

VRF-G, a New Intraocular Lens Power Calculation Formula: A 13-Formulas Comparison Study

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Purpose: To compare the accuracy of a newly developed intraocular lens (IOL) power formula (VRF-G) with twelve existing formulas (Barret Universal II, EVO 2.0, Haigis, Hill-RBF 2.0, Hoffer Q, Holladay 1, Kane, Næser 2, PEARL-DGS, SRK/T, T2 and VRF).

Methods: Retrospective case series including 828 patients having uncomplicated cataract surgery with the implantation of a single IOL model (SN60WF). Using optimised constants, refraction prediction error of each formula was calculated for each eye. Subgroup analysis was performed based on the axial length (short ≤ 22.0 mm; medium >22.0 mm to <26.0 mm; long ≥ 26.0 mm). Main outcomes included mean prediction error (ME) mean (MAE) and median absolute error (MedAE), in diopters (D), and the percentage of eyes within ± 0.25 D, ± 0.50 D, ± 0.75 D and ± 1.00 D.

Results: Formulas absolute errors were statistically different among them ($p < 0.001$), with Kane having the lowest MAE of all formulas, followed by EVO 2.0 and VRF-G, which had the lowest MedAE. The Kane formula had the highest percentage of eyes within ± 0.25 D (47.0%) and ± 1.00 D (97.7%) and the VRF-G formula had the highest percentage of eyes within ± 0.50 D (79.5%). For all AL subgroups, Kane, EVO 2.0 and VRF-G formulas had the most accurate performances (lowest MAE).

Conclusion: New generation formulas may help us in achieving better refractive results, lowering the variance in accuracy in extreme eyes – Kane, EVO 2.0 and VRF-G formulas are promising candidates to fulfil that goal.

Keywords: intraocular lens power calculation formulas, biometry, cataract, phacoemulsification, formulas accuracy

Introduction

Cataract surgery is the most frequently performed refractive procedure worldwide. Achieving the desired target refractive outcome has become a key tenet in recent years as patients' refractive expectations continue to rise.

The most widely used intraocular lens (IOL) power formulas are vergence-based,¹ estimating the effective lens position (ELP) from 2 to 7 eye parameters (Barrett Universal II, Haigis, Hoffer Q, Holladay 1 and 2 and SRK/T), and traditionally classified by generation.

Recently, some modern formulas have appeared, using newer methodologies like artificial intelligence and larger number of preoperative eye parameters for prediction, which may be outside the proposed categories for formulas classification described in 2017.²

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Previous studies, using biometers based on partial coherence interferometry (PCI), swept-source optical coherence tomography (SS-OCT) or optical low-coherence interferometry (OLCR), revealed promising results with regard to some of these new formulas.³⁻⁹ Kane formula seems to be the most accurate formula available,⁴⁻⁶ with Barrett Universal II continuing to be a very reliable option (84% of eyes within 0.50D for Kane formula and 80% of for Barrett Universal II).^{3,4} Very recently, EVO (version 2.0) also showed good results, being one of the most accurate formulas using both SS-OCT and PCI based biometers to obtain biometric data.^{6,8}

However, we are unaware of comparative studies including EVO (version 2.0) and PEARL-DGS, using an OLCR biometer.

VRF formula is a vergence-based thin-lens formula using four variables: axial length, keratometry, anterior chamber depth, and horizontal corneal diameter. However, it does not consider parameters such as lens thickness and gender and published results did not position it as one of the most accurate formulas. VRF-G formula is a modification of VRF, based on theoretical optics with regression and ray-tracing components, operating eight variables for IOL power calculation to improve previsions accuracy (VRF parameters described above plus lens thickness, preoperative refraction, central corneal thickness, gender).

Our study aimed to assess and compare the overall accuracy of the classic, vergence-based formulas, with new-generation formulas, using measurements obtained from an OLCR biometer Lenstar LS900[®] (Haag-Streit AG, Köniz, Switzerland). Moreover, we want to report the first results obtained with a newly developed formula – VRF-G.

