

2005 ARVO Highlights

Glaucoma researchers from around the world presented hundreds of posters and papers at the annual meeting in Fort Lauderdale, Florida.

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Every year, the ARVO meeting features presentations of the best in glaucoma research. In May 2005, the spotlight shone on surgery, IOP, and the detection of glaucomatous progression. From hundreds of studies, we have chosen several of the most interesting and clinically relevant.

IOP MEASUREMENT

Researchers from the University of Southern California in Los Angeles evaluated the effect of central corneal thickness (CCT) on Goldmann applanation tonometry and dynamic contour tonometry. They evaluated 806 eyes and obtained a mean IOP of 14.0 ± 3.3 mm Hg from applanation tonometry and a mean IOP of 14.8 ± 3.8 mm Hg from dynamic contour tonometry. After stratifying the data by CCT, the researchers observed that, in patients with CCTs > 500 μm , the IOP measurements from applanation tonometry were higher than those from dynamic contour tonometry, but the mean difference was greater with higher IOP levels. Conversely, they discerned the opposite relationship in patients with CCTs < 500 μm , and the mean difference (ie, applanation IOP minus dynamic contour tonometry IOP) was 2 mm Hg, regardless of IOP levels. The investigators suggested that, from a clinical perspective, dynamic contour tonometry might provide more accurate estimates of IOP in eyes with thin CCTs.¹

Two studies evaluated the biomechanical properties of the cornea, specifically corneal hysteresis (ie, corneal resistance to deformation). An Ocular Response Analyzer (Reichert, Inc., Depew, NY) measured the corneal hysteresis in both studies. The device is an air-puff tonometer that uses an applied-force–displacement relationship to determine corneal hysteresis. The study conducted at Johns Hopkins Hospital in Baltimore aimed to estimate the influence of ocular characteristics on tonometers. Researchers measured the IOP of 230 subjects, with a Goldmann applanation tonometer, the Tono-Pen (Medtronic Xomed Ophthalmics, Inc., Minneapolis, MN), and the Ocular Response Analyzer. The investigators observed that each tonometer had strengths in being less affected by particular ocular characteristics.

They suggested that the tonometric calculation of IOP could be affected by properties of the cornea other than its thickness. They observed a quadratic relationship between hysteresis and the average IOP. The lowest and highest values of hysteresis were associated with higher IOP values than midrange hysteresis. The investigators concluded that corneal bioelastic response merits further research.²

In a separate study at the Bietti Foundation in Rome and Moorfields Eye Hospital in London, researchers evaluated 105 patients, whose mean age was 60 years (range, 26 to 82 years), with the Ocular Response Analyzer. Although this study did not aim to evaluate the impact of hysteresis on IOP measurement, investigators observed that corneal hysteresis decreased with age and was significantly greater in thicker corneas.³

IOP VARIATION

A study conducted at the New York Eye and Ear Infirmary in New York City reviewed the records of open-angle glaucoma (OAG) patients admitted for 24-hour IOP monitoring. Applanation IOP was recorded at 6 AM when patients were in the supine position and every 2 hours when they were in the sitting position. Confirming previous research, 24-hour IOP monitoring revealed higher peaks and wider fluctuation than did measurements taken during office hours. Upon calculating the differences between IOP peaks detected during 24-hour monitoring and those occurring during office hours, researchers observed a difference of ≥ 2 mm Hg in 43% of OAG patients and ≥ 4 mm Hg in 19% of OAG patients. Furthermore, in 60.9% of eyes, the 24-hour peak IOP was higher than the peak IOP noted during the previous five visits. The investigators concluded that the 24-hour monitoring of IOP might reveal a greater role for an IOP-related risk of glaucomatous progression than previously suspected.⁴

