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Original Research

The evaluation of dry eye mobile apps for screening of dry eye disease and educational tear event in Japan

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ABSTRACT

Purpose: To evaluate the usefulness of a dry eye mobile application (app) for screening dry eye disease (DED) at educational tear events in Japan.

Methods: In this cross-sectional study, Japanese subjects visiting a "Tears Day" event were selected randomly. They completed questionnaires and underwent ophthalmic evaluations for DED (using Japanese revised diagnostic criteria) including a functional visual acuity (FVA) test. The app calculated FVA using the average of the continuous VA over 30 s.

Results: Sixty-three general-population subjects were included: 25 men and 38 women (average age, 50.8 ± 15.9 years). The prevalence of DED was 66.7% (42 subjects); age was significantly higher among subjects with DED (55.2 ± 3.4 vs. 48.1 ± 2.7 years, $p = 0.04$; men, 54.0 ± 7.3 vs. 47.0 ± 3.0 years, $p = 0.36$; women, 55.5 ± 3.9 vs. 50.6 ± 3.8 years, $p = 0.4$). The prevalence of DED was significantly higher in women ($p = 0.04$). Tear film breakup time was significantly shorter (3.8 ± 2.4 vs. 8.7 ± 2.0, $p = 0.04$) and the meibum score was significantly higher ($p = 0.02$) among subjects with DED. Regarding the tear film breakup pattern, line and random breaks were most prevalent among DED. FVA showed a significant negative correlation with DED ($r = -0.25$, $p = 0.047$).

Conclusions: The app might motivate people to perform quick tests with the expectation of getting easy DED screening. The number of subjects diagnosed with DED was relatively high.

1. Introduction

In 2016, the Asia Dry Eye Society announced the new definition of DED as follows: "Dry eye is a multifactorial disease characterized by unstable tear film causing a variety of symptoms and/or visual impairment, potentially accompanied by ocular surface damage [1]." This new definition stresses instability of the tear film. Since the importance of the tear film has increased, in 2016, "Tears' Day" was established to increase the public's awareness of tears in Japan.

The Dry Eye Workshop II (DEWS II) reported that VDT use can be one of the main causes of DED, and especially the evaporative DED subtype [2]. There has been a dramatic increase in work performed using VDTs including smartphones in recent years. Ocular symptoms reported by VDT users include eyestrain, tiredness, irritation, a burning sensation, redness, reduced visual acuity, ocular pain, double vision, and dry eyes [3–6]. To determine whether the current working environment with increased VDT use is causing DED, a mobile application (app) called "You Can Know Whether You Have Dry Eye in a Minute" was created in 2012. This app can be downloaded for free, which enables everyone to estimate the possibility of having DED by using combined methods: functional visual acuity (FVA) measurement and four validated DED questions [7]. FVA is an index of visual function over time obtained by continuous measurement of the dynamics of visual acuity (VA). It has been reported that FVA is decreased in patients with DED despite the demonstration of normal VA in standard testing [8–13].

The aim was to evaluate the effectiveness of using an DED screening app to predict the statuses of tears and DED among the general Japanese population and disseminate DED information at educational events.

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2. Methods

2.1. Study population

This study was conducted at Kitte-marunouchi, which located in front of Tokyo Station, Tokyo, Japan, on July 4, 2017. We randomly asked subjects who visited the "Tears Event" to participate in this study. Subjects who understood the use of apps underwent dry eye screening tests including detailed dry eye examinations using a dry eye app. Subjects with a history of refractive surgery were excluded. This cross-sectional study followed the tenets of the Declaration of Helsinki. The Institutional Review Board of Hanegino Eye Clinic, Tokyo, Japan approved the protocol prospectively. Written informed consent was obtained from all participants after an explanation of the nature and possible consequences of the study.

2.2. Dry eye symptom questionnaire

The symptoms of each subject were assessed after an objective examination using the Dry Eye-Related Quality-of-Life Score (DEQS) questionnaire [14]. The DEQS questionnaire was recently developed in Japan, and its internal consistency, test-retest reliability, discriminant validity, and responsiveness to change have all been validated. The DEQS consists of 15 questions that assess bothersome ocular symptoms and their impacts on daily life. The total score ranges from 0 (best) to 100 (worst) [14].

