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Repeatability of Anterior Chamber Dimension Measurements Performed by a Scheimpflug-Placido Analyser in Unoperated and Post-Refractive Surgery Eyes

Ameliyat Edilmemiş ve Refraktif Cerrahi Geçirmiş Gözlerde Scheimpflug-Placido Analyzer Tarafından Yapılan Ön Kamara Boyut Ölçümlerinin Tekrarlanabilirliği

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ABSTRACT Objective: We aimed to evaluate the repeatability of iridocorneal angle (IA), anterior chamber depth (ACD), and anterior chamber volume (ACV) measurements of the rotating Scheimpflug camera combined with a Placido disc anterior segment analyser in unoperated and post-refractive surgery eyes. **Material and Methods:** In this prospective study, we measured IA, ACD, and ACV using a Sirius (CSO, Florence, Italy). Glaucoma summary mode of the Sirius provides nasal and temporal IA values at different angles (specifically; 0°, +10°, +20°, +30°, -10°,-20°, and-30° degrees) automatically and an average value as IA. We calculated repeated measures one-way analysis of variance (ANOVA), intraclass correlation coefficient (ICC), within-subject standard deviation (Sw), intrasession test-retest variability, and coefficient of variation (COV) to determine repeatability. **Results:** This study included 50 eyes of 50 subjects without a history of refractive surgery with a mean age of 42.6 years and 13 eyes of 13 subjects who had undergone LASIK or PRK with a mean age of 39.1 years. We did not find any statistically significant differences between consecutive measurements using repeated measures ANOVA in both groups. For the average IA, ACD, and ACV measurements, repeatability was excellent with ICC > 0.90 in both groups. For the IA measurements at different meridians, the ICC value was below 0.9 at all nasal meridians with the exception of nasal angle 10° in operated eyes and higher than 0.8 for all temporal meridians. **Conclusion:** Iridocorneal angle measurements of the Sirius device at temporal meridians showed moderate or high repeatability, whereas at nasal meridians, it showed poor or moderate repeatability in both normal and post-refractive surgery eyes. On the other hand, ACD and ACV measurements of the Sirius showed excellent repeatability in both groups.

Keywords: Corneal topography; refractive surgical procedures; anterior chamber

ÖZET Amaç: Bu çalışmada, ameliyat edilmemiş ve refraktif cerrahi geçirmiş gözlerde Placido disk ile bağlantılı rotasyonel Scheimpflug kamera içeren bir ön segment analiz cihazı ile elde edilen iri-dokorneal açı (İA), ön kamara derinliği (ÖKD) ve ön kamara hacmi (ÖKH) ölçümlerinin tekrarlanabilirliğini değerlendirmeyi amaçladık. **Gereç ve Yöntemler:** Bu prospektif çalışmada, Sirius (CSO, Floransa, İtalya) cihazı kullanarak İA, ÖKD ve ÖKH'yi ölçtük. Sirius'un glokom özet modu, farklı açılarda (spesifik olarak 0°, +10°, +20°, +30°, −10°,−20°, and -30° dereceleri) nazal ve temporal İA değerlerini otomatik olarak ölçer ve ilaveten bir ortalama İA değeri sunar. İA, ÖKD ve ÖKH ölçümleri tekrarlanabilirliği, tek yönlü varyans analizi (ANOVA), gözlem içi korelasyon katsayısı (İKK), bireye özgü standart sapma (Sw), sınıf içi test-tekrar test değişkenliği ve varyasyon katsayısı (VK) hesaplanarak değerlendirildi. **Bulgular:** Bu çalışmada, ortalama yaşı 42,6 olan ve refraktif cerrahi öyküsü olmayan 50 hastanın 50 gözü ve yaş ortalaması 39,1 yıl olan LASIK veya PRK tedavisi geçirmiş 13 hastanın 13 gözü yer aldı. Her iki grupta ardışık ölçümler, tekrarlanan ölçümler ANOVA testi kullanılarak değerlendirildi ve istatistiksel olarak anlamlı bir fark bulunamadı. Ortalama İA, ÖKD ve ÖKH ölçümleri için her iki grupta da tekrarlanabilirlik mükemmeldi (İKK>0,90 idi). Farklı meridyenlerdeki İA ölçümleri için, İKK değerleri, ameliyat edilen gözlerde nazal 10° değeri hariç tüm nazal meridyenler için 0,9'un altında ve tüm temporal meridyenler için 0,8'in üstünde idi. **Sonuç:** Sirius cihazının iridokorneal açı ölçümleri, temporal meridyenlerde orta veya yüksek tekrarlanabilirlik gösterirken, nazal meridyenlerde hem normal hem de refraktif cerrahi geçirmiş gözlerde zayıf veya orta derecede tekrarlanabilirlik göstermiştir. Diğer yandan, Sirius'un ÖKD ve ÖKH ölçümleri her iki grupta da mükemmel tekrarlanabilirlik göstermiştir.

