Original Article

Association of pupil responses with severity of erectile dysfunction in diabetes mellitus

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Purpose: To investigate the relation between erectile dysfunction (ED) severity and pupillary functions in patients with diabetes mellitus (DM). **Methods:** This prospective and observational study included 90 patients with type 2 DM and ED. Patients divided into three subgroups according to severity of ED: (i) Mild ED, (ii) Moderate ED and (iii) Severe ED groups. Thirty age-matched healthy subjects formed the control group. Main outcome measures were pupil diameter and average speed of pupil dilation. Static and dynamic pupillometry analysis was performed using the Sirius Topographer (CSO, Firenze, Italy). **Results:** Mean pupil diameter during static and dynamic pupillometry analysis were significantly greater in the control group than in the all study groups ($P < 0.05$). Mean pupil diameter in static pupillometry analysis was significantly different in each study group and pupil was more miotic in the Severe ED group than in the both Moderate and Mild ED groups ($P < 0.05$ for each). Dynamic pupillometry analysis revealed that mean pupil diameter and mean average dilation speed were significantly different in each study group throughout measurement period and the highest speed was observed in the Mild ED group and the lowest speed was observed in the severe ED group ($P < 0.005$ for each). **Conclusion:** Our study results suggest that abnormal pupil functions due to diabetic autonomic neuropathy may indicate the associated ED in patients with DM.

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Diabetes mellitus (DM) is a common systemic metabolic disorder, and a significant proportion of the population all around the world suffers from the long-term damage related to DM, such as neuropathy.[1] Diabetic autonomic neuropathy (DAN) is associated with increased mortality and morbidity in patients with DM, and it affects the cardiovascular, gastrointestinal, and genitourinary systems as well as the eye.[2-4] Pupil functions are under the control of the autonomic nervous system, and, in the literature, DAN has been reported to be associated with abnormal pupil responses.[4,5]

DAN causes a wide spectrum of clinical manifestations including erectile dysfunction (ED)[2] which is defined as the persistent inability to attain and maintain erection sufficient for satisfactory sexual performance.[6] Cardiovascular diseases, hypertension, hyperlipidemia, smoking, and medication side effects are the common causes of ED.[7] DM also appears to be one of the most common etiologic causes of ED.[8,9] The underlying pathophysiological mechanism of diabetic ED is multifactorial, and it is based on vasculopathy and neuropathy.[8,9] Diabetic autonomic and peripheral neuropathy may cause and induce ED, since the penis is innervated by both autonomic and sensory nerves.[8,10] In the literature, several studies have highlighted that the stage of diabetic retinopathy (DR) is associated and correlated with the severity of ED.[11,12]

Previous studies have focused on the relation between the severity of DR and pupil responses and ED.[11,13] Although both pupil responses and ED share some similar underlying mechanisms, no study has directly investigated the correlation between static and dynamic pupil responses and ED. The present study aimed to investigate the relation between ED severity and pupil functions in patients with DM, and to evaluate the predictive value of static and dynamic pupil responses on the severity of ED.

Methods

This prospective and observational study was conducted at the ophthalmology department of a tertiary hospital in accordance with the ethical standards of the Declaration of Helsinki. The study protocol was approved by the institutional board of our hospital's ethics committee. All participants provided written informed consent prior to undergoing all examinations.

Patients with type 2 DM and ED, and age-matched healthy controls, who met the eligibility criteria, were included in the study. Patients with the following conditions were excluded: corrected distance visual acuity <20/50 in the Snellen chart, history of ocular trauma or surgery, uveitis, glaucoma, pseudoexfoliation syndrome,

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anterior or posterior synechiae, grade 3–4 cataract, congenital or acquired iris and pupil anomalies, history of optic neuropathy, retinal diseases that may affect pupil functions, permanent use of topical medications, panretinal laser photocoagulation at any time, and focal laser photocoagulation or intravitreal injection in the previous 6 months. Patients with systemic diseases that affect the central nervous system and the genitourinary system, except DM, were also excluded. Patients with cardiovascular diseases, arterial blood pressure >140/90 mmHg, psychological disorders, thyroidal disorders, anemia, use of drugs that may cause ED, use of drugs that increase sexual performance, history of hormone supplementation, electrolyte imbalance, and history of pelvic, penile, or perineal surgery were also excluded. Smoker subjects were excluded only in the control group to set a baseline for the outcomes, whereas they were not excluded in the study groups. Patients with proliferative DR (PDR) that have recently been diagnosed and had no treatment history were included in the study.

