CLINICAL HISTORY METHOD VERSUS CORNEAL TOMOGRAPHERS IN ESTIMATING CORNEAL POWER AFTER PHOTOREFRACTIVE SURGERY

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The authors declare that they have adhered to the tenets of the Declaration of Helsinki for research in human beings.

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SUMMARY

Aims: To investigate the concordance between the corneal power determined by various approaches with two tomographers (MS-39® and Galilei G6®) and the clinical history method (CHM) in patients undergoing photorefractive surgery with excimer laser for myopic errors.

Material and Methods: Prospective cohort study. Patients undergoing keratorefractive surgery, and having pre- and postoperative keratometries, and tomographies, were included.

Results: In 90 eyes, the differences in the power estimated by the CHM and the one determined by four approaches with the corneal tomographers, which included measurements of the posterior cornea, did not show statistically significant differences in their averages. However, the 95% limits of agreement were very wide. After obtaining regression formulas to adjust the values of these four variables, the results of the agreement analysis were similar.

Conclusion: Although certain values either directly determined or derived from measurements with the Galilei® and MS-39®corneal tomographers, approximated the estimated value of postoperative corneal power according to the CHM, due to the amplitude of their limits of agreement, these calculations must be taken with care, because they may not be accurate in a given eye.

Key words: corneal power; corneal tomography; clinical history method; refractive surgery

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INTRODUCTION

Excimer laser refractive surgery is used to correct refractive errors by modifying the corneal curvature. A disadvantage of this procedure is that, many years later, when these patients require cataract surgery, the calculation of the power of the intraocular lens can be imprecise, due, in part, to the difficulty of determining the true corneal power after photorefractive surgery. This stems from changes generated in the anterior surface of the cornea, rendering the keratometric index unsuitable [1–3]. To address this issue, numerous methods have been proposed, with the clinical history method (CHM), introduced by Holladay in 1989, standing as the earliest among them [4]. The CHM boasts a robust theoretical foundation, leading it to still be considered the gold standard for determining real corneal power after refractive surgery (Holladay JT. Personal communication. July 4/2023) [4,5]. However, this method has a critical drawback, as it heavily relies on the availability and accuracy of preoperative data prior to corneal refractive surgery. In addition, it requires a postoperative refraction that must have been obtained before cataract development, but not too long before its appearance. This precaution is necessary to avoid potential changes in the cornea, such as epithelium remodeling leading to regression, or, on the other hand, progression of refractive error, possibly caused by axial length elongation. In real-life scenarios, obtaining all this information becomes challenging, as there is often a timespan of several decades between photorefractive surgery and cataract surgery in these patients. Consequently, this lack of information significantly limits the clinical usefulness of CHM [4,5].

New alternatives that do not require preoperative data have been explored to determine the true corneal power after refractive surgery, some of them based on direct measurements performed by corneal tomographers. These devices have an optical light slit (in the visible or infrared spectrum) and many are combined with a Placido disk, which allows them to measure the radius of curvature of both the anterior and posterior corneal surfaces [2,6–10].

The objective of this study was to investigate, in patients undergoing photorefractive surgery with excimer laser, the concordance between the corneal power determined by various approaches, by the corneal tomographers MS-39® (CSO, Florence, Italy) and Galilei G6® (Ziemer, Port, Switzerland) with respect to that determined by the traditional CHM [4]. Values derived from these direct measurements, including some using formulas obtained by linear regression, were also analyzed. A variant of the CHM, the modified CHM (mCHM) used by the Amaris Schwind® laser program (Schwind, Kleinostheim, Germany) was also studied.

MATERIAL AND METHODS

In 178 eyes (90 patients), a correlation was found between both eyes with the outcome variables, so only one eye of each patient was randomly selected for the analysis, and thus the final sample in this prospective study was 90 eyes of 90 patients. The mean age of the patients was 31.0 ±12.2 years. 28 patients (31.1%) were male. 39 eyes (43.3%) were right.

All the subjects underwent excimer laser photorefractive surgery to correct myopia or myopic astigmatism (LASIK, PRK, TransPRK) from November 2020 to February 2022. The patients included were older than 18 years, without any signs of corneal ectasia, according to the corneal tomographic findings with both MS-39 and Galilei G6® [11,12]. Those who presented some complication during surgery, in whom some retinal comorbidity was identified, or who for some reason did not return for a postoperative visit, were excluded. The study was approved by the institutional Ethics Committee and adhered to the principles of the Declaration of Helsinki.

Surgical technique

53 patients underwent LASIK surgery, 19 PRK, and 18 TransPRK. All procedures were performed by 4 surgeons trained in refractive surgery, using the excimer laser Amaris Schwind® with a repetition rate of 1050 Hz. The optimized ablation option (Aberration Free®) was used in all cases. The diameter of the optic zone was between 6.2 and 7.0 mm for LASIK, between 6.5 and 7.0 mm for PRK, and between 6.9 and 7.2 mm for single-step transepithelial photorefractive keratectomy (TransPRK) [13]. Topical anesthesia was administered for the procedure, after which, in PRK, the corneal epithelium was manually removed with a spatula and photoablation was performed on Bowman's membrane and the anterior stroma. In the case of TransPRK, the epithelium, Bowman's membrane and stroma were ablated in a single step, with the excimer laser. In LASIK patients, a flap approximately 110 µm thick was created with a microkeratome (Hansatome®, Bausch & Lomb Surgical Inc., Bridgewater, NJ, USA), which was then lifted to perform photoablation directly on the stroma.

Pre- and postoperative exams

Preoperatively and postoperatively (at least 1 month and up to 12 months after surgery for LASIK patients, and at least 3 months and up to 12 months later for PRK and TransPRK patients), uncorrected distance visual acuity, corrected distance visual acuity, slit lamp biomicroscopy, subjective refraction, manual keratometry (OM-4®, Topcon, Tokyo, Japan) and corneal tomographies with Galilei G6® and MS-39® devices, were performed.

Determination of postoperative corneal power

Corneal power was determined using the CHM (considered the gold standard) and compared with the corneal power obtained in various approaches, including one always determined in clinical routine examination (manual keratometry) and several alternatives with the Galilei-G6® and MS-39® tomographers. Additional values derived from the direct measurements with these devices, including some using formulas obtained by linear regression, were also analyzed. Similar comparisons were also made for the mCHM, as incorporated within the Schwind CAM program of the Amaris® excimer laser.

Each method is briefly explained below.

- **Clinical History Method (CHM)**

This method, applied to eyes operated on for myopic errors, consists of subtracting from the preoperative keratometric power, the change induced in the refraction (that is, postoperative minus preoperative spherical equivalent, both already adjusted to the corneal vertex), to thus determine the real flattening generated to the cornea by the surgical procedure. [4] The method is summed up in the following formula:

Kc = Kpre - RC,

where Kc = postoperative corrected keratometry by the CHM, Kpre = preoperative keratometry, RC = spherical equivalent refractive change, adjusted to the corneal vertex.

To correct the refraction for vertex distance, the following formula was used:

Rc = Rg / [1 - (g x Rg)],

where Rc = refraction corrected to the plane of the cornea, Rg = refraction measured in the plane of the glasses, g = distance to the corneal vertex, corresponding to the measurement between the cornea and the back surface of a corrective lens (generally 12 mm = 0.012 m).

Clinical History Method modified by Schwind CAM (mCHM)

This modification of the original method is based on the principles proposed by Holladay and Mandell, among others, taking into account that the modification of photorefractive surgery occurs almost exclusively on the anterior surface of the cornea, and not on its posterior surface [14–16]. The modifications included in the Schwind mCHM not only took into account the exclusive refractive change of the anterior surface of the cornea, but also the amount of ablated tissue, and this calculation base was later refined considering the lensmaker equation [17–19].

