A Comparison between Wavefront-Optimized and Wavefront-Guided Photorefractive Keratectomy in Patients with Moderate-to-High Astigmatism: A Randomized Clinical Trial

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Abstract

Purpose: To compare clinical outcomes of wavefront-optimized (WFO) and wavefront-guided (WFG) photorefractive keratectomy (PRK) in patients with moderate-to-high astigmatism.

Methods: Patients with corneal cylinder above 2 diopters and myopic spherical equivalent were randomized into WFO or WFG PRK. Visual acuity (VA), refraction, contrast sensitivity, higher-order aberrations (HOAs), and astigmatic vector differences were documented and compared for 6 months after surgery.

Results: The total number of 362 eyes from 181 patients was analyzed. The amount of total aberration was reduced 2.7 root mean square (RMS) and 2.9 RMS in the WFO and WFG groups, respectively (P < 0.001 in each group and between the groups). HOAs including coma, trefoil, and spherical aberrations increased in both the groups (P < 0.001) but were significantly more in the WFO group (P < 0.001). The increased spherical aberration was similar in both the groups (P = 0.12). Surgically induced astigmatism was not significantly different between the groups (P = 0.20). The magnitude of error was significantly higher in the WFO group (P < 0.001), but the absolute angle of error and the arithmetic angle of error were not significantly different between the groups (P = 0.20 and P = 0.30, respectively).

Conclusion: WFO and WFG platforms of PRK appear comparable in terms of VA, refractive correction, and total aberration. Yet, HOAs may increase especially after WFO PRK.

Keywords: Photorefractive keratectomy, Wavefront-guided photorefractive keratectomy, Wavefront-optimized photorefractive keratectomy

INTRODUCTION

Photorefractive keratectomy (PRK) is an efficient technique for correcting refractive errors of myopia, hyperopia, and astigmatism.¹ All of the available PRK profiles involve laser ablation of the corneal stromal bed to a certain depth that reshapes the cornea to assist the eye reaching the state of optical neutrality.²,³ Although many patients are satisfied with their spectacle-free status, there are a number of postoperative complaints that adversely affect their quality of vision. In fact, despite proven efficacy of corneal laser ablation in eliminating lower-order aberrations (i.e., myopia, hyperopia, and regular astigmatism), it is considered a culprit for increasing the higher-order aberrations (HOAs) (i.e., coma, trefoil, and spherical aberration) which leads to symptoms of glare, halo, starburst, and reduced contrast sensitivity (CS).²

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To alleviate this problem, some modifications to the traditional ablating patterns have been made. These included wavefront-optimized (WFO) and wavefront-guided (WFG) ablation patterns, both of which were demonstrated to be efficient and safe in reducing symptoms associated with HOA, especially in myopic eyes.4-11

Although both platforms consider preoperative wavefront analysis of the eye, some investigators have proposed that WFG profile may be superior to WFO in myopic and astigmatic correction, reflecting the individualized nature of the former.12-15 However, the majority of the evidence in this area comes from laser-assisted in situ keratomileusis (LASIK), not PRK, patients. On the other hand, only few studies have considered the astigmatic vector analysis of patients with moderate-to-high astigmatism in their study designs.2,16-18

The aim of this randomized clinical trial (RCT) was to compare the clinical outcomes of WFO versus WFG two-step PRK in patients with moderate-to-high astigmatism in terms of visual acuity (VA), manifest refraction, CS, astigmatic and aberrometric vector changes for a period of 6 months after intervention.

**METHODS**

This is a nonmasked RCT performed in Feiz Teaching Hospital, Isfahan University of Medical Sciences, Isfahan, Iran. The study design was approved by the Ethics Committee of the Isfahan University of Medical Sciences for accordance with tenets of the Declaration of Helsinki. The study protocol was registered in the Iranian Clinical Trials Registry (IRCT no. IRCT20190806044459N1; Ethics ID: IR.MUI.MED.REC.1398.047). The recruitment started in September 2018, and each patient was followed for 6 months, concluding the trial in January 2020.