All subjects underwent a complete physical examination, and all the findings and previous medical history were noted. Body mass index (BMI) was calculated as body weight (in kg) divided by the square of the person's height (in cm). Duration of DM, history of smoking, use of antihypertension medication and lipid-lowering medication was noted. Type 2 DM diagnosis was approved by the Endocrinology Department at our hospital. The most recent glycated hemoglobin (HbA1c) level was noted. All ophthalmological examinations were performed by the same clinician. All patients underwent a complete ophthalmological examination including corrected distance visual acuity testing with Snellen chart, non-contact tonometry, and slit-lamp biomicroscopy. Following full mydriasis, slit-lamp biomicroscopy of the fundus were performed. DR stage classified based on the finding of fundus examination, fundus photography, fundus florescein angiography, and optical coherence tomography. Patients with DR were classified as non-proliferative DR (NPDR) and PDR based on the Early Treatment of Diabetic Retinopathy Study criteria.[14] Only the data of the right eye of all patients were used in the statistical analysis. ED was diagnosed according to physical examination, sexual activity history, and the Turkish version of the International Index of Erectile Function (IIEF)[15] questionnaire scores. All patients completed the Turkish version of the IIEF in a single session without any assistance. The IIEF is a reliable screening test; it evaluates the clinical severity of ED within the past 6 months.[15] Cronbach's alpha reliability coefficient of the Turkish version of the IIEF was 0.959.[15] The IIEF score ranges between 1 and 25, and a score <22 indicates ED.[15] The severity of ED was evaluated according to the total IIEF score; a score of 1–7 indicates severe ED, a score of 8–11 indicates moderate ED, a score of 12–21 indicates mild ED, and a score of 22–25 indicates no ED.[15]

The study group consisted of patients with type 2 DM and ED; the study group was divided into three subgroups based on the severity of ED. Patients with mild ED comprised the Mild ED group, patients with moderate ED comprised the Moderate ED group, and patients with severe ED comprised the Severe ED group. The control group consisted of age-matched healthy and non-smoker subjects.

Pupil responses were evaluated with the automated pupillometry function of the Sirius Topographer (CSO, Firenze, Italy) using Phoenix v2.1 software (Costruzione Strumenti Oftalmici, CSO, Firenze, Italy). All measurements were performed on the right eye of the subjects in the study group and the control group. All measurements were performed by the same experienced clinician who was blinded to medical conditions of the subjects; measurements were taken at the same time of the day (10:00–12:00 am) to minimize the effect of circadian changes in the pupillary response.[16] All measurements were performed based on Prakash *et al.*'s method.[17] The measurements were performed after a dark adaptation interval of 5 minutes, which was followed by scotopic measurement at illumination of 0.4 lux, mesopic measurements at illumination of 4 lux, and photopic measurements at illumination of 40 lux. LED lighting was the only light source in the room, and the illumination conditions were tested and adjusted using a photometer. During the measurements, the subjects were advised to look straight ahead, not at the light source, to prevent the accommodative response. After the static pupil measurements were completed, dynamic pupil measurements were performed. Dynamic measurement started at illumination of 500 lux; after the measurement began the illumination was switched off until the end of the session. Thus, this technique makes it possible to monitor pupil responses in conditions ranging from photopic to scotopic, and to evaluate the pupil size and offset instant by instant [Fig. 1].

For dynamic pupil measurements, the following equation was used to calculate the speed of change in pupillary diameter: Average speed (mm/s) was the overall average speed until that time,

$$V_{average} = ([\delta\Phi_t - \Phi_{t0}]/t)$$

Where δΦ is the difference in the pupil diameter (mm) between time (s) at the time of measurement and at $t = 0$.

