

# Quality of life in keratoconus patients in a tertiary hospital in Thailand.

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## Abstract

**Background:** Keratoconus is a progressive corneal ectatic disease that significantly impacts visual function and quality of life (QoL) in affected individuals.

**Objective:** This primary objective of this study aimed to evaluate the QoL of keratoconus patients in Thammasat University Hospital and compare it with a control group. The secondary objective was a subgroup analysis aimed to compare the QoL between keratoconus patients who underwent collagen cross-linking (CXL) with those who received supportive treatment. The study was conducted at Thammasat University Hospital, Pathumthani Province, Thailand.

**Methods:** Keratoconus patients were recruited from Thammasat University Hospital by random sampling. Control patients were recruited by consent at the General Practice Outpatient Department. The Thai version of the National Eye Institute of Visual Functioning Questionnaire (T-NEI-VFQ-25) was used to assess quality of life in both groups. The questionnaire had 25 items grouped into seven categories related to quality of life. For every response, choices of worded answers were converted into integer scores ranging 1 to 5 associated with the lowest to highest quality of life respectively. Two-sample two-tailed t-test was used to determine statistical significance at alpha = 0.05.

**Results:** The results showed that all QoL domains were negatively impacted in keratoconus patients, with the most significant compromise observed in mental health (mean score = 3.961, s.d. = 0.711). The least disrupted component were social aspects (mean score = 4.597, s.d. = 0.382). The domain with the greatest difference between keratoconus and control were social aspects (p = 0.00000420). Subgroup analysis revealed no statistically significant difference between the two groups of keratoconus patients regarding QoL, though the CXL group reported lower scores in mental health (mean score of 4.175 versus 3.733, s.d. 0.903 versus 0.827, p = 0.000162). Those who underwent CXL had better scores in ocular symptoms, activities of daily living and transportation.

**Conclusions:** These findings suggest that keratoconus affects various aspects of QoL, with mental health being a key concern. The study underscores the importance of integrating QoL assessments into clinical management to tailor treatments, including the consideration of mental health in treatment plans. Further research is needed to explore the long-term effects of collagen cross-linking and other surgical treatments on QoL in keratoconus patients.

**Keywords:** Collagen cross-linking, Keratoconus, Quality of life, Thailand, VFQ-25

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## Introduction

The Global Consensus on Keratoconus and Ectatic Diseases 2015 states that Keratoconus is a primary ectatic disease characterised by abnormal posterior ectasia, abnormal corneal thickness distribution and clinical noninflammatory corneal thinning with a typical pattern of thinning and protrusion distinguishing it from other ectatic diseases such as pellucid marginal degeneration and keratoglobus.<sup>1</sup>

Due to the slow progressive nature of Keratoconus and its lower prevalence to fellow eye diseases, there are few studies investigating the impact of keratoconus on quality of life of the Thai population. Al Zabadi et al's cross-sectional study performed in Nablus University Hospital, Palestine demonstrated the significant impact keratoconus has on patient's quality of life in terms of near and distant vision, general vision, mental health and social health.<sup>2</sup>

Piyacomn et al's recent cross-sectional study performed in King Chulalongkorn Memorial Hospital, Thailand had described the prevalence, ocular findings, pachymetry, keratometry and topography of keratoconus patients but did not report quality of life.<sup>3</sup> To the researchers' understanding, currently, there is no study on the quality of life of keratoconus patients performed in Thailand.

Evaluation of quality of life, not only adds value to the holistic approach of medical care, but may be an important factor in guiding the ophthalmologist in choice of treatment and timing of treatment but is often overlooked. Furthermore, from an epidemiological standpoint, keratoconus patients are usually young adults, and hence addressing their concerns and attending to their needs and wants not only can have a positive impact on public health but also the overall national productivity.

From literature review, with lack of studies on the quality of life between keratoconus patients and their respective baseline population, and between those who have undergone collagen cross-linking and those who have not, the authors aim to examine how quality of life can be affected in keratoconus patients with hopes of adding value to practical care and assist further studies regarding quality of life.

## Methods and Materials

The study was approved by The Human Research Ethics Committee of Thammasat University (MTU-EC-OP-1-295/66). The primary outcome of this quantitative study is to compare the quality of life between keratoconus patients and their respective baseline population using the Thai version of the National Eye Institute of Visual Functioning Questionnaire (T-NEI-VFQ). The secondary outcome is to compare the quality of life of patients who underwent collagen cross-linking with those who have not in keratoconus patients also using the Thai version of the National Eye Institute of Visual Functioning Questionnaire (T-NEI-VFQ).

