

Glaucoma Filtration Surgery and Retinal Oxygen Saturation

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PURPOSE. Glaucoma may involve disturbances in retinal oxygenation and blood flow. The purpose of this study was to measure the effect of glaucoma filtration surgery on retinal vessel oxygen saturation.

METHODS. A noninvasive spectrophotometric retinal oximeter was used to measure hemoglobin oxygen saturation in retinal arterioles and venules before and after glaucoma filtration surgery. Twenty-five consecutive patients were recruited, and 19 had adequate image quality. Fourteen underwent trabeculectomy and five glaucoma tube surgery. Twelve had primary open-angle glaucoma and seven had exfoliative glaucoma. IOP decreased from 23 ± 7 to 10 ± 4 mm Hg (mean \pm SD, $P = 0.0001$).

RESULTS. Oxygen saturation increased in retinal arterioles from $97\% \pm 4\%$ to $99\% \pm 6\%$ ($n = 19$; $P = 0.046$) after surgery and was unchanged in venules ($63\% \pm 5\%$ before surgery and $64\% \pm 6\%$ after, $P = 0.76$). There were no significant changes in saturation in the fellow eyes ($P > 0.60$). The arteriovenous difference was 34% before and 36% after surgery ($P = 0.35$).

CONCLUSIONS. Glaucoma filtration surgery had almost no effect on retinal vessel oxygen saturation. (*Invest Ophthalmol Vis Sci.* 2009;50:5247-5250) DOI:10.1167/iovs.08-3117

The exact pathogenesis of glaucoma is not known. The role of hypoxia is supported by increased staining of hypoxia-induced factor (HIF-1 α) in the retina and optic nerve of patients with glaucoma compared with that present in healthy individuals.¹ Animal studies have demonstrated that optic nerve oxygen tension decreases if intraocular pressure (IOP) rises to high levels and increases if IOP is lowered again.^{2,3} Decreased or poorly controlled ocular blood flow, has been shown in patients with glaucoma in many studies (for review, see Refs. 4, 5).

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Glaucoma filtration surgery is one of many treatment options used in glaucoma management. It decreases IOP, which remains the primary goal of glaucoma therapy. To our knowledge, no studies have examined oxygenation of the retina before and after glaucoma surgery. However, several studies have been conducted to determine the effect of glaucoma surgery on ocular blood flow, with varying results. An increase in blood flow velocity in the central retinal artery was demonstrated by Tribble et al.⁶ while Cantor⁷ found no change. Superficial optic nerve head blood flow was found to increase after surgery in two studies,^{8,9} whereas others found no change in optic nerve head blood flow⁷ or flow velocity.¹⁰ Two studies have found no change in capillary blood flow in the peripapillary area.^{7,9} Increased pulsatile ocular blood, which is presumed to reflect increased choroidal blood flow, was found after glaucoma surgery in three studies.^{8,11,12} Blood flow velocity in short posterior ciliary arteries, which partly supply the choroid, has been found to be increased⁶ or unchanged.⁷

Previous studies, therefore, indicate that glaucoma may involve hypoxia and poor or poorly controlled blood flow. However, the influence of glaucoma surgery on blood flow is uncertain and the influence on retinal oxygenation has not been studied. The purpose of this study is to investigate changes in retinal vessel oxygen saturation after glaucoma filtration surgery.

METHODS

The automatic retinal oximeter has been described previously.¹³ It is based on a fundus camera (Canon CR6-45NM, Canon Inc., Tokyo, Japan), which is coupled with a beam splitter (MultiSpec Patho-Imager; Optical Insights, Tucson, AZ) and a digital camera (SBIG ST-7E; Santa Barbara Instrument Group, Santa Barbara, CA). It yields fundus images with four wavelengths of light simultaneously. Specialized software automatically selects measurement points on the oximetry images and calculates the optical density (absorbance) of retinal vessels at two wavelengths: 605 and 586 nm. Optical density is sensitive to oxygen saturation at 605 nm but not at the reference wavelength, 586 nm. The ratio of these optical densities is approximately linearly related to hemoglobin oxygen saturation,^{14,15} and the oximeter yields relative oxygen saturation levels. Although the saturation data are not absolute, the oximeter has been shown to give reproducible results and to be sensitive to changes in oxygen saturation.¹³ The comparison of data in the same eye before and after surgery is therefore valid.

Pupils were dilated with 1% tropicamide (Mydracil; Alcon-Couvreur NV, Puurs, Belgium), which was in some cases supplemented with 10% phenylephrine hydrochloride (AK-Dilate; Akorn Inc., Lake Forest, IL). Oximetry was performed in first- and second-degree retinal arterioles and venules. Oximetry was performed before glaucoma surgery and again approximately 1 month after surgery (Fig. 1). Infrared light was used to align the fundus camera (oximeter), and the images were taken in a dark room. The time between images (flashes) of the same eye was on average 1 to 2 minutes. An average was taken of measurable arterioles and venules in each eye and the same vessels' segments were averaged before and after surgery.