Materials and Methods

Patients

This was a retrospective review study that included consecutive patients who underwent cataract surgery and implantation of a monofocal in-the-bag IOL from 2017 to 2019 at Centro Hospitalar Universitário de Lisboa central, performed by six different surgeons. The study adhered to the principles of the Declaration of Helsinki and approval was obtained by Centro Hospitalar Unversitário de Lisboa Central Ethics Committee. Written informed consent was obtained from all patients regarding the use of their medical records for a scientific investigation.

Inclusion criteria were patient's age of at least 18 years-old and the implantation of an Acrysof IQ SN60WF (Alcon Laboratories, Geneva, Switzerland) IOL through a 2.75mm clear corneal incision. Exclusion criteria were: (1) incomplete biometry data; (2) postoperative corrected distance visual acuity inferior than 20/40; (3) keratometric astigmatism > 4D; (4) any intraoperative or postoperative complication; (5) previous intraocular or refractive surgery; (6) any corneal disease, as keratoconus or corneal scarring of any aetiology.

Based on Hoffer K.J. et al¹⁰ recommendations, only one eye per patient was included. If both eyes of the same patient fulfilled the above-mentioned criteria, the eye included was chosen randomly.

Preoperative optical biometry was performed with optical low-coherence reflectometry (OLCR) – Lenstar LS-900[®] (Haag-Streit AG, Köniz, Switzerland), obtaining the following data for each patient: axial length (AL), anterior chamber depth (ACD), central corneal thickness (CT), keratometry (K), lens thickness (LT) and horizontal corneal diameter (HCD). The keratometric index used was 1.3375. Postoperative manifest refraction was assessed 4 weeks after surgery by an ophthalmologist.

Formula Calculation

Spherical equivalent predictions from thirteen IOL power calculation formulas were obtained. Calculations were performed as follows:

- Barrett Universal II (UII), a multiple-parameter vergence-based thick-lens formula is included in the software of Lenstar LS900[®]. The formula is also freely available online.²³ Constant optimisation and data analysis were performed for us by the author, Graham Barrett, FRANZCO.
- Emmetropia Verifying Optical (EVO) formula²⁶ (version 2.0) is a thick-lens formula based on the theory of emmetropization and is freely available online. Constant optimisation and data analysis were performed by the author Tun Kuan Yeo, FRCOphth.
- Vergence-based Haigis,¹¹ HofferQ¹² Holladay 1,¹³ and SRK/T¹⁴ formulas were calculated by Jack Kane, MD, using an already validated Excel (Microsoft Corporation, Redmond, WA, USA) spreadsheet.¹⁵ The results were confirmed and validated against optical biometer printouts by one of the authors (DHF).

- Hill-RBF 2.0 uses adaptive learning from a large dataset to predict refractive outcomes through artificial intelligence – it was calculated using its online platform.²⁴ Constant optimisation and data analysis were performed Jack Kane, MD and the results were confirmed by one of the authors (DHF)
- Kane formula²⁵ is based on theoretical optics and incorporates both regression and artificial intelligence components to refine predictions. Constant optimisation and data analysis were performed by the author Jack Kane, MD.
- Næser2¹⁶ is a thick-lens vergence formula that predicts the geometric ACD, instead of ELP. The formula is available in Excel (Microsoft Corporation, Redmond, WA, USA) from its author. Optimisation and data analysis were performed by one of this study authors (O.V.V) following the recommendations of the formula's author (Kristian Næser, MD).
- PEARL-DGS²⁷ formula uses machine learning modelling and output linearization to predict ELP and adjustments for extreme biometric values. Constant optimisation and data analysis were performed by one of the authors (Guillaume Debellemière, MD).
- T2 formula was developed as an improvement to the SRK/T.¹⁷ The formula was computed on Excel (Microsoft Corporation, Redmond, WA, USA) and constant optimisation was performed by one of this study authors (O.V.V)
- VRF formula¹⁸ is a vergence-based thin-lens formula, developed by Oleksiy V. Voytsekhivskyy, MD and available on its software (VIOL Commander V.2.0.0.0.) Constant optimisation and data analysis were performed by the author.
- VRF-G formula is an unpublished new formula developed by Oleksiy V. Voytsekhivskyy. This is a next-generation formula based on theoretical optics with regression and ray-tracing components. It operates eight variables for IOL power calculation. It was programmed into Excel (Microsoft Corporation, Redmond, WA, USA) – constant optimisation, and data analysis were performed by the formula's author.