Researchers from the University of São Paulo in Brazil compared the IOP variation detected in a modified diurnal tensional curve (five IOP measurements in the sitting position, 2 hours apart, from 8 AM to 4 PM) to the variation observed by moving the body from a seated to a supine position and by a water-drinking test. Because these tests

have been proposed to assess IOP control in OAG patients, the investigators aimed to compare them in 31 OAG patients under topical antiglaucoma treatment. The mean IOP detected in the modified diurnal tensional curve was 15.56 ± 3.25 mm Hg. IOPs in OAG patients significantly increased after patients assumed a supine position and after a water-drinking test (mean IOP increased 2.84 ± 2.21 mm Hg and 4.13 ± 2.33 mm Hg, respectively). The mean IOP peak detected by a modified diurnal tensional curve was not different than the one detected when patients became supine ($P=.75$), but, the water-drinking test demonstrated a higher mean IOP peak than the modified diurnal tensional curve and supine position ($P=.003$ and $P=.013$, respectively). The researchers suggested that, in OAG patients under treatment, the peak IOP detected after postural changes during office hours may not detect their maximum IOP during the day.⁵

CLINICAL TREATMENT

Japanese researchers evaluated the intraindividual difference in the efficacy of some antiglaucoma topical drugs (including timolol and latanoprost) in 26 primary OAG patients. Using a pneumatic tonometer, IOPs were measured for the seated and supine positions immediately after the patients assumed the positions. The mean baseline IOP was 17.7 ± 2.9 mm Hg in the seated position and 22.3 ± 2.8 mm Hg when patients were recumbent. The researchers found that latanoprost was the most effective agent for both postures, but its efficacy was markedly reduced in supine patients. The investigators concluded that a supine position may increase IOP considerably and that the efficacy of medicines varies individually according to the body's position.⁶

A study conducted at the Federal University of São Paulo evaluated the effects of a topical inhibitor of prostaglandin (indometacin) in OAG patients already using bimatoprost. In this randomized, double-masked clinical trial, investigators divided 28 OAG patients into groups A (indometacin; $n = 13$) and B (placebo; $n = 15$). At the end of 6 months, the groups displayed no significant difference in IOP during the seven follow-up visits. Researchers concluded that blocking endogenous prostaglandins with topical indometacin did not affect the IOP-lowering effect of bimatoprost.⁷

EPIDEMIOLOGY

A study conducted in an urban Chinese population detected a higher prevalence of primary OAG in mainland China than previous reports. The examination of 1,504 subjects older than 50 years yielded a crude prevalence of 3.8% for all glaucoma (95% confidence interval [CI]: 2.8, 4.8). Primary OAG was observed in 2.1% (95% CI: 1.4, 2.8) and primary angle-closure glaucoma in 1.5% (95% CI: 0.8, 2.1).⁸

ANGLE-CLOSURE GLAUCOMA

A study conducted at the National University Hospital in Singapore compared the capability of an anterior segment optical coherence tomography (OCT) prototype with gonioscopy in the detection of occludable angles. Gonioscopy under dim lighting conditions and imaging with anterior segment OCT under dark and light conditions were obtained at the inferior, temporal, and nasal quadrants. The researchers removed the superior quadrant from the protocol due to technical difficulty acquiring the image by anterior segment OCT. A quadrant of the angle was defined as *occludable* on gonioscopy if the trabecular meshwork was not visible without indentation. During anterior segment OCT, the angle quadrant was considered *closed* if the peripheral iris were apposed to the trabecular meshwork, and it was defined as *narrow* if a small slit were visible. Anterior segment OCT identified 81 of 93 (87.1%) occludable-angle quadrants as narrow or closed. The researchers concluded that the new prototype of the anterior segment OCT may be a promising, rapid, noncontact method of imaging the drainage angle.⁹