Inclusion criteria for the study (keratoconus) group includes patients diagnosed with any grade of keratoconus in Thammasat University Hospital with or without vision problems, with or without refractive error correctable by glasses or contact lenses, aged 18 to 80 years, with good competency of Thai language and access to mobile communicative devices. Whether or not the patient underwent collagen cross-linking was noted.

Inclusion criteria for the control group includes respondents with or without vision problems, with or without refractive error correctable by glasses or contact lenses, aged 18 to 80 inclusive, with good competency of Thai language.

Exclusion criteria for the keratoconus group include those who have undergone corrective surgery for keratoconus or any other ocular surgery. Exclusion criteria for both groups include those who have chronic ocular or systemic diseases, those who underwent ocular surgery and those with mental illnesses.

Keratoconus patients were recruited from Thammasat University Hospital's Information Technology Services database according to aforementioned criteria. Random sampling method was used to select 31 patients, determined by sample size calculation. We ended up with 16 patients who have not undergone collagen cross-linking and 15 who have undergone collagen cross-linking. After informed consent, the questionnaire was conducted by a phone interview in Thai language by two Ophthalmology Residents who are fluent in Thai language.

Control patients were recruited at the General Outpatient Department Clinic at Thammasat University Hospital according to aforementioned criteria. Sample size was calculated using the n4Studies online calculator. Sample size for estimating a finite population proportion (of N = 100,000) assuming an expected prevalence of 0.005 (from Gomes et al.' study<sup>4</sup>), confidence level of 95% and a precision of 0.025. A minimum of 31 patients was needed determined by sample size calculation. After informed consent, a total of 43 patients were recruited. The questionnaire was done at the OPD by General Practitioners who are fluent in Thai language.

The NEI-VFQ-25 or 25-item National Eye Institute-Visual Function Questionnaire is widely accepted tool that takes into account the patient's perspective of visual function and is well able to assess the effect of visual function on personalised patient aspects such as lifestyle and daily activities, better than visual acuity alone.<sup>5</sup> The NEI-VFQ-25 is a standard questionnaire developed from the original 51-item NEI VFQ to ease settings where time may be a limiting constraint. According to Mangione et al's study, with regards to the questionnaire items, it was primarily concluded that the NEI VFQ-25 is versatile in evaluation of varying patient profiles such as age-related cataracts, age-related macular

degeneration, diabetic retinopathy, primary open-angle glaucoma and cytomegalovirus retinitis.<sup>6</sup>

In terms of practicality, under the setting of a suburban hospital, the Thai translated version of the NEI-VFQ-25 or T-NEI-VFQ-25 is often utilised in evaluation of quality of life of ophthalmologic patients due alleviated language and communication barrier.

Setthawatcharawanich et al's study validated the use of T-NEI-VFQ-25 in comparison to the existing Thai SF-36 questionnaire in assessment of blepharospasm and their response to botulinum toxin treatment.<sup>7</sup> Hence, in our study population with the majority of patients being Thai natives, evaluation will be done using the T-NEI-VFQ-25.

From the T-NEI-VFQ-25, we categorised 25 items of the questionnaire into seven categories related to quality of life. Mental aspects, ocular symptoms, activities of daily living, social aspects, transportation, work and dependency. The items and their subsequent categorisation can be seen in **Table 1**. For ease of calculation, for every response, we converted worded choices of answers into integer scores with 5 associated with the best possible quality of life and 1 being least favourable quality of life. Questions 15, 15a, and 15b were omitted from mathematical analysis due to inability to compare those who drive with those who do not drive.