Information on age, sex, and smoking status (current smoker or not) was also obtained. Based on our previous studies [3,5,6], we assessed the duration of VDT use (stratified, none to over 10 h in 1-h increments) and contact lens (CL) use (yes or no). A current history of certain common systemic diseases (hypertension, diabetes mellitus) was determined by asking participants whether their physician had ever told them they had these conditions. We defined systemic medication use as medication prescribed only by a doctor and not over-the-counter supplements.

2.3. Tear function and ocular surface evaluation

Ophthalmic examinations included assessments of conjunctival and corneal vital staining with fluorescein. Tear stability was assessed by the standard tear film breakup time (TBUT) measurement before the evaluation of keratoconjunctival epithelial damage. To determine the TBUT, fluorescein vital staining was performed, and patients were asked to blink three times to ensure adequate mixing of the fluorescein dye with tears. The time interval between the last complete blink and the appearance of the first corneal dark spot was measured with a stopwatch, with the mean of three measurements regarded as the TBUT in this study. Corneal and conjunctival epithelial damage were assessed separately by fluorescein staining. The eye was categorized into three equal parts representing the temporal conjunctiva, nasal conjunctiva, and cornea. All three parts were scored separately with a maximum staining score of 3 points. Overall epithelial staining severity was scored on a scale of 0–9 points. The tear film breakup pattern (TBUP) was categorized using Yokoi's classification [15]. Briefly, this classification includes five TBUPs as follows: area, spot, line, dimple, and random breaks. Area and line breaks were considered aqueous tear deficiencies; on the other hand, spot, dimple, and random breaks corresponded to the short TBUT type of DED.

Meibomian gland dysfunction (MGD) grading was performed according to a modified Bron's classification [16] as follows: grade 0, no glandular dropout and easy meibum expressibility with clear transparent meibomian secretion; grade 1, glandular dropout in one-third of the eyelid length with acinar cluster visibility in the remaining eyelid, granular secretion, difficult expressibility, and turbid, non-sticky secretion; grade 2, glandular dropout in one-third of the eyelid with loss of acinar cluster visibility but with observable yellow stripes, meibomian secretion not easily expressible, and opaque, white granular secretion; and grade 3, meibomian seborrhea with increased sticky secretion.

To avoid the influence of CL use, these examinations were performed at least 20 min after removal. To avoid variation among the examiners, N.Y. performed all tear film assessments and the MGD evaluation was performed by two ophthalmologists (M.K. and Y.U.). All examiners are members of the Japanese Dry Eye Society and specialize in ocular surface disease.

2.4. Diagnosis of dry eye disease

The latest revised version of the Japanese DED diagnostic criteria was used. Briefly, the new diagnostic criteria include only two parameters: the presence of subjective dry eye symptoms and a TBUT ≤ 5 s. A diagnosis of DED was made in the presence of two positive parameters [6].

2.5. The app "You Can Know Whether You Have Dry Eye in a minute"

The app called "You Can Know Whether You Have Dry Eye in a Minute," which is freely available, was utilized in this study (Tsubo Labo, Tokyo, Japan; Fig. 1). In detail, the app consists of two parts. One is the subjective symptom questionnaire and the other is an assessment of FVA. The questionnaire consists of four questions in total. Two are from the Women's Health Study [7], which are used commonly in epidemiological studies worldwide. In addition, two questions are included that are commonly used to screen for dry eye disease in Japan. In total, the questionnaire was as follows: 1) Do you have ocular fatigue? 2) Do your eyes feel irritated? 3)Do your eyes feel dry? 4) Do you have photophobia? The other part consisted of an FVA assessment. FVA was measured for 30 s under daily visual correction without topical anesthesia [17,18]. Subjects were allowed to blink naturally during the measurement period. Patients delineated the orientation of automatically presented Landolt rings by pressing an arrow on the smartphone. FVA was defined as the mean value change in VA over time during the examination [17,18]. If the subject fails to select the correct answer or did not provide any answer within 5 s, the Landolt rings increase in size. On the other hand, if the subject answers correctly, the Landolt rings become smaller. The FVA test was performed before all tear function examinations. From the combination of the questionnaire and FVA results, the app automatically estimated the possibility of having DED on a scale from 0 to 100. The algorithm to calculate the dry eye possibility was as follows: dry eye possibility $= -6.113 + 4.907 \times$ FVA + (eye fatigue is YES -1 or No +1) x 0.544 + (eye irritation is YES -1 or No +1) x 0.452 + (dry sensation is YES -1 or No +1) x 0.397 + (sensitivity to bright light is YES -1 or No +1) * 0.350. Finally, the app provides the user with information about the nearest ophthalmological clinic using a global positioning system. All subjects who consented to participating in this study tested the app first, which was then followed by the clinical evaluation. The clinical examiner was blinded to the results of the app test to avoid bias.