Galilei® Tomographer

The parameters obtained from the Galilei® tomographer to determine the corneal power were the following [12]:

- Average Simulated Keratometry (SimK): Average of keratometry corneal curvature over central area of diameter around 3 mm, using the keratometric index (1.3375). The considered zone has a variable amplitude depending on the curvature of the measured cornea (it is slightly larger in flatter corneas).
- Total Corneal Power (TCP): total corneal power, considering both anterior and posterior corneal surfaces, calculated by ray tracing.
- Mean TCP: average total corneal power over an annulus of central and peripheral radii of 0.5 mm and 2.0 mm, respectively.
- Central TCP: average total corneal power over a central area of a radius of 2.0 mm.
- Mid TCP: average total corneal power over an annulus of central and peripheral radii of 2.0 mm and 3.5 mm, respectively.

In addition, a parameter called Postoperative Galilei average was analyzed, calculated by obtaining the mean of average SimK and Mid TCP.

Finally, linear regression formulas were calculated to predict the value estimated by the CHM, from those measurements that included information from both the anterior and posterior surfaces of the cornea, and which initially did not show a statistically significant difference when comparing their average to the estimated value with the CHM, as well as the regression formula to predict the value estimated by the CHM from the Postoperative Galilei average. [4]

MS-39® Tomographer

The parameters obtained from the MS-39® tomographer to determine the corneal power were the following [11]:

- Average SimK: SimK represents the simulation of the readings that would be obtained with a keratometer, (i.e. the mean sagittal curvature from the 4th to the 8th Placido ring) using the keratometric index. The considered zone has a variable amplitude depending on the curvature of the measured cornea (it is slightly larger in flatter corneas).
- Meridian 3 mm (3 mm K): Mean curvature for the main meridians in the 3 mm zone of the anterior surface of the cornea.
- Mean Pupil Power 3 mm (MPP 3 mm): The equivalent corneal power calculated from the corneal wavefront related to an entrance pupil located in the position of the patient's pupil, for a diameter of 3 mm. Both the measured anterior and posterior corneal surfaces are taken into account and ray tracing is performed.
- MPP 5.5 mm: MPP determined for a diameter of 5.5 mm.

In addition, a parameter called Postoperative MS-39 average was analyzed, calculated by obtaining the mean of average SimK and MPP 3 mm.

Finally, linear regression formulas were calculated to predict the value estimated by the CHM, from those measurements that included information from both the anterior and posterior sides of the cornea, and which did not initially show a statistically significant difference from their average with regard to the estimated value with the CHM, as well as the regression formula to predict the value estimated by the CHM from the Postoperative MS-39 average [4].

Statistical analysis

The correlation between the two eyes of each patient was evaluated, using the Pearson correlation coefficient, obtaining a value greater than 0.70, for which it was decided to randomly select one eye per patient for this study.

The data were analyzed with the software R version 4.1.1. A descriptive analysis was performed on the qualitative variables with relative and absolute frequencies, and for the quantitative variables, measures of central tendency and dispersion were used. For quantitative variables, the Shapiro Francia Wilk normality test was performed.

To determine the difference in means between the various methods for determining corneal power, a repeated measures ANOVA was used, and the Bonferroni test was applied as a post hoc test (multiple comparison test). The Bland-Altman graphical method was used to establish the agreement between the methods, and the absolute intraclass correlation coefficient (ICC) was applied to determine the agreement between formulas. It is considered that an ICC > 0.90 implies excellent relative reliability; an ICC between 0.75 and 0.90 implies good reliability; an ICC between 0.50 and 0.75, implies moderate reliability; and an ICC < 0.50, implies poor reliability [20,21].

After estimating postoperative corneal power with the CHM, the difference from the actually measured postoperative keratometry was quantified and a cor-

Table 1. Comparison of other methods versus the Clinical History Method

	Mean ±SD (D)	ΔMean ±SD (D) (versus CHM)	P -value *	95% LoA (Lower; Upper) versus CHM (D)	ICC (vs. CHM)**
CHM	40.3 ±2.3				
mCHM (Schwind CAM)	40.8 ±2.1	-0.46 ±0.36	**< 0.001**	-1.17; 0.25	0.96
Pop. Mean Keratometry	40.6 ±2.1	-0.29 ±0.62	**0.001**	-1.51; 0.93	0.95
Pop. Ave. SimK (Galilei)	40.5 ±2.2	-0.16 ±0.61	> 0.999	-1.36; 1.04	0.96
Pop. Mean TCP (Galilei)	38.9 ±2.3	1.44 ±0.69	**< 0.001**	0.07; 2.80	0.80
Pop. Central TCP (Galilei)	38.8 ±2.4	1.48 ±0.68	**< 0.001**	0.14; 2.81	0.79
Pop. Mid TCP (Galilei)	40.1 ±2.1	0.18 ±0.88	> 0.999	-1.53; 1.91	0.91
Pop. Ave. SimK (MS39)	40.8 ±2.0	-0.46 ±0.65	**< 0.001**	-1.74; 0.82	0.99
Pop. 3mm K average (MS39)	40.7 ±2.2	-0.36 ±0.58	**< 0.001**	-1.51; 0.77	0.95
Pop. MPP 3.0mm (MS39)	39.6 ±2.4	0.74 ±0.58	**< 0.001**	-0.40; 1.88	0.92
Pop. MPP 5.5mm (MS39)	40.4 ±2.2	-0.06 ±0.68	> 0.999	-1.39; 1.26	0.95
Pop. Galilei average	40.3 ±2.1	0.01 ±0.71	> 0.999	-1.38;1.41	0.94
Pop. MS39 average	40.2 ±2.2	0.13 ±0.57	> 0.999	-0.98; 1.26	0.96

*D – Diopters; * P-values calculated using repeated measures ANOVA for the difference against CHM. Statistically significant values are indicated in bold; **It is considered that an ICC > 0.90 implies excellent relative reliability; an ICC between 0.75 and 0.90 implies good reliability; an ICC between 0.50 and 0.75, implies moderate reliability; and an ICC < 0.50, implies poor reliability [18,19]; LoA – limit of agreement, ICC – intraclass correlation coefficient, Pop. – postoperative, CHM – Clinical History Method, mCHM – Modified Clinical History Method. SimK – Average Simulated Keratometry, TCP –Total Corneal Power, MPP – Mean Pupil Power, K – Keratometry*

Table 2. Comparison of other methods versus the modified Clinical History Method (Schwind CAM)