Statistical analyses were performed with SPSS Statistics (Version 22.0, Armonk, NY: IBM Corp). The assumption of normal distribution of data was tested by the Shapiro-Wilk test. Differences in descriptive data between groups were tested with the Chi-square test. Differences in the outcomes between the groups were tested with one-way analysis of variance and Kruskal-Wallis test. LSD post-hoc test was used for subgroup analysis. A level of $P < 0.05$ was assumed statistically significant for all tests.

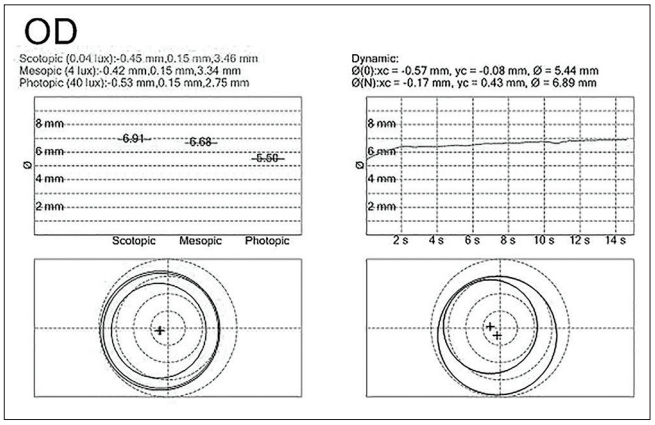


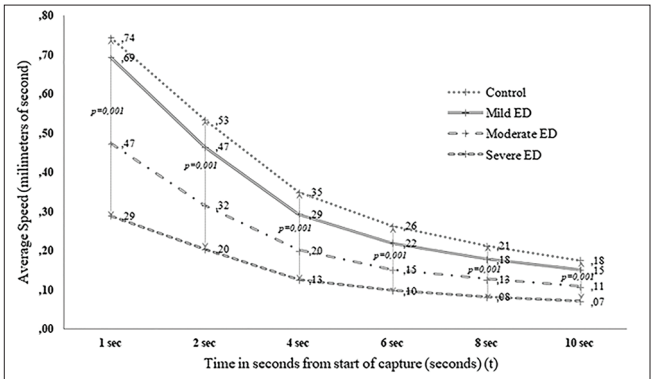
Figure 1: An output of pupillometry analysis of Sirius Topographer (CSO, Italy). The pupil diameters under different illumination conditions are shown and the legends indicate the centroid location (x, y) and pupil diameter on the left side of the output graph. Right side of the graph shows the output of dynamic pupillometry analysis and the legend indicates centroid location (x, y) and the pupil diameter at a particular time

Results

A total of 120 men who met the eligibly criteria were included in the study. The control group consisted of 30 healthy men with a mean age of 53.8 ± 6.5 years (min: 38 years, max: 62 years). The study group consisted of 90 men with DM and ED. Of the 90 men in the study group, 30 were included in the Mild ED group, 30 were included in the Moderate ED group, and 30 were included in the Severe ED group. Table 1 shows the demographic data and clinical characteristics of the study groups and a comparison of the groups. No statistically significant difference was found between the study and control groups regarding mean age ($P > 0.05$). The mean duration of DM was significantly higher in the Severe ED group than in the Mild ED group, while no significant difference was observed between Mild and Moderate ED groups and Moderate and Severe ED groups. No significant difference was observed between the study groups regarding the last HbA1c levels, BMI, smoking, use of anti-hypertension medications, and use of lipid-lowering medications ($P > 0.05$ for each). Distribution of DR classification among the subjects showed that the number of the subjects with PDR was significantly higher in the Severe ED group; the number of the patients with no DR was significantly higher in Mild ED group than the other study groups ($P < 0.001$).