Differences regarding metrics used by each formula are summarized in [Supplementary Table 1](#).

As above-mentioned, each formula constant used was optimised for the entire dataset of patients, to achieve an arithmetic mean prediction error (ME) of zero, following recommended protocols.^{10,19} Any small residual ME was

nulled by adjusting the refractive prediction error for each eye up or down by an amount equal to the ME of that group, as described by Wang L et al.²⁰

Outcome Measurements

Refractive prediction error was calculated as the difference between the spherical equivalent of the post-operative manifest refraction and the formula prediction error. A negative refractive prediction error represents a myopic error, and a positive prediction error represents a hyperopic error.²⁰

Study outcome measures included ME and its standard deviation (SD), mean absolute error (MAE) and median absolute error (MedAE) of each formula, following Hoffer K. and Savini G.¹⁹ and Wang L et al²⁰ recommendations. The percentage of eyes with a prediction error within ± 0.25 , ± 0.50 , ± 0.75 and ± 1.00 dioptres were also calculated.

The subgroup analysis was performed based on AL intervals: short ($AL \leq 22.0$ mm), medium (22.0 mm $< AL < 26.0$ mm) and long ($AL \geq 26$ mm) eyes.

Statistical Analysis

Demographics and biometric data of patients were described with frequencies (percentages) and mean (SD: standard deviation). Data normality was assessed by the Kolmogorov–Smirnov test. The parametric one sample *t*-test or non-parametric Wilcoxon signed-rank test (1 sample) were used, as appropriate, to evaluate whether the mean refractive prediction error of each formula was different from zero. ANOVA with repeated measures were used to compare formulas prediction error. The comparisons of the absolute errors were assessed using the Friedman test (non-parametric ANOVA) with Bonferroni correction, as recommended,^{20,21} using Wilcoxon rank sum test for pairwise comparisons. The Cochran Q test was used to compare the percentage of eyes within $\pm 0.25D$, $\pm 0.50D$ and $\pm 1.00D$, with Bonferroni adjustment, using Dunn post-test. A p-value of less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS for Windows Software (version 24.0, SPSS, Inc.).

Results

Demographics and Biometric Data

A total of 828 eyes of 828 Caucasian patients fulfilled the inclusion criteria. Patients' demographics and biometric data are presented in [Table 1](#).

Table 1 Demographic and Biometric Data of Patients

Parameter	Mean \pm SD	Range
Age, years	76.03 \pm 8.33	45–94
Female gender, n (%)	544 (65.7%)	–
Axial length, mm	23.41 \pm 1.30	20.82–29.21
Anterior chamber depth, mm	3.20 \pm 0.43	2.06–4.83
Mean Keratometry, D	44.25 \pm 1.47	37.70–48.95
Corneal Thickness, μ m	540.39 \pm 34.03	442–640
Lens Thickness, mm	4.46 \pm 0.42	2.74–5.73
White-to-white, mm	11.85 \pm 0.43	10.09–13.13
Implanted IOL power, D	21.44 \pm 3.67	6.0–29.5

Abbreviations: SD, standard deviation; D, diopter.

Based on AL, 82 eyes (9.9%) were classified as short, 695 (83.9%) as medium and 51 (6.2%) as long. Optimised constants used are shown in [Supplementary Table 1](#).

Overall Formulas Accuracy

There was no statistically significant difference between the ME of formulas, since all formulas were optimised to have a ME of zero ($p=0.998$).

