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The effect of Neodymium Yttrium Aluminium Garnet laser capsulotomy on intraocular pressure and retinal nerve fibre thickness

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Introduction

Posterior capsular opacity (PCO) is the most common delayed complication of cataract surgery with an incidence of 20.7% at two years and 28.5% at five years.(1,2) Risk factors for the development of PCO after cataract surgery include diabetes, uveitis and young age.(3) Neodymium Yttrium Aluminium Garnet (Nd:YAG) laser capsulotomy is the gold standard for the management of PCO and is an improvement on the previous treatment options.(2) Although it is usually an effective and safe outpatient treatment, complications can occur, including an increase in intraocular pressure (IOP), corneal injury, iritis, intraocular lens (IOL) dislocation, retinal detachment and increase in macular thickness.(1,4) Complications are related to the amount of energy used during the procedure,(1) larger size of the capsulotomy,(1,5) the timing of the capsulotomy post cataract surgery and the patient's pre-existing conditions such as glaucoma, aphakia, vitreoretinal disease and high myopia.(4)

An increase in IOP post Nd:YAG laser capsulotomy is the most common complication reported, with an incidence of 15-30%.(1,2) The severity of the IOP increase and the timing of the increase varies between studies, with higher IOPs reported in studies shortly after Nd:YAG capsulotomy was introduced.(1,4) In an early study by Channell and Beckman shortly after Nd:YAG laser capsulotomy was first introduced an increase in IOP of 5mmHg in 95% of their patients was reported.(6) Increases in IOP have been reported at different time points, especially at 1 (2,7–9), 2(10) , and 3 – 4 hours (7,11) after Nd:YAG capsulotomy, after which the IOPs returned to baseline (except for two studies (10,12) which reported a persistent increase in IOP until 1 week post Nd;YAG laser capsulotomy). Conversely other studies showed no change in IOP after Nd:YAG laser capsulotomy.(13–15) No studies have been done in Africa looking at the response in IOP after Nd:YAG laser capsulotomy.

Diabetes has been reported to increase a patient's likelihood of developing complications from Nd:YAG laser capsulotomy.(16) There is no evidence to suggest that diabetic patients are at greater risk of an IOP increase after Nd:YAG laser capsulotomy, despite diabetes being associated with primary open angle glaucoma.(17) In a study comparing post Nd:YAG laser capsulotomy IOP outcomes between diabetic and non-diabetic patients,despite IOP elevation occurring at 1 week in all the patients there was no difference in the IOP change between the two groups of patients at this time point.(12) In another study looking at visual acuity improvement in diabetic patients after Nd:YAG laser capsulotomy, two patients (4%) developed glaucoma after the procedure.(16)

Studies on retinal nerve fibre layer (RNFL) thickness after Nd:YAG laser capsulotomy are sparse. Although one study reported no significant change in RNFL thickness after

Nd:YAG laser capsulotomy(18), there are no studies reporting on RNFL thickness in diabetic patients after Nd:YAG laser capsulotomy.

Due to the contrasting reports regarding whether or not IOP increases after Nd:YAG laser capsulotomy and the timing thereof in patients with increase IOP, we aimed to study the effect of Nd:YAG laser capsulotomy on IOP at different time points and on RNFL thickness at 1 month in all patients in a tertiary hospital in sub-Saharan Africa. Because of the lack of data on IOP and RNFL changes in diabetic patients, we further aimed to study the effect of the laser on IOP at different time points and on RNFL thickness at 1 month in this subgroup of patients.

Methods

We conducted a prospective cohort study of adult patients (≥ 21 years) requiring Nd:YAG laser capsulotomy for PCO after uncomplicated cataract surgery at St John Eye Hospital – Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa from 11/12/2020 until 26/8/2022.

Inclusion criteria were in-the-bag IOL placement, a visual acuity (VA) of 6/9 or worse,and normal RNFL and central retinal thickness(CRT) before laser capsulotomy; and laser capsulotomy ≥ 3 months after cataract surgery. Exclusion criteria were elevated IOP before laser capsulotomy; diagnosis of intraocular disease, including glaucoma, uveitis and corneal disease; and previous laser capsulotomy in the same eye.One eye per patient was enrolled in the study. The study was approved by the University of the Witwatersrand Human Research Ethics Committee (M200832) and was conducted in accordance with the tenets of the Declaration of Helsinki. Written informed consent was obtained from all participants.

