LABORATORY SCIENCE

Histopathological trabecular meshwork remodeling after cataract surgery detected with an advanced image analyzer

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Purpose: To compare the histopathological morphometry of the trabecular meshwork and ciliary processes in pseudophakic eyes and phakic eyes using advanced image analyzer technology.

Setting: McGill University, Montreal, Quebec, Canada.

Design: Retrospective case series.

Methods: Thirty-five pseudophakic eyes and 25 phakic eyes were sectioned and converted into digital slides. The total trabecular meshwork area and the ciliary body stroma were demarcated. The area of the trabecular meshwork, cellular and noncellular trabecular meshwork compartments, trabecular space, distance from scleral spur to inner uveal trabecular portion, and degree of fibrosis of the ciliary processes were evaluated.

Results: The trabecular meshwork area was larger in the pseudophakic group than the phakic group ($P = .03$). Furthermore, a trend of larger trabecular space recorded was seen in the pseudophakic group than the phakic group ($P = .14$). No differences in the proportion of cellular ($P = .88$) and noncellular trabecular meshwork compartments ($P = .4$) were seen between groups. The scleral spur to inner uveal trabecular portion distance was longer in the pseudophakic group than the phakic group ($P = .008$) and correlate with the trabecular meshwork area ($P = .0001$, $r = 0.56$). In the ciliary processes, a higher degree of fibrosis was measured in the pseudophakic group than the phakic group ($P = .02$).

Conclusions: There were significant histopathological changes in the trabecular meshwork and higher fibrosis in the ciliary processes in pseudophakic eyes compared with phakic eyes. These findings support the hypothesis that trabecular meshwork remodeling after cataract surgery is involved in lowering intraocular pressure.

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Cataract and glaucoma are the leading causes of blindness worldwide; moreover, cataract surgery is among the most commonly performed surgical procedure.[1–3] Numerous previous studies[4–11] found that uneventful cataract surgery with a posterior intraocular lens (IOL) replacement lowers intraocular pressure (IOP) in most patients, independent of coexisting glaucoma or surgical technique. The postoperative IOP has been reported in the literature to decrease by up to 16.5%[4] and to be stable for up to 10 years.[6] The major predictor of IOP reduction after cataract surgery is the preoperative IOP; individuals with higher preoperative pressures are more likely to have a greater decline in IOP after surgery.[4–7,11] Other factors that have been associated with the decrease in IOP after cataract surgery include a shallower anterior chamber depth (ACD), narrower angle, a steeper iris curvature, and a wider lens vault, as measured via clinical evaluation using ultrasound and optical coherence tomography.[11–14] Nevertheless, clinical data regarding the magnitude and the long-term clinical importance of this decrease in the IOP is still under debate.[15]

Impaired aqueous secretion and improved outflow are the mechanisms proposed to explain this phenomenon. Impairment of aqueous production because of

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hyposecretion by the ciliary body secondary to partial detachment of the ciliary epithelium or because of surgical manipulation has been suggested.[16] Increased outflow has been attributed to biochemical changes in the aqueous humor, prostaglandin release, increased permeability of the blood–aqueous barrier, particulate washout, and structural changes in the outflow tract.[16]

Progressive thickening of the aging lens is thought to impede flow to the trabecular meshwork; as such, its extraction and replacement with a thinner lens relieves obstruction and improves outflow. Accordingly, deepening of the anterior chamber and iridocorneal angle has been well documented in pseudophakic eyes.[11–14] In addition, repositioning the lens capsule to a more posterior location after surgery allows the zonular fibers to exert backward traction on the ciliary body and the scleral spur, allowing the expansion of the trabecular meshwork.[17] The aim of this study was to compare the histopathological morphometry of the trabecular meshwork and ciliary processes between pseudophakic eyes and phakic eyes using advanced image analyzer technology and therefore recognize structural changes that might be related to the decrease in IOP after cataract surgery.

MATERIALS AND METHODS

Tissue Samples

Clinicopathologic data from 76 normal human eyes from the Eye Bank of Canada (Toronto, Ontario, Canada) were obtained. All data accumulation was in accordance with the Canada and Province of Quebec legislation and the tenets of the Declaration of Helsinki. Data included age and sex. All eyes were fixed in formalin and cut along the coronal axis. A Miyake-Apple view was obtained to verify the lens status (phakic, pseudophakic, or aphakic). The anterior segment was further bisected in the sagittal axis through the center of the pupil, processed routinely, and embedded in paraffin. The lens was removed to be processed histopathologically only for eyes with a hard IOL. Slides were stained with Masson trichrome and digitalized using a digital slide scanner (Aperio AT Turbo, Leica Biosystems Imaging, Inc.) (Figure 1).