**Table 1:** Thai version of the National Institute of Visual Functioning Questionnaire (T-NEI-VFQ-25) and categorisation

| Question |                                                                                            | Category        | Response and Integer score |            |         |                |           |
|----------|--------------------------------------------------------------------------------------------|-----------------|----------------------------|------------|---------|----------------|-----------|
|          |                                                                                            |                 | 5                          | 4          | 3       | 2              | 1         |
| 1        | โดยทั่วไป ท่านถือเป็นคนสุขภาพเช่นไร                                                        | Mental aspects  | ดีที่สุด                   | ดีมาก      | ดี      | ปานกลาง        | ไม่ดี     |
| 2        | ปัจจุบัน ท่านคิดว่าสายตาของท่าน โดย การมองด้วยสองตา โดยใส่แว่นหรือ คอนแทคเลนส์ เป็นอย่างไร | Mental aspects  | ดีที่สุด                   | ดีมาก      | ดี      | ปานกลาง        | ไม่ดี     |
| 3        | ท่านมีความกังวลเกี่ยวกับสายตาของท่านบ่อยแค่ไหน                                             | Mental aspects  | ไม่เคย                     | นานๆ ครั้ง | บางเวลา | เกือบ ตลอดเวลา | ตลอดเวลา  |
| 4        | ท่านรู้สึกเจ็บปวดหรือไม่สบายบริเวณ ในดวงตา หรือรอบดวงตามากแค่ไหน เช่น แสบตา คันตา          | Ocular symptoms | ไม่                        | เล็กน้อย   | ปานกลาง | มาก            | มากที่สุด |

**Table 1:** Thai version of the National Institute of Visual Functioning Questionnaire (T-NEI-VFQ-25) and categorisation (Cons.)

|     | Question                                                                                      | Category                   | Response and Integer score       |                 |                    |                |                      |
|-----|-----------------------------------------------------------------------------------------------|----------------------------|----------------------------------|-----------------|--------------------|----------------|----------------------|
|     |                                                                                               |                            | 5                                | 4               | 3                  | 2              | 1                    |
| 5   | ท่านมีปัญหากับการอ่านตัวพิมพ์ในหนังสือมากน้อยแค่ไหน                                           | Activities of daily living | ไม่มีปัญหา                       | มีปัญหา<br>น้อย | มีปัญหา<br>ปานกลาง | มีปัญหา<br>มาก | มีปัญหา<br>มากที่สุด |
| 6   | ท่านมีปัญหาในการทำงานหรืองานอดิเรกที่ใช้การเพ่งในระยะใกล้มากแค่ไหน เช่นการเย็บผ้า             | Activities of daily living | ไม่มีปัญหา                       | มีปัญหา<br>น้อย | มีปัญหา<br>ปานกลาง | มีปัญหา<br>มาก | มีปัญหา<br>มากที่สุด |
| 7   | ท่านมีปัญหาในการมองหาของบนชั้นวางที่มีสิ่งของเยอะมากแค่ไหน                                    | Activities of daily living | ไม่มีปัญหา                       | มีปัญหา<br>น้อย | มีปัญหา<br>ปานกลาง | มีปัญหา<br>มาก | มีปัญหา<br>มากที่สุด |
| 8   | ท่านมีปัญหาในการอ่านป้ายจราจรหรือขึ้นร้านมากแค่ไหน                                            | Transport                  | ไม่มีปัญหา                       | มีปัญหา<br>น้อย | มีปัญหา<br>ปานกลาง | มีปัญหา<br>มาก | มีปัญหา<br>มากที่สุด |
| 9   | ท่านมีปัญหาในการเดินลงบันได หรือพื้นต่างระดับในที่มืดหรือตอนกลางคืนเพราะสายตาของท่านมากแค่ไหน | Transport                  | ไม่มีปัญหา                       | มีปัญหา<br>น้อย | มีปัญหา<br>ปานกลาง | มีปัญหา<br>มาก | มีปัญหา<br>มากที่สุด |
| 10  | ท่านมีปัญหาในการมองเห็นวัตถุทางด้านข้างระหว่างเดินมากแค่ไหน                                   | Transport                  | ไม่มีปัญหา                       | มีปัญหา<br>น้อย | มีปัญหา<br>ปานกลาง | มีปัญหา<br>มาก | มีปัญหา<br>มากที่สุด |
| 11  | ท่านมีปัญหาในการสังเกตสีหน้าผู้อื่นระหว่างคุยเพราะปัญหาสายตาท่านมากแค่ไหน                     | Social                     | ไม่มีปัญหา                       | มีปัญหา<br>น้อย | มีปัญหา<br>ปานกลาง | มีปัญหา<br>มาก | มีปัญหา<br>มากที่สุด |
| 12  | ท่านมีปัญหาในการเลือกเสื้อผ้าที่เข้ากันเพราะปัญหาสายตาท่านมากแค่ไหน                           | Social                     | ไม่มีปัญหา                       | มีปัญหา<br>น้อย | มีปัญหา<br>ปานกลาง | มีปัญหา<br>มาก | มีปัญหา<br>มากที่สุด |
| 13  | ท่านมีปัญหาในการพบปะผู้อื่นที่บ้านงานเลี้ยง หรือร้านอาหาร เพราะปัญหาสายตาท่านมากแค่ไหน        | Social                     | ไม่มีปัญหา                       | มีปัญหา<br>น้อย | มีปัญหา<br>ปานกลาง | มีปัญหา<br>มาก | มีปัญหา<br>มากที่สุด |
| 14  | ท่านมีปัญหาในการดูหนัง ดูละครเวที ดูการแข่งขันกีฬา เพราะสายตามากแค่ไหน                        | Social                     | ไม่มีปัญหา                       | มีปัญหา<br>น้อย | มีปัญหา<br>ปานกลาง | มีปัญหา<br>มาก | มีปัญหา<br>มากที่สุด |
| 15  | ในปัจจุบันท่านขับรถหรือไม่                                                                    | Transport                  | ใช่ หรือ ไม่ใช่                  |                 |                    |                |                      |
| 15A | ถ้าไม่ ท่านไม่เคยขับรถหรือเลิกขับรถ                                                           | Transport                  | ไม่เคยขับรถมาก่อน หรือ เลิกขับรถ |                 |                    |                |                      |
| 15B | ถ้าท่านเลิกขับรถ สาเหตุหลักที่เลิกเกิดจากเรื่องสายตา สาเหตุอื่น หรือทั้งสายตาและสาเหตุอย่าง   | Transport                  | ปัญหาสายตา หรือ สาเหตุอื่น       |                 |                    |                |                      |
| 15C | ท่านมีปัญหาเล็กน้อยแค่ไหนในการขับรถในพื้นที่ที่คุ้นเคยมากตอนช่วงกลางวัน                       | Transport                  | ไม่มีปัญหา                       | มีปัญหา<br>น้อย | มีปัญหา<br>ปานกลาง | มีปัญหา<br>มาก | มีปัญหา<br>มากที่สุด |