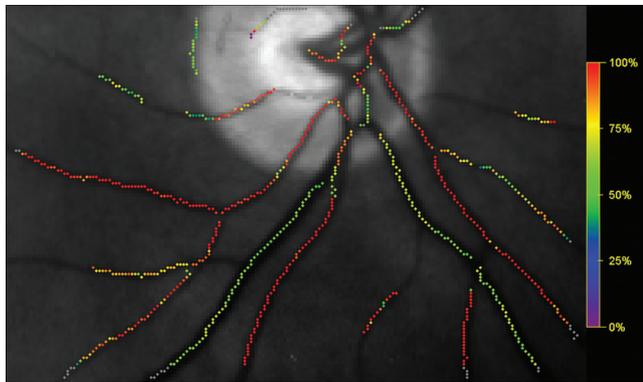


FIGURE 1. The pseudocolor fundus image shows a typical map of the hemoglobin oxygen saturation in the human fundus. This image was taken before surgery. *Right:* oxygen saturation color scale.

All consecutive patients with open-angle glaucoma, with and without pseudoexfoliation syndrome, undergoing glaucoma surgery in Iceland in a 6-month period were invited to participate in the study. All patients were using topical glaucoma drugs before their surgery, and one was also taking oral acetazolamide (Table 1). None of the patients used glaucoma drugs at the time of postoperative oximetry. Twenty-five patients were measured before and after surgery. Six patients were excluded from analysis because of poor optical quality of the eye.

Fourteen patients underwent trabeculectomy with mitomycin C and five patients underwent glaucoma drainage device surgery with the Ahmed tube. All surgeries were performed by the same surgeon.

Statistical analysis was performed with R ver. 2.6.1 (provided in the public domain by the R Foundation for Statistical Computing, Vienna, Austria, available at <http://www.r-project.org/>). Paired *t*-tests were used for comparing the means. Post hoc power analyses were performed separately for arterioles, venules, and arteriovenous differences. An effect size of five percentage points and standard deviations of differences between measurements before and after surgery (surgical eye) were used to calculate the power. The study was approved by the National Bioethics Committee of Iceland and The Icelandic Data Protection Authority and adhered to the tenets of the Declaration of Helsinki.

TABLE 1. Clinical and Medication Data

Demographic Data of the 19 Study Patients

Age	73 ± 7 years (mean ± SD)
Sex	12 M, 7 F
Pseudoexfoliation, <i>n</i>	7
Trabeculectomy, <i>n</i>	14
Shunt surgery (Ahmed tube), <i>n</i>	5
IOP in surgical eye before surgery, mm Hg	23 ± 7 (mean ± SD)
IOP in surgical eye after surgery, mm Hg	10 ± 4 (mean ± SD)
	Postoperative IOP decreased ($P < 0.0001$)

Eyes Receiving Topical Medication before Glaucoma Filtration Surgery, *n*

Timolol+ dorzolamide+latanoprost	7
Latanoprost	3
Betaxolol+latanoprost	2
Timolol gel+latanoprost	2
Timolol+pilocarpine+latanoprost	1
Timolol+brimonidine+latanoprost	1
Pilocarpine+propine+travoprost	1
Brimonidine+latanoprost+acetazolamide	1
Timolol gel	1

TABLE 2. Hemoglobin Oxygen Saturation in First- and Second-Degree Retinal Vessels in 19 Patients before and after Glaucoma Filtration Surgery

	Surgical Eye		Fellow Eye	
	Pre-op	Post-op	Pre-op	Post-op
Arterioles	97 ± 4	99 ± 6*	96 ± 5	96 ± 5
Venules	63 ± 5	64 ± 6	64 ± 6	63 ± 8
AV difference	34 ± 6	36 ± 8	32 ± 6	32 ± 8

AV difference denotes the difference in oxygen saturation between arterioles and venules. The table shows the mean percentage ± SD.

*The increase in arterioles in the surgical eye was statistically significant; $P = 0.046$ (paired *t*-test).

