Mastering Advanced Corneal Diagnostics for Early Detection of Keratoconus

COPE Category: Anterior Segment

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Abstract:

This course will present diagnostic parameters derived from the peer-reviewed literature for nearly every advanced corneal diagnostic technology currently available in clinical practice. It will also offer data on low-tech signs from simple common tests, such as refraction and simulated keratometry, which all doctors can use to recommend further testing for workup of keratoconus. Additionally, it will touch on diagnostic devices being developed, which may become part of our future methods of diagnosis.

Course Learning Objectives:

1. Learn what devices are helpful in the diagnosis of keratoconus
2. Learn the established diagnostic parameters for keratoconus
3. Learn about devices being developed to diagnose keratoconus
4. Understand the core components of keratoconus and how each diagnostic device can contribute to finding the disease
5. Learn the value of refraction and keratometry in keratoconus
6. Understand when to refer for further testing based on these parameters

Outline: (50 minutes)

1. KC Background (5 mins)
    a. Description of KC
        i. Incidence
            1. More common than previously thought/reported
    b. Prevalence studies
        i. Historical prevalence is 1:2000
            1. Rabinowitz 1998
            2. Kennedy et al 1986
        ii. Most recently
            1. Hashemi et. al in 2020 - Worldwide = 1:725
            2. Godefrooij et. al in 2017 - Netherlands = 1:375
            3. Papali'i-Curtin et. al in 2019 - New Zealand = 1:191
            4. Chen et. al in 2020 - Australia = 1:84
        iii. Increases in prevalence are related to improvements in diagnostic technology.
    c. KC diagnosis is delayed
        i. Godefrooij et. al in 2017: Mean dx at 28.3 y/o
            1. Early signs missed
    d. Traditional KC Management in the US
        i. Dx and watch as the disease progresses
        ii. Visual Rehab with GP

iii. PKP with CL intolerance, poor VA, central scarring

e. Paradigm Shift in KC Management in the US
    i. Dx Early
        1. Intervene Early
    ii. CXL
        1. Stop progression
            a. Prevent advanced disease
    iii. Visually Rehabilitate
        1. Specialty contact lenses
        2. Surgical interventions
    iv. Corneal Transplantation
        1. Modern transplantation
            a. Dalk vs PK
            b. Femto vs Trephine
                i. Treatment of last resort

2. Diagnose Early? (5 mins)
    a. Visual Symptoms and Common Complaints
        i. Poor refractive endpoint
        ii. Poor VA in absence of apparent disease
    b. Classic Diagnostics
        i. Keratometry
        ii. Reflex: O-Scope/Ret Reflex
        iii. Ultrasonic Pachy
        iv. Rigid Lens Pattern Analysis
    c. Slit Lamp Signs
        i. Visible with advanced disease
        ii. Invisible in early disease
    d. AK grading
        i. Out of date
3. Debunking AK grading and learning when to refer for more testing (10 mins)
    a. Chung et al. 2020
        i. Purpose: To evaluate the baseline refraction measurements of eyes with keratoconus (KC).
            1. Methods: A retrospective analysis of the baseline manifest refraction of 1024 KC eyes
            2. Results:
                a. The average manifest refraction of all eyes was -2.2-3.4 x 93.2.
                b. The manifest refractive spherical equivalent (MRSE) of 78.9%, 13%, and 8.1%, of eyes, were myopic, emmetropic (-0.5D<0>0.5D), and hyperopic, respectively.
                c. 59.1%, 24.6%, 11.6%, and 4.6% had myopic, mixed, hyperopic, and no astigmatism, respectively.

d. 53.9%, 25.3%, and 20.8% of eyes had ATR, oblique, and WTR astigmatism, respectively.
e. Patients with higher maximum keratometry (Kmax) had a higher percentage of myopic MRSE ($p<0.001$).
f. Irrespective of Kmax and age≥ 20, ~50% about eyes had ATR astigmatism. In patients <20, 37% and 32.9% had ATR and oblique astigmatism, respectively.