**Table 1:** Thai version of the National Institute of Visual Functioning Questionnaire (T-NEI-VFQ-25) and categorisation (Cons.)

| Question |                                                                                                                                                      | Category       | Response and Integer score |                   |                 |                  |                   |
|----------|------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|----------------------------|-------------------|-----------------|------------------|-------------------|
|          |                                                                                                                                                      |                | 5                          | 4                 | 3               | 2                | 1                 |
| 16       | ท่านมีปัญหาในการขับรถตอนกลางคืนมากแค่ไหน                                                                                                             | Transport      | ไม่มีปัญหา                 | มีปัญหา น้อย      | มีปัญหา ปานกลาง | มีปัญหา มาก      | มีปัญหา มากที่สุด |
| 16A      | ท่านมีปัญหาในการขับรถในสภาพที่ทำให้การขับร่นั้นยากขึ้นอย่างเช่น เมื่อสภาพอากาศไม่ดี หรือในชั่วโมงเร่งด่วน หรือบนทางด่วน หรือในพื้นที่รถติด มากแค่ไหน | Transport      | ไม่มีปัญหา                 | มีปัญหา น้อย      | มีปัญหา ปานกลาง | มีปัญหา มาก      | มีปัญหา มากที่สุด |
| 17       | ท่านปฏิบัติงานได้น้อยลง เพราะปัญหาทางด้านสายตา                                                                                                       | Work           | ไม่เป็น                    | เป็นเวลา ส่วนน้อย | เป็นบางเวลา     | เป็นเวลา ส่วนมาก | เป็นตลอดเวลา      |
| 18       | ท่านถูกจำกัดความสามารถ ในการทำงานทำให้ทำงานและกิจกรรมต่างๆ ในระยะเวลาสั้นลง                                                                          | Work           | ไม่เป็น                    | เป็นเวลา ส่วนน้อย | เป็นบางเวลา     | เป็นเวลา ส่วนมาก | เป็นตลอดเวลา      |
| 19       | ท่านรู้สึกปวดหรือระคายเคือง บริเวณดวงตา เช่น แสบ ร้อน คัน ทำให้ท่านต้องหยุดทำงาน                                                                     | Work           | ไม่เป็น                    | เป็นเวลา ส่วนน้อย | เป็นบางเวลา     | เป็นเวลา ส่วนมาก | เป็นตลอดเวลา      |
| 20       | ในเวลาส่วนมากท่านมักจะอยู่บ้านเนื่องจากปัญหาสายตา                                                                                                    | Transport      | ไม่จริง                    | ไม่จริง บ้าง      | จริงปานกลาง     | จริงบ้าง         | จริง              |
| 21       | ท่านเป็นกังวลตลอดเวลา เนื่องจากปัญหาทางด้านสายตา                                                                                                     | Mental aspects | ไม่จริง                    | ไม่จริง บ้าง      | จริงปานกลาง     | จริงบ้าง         | จริง              |
| 22       | ท่านเสียการควบคุมในสิ่งที่กำลังทำอยู่ เนื่องจากปัญหาทางสายตา                                                                                         | Work           | ไม่จริง                    | ไม่จริง บ้าง      | จริงปานกลาง     | จริงบ้าง         | จริง              |
| 23       | ท่านจำเป็นต้องพึ่งผู้อื่นอย่างมากเนื่องจากปัญหาทางด้านสายตา                                                                                          | Dependency     | ไม่จริง                    | ไม่จริง บ้าง      | จริงปานกลาง     | จริงบ้าง         | จริง              |
| 24       | ท่านจำเป็นต้องได้รับความช่วยเหลืออย่างมาก เนื่องจากปัญหาทางด้านสายตา                                                                                 | Dependency     | ไม่จริง                    | ไม่จริง บ้าง      | จริงปานกลาง     | จริงบ้าง         | จริง              |
| 25       | ท่านกังวลเกี่ยวกับสิ่งที่ท่านกำลังจะทำเพราะมันอาจจะทำให้ ท่านละอายใจในภายหลัง                                                                        | Mental aspects | ไม่จริง                    | ไม่จริง บ้าง      | จริงปานกลาง     | จริงบ้าง         | จริง              |