2.6. Satisfaction questionnaire

The satisfaction questionnaire was distributed to subjects who completed the DED screening. The questionnaire consisted of two questions as follows: 1) Do you think that the dry eye testing was useful? and 2) After seeing the results, do you intend to visit an ophthalmology clinic? The possible answers were yes, no, or unknown for all questions.

2.7. The educational approach to disseminate the importance of the tear film and dry eye disease

To educate subjects about the importance of the tear film, a 12-page

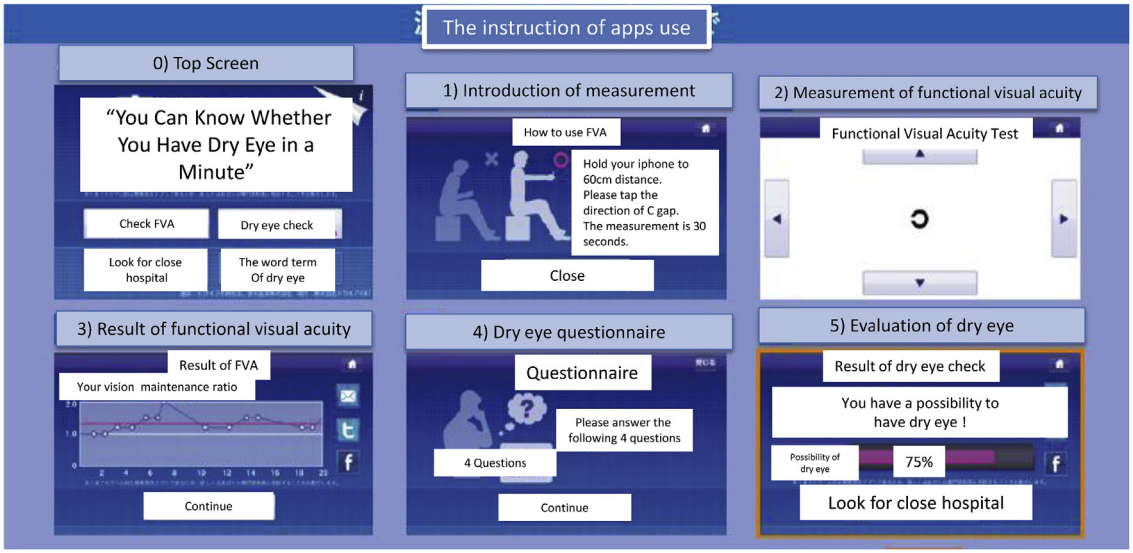


Fig. 1. The mobile application "You Can Know Whether You Have Dry Eye in a Minute".
The smartphone application enables subjects to measure functional visual acuity at anytime and anywhere.

brochure was created, and 1000 copies were distributed among Kittemarunouchi visitors on Tears Day. In addition, 712 members of the Japanese Dry Eye Society, 2245 members of the Tokyo Association of Ophthalmologists, and almost all clinics in Japan received brochures to educate patients. In addition to education regarding tears, we had two 30-min lectures about tears by M.U. and one talk show featuring a celebrity and T.K. The audience numbered approximately 100 in total. Moreover, an online educational lecture targeting ophthalmologists in Japan was performed by Y.H.

