Characteristics and clinical outcomes of patients diagnosed with keratocone

Características e desfechos clínicos dos pacientes diagnosticados com ceratocone

Alexandre Batista Esperidião[1] https://orcid.org/0000-0002-7984-5561
Fernando dos Reis Spada[2] https://orcid.org/0000-0001-9829-5270
Astor Grumann Júnior[3] https://orcid.org/0000-0002-6017-7671

ABSTRACT

Objectives: *To describe the epidemiological and clinical profile, evolution and outcomes of keratoconus patients diagnosed in the ophthalmologic reference service of the state of Santa Catarina, Brazil.* ***Methods:*** *The medical records of all patients with keratoconus attended at the Cornea service of the Regional Hospital of São José, between January 2016 and December 2018 were retrospectively analyzed. The following data were extracted: sex, age, disease stage, systemic diseases, ophthalmological symptoms, adaptation of contact lenses, previous treatments, best monocular visual acuity, keratometric measurements, ophthalmological procedures, clinical outcomes.* ***Results:*** *The medical records of 267 patients were analyzed. The average age was 23 years (range: 06 - 60 years), 159 (59.55%) were male. 12 (4.49%) patients had already performed penetrating keratoplasty; 22 (8.24%) had performed crosslinking; 07 (2.62%) had already an intrastromal ring implant. 81 (30.34%) patients had already adapted contact lenses. 168 (62.92%) had best corrected visual acuity, of the better eye, equal to or greater than 20/40. A distribution between cases was found light, moderate and severe of: 03 (1.12%), 78 (29.21%), 157 (58.80%), respectively. Throughout the period, a total of 51 (73,9%) corneal transplants, were performed 09 (90,0%) intrastromal ring implants, 35 (32,4%) crosslinking, 22 (23,4%) contact lens adaptations were performed; 205 (76.77%) patients lost follow-up, 12 (4.49%) were discharged.* ***Conclusion:*** *The patients are mostly young, with moderate to severe illness and good visual acuity in the best eye. Even so many received a surgical management. The loss of clinical follow-up is an important factor in the quality of ophthalmic care in this population.*

Keywords: *Keratoconus/epidemiology; Tertiary referral center*

RESUMO

Objetivos: Traçar o perfil epidemiológico, clínico, evolução e desfechos dos pacientes com ceratocone diagnosticados no serviço de referência oftalmológica do estado de Santa Catarina, Brasil. **Métodos:** Foram analisados retrospectivamente os prontuários de todos os pacientes com ceratocone do setor de córnea do Hospital Regional de São José, entre Janeiro de 2016 e dezembro de 2018. Os seguintes dados foram extraídos: sexo, idade, estágio da doença, doenças sistêmicas, sintomas oftalmológicos, adaptação de lentes de contato, tratamentos prévios, melhor acuidade visual monocular, medidas ceratométricas, condutas oftalmológicas, desfechos clínicos. **Resultados:** Os prontuários de 267 pacientes foram avaliados. A média de idade foi de 23 anos (intervalo: 06 – 60 anos), 159 (59,55%) eram do sexo masculino. 12 (4,49%) pacientes já haviam realizado ceratoplastia penetrante; 22 (8,24%) haviam realizado crosslinking; 07 (2,62%) já possuíam implante de anel intraestromal. 81 (30,34%) pacientes já haviam adaptado lentes de contato. 168 (62,92%) possuíam acuidade visual corrigida, do melhor olho, igual ou superior a 20/40. Encontrou-se uma distribuição entre casos leves, moderados e graves de: 03 (1,12%), 78 (29,21%), 157 (58,80%), respectivamente. Ao longo do período, efetivaram-se 51 (73,9%) transplantes de córnea, 09 (90,0%) implantes de anel intraestromal, 35 (32,4%) crosslinking, 22 (23,4%) adaptações de lentes de contato; 205 (76,77%) pacientes perderam seguimento, 12 (4,49%) receberam alta. **Conclusão:** Os pacientes são em sua maioria jovens, com doença moderada a grave, e boa acuidade visual no melhor olho. Ainda assim, muitos receberam indicação de tratamento cirúrgico. A perda de seguimento clínico constitui um fator importante na qualidade da assistência oftalmológica desta população.

Descritores: Ceratocone/epidemiologia; Centro de atenção terciária

[1]Ophthalmology Residency Program, Dr. Homero de Miranda Gomes Regional Hospital of São José, São José County, SC, Brazil.
[2]Cornea Department, Dr. Homero de Miranda Gomes Regional Hospital of São José, São José County, SC, Brazil.
[3]Oculoplastic Department, Dr. Homero de Miranda Gomes Regional Hospital of São José, São José County, SC, Brazil.

