

Original Research Article

EVALUATING AUTOMATED PERIMETRY FOR EARLY DETECTION OF RETINAL CHANGES IN DIABETIC RETINOPATHY: A COMPARATIVE ANALYSIS OF SITA-SAP AND SITA-SWAP

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ABSTRACT

Background: DR causes most working-age blindness in industrialised and underdeveloped countries. Conventional Achromatic White on White Perimetry (WWP) or Standard Automated Perimetry (SAP) can detect retinal alterations caused by diabetes early on, while SWAP detects short wavelength visual pathway sensitivity loss. This study compared SITA-SAP and SITA-SWAP as early indicators of diabetic retinopathy and assessed the effect of automated perimetry in detecting functional retinal abnormalities.

Material and Methods: The Department of Ophthalmology, Vivekananda Institute of Medical Sciences, Kolkata, did an observational, prospective investigation. Cases consisted of 90 eyes of 47 Type 2 diabetes mellitus patients without retinopathy or varied degrees of retinopathy, and Control group consisted of 30 eyes of 15 otherwise healthy volunteers. Four groups of 30 eyes were formed. Group A: no DR, Group B: mild to moderate NPDR, Group C: severe NPDR, and Group D: control non-diabetics. Swedish Interactive Threshold Algorithms (SITA) was used for 24-2 program. Before the test, five minutes were given for adaptation and practice.

Results: The study demonstrated a significant difference between SAP and SWAP for FT in Groups A and B (p value <0.001), but not in Groups C (p value 0.134) and D (p value 0.184). Significant difference (p < 0.001) was observed between SAP and SWAP in Groups A and B. MD was not significantly different between SAP and SWAP in Group C [0.062] and Group D [0.224]. We discovered significant differences between all groups except Group A and C for FT SWAP [p=0.785] and Group A and Group D for PSD SAP [p=0.053]. However, SAP and SWAP MD differed significantly among all groups.

Conclusion: In diabetic individuals with no DR and mild to moderate NPDR, SITA SWAP is more sensitive than SITA SAP in detecting Koniocellular pathway retinal impairment, probably with a higher edge in those without clinical indications of DR. SITA SWAP can supplement photographic documentation of diabetic retinopathy and detect early retinopathy.

Key Words: Diabetes mellitus, Diabetic Retinopathy, Standard Automated Perimetry, Swedish Interactive Threshold Algorithms.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycaemia resulting from defects of insulin secretion and/or increased cellular resistance to insulin. Chronic hyperglycaemia and other metabolic disturbances of DM lead to long-term tissue and organ damage as well as dysfunction involving the eyes, kidneys, and nervous and vascular systems.^[1,2,3] Patients with diabetes often develop ophthalmic complications, such as corneal abnormalities, glaucoma, iris neovascularization, cataracts, and neuropathies. The most common and potentially most blinding of these complications, however, is diabetic retinopathy [DR].^[4,5]

DR is a vascular disorder affecting the microvasculature of the retina. DR has become the leading cause of blindness in working age adults in both developed and developing countries.^[6,7,8] It is not only a major cause of acquired blindness before 65 years of age in the industrialised countries in the western world, but also a rapidly increasing problem in urban areas in the developing countries. DR occurs both in type 1 and type 2 DM and has been shown that nearly all type 1 and 75 per cent of type 2 diabetes patients will develop DR after 15 years duration of diabetes as shown in earlier epidemiological studies.^[9,10,11] In the western population, DR has been shown to be the cause of visual impairment in 86 percent of type 1 diabetic patients and in 33 per cent of type 2 diabetic patients.^[12] It is difficult to treat once sight-threatening vascular changes have developed and only laser therapy can substantially reduce the risk of visual loss. It is necessary to regulate the hyperglycaemic and related metabolic disturbances to prevent or delay progression of vascular abnormalities.^[13]