2.8. Statistical analysis

Fisher's exact test, the *U* test, and *t*-test were used to compare parameters between subjects in the DED and non-DED groups. All statistical analyses were performed using SAS software (version 9.4; SAS Inc., Cary, NC, USA). A p-value < 0.05 was considered statistically significant.

3. Results

Among the 63 subjects who consented, all completed the study, including 25 men (39.7%) and 38 women (60.3%) aged between 24 and 84 years (50.8 ± 15.9 years, average ± standard deviation [SD]; Table 1). No difference was observed between the sexes in CL or medication use ($p = 0.7$ and 0.67, respectively). However, men reported significantly longer VDT working hours than did women (7.5 ± 3.5 vs. 3.1 ± 3.3 h, $p \leq 0.001$). There was a significant sex difference between subjects in the DED and non-DED groups ($p = 0.04$). Women had a higher prevalence of DED (61.9%) compared with men (42.9%, $p = 0.04$). However, CL and systemic medication use did not show any significant difference between subjects in the DED and non-DED groups ($p = 0.1$ and 0.9, respectively).

Regarding ocular findings, subjects with DED had significantly shorter TBUTs than did subjects without DED (3.8 ± 2.4 vs. 8.7 ± 2.0, $p = 0.04$; Table 2). Almost all subjects had no ocular fluorescein staining in either group (0.07 ± 0.3 vs. 0, $p = 0.33$). In the DED group, random and line breaks were the top two TBUPs (44.7% and 36.8%) followed by dimple breaks (13.2%) and spot breaks (5.3%). No subject demonstrated an area break in this study. Almost half of the non-DED group showed no breakup within 10 s (57.1%); the remainder of the subjects who had TBUTs within 10 s all showed a random break (100%). Significant differences in TBUPs were observed between subjects with and without DED ($p = 0.03$). The most prevalent dry eye pattern was impaired wettability of the corneal surface at the breakup spot caused by tear film instability. The DED group showed higher MGD and meibum grades ($p = 0.06$ and 0.02, respectively). Among subjects diagnosed with DED, one-quarter had MGD scores of 2 or greater. However, we did not observe a significant difference in the relationship between the TBUP and meibum grade ($p = 0.46$). In detail, among subjects with a line break, 75% were MGD grade 0, 12.5% were MGD grade 1, and 12.5% were MGD grade 2. Among those with a spot break, 100% were MGD grade 0; additionally, 93.3% of subjects with a random break were grade 0. Lastly, regarding subjects with a dimple break, 40% were MGD grade 0, 20% were MGD grade 1, and the remaining 40% were MGD grade 2. The presence of conjunctivochalasis did not show significance, and no subject with or without DED had lid wiper epitheliopathy ($p = 0.2$ and 1.0, respectively). For subjective DED symptoms related to QOL, the DED group showed worse scores than the non-DED group; however, there was no statistical difference (Table 3; 16.9 ± 2.1 vs. 12.1 ± 1.8, $p = 0.14$). DED prediction results using the app did not show statistical significance between subjects with and without DED (82.5 ± 2.6 vs. 76.9 ± 4.6, $p = 0.26$). The FVA maintenance ratio measured by the app showed a significant difference between subjects with and without DED (0.76 ± 0.04 vs. 0.91 ± 0.55, $p < 0.0047$). There were significant associations between the app's DED evaluation and the total DEQS score ($r = 0.39$, $p = 0.002$) and between the app's DED evaluation and the TBUT result ($r = -0.30$, $p = 0.018$).

On the satisfaction questionnaire, 69% of subjects felt the evaluation was useful and 47% felt the need to visit an ophthalmologist for treatment.

