Something Old (Trabeculectomy), Something New (Ab Interno Gelatin Microstent): Finally, a Marriage of Innovation and Outcome Data (without Concurrent Cataract Surgery)!

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We thank Schlenker et al1 (see http://www.aaojournal.org/article/S0161-6420(17)30464-5/fulltext) for providing a much-needed substantive comparison of one of the newer less-invasive glaucoma procedures (ab interno gelatin microstent) with trabeculectomy, the gold standard glaucoma filtering procedure for nearly 50 years. We have all been seeking a more predictable and successful treatment than trabeculectomy, and our patients are potential beneficiaries of a surge of innovation exploring techniques and devices to afford enhanced aqueous outflow via Schlemm canal, suprachoroidal, and subconjunctival approaches. The Food and Drug Administration-approved devices in the 2 former categories have been studied and approved in the context of combination treatment with cataract surgery. Partly because of the intraocular pressure (IOP) reduction achieved by cataract surgery alone,2 the seminal studies3,4 for those devices in combination with cataract surgery have demonstrated only modestly greater reduction in IOP, ocular hypotensive medication burden, or both than cataract surgery alone. Furthermore, the IOP outcomes have clustered in the mid to high teens in most patients, such that many patients for whom lower IOPs are desirable may not be sufficiently well served by those devices.

Because both of us are somewhat skeptical by nature (one of us by virtue being sufficiently senior to have personally lived through Scott’s parabola5 with such devices as the Mendez Glaucoma Seton,6 Krupin-Denver valve,7 thulium-holmium-chromium-doped:yttrium—aluminum—garnet laser sclerostomy,8 and Ex-PRESS (Optonol, Ltd., Neve-Ilan, Israel) implant [not under scleral flap]), we enthusiastically welcome the retrospective comparison by Schlenker et al of the ab interno gelatin microstent and trabeculectomy without the confounding variable of cataract surgery. The authors exhibit considerable understanding of clinical research, as well as very sophisticated and effective application of statistical methods. We wish that, as soon as the authors had achieved reasonable facility and comfort with the microstent procedure, they had seized the opportunity to undertake a randomized clinical trial (RCT) for a more direct comparison. Too frequently, the early adopters among us perform relatively high volumes of a new procedure without subjecting that procedure to the rigor of an RCT, from which fellow physicians would derive invaluable insight into the relative merits of and indications for that procedure versus an appropriate gold standard. Retrospective cohort studies are certainly informative, but RCTs minimize bias, especially in patient selection, and a well-performed RCT is more likely to influence care provided by colleagues. A new device or technique deserves a period of exploration and trial before the cost and effort of a randomized comparison with the current gold standard and also deserves the best chance possible to supplant the gold standard in ways that maximize both effect and safety. We believe that a well-designed RCT is the best path forward for these innovations and suggest that the most responsible (and ultimately effective) way to advance a good idea is to obtain enough data to justify an RCT and then to proceed immediately to the RCT.

Drawn from consecutive patients treated at 4 tertiary referral centers in Canada, Germany, Austria, and Belgium, the authors retrospectively reviewed 354 eyes (293 patients; 185 microstents and 169 trabeculectomies) with no prior incisional glaucoma or conjunctival surgery. This multicenter collaboration and its sample size improve the generalizability of the findings; however, compared with most United States tertiary referral glaucoma practices, patients of African ancestry were underrepresented consistent with the Canadian and European location of the study centers.

One of the common limitations of studies of new techniques is the associated early learning curve. To avoid this issue, the authors selected their study period to balance “the need to ensure the surgeons were over the initial learning curve required to insert the microstent, while early enough in their experience to preclude significant preconceived notions regarding which procedure was best for a given patient (to minimize confounding by indication).” However, there was disparate allocation of patients between microstents and trabeculectomies among centers overall (P = 0.003) that resulted from more microstents at the Canadian center (63%) and more trabeculectomies at the German and Austrian centers (57% and 60%, respectively); Belgium was relatively balanced (51% microstents). This suggests that surgeons at the Canadian, German, and Austrian centers did have some “preconceived notions regarding which procedure was best for a given patient,” and given the large number of patients and the 55-month study period, one would expect surgeons (particularly those past the initial learning curve) to have formed some preliminary (perhaps unconscious) selection biases. Consequently, it is reassuring that the authors confirmed that, at least with respect to expected potential confounders, the groups were relatively well matched, with only the following demographic characteristics being statistically significantly different for the microstent group compared with the trabeculectomy group, respectively: median age (65.0 years [range, 53.7–73.6 years]) vs. 67.2