Patients seeking refractive surgery aged 21 years or more, with corrected distance VA (CDVA) of at least 20/20, corneal astigmatism above 2 diopters (either with or against the rule astigmatism), myopic spherical equivalent (SE) were randomized into two treatment groups after consultation and documentation of informed consent. Figure 1 demonstrates the steps of the study, recruitment, and follow-up of the patients. We excluded patients with ocular surface disease, history of past or current use of rigid gas permeable contact lens, corneal opacity of any reason, cataract of any kind and any severity, previous ophtalmic surgery, atopic disease (ocular and/or nonocular), connective tissue disease (with or without ocular involvement), glaucoma and/or uncontrolled intraocular pressure (IOP), vitreoretinal disease, macular disease, use of systemic and ophtalmic immunosuppressive medications, pregnancy, and lactation.

To facilitate follow-ups, we decided to enter those patients who had both eyes eligible for treatment by one modality. Computerized randomization was used to deploy each patient into the treatment groups.

![Figure 1: Flow diagram demonstrating the steps of the study, recruitment, and follow-up of the patients](image-url)
Each patient underwent a comprehensive ophthalmologic examination and appropriate consultations were performed for suspicious cases. VA with and without correction and best spectacle CDVA were documented.

Slit-lamp examination, retinal assessment, IOP measurement (using noncontact air-puff device [Topcon CT-80; Topcon Corporation, Tokyo, Japan]), and corneal tomography (Pentacam HR, Oculus GmbH, Wetzlar, Germany) were performed. Wavefront aberrometry (Zywave II Wavefront Aberrometer, BAUSCH and LOMB Inc., USA) was done in all patients.

In the case of a significant difference between aberrometric and subjective astigmatism (defined as more than 0.75 diopter of the astigmatic amount and more than 15° of an axis), we repeated the subjective and aberrometry evaluations. With the persistent difference, the case was excluded from the study. For axis difference of smaller than 15°, the aberrometry axis was used for treatment.

The Pentacam (Oculus GmbH, Wetzlar, Germany) was mainly used to look for stigmata of corneal ectasia such as skewed axis deviation, anterior and posterior best fit sphere elevations, inferior-superior difference, and the Belin-Ambrosio map reconstruction. The aberrations including coma, trefoil, spherical aberration, and total HOAs were calculated using Zywave Wavefront Aberrometer. The values for target-induced astigmatism (TIA) and surgically induced astigmatism (SIA), angle of error (AofE), and flattening effect were measured using both devices.

We report the values for CDVA (in logMAR) measured with Snellen acuity chart, refractive error, and SE; CS measured with CSV-1000 chart (in four spatial frequencies: 3, 6, 12, and 18 cycles per degree [cpd]); aberrometric findings; and vector analysis of the astigmatic error.

The variables related to vectors include the following:
- **TIA**: The amount of required change in the magnitude and axis that should be induced to neutralize a preexisting astigmatism
- **SIA**: The amount and axis of astigmatic change that have been actually induced by the surgery.
- **Magnitude of error (MoF):** The dioptric translation of intended correction minus-induced correction
- **Correction index (CI):** The ratio of SIA to TIA
- **AofE**: The angle formed by the vectors of the intended correction and the achieved correction
- **Index of success (IOS):** Calculated from dividing the difference vector (DV) by the TIA, it is a measure of relative effectiveness.

A single surgeon masked to the patient recruitment and randomization processes was in charge of handling the surgeries. The technique included applying 20% alcohol for 20 s over the cornea to facilitate corneal epithelium peeling, followed by excimer laser ablation of the stromal bed (TECHNOLAS TENEo 317 Model 2 Excimer Laser, BAUSCH + LOMB Surgical [ZYOPTIX HD module for WFG and PROSCAN module for WFO ablations], NY, USA). To reduce postoperative haziness, we applied mitomycin-C (MMC) in all subjects. The minimum touch time for the sponge impregnated with MMC before irrigation was 30, and the maximum was 60 s. The MMC time was decided by the surgeon in each case according to the ablation depth and predicted postoperative ultraviolet exposure. Finally, the surgery was concluded by putting on a therapeutic contact lens.

We used the exported iris image for static iris registration before ablation in all cases.

Optical zone of ablation was 6 mm. To compensate cyclotorsion of the eyes while supine, the in-built tracker of the TECHNOLAS system was used.

Postoperative visits were scheduled for days 1 and 7 after surgery. Patients were followed for repeating measurements at months 1 and 6 postoperative. The medications used included a topical steroid (betamethasone 0.1% eye drop, Sina Darou, Tehran, Iran) and a topical antibiotic (ciprofloxacin 0.3% eye drop, Sina Darou, Tehran, Iran) for the 1st week. After removal of the bandage contact lens in the follow-up visit at day 7, the topical antibiotic was discontinued and a weekly tapering schedule of topical steroid was continued.