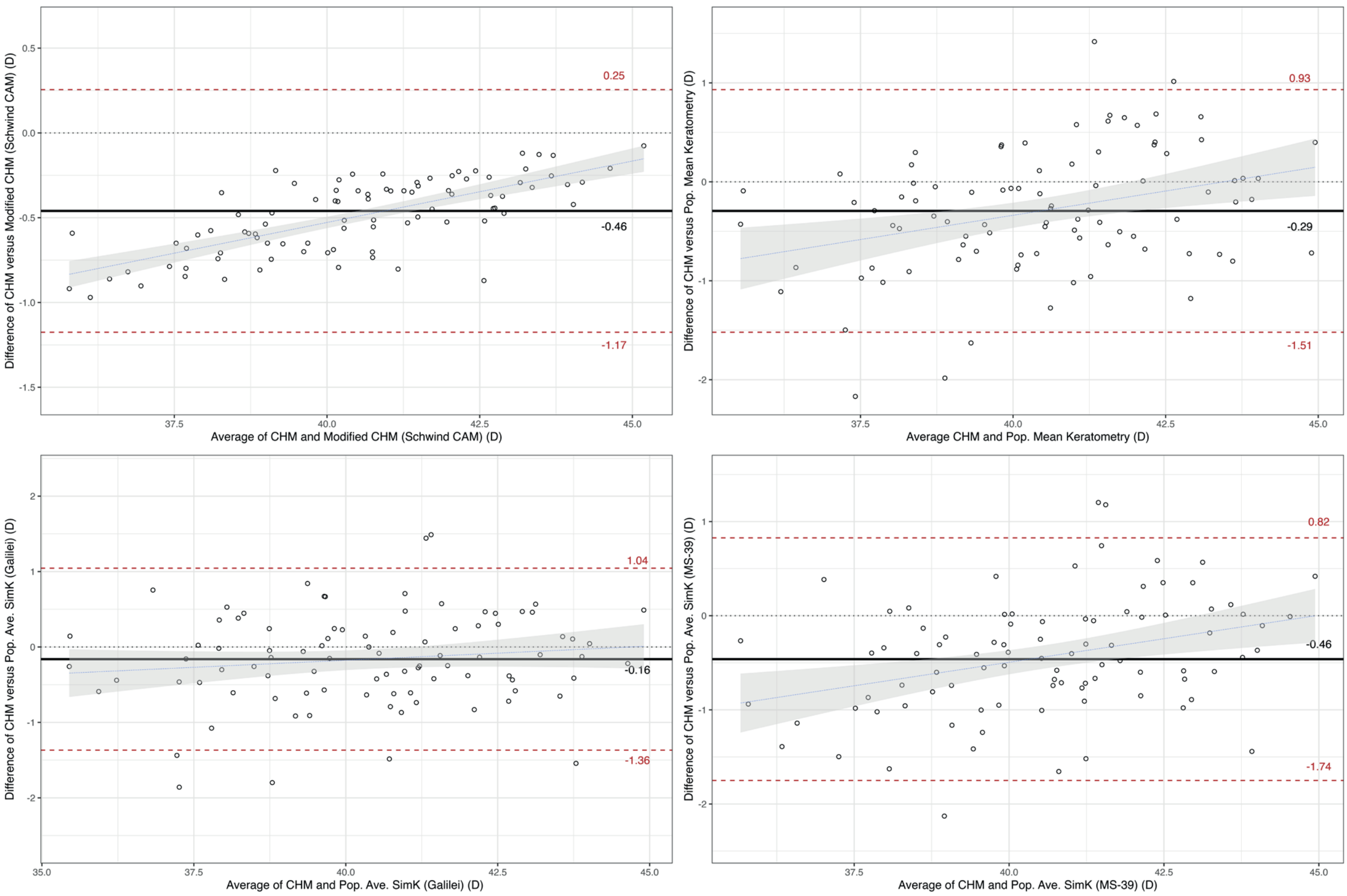
	Mean ±SD (D)	Δ Mean ±SD (versus Modified mCHM) (D)	P -value *	95% LoA (Lower; Upper) versus mCHM (D)	ICC (versus mCHM)**
mCHM (Schwind CAM)	40.8 ±2.1				
CHM	40.3 ±2.3	0.46 ±0.36	**< 0.001**	-0.25; 1.17	0.96
Pop. Mean Keratometry	40.6 ±2.1	0.16 ±0.59	> 0.999	-0.99; 1.32	0.94
Pop. Ave. SimK (Galilei)	40.5 ±2.2	0.29 ±0.61	**< 0.001**	-0.90; 1.50	0.95
Pop. Mean TCP (Galilei)	38.9 ±2.3	1.90 ±0.70	**< 0.001**	0.40; 3.39	0.69
Pop. Central TCP (Galilei)	38.8 ±2.4	1.94 ±0.74	**< 0.001**	0.47; 3.40	0.68
Pop. Mid TCP (Galilei)	40.1 ±2.1	0.64 ±0.85	< 0.001	-1.01; 2.31	0.87
Pop. Ave. SimK (MS39)	40.8 ±2.0	-0.001 ±0.61	> 0.999	-1.19; 1.19	0.95
Pop. 3mm K average (MS39)	40.7 ±2.2	0.09 ±0.59	> 0.999	-1.08; 1.26	0.86
Pop. MPP 3.0mm (MS39)	39.6 ±2.4	1.20 ±0.65	**< 0.001**	-0.09; 2.49	0.83
Pop. MPP 5.5mm (MS39)	40.4 ±2.2	0.3 9±0.70	**< 0.001**	-0.98; 1.77	0.93
Pop. Galilei average	40.3 ±2.1	0.47 ±0.69	**< 0.001**	-0.88; 1.83	0.92
Pop. MS39 average	40.2 ±2.2	0.59 ±0.58	< 0.001	-0.55; 1.75	0.92

*D – Diopters; * P-values calculated using repeated measures ANOVA for the difference against mCHM. Statistically significant values are indicated in bold; **It is considered that an ICC > 0.90 implies excellent relative reliability; an ICC between 0.75 and 0.90 implies good reliability; an ICC between 0.50 and 0.75, implies moderate reliability; and an ICC < 0.50, implies poor reliability [18,19]; LoA – limit of agreement, ICC – intraclass correlation coefficient, Pop. – postoperative, CHM – Clinical History Method, mCHM – Modified Clinical History Method. SimK – Average Simulated Keratometry, TCP –Total Corneal Power, MPP – Mean Pupil Power, K – Keratometry* relation was plotted against the preoperative spherical equivalent. A linear regression was also used to predict CHM estimated postoperative keratometry from the postoperatively determined corneal data from the tomographers. The entire data set was randomly shuffled and divided (computer-assisted process) into 2 subsets: a training subset with 80% of the full data set (72 eyes), and a validation subset with 20% of the data set (18 eyes). During the fitting of the model, 69 eyes were included to calculate the regression formula from the MPP MS-39 5.5 mm. The training dataset was used to derive the formulas of the above-mentioned linear regression, which were then tested on the validation dataset (18 eyes). In the frame of validation, a paired t - Student test was performed to determine the mean difference between the expected value of the CHM and its prediction obtained from the linear regression, as well as an analysis of the agreement with the Bland-Altman plot. For this study, we established in advance, according to the judgment of the two participating researchers, experts in refractive surgery (AT and VG), that the limits of maximum clinically acceptable differences of a given method compared to CHM would be +/-0.50 D (i.e. a 95% limit of agreement on the Bland Altman plot of maximum 1.00 D of amplitude). An alpha of 0.05 was considered as statistical significance.

Since one of the most commonly used methods, at least in our country, to determine corneal power in a clinical setting is still manual keratometry, the correlation between the difference of the mean manual keratometry measured postoperatively minus the corneal power determined by the CHM, and the magnitude of the preoperative spherical equivalent, was analyzed.