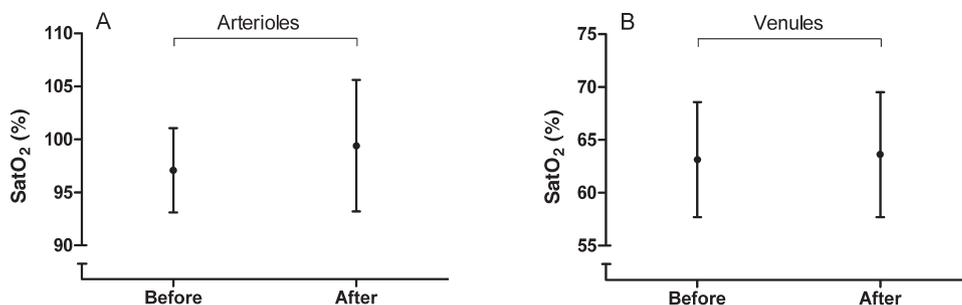
RESULTS

A statistically significant increase from 97% ± 4% to 99% ± 6% ($n = 19$; $P = 0.046$, paired *t*-test, Table 2; Fig. 2) was found in arteriolar oxygen saturation after glaucoma filtration surgery. No change ($P = 0.76$) was seen in oxygen saturation in the venules, and the oxygen saturation in the fellow eyes remained stable ($P > 0.60$). The arteriovenous difference in oxygen saturation was 34% before surgery and 36% after surgery ($P = 0.35$). Assuming an effect size of 5 percentage points, post hoc power analysis yields a power of 99% for arterioles, 87% for venules, and 70% for arteriovenous difference.

DISCUSSION

Our results show almost no change in oxygen saturation with glaucoma filtration surgery. We found a statistically significant 2% increase in arteriolar oxygen saturation and no change in venules after dramatic lowering of IOP with surgery. Changes in arteriovenous difference did not reach statistical significance. Although the sample size is small, a post hoc power analysis demonstrates that it is unlikely that a difference of 5 percentage points or larger was missed in retinal venules (or in arteriovenous difference). It can therefore be concluded that the surgery had almost no effect on oxygen saturation.

FIGURE 2. Hemoglobin oxygen saturation (SatO₂ %) in (A) retinal arterioles and (B) venules before and after glaucoma filtration surgery. Data are the mean and standard deviation. The measurements are the same as those in Table 2.



The absence of change in retinal vessel oxygen saturation does not necessarily mean that glaucoma filtration surgery has no effect on oxygenation of the retina. Oxygen delivery from the retinal circulation to the tissue depends on both the arteriovenous difference in saturation and on the retinal blood flow. We found almost no change in oxygen saturation, but the question remains whether there could be an increase in retinal blood flow with surgery.

Retinal blood flow can be described (at least qualitatively) by the Hagen-Poiseuille law, which states that flow is equal to the arteriovenous pressure difference (perfusion pressure) divided by the resistance to flow. Since the retinal venous pressure is equal to¹⁶⁻¹⁸ or at least positively correlated with^{19,20} IOP, the flow, F , can be calculated as:

$$F = \frac{OAP - IOP}{R}$$

where OAP is the ophthalmic artery pressure and R is the resistance to flow. Therefore, if IOP is decreased after surgery and if other factors are constant, the flow should increase. Whether the other factors are constant, however, is not certain. Autoregulation of blood flow may, for example, increase the resistance, R , and limit the change in flow, F . Some studies have found an increase in blood flow after glaucoma filtration surgery, whereas others have found no change (see the introduction). Whether the retinal blood flow changed in the present study is uncertain. It should be noted, however, that the small increase found in arteriolar saturation is consistent with an increase in retinal blood flow (i.e., less oxygen is lost per unit volume of blood through the arteriolar walls when the blood flow increases).

Oxygen delivery by the retinal vasculature mostly reflects oxygen consumption by the inner retina, whereas the choroid mostly supplies the outer retina, although these boundaries shift a little depending on light conditions.²¹⁻²³ Choroidal blood flow increases with dramatic increases in perfusion pressure,²⁴⁻²⁹ and some studies have indicated an increase after glaucoma surgery.^{8,11,12} However, oxygen was not measured in the choroid in this study and it is uncertain whether the decrease in IOP in this study has an effect on oxygenation. If there is any effect of the surgery on oxygen delivery from the choroid, an increase is more likely than a decrease.

One limitation of the present study is that the patients received glaucoma drug treatment before but not after surgery and this may influence the oxygen saturation. However, despite the withdrawal of drugs, the IOP was dramatically decreased between the pre- and postoperative measurements. Unfortunately, blood pressure data are not available to confirm that perfusion pressure was increased. Most of the patients (14/19; Table 1) were using ocular β -blockers before surgery and not after surgery, and the cessation of the medication may have increased blood pressure after surgery. The oxygen saturations are relative, although comparison between the same

eye before and after surgery is valid (see the Methods section). Finally, although the retinal oximeter has been systematically defined and tested,¹³ clinical oximetry studies are limited so far.

We conclude that glaucoma filtration surgery, which lowers IOP, results in almost no change in retinal vessel oxygen saturation. Coupled with an increase in retinal blood flow, the sustained oxygen saturation would result in increased oxygen delivery to the retina after surgery. Changes in retinal blood flow are uncertain, however, and further studies are needed. It should also be stressed that the present study only includes retinal measurements, with no evaluation of potential changes in optic nerve oxygenation.

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