Assessment of Dry Eye Symptoms: Current Trends and Issues of Dry Eye Questionnaires in Japan

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Dry eye disease (DED) is one of the most common disease in the ophthalmic clinic, and the reasons DED patients visit ophthalmic clinics are symptoms such as stinging, burning, or scratchy sensations. The symptoms and visual disturbances of DED have a negative impact on the daily routines and social lives of the patients (i.e., their quality of life [QOL]). The presence of symptoms was required in the definition of DED by the National Eye Institute/Industry Workshop in 1995; therefore, disease-specific questionnaires were essential for monitoring and managing patients with DED. Thereafter, many questionnaires have been developed to evaluate the specific symptoms of dry eyes. Although many questionnaires are available to assess the dry eye symptoms, it is essential that they provide valid answers and are easy to use to assess the effects of DED on the QOL. The Asia Dry Eye Society and Japan Dry Eye Society have proposed a new definition of DED that is a combination of symptoms and an unstable tear film, and information on these two factors is sufficient to make a definitive diagnosis of DED. Therefore, the assessments of the symptoms are fundamental in the diagnosis of DED.

Keywords: dry eye, questionnaires, symptoms, quality of life

The aim of this study was to perform a systematic review of the dry eye-specific questionnaires and to discuss the future directions of diagnosing and treating DED in Japan.

The World Health Organization defines the quality of life (QOL) as “an individuals’ perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.”

It is a broad-ranging concept that is affected in complex ways by the person’s physical health, psychological state, level of independence, social relationships, personal beliefs, and the relationship to salient features in the environment. It has been reported that patients with dry eye disease (DED) were more negatively affected than patients without DED in performing everyday activities such as reading, computer use, professional work, driving, and watching television. Thus, the bothersome symptoms and visual disturbances of DED are recognized to have negative impacts on the daily routines and social lives of individuals, that is, their QOL. Because DED patients seek medical treatment to alleviate the irritative ocular symptoms, the goals of treating DED are to improve the patient’s ocular comfort and QOL by restoring the ocular surface and tear film to the normal homeostatic state.

Thus, a comprehensive questionnaire that assesses the symptoms and the impact of DED on the QOL is as important as the clinical findings. The report of the National Eye Institute/Industry Workshop on Clinical Trials on Dry Eyes proposed the first definition of DED in 1995, and the presence of symptoms were required in the definition of DED. In 2007, the definition of DED expanded the concept of symptoms to include visual disturbances. Thus, it has been recognized that in diagnosing DED and evaluating the therapeutic effects of different protocols on the DED, clinicians should consider the patients’ reported symptoms as well as the clinical signs.

Several studies have shown that the symptoms and their impact on the QOL in patients with DED were poorly associated with the clinical findings. This discrepancy can be explained by the natural variations of the disease processes, the subjective nature of symptoms, and the variability in pain thresholds and cognitive responses to questions about physical sensations of the eyes. Recently, the relationship between the corneal sensitivity and pain and DED have been intensively studied (e.g., severe irritations associated with reduced corneal sensitivity, corneal neuropathy in DED, and nociceptor hypersensitization from inflammation and tear hyperosmolarity).

Recently, the Tear Film and Ocular Surface Society Dry Eye Work Shop II (TFOS DEWS II) reported that the presence of both discomfort and visual disturbances were fundamental to DED. However, to avoid restrictions and maximize the relevance of this definition across the world, the current definition has added the phrase, “accompanied by ocular symptoms” to encompass a broader range of possible symptoms associated with DED. Thus, the ocular symptoms of DED remained a fundamental component and needed further discussions.

In 2014, the Asia Dry Eye Society (ADES) agreed to the following definition of DED: “Dry eye is a multifactorial disease characterized by unstable tear film causing a variety of symptoms and/or visual impairments, potentially accompanied by ocular surface damage.” The new definition also emphasized that the presence of a combination of symptoms, an unstable tear film, and a short tear film breakup time (TFBUT), was sufficient to make a definite diagnosis of DED. The criteria for diagnosing DED presented by the ADES group was followed by the Japan Dry Eye Society proposal publication titled, “Definition and Diagnosis of Dry Eye in Japan, 2016.” Thus, the assessments...
of symptoms were fundamental for diagnosing and monitoring the therapeutic effects of any type of treatment on eyes with DED.

The aim of this study was to perform a systematic review of the dry eye–specific questionnaires and to discuss the future directions of diagnosing and treating DED, especially in Japan.