Place where the research was carried out: Ophthalmology Service of Dr. Homero de Miranda Gomes Regional Hospital of São José, at Adolfo Donato da Silva Street, s/n, Praia Comprida, São José County – SC

INTRODUCTION

Keratoconus is a pathological condition that gives the cornea a conical and protruding shape due to progressive non-inflammatory stromal thinning, also known as ectasia.[1] This pathophysiological process and other issues such as pellucid marginal degeneration, keratoglobus and post-refractive surgery progressive ectasia, belong the group of ectatic corneal diseases.[2] The clinical outcome of this condition lies on decreased visual acuity due to irregular astigmatism, high myopia, higher-order visual aberrations and, sometimes, corneal scar development.[3]

The global incidence and prevalence of keratoconus presents great variability in the literature - estimates range from 5 to 23 and 54 cases per 100,000 inhabitants, respectively.[1,4-7] However, besides ethnic differences, keratoconus incidence and prevalence have recently shown annual rates 5 to 10 times higher than previously reported data.[8] Assumingly, this discrepancy may result from the use of different clinical definitions and diagnostic criteria, in association with progressively more accurate and early disease diagnosis.[8,9]

Divergences emerge at the time keratoconus' etiology, heredity, pathogenesis and biochemistry are addressed. Most likely, the aforementioned disease is the final outcome of a course shared by different pathological conditions, such as systemic collagen diseases, trauma and pre-existing tissue abnormalities.[5] However, there is consensus about the main risk factors linked to the disease, namely: Down syndrome, affected relatives (mainly if they are young), eye allergy, ethnic factors (Asian and Arab), mechanical factors (such as eye friction), loose eyelid syndrome, atopy, connective tissue disorders (Marfan syndrome), Ehlers-Danlos syndrome and Leber congenital amaurosis.[2]

Symptoms associated with keratoconus can change depending on disease severity and/or stage; it can even be asymptomatic and imperceptible at clinical examination, unless specific tests, such as corneal topography, are carried out. [9] Nevertheless, disease progression leads to steady visual acuity decrease, even after optical correction application. In addition, biomicroscopic findings become increasingly prevalent as the disease progresses, namely: inferior off-center corneal protrusion and thinning, Munson's sign, Vogt's striae in posterior stroma, Bowman's layer scar, Fleischer ring. [9,10] Thus, keratoconus patients' management and treatment depends on disease stage and severity. [1,2,5,9]

Therapeutic options are traditionally divided into non-surgical and surgical. Optical correction procedures based on glasses and contact lens using are classic alternatives focused on the clinical management of patients with mild-to-moderate keratoconus degree. [2,10] Progression and severity of signs and symptoms eventually make these initial therapeutic strategies intolerable and uncapable of visually rehabilitate patients. Penetrating keratoplasty is the most common and successful surgical treatment available for the most advanced stages associated with corneal sequelae, such as post-hydrops scars – this treatment often presents satisfactory visual outcomes. [1,5,11] Recently, lamellar keratoplasties, mainly deep anterior lamellar keratoplasty (DALK), have been preferred over penetrating transplantation in cases without history of hydrops. In addition, newer alternative procedures, such as intrastromal ring implantations, have led to satisfactory visual outcomes. [2,9,11] Nevertheless, it was only in the late 20th century that corneal cross-linking emerged as the new treatment modality primarily aimed at changing the natural history of the disease, mainly for patients with documented disease progression. This treatment modality helps stabilizing the disease, preserving patients' visual acuity and postponing the need of adopting highly-invasive approaches. [6,12,13]

In short, keratoconus is an expressive and globally-compromising ophthalmological pathology, whose natural evolution generates significant visual morbidity. Thus, understanding its individual and population-related features helps implementing measures focused on the early diagnosis and treatment of affected patients. The aim of the current research was to feature the epidemiological profile, initial clinical stage, conduct and outcomes of keratoconus patients diagnosed at the reference ophthalmology service in Santa Catarina State, Brazil.

METHODS

Observational, analytical, historical cohort study focused on analyzing medical records of patients referred to the cornea sector of the reference ophthalmology service belonging to the public health network in Santa Catarina State, from January 1st, 2016 to December 31st, 2018. The study was carried out at Dr. Homero de Miranda Gomes Regional Hospital of São José, which is located at Adolfo Donato da Silva Street, s/n, Praia Comprida, São José County, SC.

Among all patients referred to the aforementioned hospital from January 1st, 2016 to December 31st, 2018, those who were diagnosed with, or suspected to have, keratoconus at the first visit, and in subsequent visits after clinical investigation, as well as those who had already been diagnosed with the disease at referral time, were selected to participate in the current study. Clinical data recorded in patients' electronic medical records were thoroughly analyzed.

The medical records of patients who were not treated in the cornea sector of the aforementioned hospital; whose first visits took place outside the investigated period, despite the diagnosis of keratoconus; as well as patients diagnosed with other ophthalmological pathologies were excluded from the study. Finally, patients whose medical records had missing or conflicting data that made statistical analysis unfeasible were also excluded from it.

Selected patients' clinical data were collected based on the collection protocol pre-defined by researchers, by taking into consideration the following variables: sex; age at first consultation date; initial diagnosis; previous diagnosis; ophthalmological symptoms; disease stage (severity); systemic comorbidities; previous attempts to contact lens fitting, either reported by patients themselves or in their medical record; previous surgical treatments, either reported by patients themselves or in their medical record; better monocular visual acuity measured through Snellen table at first consultation; initial keratometric measurements [steep keratometry (Ks), flat keratometry (Kf) and maximum keratometry (Kmax)] taken at first consultation by using the same topographer, Tomey TMS-4N Topographic Modeling System, Nagoya, Japan; initial medical conduct/indication; clinical developments over the ophthalmological follow-up period; and final outcomes associated with proposed and performed treatments, follow-up time and loss of ophthalmological follow-up (recorded in the latest evolution available)

Lack of consistent information about corneal thinning degree, apical healing, cone location, presence or absence of Fleischer ring, Vogt's striae or Munson's sign has prevented the analysis of these data.

