ORIGINAL ARTICLE

Long-term Biomechanical Properties and Intraocular Pressure in Patients with Keratoconus After Penetrating Keratoplasty and Deep Anterior Lamellar Keratoplasty

Propriedades Biomecânicas e Pressão Intraocular a Longo Prazo em Doentes com Queratocone Submetidos a Queratoplastia Penetrante e Queratoplastia Lamelar Anterior Profunda

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ABSTRACT

INTRODUCTION: Our aim was to compare long-term biomechanical properties and intraocular pressure between eyes treated with penetrating keratoplasty (PKP) and deep anterior lamellar keratoplasty (DALK) in patients with keratoconus and healthy patients.

METHODS: Retrospective observational case-control study with corneal biomechanical evaluation by ultra-high-speed Scheimpflug imaging during noncontact tonometry (Corvis ST, OCULUS®). The intraocular pressure (IOP) was assessed with: Goldmann applanation tonometer; noncontact tonometer and biomechanically corrected by the Corvis ST and Pentacam corrected system (Ehlers, Shah, Dresden, and Spoerl correction).

RESULTS: The study included 104 eyes: 18 PKP-treated eyes, 34 DALK-treated eyes, and 52 healthy eyes. The average age at biomechanical assessment was similar between treated and healthy eyes (p=0.980). The mean follow-up time was similar between PKP- and DALK-treated eyes (p=0.273). PKP- and DALK-treated eyes showed significantly softer behaviour in 1st (19/28 and 21/28, respectively) and 2nd (8/11 and 9/11, respectively) generation biomechanical corneal parameters compared to the control group. There was no difference in 1st and 2nd generation biomechanical corneal parameters between PKP and DALK-treated eyes and between "big bubble" and "manual dissection" DALK techniques. When analysed postoperative IOP measured by different methods, mean values were similar between PKP- and DALK-treated eyes.

CONCLUSION: Neither of the two keratoplasty techniques fully restored corneal biomechanics to those of healthy corneas. When comparing directly PKP and DALK-treated eyes, there were no significant differences in biomechanical behaviour. Mean postoperative IOPs measured by different methods were similar between PKP and DALK-treated eyes.

KEYWORDS: Biomechanical Phenomena; Cornea/physiology; Intraocular Pressure; Keratoconus; Keratoplasty, Penetrating.

RESUMO

INTRODUÇÃO: O nosso objectivo foi comparar as propriedades biomecânicas e a pressão intraocular a longo prazo entre olhos tratados com queratoplastia penetrante (PKP) e queratoplastia lamelar anterior profunda (DALK) em doentes com queratocone e doentes saudáveis.

MÉTODOS: Estudo retrospetivo observacional caso-controlo com avaliação biomecânica da córnea por imagem de Scheimpflug de alta velocidade durante tonometria de não contacto (Corvis ST, OCULUS®). A pressão intraocular (PIO) foi avaliada com: tonómetro de aplanação de Goldmann; tonómetro de não contacto, corrigido biomecanicamente pelo Corvis ST e corrigido pelo Pentacam (correção de Ehlers, Shah, Dresden e Spoerl).

RESULTADOS: O estudo incluiu 104 olhos: 18 olhos tratados com PKP, 34 olhos tratados com DALK e 52 olhos saudáveis. A média de idade na avaliação biomecânica foi semelhante entre olhos tratados e olhos saudáveis (p = 0,980). O tempo médio de acompanhamento foi semelhante entre os olhos tratados com PKP e DALK (p = 0,273). Olhos tratados com PKP e DALK mostraram um comportamento significativamente menos rígido nos parâmetros corneanos biomecânicos de 1ª (19/28 e 21/28, respetivamente) e 2ª (8/11 e 9/11, respetivamente) geração em comparação com o grupo de controlo. Não houve diferença nos parâmetros biomecânicos da córnea de 1ª e 2ª geração entre os olhos tratados com PKP e DALK e entre as técnicas de "big bubble" e "dissecção manual" no grupo DALK. Quando analisada a PIO pós-operatória medida por métodos diferentes, os valores médios foram semelhantes entre os olhos tratados com PKP e DALK.

CONCLUSÃO: Nenhuma das duas técnicas de queratoplastia conseguiu a restauração completa da biomecânica da córnea. Ao comparar diretamente os olhos tratados com PKP e DALK, não houve diferenças significativas no comportamento biomecânico. As médias das PIOs pós-operatórias medidas por métodos diferentes foram semelhantes entre os olhos tratados com PKP e DALK.

PALAVRAS-CHAVE: Córnea/fisiologia; Fenómenos Biomecânicos; Pressão Introcular; Queratoconus; Queratoplastia Penetrante.