METHODS

Search Strategy and Article Selection

A structured search in the PubMed/Medline databases was performed using the following medical subject headings search terms (MeSH): (surveys and questionnaires OR questionnaire OR psychometrics), (signs and symptoms OR sign OR symptom), and (ocular surface OR dry eye). We included all original articles in English describing the development and/or evaluation of one or more measurement properties, for example, internal consistency, reliability, validity, responsiveness, and symptom measurements specific for patients with DED. Articles were included if they sought to assess at least one symptom of patients with DED.

The evaluations of the articles and quality assessments were performed by two trained ophthalmologists (AS and YS). All articles were screened based on the title and abstract. Articles meeting the inclusion criteria were selected for full-text review. References of selected articles were scanned and, if suitable, included. Content validity refers to the extent to which the instrument measured the symptoms that are indicative of the objectivity.

RESULTS

The search strategy extracted 421 articles. The two reviewers screened the titles, abstracts, and the references of these articles to obtain any additional articles of relevance. All original articles describing the development and/or evaluation of one or more of the measurement properties, for example, internal consistency, reliability, validity, and responsiveness of the measures specific for patients with DED were selected for full-text review. In the end, 13 questionnaires were identified as validated questionnaires to be used for various purposes on eyes with DED.

Most questionnaires were developed to evaluate specific symptoms of dry eyes. Although the 25-item National Eye Institute Visual Function Questionnaire (VFQ-25) was not developed as a dry eye–specific questionnaire, we listed this questionnaire because it has been used to evaluate the impact of DED on the patient's QOL as an established instrument.5–5,12,21,22 The 13 listed questionnaires were developed for different purposes, for example, for clinical studies or practices to evaluate the effect of DED on the patient's QOL.5–5,12,21,22 and it has been found to be significantly correlated with the OSDI, especially the ocular pain scores.21

The OSDI is made up of 12 questions that are designed to assess both the frequency of the DED symptoms and their impact on vision-related everyday functions.20 The 12 OSDI questions are divided into three subscales: ocular symptoms, vision-related functions, and environmental triggers. Although the OSDI is widely used for diagnosis and evaluations of the severity of the symptoms, it does not fully cover the impact of DED on everyday lives, such as the psychological and social aspects of the patients.

The IDEEL is a 57-item questionnaire that was developed to evaluate the QOL, dry eye symptoms, and treatment satisfaction.27 The IDEEL has been found to have good validity and reliability and covers all relevant domains of DED. However, the IDEEL requires approximately 30 minutes for completion, and it is not easy to use routinely in a clinical practice.

The DEQs questionnaire was developed to assess the relationship between DED and QOL in Japanese. It consists of 15 items and two subscales: the impact of DED on daily life and bothersome effects of the ocular symptoms.28 The DEQs scores are significantly correlated with the mental component of the generic QOL questionnaire (SF-8; Short Form 8-Item health survey)29 and the four subscales of the VFQ-25 questionnaire, namely, ocular pain, near vision, distance vision, and mental health. The relatively short DEQs questionnaire can be used routinely in a clinical practice. The DEQs has been validated only in Japan. Therefore, translations and cross-cultural adaptation will be necessary for use of the DEQs in other countries.

The UNC DEMS is a single-item instrument that asks patients to rate their symptoms and effects of those symptoms on daily life on a scale of 1 to 10. It was created for use in clinical settings with ease of use and rapid interpretability.30 It has been validated using DED and non-DED and was found to be highly correlated with the longer OSDI test and the Minimal Clinically Important Difference Questionnaire.30–52

Two instruments, the McMonnies Dry Eye Questionnaire (MQ) and the Dry Eye Screening Questionnaire for Dry Eye Epidemiology Projects (DEEP), have been used to screen DED. The MQ consists of 12 items, most of which are dichotomous questions.53 The questions include age, sex, contact lens wear, previous diagnosis of DED, and triggers, and it assesses the frequency of dryness, grittiness, soreness, redness, tiredness, and medications used. The questionnaire has been used for DED screening in dry eye clinics.20,52

The DEEP contains 19 questions used as a screening phone interview questionnaire for cost savings and for large epidemiologic studies.34 The resulting sensitivity and specificity values are reasonably high (60% and 94%), suggesting that it could be a useful screening tool for DED in epidemiologic studies.

The Dry Eye Questionnaire (DEQ), the Standard Patient Evaluation of Eye Dryness (SPEED), the Subjective Evaluation of Symptom of Dryness (SESd), Symptoms Assessment in Dry Eye (SANDE), the Women's Health Study Questionnaire (WHS), and the Ocular Comfort Index (OCI) were developed for clinical studies or practices to diagnose or assess the severity of the DED.