**Statistical analysis**

The statistical analysis was accomplished using SPSS 25 for Windows (IBM Corporation, Armonk, New York, USA). Quantitative and qualitative data are presented as mean ± standard deviation and number (percent), respectively.

Statistical tests including independent Student’s t-test, paired t-test, analysis of covariance (ANCOVA), Mann–Whitney U-test, and Chi-square test were utilized where applicable to compare measures of interest in each group and between the groups. Generalized estimating equation (GEE) was used in analysis to consider the correlation between the two eyes of a patient participated in the study. $P < 0.05$ was considered statistically significant.

**Results**

A total number of 362 eyes from 181 patients completed the study course and underwent analysis [Table 1]. We found no difference between the two groups in terms of age, gender, and the preoperative parameters including CDVA, sphere and cylinder power, SE, and the cylinder axis.

After 6-month follow-up, the amount of sphere and cylinder powers showed significant improvement after operation in both the groups ($P < 0.001$). Both variables were significantly more in the WFG group (sphere $0.1 ± 0.6$ vs. $0.24 ± 0.7$, $P = 0.02$; cylinder $−0.6 ± 0.3$ vs. $−0.45 ± 0.2$, $P < 0.001$ [based on ANCOVA test]). Nonetheless, the CDVA in both the groups showed significant improvement ($P < 0.001$) with no significant difference between the groups ($0.01 ± 0.02$ vs. $0.02 ± 0.03$, $P = 0.70$).

In the WFO group, we found that the total aberration was reduced 2.7 root mean square (RMS), postoperatively ($3.4 ± 1.5$ vs.
0.7 ± 0.4; \( P < 0.001 \); Wilcoxon ranked test). This was also the case for the WFG group as we found 2.9 RMS reduction in the total aberration (3.65 ± 1.0 vs. 0.75 ± 0.3; \( P < 0.001 \); Wilcoxon ranked test). The greater reduction of the total aberration in the WFG group in comparison to the WFO group was not statistically significant (\( P = 0.30 \); GEE test).

In the WFO group, both the total HOA and the third-order aberrations increased 0.12 RMS (0.25 ± 0.08 vs. 0.37 ± 0.14; \( P < 0.001 \); Wilcoxon ranked test) and 0.11 RMS (0.22 ± 0.07 vs. 0.33 ± 0.10; \( P < 0.001 \); Wilcoxon ranked test), respectively, after operation. In the WFG group, both the total HOA and the third-order aberrations increased 0.02 RMS (0.27 ± 0.05 vs. 0.29 ± 0.05; \( P < 0.001 \); Wilcoxon ranked test) and 0.01 RMS (0.24 ± 0.04 vs. 0.25 ± 0.05; \( P < 0.001 \); Wilcoxon ranked test), respectively.

The increased total HOA in the WFO group was significantly more than the WFG group (\( P < 0.001 \); ANCOVA test) the same as third-order aberrations. Accordingly, in both the groups, the preoperative spherical aberration was 0.03 RMS which increased to 0.04 RMS postoperatively with no statistically significant difference (\( P = 0.12 \); ANCOVA test).

Table 2 demonstrates the logarithmic values of CS as measured in four spatial frequencies: 3, 6, 12, and 18 cpd. It is evident that at different spatial frequencies, the CS differs between the groups. The WFG group demonstrated better CS at 3 cpd while the sensitivity was better in the WFO group at 6, 12, and 18 cpd. Figure 2 illustrates the spatial difference in CS between the two groups.

The comparison of the astigmatic vectors is summarized in Table 3. We found that target-induced vector (TIA) was significantly more in the WFO group (\( P < 0.001 \)) while its axis difference remained statistically insignificant (\( P = 0.50 \); Mann–Whitney U-test) [Figure 3]. The surgically induced vector (SIA) and its axis were not significantly different between the groups (\( P = 0.10 \) and \( P = 0.20 \), respectively; based on Mann–Whitney U-test) [Figure 3]. On the other hand, although the MofE was significantly higher in the WFO group, the absolute AofE (AAofE) and the arithmetic AofE (aAofE) were not significantly different between the two groups [Table 3]. The CI was significantly higher in the WFG group (\( P = 0.001 \)) while the IOS was significantly more in the WFO group (\( P = 0.002 \)). Both of the attempted and the achieved SE values were higher in the WFG group (\( P < 0.001 \)). We also found that final flattening