INTRODUCTION

Keratoconus is a noninflammatory corneal ectasia that induces irregular astigmatism, myopia, and protrusion, leading to impairment in the quality of vision.[1] Corneal transplant is a frequent therapeutic option for advanced disease when spectacle correction is insufficient, contact lens wear is intolerable and visual acuity is at an unacceptable level.[2] Although other treatments had been extended for advanced disease (ultraviolet crosslinking, intrastromal corneal ring segments, bowman layer transplant), visual gains rarely exceed one or two lines at this stage of the disease.[3]

Comparing the two main corneal transplant techniques for keratoconus, penetrating keratoplasty (PKP) is less time-consuming and less surgical experience-dependent than deep anterior lamellar keratoplasty (DALK).[3] However, nowadays, it is more reserved for those where endothelial dysfunctions are present or when deep corneal scarring severely affects the visual axis up to the Descemet membrane level. The advantages of DALK over PKP are as follows: the immune rejection of the corneal endothelium cannot occur; topical corticosteroids can usually be discontinued earlier with decreased risk of secondary glaucoma; sutures can be removed earlier; DALK may have superior resistance to rupture to the globe after blunt trauma.[4] This last point is a theoretical advantage because it is difficult to prove this assertion due to smaller numbers and shorter postoperative follow-up available on DALK eyes.[5]

A corneal biomechanical assessment is increasingly used for ectatic corneal diseases, among other diseases, as it is a safe, non-invasive procedure and capable to evaluate corneal stiffness, relevant for the diagnosis, staging, and prognosis. The assessment of biomechanical properties for intraocular pressure (IOP) is another potential application.[6] To this date, in the literature, there are few published studies with results of the application of this technology in keratoconus after transplantation.

This study aimed to compare the ocular biomechanical properties of patients with keratoconus submitted to PKP or DALK and healthy patients.

MATERIAL AND METHODS

STUDY DESIGN

A retrospective observational case-control study was performed, and it included a group of patients with a diagnosis of keratoconus who previously underwent PKP or

DALK surgeries (Group 1) and a control group of healthy patients (Group 2) observed at the ophthalmology department at the Centro Hospitalar Universitário do Porto (CHUP) between July 2021 and August 2021. All patients underwent a complete eye examination, and tomographic and biomechanical assessment of the cornea. This study was conducted following the norms of the Declaration of Helsinki (1964) and its latest amendment (Brazil, 2013). The authors ensured that all patients' anonymity was carefully protected. Approval was obtained from the "Departamento de Ensino, Formação e Investigação" (DEFI).

PARTICIPANTS

The inclusion criteria for Group 1 were: diagnosis of keratoconus and previous PKP or DALK surgeries. The exclusion criteria for Group 1 were: endothelial keratoplasty, laser treatments, corneal sutures, previous vitrectomy, regrafts, graft failure, graft rejection, cataract, glaucoma, retinal disorders, ocular trauma history, non-compliant patients, and follow-up less than 1 year.

The inclusion criteria for Group 2 were: age-matched patients with the study group and absence of known ocular (such as uveitis, glaucoma, dry eye, high myopia, amblyopia) and systemic pathology (microvascular, neurological, inflammatory, infectious, metabolic, or genetic). Eyes with previous ocular surgery were excluded.

All exclusion criteria allowed us to control factors that could influence clinical, biomechanics and tomographic outcomes.

PARAMETERS

The following variables were analysed:

- Demographic characteristics of the study population (gender, age at surgery, type of surgery, recipient trephine diameter, donor trephine diameter, type of sutures);
- Clinical features pre and postoperative [best-corrected distance visual acuity (CDVA), sphere and cylinder refraction, cylinder axis, spherical equivalent (SE), IOP, and time of follow-up];
- Corneal biomechanics parameters [dynamic corneal response first and second-generation parameters].
- Cornea tomographic parameters [the deviation index (D) of Belin/Ambrósio Enhanced Ectasia Display (BAD-D), average pachymetry progression index (RPIavg), maximum Ambrosio Relational Thickness (ARTmax), maximum keratometry (Kmax), index of vertical asymmetry (IVA), index of surface variance (ISV), index of height decentration (IHD), and index of height asymmetry (IHA)];

Demographic and clinical data were collected from the patient's clinical records. For numerical analysis, "counting fingers" was replaced by a decimal acuity of 0.014 (≈20/1500) and "hand motion" of 0.005 (=20/4000).[7] Then, decimal visual acuity was converted to the logarithm of the minimum angle of resolution (logMAR) values. The IOP was assessed with Goldmann applanation tonometer (gIOP); noncontact tonometer (ncIOP) and biomechanical corrected (bcIOP) by the Corvis ST; Ehlers (eIOP), Shah (sIOP), Dresden (dIOP) and Spoerl (spIOP) correction by the Pentacam corrected system. Tomographic data was assessed with a Scheimpflug camera (Pentacam, OCULUS®). The corneal biomechanical assessment was made through ultra-high-speed Scheimpflug imaging during noncontact tonometry (Corvis ST, OCULUS®). The dynamic corneal response first and second-generation parameters included were detailed in our previous study.[8] The ABCD keratoconus grading system was used to grade the cases included.[9]

SURGICAL TECHNIQUE

All surgical procedures were carried out by three experienced cornea surgeons and performed under general anaesthesia. Regarding the PKP procedure, the host corneal opening varied between 7.50 and 8.00 mm. A corneal button 0.25 mm larger than the diameter of the host corneal opening was used and the donor cornea is sutured in place with 16 interrupted sutures, except in 2 cases where continuous suture was performed (Table 1). The DALK procedure was performed using the big-bubble technique, whenever possible, with the host corneal opening varying between 7.50 and 8.00 mm. When a big bubble was not formed even after several failed attempts at formation, a layer-by-layer manual stromal or viscoelastic dissection was tried. Even so, seven (17%) cases were converted to PKP and included in the PKP group. The donor grafts were sutured with 16 interrupted sutures, except in 1 case where continuous sutures were performed. Sutures were removed according to the clinical judgment during the follow-up.