Table 2 shows the results of the static (scotopic, mesopic, and photopic) and dynamic pupillometry analysis, and a comparison of the groups. Mean pupil diameter during static (scotopic, mesopic, and photopic) and dynamic pupillometry analysis were significantly greater in the control group than the study groups. In the scotopic pupillometry analysis, the mean pupil diameter was significantly different in each of the study groups; it was highest in the Mild ED group and lowest in the Severe ED group. In the mesopic pupillometry analysis, the mean pupil diameter was significantly lower in the Severe ED group, but no significant difference was observed between the Mild ED and Moderate ED groups. Dynamic pupillometry analysis revealed that the mean pupil diameter was significantly different in each study group at the 1st, 2nd, 4th, 6th, 8th, and 10th second after the measurement started; it was highest in the Mild ED group and lowest in the Severe ED group.

Fig. 2 shows the change of average speed of pupil dilation based on the time; it also shows a comparison of the results between the groups. Mean average speed of pupillary dilation at the 1st, 2nd, 4th, 6th, 8th, and 10th second after the measurement started was significantly lower in the study groups than the control group ($P < 0.05$ for each). Mean average pupillary dilation speed during the measurement period was significantly different in each study group; the highest speed was observed in the Mild ED group and the lowest speed was observed in the Severe ED group.



1st second (mm/s): p=0.05 in Control vs. Mild ED, p <0.001 in Control vs. Moderate ED, p <0.001 in Control vs. Severe ED, p<0.001 in Mild ED vs. Moderate ED, p <0.001 in Mild ED vs. Severe ED.and p <0.001 in Moderate ED vs. Severe ED.**

2st second (mm/s): p=0.02 in Control vs. Mild ED, p <0.001 in Control vs. Moderate ED, p <0.001 in Control vs. Severe ED, p<0.001 in Mild ED vs. Moderate ED, p <0.001 in Mild ED vs. Severe ED,and p <0.001 in Moderate ED vs. Severe ED.**

4th second (mm/s): p=0.003 in Control vs. Mild ED, p <0.001 in Control vs. Moderate ED, p <0.001 in Control vs. Severe ED, p<0.001 in Mild ED vs. Moderate ED, p <0.001 in Mild ED vs. Severe ED,and p <0.001 in Moderate ED vs. Severe ED.**

6th second (mm/s): p=0.004 in Control vs. Mild ED, p <0.001 in Control vs. Moderate ED, p <0.001 in Control vs. Severe ED, p<0.001 in Mild ED vs. Moderate ED, p <0.001 in Mild ED vs. Severe ED,and p <0.001 in Moderate ED vs. Severe ED.**

8th second (mm/s): p=0.005 in Control vs. Mild ED, p <0.001 in Control vs. Moderate ED, p <0.001 in Control vs. Severe ED, p<0.001 in Mild ED vs. Moderate ED, p <0.001 in Mild ED vs. Severe ED,and p <0.001 in Moderate ED vs. Severe ED.**

10th second (mm/s): p=0.11in Control vs. Mild ED, p <0.001 in Control vs. Moderate ED, p <0.001 in Control vs. Severe ED, p<0.001 in Mild ED vs. Moderate ED, p <0.001 in Mild ED vs. Severe ED,and p <0.001 in Moderate ED vs. Severe ED.**

*One-way analysis of variance was used.

**LSD post-hoc test was used

Figure 2: The average speed of pupillary dilatation by the given time and comparison of the results between groups

Table 1: Demographic and clinical characteristics of the Mild ED (*n*=30), Moderate ED (*n*=30), and Severe ED (*n*=30) groups