3. Conclusions: 78.9% of eyes with KC had a myopic MRSE. 24.6% and 11.6% of eyes had mixed and hyperopic astigmatism, respectively. **These findings suggest that younger patients with ATR and oblique astigmatism may benefit from keratoconus screening. KC patients not as myopic as suggested by AK grading.**

b. Gelles et al. 2021
   i. Purpose: To evaluate cone location, topography measurements, and determine which keratometric values are most valuable in keratoconus (KC).
      1. Methods: A retrospective analysis of maximum (Kmax), steep (Ksteep), flat (Kflat), and mean keratometry (Kmean) of 497 KC eyes
      2. Results:
         a. The average Kmax, Ksteep, Kflat, Kmean were 58.0±9.4D, 50.4±6.4D, 46.7±5.8D, 48.5±6.0D, respectively.
         b. The correlations between Ksteep, Kflat and Kmean compared with Kmax were poor below 55D
            i. Kmax>55D: R^2 steep 0.65, R^2 flat 0.56, R^2 mean 0.63
            ii. Kmax<55D: R^2 steep 0.34, R^2flat 0.08, R^2mean 0.19
      3. Conclusions: **Ksteep, Kflat, and Kmean, are poor indicators for the severity of KC in mild and moderate disease.** Eyes with more severe KC have a more central cone location.

4. Dx Early: Advanced Diagnostics for Earliest Dx (5 mins)
   a. KC is a Progressive Disease
      i. Progressive age range
      ii. Pediatric onset
   b. What is Progressive KC
      i. No current definitive definition
      ii. Subjective and Objective findings indicate progression
   c. Importance of Global Data
      i. Full cornea
5. Think like glaucoma (20mins)
   a. Structure vs Function

i. Vision
    1. Aberrometry
ii. Shape
    1. Tomography
iii. Strength
    1. Biomechanics

b. Aberrometry
    i. Hartmann Shack
    ii. Ray trace
    iii. Tshering
        1. Total HORMS> Coma> Trefoil
            a. Li et al
            b. Kosaki et al
            c. Prakash et al
        2. Wavefront plus corneal curvature ray trace
            a. Subtractive values to localize irregularity
                i. Internal vs Corneal
                    1. Gantel et al
                    2. Rabinowitz et al

c. Topography
    i. History
        1. Placido Based
            a. Anterior Curvature ONLY
                i. IS
                ii. Kmax and Kmean
                iii. Axis Skew
                    1. Rabinowitz et al
                    2. Klyce et al

d. Tomography
    i. Scheimpflug Based
        1. Full corneal metrics
            a. Low resolution
                i. Topography +
                    1. Anterior elevation
                    2. Pachymetry
                    3. Posterior elevation
                        a. Shetty et al
                        b. Motlagh et al
                        c. Moshirfar et al
    ii. Ultrasound Based
        1. Full corneal metrics
            a. Difficult scan acquisition
            b. Low resolution

i. +Epi mapping
1. Epi donut
a. Reinstein et al

iii. OCT
1. Full corneal metrics
2. High resolution
a. +Epi mapping and bowman mapping
i. Subtractive epi to stroma
1. Li et al
ii. Bowman's thinning
1. Pircher et al

e. BioMechanics
i. Etiology
1. Biomech
a. Collagen Structure
b. Lamellar Architecture
i. Meek et al
ii.

ii. Waveform
1. Non-contact applanation with I-R sensor
a. Corneal hysteresis
b. Corneal resistance factor
i. Ortiz et al
ii. Shah et al
1. +CCT increase sens & spec
a. Galletti et al
c. Low diagnostic power for subclinical vs normal
i. Refuted by Dupps et al
1. MatLab values find a statistically significant difference
2. Non-contact applanation with Scheimpflug camera
i. Non-contact applanation with I-R sensor
1. AT1 value
a. Roberts et al
i. High diagnostic value
3. Brillouin Spectroscopy
a. Global data
b. The specific location of biomechanical instability
i. Shao et al
ii. Scarcelli et al
4. OCT elastography
a. Sectoral data
i. Depth of biomechanical instability

ii. Changes to tissue with treatment
1. Dupps et al
2. De Stephano et al

f. Combine for earliest Dx
i. Multimetrics topography
1. Rabinowitz et al
ii. Multimetric tomography
1. Shetty et al
iii. Multimetric biomechanics
1. Vinciguerra et al
iv. Multimetric tomography and biomechanics
1. Ferriera-Mendes et al
g. Finite Element Analysis
i. Predictive corneal modeling based on metrics
1. Dupps et al
2. Roberts et al
3. Roy et al
4. Seven et al

6. Genetics: The earliest piece of the puzzle? (5 mins)
a. Genetics
i. Buccal mucosal swab
1. LOX regulation
a. Rabinowitz et al
b. Bykhovskaya et al
c. Hardcastle et al
ii. Polygenic
1. Results = a risk score, not positive/negative
iii. Who gets tested?
1. Positive family hx
2. Suspicious findings or lack of tech
3. Corneal treatment candidates