Lack of new information about outpatient consultations, when patients' medical records lacked clearly stated discharge from medical follow-up in the most recent consultation available, was the criterion used to define loss of ophthalmological follow-up.

Participants subjected to outpatient follow-up after February 2020 (when the final collection of data recorded in patients' electronic medical records was carried out) were classified as patients who maintained ophthalmological care with the corresponding corneal team.

Criteria proposed in the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) (10) study were used to categorize keratoconus severity in each patient, based on Ks. According to these criteria, keratoconus was classified as mild, when Ks value was lower than 45D; moderate, when Ks value ranged from 45D to 52D; and severe, when Ks value was higher than 52D.

Data about all selected patients were organized in Microsoft Excel® spreadsheet (version 16.41) and exported to R software. They were analyzed based on descriptive statistics, absolute and relative frequency (categorical variables), and on data position and dispersion measurements (numeric variables). Results were presented in tables and figures.

The research was carried out after approval by the Research Ethics Committee of Santa Catarina State Cardiology Institute, on December 11th, 2019 (CAAE number 26430019.1.0000.0113). It has followed the rules set by the National Health Council Resolution n. 466/2012, which addresses operational and ethical aspects of scientific studies conducted with human beings in Brazil.

RESULTS

In total, 912 patients were referred to the cornea sector for their first consultation with the specialist throughout the investigated period; 267 of them were suspected to have, or diagnosed with, keratoconus in at least one eye, which corresponded to 29.28% of all referred patients. Of these, 219 patients (82.02%) had been previously diagnosed with the disease, which was the reason why they were referred to the reference service.

All 267 selected patients were assessed based on the following parameters: age, sex, comorbidities, ophthalmic symptoms, disease stage, prior attempts to contact lens fitting, previous surgical treatments, visual acuity and keratometric measurements.

Age and sex
Patients' mean age was 23 years (standard deviation: 10.41 years; range: 06 - 60 years old), as shown in Figure 1. In addition, 13- and 17-year-old patients presented equivalent prevalence in the sample, which configured bimodal distribution. Most patients (n = 159; 59.55%) were male, whereas 108 (40.45%) were female.

Comorbidities and ophthalmic symptoms
Based on the survey about associated comorbidities investigated at the first consultation, 4 (1.5%) patients were diagnosed with Down syndrome; 12 (4.49%) were diagnosed with asthma; 9 (3.36%), with atopy (atopic dermatitis); 11 (4.11%) patients had cardiovascular diseases; 1 (0.37%) patient had diabetes mellitus; and 160 (59.93%) patients reported to not have comorbid systemic diseases.

With respect to ophthalmic symptoms, 73 (27.34%) patients reported moderate-to-severe itchy eyes. In total, 126 (47.19%) patients reported low visual acuity at the first consultation.

Initial severity
Disease severity presented numerical and percentage distribution among mild (n = 3; 1.12%), moderate (n = 78; 29.21%) and severe (n = 157; 58.80%) cases.

Prior attempts to contact lens fitting
All 219 patients with previous keratoconus diagnosis were asked about previous attempts to contact lens fitting. In total, 79 (36.07%) had already tried this therapeutic alternative; 55 of them (69.62%) did not tolerate the use of contact lenses over time and abandoned the therapy, whereas 23 (29.11%) used contact lenses in both eyes at first consultation time. Only 2 individuals in the group of patients whose keratoconus remained undiagnosed until the first consultation had previously tried to use contact lenses, although unsuccessfully.

Previous surgical treatments
Twelve (n = 12; 4.49%) patients had been subjected to penetrating keratoplasty before the initial consultation (6, in the
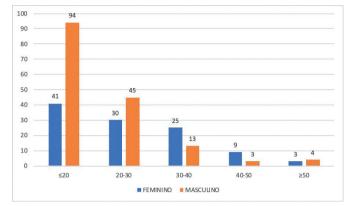

Figure 1: Patients' distribution based on age group

right eye; 3, in the left eye; and 3, in both eyes). In total, 22 (8.24%) patients had already been subjected to crosslinking (5, in the right eye; 7, in the left eye; and 10, in both eyes) and 7 (2.62%) patients had already undergone intrastromal ring implantation (1, in the right eye; 4, in the left eye; and 2, in both eyes).

Visual acuity
The best corrected visual acuity was recorded at the first consultation. Table 1 summarizes data about each patient's best eye. Only 45 (16.85%) patients presented equal visual acuity in both eyes; 168 (62.92%) presented visual acuity in the best eye equal to, or better than, 20/40; and 21 (7.87%) presented visual acuity of the best eye equal to, or worse than, 20/200.