The DEQ includes categorical scales to measure the incidence, frequency, diurnal intensity, and intrusiveness of vision activities, limitation of social functioning, mental health, role limitations, dependency on others due to vision, driving difficulties, difficulty with color vision, and difficulty with peripheral vision. Although the VFQ-25 is not disease specific, it has been used on patients with DED. The VFQ-25 has also been used in many studies to evaluate the impact of DED on the patient's QOL.5–5,12,21,22 and it has been found to be significantly correlated with the OSDI, especially the ocular pain scores.21
The DEQ consists of a three-item questionnaire that is used to evaluate the patients’ perception of ocular discomfort related to dryness for a clinical assessment (Simmons PA, et al. IOVS 2003;44:ARVO E-Abstract 2448). The key questions are the frequency of symptoms, the presence of discomfort, and any interference with daily activity. The SESoD assesses DED using a 5-point scale of 0 to 4. The results of this questionnaire do not differ significantly from the scores obtained by the SPEED, OSDI, DEQ, and MQ history questionnaires.

The SANDE is a short questionnaire that is based on a visual analog scale (VAS) and is used to assess the frequency and severity of the dry eye symptoms. The two items are assessed with a 100-mm VAS and scored from 0 to 100. It has not been well refined, but a recent study reported a good correlation with the OSDI and SANDE scores. The short and quick SANDE may be useful for clinical practice.

The WHS questionnaire has been used widely in population-based studies of DED, and it includes three questions pertaining to the diagnosis or the symptoms of patients with DED. An individual is considered positive for DED with reported rates of disease based on the symptoms of dryness and irritation with an answer of “often” and/or by a physician’s

<table>
<thead>
<tr>
<th>Purpose</th>
<th>Instrument Title</th>
<th>Items</th>
<th>Contents</th>
<th>Characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evaluate the impact of DED on QOL</td>
<td>National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ 25)</td>
<td>25</td>
<td>• Visual function</td>
<td>Comparable with patients with various chronic eye disease</td>
</tr>
<tr>
<td></td>
<td>Ocular Surface Disease Index (OSDI)</td>
<td>12</td>
<td>• Visual function</td>
<td>Diagnosis and assessment of severity are possible</td>
</tr>
<tr>
<td></td>
<td>Impact of Dry Eye on Everyday Life (IDEEL)</td>
<td>57</td>
<td>• Symptoms, • Visual function, • Other factors (environmental triggers)</td>
<td>Covering all relevant domains of DED and useful for assessment of the impact of dry eye on QOL, impact of treatment on patient outcomes in clinical trials</td>
</tr>
<tr>
<td></td>
<td>Dry Eye-Related Quality of Life Score Questionnaire (DEQS)</td>
<td>15</td>
<td>• Symptoms, • Visual function, • HRQL</td>
<td>Evaluates the multifaceted impact of dry eye on the patient’s daily life</td>
</tr>
<tr>
<td></td>
<td>University of North Carolina Dry Eye Management Scale (UNC DEMS)</td>
<td>1</td>
<td>• Symptoms, • HRQL</td>
<td>Single-item scale that provides a snapshot of a patient’s symptoms and QOL over the last week</td>
</tr>
<tr>
<td>Screening of DED</td>
<td>McMonnies Dry Eye Questionnaire (MQ)</td>
<td>14</td>
<td>• Symptoms, • Other factors (previous treatment, systemic condition, environment)</td>
<td>Effective for screening dry eye, but not an effective to grade disease severity</td>
</tr>
<tr>
<td></td>
<td>Dry Eye Screening Questionnaire for Dry Eye Epidemiology Projects (DEEP)</td>
<td>19</td>
<td>• Symptoms, • Other factors (contact lens wear, dry mouth, ocular allergies)</td>
<td>Useful screening tool of diagnosis dry eye</td>
</tr>
<tr>
<td>Diagnosis or assessment severity of DED</td>
<td>Dry Eye Questionnaire (DEQ)</td>
<td>21</td>
<td>• Symptoms</td>
<td>Diagnosis and assessment of severity are possible by evaluating the presence of dry eye symptoms and their severity and the time of day when they are most severe</td>
</tr>
<tr>
<td></td>
<td>Standard Patient Evaluation of Eye Dryness Questionnaire (SPEED)</td>
<td>4</td>
<td>• Symptoms, • Other factors (use of eye drops)</td>
<td>Useful as a measure of dry eye severity by monitoring diurnal and longer-term symptom changes over the course of 3 months</td>
</tr>
<tr>
<td></td>
<td>Subjective Evaluation of Symptoms of Dryness (SESoD)</td>
<td>3</td>
<td>• Symptoms</td>
<td>Evaluates a patient’s perception of ocular discomfort related to dryness for the purpose of clinical practice</td>
</tr>
<tr>
<td></td>
<td>Symptom Assessment in Dry Eye (SANDE)</td>
<td>2</td>
<td>• Symptoms</td>
<td>VAS for dry eye diagnosis and follow-up</td>
</tr>
<tr>
<td></td>
<td>Women’s Health Study Questionnaire (WHS)</td>
<td>3</td>
<td>• Symptoms, • Other factors (history of dry eye)</td>
<td>Useful for large population-based prevalence survey</td>
</tr>
<tr>
<td></td>
<td>Ocular Comfort Index (OCI)</td>
<td>12</td>
<td>• Symptoms</td>
<td>Useful for monitoring the effect of topical treatment and assessing contact lens-induced bothersome ocular symptoms</td>
</tr>
</tbody>
</table>