STATISTICAL ANALYSIS

Statistical analysis was performed using the SPSS program (SPSS Statistics, version 22.0 for Windows, SPSS Inc., IBM, Somers, NY). The normality of the variables was evaluated by the Shapiro-Wilk test. When this test revealed a value of $p \geq 0.05$, the asymmetry coefficient was calculated, and values of modulus less than 2 were tolerated. For pre- and post-treatment analysis, the Wilcoxon test and paired sample T-test were used for variables with non-normal distribution and normal distribution respectively. The comparison between independent continuous variables was performed using the Mann-Whitney test and T-Student test for variables with non-normal distribution and normal distribution respectively. The Fisher exact test was used for nominal scaled data. Pearson and Spearman's bivariate correlation tests were used to study linear correlations for variables with normal distribution and non-normal distribution respectively. For interpretation, a correlation coefficient was considered "very weak" if between 0 and ±0.19, "weak" if between ±0.20 and ±0.39, "moderate" if between ±0.40 and ±0.59, "strong" if between ±0.60 and ±0.79, and "very strong" if between ±0.80 and ±1.0. *P* values less than 0.05 were considered statistically significant.

RESULTS

DEMOGRAPHIC DATA

Seventy four patients (104 eyes) were included, 62% male and 38% female, aged 21 to 57 years, with a mean age of 33.59±8.53 years.

Group 1 included 52 eyes (42 patients), 35% (18 eyes) had undergone PKP and 65% (34 eyes) had undergone DALK. For PKP-treated eyes, the mean age at surgery was 32.99±8.93 years and the mean follow-up was 5.72±4.56 years. For DALK-treated eyes, the mean age at surgery was 27.33±7.04 years, lower than PKP cases (*p*=0.015), and the mean follow-up time was 3.61±1.69 years, similar to PKP cases (*p*=0.273). Within DALK-treated eyes, the "big-bubble" technique was performed in 25 eyes, manual dissection in 7 eyes, and viscoelastic dissection in 2 eyes (Table 1)

Group 2 included 52 eyes (32 patients). The average age at biomechanical assessment was 33.61±8.57 years, similar to group 1 (*p*=0.980).

Table 1. Demographic variables.

	Group 1		Group 2	
	PKP	DALK	Control	*p*-value
Demographic variables	**Mean+SD**	**Mean +SD**	**Mean+SD**	
N (Eyes/patients)	18/14	34/28	52/32	-
Gender (Female/Male)	6/8	6/22	16/16	-
Age at biomechanical assessment	33.57±8.58		33.61±8.57	0.980*
Age at surgery	32.99±8.93	27.33±7.04	NA	**0.015****
Recipient trephine diameter	7.72±0.15	7.76±0.13		0.379**
Donor trephine diameter	7.97±0.15	8.01±0.13		0.379**
Type of sutures				
16 interrupted sutures	16/18	33/34	NA	0.272**
Continuous suture	2/18	1/34		
Subtype of surgery				
Big Bubble	NA	25/34	NA	-
Manual dissection		7/34		
Viscoelastic dissection		2/34		
Time of follow-up	5.72±4.56	3.61±1.69		0.273**

* *p*-value when comparing group 1 vs group 2
** *p*-value when comparing PKP vs DALK subgroups
DALK, deep anterior lamellar keratoplasty; N, number; NA, not applicable; PKP, penetrating keratoplasty; SD, standard deviation.

CLINICAL OUTCOMES

Preoperative CDVA increased from 1.45±0.54 logMAR to 0.13±0.08 logMAR (*p*<0.001) in PKP-treated eyes and from 1.40±0.44 logMAR to 0.32±0.29 logMAR (*p*<0.001) in DALK-treated eyes (Table 2). Preoperative CDVA was similar (*p*=0.731) in both subgroups, but postoperative CDVA was higher in PKP-treated eyes (*p*<0.001). For PKP-treated eyes, the postoperative SE and cylinder refraction values were similar (*p*=0.494 and *p*=0.770, respectively); and for DALK-treated eyes, the postoperative SE was similar (*p*=0.310) and cylinder refraction was higher (*p*=0.040) compared to preoperative values. There were no significant differences in mean postoperative SE and cylinder refraction (*p*=0.199 and *p*=0.151, respectively) between PKP- and DALK-treated eyes.

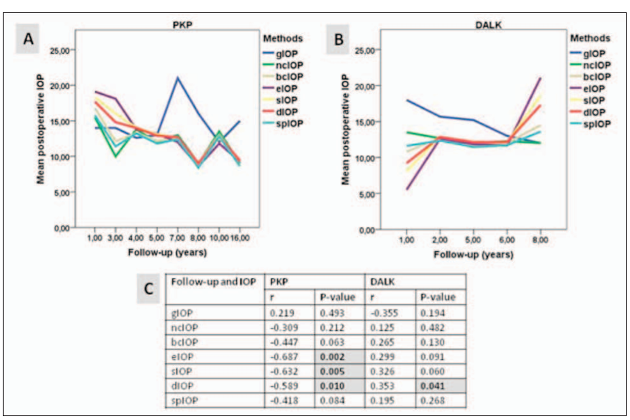
Mean postoperative gIOP was similar compared to preoperative values in both PKP- and DALK-treated eyes (*p*=0.205 and *p*=0.214, respectively). When analysed postoperative IOP measured by different methods, mean values were similar between PKP- and DALK-treated eyes (Table 2). Compared to the control group, PKP- and DALK-treated eyes had a lower mean ncIOP (*p*=0.001 and *p*<0.001, respectively), bcIOP (*p*=0.020 and *p*=0.001, respectively) and spIOP (*p*=0.006 and *p*<0.001, respectively). Additionally, DALK-treated eyes had also a lower mean sIOP (*p*=0.015) and dIOP (*p*=0.004).