Given the overall panorama regarding patients' features, it is important addressing the follow-up carried out after patients' admission to the cornea sector. Participants were assessed based on initial medical procedures, disease evolution, outcome, follow-up time and loss of follow-up, as detailed below.

Initial medical procedures
All patients referred to the cornea sector were subjected to initial clinical procedures based on the ophthalmological assessment performed at the first visit, as well as on previous complementary exams and/or history of follow-up in other ophthalmology services. In total, 110 (41.20%) patients already had this information before their first consultation at the service.

Ophthalmic procedures were condensed into six main ones: clinical follow-up (CF), request for complementary exams (CE), referral to contact lens fitting (CL), referral to crosslinking (CLX), keratoplasty (KP) (cornea transplantation), intrastromal ring implant (IR).

Figure 2 and Table 2 show the number of patients subjected to each of the aforementioned initial ophthalmic procedures, as well as those subjected to more than one procedure. Of the total number of patients, 48 (15.69%) were prescribed corneal transplantation (43 penetrating keratoplasties and 5 DALK), 5 (1.63%) were prescribed intrastromal ring implantation, 72 (23.53%) were referred to crosslinking, 70 (22.88%) were referred to attempt to contact lens fitting, and 44 (14.38) patients were only referred to clinical follow-up.

Follow-up
Based on the analysis applied to the follow-up carried out after the initial medical procedure, 103 (38.57%) patients did not return to the service after the first consultation. The distribution of each of these patients, based on their therapeutic indication, is shown in Figure 3 and the total number of patients per procedure is summarized in Table 3.

Table 4 describes the initial procedures applied to the other

Table 1
**Patients' distribution based on the best corrected
visual acuity in the best eye, or in both eyes**

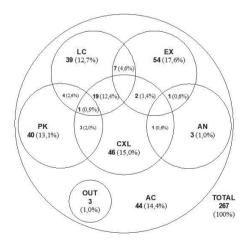| VA	RE	LE	RE and LE	N (%)
20/20 or better	25	21	11	57 (21,35)
20/21 to 20/40	59	39	13	111 (41,57)
20/41 to 20/69	15	14	5	34 (12,73)
20/70 to 20/199	22	16	6	44 (16,48)
20/200 or worse	5	6	10	21 (7,87)

VA (visual acuity); RE (right eye); LE (left eye); N (total number and percentage of patients per group)

patients, who returned for surgical procedures or clinical follow-up. Complementary exams

Pachymetric mapping and/or posterior corneal curvature evaluation were requested in order to complete the ophthalmological assessment of 64 (20.92%) patients. Of them, only 35 (11.44%) presented the required complementary exams in the following consultation. The complementary assessment helped the corneal team to apply the proper procedure to each case. Thus, 21 (6.86%) of the aforementioned patients were referred to crosslinking, 5 (1.63%) were referred to intrastromal ring implantation and 4 (1.31%) were referred to corneal transplantation.

Crosslinking

With respect to the 72 (23.53%) patients who received initial recommendation of crosslinking, only 14 (4.57%) underwent the procedure. Three (3) (2.23%) among 9 (2.94%) patients who did not undergo this procedure but returned for the follow-up visit had their clinical indication changed into corneal transplantation and 1 (0.74%) was referred to intrastromal ring implantation. All 4 patients underwent the surgical procedure indicated at that time.

CF (clinical follow-up); CE (complementary exams); CL (contact lens); CLX (crosslinking); IR (intrastromal ring); KP (keratoplasty); OT (others).

Figure 2: Distribution of ophthalmologic procedures at the first consultation, per patient

Corneal transplant

Of all 48 (15.69%) patients who were prescribed corneal transplantation at first consultation, 22 (7.19%) had already tried contact lens fitting. However, only 3 (0.98%) of them kept on using it in the contralateral eye to the one indicated for surgical

Table 2
**Distribution of ophthalmic procedures
at the first consultation, per procedure**

Procedures	N (%)
Follow-up	44 (14,38)
Complementary exams	64 (20,92)
Contact lens	70 (22,88)
Crosslinking	72 (23,53)
Intrastromal ring	5 (1,63)
Keratoplasty	48 (15,69)
Others	3 (0,98)
Total	306 (100)

N (total number and percentage of conducts/procedures per group)

Table 3
**Distribution of ophthalmologic procedures among
patients who lost follow-up after the first consultation.**

Procedures	N (%)
Follow-up	19 (16,24)
Complementary exams	17 (14,53)
Contact lens	35 (29,91)
Crosslinking	35 (29,91)
Intrastromal ring	3 (2,56)
Keratoplasty	8 (6,84)

N (total number and percentage of conducts/procedures per group)

Table 4
**Distribution of procedures effectively performed after
they were recommended at the first consultation**

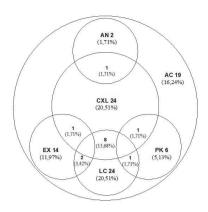| Procedures	N(%)
Complementary exams	35 (11,44)
Contact lens	14 (4,58)
Crosslinking	14 (4,58)
Intrastromal ring	1 (0,33)
Keratoplasty	36 (11,76)

N (total number and percentage of conducts/procedures per group)

procedure. There were patients among this group of 48 patients who had already undergone some surgical treatment prior to being referred to the service, namely: 3 (0.98%) patients had already undergone corneal transplantation in one eye, 1 (0.33%) of them also had intrastromal ring implant in the contralateral eye; 3 (0.98%) patients had already undergone crosslinking, 1 (0.33%) of them, in both eyes. Finally, 1 (0.33%) of the investigated patients underwent penetrating transplantation in both eyes during the follow-up period.