4. Discussion

Recently, smartphones have become used widely and smartphone-based apps are available anywhere; thus, there is an increased need for apps that can easily evaluate health conditions. In resource-poor countries, the diagnosis of certain diseases such as cattle diseases has been performed using a smartphone-based app and was shown to be useful [19]. In the field of ophthalmology, an application supporting primary care physicians in diagnosing ocular disease has been developed, but there is no application that a patient can use to estimate their ocular conditions. Among eye diseases, DED is one of the most prevalent for which patients seek eye care, and there is an increased need

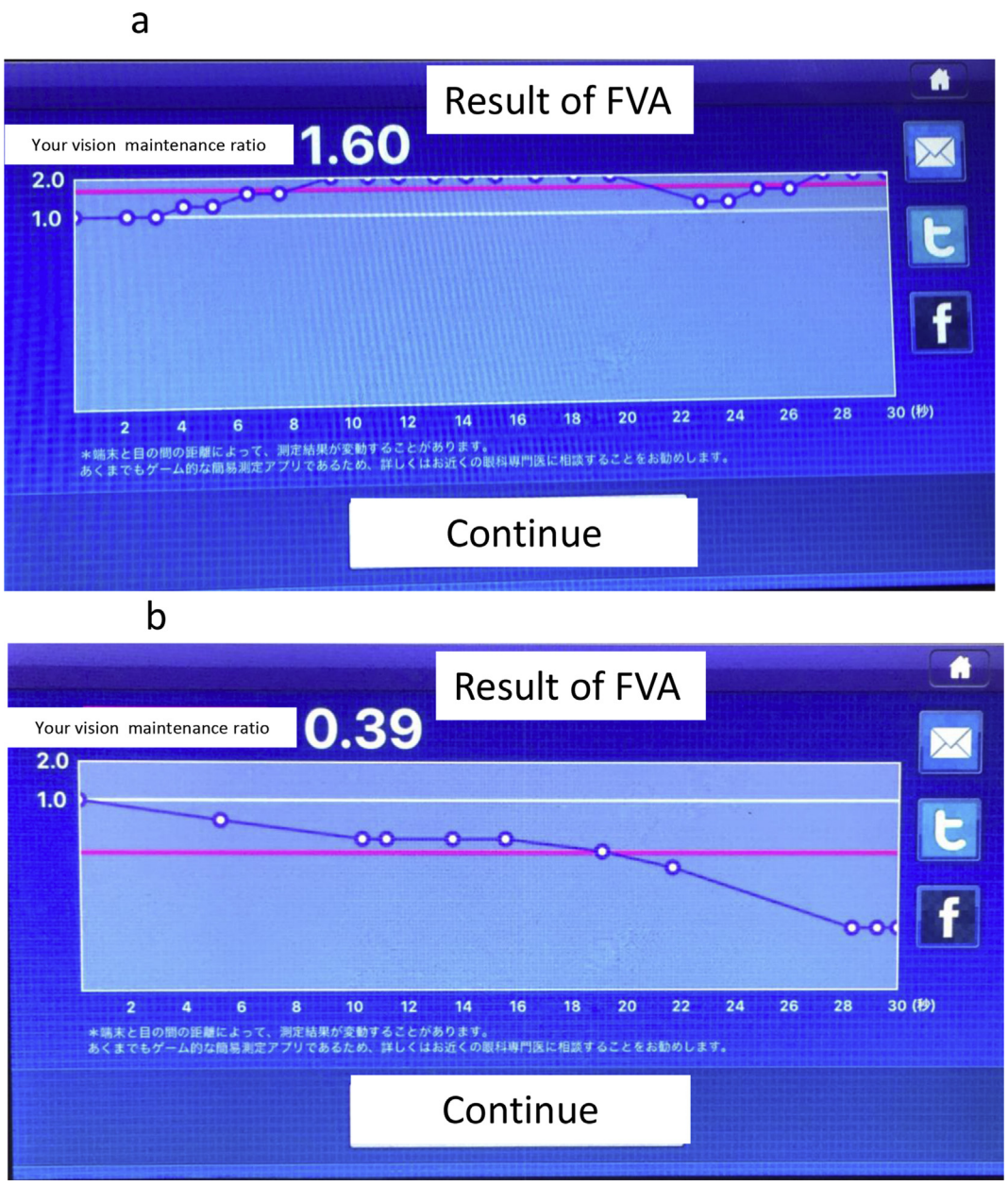


Fig. 2. A representative functional visual acuity result. **a**: The functional visual acuity of a subject with dry eye disease; functional visual acuity is maintained. **b**: The functional visual acuity of a subject without dry eye disease; functional visual acuity decreases as time elapses.

Table 1
Characteristics of the study population.

