with alteration of subsequent tests. However, excluding upper eyelid meibography may have tackled the comprehensiveness of our workup. Moreover, we are aware of the bias of using OSDI questionnaire in patients with cataract since this score has a high correlation with visual acuity being composed of a subsection of vision-related functions.[22] This aspect could explain the high rate of otherwise healthy and apparently asymptomatic patients reporting pathological OSDI score during this study. Finally, excluding patients with OSD/DED from the analysis could have reduced the prevalence and severity of pathological parameters detected by our workup.

In conclusion, the proposed noninvasive screening of the ocular surface status in otherwise healthy patients scheduled for senile cataract surgery documented a high prevalence of pathological findings. Since it is likely to hypothesize that these alterations could impact overall surgical outcomes, ocular surface investigation is useful before cataract surgery regardless of the presence of risk factors or the history of previous diagnosis of DED.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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