Morphological changes in the retina in DR is assessed according to a gold standard based on findings from seven stereo fundus photographs of specified retinal fields, presented by ETDRS. However, it would be extremely useful to assess the course of DR not only morphologically but also functionally. Several studies have shown that DR may influence the visual field; such changes are clear at advanced stages of the disease.^{14,15,16} A variable amount of visual field loss is often found in DR and the extent of the loss depends on the severity of the illness.^[17,18]

The introduction of automated static perimetry has become a new approach to study retinal function. Automated perimetry may detect retinal changes at an early stage. Conventional Achromatic White on White Perimetry (WWP) or Standard Automated Perimetry (SAP) has been reported to identify retinal changes caused by diabetes at early stages whereas Short Wavelength Automated Perimetry (SWAP) detects loss of short wavelength visual pathway sensitivity. Blue on yellow perimetry

known as short wavelength automated perimetry (SWAP) represents recent and existing advance in early identification of ischemic change in diabetes. It differs from standard automated perimetry (SAP) only in that carefully chosen wavelength of blue light is used as the stimulus and specific colour and brightness of yellow light is used for background illumination. SWAP is considered an earlier indicator of function loss in ischemic change in DR than SAP. SWAP has been shown to yield more extensive visual field loss than SAP in diabetic changes.

SWAP is a functional test to detect visual field abnormality in patients at high risk of developing DR where white on white (SAP) still within normal.^[20]

The Swedish interactive threshold algorithm (SITA) is a new automated perimetry test strategy that was developed to shorten test duration without compromising its sensitivity. The SITA strategy is based on a forecasting procedure that employs Bayesian statistics. SITA has reduced both testing time and variability in SAP and SWAP. A number of clinical studies have shown that the thresholds returned by SITA and the full threshold strategy are very similar in terms of test-retest variability, sensitivity and specificity.^[21]

A number of studies have compared SWAP and WWP in patients with diabetes but the results are not conclusive regarding the relative usefulness of these two tests.^[22-26] Few studies have assessed role of perimetry in detecting functional loss due to diabetes induced damage of the perifoveal capillary network.^[22] This study was done to assess the role of automated perimetry in early detection of functional retinal changes in diabetic retinopathy as well as compare between SITA-SAP & SITA-SWAP as early indicator of diabetic retinopathy.

MATERIALS AND METHODS

This study was designed to be observational, prospective and was conducted in the Department of Ophthalmology, Vivekananda Institute of Medical sciences, Kolkata. The period of study was of eighteen (18) months.

Subjects were selected randomly from patients, visiting the Outpatient Department, under the Department of Ophthalmology, Vivekananda Institute of Medical Sciences, Kolkata. Total 120 eyes of 62 patients were included in the study. Cases was comprised of 90 eyes of 47 patients with Type 2 diabetes mellitus, having no retinopathy or varying degree of retinopathy and Control group included 30 eyes of 15 otherwise healthy patients, who had agreed to volunteer. Age of the patients in cases ranged between 32-51 years. Age of the patients in control ranged between 35-49 years. Both the Case and the Control were sex-matched. There was total 26 males and 36 females in the present research. After approval of the local ethical committee

(Institutional Reviewing Board, Ethical Committee of Vivekananda Institute of Medical Sciences, Kolkata.), informed consents were taken from patients and controls.

Subjects were selected after diagnosing them as 'Diabetic' by Department of Endocrinology, as per American Diabetic Association, Preferred Practice Pattern criteria, release 2011. Then, they were subjected to full clinical evaluation, detailed medical history, ophthalmic history, careful drug history, Best corrected visual acuity, Slit lamp examination, Intra Ocular Pressure(IOP) measurement by Goldmann's Applanation Tonometry, Gonioscopy, Fundus examination by ophthalmoscopy, +90D stereo evaluation and documentation by fundus photography, Digital Fluorescein Angiography (DFA) and later Visual Field (VF) evaluation by Humphrey Field Analyzer (Model HFA II-750) for static perimetry with 24-2 SITA SAP and SITA SWAP programs from January 2013 to June 2014.

The selected patients were divided into 4 groups:

Group A: 30 eyes of 15 diabetics with no diabetic retinopathy.