The Nd:YAG laser (OptoYag; Optotek, Slovenia) was used to make an inverted D-shape capsulotomy with the least number of shots and laser power required for the patient. Post procedure, all patients received topical Ketorolac tromethamine 0.5% solution (Acular®, Allergan) one drop three times a day for four weeks.

Prior to the procedure, the Evaluation of Posterior Capsule Opacification (EPCO) grading score was used to grade PCO from 0 - 4 i.e., none, minimal, mild, moderate and severe.(19) Intraocular pressures were measured with the Goldmann applanation tonometer just before the Nd:YAG capsulotomy, and then at 15 minutes, 2 hours, 1 week and 1 month after the procedure. The CRT and the RNFL thickness were measured just before and 1 month after the laser capsulotomy, using the Spectralis SD-OCT (Heidelberg Engineering, Germany).

Data recorded included age; gender; comorbidities, including diabetes mellitus; type of cataract surgery; and time between cataract surgery and laser capsulotomy; PCO grading before laser capsulotomy; laser power/number of shots; and IOP, CRT and RNFL thickness measurements before and after laser capsulotomy.

Data was statistically analysed using STATA 16.1 (Statacorp, Texas, USA). A two-sided paired-means test was used to calculate the sample size for the mean-IOP before and after Nd:YAG laser treatment. Using a mean difference of 1mmHg at 2 hours post Nd:YAG capsulotomy, with an alpha level of 0.05 and SD=3mmHg, we calculated a sample size of 73 patients with 80% power. We added a loss to follow up rate and have a final sample size of 80 patients. Since IOP, RNFL and macula OCT data were normally distributed, a paired t-test was used to compare the data at each of the time points after Nd:YAG laser capsulotomy to that before the laser capsulotomy. An unpaired t-test was used to compare IOP between diabetic and non-diabetic patients at each of the time points (before, and 15 min, 2-hour, 1-week and 1-month after laser capsulotomy). A multivariate mixed-effects linear regression model was used to model IOP levels at the various time points in all the patients and in the subgroup of diabetic patients.

Results

Of the 80 patients included in the study, the mean age (SD) was 65.5 (13.9) years with predominantly females (62.5%); diabetics (41.3%); grade 1 PCO (43.8%); and phacoemulsification surgery (75%) (table 1). The mean (SD) number of shots and total energy used during Nd:YAG laser capsulotomy was 62.6 (25.9) and 108.2 (47.6) mJ, respectively (table 1). The median (IQR) time from cataract surgery to laser capsulotomy was 2.5 (0.7-4.2) years.

Table 1: Baseline characteristics of patients and Nd:YAG capsulotomy procedure data

Parameter	n= 80
Age (years) Mean (SD)	65.5 (13.9)
Sex Female n (%)	 50 (62.5)
Diabetes mellitus n (%)	33 (41.3)
Type of surgery Phacoemulsification n (%) Manual Small Incision cataract surgery n (%)	 60 (75) 20 (25)
Eye included Right n (%) Left n (%)	 41 (51.2) 39 (48.8)
PCO Grade 1 n (%) 2 n (%) 3 n (%)	 35 (43.8) 29 (36.2) 16 (20.0)

Time from cataract surgery to laser capsulotomy (years) Median (IQR)	2.5 (0.7-4.2)
Number of shots Mean (SD)	62.6 (25.9)
Total energy used (mJ) Mean (SD)	108.2 (47.6)

In all the patients there was an increase in IOP at 2 hours (p = 0.0138) and a decrease at 1 month (p = 0.0338) (table 2).

Table 2:Intraocular pressure (IOP) at different timepoints after Nd:YAG laser capsulotomy compared to baseline IOP

Variable	Number of patients	Mean	Std. Deviation	95% confidence interval		P value
IOP at baseline	80	11.850	2.52	11.289	12.411	
IOP 15 minutes	80	12.321	3.43	11.550	13.075	0.130
IOP 2 hours	80	12.750	3.46	11.980	13.520	**0.014**
IOP 1 week	79	11.949	3.01	11.271	12.626	0.847
IOP 1 month	75	11.324	2.37	10.775	11.874	**0.034**

* Paired t-test

In the diabetic patients,there was an increase in IOP at 15 minutes after Nd:YAG laser capsulotomy compared to non-diabetic patients (p= 0.035) (table 3). No difference in IOP between the two groups at 2 hours(p= 0.790), 1 week (p= 0.614) and 1 month (p=0.626) was noted after laser capsulotomy.