## Results and data analysis

Baseline demographic data were compared and analysed with a significance level ( $\alpha$ ) of 0.05. There is no statistically significant difference between the two groups (study group and control group) in terms of baseline demographic data, namely age,  $t(72) = 1.015$ ,  $p = 0.3128$ , and gender,  $\chi^2(1, n = 74) = 0.0015$ ,  $p = 0.969511$ . For the subgroup analysis of the study group, there is no statistically significant difference between keratoconus patients who underwent collagen cross-linking and keratoconus patients who had supportive treatment in terms of age  $t(29) = 0.386$ ,  $p = 0.7006$ . However, there is

a statistically significant difference in terms of sex between the two subgroups,  $\chi^2(1, n = 31) = 3.889$ ,  $p = 0.048619$ . Namely, the collagen cross-linking group is predominantly male (10:5) whilst the supportive group is predominantly female (11:5). The summary of demographic data is shown in **Table 2**.

Of note, in the control group, 1 patient had migraine, 1 patient had adjustment disorder and 1 patient had gastroesophageal reflux disease. In the study group, 4 patients had allergic rhinitis, 2 patients had obesity, 1 patient had obstructive sleep apnoea and 1 patient had autism spectrum disorder.

**Table 2:** Summary of baseline demographic data of the study group and control group in terms of mean age and sex. Subgroup data is also shown.

|                        | Sample size | Mean age (years) | Standard deviation | Sex  |        |
|------------------------|-------------|------------------|--------------------|------|--------|
|                        |             |                  |                    | Male | Female |
| Study group            | 31          | 26.806           | 13.713             | 15   | 16     |
| Supportive treatment   | 16          | 26.250           | 7.326              | 5    | 11     |
| Collagen cross-linking | 15          | 27.400           | 9.117              | 10   | 5      |
| Control group          | 43          | 29.395           | 8.122              | 21   | 22     |

Two-sample two-tailed  $t$  scores assuming unequal variances were used to analyse both the primary and secondary outcomes ( $\text{Alpha} = 0.05$ ). The mean score and standard deviation for both the study group and control group for each category was calculated. Subgroup analysis was done for the study group in terms of whether or not the patient underwent collagen cross-linking.

The mean score and standard deviation for each group and subgroup are shown in **Table 3 and 4**. The difference in means between study and control, and collagen cross-linking and supportive treatment were analysed with confidence interval and  $p$ -values shown.

