SCIENTIFIC REPORT

Evaluation of ocular surface temperature and retrobulbar haemodynamics by infrared thermography and colour Doppler imaging in patients with glaucoma

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Background: Ocular surface temperature (OST) could berelated to retrobulbar haemodynamics in patients with glaucoma.
Aims: To compare OST measurements in patients with glaucoma and healthy controls, and to investigate the correlation between OST, intraocular pressure (IOP) and retrobulbar haemodynamics in patients with glaucoma.
Methods: 32 patients with primary open-angle glaucoma (POAG) and 40 controls were included in the study. The parameters considered both in patients with POAG and in controls were IOP and OST values measured by infrared ocular thermography. Colour Doppler imaging was used to determine haemodynamic parameters in ophthalmic artery (OA), central retinal artery (CRA) and short posterior ciliary arteries (SPCAs) in patients with POAG.
Results: OST values were significantly lower in patients with POAG than in controls ($p<0.001$). OST was negatively related with resistivity index of OA ($p<0.001$), CRA ($p=0.001$) and SPCAs ($p<0.001$), and positively related with end-diastolic velocity of OA ($p=0.02$) and SPCAs ($p=0.05$).
Conclusion: This study suggested that OST could be a marker of impaired retrobulbar haemodynamics in patients with glaucoma.

Glaucoma pathogenesis is multifactorial and not yet well established. Ocular hypertension is the main risk factor for the development and progression of the disease.[1–4] Vascular factors have assumed an increasing relevance in the past years. A reduction or an impaired autoregulation of blood supply to the optic nerve head (ONH), at least in some types of glaucoma, has been demonstrated.[5–10] Colour Doppler imaging (CDI) gives important information about the retrobulbar circulation. In patients with glaucoma, changes in retrobulbar haemodynamics are correlated with a progression in functional damage.[11–16]

A vascular imaging method widely used to study the abnormalities in blood flow is the infrared thermography. This technique measures the radiated heat from the body surface, which is related to the local blood flow. A recent review displayed the clinical applications of infrared thermography.[17] The characteristics of the ocular thermographic profiles have been clarified by previous investigations.[18–22] The real-time measurements of ocular surface temperature (OST) by infrared thermo-cameras proved their utility in ophthalmology. Changes in OST have been described in several pathological states of the adnexa and in the anterior segment of the eye, as well as in the cataract and refractive surgery.[23–27] Some studies showed a correlation between OST and ocular blood flow. An increase of intraocular pressure (IOP) was found to be related to a contemporary decrease of ocular perfusion pressure and ocular temperature in monkeys.[28] In normal human subjects, a correlation between ocular temperature and finger temperature has been displayed.[29] In carotid artery stenosis, the eye on the affected side showed a reduction in corneal temperature and impaired retrobulbar haemodynamics.[18 30] Thermography could be suitable to provide information about the role of vascular factors in the physiopathology of glaucomatous optic neuropathy. Changes in OST would be expected in affected eyes, presumably correlated to the impairment of retrobulbar haemodynamics. Gugleta *et al*[31] demonstrated a relationship between corneal temperature and retrobulbar haemodynamics.

In the present study, OST measurements were evaluated in a group of patients with primary open-angle glaucoma (POAG) and in a group of healthy controls. The correlation between OST, IOP and retrobulbar haemodynamics was investigated using CDI in patients with glaucoma.

MATERIALS AND METHODS

A total of 32 patients with POAG and 40 controls were evaluated. Written informed consent was obtained from each subject. The procedures conformed with those of the Declaration of Helsinki and of the local committee of the University of Florence, Florence, Italy. All the subjects underwent the following ophthalmic examinations: best-corrected visual acuity measurement with Snellen chart; Goldmann applanation tonometry; slit-lamp examination of the anterior and posterior segments; Schirmer's test; break-up time test; and, only in patients with POAG, Humphrey 24–2 full-threshold visual field test. The following exclusion criteria were applied: myopia or hyperopia $\geqslant$4 diopters; astigmatism $\geqslant$1.5 diopters; contact lens wear; any inflammation of the adnexa, the anterior or posterior segments of eye; abnormal Schirmer's test (<10 mm/5 min); reduced break-up time (<10 s); any cardiovascular pathologies; systemic or topical therapy with drugs acting on cardiovascular system; and body temperature <36.4℃ or >36.7℃. In each subject one eye was evaluated. All the study eyes of patients with POAG were treated with prostaglandins and showed similar visual field defects. The study eye of the controls was chosen randomly. Table 1 lists the data of patients with POAG and controls.