Over the entire sample, there was a significant difference between the formulas' absolute prediction errors ($p<0.001$). The lowest MAE and MedAE were obtained with Kane, EVO 2.0 and VRF-G formulas – their absolute errors were lower than SRK/T, Holladay 1, Hoffer Q, Haigis and Næser 2 ($p<0.001$ for each comparison). The Kane formula absolute error was also lower than the error obtained with Hill-RBF 2.0, Barrett UII, PEARL-DGS, VRF and T2 formulas ($p<0.001$). EVO 2.0 revealed

a better performance compared to Barrett UII, PEARL-DGS and VRF ($p<0.001$). On the other hand, Hoffer Q had the highest absolute error, which was significantly higher than all other formulas ($p<0.001$), except Haigis and Næser 2. [Table 2](#) reveals the outcomes of each formula ranked by MAE. [Supplementary Table 2](#) includes the formulas ranked by MedAE.

[Figure 1](#) displays the proportion of eyes within a prediction error of $\pm 0.25D$, $\pm 0.50D$, $\pm 0.75D$ and $\pm 1.00D$, which were statistically different among the investigated formulas ($p=0.001$ for $\pm 0.25D$ and $p<0.001$ for the remaining). Every formula, except Næser 2, Haigis, Holladay 1 and Hoffer Q had a percentage of eyes within $\pm 0.50D$ higher than 75%.

The Kane formula had a higher percentage of eyes within $\pm 0.25D$ compared to the Holladay 1, Haigis and Hoffer Q formulas ($p<0.05$). The Hoffer Q formula had the lowest percentage of eyes within $\pm 0.50D$, being significantly lower than all other formulas ($p<0.05$), except Holladay 1. Kane and VRF-G also had a significantly higher percentage of eyes within $\pm 0.50D$ than Holladay 1, Næser 2 and Haigis ($p<0.05$). The T2 also had significantly better percentages than the Haigis formula ($p=0.002$).

Regarding the proportion of eyes within $\pm 0.75D$, the Hoffer Q formula had a significantly lower outcome compared to all other formulas except Haigis and Næser 2. Moreover, Kane, EVO 2.0, VRF-G, Barrett UII and Hill-RBF 2.0 formulas produced a higher percentage compared to Næser 2 and Haigis ($p<0.05$). Næser 2's percentage was inferior compared to SRK/T ($p=0.006$).

Table 2 Refractive Outcomes of Each of the Investigated Formulas, Over the Entire Axial Length Range, Ordered by MAE (n=828)

Formula	ME	SD	MAE	MedAE	Percentage of Eyes Within			
					$\pm 0.25D$	$\pm 0.50D$	$\pm 0.75D$	$\pm 1.00D$
Kane	0.000	0.418	0.324	0.274	47.0	79.3	93.6	97.7
EVO 2.0	0.000	0.419	0.329	0.282	44.9	78.5	93.6	97.6
VRF-G	0.000	0.423	0.332	0.273	45.4	79.5	93.5	97.1
Barrett UII	0.000	0.429	0.339	0.291	42.4	77.8	93.5	97.2
Hill-RBF 2.0	0.000	0.433	0.342	0.291	43.2	76.7	93.2	97.6
PEARL-DGS	0.000	0.436	0.344	0.290	42.0	76.9	92.4	97.2
VRF	0.000	0.440	0.347	0.293	42.3	76.7	91.7	97.0
T2	0.000	0.441	0.346	0.291	43.0	75.5	92.6	97.1
SRK/T	0.000	0.454	0.356	0.303	42.5	75.1	92.1	97.2
Næser 2	0.000	0.455	0.357	0.309	41.4	74.9	90.3	96.3
Haigis	0.000	0.459	0.359	0.309	40.7	74.5	90.0	95.4
Holladay 1	0.000	0.461	0.361	0.299	40.8	74.3	91.5	96.1
Hoffer Q	0.000	0.489	0.383	0.317	40.6	69.9	88.3	95.7

Abbreviations: ME, mean prediction error; SD, standard deviation; MAE, mean absolute error; MedAE, median absolute error; D, diopter.