From the study, the most compromised aspect of quality of life by T-NEI-VFQ in those with keratoconus was mental aspects (mean score = 3.961,  $\text{s.d.} = 0.711$ ), whilst the least disturbed aspect of quality of life was social aspects (mean score = 4.597,  $\text{s.d.} = 0.382$ ). In those without keratoconus, the sample reports the lowest score for mental aspects (mean score = 4.549,  $\text{s.d.} = 0.419$ ), whilst the least disturbed aspect of quality of life was dependency with a full score of 5.00.

Looking at the standard deviations, the aspect of quality of life with the greatest standard deviation in the study group was dependency ( $\text{s.d.} = 0.880$ ) in contrast to a standard deviation of zero in the control group for the corresponding aspect. The aspect of quality of life with the smallest standard deviation in the keratoconus group was ocular symptoms ( $\text{s.d.} = 0.342$ ) in contrast to this aspect having the greatest standard of deviation in the control group ( $\text{s.d.} = 0.529$ ).

It was found that there is a statistically significant difference in all aspects of quality of life between keratoconus patients and control patients. The domains with the greatest statistical significance were social aspects of quality of life (mean difference = -0.588, CI (-0.876, -0.300),  $p = 0.00000420$ ), followed by ocular symptoms (mean difference = -0.49, CI (-0.692, -0.288),  $p = 0.00000749$ ) and followed by work (mean difference = -0.527, CI (-0.746, -0.308),  $p = 0.0000222$ ). The domain with the least level of significance was dependency (mean difference = -0.532, CI (-0.855, -0.209),  $p = 0.0210$ ) but was still statistically significant.

In the subgroup analysis of keratoconus patients, mental aspects of quality of life had the lowest score in the collagen cross-linking subgroup (mean score = 3.733, s.d. = 0.827) in contrast to both ocular symptoms and activities of daily living equally having the lowest score among the subgroup who had supportive treatment (mean score = 4.125, s.d. = 0.775 and mean score = 4.125, s.d. = 0.981, respectively).

Both subgroups reported the highest score in terms of social aspects of quality of life (mean score = 4.450 and 4.734 respectively). The aspect of quality of life with the greatest standard deviation was dependency in both subgroups (s.d. = 1.064 and 1.249, respectively). The aspect of quality of life with the smallest standard deviation was ocular symptoms in both groups (s.d. = 0.583 and 0.775, respectively).

**Table 3:** Table showing the mean and standard deviation of the integer score for both the study group and control group. The differences in means between the two groups are shown in terms of confidence interval and p-value for the corresponding degrees of freedom with a significance level of 0.05.

|                            | Study group<br>(n = 31) |       | Control group<br>(n = 43) |       | Difference in means<br>(study – control) |          |            |
|----------------------------|-------------------------|-------|---------------------------|-------|------------------------------------------|----------|------------|
|                            | Mean                    | S.D.  | Mean                      | S.D.  | CI lower                                 | CI upper | p-value    |
| Mental aspects             | 3.961                   | 0.711 | 4.549                     | 0.419 | -0.876                                   | -0.300   | 0.000162   |
| Ocular symptoms            | 4.161                   | 0.342 | 4.651                     | 0.529 | -0.692                                   | -0.288   | 0.00000749 |
| Activities of daily living | 4.172                   | 0.708 | 4.845                     | 0.426 | -0.961                                   | -0.385   | 0.0000233  |
| Social aspects             | 4.597                   | 0.382 | 4.983                     | 0.084 | -0.528                                   | -0.244   | 0.00000420 |
| Transportation             | 4.395                   | 0.790 | 4.959                     | 0.144 | -0.857                                   | -0.271   | 0.000438   |
| Work                       | 4.403                   | 0.576 | 4.930                     | 0.199 | -0.746                                   | -0.308   | 0.0000222  |
| Dependency                 | 4.468                   | 0.880 | 5.000                     | 0.000 | -0.855                                   | -0.209   | 0.00210    |

Comparing the two subgroups, the group who underwent collagen cross-linking had better scores in ocular symptoms, activities of daily living and transportation whilst the supportive group had better scores in mental aspects, social aspects, work and dependency. However, there is no statistically significant difference between keratoconus patients who underwent collagen-cross linking and those who have not undergone collagen cross-linking across all categories of quality of life ( $p > 0.05$ ). The domain with the greatest difference was mental aspects with those who had supportive treatment having a better

score than those who underwent collagen cross-linking (mean difference = -0.442, CI (-1.078, 0.194),  $p = 0.166$ ). However, again, this was not statistically significant ( $p > 0.05$ ).

