Outflow Resistance

Implications for canal-based surgery.

BY HAIYAN GONG, MD, PhD


Welcome to Glaucoma Today's *third installment of "Bench to Bedside: How Laboratory Studies May Better Explain Why Procedures Work and Why They Fail." The essence of this column is to explain the "why" of the clinical quandaries we glaucoma specialists often face. This group of articles tackles why canal-based surgery does not lower IOP to episcleral venous pressure (EVP). One would think it should, but on average, it does not. Basic laboratory experiments may improve our understanding.*

We asked three basic and clinician scientists critical questions about outflow to bridge the gap in this clinical puzzle from bench to bedside. In the first installment, Murray Johnstone, MD, analyzed past and recent research on outflow resistance and discussed how high-resolution optical coherence tomography and optical microscope platforms permit the real-time observation of collector channel motion. (See Dr. Johnstone's article in the January/February issue of GT, *and watch his video [http://bit.ly/1OFsPgA] on the opening and closing of collector channels.) In the second installment, Arthur J. Sit, SM, MD, shared his expertise on outflow. (See Dr. Sit's article in the July/August issue of GT.) In this final installment, Haiyan Gong, MD, PhD, provides her answers to four questions about outflow.*

—Ronald L. Fellman, MD, and Davinder S. Grover, MD, MPH, section editors

CLINICAL PUZZLE

Canal-based surgery does not lower IOP to EVP, which is reported to be around 10 mm Hg. Why?

The classic outflow experiment by Rosenquist et al[1] found greater downstream resistance to aqueous outflow than Grant's classic study.[2] Why? Does this article at least partially explain IOP control after canal-based surgery?

Rosenquist et al reported that, after a complete trabeculotomy, 49% of outflow resistance is eliminated at a perfusion pressure of 7 mm Hg (corresponding to the normal IOP in enucleated human eyes with no EVP).[1] Grant reported that 71% of outflow resistance was eliminated at a perfusion pressure of 25 mm Hg.[2] Schuman et al reported that 35% of outflow resistance was eliminated after a 1-clock hour ablation of the tissue from the outer wall of Schlemm canal (SC) and distal by using the excimer laser at a perfusion pressure of 10 mm Hg.[3]

These studies suggest that one-third to one-half of the outflow resistance lies distal to the inner wall of SC at normal pressure[1,3] and that a portion of outflow resistance is related to pressure-dependent changes in the outflow pathway.[2] SC becomes narrower or collapses with elevated IOP, which is associated with decreases in outflow facility and effective filtration area.[4,5] Blockages of collector channel (CC) ostia were also reported clinically and histologically.[5-7] These structural changes would contribute to distal outflow resistance. If canal-based surgery can dilate or maintain dilation of SC and remove or reverse the blockage of CC ostia, it will lower IOP. The success of canal-based surgery intended to restore outflow into the episcleral venous system would depend on whether there are some permanent changes in the distal outflow pathway.[6-8]

If distal outflow resistance is higher than initially anticipated, is most of the resistance coming from deep in the sclera, or is it more superficial?

This question has not been carefully investigated in healthy and glaucomatous eyes.

What is outflow facility, and how is it measured? What is the correlation between outflow facility and outflow resistance?

The flow of aqueous humor through the trabecular meshwork is driven passively by gradients in osmotic and/or hydrostatic pressures. Because there is no

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osmotic difference between aqueous and the blood into which it flows, what is left is hydrostatic pressure as the dominant force.[9] So, it is the pressure difference (P) between the IOP in the anterior chamber and that in the episcleral veins (P = 5 mm Hg) that drives aqueous humor through this system. The ratio of this pressure difference to that of aqueous flow (assuming a typical flow rate [Q] of 2-3 µL/min) equals the flow resistance (R).[10]

R = P/Q

The inverse of the outflow resistance is known as the *outflow facility* (Ctm).

Ctm = Q/(Pi-Pe), where Pi equals IOP and Pe equals EVP.

To learn how to measure the outflow facility, please read the article by Toris and Camras in the September 2007 issue of *GT*.[11]

In your opinion, why is circumferential flow in SC limited, and does this influence canal-based surgery?

Based on a previous tracer study by my colleagues and me in enucleated human eyes, aqueous humor outflow through the trabecular outflow pathway is segmental or circumferentially nonuniform.[12] We found that only 39.9% ±5.8% of the outflow pathways was actively involved in aqueous humor drainage in normal control eyes at 15 mm Hg (more than 2 clock hours). This active flow area was measured through the percent effective filtration length, which equals the length of the inner wall exhibiting tracer labeling/total length of inner wall. We observed a greater concentration of tracer in the trabecular meshwork adjacent to CC ostia, but not all the CC ostia are active at a given time.

In another ongoing study in my laboratory, we found that a similar percentage of active flow area reached the inner wall of SC (35.32 ±5.0%) and continued in the episcleral veins with significant preferential flow to the nasal quadrant ($P < .05$).[13] Further studies are needed to understand why there is lower outflow resistance in the nasal quadrant. When performing canal-based surgery, such as with the iStent Trabecular Micro-Bypass Stent (Glaukos), the success of the procedure depends on the circumferential location (ie, whether the implant is placed near a large and active CC ostium).

In another tracer study designed to investigate changes in outflow facility and outflow pattern after implanting either one Hydrus Microstent (Ivantis; not available in the United States) or two iStents in one enucleated human eye, we accidently placed two iStent implants in the temporal region instead of the nasal region.[14] The fluorescent tracer, perfused into the anterior chamber, still preferentially flowed to the nasal region, not the regions with implants, which suggests that the nasal region has lower outflow resistance than the temporal region, even with implants.[14] More studies are needed to confirm this finding. ■

Section Editor Ronald L. Fellman, MD, is a glaucoma specialist at Glaucoma Associates of Texas in Dallas and clinical associate professor emeritus in the Department of Ophthalmology at UT Southwestern Medical Center in Dallas. Dr. Fellman may be reached at (214) 360-0000; rfellman@glaucomaassociates.com.

Section Editor Davinder S. Grover, MD, MPH, is a glaucoma specialist at Glaucoma Associates of Texas in Dallas and a clinical instructor in the Department of Ophthalmology at UT Southwestern Medical Center in Dallas. Dr. Grover may be reached at dgrover@glaucomaassociates.com.

Haiyan Gong, MD, PhD, is a professor of ophthalmology, anatomy, and neurobiology at Boston University School of Medicine in Boston. *She acknowledged no financial interest in the products or companies mentioned herein, but she has received grant support from Aerie Pharmaceuticals, the Massachusetts Lions Eye Research Fund, and the National Institutes of Health (EY022634 and EY019696). Dr. Gong may be reached at hgong@bu.edu.*

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