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Anatomic Predictive Factors of Acute Corneal Hydrops in Keratoconus

An Optical Coherence Tomography Study

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Purpose: To define the optical coherence tomography (OCT) corneal changes predisposing to acute corneal hydrops among patients with advanced keratoconus.

Design: Retrospective cohort study.

Participants: A total of 191 advanced keratoconic eyes from 191 patients with advanced keratoconus cases were studied.

Methods: Data collected from patients with advanced keratoconus cases were studied during a minimum period of 24 months of follow-up. High-resolution Fourier-domain corneal OCT (5 μm of axial resolution) and corneal topography were performed every 4 months during the follow-up. Several anatomic features at the keratoconus cone were analyzed with OCT, including epithelial and stromal thicknesses, the aspect of Bowman's layer, the presence of Vogt's striae, and stromal opacities. A comparative analysis between anatomic corneal features in eyes that developed corneal hydrops and those that did not develop this complication during the follow-up was performed.

Main Outcome Measures: Evaluation of anatomic corneal changes at risk of developing a corneal hydrops on the basis of OCT findings.

Results: Eleven cases of corneal hydrops (5.8%) occurred in our series during a mean follow-up of 30 months (24−36 months). All of these patients were male and younger (23.7±5.9 years) than patients with no acute keratoconus (32.7±11.3 years). Increased epithelial thickening with stromal thinning at the conus and the presence of anterior hyperreflectives at the Bowman's layer level were significantly associated with corneal hydrops, whereas the presence of corneal scarring was a preventive factor. At the healing stage, a pan-stromal scar occurs, with a significant stromal thickening and cornea flattening.

Conclusions: Increased epithelial thickening, stromal thinning at the keratoconus cone, anterior hyperreflectives at the Bowman's layer level, and the absence of stromal scarring are associated with a high risk of developing corneal hydrops. These aspects should be taken into account by the clinician in the evaluation of keratoconus eyes and in the planning of corneal keratoplasty. *Ophthalmology 2015;122:1653-1659 © 2015 by the American Academy of Ophthalmology.*

Acute corneal hydrops is a condition characterized by marked corneal edema after a break in Descemet's membrane. This complication typically affects young individuals with progressive disease and occurs in approximately 3% of patients with keratoconus.[1−4] The patients generally present with a sudden onset of decrease in visual acuity, ocular irritation or pain, and photophobia.[5,6] Acute keratoconus has been associated with various clinical risk factors, including young age at onset, eye rubbing, atopy, vernal keratoconjunctivitis, and Down syndrome.[3,5−8] However, no anatomic predictive risk factors for developing corneal hydrops have been described to date.

The detection of patients with keratoconus with a higher risk of corneal hydrops is important because the visual prognosis and surgical outcomes after deep anterior lamellar keratoplasty (DALK) are better in patients without a history of acute keratoconus and in whom the big bubble technique allowing a complete stromal dissection is contraindicated.[9−11] Penetrating keratoplasty is still possible in eyes with a history of hydrops with good visual recovery after surgery. Although DALK is a physiologic approach preserving the healthy endothelial layer in eyes with keratoconus, an Australian graft registry study demonstrated contradictory results, attributing a better prognosis to penetrating keratoplasty over DALK.[12] This multicenter study shows "real-life" results from several surgeons with various levels of experience, which differ from selected monocentric studies performed by 1 experienced surgeon.[13,14]

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Table 1. Amsler–Krumeich Keratoconus Classification

Stage	Characteristics
I	Eccentric steepening Induced myopia and/or astigmatism of ≤5.00 D Keratometric reading ≤48.00 D Vogt's lines, typical topography
II	Induced myopia and/or astigmatism >5.00 to ≤8.00 D Keratometric reading ≤53.00 D Pachymetry ≥400 μm
III	Induced myopia and/or astigmatism >8.00 to ≤10.00 D Keratometric reading >53.00 D Pachymetry 200 to 400 μm
IV	Refraction not measurable Keratometric reading >55.00 D Central scars Pachymetry ≤200 μm

D = diopters.
Stage is determined if 1 of the characteristics applies. Pachymetry is measured at the thinnest site of the cone.