Sex	Male	Female	Total	P-value
Number	25 (%)	38 (%)	63	
Age, years (± the SD)	48.1 ± 13.7	52.5 ± 17.1	50.8 ± 15.9	0.29
VDT working hours	7.5 ± 3.5	3.1 ± 3.3	4.8 ± 3.9	< 0.001
CL use	7 (28.0)	9 (23.7)	16 (25.4)	0.7
Medication use	7 (29.2)	9 (24.3)	16 (26.2)	0.67

SD: standard deviation, VDT: visual display terminal, CL: contact lens.

Table 2
Associations between dry eye disease and demographic characteristics.

Number	Dry Eye	Non Dry Eye	P value
	42 (%)	21 (%)	
Age, years (± the SD)	53.7 ± 15.9	44.9 ± 10.8	0.04
The female sex	29 (61.9)	9 (42.9)	0.04
VDT working hours	4.1 ± 4.0	6.2 ± 3.8	0.04
CL use	8 (19.1)	8 (38.1)	0.1
Medication use	11 (26.8)	5 (25.0)	0.9

SD: standard deviation, VDT: visual display terminal, CL: contact lens.

for applications that can evaluate the ocular condition including TBUT. This study evaluated the effectiveness of using an app called “You Can Know Whether You Have Dry Eye in a Minute.” This application does not directly evaluate the status of the cornea including the TBUT; however, it enables patients to calculate their FVAs. FVA is well known to have a statistically negative correlation among DED subjects [9], and the measurement of FVA can be an alternate method to screen for DED. In this study, we found a significant reduction in FVA among subjects with DED. Subjects without DED had higher VA maintenance ratios, which imply stable VAs over 30 s (0.91 ± 0.55%). On the other hand, subjects with DED had lower VA maintenance ratios and unstable VAs

Table 3
Associations between dry eye disease and ocular findings.

Number	Dry Eye	Non Dry Eye	P value
	42	21	
TBUT	3.8 ± 2.4	8.7 ± 2.0	0.04
Fluorescein staining	0.07 ± 0.3	0	0.33
MGD			
0	1 (2.4)	21 (100)	0.06
1	30 (71.4)	0	
2	8 (19.1)	0	
3	3 (7.1)	0	
Meibum	0.45 ± 0.1	0.10 ± 0.1	0.02
Chalasis	0.28 ± 0.1	0.10 ± 0.1	0.2
Lid Wiper	0	0	1
Total DEQS score	16.9 ± 2.1	12.1 ± 1.8	0.14

SD: standard deviation; TBUT: tear film breakup time; MGD: meibomian gland dysfunction; DEQS: Dry Eye-Related Quality-of-Life Score.

(0.76 ± 0.04%, p = 0.0047). Kaido et al. reported using a discriminant equation obtained using FVA measurements combined with symptoms and stated that it can be a screening method for DED [11]. They used standard FVA measurements in the clinic rather than app-based FVA measurements. It used to be difficult for subjects to measure their FVAs at anytime and anywhere. A screening instrument is ideal if it is demonstrably simple, quick to administer, and easy to use. In this light, our app is a useful tool that can measure FVA at anytime as long as there is a smartphone available.

The app also showed the possibility of detecting DED based on a score ranging from 0–100. Interestingly, our results show that subjects with DED had a higher probability of having DED according to the app; however, there was no statistical significance (82.5 ± 2.6 vs. 76.9 ± 4.6, r = −0.24, p = 0.26). The reasons for the lack of significance remain unknown; however, it is possible that the questions included in the app might not be adequate to detect Japanese dry eye symptomatology. In addition, the revised Japanese criteria include only the TBUT and a questionnaire; therefore, it might lack specificity in evaluating DED. There was a significant association between the app's evaluation and the total DEQS score (p = 0.002). Interestingly, we also found an association between the result from the app and the TBUT (p = 0.018). The app itself might similarly detect and measure TBUT in addition to providing an evaluation of DED for users worldwide.