Group B: 30 eyes of 16 diabetics with mild to moderate non-proliferative diabetic retinopathy.

Group C: 30 eyes of 16 diabetics with severe non-proliferative diabetic retinopathy.

Group D: 30 eyes of 15 healthy patients without diabetes mellitus and no retinopathy.

Inclusion Criteria

Patients were selected on fulfilment of all the laid down criteria as detailed below:

1. Age- > 30 years
2. BCVA > or =6/18
3. Normal anterior segment by slit lamp examination

Exclusion Criteria

1. Co-existent Glaucoma.
2. Co-existent Ocular hypertension.
3. Past history of laser treatment.
4. Past history of any eye surgery.
5. Nuclear opacities in Lens.
6. Refractive error >3D

For SITA-SAP stimulus size of Goldmann III (0.43-degree visual angle) and background luminance of 31.5asb unit was taken. For SITA-SWAP Standard broadband yellow filter (OG530 Schott filter – a 530 nm short wavelength cutoff filter), a background luminance of 100 cd/m² a large stimulus Goldmann Size V[1.7 degrees diameter] with a narrow band short wavelength interference filter (440 nm peak transmission, with a 15 nm bandwidth) and a 200 millisecond stimulus duration was used. A Swedish Interactive Threshold Algorithms (SITA) strategy was applied for using 24-2 program. Five minutes of adaptation period and five minutes of practice session were provided before starting the test. All patients were provided required rest to avoid fatigue effects. Test was conducted by single observer masked to the diagnosis.

Criteria for visual field abnormality

Caprioli strict

≥ 4 adjacent points of ≥ 5 dB loss each
≥ 3 adjacent points of ≥ 10 dB loss each
Difference of ≥ 10 dB across nasal horizontal meridian at ≥ 3 adjacent points

Caprioli moderate

≥ 3 adjacent points of ≥ 5 dB loss each
≥ 2 adjacent points of ≥ 10 dB loss each
Difference of ≥ 10 dB across nasal horizontal meridian at ≥ 2 adjacent points

Caprioli liberal

≥ 2 adjacent points of ≥ 5 dB loss each
≥ 1 adjacent points of ≥ 10 dB loss each
Difference of ≥ 5 dB across nasal horizontal meridian at ≥ 2 adjacent points

Anderson modified

≥ 3 adjacent points in an expected location of the central 24° field that have p < 5% on the pattern deviation plot, one of which must have p < 1%
Glaucoma hemifield test "outside normal limits"
PSD with a p value < 5%

Statistical Methods

Data was analyzed by using SPSS version 20.0 & R software. Statistical methods used were descriptive and inferential statistical analysis. Sex and Age group were expressed as number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes. Duration of diabetes, HbA1C, SAP and SWAP values for FT, MD and PSD were expressed as Mean ± Standard Deviation and compared across the groups using one-way ANOVA. Comparison of SAP and SWAP values for FT, MD and PSD were done using paired t test. We used Mann-Whitney U test to compare group A and B. An alpha level of 5% was taken, i.e. if any p value was less than 0.05 it was considered as significant.

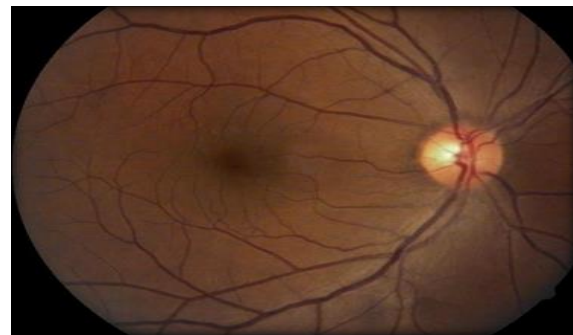


Figure 1: Colour fundus photograph OD [patient 1]



Figure 2: Colour fundus photograph OD [patient 2]