IMAGING TECHNOLOGY

A study conducted at the New York Eye and Ear Infirmary examined the validity of the ISNT rule (ie, the decreasing order of rim thickness width should be inferior, superior, nasal, temporal) in black and white subjects. The investigators evaluated 47 healthy subjects (24 blacks and 23 whites) and 48 OAG patients (18 blacks and 30 whites) by means of simultaneous stereo disc photos and optic nerve imaging using the HRT II (Heidelberg Engineering GmbH, Dossenheim, Germany) and the Stratus OCT (Carl Zeiss Meditec Inc., Dublin, CA). Glaucoma diagnosis was based on the visual field and not on any optic nerve criteria. Clinical evaluation of disc photos revealed that the ISNT rule was applicable to 38 of the 47 (80.9%) normal eyes, with no significant difference between blacks and whites ($P=.46$, Fisher exact test). The investigators concluded that the ISNT rule is clinically applicable to healthy, black subjects but is disobeyed in glaucoma patients. They also observed that, likely due to the way the data are processed using current software, automated optic nerve topography using the HRT II and the Stratus OCT was not consistent with a clinical assessment of the ISNT rule in healthy subjects.¹⁰

Researchers from Nottingham, United Kingdom, evaluated HRT II parameters from 459 normal elderly subjects (mean age = 72.6 ± 5.1 years; range, 65 to 89 years). Because an elderly age is more relevant to glaucoma, the investigators asserted that their dataset of normal subjects would be more pertinent for discriminant an-

analyses separating healthy patients from those with glaucoma. They found that disc size significantly influenced most HRT II parameters. Researchers also reported that, in this cohort, even though disc area did not differ significantly based on sex, women had significantly smaller cup areas/volumes and cup-to-disc ratios than men as well as larger rim volumes, mean retinal nerve fiber layer thicknesses, and cross-sectional areas. The investigators suggested that, given the systematic differences between male and female parameters, a normal range should be quoted for each sex.^{11,12}

This year's ARVO meeting included many presentations on new technological enhancements for the Stratus OCT. Researchers from the Massachusetts Institute of Technology in Cambridge, the New England Eye Center in Boston, and the University of Pittsburgh Medical Center demonstrated a new three-dimensional high-speed, ultrahigh-resolution OCT.¹³ According to the researchers, measurements such as nerve fiber layer thickness, optic disc topography, and macular thickness can be performed with improved coverage and resolution compared to standard OCT. Researchers from Andover, Massachusetts, and the University of Pittsburgh Medical Center demonstrated a tracking system integrated into a new OCT instrument. They concluded that tracking systems are expected to augment the capabilities of future high-speed OCT systems.¹⁴ These studies represent promising new technologies for better imaging of posterior segment structures.

BIOMECHANICS OF THE OPTIC NERVE HEAD

In a study conducted at Louisiana State University in New Orleans, axon loss was modest and diffuse at the onset of HRT-detected early experimental glaucoma in young adult monkey eyes. The investigators hypothesized that young adult monkeys' lamina cribrosa might be more compliant and more susceptible to early plastic deformation. The researchers concluded that HRT-detected early experimental glaucoma may reflect more laminar deformation and less axonal loss in a young adult monkey's eye. Further studies will evaluate these findings in older (less compliant) monkeys.¹⁵

According to researchers at the University of Toronto, scleral biomechanical properties are a major determinant of the optic nerve head's biomechanics. They evaluated the biomechanical responses of the optic nerve head under different conditions using previously validated computed modeling techniques. Scleral deformations induced by the indirect effects of IOP would be directly transmitted to tissues of the optic nerve head through mechanical coupling. They asserted a need for carefully studying the mechanical properties of the sclera

in healthy and glaucomatous eyes as well as for developing an individualized biomechanical model.¹⁶

DETECTING GLAUCOMATOUS PROGRESSION

A study conducted at the Hamilton Glaucoma Center in San Diego evaluated the effect of proximity to existing scotomas on the progression of visual field defects. Among glaucoma subjects with two or more abnormal results on standard automated perimetry, 48 subjects with progressive glaucomatous optic neuropathy were selected. The mean follow-up was 5.09 ± 2.68 years, and only the first and last standard visual field tests were considered for analysis. Using a specific algorithm to determine where new abnormal locations develop, the investigators observed a trend toward more progression in areas closer to initially abnormal locations. They plan to use these findings to develop a new algorithm for individualized follow-up on visual fields.¹⁷