HRQL, health-related quality of life.
diagnosis of dry eye as reported by the participant. The results of a short WHS questionnaire has been compared with two large cohort questionnaire studies composed of 16 questions pertaining to the symptoms, and the results showed comparable sensitivity and specificity values. It was also validated against a standardized clinical examination.

The OCI was developed using Rasch analysis for a quick assessment of ocular comfort in clinical trials. It contains 12 items that assess the degree of ocular surface irritation on a linear interval scale. It has been demonstrated to have robust psychometric properties and has also been shown to be able to detect the symptoms of DED in individuals before and after treatment. It has been used to monitor the effect of topical treatments on DED symptoms and in assessing contact lens-induced DED.

**Dry Eye Questionnaires in Japan**

The report of the National Eye Institute/Industry Workshop on Clinical Trials on Dry Eyes proposed the first definition of DED in 1995, and the presence of symptoms were required in that definition. Although this requirement was absent from the Japanese definition of DED in 1995, the Japanese Dry Eye Society modified the definition and diagnostic criteria of DED, incorporating symptoms in 2006. Thus, a reliable assessment of the symptoms has also become necessary for the diagnosis or evaluating the therapeutic effects for DED in Japan. In addition, the Japan Dry Eye Society proposed in “Definition and Diagnosis of Dry Eye in Japan, 2016” that DED be defined as a “combination of symptoms and an unstable tear film.” Information on these items were sufficient to make a definitive diagnosis of DED. Thus, the assessments of symptoms are fundamental in DED for diagnosing and monitoring the therapeutic effects of any type of treatment.

The OSDI and the VFQ-25 have been used to measure the severity of the DED and as patient-reported outcomes in clinical trials and clinical studies in Japan. However, the terminology varies with the language and between different cultures and lifestyles.

The VFQ-25 is probably the most widely used questionnaire in the ophthalmic field that assesses the visual function and vision-related QOL, even though it is not a disease-specific questionnaire. The VFQ-25 has been translated into other languages, including Italian, French, German, Spanish, Turkish, Chinese, Greek, Portuguese, Arabic, and Serbian. In response to the need for evaluating vision-related QOL in the Japanese, a Japanese version of the NELVFQ-25 was developed in 2005. Because the VFQ-25 is not a dry eye-specific questionnaire, the OSDI has been often used to measure the severity or QOL in DED as a validated DED-specific questionnaire. However, there are different diagnostic criteria in different countries, especially between Japanese Dry Eye Society and TFOS DEWS II, and it is necessary to develop a specific questionnaire that can be used to evaluate the severity of the DED and QOL in Japan.

The DEQS was developed as a dry eye-specific questionnaire to respond to the increasing need for a reliable assessment of the symptoms for diagnosing and evaluating the therapeutic effect of different agents for DED in Japan. The DEQS was developed by referring to the U.S. Food and Drug Administration (FDA) guidelines for patient-reported outcome measures. A validation study was conducted to verify the psychometric validity and reliability of this questionnaire. The DEQS consists of 15 items and two subscales: impact on daily life and bothersome ocular symptoms. In the validation study, the DEQS scores were compared to the Japanese version of VFQ-25 and the SF-8. The score of each component, especially the mental component summary of the SF-8, was significantly correlated with the DEQS. When compared with the VFQ-25 “ocular pain,” which is only a subscale of the VFQ-25 and is apparently related to the typical symptoms of DED, it was strongly correlated with the summary score and each subscale score of the DEQS. A subscale of the DEQS that represents the impact on daily life was also strongly correlated with the three subscales: near vision, distance vision, and mental health. The DEQS can be easily applied in routine clinical practice and be completed in 5 minutes. It can evaluate the multifaceted impact of DED on the patient’s daily life. However, the DEQS is not a suitable questionnaire to diagnose or to assess the degree of severity of the DED, although it is a useful tool for evaluating the effect of DED on the QOL or to evaluate the treatment effects on DED.