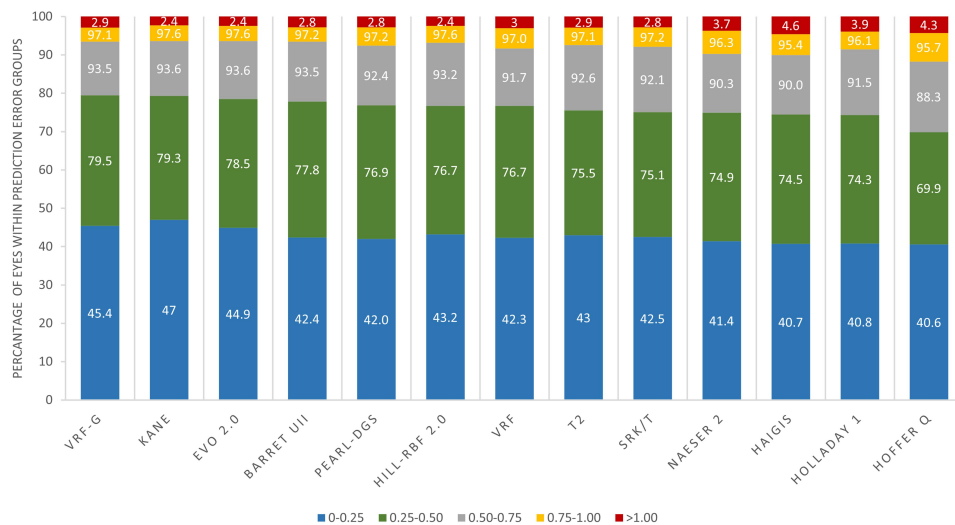


Figure 1 Stacked histogram comparing the percentages of eyes within $\pm 0.25D$, $\pm 0.50D$, $\pm 0.75D$ and $\pm 1.00D$ of prediction error. Formulas are ranked according to the higher percentage of eyes within $\pm 0.50D$.

With respect to the proportion of eyes within $\pm 1.00D$, Haigis had a significantly lower percentage than all other formulas ($p < 0.05$), except for VRF, Hoffer Q and Næser 2. Hoffer Q also had a lower percentage compared to Kane, EVO 2.0 and Hill-RBF 2.0 ($p < 0.05$).

Globally, the Kane formula had the lowest SD, MAE, and the highest percentage of eyes within $\pm 0.25D$ and $\pm 0.75D$. VRF-G formula produced the lowest MedAE and the highest percentage of eyes within $\pm 0.50D$. Kane (3.3%), followed by EVO 2.0 and Hill-RBF 2.0 (3.4% for both) had the lowest risk of a refractive surprise (refractive error greater than 1.00D).

Formulas Accuracy According to the Axial Length

In all axial length subgroups, a statistically significant differences between formulas absolute errors were found ($p < 0.001$) – each formula results are shown in Table 3.

In short eyes ($n = 82$), Hoffer Q produced a higher absolute error when compared to VRF-G, EVO 2.0, Kane and VRF ($p < 0.001$). In medium eyes ($n = 695$), Kane and EVO 2.0 were more accurate than Haigis and Næser 2 ($p < 0.001$). Moreover, the Kane formula absolute error was also significantly lower than the MAE of SRK/T, Hoffer Q and VRF.

Finally, in long eyes ($n = 51$), Hoffer Q and Holladay 1 performance was worse than any other formulas ($p < 0.05$).

For all AL subgroups, Kane, EVO 2.0 and VRF-G formulas had the most accurate performances.

Figure 2 presents a smooth-line graph representing the mean prediction error of each formula according to the AL.

The graph reveals a tendency for a myopic shift in short eyes and a more pronounced hyperopic shift in long eyes. Kane, EVO 2.0, VRF-G and Hill-RBF 2.0 formulas did not present a mean prediction error significantly different from zero across the entire AL range. Interestingly, despite not reaching the most accurate absolute errors among all formulas, Næser 2 also did not have a ME significantly different from zero, independent of the AL range.