	Mild ED group Mean±SD (range)	Moderate ED group Mean±SD (range)	Severe ED group Mean±SD (range)	*P**
Age (years)	54.96±7.03 (39-64)	54.36±7.37 (40-60)	56.66±5.20 (44-63)	0.512*
HbA1c (%)	9.12±2.14 (6.20-13.60)	9.11±2.42 (6.0-15.80)	9.15±1.94 (6.0-14.20)	0.967*
DM duration (years)	11.90±5.78 (5-23)	14.16±4.63 (8-26)	16.66±5.38 (8-32)	<0.003*[a]
BMI (kg/m^2)	30.32±3.68 (23.73-42.77)	29.09±3.97 (18.81-36.29)	29.01±4.58 (20.98-39.25)	0.436*
Smokers/Non-smokers, (*n*/*n*)	15/15	17/13	15/15	0.837**
Anti-hypertension medication (*n*, %)	13 (29.5)	14 (31.8)	17 (36.6)	0.561**
Lipid lowering medication (*n*, %)	12 (34.3)	11 (31.4)	12 (34.3)	0.954**
DM classification				
No-DR (*n*, %)	14 (70)	4 (20)	2 (10)	0.001**
NPDR (*n*, %)	13 (37.1)	13 (37.1)	9 (25.7)	
PDR (*n*, %)	3 (8.6)	13 (37.1)	19 (54.3)	

ED=Erectile dysfunction; HbA1c=Glycated hemoglobin; DR=Diabetic retinopathy; NPDR=Non-proliferative diabetic retinopathy; PDR=Proliferative diabetic retinopathy; SD=Standard deviation; DM=Diabetes mellitus; BMI=Body mass index. *Kruskal-Wallis test. *Chi-square test. [a]*P*=0.071 in Mild ED vs Moderate ED, *P*=0.001 in Mild ED vs Severe ED, and *P*=0.644 in Moderate ED vs Severe ED

Table 2: The results of pupil responses in the control (*n*=30), Mild ED (*n*=30), Moderate ED (*n*=30), and Severe ED (*n*=30) groups

	Control group mean±SD (range)	Mild ED group mean±SD (range)	Moderate ED group mean±SD (range)	Severe ED group mean±SD (range)	*P**
Static Pupillometry					
Scotopic (mm)	5,19±0,51 (4,22-6,39)	4,44±0,82 (3,3-6,42)	4,16±0,81 (2,58-5,86)	3,66±0,77 (2,01-5,21)	<0.001[a]
Mesopic (mm)	4,60±0,64 (3,46-5,84)	3,98±0,72 (3,09-5,95)	3,82±0,69 (2,33-5,41)	3,45±0,72 (1,81-4,59)	<0.001[b]
Photopic (mm)	3,59±0,55 (2,48-5,12)	3,27±0,48 (2,58-4,45)	3,20±0,62 (2,16-4,32)	3,05±0,65 (1,7-4,38)	<0.003[c]
Dynamic pupillometry					
0th second (mm)	3,40±0,46 (2,68-4,59)	3,08±0,39 (2,49-4,04)	3,03±0,52 (2,06-3,96)	2,94±0,66 (1,66-4,31)	<0.004[d]
1st second (mm)	4,15±0,42 (3,53-5,32)	3,77±0,43 (3,14-4,64)	3,50±0,61 (2,42-4,75)	3,23±0,64 (1,71-4,37)	<0.001[e]
2nd second (mm)	4,47±0,39 (3,88-5,47)	4,01±0,46 (3,3-4,84)	3,66±0,66 (2,42-5,18)	3,34±0,67 (1,76-4,5)	<0.001[f]
4th second (mm)	4,80±0,41 (4,07-5,77)	4,26±0,52 (3,45-5,24)	3,84±0,72 (2,53-5,47)	3,44±0,72 (1,76-4,59)	<0.001[g]
6th second (mm)	4,98±0,44 (4,41-5,97)	4,40±0,58 (3,57-5,47)	3,94±0,76 (2,56-5,73)	3,53±0,73 (1,78-4,73)	<0.001[h]
8th second (mm)	5,11±0,47 (4,29-6,29)	4,51±0,61 (3,65-5,80)	4,05±0,77 (2,65-5,73)	3,60±0,75 (1,79-4,83)	<0.001[i]
10th second (mm)	5,16±0,43 (4,29-6,37)	4,59±0,60 (3,75-5,8)	4,12±0,76 (2,72-5,83)	3,65±0,76 (1,8-5,0)	<0.001[j]