Thermography was performed in all the subjects using an infrared detector (Agema Thermovision 800 LWB, AGEMA Infrared Systems 1991 AB, Donderyd, Sweden). OST was always measured between 9:00 and 10:00, to avoid bias due to an increase in OST throughout the day.[17] Before each examination, room temperature, humidity and air flow were recorded, to make sure to have relatively constant environmental parameters. At each examination, the subject was requested to keep the eyes closed for 3–5 s, then to open both eyes wide. OST measurements lasted for 20 s, and the data were registered every second,

Abbreviations: CDI, colour Doppler imaging; CRA, central retinal artery; EDV, end-diastolic velocity; IOP, intraocular pressure; OA, ophthalmic artery; ONH, optic nerve head; OST, ocular surface temperature; POAG, primary open-angle glaucoma; PSV, peak-systolic velocity; RI, resistivity index; SPCA, short posterior ciliary artery

Table 1 Characteristics of the enrolled subjects

	Controls	Patients with POAG	p Value
n	40	32	
Mean (SD) age (years)	65.10 (11.81)	64.75 (11.21)	0.899
Sex (M:F)	20:20	15:17	0.796
Mean (SD) IOP (mm Hg)	12.90 (1.53)	19.12 (3.98)	<0.001
Mean (SD) deviation	Not done	6.77 (1.04)	
Mean (SD) corrected pattern	Not done	3.56 (0.83)	
Hypotensive therapy (prostaglandins)	None	Yes	

F, female; POAG, primary open-angle glaucoma; IOP, intraocular pressure; M, male.

Table 2 Ocular surface temperature values at frame 0

Mean (SD) OST	Controls	Patients with POAG	p Value
Point 1	36.40 (0.10)	35.86 (0.41)	<0.001
Point 2	36.00 (0.18)	35.50 (0.60)	<0.001
Point 3	35.40 (0.15)	34.83 (0.52)	<0.001
Point 4	35.60 (0.16)	34.92 (0.49)	<0.001
Point 5	35.90 (0.12)	35.27 (0.49)	<0.001

OST, ocular surface temperature; POAG, primary open-angle glaucoma.

Table 3 Ocular surface temperature values at frame 109

Mean (SD) OST	Controls	Patients with POAG	p Value
Point 1	36.39 (0.17)	35.84 (0.54)	<0.001
Point 2	35.81 (0.13)	35.22 (0.66)	<0.001
Point 3	35.20 (0.10)	34.55 (0.68)	<0.001
Point 4	35.30 (0.20)	34.67 (0.50)	<0.001
Point 5	35.88 (0.17)	35.10 (0.51)	<0.001

OST, ocular surface temperature; POAG, primary open-angle glaucoma.

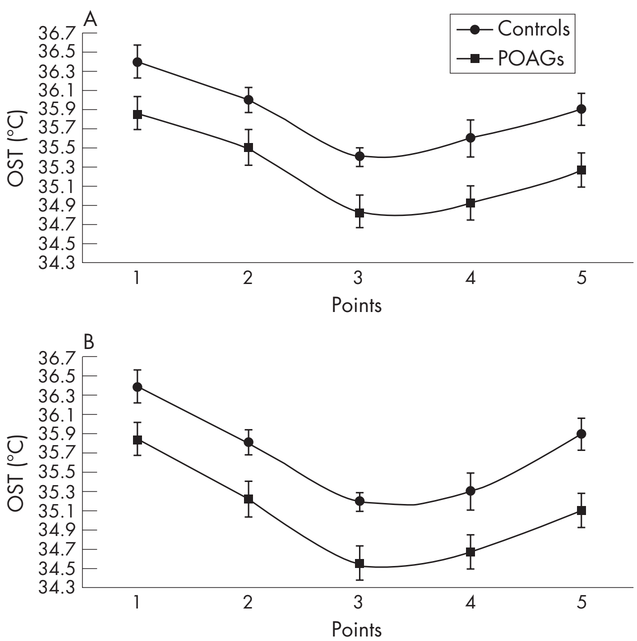

Figure 1 Comparison between ocular surface temperature (OST) values in patients with glaucoma and in controls ($p<0.001$ in both frames). (A) Analysis at frame 0. (B) Analysis at frame 109. POAG, patients with primary open-angle glaucoma. The numerical data for the (A) and (B) are listed in tables 2 and 3, respectively.

