Predictors of progression in untreated keratoconus: a Save Sight Keratoconus Registry study

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ABSTRACT

Aims We set out to identify risk factors for progression in untreated keratoconus patients from 34 centres across Australia, New Zealand, Spain and Italy.

Methods Patients were divided into 'progressors' and 'stable' patients for each clinical parameter: visual acuity (VA), steepest keratometry (maximum keratometry (Max-K)) and thinnest corneal thickness (TCT). Primary outcomes were the proportion of eyes with sustained progression in VA, Max-K or TCT within 3 years. Secondary outcomes included predictors of progression.

Results There were 3994 untreated eyes from 2283 patients. The proportion of eyes with VA, Max-K and TCT progression at 1 year were 3.2%, 6.6% and 3.1% respectively. Factors associated with VA loss were higher baseline VA (HR 1.15 per logMAR line increase in VA; p<0.001) and steeper baseline Max-K (HR 1.07 per 1D increase; p<0.001). Younger baseline age was associated with Max-K steepening (HR 0.96 per year older; p=0.001). Thicker baseline TCT, steeper baseline Max-K and younger baseline age were associated with TCT thinning: (HR 1.08 per 10 µm increase in TCT; p<0.001), (HR 1.03 per 1D increase; p=0.02) and (HR 0.98 per year younger; p=0.01), respectively.

Conclusions Steeper Max-K and younger age were the most clinically useful baseline predictors of progression as they were associated with worsening of two clinical parameters. Every 1D steeper Max-K was associated with a 7% and 3% greater risk of worsening VA and thinning TCT, respectively. Each 1 year younger was associated with a 4% and 2% greater risk of steepening Max-K and thinning TCT, respectively.

INTRODUCTION

Keratoconus is a progressive corneal ectasia that typically begins during the second decade of life[1] and affects 265 per 100 000 people.[2] As the disease progresses, the cornea becomes increasingly irregular and steep leading to irregular astigmatism, permanent visual loss and impacts on patients' quality of life.[3–6] Identifying keratoconus patients at high risk of progression is important in monitoring and can facilitate timely corneal cross-linking (CXL), but modern evidence on progression in keratoconus and its risk-factors are lacking.

CXL is a procedure that aims to stabilise the shape of the cornea thereby halting progression and has seen widespread adoption for the treatment of keratoconus over the last decade.[7] Randomised controlled trials (RCTs) have supported CXL as a relatively safe and effective treatment[8–11] but complications such as keratitis, corneal scarring,[12] severe corneal flattening[13] and irreversible vision loss can occur. The Global Consensus on Ectasia[14] recommended CXL for keratoconus patients that are progressing but conceded that progression is challenging to detect and difficult to define. Our recent meta-analysis of keratoconus natural progression,[15] including 11 529 eyes, reported that only two large studies have investigated this (Tuft *et al*'s report[16] and the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) study[17]). These studies add valuable insights into natural keratoconus progression risk factors but are difficult to apply in modern keratoconus management. With mounting evidence of the effectiveness of CXL and its uptake, there will inevitably be an increasingly limited cohort of untreated keratoconus patients. Further, given CXL's efficacy, it will become unethical to perform RCTs with untreated control arms. Registries, such as the Save Sight Keratoconus Registry (SSKR) used in this study,[18] will become an increasingly valuable resource for data on the natural history of keratoconus as well as current treatment outcomes.

The aim of this study was to identify risk factors for progression in untreated keratoconus patients using data from the SSKR and to identify at-risk patients who may imminently need CXL.

METHODS

Design and setting

We carried out an observational study analysing data from routine clinical practice. Data were captured using the Fight Corneal Blindness! Projects' SSKR, which is based on the Fight Retinal Blindness! Project.[19] This study included data from 34 contributing centres located in Australia, New Zealand, Spain and Italy. Monitoring regimes including tomographer choice, contact lens removal protocol and review frequency were at the discretion of the treating clinician and patient. At the baseline visit, demographic and clinical information were obtained, including year of birth, gender, prior CXL, refractive procedures including intracorneal ring segments (ICRS) or grafts. Data were collected at each visit on visual acuity (VA) logMAR letters read, including if spectacles or contact lenses were in use, VA pinhole letters, and the K2, steepest keratometry (maximum keratometry (Max-K)) and thinnest corneal thickness (TCT) pachymetry readings.

Study population

Study enrolment criteria included untreated keratoconus eyes that had not received any previous