Of the 76 eyes, 60 were selected for the study, including 25 phakic eyes and 35 pseudophakic eyes. The remaining 16 eyes were excluded from the analysis because they had an asymmetric globe shape, corneal depression, were aphakic, or a combination.

Trabecular Meshwork Measurements

Using the digital slide scanner, the trabecular meshwork was demarcated by an experienced ocular pathologist on a touchscreen (Flexscan T2351W, Eizo Corp.) using a stylus pen (Figure 2, *A*). The area demarcated included the corneoscleral and uveal meshwork. Using the custom TMAN software (Medical Parachute), the trabecular area, trabecular space, and trabecular lamellae area were obtained. The cellular and extracellular matrix (ECM) compartments of the trabecular lamellar area were also evaluated (Figure 2, *B*). Moreover, a trabecular meshwork fibrosis score corresponding to the intensity of the ECM collagen staining (blue in Masson trichrome) was obtained. To standardize the intensity of the Masson staining across the samples, internal controls were established in each section as follows: The maximum intensity was acquired by demarcating the darkest area in the sclera and the lower intensity from the loose stroma of the iris on each eye (Table S1 in Supplement 1, available at http://jcrsjournal.org). A relative intensity was then obtained considering these internal controls as detailed in Supplement 1 (available at http://jcrsjournal.org).The distance between the scleral spur and the inner uveal trabecular portion was also recorded in each case (Figure 3, *A*) using the Aperio image scope analyzer (Leica Biosystems Imaging, Inc.)

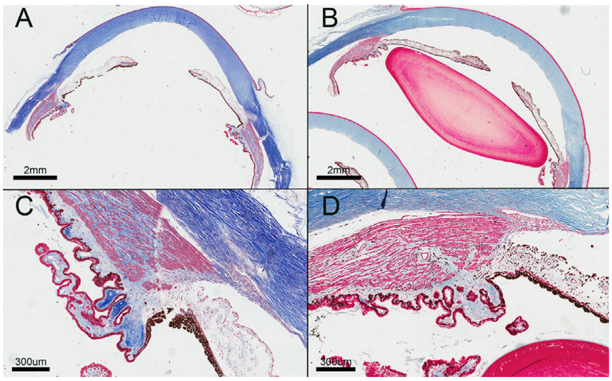

Figure 1. Anterior segment of the eye stained with Masson trichrome. Low-power view of a pseudophakic (*A*) and phakic eye (*B*) (original magnification ×2). Medium-power view of the angle and ciliary process of the same pseudophakic (*C*) and phakic eye (*D*).

Ciliary Process Fibrosis Measurements

Demarcation of the stroma above the muscular bundles of the ciliary body was performed. A fibrosis score that considers the area and the intensity of the structure were evaluated (Figure 4, *A*, and Supplement 1, available at http://jcrsjournal.org).

Statistical Analysis

The means for the pseudophakic group and phakic group were compared using the Mann-Whitney test as determined by the D'Agostino and Pearson omnibus normality test. To test whether age was a confounding factor, a correlation matrix coefficient was calculated for each measurement. Statistics were performed using Excel software (Microsoft Corp.) and Graphpad Prism software (version 5.0, Graphpad Software, Inc.).

RESULTS

A larger trabecular meshwork area was observed in the pseudophakic group than the phakic group ($P = .0262$) (Figure 2, *C*, *left*). Furthermore, trabecular meshwork structural compartments were analyzed separately. A trend of larger trabecular space area in pseudophakic eyes than in phakic eyes was noted ($P = .14$) (Figure 2, *C*, *center*). For the trabecular lamellae, a larger area was observed in the pseudophakic group than in the phakic group ($P = .01$) (Figure 2, *C*, *right*). Moreover, within the trabecular lamellae, no differences in the percentage area of the cellular and ECM area compartments between the pseudophakic group and in phakic group were noted ($P = .88$ and $P = .40$, respectively) (Figure 2, *D*). In addition, the trabecular meshwork fibrosis score was comparable between the 2 groups ($P = .25$) (Figure 2, *D*). Last, the scleral spur to uveal trabecular meshwork distance was longer in the pseudophakic group than in the phakic group ($P = .008$) (Figure 3, *B*, *left*) and correlated with the trabecular meshwork area ($P = .0001$, $R = 0.56$) (Figure 3, *B*, *right*).

The evaluation of the fibrosis of the ciliary processes showed that the pseudophakic eyes had significantly