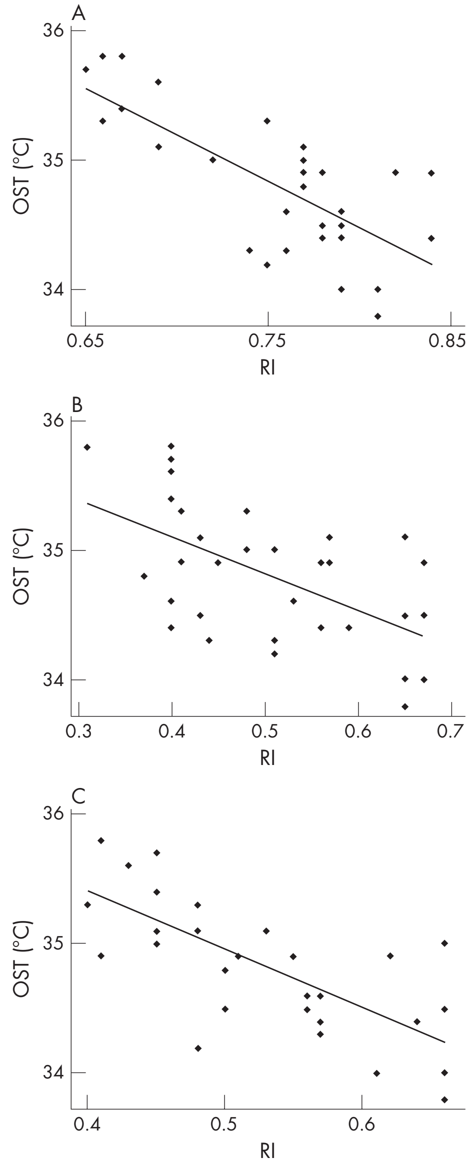

Figure 2 Linear regression between ocular surface temperature (OST) and resistivity index (RI). Correlation in (A) ophthalmic artery ($p<0.001$), (B) central retinal artery ($p=0.001$) and (C) short posterior ciliary arteries ($p<0.001$). Numerical data for fig 2 are listed in table 4.

but only the thermograms taken at the eye opening and at the 20th second after opening (frames 0 and 109, respectively) were evaluated in the statistical analysis. The temperature of five anatomical points across a line running horizontally through the centre of the cornea was recorded: the internal canthus (point 1), half-way from the internal canthus and nasal limbus (point 2), the centre of the cornea (point 3), half-way from the temporal limbus and external canthus (point 4) and the external canthus (point 5).

Patients with POAG underwent a retrobulbar haemodynamic evaluation by Colour Doppler Dynaview TM II SSD-1700 (Aloka, Tokyo, Japan), using a 6 MHz probe. The peak-systolic velocity (PSV), the end-diastolic velocity (EDV) and the resistivity index (RI) were recorded in ophthalmic artery (OA), central retinal artery (CRA) and short posterior ciliary arteries (SPCAs).

Student's t test for unpaired data was used to compare the values obtained from patients with POAG and controls. Linear