In terms of questions 15, 15a, and 15 b relating to transport issues, 3 out of 43 patients in the control group reported cessation of driving with 1 out of 3 reporting cessation due to problems related to vision. In comparison, in the study group, 3 out of 31 patients reported cessation of driving, with all three patients reporting cessation due to problems related to vision.

**Table 4:** Table showing the mean and standard deviation of the integer score for both the collagen cross-linking group and supportive group. The differences in means between the two groups are shown in terms of confidence interval and p-value for the corresponding degrees of freedom with a significance level of 0.05.

|                            | Collagen cross-linking (n = 15) |       | Supportive treatment (n = 16) |       | Difference in means (collagen – supportive) |          |         |
|----------------------------|---------------------------------|-------|-------------------------------|-------|---------------------------------------------|----------|---------|
|                            | Mean                            | S.D.  | Mean                          | S.D.  | CI lower                                    | CI upper | p-value |
| Mental aspects             | 3.733                           | 0.827 | 4.175                         | 0.903 | -1.078                                      | 0.194    | 0.166   |
| Ocular symptoms            | 4.200                           | 0.583 | 4.125                         | 0.775 | -0.428                                      | 0.578    | 0.762   |
| Activities of daily living | 4.222                           | 0.838 | 4.125                         | 0.981 | -0.572                                      | 0.766    | 0.769   |
| Social aspects             | 4.450                           | 0.628 | 4.734                         | 0.803 | -0.812                                      | 0.924    | 0.280   |
| Transportation             | 4.400                           | 0.889 | 4.391                         | 1.012 | -0.690                                      | 0.708    | 0.979   |
| Work                       | 4.333                           | 0.721 | 4.469                         | 0.864 | -0.720                                      | 0.448    | 0.637   |
| Dependency                 | 4.333                           | 1.064 | 4.594                         | 1.249 | -1.112                                      | 0.590    | 0.535   |

## Discussion

Keratoconus is a common ectatic disease characterised by progressive corneal protrusion and thinning at the point of protrusion. Progression of keratoconus can lead to severe visual loss and can impact the life of the individual. This condition is fairly common, affecting 1 in 2000 individuals worldwide with a higher incidence in South Asia. Gomes et al.' study reviewed a variable prevalence of up to 5% in Middle Eastern population.<sup>4</sup> Another study conducted by Munir et al. in the United States estimated the prevalence among vision service plan enrollees in 2016 to be 0.15%.<sup>8</sup> In Thailand, there is no study reporting the prevalence of keratoconus. Piyacomn et al.'s cross-sectional study, conducted from 2015 to 2018 inclusive, studied the prevalence and characteristics of keratoconus in patients seeking refractive surgery and found the prevalence of keratoconus to be 1.66%.<sup>3</sup> Early keratoconus may be undetected due to its asymptomatic manifestation, but as highlighted its prevalence may be greater than expected. Thus its effect on quality of life may also be under detected.

Keratoconus causes an array of symptoms and functional impairment in those affected. Fournié et al's recent study performed in 2023 examined the impact of keratoconus on quality of life via phone interview. Inspired by Wilson & Cleary's model of patient outcomes, aspects of quality of life were grouped into domains, namely "psychological", "social life", "professional life", "financial costs" and "student life". It was found that all domains, regardless of prior treatment or intervention, were all affected by keratoconus.<sup>9</sup> Our study attempted to categorise some domains of quality of life using the T-NEI-VFQ.

With the investigation conducted in Thai language, we were able to alleviate some barriers of communication. With our results, we showed that all domains of quality of life are affected by keratoconus in varying degrees with some aspects more greatly impacted than others.

One limitation of the T-NEI-VFQ is the absence of quantitative measurement. Converting ordinal qualitative measurements into numerical integer scores may not be the most accurate way of data analysis despite ease. Furthermore, some questions, as previously aforementioned,

could not be assessed numerically. Another pitfall is the difference in method of delivering the questionnaire among the two groups. The keratoconus group had a phone interview whilst the control group had an on-site interview. To reduce bias, future studies should have questionnaires be conducted using the same method in both groups with the same interviewer collecting data for the entire sample size.