Table 3: Comparing intraocular pressure (IOP) in diabetic patients vs. non-diabetic patients

	Non diabetics		Diabetics		
Timepoints	Mean (SD)	95% CI	Mean (SD)	95% CI	P value
Baseline	11.96 (2.39)	11.26 -12.66	11.70 (2.73)	10.73-12.67	0.652

15 minutes	11.64 (2.86)	10.80-12.48	13.27 (3.95)	11.87-14.67	**0.035**
2 hours	12.34 (3.46)	11.62-13.65	12.91 (3.50)	11.67-14.15	0.790
1 week	11.80 (3.10)	10.89-12.72	12.16 (2.91)	11.11-13.20	0.614
1 month	11.21 (2.38)	10.48-11.94	11.48 (2.39)	10.61-12.36	0.626

The multivariate mixed effects linear regression model showed that, compared to baseline, the IOP increased only at 2 hours in all the patients (p= 0.01), and at 15 minutes (p= 0.01) and 2 hours (p= 0.006) in diabetic patients (table 4). There was also a relationship found between grade 3 PCO and the IOP in all patients, and in diabetic patients.

Table 4: Mixed-effects linear regression model of the change in IOP over time in all patients and diabetic patients

	Beta coefficient	95% confidence interval		P-value
<u>All patients</u>				
Age	-0.02	-0.05	0.02	0.384
IOP change compared to Baseline 15 minutes 2 hours 1 week 1 month	 0.46 0.9 0.13 -0.53	 -0.18 0.26 -0.52 -1.19	 1.1 1.54 0.77 0.12	 0.156 **0.006** 0.695 0.11
PCO grade 2 3	 -0.42 1.44	 -1.51 0.13	 0.67 2.76	 0.454 **0.031**
<u>Diabetic patients</u>				
IOP change compared to baseline 15 minutes 2 hours 1 week	 1.58 1.21 0.50	 0.71 0.34 -0.38	 2.44 2.10 1.37	 **< 0.001** **0.006** 0.266

1 month	-0.22	-1.11	0.66	0.62
PCO grade compared to Grade 1 2 3	 0.16 2.77	 -1.66 0.56	 1.98 4.98	 0.864 **0.014**