Effectively-performed surgical procedures

Table 5 shows the total number of monocular surgical procedures performed by the corneal sector within the evaluated period-of-time. In total, 51 (73.9%) corneal transplantations, 9 (90.0%) intrastromal ring implants and 35 (32.4%) crosslinking procedures were performed in at least one of patients' eyes. Of the 51 corneal transplants performed throughout the study, there were 2 re-transplants due to failure in the first graft - 6 patients were subjected to surgery in both eyes.

Loss of follow-up

Legend: CF (clinical follow-up); CE (complementary exams); CL (contact lenses); CLX (crosslinking); IR (intrastromal ring); KP (keratoplasty)

Figure 3: Distribution of patients who missed the follow-up after the first consultation.

Table 5
Total number of surgical procedures performed throughout the study

Procedures	Recommended	Performed	%
Crosslinking	108	35	32.4
Intrastromal ring	10	9	90.0
Keratoplasty	69	51	73.9

%, rate calculated based on the association between the number of performed procedures and the number of times they were indicated.

Based on the analysis applied to the outpatient follow-up conducted with 267 patients, 205 (76.77%) of them missed the ophthalmic follow-up with the assistant team within the investigated period, 12 (4.49%) patients were discharged from the service (4 of them were referred to follow-up with assistant ophthalmologist) and 50 (18.72%) remain under follow-up with the corneal team. The mean clinical follow-up time comprised 168 days, if one takes into consideration all 267 patients.

DISCUSSION

The current study has shown that most patients referred to specialized corneal teams, at the state ophthalmology reference center, were diagnosed with keratoconus. Almost a third of the referred patients had the disease and 82.02% of them had already been diagnosed at the time of their first consultation. Studies about keratoconus patients treated in contact lens clinics, tertiary hospitals and anterior segment-specialized clinics have shown lower demand by this group when it comes to the total number of consultations, which ranged from 3.21% to 16.4%. [14–16] Other studies recorded similar absolute numbers of care services provided to keratoconus patients on a yearly basis, although they did not compare this demand to the overall demand of each reality. [16–19]

However, these data do not reflect the incidence or prevalence of the disease, which present significant variations in the literature. Factors such as geographical location, diagnostic criteria, increasing improvement in the sensitivity of diagnostic instruments and cohorts of selected patients can contribute to this variability. [8,20] Nevertheless, major epidemiological reviews have reported disease incidence values ranging from 1:3,000 to 1:80,000 a year, and prevalence estimates as low as 2 cases per 100,000 individuals, and as high as 265 cases per 100,000 individuals. [4,8]

The numbers in the present study were already expected to be higher than those of the overall population, since patients' selection process took place in a tertiary ophthalmic center of referenced demand (selection bias).

Although the current study has found higher proportion of male patients (59.55%), in compliance with previous studies, [10,19,21,22] major reviews on the topic, such as the study by Krachmer et al. [5], have shown higher disease prevalence in female patients. On the other hand, other studies did not find difference in disease prevalence between sexes. [4] Thus, it remains uncertain in the literature whether there are significant differences between men and women. [20]

Mean age among patients (23 years old) was lower than that observed in major reviews, such as the American study CLEK, [10] whose investigated patients (n = 1,209) presented mean age of 39.2 years. A South Korean study [23] has found mean age of 31.2 years among 17,931 patients. There is evidence that younger patients present more aggressive disease progression. Besides, factors such as keratometry, cylindrical refraction, visual acuity, ethnicity can lead to greater risk of having patients in need of corneal transplant. [24–26]

It is possible inferring a window of opportunity for the early follow-up and treatment of patients served in the investigated center, if one only takes into account the aforementioned epidemiological factors, since younger members of the population with keratoconus would mostly tend to show unfavorable disease evolution. However, they would still have functional visual acuity at the time they started their ophthalmological follow-up.

Comorbidities classically associated with keratoconus, such as Down's syndrome, Leber congenital amaurosis and connective tissue diseases, [1,2,5] were uncommon in the patient pool of the current study, as also reported by other scholars. [1,4,10,19]

Given the epidemiological profile of the herein investigated patients, decreased visual acuity was the symptom mostly reported at the first consultation (47.19%) - this symptom was the main and earliest complaint by keratoconus patients in previous studies. [14,27] However, it is important highlighting that keratoconus patients may experience reduced visual function before visual acuity loss can be measured. [5] Results in the current study have shown that 21.35% of patients recorded the best corrected visual acuity in the best eye equal to, or better than, 20/20 (based on the Snellen chart), whereas 62.92% of them presented visual acuity equal to, or better than, 20/40.