Despite the keratoconus group having the lowest score for mental aspects, the control group also had the lowest score for mental aspects among domains of quality of life. This possibly highlights masked factors which may be a common ground for low quality of life in terms of mental aspects that may be among the Thai population regardless of their corneal ectatic status. Although chronic underlying illnesses were excluded from the study, mental illness was not one of the criteria. With the increasing incidence of stress in the current era, psychiatric disorders may be an influence to poor psychosocial quality of life. A study conducted by Mahikul et al. published in 2024 investigated both the prevalence and associations between mental health and quality of life after the COVID-19 outbreak and found that depression was present in 19.4% of the participants using Patient Health Questionnaire-9 (PHQ-9). A higher number of depression (32.4%), anxiety (45.4%) and stress (24.1%) was found using the Depression Anxiety Stress Scales (DASS-21) instrument. All of these were associated with poor mental health and quality of life.<sup>10</sup> Hence further attention to baseline mental health status may need to be accounted for in order to fully establish keratoconus as the independent factor in subsequent studies.

With our given data, more focus should be made in mental and psychological counseling in patients with keratoconus in our outpatient care. This may suggest that meticulous evaluation of mental status should be made at the time of diagnosis as well as during follow-up visits in order to detect any impairment in their mental wellbeing and attend to, in attempt to preserve and maintain their mental aspect of quality of life.

From our study, ocular symptoms had the smallest standard deviation in the keratoconus group. This possibly highlights that most keratoconus patients recruited in this study had

a similar degree of severity of keratoconus. However, what is lacking in this study is qualitative evidence of severity by slit lamp examination and quantitative evidence of severity by pachymetry or topography. But, this reiterates that symptomatic relief for all patients regardless of their severity, may be useful. Despite knowing that keratoconus is a disease with a wide spectrum of signs and symptoms, our selection of patients in this study may have been limited to those with a certain degree of symptoms. In future studies, more attention to patients who are asymptomatic or have less symptoms may be useful.

Concurrently, collagen cross-linking is a relatively new - and in some places rare - modality of non-surgical treatment aimed to combat or slow the progression of keratoconus. Sykakis et al's systematic review carried out in 2015, on the effectiveness of corneal collagen cross-linking for treating keratoconus has evaluated various parameters such as change in maximal keratometry, uncorrected visual acuity (UCVA), corneal thickness at the thinnest part of the cornea, spherical equivalent as well as its adverse effects. However, no studies have yet to address its impact of collagen cross-linking on quality of life.<sup>11</sup> Despite not finding any statistically significant difference in quality of life between those who underwent collagen cross-linking and those who had supportive treatment, our study found that those who underwent collagen cross-linking had a lower mental aspect of quality of life in contrast to those who had supportive treatment despite not having statistically significance. It may be possible that performance of procedures on patients may induce psychological trauma. Furthermore, the number of collagen cross-linking the patient underwent or the duration after collagen cross-linking was not taken into account. As stated in Agrawal's study, improvement in visual function may start beyond 3 months after the procedure. In fact, during the early post-procedural period, there may even be a decline in visual function due to stromal oedema. Furthermore, most improvement in visual function may take years to become evident.<sup>12</sup> Further studies should be conducted pre-operatively and post-operatively with regular follow-up intervals on those who undergo collagen cross-linking to visualise positive and negative influence on both mental health and visual function.

Currently, other surgical options of treatment for keratoconus for example deep anterior lamellar keratoplasty (DALK), penetrating keratoplasty (PKP) and intrastromal corneal ring segments (ICRS) are available. Visual rehabilitation by these surgical procedures may have a significant effect on keratoconus patients. In evaluation of the benefits of these surgery, parameters apart from visual acuity, keratometry, topography and pachymetry should be considered given that quality of life is one aspect that influences the success of surgery for these patients.

### Conclusion

As shown, keratoconus does have a negative influence on all aspects of quality of life. With more focus on how much the disease impacts the quality of life, we may have greater guidance on the choice of management for each individual patient. Quality of life may also be a measurable outcome which may help determine success of any medical or surgical intervention, such as collagen cross-linking. As demonstrated, we hope that quality of life is not regarded inferior to other measured biometric parameters and can give insight to help tailor treatment for our keratoconus patients in the clinic.

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