ED=Erectile dysfunction, SD=Standard deviation. * One-way analysis of variance was used. a) *P*<0.001 in Control vs Mild ED, *P*<0.001 in Control vs Moderate ED, *P*<0.001 in Control vs Severe ED, *P*=0.046 in Mild ED vs Moderate ED, *P*<0.001 in Mild ED vs Severe ED, and *P*<0.001 in Moderate ED vs Severe ED. **b) *P*<0.001 in Control vs Mild ED, *P*<0.001 in Control vs Moderate ED, *P*<0.001 in Control vs Severe ED, *P*=0.391 in Mild ED vs Moderate ED, *P*=0.004 in Mild ED vs Severe ED, and *P*=0.037 in Moderate ED vs Severe ED.** c) *P*<0.001 in Control vs Mild ED, *P*=0.03 in Control vs Moderate ED, *P*=0.09 in Control vs Severe ED, *P*=0.66 in Mild ED vs Moderate ED, *P*=0.14 in Mild ED vs Severe ED, and *P*<0.30 in Moderate ED vs Severe ED.** d) *P*=0.016 in Control vs Mild ED, *P*=0.005 in Control vs Moderate ED, *P*=0.001 in Control vs Severe ED, *P*=0.69 in Mild ED vs Moderate ED, *P*=0.27 in Mild ED vs Severe ED, and *P*=0.49 in Moderate ED vs Severe ED.** e) *P*<0.001 in Control vs Mild ED, *P*=0.007 in Control vs Moderate ED, *P*<0.001 in Control vs Severe ED, *P*=0.05 in Mild ED vs Moderate ED, *P*<0.001 in Mild ED vs Severe ED, and *P*=0.046 in Moderate ED vs Severe ED.** f) *P*<0.001 in Control vs Mild ED, *P*=0.002 in Control vs Moderate ED, *P*<0.001 in Control vs Severe ED, *P*=0.017 in Mild ED vs Moderate ED, *P*<0.001 in Mild ED vs Severe ED, and *P*<0.001 in Moderate ED vs Severe ED. **g) *P*<0.001 in Control vs Mild ED, *P*<0.001 in Control vs Moderate ED, *P*<0.001 in Control vs. Severe ED, *P*=0.008 in Mild ED vs Moderate ED, *P*<0.001 in Mild ED vs Severe ED, and *P*<0.013 in Moderate ED vs Severe ED. **h) *P*<0.001 in Control vs Mild ED, *P*<0.001 in Control vs Moderate ED, *P*<0.001 in Control vs Severe ED, *P*=0.06 in Mild ED vs Moderate ED, *P*=0.013 in Mild ED vs Severe ED, and *P*<0.001 in Moderate ED vs Severe ED. **i) *P*<0.001 in Control vs Mild ED, *P*<0.001 in Control vs Moderate ED, *P*<0.001 in Control vs Severe ED, *P*=0.08 in Mild ED vs Moderate ED, *P*<0.001 in Mild ED vs Severe ED, and *P*<0.001 in Moderate ED vs Severe ED. **j) *P*<0.001 in Control vs Mild ED, *P*<0.001 in Control vs Moderate ED, *P*<0.001 in Control vs Severe ED, *P*<0.001 in Mild ED vs Moderate ED, *P*<0.001 in Mild ED vs Severe ED, and *P*<0.001 in Moderate ED vs Severe ED.** **LSD *P*ost-hoc test was used

Discussion

In the literature, previous studies have revealed the relation between DM and both ED and pupil functions,[3,11,12,18] however, the direct relation between ED severity and pupil functions in patients with DM has not been investigated. Our results showed that both static and dynamic pupil functions were better in healthy patients than in patients with both DM and ED. Furthermore, our results provided significant evidence for the association between the severity of ED and the severity of impairment of static and dynamic pupil functions in patients with type 2 DM.