Disease bilaterality was not evaluated in the current study; however, it is possible inferring that eyes with initial keratoconus, or subclinical keratoconus in the contralateral eye presenting good visual acuity, have contributed to the larger number of patients with visual acuity better than, or equal to, 20/40. It is worth mentioning that keratoconus is, by definition, bilateral and asymmetric [1,2,5] and that unilateral keratoconus does not exist. [2]

With respect to patients' classification based on disease severity, the 2015 Global Consensus on Keratoconus and Ecstatic Diseases [2] has concluded that there would be no adequate clinical classification system for the disease and that, in fact, its classification presents great variability among studies. [9,28,29] The current study has accessed the severity of the investigated cases based on the criterion proposed by the CLEK study, [10] which used a keratometric parameter, more specifically the Ks (steep keratometry), in order to classify the investigated cases as mild, moderate and severe. Results have shown considerable trend to find severe cases (n = 157; 58.80%), which was also found in, and expected by, the CLEK study, [10] when it used Ks as parameter. In addition, the selection bias observed for the herein investigated ophthalmic center has contributed to this trend. Sray et al. [30] have found increasing trend towards the need of corneal transplant in patients presenting higher Ks values. Nevertheless, finding patients at advanced disease stages is extremely valuable to help improving the knowledge of health professionals and managers in charge of ophthalmic services, since they can reason about the ophthalmological care to be provided to these patients.

Disease severity classification, as well as the initial assessment and follow-up of all patients, were based on video-keratographic findings. In light of the current technological advancements in corneal imaging tests, the evaluation of more sensitive and early parameters mainly associated with keratoconus diagnosis and progression [2,31] enables speculating that disease severity and even the number of cases may have been underestimated due to limitations in the adopted technologies.

With respect to non-surgical therapies available for keratoconus patients, contact lenses (gelatinous, rigid gas-permeable, hybrid, scleral) are a consolidated and widely recommended tool to help improving the visual acuity of these patients. [2,9,32] However, the current study has found a small number of individuals who had been offered treatment, even those who had been previously diagnosed with the disease by another ophthalmologist. On the other hand, there was consensus that wearing contact lenses does not help reducing or stabilizing ectasia progression. [2] In addition, there is evidence that the most severe cases are more likely to develop corneal scarring due to contact lenses wearing. [33] However, it does not mean that patients with mild-to-moderate keratoconus cannot benefit from the adequate fitting of several options and types of lenses capable of providing good visual correction and of reducing the need of surgical interventions aimed at improving patients' visual acuity.

With respect to surgical treatment modalities, 44.94% of investigated patients received surgical recommendations such as crosslinking, intrastromal ring implantation and corneal transplantation, at their first consultation. Other studies have reported greater proportion of patients whose recommendation for non--surgical treatment has prevailed. [3,9,19,34] Similar studies have conducted retrospective analysis of keratoconus patients' follow-up and found initially indicated corneal transplant rates compatible to those reported in the current study. Nevertheless, most of these studies have selected longer periods-of-time to observe the outcomes of each patient, which would increase the likelihood of having patients progressing towards keratoplasty. [3,19,26] Kennedy et al. [4] have followed-up a group of patients for 48 years; their data have shown that patients' cumulative likelihood of surviving and not undergoing keratoplasty remained higher than 80%, more than 20 years after disease diagnosis.

The need of improving ophthalmological assessment through complementary exams external to the investigated service was the initial procedure applied to 64 (20.92%) patients. Almost half of them received surgical recommendation after complementary evaluation. This finding emphasizes one of the weak points in the medical care provided by the investigated institution, namely: the follow-up of this potentially progressive chronic disease, whose early diagnosis and procedures can influence its outcome and prognosis. Early keratoconus diagnosis can help decision-making processes, such as assessing the need of early intervention based on crosslinking. [35,36] In addition, undiagnosed early-stage keratoconus is the leading cause of iatrogenic ectasia after laser in situ keratomileusis (LASIK) and remains the major challenge of preoperative screening for refractive surgery. [5,37-40]

Data about effectively performed procedures and conducts, and ophthalmological follow-up maintenance records, have also shown vulnerability in the ophthalmological care provided by the investigated service. Such a vulnerability ends up being transferred to patients themselves, who do not know their own disease and have a hard time accessing diagnostic and therapeutic resources. Half of patients who missed follow-up in the current study only went to the first consultation; non-surgical approach was recommended to 58.25% of them.

With respect to consolidated surgical therapies recommended for keratoconus, the investigated service presented small number of recommendations for intrastromal ring implantations. This limitation can be explained by lack of material available for this procedure in the Unified Health System (SUS) and by the obstacle faced by most patients to have access to other alternatives, such as the complementary system. Nevertheless, intrastromal ring implantation, together with deep anterior lamellar keratoplasty and penetrating keratoplasty, are the most important surgical techniques used to restore the best uncorrected visual acuity in keratoconus patients. [2]