Discussion

Our study evaluated the accuracy of new-generation formulas along with the well validated vergence-based formulas, using one single IOL model AcrySof SN60WF

Table 3 Mean Absolute Error of Each Formula by Axial Length Group

Formula	Short AL ≤ 22.0 mm	Medium 22.0 mm $< AL < 26$ mm	Long AL ≥ 26.0 mm
Kane	0.348	0.323	0.301
EVO 2.0	0.347	0.329	0.308
VRF-G	0.345	0.333	0.309
Barrett UII	0.367	0.338	0.319
Hill-RBF 2.0	0.368	0.339	0.325
PEARL-DGS	0.368	0.339	0.377
VRF	0.365	0.346	0.329
T2	0.400	0.340	0.339
SRK/T	0.384	0.352	0.364
Næser 2	0.380	0.357	0.319
Haigis	0.397	0.357	0.352
Holladay I	0.409	0.339	0.579
Hoffer Q	0.478	0.357	0.592

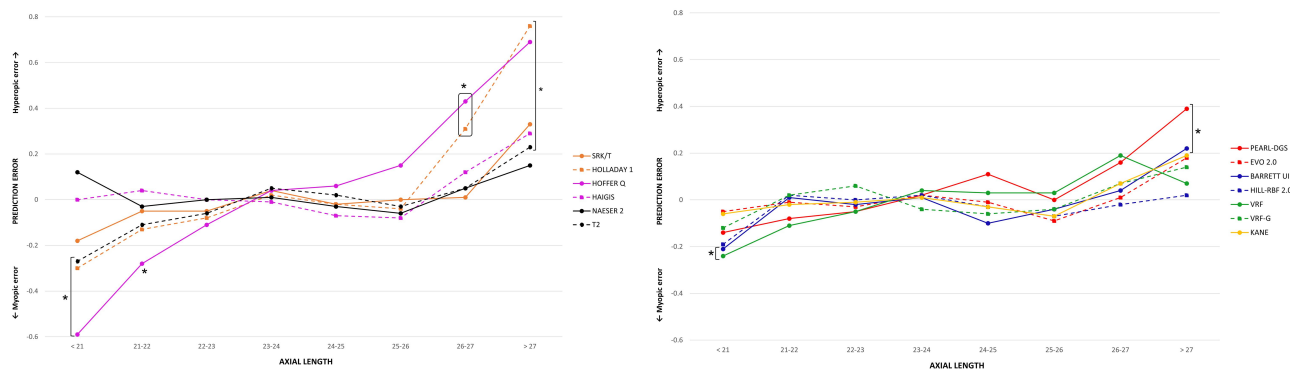


Figure 2 Mean Arithmetic Prediction Error (in diopters) of each formula versus axial length (in millimetres). *p<0.05 – one sample t-test/wilcoxon signed-rank test.

(Alcon Laboratories, Geneva, Switzerland). To the best of our knowledge this is the first clinical study evaluating some of these new formulas (EVO 2.0 and PEARL-DGS) using data obtained from an OLCR-biometer (Lenstar LS900). Furthermore, we report the first results of a newly developed, unpublished formula – VRF-G.

Overall, the Kane and VRF-G formulas presented the most accurate outcomes. The Kane formula had the lowest SD and MAE and the highest percentage of eyes within ±1.00D. On the other hand, VRF-G formula revealed the lowest MedAE and the highest percentage of eyes within ±0.50D. Regarding short eyes, VRF-G presented the lowest MAE and in medium and long eyes Kane obtained the most accurate results.

Regarding the Kane formula, these results are in agreement with recently published literature,^{4,5,9} independent of OLCR or PCI biometers. With new SS-OCT biometers, similar results were also reported.^{6–8} With respect with VRF-G formula, it is a newly developed formula based on theoretical optics with regression and ray-tracing components. We are unable to discuss the results due to lack of literature. However, based on our outcomes, both the Kane and VRF-G formulas are shown to be promising formulas.

EVO formula, in its earlier version, had relatively more myopic and hyperopic outcomes in short and long eyes.³ However, our results suggest that with an OLCR biometer, the improved 2.0 version is considerably more accurate, confirming reported outcomes by authors who used other biometer technologies.^{6–8} In fact, it had the second lowest MAE for all AL subgroups, revealing its regularity across the entire AL range.