Researchers from Moorfields Eye Hospital recommended employing both structural and functional tests to improve the detection of glaucomatous progression. The study evaluated 198 ocular hypertensive subjects (median follow-up = 6.1 years) and 21 healthy controls (median follow-up = 5.3 years). All subjects underwent Humphrey Visual Field (Carl Zeiss Meditec Inc.) analysis and HRT imaging on more than five occasions. Linear regression of rim area over time was performed for each disc sector. Variability was estimated from the residual standard deviation. Subjects were classified as having high or low variability based on a 50th percentile residual standard deviation cut-off. Progression was defined as a significant negative slope of $>1\%$ of baseline rim area/year ($P < .01$, low variability series, and $P < .002$, high variability series) in at least one disc sector. Visual fields were analyzed by pointwise linear regression of sensitivity over time. The investigators noted progression in 14 (7.1%) ocular hypertensive subjects by both visual field and HRT criteria, 33 (16.7%) by only HRT criteria, and 19 (9.6%) by visual fields alone. Interestingly, HRT detected a significant sector of improvement in rim area in 14 (6.4%) of the 219 subjects and detected a significant improvement in visual field in four (1.8%) subjects.¹⁸

SURGERY

Italian researchers evaluated the long-term outcome of deep sclerectomy versus trabeculectomy in a randomized study with 7 years' follow-up. Group A consisted of 41 subjects who underwent deep sclerectomy, and group B comprised 38 subjects who underwent trabeculectomy. As the main efficacy outcome, 43% in group A and 68% in group B met a 21-mm Hg cut-off;

3% of group A and 45% of group B met the 16-mm Hg cut-off. If YAG laser goniopuncture were considered as a regular postoperative step, the efficacy outcome for deep sclerectomy would increase to 61% for the 21-mm Hg cut-off and to 23% for the 16-mm Hg cut-off. Although the researchers concluded that trabeculectomy offers better IOP control than deep sclerectomy, the former procedure was associated with a higher incidence of subsequent cataract extraction.¹⁹

According to a study performed at Moorfields Eye Hospital, the use of intraoperative 5-fluorouracil (5-FU) results in a lower IOP than a placebo for the same sized bleb. Using the Moorfields Bleb Grading System, the investigators assessed the change in photographic appearance of 368 blebs over 4 years after trabeculectomy. They also associated moderate-to-severe vascularity outside the central bleb zone with a higher risk of future failure. Hazard ratios for future IOP failure were graded as 2.89 (95% CI: 1.60-5.19) in patients with 2 weeks of exposure to an increased vascularity and 6.17 (95% CI: 2.19-17.40) with 6 weeks' exposure. Interestingly, intraoperative 5-FU as an independent covariate did not influence the vascularity of the peripheral bleb zone, but an increase in central bleb thinning was observed with 5-FU. At the end of the first year of follow-up, researchers observed that 14% of blebs were graded as cystic in the 5-FU group compared to 5.5% in the placebo group.²⁰

SELECTIVE LASER TRABECULOPLASTY

A study conducted at the Long Island Jewish Medical Center in New York evaluated eight eyes of seven patients to determine the effect of selective laser trabeculoplasty (SLT) on ocular hypertension secondary to intravitreal steroid injection. In this prospective case series, the mean IOP after steroid injection was 38.1 $\pm$ 3.3 mm Hg. The patients underwent SLT and were followed for an average of 5.25 $\pm$ 1.5 months. After SLT, the mean IOP decreased to 25.3 $\pm$ 3.4 mm Hg ($P < .01$). According to the researchers, SLT may be an effective treatment modality in the management of ocular hypertension induced by intravitreal steroid injection, but multiple procedures may be necessary to lower IOP successfully.²¹ □

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