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years [range, 59.2–74.8 years]), gender (43.8% vs. 57.4% women), preoperative visual acuity (median, 0.2 logarithm of the minimum angle of resolution [logMAR; interquartile range, 0.1–0.3 logMAR] vs. 0.2 logMAR [interquartile range, 0.1–0.6 logMAR]), preoperative visual acuity of 0.4 logMAR or less (21.6% vs. 32.0%), and previous laser trabeculoplasty (52.4% vs. 29.6%). Although those factors were statistically significantly different, we are reassured that the differences, except for previous trabeculoplasty, were small and therefore probably not clinically significant. The authors appropriately acknowledge that their statistical analyses cannot adjust for unrecognized confounders, which is an inherent disadvantage of any retrospective study.

The success rates were not dissimilar between microstents and trabeculectomies for IOP ranges of 6 to 14 mmHg, 6 to 17 mmHg, and 6 to 21 mmHg, both without (complete success) and with (qualified success) ocular hypertensive medication (or laser trabeculoplasty). Eyes of nonwhite patients and those with diabetes had statistically significantly higher failure rates overall. Statistically significant differential interactions of the intervention (i.e., microstent versus trabeculectomy) were observed vis-à-vis preoperative visual acuity, preoperative IOP, and ethnicity. Eyes with preoperative vision better than 0.4 logMAR showed statistically significantly better results with microstents; whereas those with worse vision trended better with trabeculectomies. Eyes with preoperative IOP of more than 21 mmHg trended better with microstents, whereas those 21 mmHg or less trended better with trabeculectomies. The influence of ethnicity was apparently driven by eyes of nonwhite patients that had undergone trabeculectomies that had failed more frequently than eyes of white patients that had undergone microstents. Many patients in both groups underwent postoperative interventions, most frequently the following: needling (43.2% vs. 30.8%), anterior chamber reformation (11.9% vs. 6.9%), and bleb revision or conjunctival suturing (1.1% vs. 5.9%). Serious complications were limited to malignant glaucoma (2.2% vs. 1.2%) and blebitis (0% vs. 0.6%).

Given the authors’ otherwise sophisticated application of statistical methods, it is surprising that they chose to exclude patients with less than 1 month of follow-up, an approach that is not consonant with the principles of survival analysis. The 12.8% and 9.2% of eyes, respectively, that were excluded because the treating physicians (of out-of-town patients) did not respond to data inquiries raises concerns regarding how much and how many of the remaining patients’ early care was managed by treating physicians rather than the study physicians. This is important given the potential impact of less expert early postoperative management on the successful outcome of filtering surgery (especially for trabeculectomies, but presumably also for microstents).

In summary, this study provides the first large comparison of one of the newer less-invasive glaucoma procedures with trabeculectomy. As such, it demonstrated similar IOP and visual acuity outcomes, reductions in ocular hypertensive medication burden, postoperative interventions (more with trabeculectomy if laser suture lysis is considered an intervention), and complications with both approaches. The groups seem relatively comparable, but the authors and other early, high-volume adopters are encouraged to undertake RCTs relatively early with new techniques, specifically as soon as device development and experience with the devices is sufficient to warrant an RCT. Better approaches will be adopted more quickly as soon as they have been proven objectively superior to current preferred practices. Our patients deserve the best care possible, so having better evidence sooner is essential. To achieve more rapid acceptance of new techniques when appropriate by colleagues, we call on all potential sources of funding to support earlier RCTs during the development of innovative devices and procedures, and thereby to expedite the application of better surgical approaches to benefit our patients.

References