Similarly, crosslinking unavailability in the service itself may have been the determining factor for this group to present the highest rate of missing patients (together with the group of patients referred to contact lens fitting). According to the 2015 Global Consensus on Keratoconus and Ecstatic Diseases [2], crosslinking plays key role in the treatment of keratoconus cases with perceived or documented risk of progression in patients previously subjected to other corneal surgeries. Thus, there are no formal restrictions regarding patients' minimum or maximum age, or visual acuity threshold, for this procedure to be performed. Evidence has indicated that crosslinking was capable of effectively stopping keratoconus progression and improving patients' visual acuity - it even presented late effects such as reduced keratometric values. [6,13,35,41]

CONCLUSION

The present study has epidemiologically and evolutionarily featured a population lacking data about a disease of increasing interest in the global ophthalmological literature, namely: keratoconus. Overall, patients were young, presented moderate-to-severe disease, according to the keratometric criterion, as well as good visual acuity. Few patients presented systemic diseases associated with keratoconus. Yet, many of them were referred to surgical treatment. The follow-up of this population was overall severely hampered due to loss of follow-up by most patients. Moreover, some procedures in the arsenal necessary for clinical and surgical keratoconus management processes were not available at the center where they were treated in.

The limitations of the current study lie on its retrospective nature, on the selection bias due to the role played by the institution within the healthcare system it operates in and on limitations intrinsic to each healthcare service reality with respect to access, resources and assistance. Prospective and well-controlled studies should be conducted to help broadening the scientific knowledge about the topic. Nevertheless, retrospective analysis application to baseline features of the investigated population, and to its evolution over time, can be used as consistent model to help designing further studies focused on promoting the best ophthalmological management possible.

REFERENCES

1. Rabinowitz YS. Keratoconus. Surv Ophthalmol. 1998;42(4):297–319.
2. Gomes JA, Tan D, Rapuano CJ, Belin MW, Ambrósio R Jr, Guell JL, et al.; Group of Panelists for the Global Delphi Panel of Keratoconus and Ectatic Diseases. Global consensus on keratoconus and ectatic diseases. Cornea. 2015;34(4):359–69.
3. Rafati S, Hashemi H, Nabovati P, Doostdar A, Yekta A, Aghamirsalim M, et al. Demographic profile, clinical, and topographic characteristics of keratoconus patients attending at a tertiary eye center. J Curr Ophthalmol 2019;31(3):268–74.
4. Kennedy RH, Bourne WM, Dyer JA. A 48-year clinical and epidemiologic study of keratoconus. Am J Ophthalmol. 1986;101(3):267–73.
5. Krachmer JH, Feder RS, Belin MW. Keratoconus and related noninflammatory corneal thinning disorders. Surv Ophthalmol. 1984;28(4):293–322.
6. Mohammadpour M, Masoumi A, Mirghorbani M, Shahraki K, Hashemi H. Updates on corneal collagen cross-linking: Indications, techniques and clinical outcomes. J Curr Ophthalmol. 2017;29(4):235–47.

7. Mas Tur V, MacGregor C, Jayaswal R, O'Brart D, Maycock N. A review of keratoconus: Diagnosis, pathophysiology, and genetics. Surv Ophthalmol. 2017;62(6):770–83.

8. Godefrooij DA, de Wit GA, Uiterwaal CS, Imhof SM, Wisse RP. Age-specific Incidence and Prevalence of Keratoconus: A Nationwide Registration Study. Am J Ophthalmol. 2017;175:169–72.

9. Romero-Jiménez M, Santodomingo-Rubido J, Wolffsohn JS. Keratoconus: a review. Cont Lens Anterior Eye. 2010;33(4):157–66.

10. Zadnik K, Barr JT, Edrington TB, Everett DF, Jameson M, McMahon TT, et al. Baseline findings in the collaborative longitudinal evaluation of keratoconus (CLEK) study. Invest Ophthalmol Vis Sci. 1998;39(13):2537–46.

11. Parker JS, van Dijk K, Melles GR. Treatment options for advanced keratoconus: A review. Surv Ophthalmol. 2015;60(5):459–80.

12. Brasil. Ministério da Saúde. CONITEC. Crosslinking corneano para ceratocone. Brasília (DF): Ministério da Saúde; 2016. [Relatorio de Recomendação, 225].

13. Horovitz RN, Garcia R, Bechara SJ. Crosslinking: an updated and effective insight. Rev Bras Oftalmol. 2015;74(2):119–23.

14. Lim N, Vogt U. Characteristics and functional outcomes of 130 patients with keratoconus attending a specialist contact lens clinic. Eye (Lond). 2002;16(1):54–9.

15. Mahadevan R, Arumugam AO, Arunachalam V, Kumaresan B. Keratoconus - a review from a tertiary eye-care center. J Optom. 2009;2(4):166–72.

16. El-Khoury S, Abdelmassih Y, Hamade A, Slim E, Cherfan CG, Chelala E, et al. Pediatric keratoconus in a tertiary referral center: Incidence, presentation, risk factors, and treatment. J Refract Surg. 2016;32(8):534–41.

17. Alabdelmoneam M. Retrospective analysis of keratoconus at King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia. Clin Optom (Auckl). 2012;2012:7-12.

18. Agrawal VB. Characteristics of keratoconus patients at a tertiary eye center in India. J Ophthalmic Vis Res. 2011;6(2):87–91.