RESULTS AND DISCUSSION

Table 1: Age distribution of patients studied

Group	Mean	N	Std. Deviation	Minimum	Maximum
	41.13	15	5.222	32	51
Group B [Mild to Moderate diabetic retinopathy]	42.50	16	3.777	35	48
Group C [Severe diabetic retinopathy]	44.31	16	3.459	38	48
Group D [Non Diabetic /Control]	43.27	15	4.527	35	49
Total	42.82	62	4.333	32	51

Table 2: Duration of diabetes of patients studied

	Group				p Value						
	Group A [No diabetic retinopathy]	Group B [Mild to Moderate diabetic retinopathy]	Group C [Severe diabetic retinopathy]	Group D [Non Diabetic Control]	Overall	No vs Mild/Moderate	No vs Severe	No vs Control	Mild/Moderate vs Severe	Mild/Moderate vs Control	Severe vs Control
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation							
Duration of diabetes	3.37 ± 1.07	8.8 ± 1.6	14.23 ± 2.22	0 ± 0	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Table 3: Comparison of FT SAP and FT SWAP in the studied groups

	Group				p Value						
	Group A [No Diabetic Retinopathy]	Group B [Mild to Moderate Diabetic Retinopathy]	Group C [Severe Diabetic Retinopathy]	Group D [Non Diabetic Control]	Overall	No vs Mild/Moderate	No vs Severe	No vs Control	Mild/Moderate vs Severe	Mild/Moderate vs Control	Severe vs Control
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation							
FT SAP	29.87 ± 3.8	26.37 ± 3.55	22.33 ± 2.64	31.87 ± 3.27	<0.001	0.001	<0.001	0.033	<0.001	<0.001	<0.001
FT SWAP	22.37 ± 3.03	17.7 ± 2.41	22.17 ± 2.59	31.77 ± 3.18	<0.001	<0.001	0.785	<0.001	<0.001	<0.001	<0.001
P Value Between SAP & SWAP	<0.001	<0.001	0.134	0.184							

Table 4: Comparison of MD SAP and MD SWAP in the studied groups

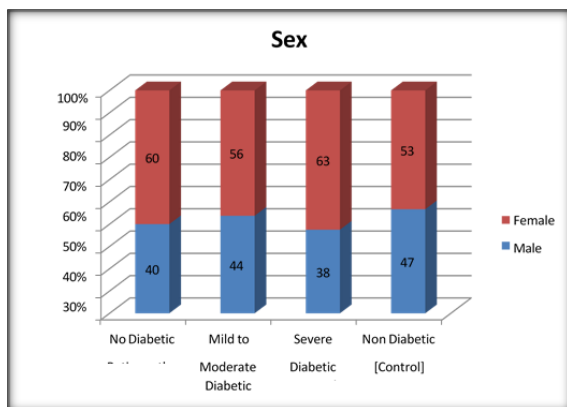
Variables	Group				P value						
	Group A [No Diabetic Retinopathy]	Group B [Mild to Moderate Diabetic Retinopathy]	Group C [Severe Diabetic Retinopathy]	Group D [Non Diabetic Control]	Overall	No vs Mild/Moderate	No vs Severe	No vs Control	Mild/Moderate vs Severe	Mild/Moderate vs Control	Severe vs Control
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation							
MD SAP	-3.83 ± 0.98	-5.53 ± 1.05	-7.61 ± 1.45	-2.39 ± 0.89	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

MD SWAP	-5.65 ± 1.57	-8.55 ± 1.43	-7.64 ± 1.49	-2.42 ± 0.9	<0.001	<0.001	<0.001	<0.001	0.02	<0.001	<0.001
P Value Between SAP & SWAP	<0.001	<0.001	0.062	0.224							

Table 5: Comparison of PSD SAP and PSD SWAP in the studied groups

Variables	Group				Overall	p Value					
	Group A [No Diabetic Retinopathy]	Group B [Mild to Moderate Diabetic Retinopathy]	Group C [Severe Diabetic Retinopathy]	Group D [Non Diabetic Control]		No vs Mild/Moderate	No vs Severe	No vs Control	Mild/Moderate vs Severe	Mild/Moderate vs Control	Severe vs Control
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation							
PSD SAP	1.49 ± 0.23	2.62 ± 0.27	3.22 ± 0.65	1.39 ± 0.15	<0.001	<0.001	<0.001	0.053	<0.001	<0.001	<0.001
PSD SWAP	4.25 ± 0.71	5.41 ± 0.9	3.23 ± 0.66	1.4 ± 0.15	<0.001	<0.001	0.001	<0.001	<0.001	<0.001	<0.001
P Value Between SAP & SWAP	<0.001	<0.001	0.184	0.186							