Table 4 Numerical data for ocular surface temperature and resistivity index

Eye	OST	RI OA	RI CRA	RI SPCA
1	35.3	0.75	0.48	0.48
2	35.1	0.77	0.57	0.48
3	34.8	0.74	0.37	0.50
4	34.5	0.79	0.65	0.66
5	34.9	0.78	0.57	0.51
6	34.9	0.77	0.45	0.62
7	34.9	0.84	0.67	0.55
8	34.9	0.82	0.56	0.62
9	34.5	0.78	0.43	0.50
10	34.6	0.79	0.40	0.56
11	34.2	0.75	0.51	0.48
12	34.4	0.79	0.40	0.64
13	33.8	0.81	0.65	0.66
14	34	0.81	0.65	0.66
15	34.5	0.79	0.67	0.56
16	34.3	0.79	0.67	0.61
17	34.3	0.76	0.51	0.57
18	34.4	0.84	0.59	0.64
19	34.3	0.74	0.44	0.57
20	34.4	0.78	0.56	0.57
21	34.9	0.78	0.41	0.41
22	34.6	0.76	0.53	0.57
23	35	0.77	0.51	0.66
24	35	0.72	0.48	0.45
25	35.3	0.66	0.41	0.40
26	35.1	0.69	0.43	0.45
27	35.5	0.69	0.65	0.53
28	35.4	0.67	0.40	0.45
29	35.6	0.69	0.40	0.43
30	35.8	0.66	0.31	0.41
31	35.8	0.67	0.40	0.41
32	35.7	0.65	0.40	0.45

CRA, central retinal artery; OA, ophthalmic artery; OST, ocular surface temperature; RI, resistivity index; SPCA, short posterior ciliary artery.

regression was applied to analyse the correlation between OST, IOP and CDI parameters. A $p \leqslant 0.05$ was regarded as significant.

RESULTS

Tables 2 and 3 outline the mean (SD) values of OST, expressed in degrees Celsius (℃), in patients with POAG and in controls.

OST values are significantly lower in patients with POAG than in controls at every point in the two frames ($p<0.001$; fig 1). The measurements at point 3 were considered the most reliable values of OST, because the avascularity of the cornea should minimise the influence of the conjunctival vascular network on thermographic analysis.[20] The data recorded immediately after eye opening (frame 0) are less influenced by environmental conditions and tear-film evaporation, so they were used to perform the subsequent statistical analyses in patients with glaucoma—that is, the correlation between OST, IOP and CDI parameters.[22] OST did not correlate with IOP values ($R^2 = 0.008$, $p = 0.62$). A negative correlation between OST and RI was found in OA ($R^2 = 0.542$, $p<0.001$), CRA ($R^2 = 0.321$, $p = 0.001$) and SPCAs ($R^2 = 0.525$, $p<0.001$; fig 2). A positive correlation between OST and EDV was reported in OA ($R^2 = 0.156$, $p = 0.02$) and in SPCAs ($R^2 = 0.115$, $p = 0.05$), not in CRA ($R^2 = 0.009$, $p = 0.60$; fig 3). Regarding PSV, it was not related to OST in OA ($R^2 = 0.037$, $p = 0.29$), whereas in CRA and SPCAs, there was a negative correlation ($R^2 = 0.320$, $p = 0.001$ and $R^2 = 0.144$, $p = 0.03$, respectively).

DISCUSSION

In the present study, OST measurements in a group of patients with POAG and a group of controls were compared. Our results display a significant difference between the two groups, with lower OST values in patients with POAG. This finding may suggest an altered perfusion of the ONH in patients with POAG. Interestingly, the measurements at point 3, considered the most reliable, were lower than the values regarded as normal for corneal temperature (35.9℃ (0.7℃)) in patients with POAG, whereas they were in the normal range in controls.[20] To clarify this finding, the relationship between OST, IOP and CDI parameters was investigated in patients with POAG. OST does not correlate with IOP values, although it does with some CDI parameters. In fact, lower OST measurements are significantly associated with higher RI values in all the retrobulbar vessels and with lower EDV values in OA and SPCAs.