Anahtar Kelimeler: Kornea topografisi; refraktif cerrahi işlemler; ön kamara

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Precise assessment of iridocorneal angle (IA), anterior chamber depth (ACD) and anterior chamber volume (ACV) are essential for the diagnosis and the follow-up of primary open-angle glaucoma (POAG) and angle-closure glaucoma. ACD and ACV were previously described among the primary risk factors for angle closure.[1,2] Additionally, ACD is a crucial parameter in converting the cylindrical power of toric intraocular lens (IOL) from the IOL plane to the corneal plane, for selection of patients and IOL size in phakic IOL implantation, and in the accurate determination of IOL power along with corneal power and axial eye length measurements.[3-5]

The present gold standard for IA assessment is gonioscopy. However, ophthalmologists do not perform gonioscopy in more than half of their POAG patients at the initial examination.[6] Gonioscopy has several limitations; it is a relatively time-consuming procedure, and performing gonioscopy and interpreting its findings require considerable experience.[7] Because of the above-mentioned reasons, ultrasound biomicroscopy, anterior segment optical coherence tomography (AS-OCT), and Scheimpflug camera-based devices were introduced for iridocorneal angle imaging. Ultrasound biomicroscopy can directly visualise the iridocorneal angle. However, similar to gonioscopy, it is a contact method and requires considerable time and skill for examination.[8] Scheimpflug analysers provide noncontact, quick, comfortable, and less operator-dependent anterior segment evaluation and have the potential for screening narrow angles.[9,10] The Sirius rotating Scheimpflug camera combined with Placido disc corneal topography (CSO, Florence, Italy) is a relatively new eye anterior segment analyser; its agreement with other devices has been reported previously.[11-14] As for every new device, it needs to be validated by assessing its repeatability. Several studies have shown the repeatability of IA, ACD, and ACV measurements of the Sirius in normal eyes, but only one study has described ACD and ACV measurements in post-refractive surgery eyes.[11-18] To the best of our knowledge, repeatability of IA measurements of the Sirius in post-refractive surgery eyes were not investigated to date. Thus, the aim of this study was to investigate the repeatability of IA, ACD, and ACV measurements of the Sirius in eyes of people who had undergone myopic excimer laser surgery and to compare them with the measurements done in healthy eyes.

MATERIAL AND METHODS

The Medical Ethics Committee of the Bakırköy Dr Sadi Konuk Training and Research Hospital of the Ministry of Health University approved the present study; the study was conducted in accordance with the principles of the Declaration of Helsinki (Etik kurul sayı: 2018-15-03, Etik kurul tarih: 03.Eylül.2018). Informed consent was obtained from all participants. We prospectively enrolled subjects who are older than 18 years old, do not use contact lenses, did not have any ocular surgery, are without ocular pathologies other than refractive errors, and underwent laser-assisted in situ keratomileusis (LASIK) or photorefractive keratectomy (PRK) for the treatment of myopia and/or myopic astigmatism. Preoperative and postoperative cycloplegic refraction, air-puff tonometry, anterior segment evaluation, and dilated fundus examination were performed on all patients. The mean spherical equivalent refraction was -0.46±1.77 Diopters (D) in unoperated eyes and -0.92±2.48 D in postrefractive surgery eyes.