The minimum age was 32 years and the maximum age was 51 years. Mean age of the case series was 42.5 ± 4.29 [Mean ± Std. Deviation] and control series was 43.27 ± 4.527 [Mean ± Std. Deviation] years.



Graph 1: Sex Distribution of Study Participants

DR is a vascular disorder affecting the microvasculature of the retina. Early detection of DR and timely intervention by laser photocoagulation can reduce the incidence of moderate visual loss in macular edema by 50–60% and severe visual loss in proliferative diabetic retinopathy (PDR) by 90%.⁶⁰ SWAP is a subjective measure of local S-cone function across the retina.

It has been suggested that SWAP (Blue on yellow) is more sensitive than WWP for detection of early retinal changes.^[13] SWAP has been shown to offer improved sensitivity for the detection of clinically significant macular edema (CSME)²⁴ and diabetic visual field defects.^[25]

In the current study, the duration of diabetes was significantly [p value <0.001] longer in diabetic patients with non-proliferative retinopathy Group B [8.8 ± 1.6 years,] and Group C [14.23 ± 2.22 years] compared with those without retinopathy Group A [3.37 ± 1.07 years]. The duration of diabetes further corroborated with the severity of DR. Our findings are consistent with Mackey et al.⁶⁴ According to them the prevalence of DR was statistically significantly higher with longer diabetes disease duration (P < 0.001).

Hohenstein et al.⁶⁵ in their study found the mean duration of diabetes 12.9 years. Othman Ali Zico et al.⁵⁹ in their study found Mean duration [Mean ± Std. Deviation] of DM in no diabetic retinopathy group (6.70 ± 5.61 years) was significantly lower than in early diabetic retinopathy group (10.05 ± 5.10 years) (P = 0.03). This is in agreement with the current study.

In The United Kingdom Prospective Diabetes Study, Stratton et al.³⁵ found that good blood sugar control does reduce the risk of DR as well as does reduce the progression of retinopathy. The diabetes control and complications trial (DCCT),⁶⁶ diabetic

retinopathy study (DRS) and ETDRS66 also support that good glycaemic control is important in the early stage of diabetes and helps in delaying the onset of retinopathy and halting the rate of progression.

In the present study FT (expressed in Decibel Sensitivity-dB) was found to be different among various groups in both SAP and SWAP techniques. Difference was statistically significant between all the groups except between group A and C in SWAP. It was also found that the more severe the diabetic retinopathy the more decrease in the FT. L. Lobefalo et al,^[56] showed significant difference in diabetic subgroup on SWAP only. On intra-group analysis, we found significant difference in FT in SAP and SWAP methods in Group A[SAP 29.87 ± 3.8,SWAP 22.37 ± 3.03] and Group B[SAP26.37 ± 3.55, SWAP 17.7 ± 2.41][p value< 0.001].However FT was not significantly different between SAP and SWAP in Group C [p value 0.134] and Group D [p value 0.184].

In this study we compared SITA SAP and SITA SWAP for detecting abnormality in the visual field of diabetic retinopathy. We compared Foveal threshold [FT], Mean Deviation [MD] and Pattern standard deviation [PSD] to analyze all perimetric test results. MD is the average elevation or depression of the patient's overall field compared with the normal age-corrected reference field. On intergroup comparison MD was significantly different among different groups in both SAP and SWAP techniques. We found more marked decrease of MD in SWAP than SAP among different groups. This finding is consistent with the studies of A. Verrotti et al,^[56] and Pathor D. et al.^[57]