The graphical representation of the variation of IOP (measured by different methods) over follow-up in the PKP- and DALK-tread eyes can be seen in Fig. 1A and 1B. In PKP-treated eyes, the linear correlation study showed moderate and strong negative correlations between the duration of follow-up and the following IOP measurements: eIOP (r=-0.687, *p*=0.002), sIOP (r=-0.632, *p*=0.005) and dIOP (r=-0.589, *p*=0.010) (Fig. 1C). In DALK-treated eyes, the linear correlation study showed one weak positive correlation between the duration of follow-up and dIOP (r=0.353, *p*=0.041).

Fig. 2 (A-C) represents the mean postoperative CDVA, SE, and bcIOP by subgroups. DALK-treated eyes had a weak negative correlation with logCDVA (r=-0.360, *p*=0.036).

Table 2. Clinical parameters.

Clinical parameters (Mean +SD)	Group 1 PKP (n=18)	Group 1 DALK (n=34)	Group 2 Control (n=52)	*p*-value Control vs PKP	*p*-value Control vs DALK	*p*-value PKP vs DALK
Preoperative						
logBCVA	1.45±0.54	1.40±0.44	NA	NA	NA	0.731
SPH	-2.69±1.69	-4.20±4.28				0.358
CYL	-3.41±2.14	-2.59±2.90				0.511
AXIS	77.88±51.76	68.64±72.46				0.762
SE	-4.39±2.53	-5.52±5.34				0.587
gIOP	14.00±2.30	12.75±2.22				
Postoperative						
logBCVA	0.13±0.08	0.32±0.29	NA	NA	NA	**0.001**
SPH	-0.96±2.47	-1.43±2.10				0.522
CYL	-3.05±1.64	-4.00±2.55				0.151
AXIS	82.86±54.34	87.41±62.52				0.817
SE	-2.49±2.63	-3.43±1.99				
gIOP	14.00±2.83	15.07±3.13	14.43±2.04	0.553	0.472	0.367
ncIOP	12.17±2.45	12.22±1.87	14.50±2.38	**0.001**	**<0.001**	0.930
bcIOP	12.46±2.30	12.30±1.78	13.94±2.27	**0.020**	**0.001**	0.788
eIOP	13.52±3.40	12.48±3.28	13.46±2.75	0.943	0.138	0.289
sIOP	13.38±2.85	12.63±2.54	14.01±2.53	0.378	**0.015**	0.336
dIOP	13.14±2.63	12.55±2.25	14.11±2.45	0.158	**0.004**	0.401
spIOP	12.01±2.39	11.86±1.87	13.89±2.45	**0.006**	**<0.001**	0.801



Follow-up and IOP	PKP r	PKP P-value	DALK r	DALK P-value
gIOP	0.219	0.493	-0.355	0.194
ncIOP	-0.309	0.212	0.125	0.482
bcIOP	-0.447	0.063	0.265	0.130
eIOP	-0.687	**0.002**	0.299	0.091
sIOP	-0.632	**0.005**	0.326	0.060
dIOP	-0.589	**0.010**	0.353	**0.041**
spIOP	-0.418	0.084	0.195	0.268

Figure 1. **The variation of intraocular pressure (IOP) measured by different methods over follow-up.** A) The graphical representation in PKP-treat eyes. B) The graphical representation in DALK-treated eyes. c) Correlations between duration of follow-up and the IOP measured by different methods, in PKP- and DALK-treated eyes. Boxes highlighted in gray correspond to a significant p-value. Abbreviations: bcIOP, intraocular pressure biomechanically corrected by the Corvis ST; DALK, deep anterior lamellar keratoplasty; dIOP, intraocular pressure by Dresden correction; eIOP, intraocular pressure by Ehlers correction; gIOP, intraocular pressure by Goldmann applanation tonometer; IOP, intraocular pressure; ncIOP intraocular pressure by Corvis ST noncontact tonometer; PKP, penetrating keratoplasty; sIOP, intraocular pressure by Shah correction; spIOP, intraocular pressure by Spoerl correction.

CORNEAL BIOMECHANICS OUTCOMES

Concerning 1st generation corneal biomechanics parameters, PKP- and DALK-treated eyes showed a significantly softer behaviour in the same 19 of 28 parameters compared to the control group. Additionally, DALK-treated eyes showed softer behaviour in more two parameters ("A1 Velocity" and "A1 Deformation Amplitude"), totalizing 21 of 28 softer parameters.