RESULTS

The differences between the CHM-derived postoperative corneal power and all the other approaches did not show a statistically significant difference among the



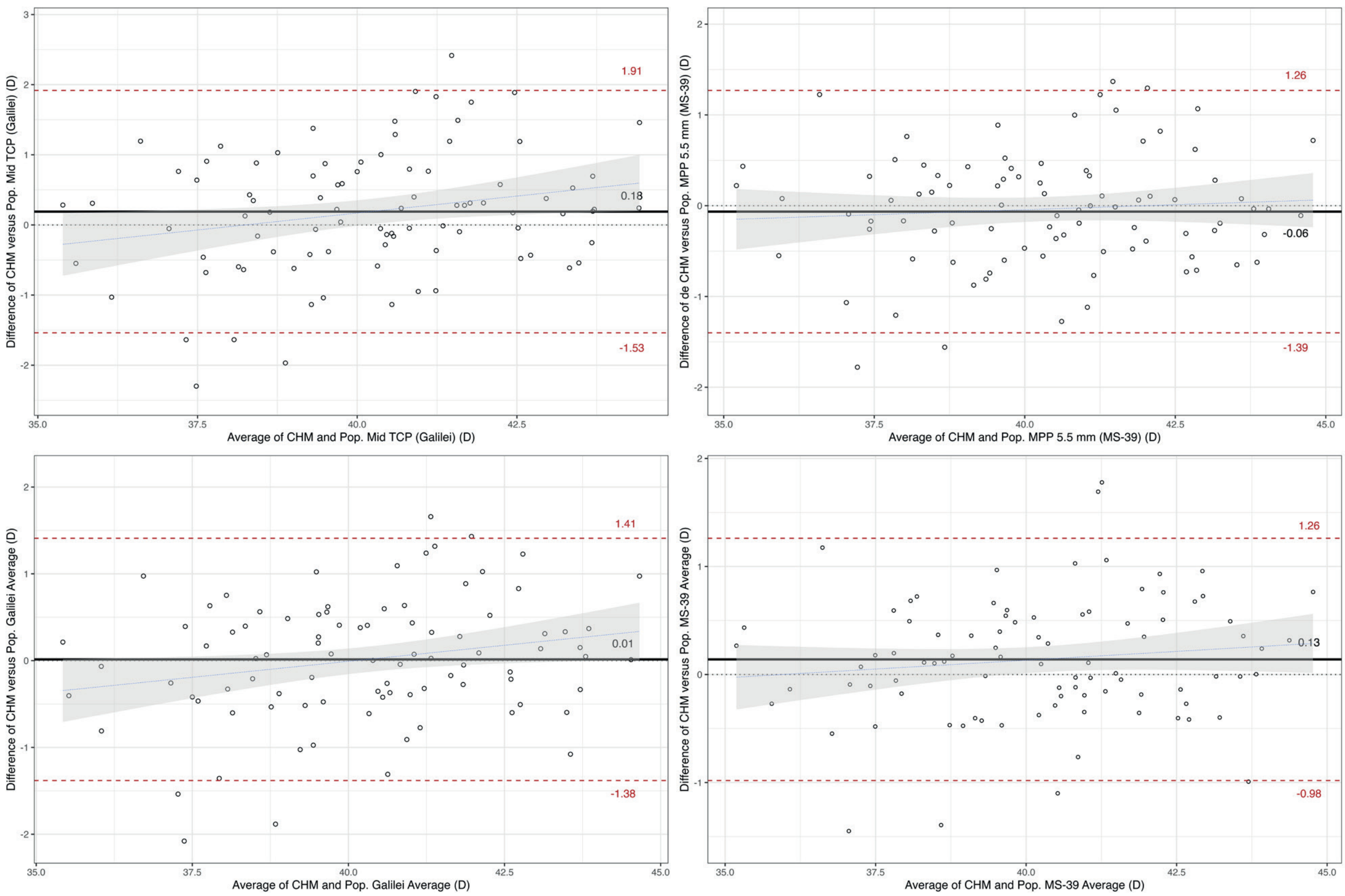
Graph 1. Bland-Altman plots comparing the estimated postoperative corneal power by CHM versus mCHM (top left), CHM versus Postoperative (Pop.) mean keratometry (top right), CHM versus Pop. Average SimK (Galilei) (bottom left), and CHM versus Pop. Average SimK (MS-39) (bottom right). The solid central horizontal black lines indicate the average bias, i.e. the average of the differences between the two methods. The mean differences in all the comparisons were negative, i.e. CHM method estimated values were lower in average than all the other three approaches, but the difference did not reach statistical significance with the SimK Galilei. The red dashed lines indicate the 95% limits of agreement of the differences (all of them with a range wider than 1.00 D). The blue dashed lines denote the trend of the differences between the compared methods, and the gray areas indicate the confidence intervals of the trends

CHM – clinical history method, mCHM – modified clinical history method (Schwind), SimK – Simulated keratometry, D – Diopters, Pop – postoperative three surgical techniques (LASIK, PRK and TransPRK). Therefore, the analysis was performed by combining all the eyes undergoing keratorefractive surgery with excimer laser.

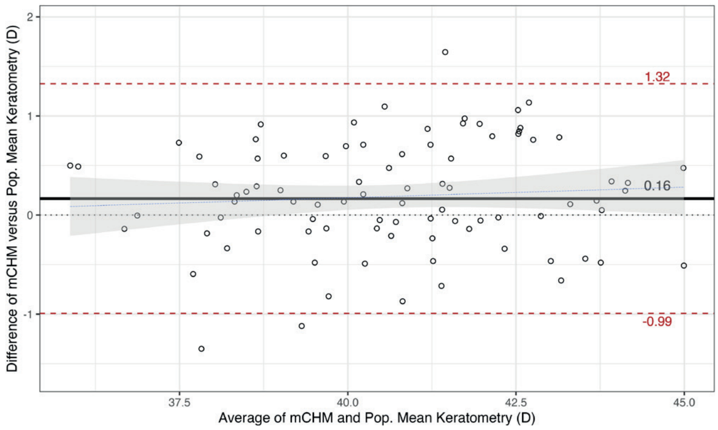
Table 1 shows the results of the comparison of corneal power determination with CHM, versus all the other approaches. The CHM-calculated corneal power was on average flatter, with statistically significant difference, than the mean manual keratometry and SimK from Galilei, but it was on average steeper, with statistically significant difference, than some of the ray-traced measurements for total corneal power with the two corneal tomographers (Mean TCP and Central TCP from Galilei, and Postoperative MPP 3.0 mm from MS-39). Only 5 of the methods did not show statistically significant difference against CHM, namely: Postoperative average value SimK (Galilei); Postoperative Mid TCP (Galilei); Postoperative MPP 5.5 mm (MS-39); Postoperative Galilei average; and Postoperative MS-39 average.

Graph 1 shows the Bland-Altman plots of the comparison between CHM and mCHM, and also between CHM and the most frequently used measurement for determining central corneal power in our country, i.e. mean manual keratometry, and SimK from both Galilei and MS-39 tomographers. In Graph 2 comparison with 4 of the other 8 alternatives for determining postoperative corneal power is shown. Those with non-statistically significant differences in their average were included.