19. Lass JH, Lembach RG, Park SB, Hom DL, Fritz ME, Svilar GM, et al. Clinical management of keratoconus. A multicenter analysis. Ophthalmology. 1990;97(4):433–45.

20. Gokhale NS. Epidemiology of keratoconus. Indian J Ophthalmol. 2013;61(8):382–3.

21. Pearson AR, Soneji B, Sarvananthan N, Sandford-Smith JH. Does ethnic origin influence the incidence or severity of keratoconus? Eye (Lond). 2000;14(Pt 4):625–8.

22. Owens H, Gamble G. A profile of keratoconus in New Zealand. Cornea. 2003;22(2):122–5.

23. Hwang S, Lim DH, Chung TY. Prevalence and Incidence of Keratoconus in South Korea: A Nationwide Population-based Study. Am J Ophthalmol. 2018;192:56–64.

24. Ferdi AC, Nguyen V, Gore DM, Allan BD, Rozema JJ, Watson SL. Keratoconus natural progression: a systematic review and meta-analysis of 11 529 eyes. Ophthalmology. 2019;126(7):935–45.

25. McMahon TT, Edrington TB, Szczotka-Flynn L, Olafsson HE, Davis LJ, Schechtman KB; CLEK Study Group. Longitudinal changes in corneal curvature in keratoconus. Cornea. 2006;25(3):296–305.

26. Gordon MO, Steger-May K, Szczotka-Flynn L, Riley C, Joslin CE, Weissman BA, et al.; Clek Study Group. Baseline factors predictive of incident penetrating keratoplasty in keratoconus. Am J Ophthalmol. 2006;142(6):923–30.

27. Khor WB, Wei RH, Lim L, Chan CM, Tan DT. Keratoconus in Asians: demographics, clinical characteristics and visual function in a hospital-based population. Clin Exp Ophthalmol. 2011;39(4):299–307.

28. Tu KL, Tourkmani AK, Srinivas S. Keratoconic cone using its keratometry, decentration, and thickness as staging parameters. Int J Keratoconus Ectatic Corneal Dis. 2016;5(3):99–104.

29. Bardan AS, Kubrak-Kisza M, Kisza KJ, Nanavaty MA. Impact of classifying keratoconus location based on keratometry or pachymetry on progression parameters. Clin Exp Optom. 2020;103(3):312–9

30. Sray WA, Cohen EJ, Rapuano CJ, Laibson PR. Factors associated with the need for penetrating keratoplasty in keratoconus. Cornea. 2002;21(8):784–6.

31. Cavas-Martínez F, De la Cruz Sánchez E, Nieto Martínez J, Fernández Cañavate FJ, Fernández-Pacheco DG. Corneal topography in keratoconus: state of the art. Eye Vis (Lond). 2016;3(1):5.

32. Peña-García P, Sanz-Díez P, Durán-García ML. Keratoconus Management Guidelines. Int J Keratoconus Ectatic Corneal Dis. 2015;4(1):1–39.

33. Barr JT, Wilson BS, Gordon MO, Rah MJ, Riley C, Kollbaum PS, et al.; CLEK Study Group. Estimation of the incidence and factors predictive of corneal scarring in the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study. Cornea. 2006;25(1):16–25.

34. Smiddy WE, Hamburg TR, Kracher GP, Stark WJ. Keratoconus. Contact lens or keratoplasty? Ophthalmology. 1988;95(4):487–92.

35. Gaster RN, Caiado Canedo AL, Rabinowitz YS. Corneal collagen cross-linking for keratoconus and post-LASIK ectasia. Int Ophthalmol Clin. 2013;53(1):79–90.

36. Kanellopoulos AJ. Collagen cross-linking in early keratoconus with riboflavin in a femtosecond laser-created pocket: initial clinical results. J Refract Surg. 2009;25(11):1034–7.

37. Amoils SP, Deist MB, Gous P, Amoils PM. Iatrogenic keratectasia after laser in situ keratomileusis for less than -4.0 to -7.0 diopters of myopia. J Cataract Refract Surg. 2000;26(7):967–77.

38. Binder PS, Lindstrom RL, Stulting RD, Donnenfeld E, Wu H, McDonnell P, et al. Keratoconus and corneal ectasia after LASIK [1]. J Cataract Refract Surg. 2005;31(11):2035–8.

39. Sorkin N, Kaiserman I, Domniz Y, Sela T, Munzer G, Varssano D. Risk assessment for corneal ectasia following photorefractive keratectomy. J Ophthalmol. 2017;2017:2434830.

40. Randleman JB, Russell B, Ward MA, Thompson KP, Stulting RD. Risk factors and prognosis for corneal ectasia after LASIK. Ophthalmology. 2003;110(2):267–75.

41. Meiri Z, Keren S, Rosenblatt A, Sarig T, Shenhav L, Varssano D. Efficacy of corneal collagen cross-linking for the treatment of keratoconus: A systematic review and meta-analysis. Cornea. 2016;35(3):417–28.

Corresponding author:
Alexandre Batista Esperidião
R. Adolfo Donato da Silva, s/n, Praia Comprida, São José – SC, CEP 88103-901
Phone number: +5548999052760
E-mail: alexesperidiao@hotmail.com