Regarding 2nd generation corneal biomechanical parameters, both PKP- and DALK-treated eyes showed softer behaviour in the same 8 of 11 parameters, compared to the control group. Additionally, DALK-treated eyes showed softer behaviour in more one parameter ("PachySlope"), totalizing 9 of 11 softer parameters. There was no difference in 1st and 2nd biomechanical corneal behaviour between PKP and DALK-treated eyes (Table 3) and between "big bubble" and "manual dissection" DALK techniques (Table 4). Central corneal thickness derived by Corvis was higher (p=0.016) in "manual dissection" (μ=577.86±41.74) compared to the "big bubble" DALK technique (μ=532.16±41.91). Due to the low number of cases, analysis with the "viscoelastic dissection" DALK technique was not performed.

The linear correlation study, between the duration of follow-up and the 2nd generation corneal biomechanics parameters, showed only one significant correlation with TBI for PKP-treated eyes (r=-0.582, p=0.047). The recipient trephine diameter and the 2nd generation corneal biomechanical parameters were not correlated (p>0.05 for all 11 parameters). Correlations between biomechanical parameters and types of sutures were not performed due to the low number of cases with continuous suture. Fig. 2 (D-E) represents the mean postoperative CBI and TBI by subgroups.

Table 3. Corneal biomechanics parameters.

Biomechanical parameters	**Group 1**		**Group 2**	***p*-value**		
(Mean +SD)	**PKP (n=18)**	**DALK (n=34)**	**Control (n=52)**	**Control vs PKP**	**Control vs DALK**	**PKP vs DALK**
Corvis-derived nc IOP	12.17±2.45	12.22±1.87	14.50±2.38	**0.001**	**<0.001**	0.930
Corvis-derived CCT (µm)	525.72±42.18	540.71±44.53	559.71±23.93	**0.004**	**0.027**	0.246
1st generation parameters						
Deformation Amp. Max (mm)	1.17±0.12	1.17±0.11	1.06±0.11	**0.001**	**<0.001**	0.902
A1 Time (ms)	7.43±0.28	7.43±0.21	7.69±0.31	**0.002**	**<0.001**	0.987
A1 Velocity (m/s)	0.15±0.02	0.15±0.01	0.14±0.02	0.150	**0.036**	0.833
A2 Time (ms)	22.56±0.44	22.48±0.41	22.18±0.45	**0.003**	**0.003**	0.517
A2 Velocity (m/s)	-0.30±0.04	-0.30±0.04	-0.27±0.04	**0.002**	**0.001**	0.757
HC Time (ms)	17.00±0.68	17.03±0.55	17.24±0.50	0.326	0.164	0.830
Peak Dist. (mm)	5.09±2.78	4.98±0.21	5.00±0.29	0.302	0.606	0.115
Radius (mm)	5.84±0.66	5.76±0.78	6.53±0.58	**<0.001**	**<0.001**	0.734
A1 Deformation Amp. (mm)	0.14±0.01	0.15±0.02	0.14±0.02	0.186	**0.012**	0.406
HC Deformation Amp. (mm)	1.17±0.12	1.17±0.11	1.06±0.11	**0.001**	**<0.001**	0.902
A2 Deformation Amp. (mm)	0.36±0.06	0.38±0.08	0.34±0.07	0.471	0.030	0.289
A1 Deflection Length (mm)	2.53±0.35	2.51±0.39	2.25±0.13	**0.003**	**<0.001**	0.858
HC Deflection Length (mm)	6.70±0.53	6.51±0.61	6.47±0.47	0.093	0.723	0.277
A2 Deflection Length (mm)	3.67±0.92	3.79±0.89	2.81±0.57	**0.001**	**<0.001**	0.646
A1 Deflection Amp. (mm)	0.10±0.02	0.11±0.02	0.09±0.01	**0.009**	**<0.001**	0.265
HC Deflection Amp. (mm)	1.03±0.10	1.01±0.10	0.90±0.11	**<0.001**	**<0.001**	0.383
A2 Deflection Amp. (mm)	0.13±0.03	0.14±0.03	0.10±0.01	**0.006**	**<0.001**	0.094
Deflection Amp. Max (mm)	1.04±0.10	1.07±0.28	0.92±0.13	**<0.001**	**<0.001**	0.294
Deflection Amp. Max (ms)	16.97±0.71	17.06±2.32	17.03±1.76	0.401	0.354	0.172
Whole Eye Mov. Max (mm)	0.24±0.05	0.26±0.09	0.25±0.12	0.637	0.649	0.303
Whole Eye Mov. Max (ms)	21.95±1.09	22.14±1.49	21.83±0.56	0.662	0.248	0.628
A1 Deflection Area (mm2)	0.21±0.08	0.21±0.08	0.16±0.02	**<0.001**	**<0.001**	0.923
HC Deflection Area (mm2)	3.74±0.54	3.52±0.49	3.23±0.55	**0.001**	**0.015**	0.139
A2 Deflection Area (mm2)	0.34±0.15	0.36±0.15	0.23±0.04	**0.005**	**<0.001**	0.750
A1 dArc Length (mm)	-0.02±0.01	-0.02±0.02	-0.02±0.00	**<0.001**	**0.030**	0.520
HC dArc Length (mm)	-0.14±0.05	-0.14±0.04	-0.12±0.03	**0.009**	**0.007**	0.924
A2 dArc Length (mm)	-0.04±0.02	-0.04±0.03	-0.02±0.00	**0.002**	**0.001**	0.839
dArcLengthMax (mm)	-0.18±0.04	-0.20±0.08	-0.14±0.03	**<0.001**	**<0.001**	0.176
2nd generation parameters						
Max InverseRadius (mm^-1)	0.21±0.02	0.20±0.02	0.19±0.02	**0.001**	**<0.001**	0.282
DA ratio max (2mm)	4.29±0.41	4.11±0.41	4.07±0.41	0.062	0.672	0.150
PachySlope (µm)	47.72±33.42	50.59±33.46	37.59±6.71	0.218	**0.032**	0.769
DA Ratio Max (1 mm)	1.53±0.04	1.51±0.05	1.52±0.05	0.890	0.225	0.273
Ambrosio Relational Thickness	349.31±180.25	333.95±172.93	662.83±120.50	**<0.001**	**<0.001**	0.781
Biomechanically-corrected IOP	12.46±2.30	12.36±1.80	13.94±2.27	**0.020**	**0.001**	0.868
Integrated radius (mm^-1)	10.60±1.36	10.30±1.24	9.10±0.97	**<0.001**	**<0.001**	0.426
Stiffness parameter in A1	78.71±33.51	73.96±20.40	107.88±16.29	**<0.001**	**<0.001**	0.528
Corvis biomechanical index	0.78±0.26	0.81±0.23	0.16±0.15	**<0.001**	**<0.001**	0.784
Tomographic biomechanical index	0.83±0.17	0.79±0.22	0.13±0.16	**<0.001**	**<0.001**	0.640
Stress Strain Index	0.80±0.14	0.84±0.20	0.95±0.16	**0.001**	**0.001**	0.526