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**Table 1: Preoperative characteristics of the study population**

| WFO (%) | WFG (%) | \( P \) |
|---------|---------|--------|
| Number of eyes | 192 | 170 | 0.900* |
| Age | 26.4±4.1 | 25.9±3.9 | >0.99* |
| Gender | | | |
| Male | 37 (38) | 37 (43) | |
| Female | 59 (62) | 48 (57) | |
| Sphere power (diopter) | −1.97±1.6 | −3.1±0.9 | 0.800* |
| Cylinder power (diopter) | −2.6±0.6 | −2.45±0.5 | 0.800* |
| WTR axis | 123 (59.1) | 112 (65.1) | 0.200* |
| ATR axis | 39 (18.8) | 25 (14.5) | 0.200* |
| Oblique axis | 46 (22.1) | 35 (20.3) | 0.200* |

*Based on Mann–Whitney U-test, *Based on analysis of covariance test.

WFO: Wavefront-optimized, WFG: Wavefront-guided, WTR: With-the-rule, ATR: Against-the-rule.

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**Figure 2:** Comparing the contrast sensitivity between wavefront-optimized and wavefront-guided groups (depicted in red and blue lines, respectively)

**Figure 3:** The diagrams illustrating target-induced astigmatism vector in the horizontal and surgically induced astigmatism vector in the vertical axes. The wavefront-optimized and wavefront-guided groups are shown in red and blue, respectively. The results of regression analysis demonstrated no significant difference between the groups.
effect was similar between the groups despite higher flattening index in the WFG group ($P < 0.001$).

None of our patients demonstrated significant complications that would have required omission from the study. Eight patients had mild conjunctivitis during the follow-up period. Two patients had faint asymptomatic haziness. No regression was noted during the study course, and all of our patients remained spectacle free.

**Discussion**

We performed an RCT to compare the outcomes of WFO versus WFG PRK in patients with moderate-to-high astigmatism over 6 months, and we found that these two profiles were fairly comparable in terms of refractive correction, VA, and complications. These findings are supported by previous evidence.2,3,12,19,20

We found that the reduction in total aberration was significant in both profiles and that this effect was larger for the WFG group.

This is mainly due to the reduction in sphere and astigmatic errors. However, both profiles showed a significant increase in HOAs, which was greater in the WFO group. This increase was related to the increase in the third-order aberration to a greater extent rather than spherical aberration. In a study by Jun et al. in 2017, WFO and WFG profiles were compared in transepithelial PRK of myopic astigmatic patients, and no difference in the induction of spherical aberrations was detected.12 The same authors have reported a comparison of WFO and WFG methods in transepithelial PRK of high astigmatism and detected a greater induction of spherical aberration and coma in the WFO group.2 However, we found that induced spherical aberration was similar in both the groups. In a RCT by He and Manche in 2014, eye-to-eye PRK results with WFO and WFG profiles were compared, and a slight predilection for WFG results was observed.3 Furthermore, LASIK was the intervention; Khalifa et al. reported that WFG protocol was more efficient in terms of visual outcomes and induction of HOAs in low-to-moderate myopic astigmatism.15 Older reports have similarly reported in favor of WFG ablation though in LASIK patients.21,22

The mathematical advantages of Alpins method for reporting astigmatism are invaluable.23 The CI, defined as the SIA divided by TIA, was significantly higher in the WFG group. Although the TIA vector was significantly more in the WFG group, the SIA was similar in both the groups. The calculated MoE, defined as the difference of attempted and achieved astigmatic vectors, was also significantly lower in the WFG group which parallels the above findings. The CI was significantly more in the WFG group. These measures altogether point to a slightly better profile of the WFG group.

We found that the aAofE and AAofE were not significantly different between the groups. In contrast to our findings, Jun et al. found a significantly higher AofE in the WFO group; however, they used the transepithelial PRK instead of alcohol-assisted protocol we used.2 At first glance, this difference may be attributed to alcohol or MMC in our protocol, but a study published by Antonios et al. in 2017 compared transepithelial and alcohol-assisted PRK in high myopia and found similar AofE between the groups.16 Albeit, Toy et al. analyzed outcomes of a randomized fellow eye comparison of WFO and WFG LASIK and reported higher AofE values in the WFO group.13 The latter authors compared WFO and WFG PRK outcomes of fellow eyes over 1 year and reported higher AaoE in the WFO group but similar MoE between the groups.14

Although the DV was higher in the WFO group, it did not reach statistical significance in our study. This is similar to previous studies.2,13 However, Khalifa et al. found better DV in the WFG group, though their patients underwent LASIK not PRK.13 We believe that according to the controversial findings of the current literature, making firm conclusions regarding the vector parameters is eluding.