Table 2 shows the results of the comparison of the determination of corneal power with mCHM, versus all the other approaches. The corneal power calculated with mCHM was on average higher than that calculated with CHM, than that measured with the manual keratometer, although without reaching statistical significance with the latter. mCHM calculated postoperative corneal power was also steeper, with statistically significant difference, than those obtained with the measurements made with the two corneal tomographers, with the exception of the SimK and 3 mm K average from MS-39. The differences between mCHM and the other methods did not show statistical significance, except with three of them: with postoperative mean manual keratometry; with Aver. SimK (MS-39), and with the Postoperative 3 mm K aver-



Graph 2. Bland-Altman plots comparing the estimated postoperative corneal power by CHM versus Postoperative (Pop.) Mid TCP Galilei (top left), versus Pop. MPP 5.5 mm MS-39 (top right), versus Pop. Galilei average (bottom left) and versus Pop. MS-39 average (bottom right).
The solid central horizontal black lines indicate the average bias, i.e. the average of the differences between the two methods. The mean differences in all the comparisons were smaller than 0.18 D, and they did not reach statistical significance. The red dashed lines indicate the 95% limits of agreement of the differences (all of them with a range wider than 1.00 D). The blue dashed lines denote the trend of the differences between the compared methods, and the gray areas indicate the confidence intervals of the trends
CHM – clinical history method, TCP – Total Corneal Power, MPP – Mean Pupil Power, D – Diopters, Pop. – postoperative



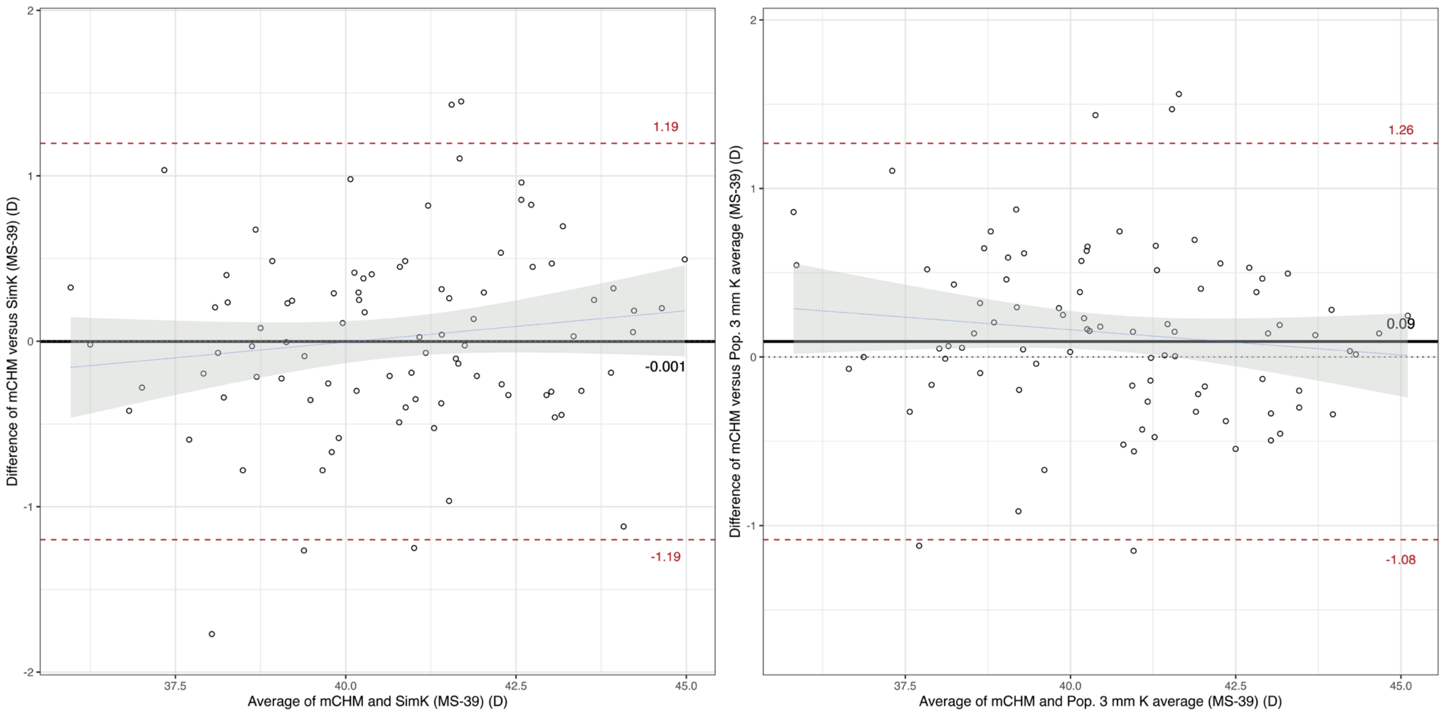
Graph 3. Bland-Altman plot comparing the estimated postoperative corneal power by mCHM versus postoperative mean keratometry. The mean difference was positive, i.e. mCHM method estimated values were higher in average than postoperative mean keratometry.
The solid central horizontal black line indicates the average bias, i.e. the average of the differences between the two methods. The mean differences in this comparison was small (0.16 D), and it did not reach statistical significance. The red dashed lines indicate the 95% limits of agreement of the differences (with a range wider than 1.00 D). The blue dashed line denotes the trend of the difference between the compared methods, and the gray area indicates the confidence intervals of the trend
mCHM – modified clinical history method (Schwind). D – Diopters, Pop. – postoperative

age (MS-39). Graphs 3 and 4 show the Bland-Altman plots of the comparison between mCHM with these three alternatives.

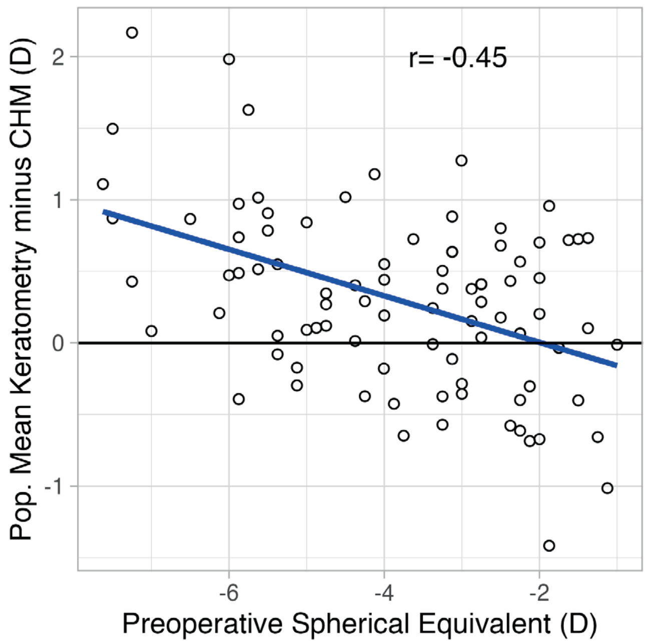
Although the mean difference between CHM and postoperative mean manual keratometry was -0.29 ±0.62 D, the manual keratometry being then, on average, higher than that determined by the CHM, in 26 eyes (28.9%) the postoperative manual keratometry was lower than that determined by the CHM, with differences of up to +1.42 D (Graph 1, top right plot).

The correlation between the difference of the mean manual keratometry measured postoperatively minus the corneal power determined by the CHM, and the magnitude of the preoperative spherical equivalent, is shown in Graph 5. A moderate, negative correlation was found, with a Pearson correlation coefficient (r) of -0.45 ($p < 0.001$). The correlation between these two parameters was analyzed, and not between CHM and others, because manual keratometry is nearly universally conducted during routine clinical examinations, at least in our country.