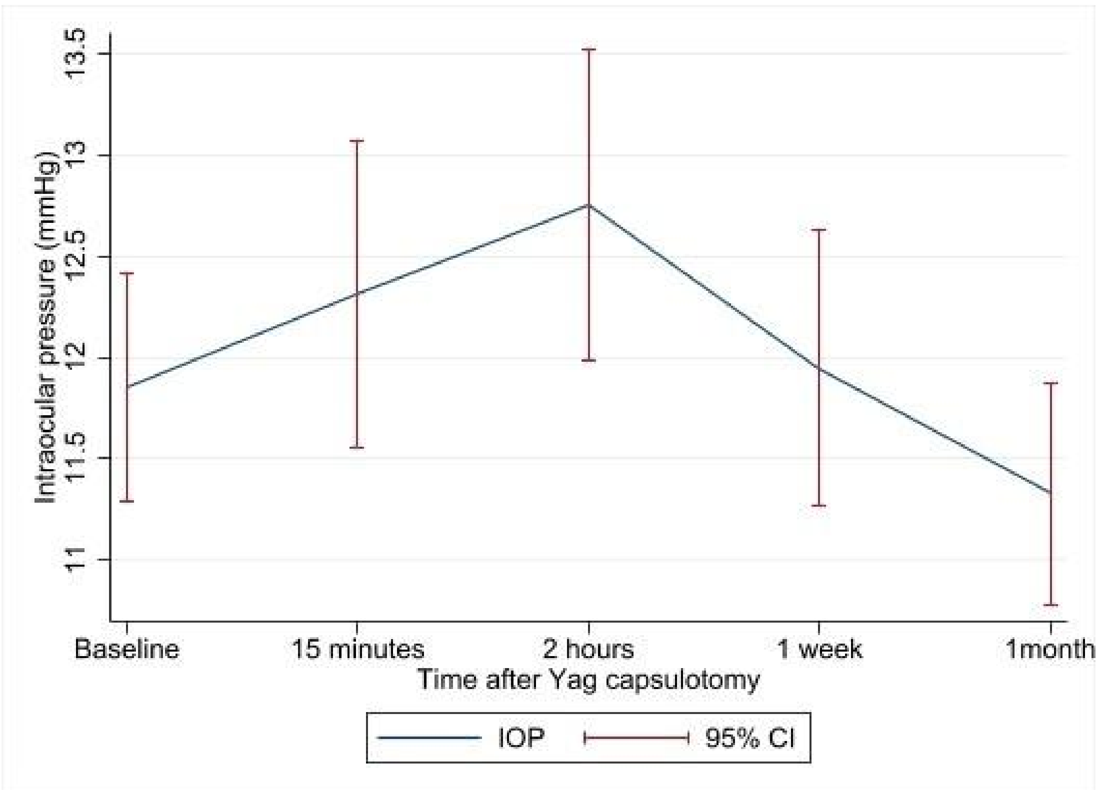

Figure 1: IOP over time in all patients

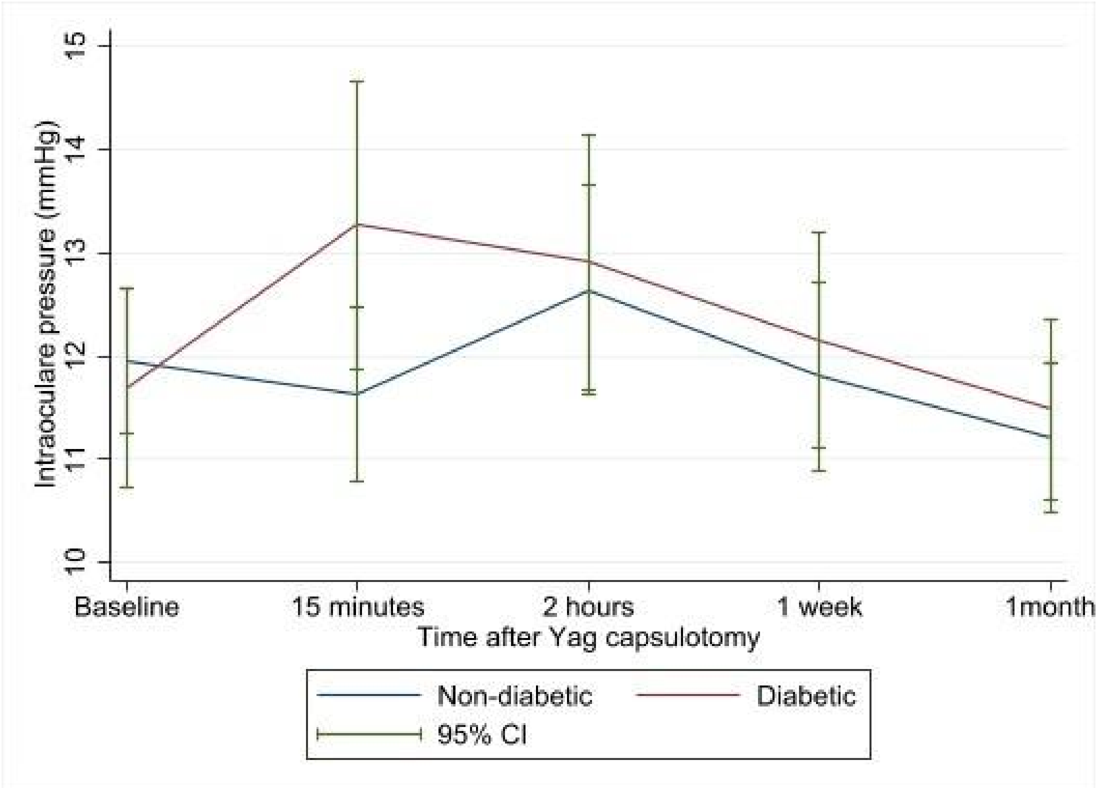

Figure 2: IOP over time in diabetics versus non-diabetic patients

There was no difference in the RNFL thickness 1 month after Nd:YAG capsulotomy compared to baseline in all patients (p= 0.217). There was a significant decrease in RNFL thickness between these timepoints in diabetic patients (p = 0.009) (table 5). There was no significant change in the CRT 1 month after Nd:YAG capsulotomy in all (p = 0.261) and diabetic patients.(p = 0.365).