ED is defined as the chronic inability to attain and maintain sufficient erection.[6] Vascular diseases, obesity, smoking, metabolic syndrome, hyperlipidemia, depression, medication side effects, DM, and neuropathy may contribute to ED.[7,19] DM is an independent risk factor for ED, and its association with neuropathy has been well documented.[5,12,20] It has been reported that DAN is a common pathophysiologic disorder of both ED and abnormal pupil function in DM.[3,4,7,9] Stimulation of the parasympathetic neural pathways relaxes the smooth muscle of the corpus cavernosum and induces erection.[21] DAN damages the transmission of the autonomic stimulation causing ED.[21] Although DAN is strongly associated with ED, it is not the only major underlying factor.[8,9,21] The multifactorial basis of ED and the technical challenges for assessing DAN complicate the diagnosis of ED, making it challenging to assess its dominance over other etiologic factors in patients with DM.[21] An appropriate assessment of DAN requires a complete physical examination, long-term screening of the clinical signs, and complete participation and compliance from patients. New, simple, and reliable assessment techniques for DAN may provide insights into DAN-related disorders.

Appropriate pupil response requires functional and robust neural pathways. Wang *et al.* emphasized that dilation of the pupil requires both parasympathetic and sympathetic innervation of the iris.[22] Basically, dynamic pupillometry analysis evaluates the change of pupil diameter based on time; thus, evaluation of the dilation speed can be used to estimate the autonomic neural activity of the iris. Our study results showed that the mean pupil dilation speed decreased as the ED severity increased in the study groups. DAN is known to affect the autonomic nerve ending in the iris muscles, thereby affecting muscle activity.[23] Consistently, Jain *et al.* noted that decreased dilatation velocity indicates dysfunction of the autonomic neural pathways in DM.[13] Yang *et al.* suggested that dilation of the pupil mediated by autonomic neural innervation, and pupillometry was a useful technique to define early DAN.[3] Moreover, Park *et al.* noted that pupillometry could be used to quantify neural dysfunction in patients with DM.[18] The dynamic and static pupillometry results of our study consistently showed that the pupils of the patients with ED tended to be more miotic compared to control group; this finding is attributed to DAN and damaged autonomic nerve terminals in literature.[23] The mean duration of DM was significantly longer in the Severe ED group than the Mild ED

group. Longer duration of DM was found to be associated with the severity of DAN.[20] Longer duration in the severe ED group may indicate more severe DAN. Based on our study results, we can speculate that DAN, and its severity, are important factors in the ED etiology of patients with DM, and dynamic pupillometry data may be used to assess the clinical burden of DAN in the ED etiology of patients with DM.

The association between abnormal pupil functions and the severity of ED cannot be attributed solely to autonomic neural dysfunction; therefore, morphological changes in the tissue structure is another underlying factor for both abnormal pupil functions and ED in DM. Decreased smooth muscle density of the corpora cavernosa and increased fibrotic processes of the penile structures were reported in DM.[24,25] Fujii *et al.* reported structural changes in the constrictor iris muscles, and Alio *et al.* suggested that myopathy in the pupil was associated with abnormal pupil size and functions in DM.[23,26] In the present study, scotopic pupillometry analysis revealed decreasing pupil diameter with increasing ED severity. Decreased static pupil diameter under scotopic conditions, and its association with ED severity, should be considered in light of structural changes in both the iris and the penis due to DM, and it would not be surprising if the severity of these changes progressed simultaneously with increasing exposure to DM.

Our study has some limitations. ED has multiple underlying factors that intersect, so it is unrealistic to completely exclude the impact of other factors or solely investigate one of these factors. ED was diagnosed based on physical examination and sexual activity history without using objective measurement methods, such as penile Doppler ultrasound, which analyses the involvement of vascular mechanism. In future studies, the exclusion of vascular involvement with penile Doppler ultrasound will improve the strength of the results. Depression is independently associated with ED.[27] Although we excluded patients with psychological disorders, occasional psychological mood changes might affect the classification of the ED severity groups.

Conclusion

In conclusion, the present study showed that both static and dynamic pupillometry measurements were altered in patients with type 2 DM and ED. The severity of abnormal pupil responses was associated with the severity of ED in patients with DM. These data indicate the importance of DAN as a causative factor in DM-associated ED.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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