It seems that WFO profile preserves CS better, especially in higher spatial frequencies. The only contrast measure that was

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**Table 2: Comparison of contrast sensitivity between wavefront-optimized and wavefront-guided groups**

| CS  | WFO          | WFG          | $P^*$ |
|-----|--------------|--------------|------|
| CS3 | 1.61±0.1     | 1.65±0.1     | 0.01 |
| CS6 | 1.98±0.1     | 1.96±0.08    | 0.09 |
| CS12| 1.8±0.1      | 1.7±0.1      | <0.001 |
| CS18| 1.24±0.1     | 1.19±0.08    | <0.001 |

$^*$Based on Mann–Whitney U-test. WFO: Wavefront-optimized, WFG: Wavefront-guided, CS: Contrast sensitivity

**Table 3: Analytical vector profile of the wavefront-optimized and wavefront-guided groups**

| Parameter          | WFO          | WFG          | $P^*$ |
|--------------------|--------------|--------------|------|
| TIA vector         | 2.43±0.52    | 2.21±0.39    | <0.001 |
| SIA vector         | 1.91±0.56    | 1.81±0.4     | 0.100 |
| TIA axis           | 83.23±63.86  | 79.66±65.22  | 0.500 |
| SIA axis           | 77.43±62.63  | 70.28±62.72  | 0.200 |
| MoE                | −0.53±0.72   | −0.4±0.2    | <0.001 |
| AAoE               | 2.7±2.9      | 2.3±2.5     | 0.200 |
| aAofE              | −0.6±3.9     | 0.03±3.4    | 0.300 |
| DV                 | 81.9±65.1    | 73.8±67.5   | 0.100 |
| CI                 | 0.78±0.12    | 0.82±0.09   | 0.001 |
| IOS                | 0.25±0.13    | 0.2±0.11    | 0.002 |
| Attempted SE       | −3.2±1.5     | −4.4±1.02   | <0.001 |
| Achieved SE        | −3.1±1.6     | −4.4±1.02   | <0.001 |
| Flattening effect  | 1.89±0.57    | 1.8±0.4     | 0.140 |
| Flattening index   | 0.77±0.13    | 0.81±0.1    | 0.001 |
| SCI                | 0.93±0.28    | 1.00±0.16   | 0.005 |
| SSI                | 0.93±0.27    | 1.00±0.15   | 0.005 |

$^*$Based on Mann–Whitney U-test. WFO: Wavefront-optimized, WFG: Wavefront-guided, TIA: Target-induced astigmatism, SIA: Surgically induced astigmatism, MoE: Magnitude of error, AAoE: Absolute angle of error, aAofE: Arithmetic angle of error, DV: Difference vector, CI:Correction index, IOS: Index of success, SE: Spherical equivalent, SCI: Spherical correction index, SSI: Spherical success index
better in the WFG group was CS at 3 cpd. This is noteworthy because the literature is scant regarding long-term results for CS after PRK in a comparative manner. Nonetheless, early post-PRK results have shown that in WFO patients, the CS decreases at month 1, then increases to normal at month 3, and may even increase thereafter up to month 6. WFG LASIK, in comparison to conventional LASIK, was also shown to increase CS 1 month after surgery. In an RCT by Ryan et al., CS was compared after WFO and WFG ablations in either PRK or LASIK, and it was found that neither the profiles nor the treatment types were different at 12 months.

Our study is limited by the fact that loss to follow-up reduced the number of patients who finished the study. Thus, the number of analyzed patients was less than the calculated sample size. Furthermore, the duration of MMC administration was not exactly the same for all patients which may theoretically affect the results.

In conclusion, although both of the WFO and WFG platforms of PRK appear efficiently comparable in terms of VA and refractive correction, there are still controversies regarding the induction of HOAs, CS, and vector parameters. We believe that until sufficient evidence or systematic reviews are not available, either method merits application at the physician’s discretion.

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Conflicts of interest
There are no conflicts of interest.

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