In the current study MD values were worse (more negative) in eyes with more advanced retinopathy consistent with the study of B. Bengtsson et al,^[13] We also found significant decrease of MD in diabetic patients than control indicating decreased retinal sensitivity. This is in agreement with Othman Ali Zico et al.^[59]

PSD is a measure of the extent to which the shape of the patient's measured visual field deviates from the normal, age-corrected reference field. In the current study PSD was significantly different among all the groups in SWAP [p value< 0.001]. However difference was not significant[p value 0.053] between group A and D in SAP. On intra-group analysis we found significant difference [p value<0.001] between SAP and SWAP in group A [SAP 1.49 ± 0.23,SWAP 4.25 ± 0.71]and B[SAP 2.62 ± 0.27,SWAP 5.41

± 0.9]. There was no significant difference in group C [p value 0.184] and group D [p value 0.186]. Othman Ali Zico et al,^[59] compared Corrected pattern standard deviation[CPSD] between SAP and SWAP. They found no significant difference in no DR and early DR group. CPSD in SWAP showed significantly higher results in early DR group compared with no DR group [P = 0.005] and control [P = 0.002]. CPSD in SAP was statistically higher in early DR group compared to control group (P =

0.007). In the current study PSD was significantly higher in group B compared to group A,C and D[p value <0.001] in SWAP. Again PSD was significantly higher in group B than group D in SAP [p value < 0.001].

In the current study we found no significant difference in FT, MD and PSD in group C and D between SAP and SWAP consistent with Othman Ali Zico et al,^[59] who found no significant difference between SAP and SWAP in MD, SF[short term fluctuation] and CPSD in non-diabetic group. Our results are in agreement with Remky et al,^[23] showing that sensitivity is significantly lower in patients with diabetes than in controls. SWAP thresholds were significantly more greatly reduced by diabetes than those of SAP (P = 0.003).

In the current study we have found significant difference [p value <0.001] between SAP and SWAP in FT, MD and PSD in group A and B indicating role of perimetry in detecting changes in the retinal sensitivity in no DR and mild to moderate NPDR group. Han et al⁶⁸ found that SWAP is a sensitive measurement of diabetic dysfunction, even prior to retinopathy.

In the current study, we found significant difference in FT among all the groups in both SAP and SWAP except between group A and D in SWAP on the contrary Nomura R. et al,^[55] in their study found no difference in Foveal sensitivity between no DR, early background DR and normal subjects.

Parameters of both techniques showed a significant difference between group A and B with more affection in the earlier group. However, both methods demonstrated significantly different values in diabetics from controls regarding FT,MD and PSD, only exception being PSD SAP between group A and D. In the current study, we demonstrated that parameters of SWAP technique yielded results that were significantly different than the SAP one regardless the presence of DR, in accordance with earlier studies showing sensitivity of shortwavelength to be affected earlier than achromatic sensitivity early in the course of DR and more recent studies reporting SWAP as a perimetric test designed to isolate and quantify the activity of shortwavelength sensitive pathways.

In diabetic patients with nonproliferative retinopathy the two techniques

showed similar sensitivity to pick up abnormal cases. This means that SWAP being more sensitive tool is capable to detect minor changes in patients without clinical overt retinopathy. However, in overt cases with nonproliferative retinopathy, changes are marked so that both techniques are capable to show, visual field changes equally. Our study indicates that perimetry is a useful tool in assessment of the retina of diabetic patients. SWAP technique is better than SAP in this regards especially when overt clinical features of DR are yet lacking so that patients can be advised for more rigorous control of

systemic parameters to delay development of overt clinical DR in future.

CONCLUSION

Automated perimetry can detect retinal functional changes in diabetic patients with or without retinopathy. SITA SWAP is more sensitive than SITA SAP in detection of retinal dysfunction involving Koniocellular pathway, in diabetic patients with no DR and mild to moderate NPDR, possibly with a higher edge in diabetics with no clinical signs of DR. SITA SWAP can provide additional useful information to photographic documentation in monitoring of diabetic retinopathy and hence can be used as a tool for detection of early diabetic retinopathy.

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