Hill-RBF 2.0 showed consistent results across the entire set of eyes (fourth lowest MAE and fifth lowest MedAE) and after AL subgroup analysis, confirming an improvement with this second version.^{4,5,9} PEARL-DGS

also revealed an overall good result, but it was not ranked among the best formulas. This may be because it is optimised for values obtained with the IOLMaster700® (Zeiss, Jena, Germany). However, in a recent study using IOLMaster700®⁶ it had a relatively lower performance compared to the other new generation formulas (Kane, EVO 2.0 and Hill-RBF 2.0) and Barrett UII, which are in agreement with our findings. This performance may be explained by its hyperopic tendency in long eyes.

Before the introduction of the most recent formulas, Barrett UII was shown to be the best-performing formula.^{3,15,22} In our study, the Barrett UII remained one of the most accurate formulas. Its accuracy was not statistically different than any of the newer formulas, confirming that it continues to be an accurate and good choice for IOL power selection. However, attention must be paid in short eyes in which the formula tends to have relatively poorer performance, based on our results, which is corroborated by some published literature.^{5,9}

The T2 formula was developed as an improvement to the SRK/T formula. Despite revealing better results than SRK/T, the improvement was not statistically significant, and the formula did not perform as well as other modern formulas, in agreement with a recently published study.⁶ The VRF formula results were similar to those obtained with the T2 formula. There are some conflicting results about which one of these two formulas perform better^{7,8,18} – differences in published outcomes may be explained by differences in biometers used. The thick-lens vergence formula Næser 2 results were not among the best, in agreement with Savini et al⁷ results.

Finally, considering mean arithmetic prediction error behaviour according to the AL, our drawn graph revealed a significant hyperopic shift of the Hoffer Q, Holladay 1 (as expected³) and PEARL-DGS in long eyes. Also, as Melles

R et al³ reported, the Hoffer Q is the formula more negatively influenced by AL variance. In contrast, Kane, VRF-G, EVO 2.0, Hill-RBF 2.0 and Næser 2 formulas did not present a mean prediction error significantly different from zero across the entire AL range. We are unable to discuss this last result due to the lack of published literature.

Our study limitations include its retrospective design, similar to most studies related to IOL formulas assessment. Moreover, a 4 m distance was used for manifest refraction which influence formulas constants values, being higher than usually reported. This methodology was consistently used in every patient and therefore does not influence formulas comparison. The inclusion of data from different surgeons may also introduce bias. However, it allows us to more accurately represent a real-world scenario and support a greater generalization of the results. Despite its limitations, this study followed the strict recommended criteria for IOL formula studies based on published literature.^{10,19,21}

Analysing our data, we conclude that newly introduced formulas, along with refined surgical techniques and improved intraocular lenses, may help us achieve better refractive outcomes after cataract surgery. These new and accurate formulas ideally should be included in the software of biometers in the future to avoid transcription errors and allow improved refractive outcomes. One of the biggest challenges for IOL formulas is to have lower variance in accuracy, even in extreme eyes, delivering more reliable and predictable results. The Kane, EVO 2.0 and VRF-G formulas are promising candidates to fulfil these goals.

Data Sharing Statement

Data are available on reasonable request (biometric measurements, implanted IOL power, postoperative refraction, prediction error by each formula) from Diogo Hipólito-Fernandes, MD (cdiogo777@gmail.com).

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Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the

article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Disclosure

Dr. Oleksiy Voytsekhivskyy reports the following patents issued: PUN $\text{\textcircled{R}}$ 101404 and PUN $\text{\textcircled{R}}$ 109842; and is the inventor and exclusive owner of the VRF and VRF-G formulas. Both formulas are the intellectual property of the doctor Voytsekhivskyy. Dr. Oleksiy Voytsekhivskyy has a patent on the method of estimation of postoperative lens position (ELP) and the calculation of its optical power and is the author and copyright holder of a computer program called ViOL Commander version 2.0.0.0 (V/B/C Systems, Kyiv, Ukraine) for PC. Dr. Tun Kuan Yeo is the creator of the EVO 2.0 formula. The following authors have no financial disclosures: Diogo Hipólito-Fernandes, Maria Elisa Luís, Pedro Gil, Vitor Maduro, João Feijão, Nuno Alves. The authors report no other potential conflicts of interest for this work.

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