Using data from 80% of the total eyes (n = 72), except for the calculation involving MPP MS-39 5.5 mm, which utilized data from 69 eyes due to model fitting constraints, we developed linear regression formulas. These formulas aimed to predict values derived from the CHM based on postoperative tomographic approaches,



Graph 4. Bland-Altman plots comparing the estimated postoperative corneal power by mCHM versus Postoperative (Pop.) SimK MS-39 (left), and versus Pop. 3 mm MS-39 (right).
The solid central horizontal black lines indicate the average bias, i.e. the average of the differences between the two methods. The mean differences in these comparisons were small (-0.001 and 0.09 D), and they did not reach statistical significance. The red dashed lines indicate the 95% limits of agreement of the differences (with a range wider than 1.00 D). The blue dashed lines denote the trend of the differences between the compared methods, and the gray areas indicate the confidence intervals of the trends
mCHM – modified clinical history method (Schwind), SimK – Simulated keratometry, D – Diopters, Pop. – postoperative



Graph 5. A scatterplot showing the relationship between the difference mean postoperative manual keratometry/ estimated corneal power by CHM, and the preoperative spherical equivalent. The r was -0.45 ($p < 0.001$) and the blue line shows the trend of the correlation

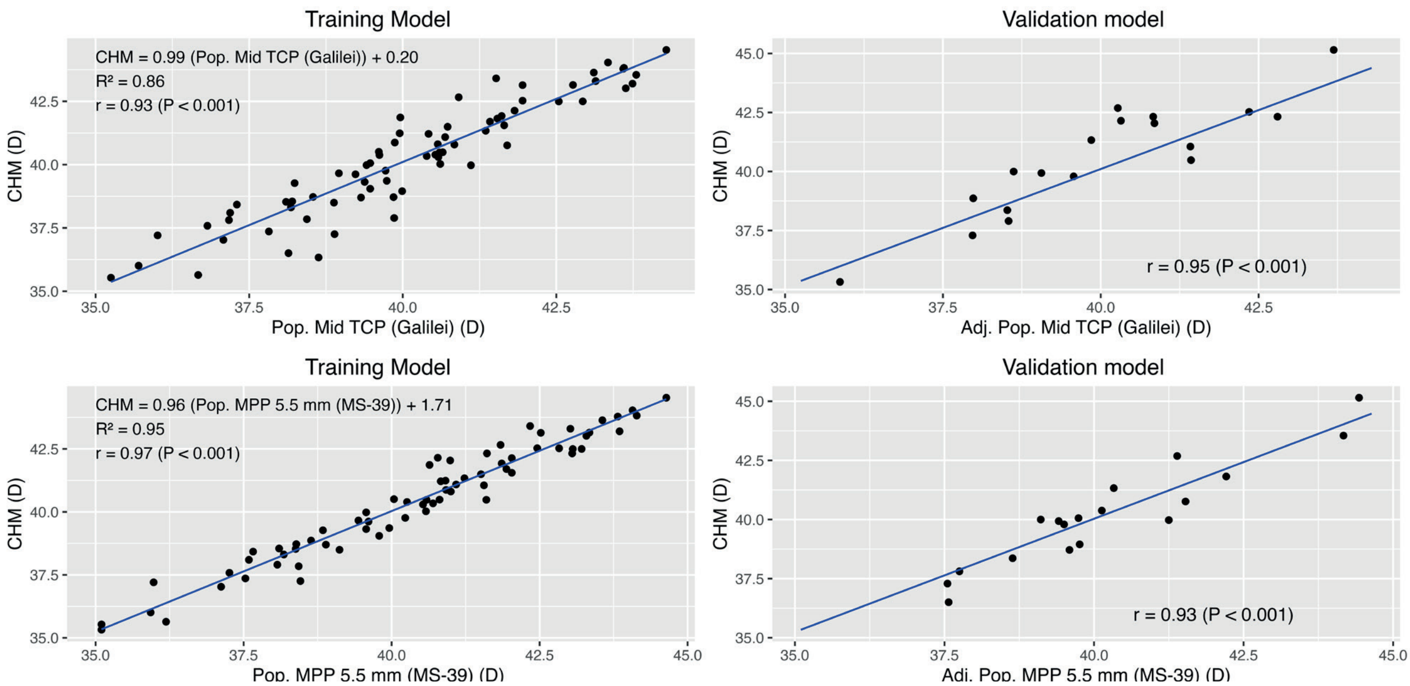
CHM – clinical history method, Pop. Mean Keratometry – mean postoperative manual keratometry, D – Diopters

meeting two criteria: they included measurements of the cornea's posterior surface, using either of the two tomographers, and they exhibited no statistically significant differences in average powers compared to the CHM-derived power. Subsequently, a validation of them was carried out with the remaining 20% of the eyes (n = 18). The results can be seen in Graphs 6 and 7, and are described below:

Prediction of CHM versus that based on postoperative mid TCP Galilei adjusted with the regression formula (Adj. Postoperative Mid TCP Galilei) (Graph 6, top plots): The results of the validation in the 18 eyes showed an average value of 40.10 D with 95% CI [39.20; 41.00], against an expected mean with the CHM of 40.52 D with 95% CI [39.42; 41.61], presenting a non-significant mean difference (-0.42, p = 0.09).

Prediction of CHM versus that based on postoperative MPP 5.5 MS-39 mm adjusted with the regression formula (Adj. Postoperative MPP 5.5 mm MS-39) (Graph 6, bottom plots): The results of the validation in the 18 eyes showed an average value of 39.86 D with 95% CI [38.84; 40.88], against an expected mean with the CHM of 40.00 D with 95% CI [39.03; 40.97], presenting a non-significant mean difference (-0.14, p = 0.43).

CHM prediction versus that based on postoperative Galilei average adjusted with the regression formula (Adj. Postoperative Galilei average) (Graph 7, top plots): The results of the validation in the 18 eyes showed an average value of 40.07 D with 95% CI [39.09; 41.04], against an expected mean with the CHM of 40.52 D with



Graph 6. Scatter diagram, regression line and regression equation relating estimations done by CHM versus postoperative (Pop.) Mid TCP Galilei, in the training model (top left), which showed an R2 = 0.86 and r = 0.93, and in the validation model using the regression formula (Adj. Pop. Mid TCP Galilei) (top right), r = 0.95; and estimations done by CHM versus postoperative MMP 5.5 mm MS-39, in the training model (bottom left), which showed an R2 = 0.95 and r = 0.97, and in the validation model using the regression formula (Adj. Pop. MMP 5.5 mm MS-39) (bottom right), r = 0.93

CHM – clinical history method, Pop. – postoperative, D – Diopters

95% CI [39.42; 41.61], presenting a significant mean difference (-0.45, p = 0.02).

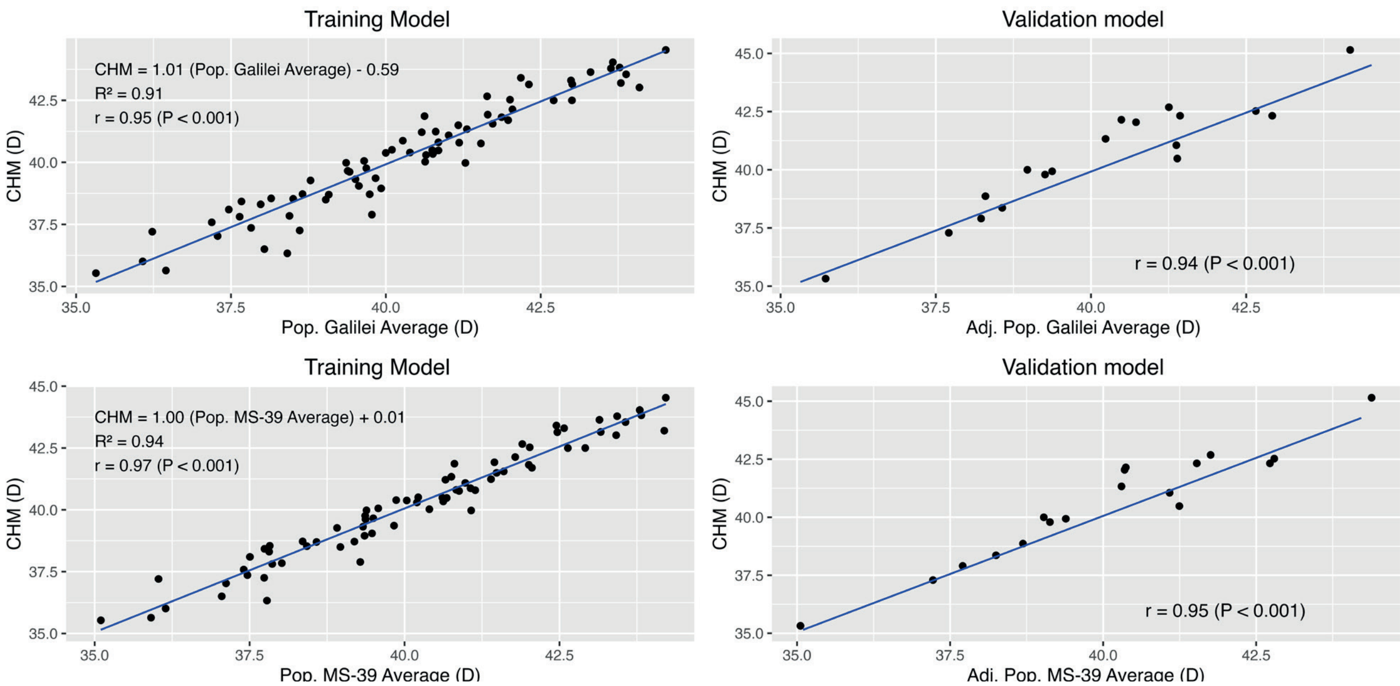
CHM prediction versus that based on postoperative MS-39 average adjusted with the regression formula (Adj. Postoperative MS-39 average) (Graph 7, bottom plots): The validation results in the 18 eyes showed a mean value of 40.11 D with 95% CI [39.06; 41.15], against an expected mean with the CHM of 40.52 D with 95% CI [39.42; 41.61], presenting a significant mean difference. (-0.41, p = 0.02).