Table 5: Retinal nerve fibre layer (RNFL) thickness at 1 month after Nd:YAG laser capsulotomy compared to baseline

	All patients		Non diabetics		Diabetic	
	Baseline Central RNFL (μm)	Central RNFL at 1 month (μm)	Baseline Central RNFL (μm)	Central RNFL at 1 month (μm)	Baseline Central RNFL (μm)	Central RNFL at 1 month (μm)
Mean	104.6	101.6	102.7	99.5	106.9	104
Std. Deviation	18.6	14.5	20.9	12.9	15.6	16.0

95% confidence interval	100.0	98.0	95.5	95.1	101.1	98.0
	109.3	105.2	109.9	103.9	112.8	110.0
P value		0.217		0.486		**0.009**

The only complications that occurred due to Nd:YAG laser capsulotomy were lens pitting in eight patients (10%) and persistent IOP >21mm Hg in one patient (1.25 %). Two patients (2.5%) required repeat Nd:YAG laser capsulotomy for incomplete clearance of the visual axis.

<u>Discussion</u>

Our study showed that, in all patients, an increase in IOP occurred 2 hours after Nd:YAG laser capsulotomy, with normalisation of the IOP at subsequent timepoints. In diabetic patients, the increase in IOP occurred earlier at 15 minutes after Nd:YAG laser capsulotomy; this increase in IOP persisted until 2 hours after the laser capsulotomy with normalisation of the IOP at subsequent timepoints. Furthermore, the RNFL thickness was found to be significantly thinner in diabetic patients 1 month after laser capsulotomy.

The increase in IOP in all our patients was 0.9mmHg at 2 hours (p = 0.006); although statistically significant it may not be clinically significant since the increase in IOP was transient. The IOP increase is similar to studies in the literature that reported an increase after Nd:YAG laser capsulotomy. These studies showed significant increases in IOP at varied timepoints, including 1 hour (2,7–9) , 2 hours (10) and 3-4 hours (7,11) post-laser capsulotomy, after which the IOP returned to normal. In contrast, other studies showed no change in the IOP after laser capsulotomy.(13–15) The elevation of IOP is thought to occur through mechanisms that lead to angle closure, such as swelling and inflammation of the iris root or ciliary body; pupillary block; and deposition of debris in the angle.(4) Mechanisms such as trabeculitis from the radiating shock waves, and neurovascular mechanisms, have also been postulated.(2,13) Risk factors for elevated IOP post Nd:Yag capsulotomy are: pre-existing glaucoma or elevated IOP, high myopia, vitreoretinal disease,diabetes and aphakia.(4,20) Except for myopia, our study did not include patients with these risk factors. IOP increased by 0.9mmHg (p = 0.006) at 2 hours in all patients, and by 1.58mmHg (<0.001) and 1.21mmHg (p = 0.006) in diabetic patients. It is worth noting that in our cohort the amount of shots and energy used for the Nd:YAG capsulotomy was higher than the 20-30 shots mentioned by the examiner. This could be because a third of the patients were diabetic,who develop a greater degree of PCO (20); more than half of the patients in our cohort had moderate to severe PCO. The amount of shots and energy used to perform an Nd:YAG capsulotomy varies based on the pattern of the opening in the posterior capsule. In the study by Kim et al they compared the amount of shots and energy comparing a cruciate pattern and a modified circular pattern. The average number of shots for the cruciate pattern was 38.9 and 97.5 for the modified round technique in their study. In our study we created an inverted D pattern to create the opening in the posterior capsule using on average 62.6 shots which falls between the two patterns compared in Kim et al's study.(21)