High-resolution optical coherence tomography (OCT) is a noncontact technique permitting high-resolution scans of different corneal layers in a few seconds. We recently established an OCT keratoconus classification containing 5 distinct keratoconus stages on the basis of structural corneal changes during the evolution of the disease.[15]

Several authors have reported the value of OCT in the diagnosis and management of patients who developed corneal hydrops.[11,16–21] However, to our knowledge, probably because of the rarity of this complication, no OCT study addresses the problem from a preventive perspective in advanced keratoconus cases before the occurrence of corneal hydrops. Furthermore, the anatomic outcomes of corneas that developed acute corneal hydrops have not been extensively studied.

The purpose of this study was to describe corneal OCT aspects predisposing to corneal hydrops and to study the anatomic outcomes of keratoconus cases that developed corneal hydrops.

Methods

Patients

We analyzed retrospectively collected data of consecutive patients followed from July 2011 to July 2014 in a reference center for keratoconus at the Quinze-Vingts National Ophthalmology Hospital (Paris, France). In accordance with French law, institutional review board and ethics committee approval was not required for this study because no modifications to French standards of treatment or follow-up were made. Eyes were assessed and patients were followed up according to the standard operative procedures of the center.

The inclusion criteria were patients with advanced keratoconus defined by stage 3 or more regarding Amsler–Krumeich classification (Table 1).[22] To avoid bias, only the most advanced eye was selected for each patient. A minimum follow-up of 24 months was required. Exclusion criteria comprised any type of prior ocular surgery, including corneal collagen cross-linking, corneal rings, or keratoplasty, and patients who showed signs of acute or healed corneal hydrops confirmed by OCT at the first consultation. Each eye had a characteristic keratoconic appearance on the topographic map (asymmetric bowtie with skewed radial axis, central or inferior steep zone, or claw shape). The keratoconic slit-lamp findings included Munson's sign, Vogt's striae, Fleischer ring, apical scar, apical thinning, Rizutti sign, and corneal scars.

Optical Coherence Tomography

A Fourier-domain OCT system (RTVue; Optovue, Inc., Fremont, CA) was used in this study. The system works at an 830-nm wavelength, with a scan speed of 26.000 axial scans per second and a depth resolution capacity of 5 μm in tissue. The corneal adaptor module provides the 6-mm scan diameter pachymetry map and the minimum corneal thickness. For each patient, 3 high-resolution scans were made across the conus to evaluate structural corneal changes. Corneal epithelial thickness and stromal thickness were measured manually as the distances between the air–tear and the epithelium–Bowman layer interfaces and between the Bowman layer–stroma and the stroma–Descemet's membrane interfaces, respectively. The cursors were placed perpendicular to the anterior ocular surface at the point of measurement.

The OCT examinations were performed every 4 months at the follow-up. To evaluate interobserver variability, all measurements were made by 2 different examiners (T.H. and I.G.). All OCT scans

Table 2. Optical Coherence Tomography Keratoconus Classification

Stage	Characteristic
1	Thinning of epithelial and stromal layers at the conus. Corneal layers have a normal aspect.
2	Hyperreflective anomalies occurring at the Bowman's layer level and epithelial thickening at the conus: 2a, clear stroma; 2b, stromal opacities.
3	Posterior displacement of the hyperreflective structures occurring at the Bowman's layer level with increased epithelial thickening and stromal thinning: 3a, clear stroma; 3b, stromal opacities.
4	Pan-stromal scar
5	Hydrops stage: 5a, acute onset, characterized by the rupture of Descemet's membrane with delamination of collagen lamellae, large fluid-filled intrastromal cysts, and the formation of epithelial edema; 5b, healing stage, pan-stromal scarring with a remaining aspect of Descemet's membrane rupture.