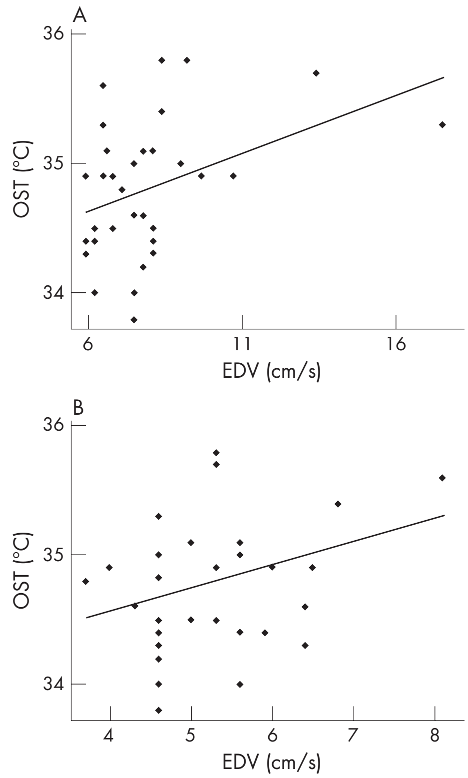

Figure 3 Linear regression between ocular surface temperature (OST) and end-diastolic velocity (EDV). Correlation in (A) ophthalmic artery ($p = 0.02$) and (B) short posterior ciliary arteries ($p = 0.05$). Numerical data for fig 3 are listed in table 5.

Among the semiologic methods used to evaluate the vascular component in glaucoma, CDI seems to be the most advisable, because of its non-invasivity and reproducibility.[32–34] It probably provides the most useful data, allowing to study the vessels that are more involved in supplying blood to the ONH—that is, OA and SPCAs. The most indicative parameters of ONH perfusion are EDV and RI. EDV, reflecting the average blood flow during the longest phase of the cardiac cycle, seems to be more suitable than PSV, which represents an instantaneous variation of blood flow. RI, the most reproducible and reliable CDI parameter, is a measure of peripheral vascular resistance, whose higher values indicate a greater impedence in the territory supplied by the examined vessel. The changes in PSV, EDV and RI in the OA and SPCAs could lead to a reduction in blood supply to ONH.[11–16] The aim of our study was not to confirm the well-known haemodynamic abnormalities in glaucoma. Therefore, CDI was performed only in patients with POAG, which showed a significant reduction of OST, when compared with normal values. Lower OST measurements are possibly related to a poorer ocular circulation. Eyes with a reduced blood supply, as in significant carotid artery stenosis, have appeared cooler than normal controls.[18 30] On the contrary, the increase in local blood flow, in case of conjunctivitis and anterior uveitis, has been

Table 5 Numerical data for ocular surface temperature and end-diastolic velocity

Eye	OST	EDV OA	EDV SPCA
1	35.3	6.5	4.6
2	35.1	7.5	5.0
3	34.8	7.1	3.7
4	34.5	6.2	4.6
5	34.9	6.5	5.3
6	34.9	9.7	6.0
7	34.9	5.9	5.3
8	34.9	10.7	4.0
9	34.5	8.1	5.0
10	34.6	7.8	4.3
11	34.2	7.8	4.6
12	34.4	8.1	5.6
13	33.8	7.5	4.6
14	34	7.5	4.6
15	34.5	6.8	5.3
16	34.3	6.2	5.6
17	34.3	8.1	6.4
18	34.4	5.9	4.6
19	34.3	5.9	4.6
20	34.4	6.2	5.9
21	34.9	6.8	6.5
22	34.6	7.5	4.6
23	35	7.5	4.6
24	35	9.0	5.6
25	35.3	17.5	8.1
26	35.1	7.8	5.6
27	35.5	8.1	5.6
28	35.4	8.4	6.8
29	35.6	6.5	8.1
30	35.8	9.2	5.3
31	35.8	8.4	5.3
32	35.7	13.4	5.3

EDV, end-diastolic velocity; OA, ophthalmic artery; OST, ocular surface temperature; SPCA, short posterior ciliary artery.

associated with an increase in OST.[18 23–25] Gugleta *et al*[31] proved a relationship between corneal temperature and retrobulbar haemodynamics comparable in patients with glaucoma and in controls. In the present analysis, a significant correlation between OST values and the most reliable CDI parameters has been demonstrated, supporting the hypothesis that retrobulbar haemodynamics could influence OST.[31]

Our study suggests that thermography could be useful in anterior eye diseases and also in glaucomatous optic neuropathy. OST, measured by this non-invasive and reliable technique, might be an indirect marker of impaired ONH perfusion. In our opinion, glaucoma would be a very interesting field of study for thermographic evaluations. Hence, further investigations are needed to obtain clinically useful information about the physiopathology of the diseases determined, at least partly, by impaired ocular perfusion.

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