In our study, the increase in IOP at 15 minutes after laser capsulotomy in diabetic patients, compared to non-diabetic patients, and the persistent increase up to 2 hours has not been reported in any prior studies. Diabetes is a risk factor for primary open-angle glaucoma. Common pathophysiologic mechanisms in diabetes and glaucoma include oxidative stress damaging retinal ganglion cells, vascular dysregulation, nitric oxide upregulation, overexpression of matrix metalloprotease-9 and glial cell dysfunction.(22) The increase in IOP in diabetic patients post-laser capsulotomy may suggest that there is a greater risk of an IOP increase in these patients. However, diabetic patients develop a greater degree of PCO (20) than non-diabetic patients, and the increase in IOP in diabetic patients may be due to the increase in energy (1,23) used with a more severe grade of PCO. In our study, the increase in IOP in diabetic patients was significant after adjusting for PCO severity. The increase in IOP may also be due to increased inflammatory response, trabeculitis, increased debris in the trabecular meshwork and poorer trabecular meshwork outflow in diabetics. More research would be required to determine the cause. The additional finding of RNFL thinning at 1 month may suggest that diabetic patients are at greater risk of developing glaucoma after Nd:YAG laser capsulotomy.This IOP response may also reflect a race-specific response as all our patients were black African patients. Black African patients are known to have RNFL thinning at a higher rate compared to other races.(24) They also develop glaucoma earlier, have higher IOPs, and have more aggressive disease.(25) This ethnic difference could be a possible reason for our findings. This ethnic difference also supports why monitoring IOP and OCT changes after Nd:YAG laser capsulotomy may be more important in our population. Since our study is the first to report these findings in diabetic patients, further cohort studies with longer follow up are needed to determine if these patients are at increased risk of developing glaucoma.

Limitations of this study were that IOP was not measured at 1 hour, the short follow up period and the different types of IOLs used. Although the IOP increase was not measured at 1 hour after Nd:YAG laser capsulotomy, this would not have mattered in diabetic patients since the IOP increase was shown to occur at 15 minutes which persisted through to the 2-hour time point. The short follow-up means that we could not definitely determine if diabetic patients were at risk of developing glaucoma after laser capsulotomy. Nevertheless, our prospective longitudinal cohort study suggests that these patients are at greater risk of developing glaucoma, and is a platform for further studies, with longer follow-up, to be conducted. Although our study did not account for the different types of IOLs, which can produce different rates of PCO(4,20) , we did adjust for PCO severity in our statistical analysis to determine if the IOP increase was significant.

In conclusion, a significant increase in IOP 2 hours post-Nd:YAG laser capsulotomy (for PCO after cataract surgery) occurred in all patients; however, in diabetic patients it occurred earlier (15 minutes post-laser capsulotomy) and was prolonged (15 minutes and 2 hours post-laser capsulotomy). Additionally, in diabetic patients, a significant decrease in RNFL thickness 1 month after laser capsulotomy occurred, which would suggest that these patients are at increased risk of developing glaucoma. Further longitudinal studies are necessary to determine if diabetic patients definitely develop glaucoma after Nd:YAG laser capsulotomy.

Conflict of interest: none

Abstract

Purpose

To study the effect of Neodymium Yttrium Aluminum Garnet (Nd:YAG) laser capsulotomy on intraocular pressure (IOP) and retinal nerve fibre layer (RNFL) thickness in all patients and diabetic patients with post-cataract posterior capsule opacification (PCO).

Design

Prospective cohort study

Methods

In all the patients, including the diabetic patients, the IOP and RNFL were measured and the PCO graded before Nd:YAG laser capsulotomy (baseline), and the IOP measured at 15 minutes, 2 hours, 1 week and 1 month after laser capsulotomy. Additionally, the RNFL was measured at 1 month after laser capsulotomy. The IOP and RNFL at the aforementioned timepoints after laser capsulotomy was compared to the baseline IOP and RNFL in all patients and in diabetic patients.

Results

Compared to baseline there was a significant increase in IOP of 0.9mmHg at 2 hours ($p = 0.01$) after laser capsulotomy in all patients. In diabetic patients there was a significant increase in IOP of 1.58mmHg at 15 minutes ($p = 0.01$) and 1.21mmHg at 2 hours (p =

0.006). There was a significant decrease in the RNFL thickness in diabetic patients 1 month after laser capsulotomy (p= 0.009); there was no decrease in RNFL thickness in all the patients at this time point.

Conclusion

The prolonged (15 minutes to 2 hours) increase in IOP and the decrease RNFL thickness at 1 month in diabetic patients suggest that these patients are at increased risk of glaucoma. Further longitudinal studies are required to determine if diabetic patients develop glaucoma after Nd:YAG laser capsulotomy.

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