The agreement was also analyzed, with the Bland-Altman plot, between the values obtained with these four approaches with the corneal tomographers, already adjusted with the respective regression formula (Graph 8).

DISCUSSION

There are three sources of error in calculating intraocular lens power after refractive surgery. The first is related to the inaccurate measurement of the radius of central curvature determined by keratometers or the SimK determined by corneal topographers [1,2]. These devices perform a paracentral measurement in a zone approximately 3.0 mm in diameter, assuming that each meridian within this zone is nearly spherical. However, they do not contemplate changes in asphericity generated by laser ablation, so they tend to overestimate power in corneas operated on for myopia, where the central area is flatter than the paracentral one, and underestimate it in corneas operated on for hyperopia, where the central area is steeper than the paracentral one. Another error factor is determined by the use of the keratometric index (1.3375), which does not work well in these patients because, by modifying the anterior corneal surface but not the posterior, the closeness with a standard relationship between both surfaces is lost, invalidating its use. And finally, the last source of error corresponds to the inaccurate prediction of the effective position of the lens due to the weight that keratometry has in this process within the third-generation biometric formulas (Hoffer Q, Holladay 1, SRK/T), which leads to an underestimation, in cases of myopic ablation, and an overestimation, in cases of hyperopic ablation, of the position where the intraocular lens will be located after cataract surgery [1,2].

In the present study, when comparing Holladay's CHM versus the mCHM with the Bland-Altman plot, a negative bias was found in general, indicating that the value estimated by the CHM was lower than that calculated by the modified method. However, in addition, a positive trend of the differences was observed as the magnitude of the estimated corneal power increased, that is, in the flatter corneas a greater difference was noted between the two approaches (Graph 1). Comparing the CHM with the average postoperative keratometry in the Bland-Altman plot, a negative bias of -0.29 D was found, as expected, but with very wide 95% limits of agreement (-1.51 to +0.93 D), which are outside the maximum determined by the authors as clinically non-significant. In addition, the regression of the differences showed

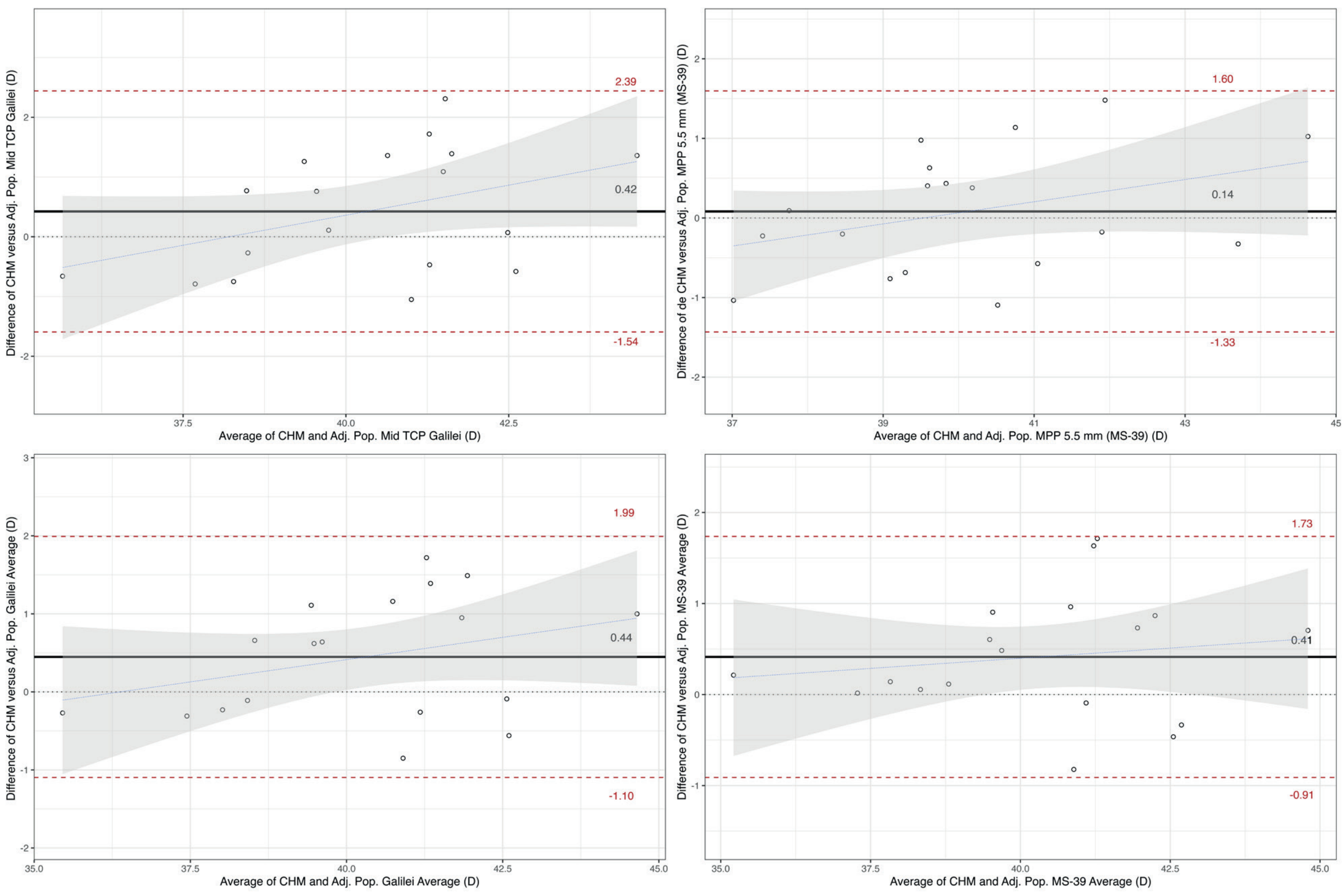


Graph 7. Scatter diagram, regression line and regression equation relating estimations done by CHM and Postoperative (Pop.) Galilei average, in the training model (top left), which showed an R2 = 0.91 and r = 0.95, and in the validation model using the regression formula (Adj. Pop. Galilei average) (top right), r = 0.94; and relating estimations done by CHM and postoperative MS-39 average, in the training model (bottom left), which showed an R 2 = 0.94 and r = 0.97, and in the validation model using the regression formula (Adj. Pop. MS-39 average), r = 0.95 (bottom right)
CHM – clinical history method, Pop. – postoperative, Adj. – Adjusted with the regression formula, D – Diopters