As listed in the Table, there are different questionnaires in use to diagnose the DED, to assess the degree of severity, or to use for epidemiologic purposes. It is necessary to develop a new Japanese questionnaire for the different purposes, especially for diagnosing.

**DISCUSSION**

The bothersome symptoms and visual disturbances of DED are recognized to strongly affect the QOL, and the symptoms have been gaining importance in assessing, diagnosing, and determining the therapeutic efficacies of different treatment protocols. Therefore, the questionnaires that assess the symptoms and the impact of DED on the QOL have been gaining in importance in assessing DED. In this systematic review, we have described 13 validated questionnaires and have presented the limitations of each questionnaire. In particular, our analyses showed that there is no standardized DED-specific questionnaire.

The currently validated DED-specific questionnaires, the OSDI and IDEEL, can be used to measure the severity of the DED and as patient-reported outcomes in clinical trials. The OSDI contains 12 questions and can assess both the frequency of the DED symptoms and their impact on vision-related functions. Although the OSDI is widely used for diagnosing and evaluating the severity of the symptoms, it does not fully cover the impact of DED on patients’ everyday lives such as the psychological and social aspects. The IDEEL, which is a 57-item questionnaire, covers all the relevant domains of DED. However, IDEEL requires approximately 30 minutes for completion, and it is not easy to use in routine clinical practice. The DEQS was developed to evaluate the symptoms and impact of DED on the patient’s daily life and can be used easily in routine clinical practice. The DEQS was developed by referring to the FDA guidelines for patient-reported outcome measures to also use the DEQS for patient-reported outcomes in clinical studies. The DEQS consist of 15 items and two subscales and requires only 5 minutes for completion. Although the DEQS is a useful method to assess the severity of the DED symptoms and their impact on the QOL in the routine clinical practice, the DEQS was validated only in Japan, and it may not be sufficient for detailed evaluations of DED.

Future questionnaires used in clinical studies of DED should focus on defining the normative data and ensuring sufficient sensitivity to detect clinically significant changes in response to treatment. In addition, it is necessary to develop a global standard questionnaire for DED with appropriate translations and cross-cultural adaptations.
and damage, and neurosensory abnormalities play etiological roles.\textsuperscript{34}

ADES agreed on the definition of DED and emphasized that the combination of symptoms and an unstable tear film would be sufficient to make a definitive diagnosis of DED.\textsuperscript{18} Thus, the symptoms are fundamental to the diagnosis of DED; however, a standardized questionnaire that can be used as a diagnostic tool for DED has not been developed. The DEEP and MQ were the validated questionnaires for screening DED. The DEEP was specifically developed for screening DED in an epidemiologic study containing 19 questions.\textsuperscript{34} Although it had relatively high sensitivity and specificity values, it may not be useful for clinical practice because it is a phone interview-screening questionnaire. The MQ consists of 12 items, most of which are dichotomous questions,\textsuperscript{5,6,11} and has been used for dry eye screening in dry eye clinics.\textsuperscript{26,32} However, the MQ was designed to screen the keratoconjunctivitis sicca as DED in 1986.

The definition and the diagnostic criteria for DED have been changed and modified with better understandings of the disease processes; therefore, the questionnaires, which were designed from old information, may not be suitable for the current studies. Thus, the questionnaires that have been validated and used should be altered or modified as required to comply with the current criteria. Furthermore, the definition and the diagnostic criteria for DED have not been standardized, even between the TFOS and ADES, under the current circumstances. For a better understanding of DED for researchers and clinicians, it will be necessary to standardize the definition and the diagnostic criteria for DED. The development of standardized questionnaires for the diagnosis of DED may be also be helpful and provide a clue for standardized definition and diagnostic criteria for DED.

In conclusion, although there are many questionnaires that can evaluate DED, more research is required to develop a questionnaire that represents the symptoms of DED and better defines the normative data and clinically significant changes. Further studies are needed to develop a standardized dry eye-specific questionnaire for clinical studies and for diagnostic tools.

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\section*{References}