Table 4. Corneal biomechanics parameters in DALK: Manual vs Big-Bubble techniques.

Biomechanical parameter	DALK: Manual *vs* Big-Bubble	
	Mean difference±SE	*p*-value
Corvis-derived nc IOP	0.71±0.78	0.374
Corvis-derived CCT (µm)	45.70±17.91	**0.016**
1st generation parameters		
Deformation Amp. Max (mm)	-0.03±0.05	0.507
A1 Time (ms)	0.08±0.09	0.356
A1 Velocity (m/s)	-0.00±0.00	0.332
A2 Time (ms)	-0.03±0.17	0.860
A2 Velocity (m/s)	0.01±0.02	0.540
HC Time (ms)	0.15±0.24	0.688
Peak Dist. (mm)	-0.06±0.09	0.544
Radius (mm)	0.42±0.34	0.216
A1 Deformation Amp. (mm)	-0.00±0.01	0.786
HC Deformation Amp. (mm)	-0.03±0.05	0.507
A2 Deformation Amp. (mm)	0.04±0.03	0.256
A1 Deflection Length (mm)	-0.32±0.16	0.062
HC Deflection Length (mm)	-0.02±0.27	0.954
A2 Deflection Length (mm)	-0.46±0.38	0.401
A1 Deflection Amp. (mm)	0.00±0.01	0.768
HC Deflection Amp. (mm)	-0.06±0.04	0.188
A2 Deflection Amp. (mm)	-0.00±0.01	0.747
Deflection Amp. Max (mm)	-0.11±0.13	0.175
Deflection Amp. Max (ms)	-0.39±1.03	0.859
Whole Eye Movement Max (mm)	0.06±0.04	0.121
Whole Eye Movement Max (ms)	-0.64±0.65	0.334
A1 Deflection Area (mm^2)	-0.02±0.03	0.324
HC Deflection Area (mm^2)	-0.32±0.21	0.132
A2 Deflection Area (mm^2)	-0.05±0.06	0.400
A1 dArc Length (mm)	0.01±0.01	0.454
HC dArc Length (mm)	0.02±0.02	0.237
A2 dArc Length (mm)	-0.01±0.01	0.408
dArc Length Max (mm)	0.03±0.04	0.357
2nd generation parameters		
Max InverseRadius (mm^-1)	-0.01±0.01	0.251
DA Ratio Max (2 mm)	-0.02±0.18	0.910
PachySlope (µm)	6.59±14.66	0.956
DA Ratio Max (1 mm)	-0.00±0.02	0.762
Ambrosio Relational Thickness	-123.02±74.45	0.110
Biomechanically-corrected IOP	-0.36±0.76	0.641
Integrated radius (mm^-1)	-0.87±0.50	0.095
Stiffness parameter in A1	10.93±8.78	0.223
Corvis biomechanical index	0.05±0.10	0.924
TBI	-0.14±0.10	0.198
Stress Strain Index	0.00±0.09	0.721

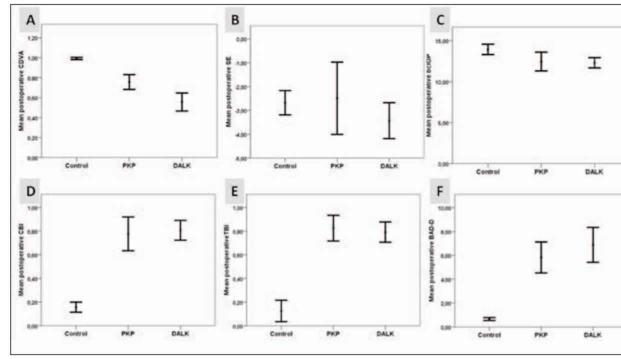


Figure 2. **The means postoperative of main clinical, corneal biomechanical, and tomographic parameters by groups.** A) CDVA. B) SE. C) bcIOP. D) CBI. E) TBI. F) BAD-D. Abbreviations: BAD-D, the final "D" of Belin/Ambrósio Enhanced Ectasia Display; bcIOP, intraocular pressure biomechanically corrected by the Corvis ST; CBI, corvis biomechanical index; CDVA, corrected distance visual acuity; DALK, deep anterior lamellar keratoplasty; PKP, penetrating keratoplasty; SE spherical equivalent; TBI, tomographic biomechanical index.