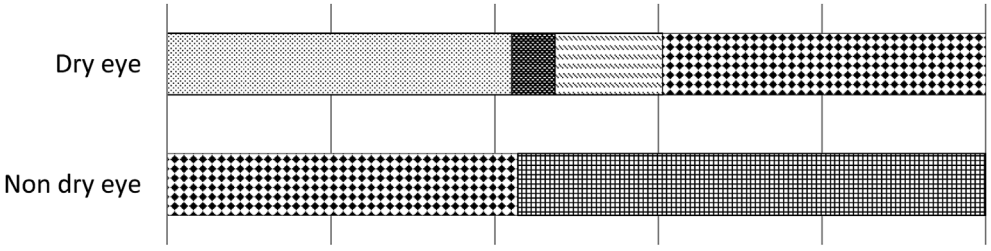
Other than the utilization of an app, this is the first study evaluating TBUPs among the general population including non-DED subjects. We found that among subjects without DED, 12 did not show any tear film breakup until 10 s (Fig. 3). Among the remaining nine subjects who showed TBUTs of 5–10 s, all showed the random-type TBUP. On the other hand, random and line breaks were most prevalent among subjects with DED (44.7% and 36.8%, respectively).

Yokoi et al. reported that a random break was considered the result of increased evaporation of aqueous tears [15]. A line break has been demonstrated to have decreased aqueous tear thickness at the lower cornea from the uptake of water by the low meniscus, and also from the upward drag of aqueous tears by the tear film lipid layer. This study revealed that subjects without DED had complete establishment of a tear film, which then showed breakup after 5 s of eye opening. The relationship between area breaks and tear volume was not clear in this study. Since we did not measure tear secretions using the Schirmer I test or another measurement system, we could not evaluate factors influencing TBUPs and tear secretion.

Interestingly, this study showed a high satisfaction rate for the DED evaluation. A campaign or educational event such as the one in this study might play an important role in determining ocular surface conditions. In addition, almost half of the subjects felt the need for DED treatment at a clinic. To reduce disease, prevention using screening tools and increasing the patient's understanding of the condition are important. This screening app might provide important information to evaluate daily FVA and maintain their current condition.

The results of this study may provide guidance for specific precautions such as brief periods of rest during VDT work, the provision of information and guidance on dry eye related problems, and the adoption of relevant policies in workplaces to prevent ophthalmic disorders such as DED during VDT work.

We acknowledge several limitations to this study. Less than 100 subjects participated in this study. To evaluate the true prevalence of DED in an urban setting, we need to establish a population-based study enrolling thousands of subjects. Second, this study was performed at a celebration of Tears Day, so this location might have included a greater proportion of subjects who were interested in tears than in the general population, which may have induced a selection bias. A decrease in FVA from other types of ocular disease has been reported previously; however, we did not consider this factor in the present study. Moreover, the symptomatology questionnaire that is included in the app should be modified to make the diagnosis more accurate. In the near future, we need to establish a study that takes ocular comorbidities and FVA into account by using a different symptomatology questionnaire to understand false-positive results.



	Non dry eye	Dry eye
Area	0	0
Line	0	16
Spot	0	2
Dimple	0	5
Random	9	15
No Brake	12	0

Fig. 3. Distributions of tear breakup patterns among the subjects. All subjects without dry eye disease show random breaks. In subjects with dry eye disease, line and random breaks are more prevalent.

In conclusion, DED App might motivate people to perform quick tests with the expectation of getting easy DED screening. By utilizing this app, subjects might be able to discern their dry eye status based on Japanese criteria anytime and anywhere without visiting an eye clinic. The features of DED in the Japanese population showed a low TBUT and higher prevalence among women. Although further studies are needed to increase our understanding of the importance of this public health problem, the results of this study may increase the awareness of methods to evaluate DED easily.

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Conflicts of interest

Miki Uchino, Motoko Kawashima, Yuichi Uchino, Hiroto Mitamura, Miki Mizuno, and Natume Sizuki declare that they have no conflicts of interest.

Yuichi Hori: Consultant and research funding from Santen Pharmaceutical Co., Ltd. and Otsuka Pharmaceutical Co., Ltd.

Norihiko Yokoi: Consultant for Kissei Co, Ltd, Alcon Japan Ltd., and Rohto Co, Ltd.

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