Role of corneal thickness in glaucoma incidence and progression becoming clearer

James Brandt MD, professor of ophthalmology and director, glaucoma service, University of California, Davis, US told the 6th International Glaucoma Symposium.

While raised IOP is the principal risk factor for glaucoma and glaucoma progression, it is well established that differences in corneal thickness can lead to the over- or underestimation of IOP as measured by GAT, he noted. For example, when patients have their corneas thinned by corneal refractive surgery, their IOP, as measured by GAT, becomes lower, although there is no change in the inflow and outflow of aqueous humour in the eye, he said.

“We owe a great deal of debt to Hans Goldmann for bringing a modern reproducible mechanism into tonometry within the workflow of an eye clinic. But Prof Goldmann recognised that corneal thickness would play a role in this device and during the 60s, 70s and 80s it became recognised that, because of variations in corneal thickness, Goldmann tonometry over- or underestimated the true IOP by a significant amount,” he added.

Corneal thickness and glaucoma progression

It was to further examine the relationship between corneal thickness, IOP measurements and the diagnosis and progression of glaucoma that the investigators in the OHTS study included corneal pachymetry findings in their analysis. Their study showed that the risk for developing glaucoma was three times higher in patients with a corneal thickness of 555 µm or less than it was in those with a corneal thickness of more than 588 µm, Dr Brandt noted.

Subsequent studies showed that patients with established glaucoma were at an increased risk of disease progression if they had thinner corneas, he noted.

One study by Felipe Medeiros MD and his associates at the University of California, San Diego (Am. ophthalmol, 2003) followed, for a mean of around four years, 98 eyes of 98 patients with evidence of damage to the optic nerve head but no visual field loss at baseline.

The study showed that in patients who developed visual field loss, the mean central corneal thickness (CCT) was 543 µm. That compared to a mean of 565 µm among those whose visual field remained unchanged (p = .005, Student t test).

“Over seven years about 60 per cent overall developed visual defects, but among patients with thin corneas almost 90 per cent converted to confirmed glaucoma, suggesting that even in those with established glaucoma this was a risk factor for disease progression,” Dr Brandt added.

Similarly, a study carried out by Leon Herrndon MD and colleagues at Duke University Durham, North Carolina (Arch Ophthalmol, January 2004) showed a significant correlation between corneal thickness and disease severity in confirmed cases.

On its own, CCT was a significant predictor of every outcome variable in the trial. There was a positive correlation between increasing CCT and higher AGIS scores (p = 0.001), improved mean deviations of visual field (p < 0.001), and smaller vertical (p = 0.001) and horizontal (p = 0.003) cup-disc ratios, and a decrease in the number of medications used for glaucoma (p = 0.04). Moreover, in a multivariate analysis CCT was the only significant predictor of AGIS score (p = 0.001).

CCT correlation an artefact?

Since the risk of glaucoma is greater in patients with thinner corneas and since low corneal thickness causes underestimation of IOP by GAT, it could appear that the association between corneal thickness and the disease are merely artefacts of GAT IOP measurement, Dr Brandt noted.

Supporting that view is the observation that when the various algorithms promoted in the literature to correct IOP for corneal thickness measured with GAT are applied to patients in the OHTS study, only half would have qualified to participate in the study. On the other hand, correcting Goldmann applanation tonometry for corneal thickness does not eliminate the parameter as a risk factor from a multivariate analysis, he pointed out.

“So does this mean that we’re dealing with an artefact or are we dealing with something else? Well, maybe we don’t have the right algorithm to adjust for corneal thickness, and that’s almost certainly true. Maybe we don’t have enough information to adjust intraocular pressure that’s also almost certainly true,” he said.

Another possibility is that corneal thickness is indirectly related to the pathophysiology of glaucoma, he suggested.

“I think the most intriguing and fascinating aspect is that maybe corneal thickness is biologically linked to other aspects of glaucoma risk whether that is the structural integrity of the lamina cribrosa or the structural integrity of the trabecular meshwork and this is a fascinating area,” he added.

Applying findings to clinical practice

The influence of corneal thickness on IOP measurements raises the question of whether physicians should base their treatment decisions on IOP adjusted for corneal thickness in individual patients. However, the correlation between corneal thickness, IOP measurements and disease progression is not completely understood. It may even be that corneal thickness is really just a surrogate for other corneal properties that are not measured by conventional tonometry, he pointed out.

For example, in a study in which engineers modelled the effects of various corneal biomechanical parameters on IOP measurements (Lu et al, JSCR, January 2005) it was corneal stiffness rather than thickness that had the strongest influence on the measurements.

“The bottom line is that it is much more complicated a situation than one which can be fixed with a simple linear algorithm,” Dr Brandt noted.

Moreover, a standard policy of adjusting IOP could actually compound the inaccuracy of IOP measurements. A study carried out in the UK showed that in 50 per cent of Goldmann applanation tonometers tested, there were calibration errors of as much as 2.5 mmHg.

“It’s a fallacy to correct a measurement that’s inherently imprecise when we try to adjust GAT in an individual patient. We are trying to add precision to what is a very noisy measurement, as opposed to the situation in OHTS, where you have an enormous data set and that noise gets washed out allowing you to explore the interesting implications of the data set,” he added.

A more profitable pursuit, in therapeutic terms, would be the closer monitoring of IOP fluctuation, Dr Brandt said. He likened the current approach in IOP measurement to that of blood sugar measurements performed for diabetes in the early part of the 20th Century, when measurements were performed in a relatively haphazard way.

“We’re still stuck with measuring individual IOP measurements and nobody would propose today the management of diabetes with individual random blood sugar measurements but that is in fact what we are doing in the management of glaucoma,” he added.

As regards corneal thickness, he suggested using a simple classification system describing corneas as being thin, average or thick, he said.

“Importing that into the whole picture may help you take better care of patients but trying to be more precise than this is not supported by any reasonable data and may in fact be harmful to patient care if you correct the individual’s pressure in the wrong direction,” he added.

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