CORNEA TOMOGRAPHIC OUTCOMES

All preoperative and postoperative tomographic parameters analysed were abnormal for both PKP- and DALK-treated eyes, compared to the control group (Table 5). There were no differences in preoperative and postoperative tomographic parameters when comparing PKP and DALK-treated eyes (Table 5). Fig. 2F represents the mean postoperative BAD-D by subgroups.

For both PKP- and DALK-treated eyes, compared to preoperative values, there were improvements on: BAD-D (p=0.012 and p<0.001, respectively), PIavg (p=0.005 and p<0.001, respectively), ARTmax (both with p<0.001), Kmax (both with p<0.001), ISV (both with p<0.001), IVA (p=0.037 and p=0.001, respectively) and IHD (p=0.004 and p<0.001, respectively). Only IHA was similar for both subgroups (p=0.133 and p=0.084, respectively) compared to preoperative values.

The PKP- and DALK-treated eyes were classified in preoperative and postoperative according to the "ABCD keratoconus grading system". Preoperative A, B, and D grades were similar between PKP- and DALK-treated eyes (p=0.849, p=0.714 and p=0.320, respectively), and C grades were better in DALK-treated eyes (p=0.014) than in PKP-treated eyes. Postoperative A, B, and C grades were similar between PKP- and DALK-treated eyes (p=0.761, p=0.249, and p=0.954, respectively), and D grades were better in PKP-treated eyes (p=0.016) than in DALK-treated eyes.

Preoperative A, B, C and D grades and postoperative 2nd generation corneal biomechanical parameters were not correlated in PKP- and DALK-treated eyes (p>0.05 for all 11 parameters).

DISCUSSION

In advanced keratoconus, keratoplasty is an option to give a more regular optical surface and strengthen corneal biomechanics. The current study investigated the biomechanical behaviour and intraocular pressure differences

Table 5. Tomographic parameters.

Tomographic parameters	Group 1		Group 2	*p*-value		
(Mean +SD)	PKP (n=18)	DALK (n=34)	Control (n=52)	Control vs PKP	Control vs DALK	PKP vs DALK
Preoperative						
BAD-D	23.53±12.29	19.14±6.33	0.66±0.38	**0.001**	**<0.001**	0.360
PI.avg	6.06±3.98	4.17±1.49	0.97±0.09	**<0.001**	**<0.001**	0.381
ARTmax	59.90±38.07	71.16±30.54	469.02±45.10	**<0.001**	**<0.001**	0.365
Kmax	81.42±15.01	71.14±10.14	44.07±1.24	**<0.001**	**<0.001**	**0.021**
ISV	183.82±58.12	152.24±47.53	18.77±8.81	**<0.001**	**<0.001**	0.095
IVA	1.25±0.73	1.16±0.48	0.11±0.05	**<0.001**	**<0.001**	0.666
IHA	64.64±36.73	53.22±33.00	5.48±5.37	**<0.001**	**<0.001**	0.362
IHD	0.27±0.16	0.22±0.11	0.01±0.01	**<0.001**	**<0.001**	0.338
Postoperative						
BAD-D	5.82±2.52	6.88±4.07	0.66±0.38	**<0.001**	**<0.001**	0.437
PI.avg	1.49±1.10	1.79±1.66	0.97±0.09	**0.015**	**<0.001**	0.331
ARTmax	230.72±138.28	238.21±145.22	469.02±45.10	**<0.001**	**<0.001**	0.858
Kmax	56.89±5.32	59.01±4.57	44.07±1.24	**<0.001**	**<0.001**	0.139
ISV	97.06±71.12	81.73±23.67	18.77±8.81	**<0.001**	**<0.001**	0.256
IVA	1.06±1.27	0.70±0.37	0.11±0.05	**0.006**	**<0.001**	0.131
IHA	55.77±70.85	38.53±30.81	5.48±5.36	**0.008**	**<0.001**	0.227
IHD	0.10±0.10	0.11±0.07	0.01±0.01	**0.001**	**<0.001**	0.716

after PKP and DALK in advanced keratoconus eyes and compared them to those healthy corneas.

Regarding biomechanical behaviour, neither of the two keratoplasty techniques achieved the full restoration of corneal biomechanics to those of healthy corneas, despite the improvement in clinical and almost all tomographic parameters. This is also shown in previous studies and this may be due to the presence of a residual peripheral host corneal rim which is affected by the ectatic process.[10] In contrast, the scar tissue may also reduce the transfer of energy to the peripheral cornea and result in higher central corneal movement inwards when compared to the healthy corneal response.[11]