a positive trend that crossed zero, i.e. in the flatter corneas, the postoperative keratometry measurement overestimated corneal power more than in the steeper corneas (Graph 1). In addition, the differences between postoperative manual keratometry and CHM estimation did not consistently show an overestimation of corneal power by the first approach, since in almost one-third of the eyes (28.9%), postoperative manual keratometry after myopic ablation was flatter than that estimated by the CHM. This might imply that manual keratometry after refractive surgery could be less reliable. Additional studies are required in this regard. The correlation between the difference of the mean manual keratometry measured postoperatively minus the corneal power determined by the CHM, and the magnitude of the preoperative spherical equivalent, showed only a moderate, negative correlation (Pearson's correlation coefficient [r] of -0.45), with an evident dispersion of values along the spectrum of preoperative magnitude of the spherical equivalent (Graph 5).

On the other hand, upon examining the agreement between mCHM and postoperative mean keratometry, it was observed that the small bias, with a positive value of 0.16 D, did not reach statistical significance (Graph 3 and Table 2). This finding (a positive difference) diverges from theoretical expectations, which suggests that measured postoperative mean keratometry would overestimate the actual postoperative corneal power following a myopic excimer laser ablation. Consequently, the average difference between mCHM (assumed to reflect the true corneal power) and the mean postoperative corneal power should theoretically be negative.

The agreement between the power estimated by the CHM and four other methods that included measurements of both the anterior and posterior surfaces of the cornea, performed by a tomographer, and that did not show statistically significant differences in their average with respect to the estimated value by the CHM, was analyzed. In addition, similarly to what was done by Jaramillo et al. with the Sirius® device (CSO, Florence, Italy) [2], and, as we also observed in the present study with the MS-39® and the Galilei®, a tendency of SimK measurements to overestimate corneal pow-



Graph 8. Bland-Altman plots comparing the estimated postoperative corneal power by CHM versus Adj. Pop. Mid TCP Galilei (top left), versus Adj. Pop. MPP 5.5. mm MS-39 (top right), versus Adj. Pop. Galilei average (bottom left), and versus Adj. Pop. MS-39 average (bottom right). The solid central horizontal black lines indicate the average bias, i.e. the average of the differences between the two methods. The mean differences were 0.42 and 0.14 D for the comparisons of CHM with Adj. Pop. Mid TCP Galilei and Adj. Pop. MPP 5.5. mm MS-39, which did not reach statistical significance. The mean differences were 0.44 and 0.41 D for the comparisons of CHM with Adj. Pop. Galilei average and Adj. Pop. MS-39 average, which reached statistical significance. The red dashed lines indicate the 95% limits of agreement of the differences (all of them with a range wider than 1.00 D). The blue dashed lines denote the trend of the differences between the compared methods, and the gray areas indicate the confidence intervals of the trends
CHM – clinical history method, Pop. – postoperative, Adj. – Adjusted with the regression formula, D – Diopters

er, and an opposite tendency of total corneal power measurements, we coined a variable averaging these measurements for each of the devices (Postoperative Galilei average and Postoperative MS-39 average). For all these mentioned approaches, in the Bland-Altman plots the mean differences with respect to the CHM estimate were low (less than 0.18 D), and clinically insignificant, but they had very wide limits of agreement, almost all in both directions greater than 1.0 D, which limits its clinical utility, since they cannot really be considered equivalent to CHM when analyzing a given eye (Graph 2).

The construction of linear regression formulas was carried out, in order to explore the ability to predict the value estimated by the CHM by modifying with these formulas some of the parameters measured by the corneal tomographers (which included the evaluation of the anterior and posterior sides of the cornea) or the averages of two of these measurements from each device (Postoperative Galilei average and Postoperative MS-39 average). Although the values of R, which determines the strength of the relationship between the model and the dependent variables, were very high, 0.93 to 0.98, and the averages of the differences in the model validated with a group of eyes, were low and could considered clinically acceptable (0.14 to 0.45 D), again in the Bland-Altman plots the 95% limits of agreement were too wide, almost all exceeding 1.0 D in both directions, exceeding the tolerance established by the authors to be considered clinically non-significant.

Lekhanont et al., in their study where they compared postoperative measurements obtained after photorefractive surgery with the Orbscan IIz® and the Pentacam®, found statistically significant differences between almost all of them with respect to the CHM, and in which no significant difference was detected (Pentacam® EKR at 3.0 mm) the 95% limits of agreement on the Bland-Altman plot were excessively wide (greater than 2.0 D in each direction) [8]. Although our results were less disparate, and the differences we found were smaller, we agree with those researchers that, due to the dispersion of the data and excessive limits of agreement, which exceed the clinically acceptable range of agreement, any direct measurement of corneal power after photorefractive surgery should be taken with great caution.

This does not mean that it is not possible to use some of these measurements or their modifications as additional data for the determination of corneal power when required (particularly with the Galilei®: the mid TCP and the mid TCP adjusted with the regression formula, and of the MS-39® the MPP MS-39 5.5 mm and the MPP MS-39 5.5 mm adjusted with the regression formula, as well as the Galilei average and the MS-39 average). For example, when a patient with a history of photorefractive surgery is going to undergo cataract surgery, the corneal power determined by one of these approaches could be entered in a newer generation biometric formula (Barrett Universal II, Hill- RBF-3.0, Kane, Pearl DGS, etc.) to calculate the power of the intraocular lens to be implanted. However, these results must be correlated with other methods that have been described to determine this power after refractive surgery. It should also be kept in mind, however, that in these cases after photorefractive surgery, there will always be a greater chance of clinically significant residual error after cataract surgery (in two recent studies almost 30% of eyes ultimately had residual errors > 0.50 D) and this should be advised to patients [22–24].

One of the limitations of this study is that the sample size was relatively small. In addition, all the eyes were operated on to correct myopia or myopic astigmatism, with the Amaris Schwind® excimer laser, with the Aberration Free® profile, and therefore their results may not be directly extrapolated to eyes operated on with other platforms, or for hyperopic refractive errors or mixed astigmatism.

CONCLUSION

While some measurements from the Galilei® corneal tomographers (mid TCP) and MS-39® (MPP MS-39 5.5 mm), along with averages derived from various measurements using these devices, including those adjusted by linear regression formulas, closely approached the anticipated postoperative corneal power value based on the CHM, caution is warranted. This is attributed to the wide limits of agreement, suggesting that these calculations may lack precision for a specific eye.

Future studies, with larger samples and patients operated on with different equipment, are needed to compare several more methods of estimating corneal power after excimer laser surgery, to try to define the best approach to measuring or estimating it.

Compliance with Ethical Standards

This study was approved by the Institutional Review Board. An Informed Consent was obtained from participants.

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Conflict of interest

V.G., A.T., V.O., S.J.V., and S.E.S. certify that they have no financial interest or non-financial interest in the subject matter or materials discussed in this study.

S.A.M. is an employee of Schwind Eye-Tech Solutions.

R.M. is an employee of ROCOL, which is the distributor for Colombia of the excimer laser devices produced by Schwind Eye-Tech Solutions and the devices produced by CSO.

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