In our study, DALK-treated corneas were significantly different from healthy corneas for a greater number of both 1st and 2nd generation biomechanical parameters than PKP-treated corneas. However, when comparing directly PKP and DALK eyes, there were no significant differences in biomechanical behaviour, which is against the theoretical advantage of DALK concerning the resistance after blunt ocular trauma.[5,12] Moreover, there are reports of in vivo animal studies that fail to show any significant biomechanical weakening following a circular Descemet's incision.[13] This fact suggests that Descemet's membrane doesn't influence the biomechanical properties in a normal cornea and therefore will not be a biomechanical advantage in DALK-treated eyes compared to PKP-treated eyes as previously suggested.[14,15] However, the possible differences in biomechanical restoration achieved by the two keratoplasty techniques could be too minor to detect with Corvis ST. It is thought that the contributions of the epithelium, Descemet's membrane, and endothelium are relatively weak; the contribution from Bowman's layer is still controversial, and the stroma is responsible for most of the corneal strength.[6,16] Although Ziaei *et al*[11] showed that PKP-treat corneas had a greater number of changed parameters from healthy corneas with Corvis ST, this study only compared 11 parameters of 1st generation and included patients with sutures not removed with low follow-up time. A recently published meta-analysis also reported better recovery of corneal biomechanical properties following DALK when compared PKP, but the analysis included only 2 parameters (the corneal hysteresis and corneal resistance factor) of Ocular Response Analyzer (ORA) (Reichert Ophthalmic Instruments, Buffalo, NY).[17] Instead of using the reflection of the infrared beam to monitor the deformation of the cornea like ORA, Corvis ST uses an ultra-high-speed Scheimpflug camera that takes 140 horizontal 8 mm frames throughout 33 ms. This approach allows a more detailed evaluation of the deformation process.[6] The meta-analysis also highlighted the less value of ORA in assessing biomechanical changes after ablative and incisional corneal surgeries and the need to complement studies with Corvis ST.[17]

Within different DALK techniques, we did not find significant differences in the biomechanical properties of the cornea between manual lamellar dissection and big bubble techniques. Thus, manual lamellar dissection was not a disadvantage considering this point. Previous reports with ORA have also failed to show these differences, even with fewer parameters analyzed.[18,19]

Concerning the analysis of postoperative IOP assessed by different methods (Goldmann applanation tonometer;

Corvis ST noncontact tonometer; and the Pentacam corrected system), mean values were similar between PKP and DALK subgroups, which does not support the hypothesis of an increased risk of ocular hypertension for PKP eyes.[5] Indeed, in our study, for PKP eyes we found moderate and strong negative correlations between the duration of follow-up and some IOPs measured by different methods, and for DALK eyes, one weak significant positive correlation. However, care must be taken when analyzing these correlations with the duration of follow-up, as there are only 2 DALK-treated eyes with more than 6 years of follow-up and 3 PKP-treated eyes with more than 10 years of follow-up in this study. At these times, we see the greatest deviations of the IOPs in Fig. 1.

One of the strengths of this study is the exclusion of patients with corneal sutures not removed which helps to understand the true behaviour of the cornea after transplantation, unlike some studies.[11] Our study is the first study comparing biomechanical behaviour in this group of patients without the presence of corneal sutures, using Corvis ST. Another strong point was the greater time between surgery and biomechanical assessment, which allowed study in the long-term, which was not assessed in other previous studies.[11,15,19,20] We think that this point is the major limitation of other studies, with lower follow-up, such as 2 months.[15] This also was mentioned as an important factor not controlled in a previous recent meta-analysis, showing better results for PKP-treated eyes after 1 year of follow-up compared to after 6 months, not verified for DALK-treated eyes, and revealing the need for more studies.[17] A shorter period of steroid treatment in the postoperative period compared to PKP, may explain the shorter time required to complete corneal remodelling in DALK and a possible advantage reported previously. We found a negative correlation between the time of follow-up and TBI for PKP-treated eyes. TBI is a new index combining tomographic and biomechanical data.[6] This means that remodelling, towards strengthening, occurs over time, even after the 1st year of follow-up. The absence of this correlation in DALK-treated eyes may mean earlier achievement of biomechanical stability.

However, this study has some limitations. A small number of patients in the study group were included and preoperative corneal biomechanical assessment was not performed, which is shared with other studies.[11,19] Donor age was not taken into account. Although the inclusion of multiple surgeons in performing the keratoplasty procedure, the type and number of sutures were similar between groups. It can also be postulated that patients undergoing PKP had more advanced keratoconus compared to patients undergoing DALK and therefore influenced host tissue viscoelastic properties. However, our subgroups were similar regarding demographic and preoperative clinical and tomographic parameters. Only Kmax and C grades accordingly to the ABCD grading system were worse in PKP-treated eyes than in DALK-treated eyes. Lastly, although the mean follow-up time was statistically similar between PKP- and DALK-treated eyes in this study, a prospective design would allow for better comparison across similar follow-up intervals and better assessment of changes over time.

This is a pioneer study as it is the first to document the long-term biomechanical properties using Corvis ST and IOP analysis with different methods in this group of patients, but further research will be needed. Prospective and longitudinal studies are needed to validate these changes, determine how they change over time and if they can be used as a surgical outcome in monitoring.

In conclusion, neither of the two keratoplasty techniques fully restored corneal biomechanics to those of healthy corneas. When comparing directly PKP and DALK-treated eyes, there were no significant differences in biomechanical behaviour and in postoperative IOPs.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

AM and CC: Responsible for gathering the data, presenting the results, and creating the manuscript;

NG: Responsible for performing complementary exams.

MMN, MG and LO: Supervised this project and contributed with their expertise to its conclusion.

All authors read and approved the final manuscript.

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