SIRIUS DATA ACQUISITION

We measured IA, ACD, and ACV using a Sirius-running Phoenix software (version 3.4.0.73). The Sirius uses 475-nm wavelength blue LED flash illumination and derives these parameters solely from its Scheimpflug camera. The scanning process acquires a series of 25 Scheimpflug images. Glaucoma mode of the Sirius provides nasal and temporal IA values at different meridians (specifically; 0°, +10°, +20°, +30°, -10°, -20°, and -30° degrees) automatically and an average IA value (specifically; average IA). The Sirius device measures central ACD from the endothelial side of the cornea to the anterior surface of the crystalline lens. The ACV is measured between the corneal endothelium and the anterior surface of the lens and is calculated on a maximum diameter of 12 mm. An experienced technician conducted all measurements consecutively for three times at the same time of the day to avoid diurnal variations, between 09:00 and 16:00.

Between the measurements, the patients were asked to sit back and blink completely.

STATISTICAL ANALYSIS

Statistical analyses were performed using Prism 7.0 software (Graphpad Software Inc). The level of significance was set at α=0.05. The D'Agostino-Pearson normality test was used to assess the normality of the data. Only one eye of each subject was included in order to avoid bias. We calculated a repeated measures one-way analysis of variance (ANOVA), intraclass correlation coefficient (ICC), within-subject standard deviation (S_w), intrasession test-retest variability, and coefficient of variation (COV) to determine repeatability. ICC is an ANOVA-based correlation, and it was calculated using the following equation: $(m \times SS_B)$- $SS_T/(m-1) \times SS_T$, where m is the number of measurements per patient, SS_B is the sum of squares between subjects, and SS_T is the total sum of squares.[19] ICC values ranged between 0 to 1 and was classified as follows: if ICC is higher than 0.9, it indicates a high agreement; if it is between 0.75 and 0.9, it indicates a moderate agreement; and if it is less than 0.75, it indicates a poor agreement. The S_w is the standard deviation of repeated measurements and a simple means of estimating measurement error. Intrasession test-retest variability is sometimes called the repeatability and calculated by $2.77 \times S_w$.[20] COV was defined as the ratio of S_w to the overall mean and expressed as a percentage.[21] Additionally, we performed independent samples *t* tests to compare age, mean values of each parameter, S_w of each parameter between the unoperated and operated group, and S_w of each parameter between the younger group (subjects younger than 40 years of age) and older group (subjects older than 40 years of age). Paired t tests were used to compare nasal and temporal IA values and S_w of each meridian (e.g. between nasal 0° and temporal 0° or nasal 20° and temporal 20°). Using Pearson's correlation coefficient (*r*), we evaluated the relationship between the magnitude of the measured parameter and the corresponding S_w value.

RESULTS

This study included 50 eyes of 50 subjects without a history of refractive surgery and with a mean age of 42.6 years (unoperated eyes, ranged between 18 to 67 years, 32 females and 18 males) and 13 eyes of 13 subjects who had undergone LASIK or PRK with a mean age of 39.1 years (operated eyes, ranged between 28 to 58 years, 6 females and 7 males). Age, IA, ACD, and ACV values passed the normality test ($p>0.05$). The difference in mean age between the operated and unoperated eyes was statistically insignificant ($p=0.387$). We did not find any statistically significant differences between the consecutive measurements using repeated measures ANOVA in both groups. Table 1 displays the mean value for each parameter in unoperated and operated eyes. Independent samples t test results showed statistically significant differences only in the nasal angle 30° and temporal angle 30° values between the two groups (Table 1).

We observed significant differences between the magnitude of the IA measurements of the same nasal and temporal meridians ($p<0.001$) in all meridians. Similarly, all S_W values for nasal angle measurements at each meridian (-30° to 30°) were significantly higher than those for temporal meridians ($p<0.001$). Table 2 displays the relationships between the S_w value and the magnitude of the corresponding parameter. For IA measurements, with the exception of temporal angle 10°, S_w negatively and significantly correlated with the angle magnitude of the corresponding meridian. Namely, variability of the IA measurements of the device was higher in narrow angles and lower in wider angles. Moreover, S_w for ACD measurements was positively correlated with the ACD magnitude. Finally, S_w for ACV measurements did not show any correlation with ACV magnitude.

Table 3 and Table 4 present the ICC, test-retest variability, and COV for each parameter examined in the present study for unoperated eyes and operated eyes, respectively. Repeatability of average IA was good with ICC > 0.90 and COV ≤ 4.18%. For the IA measurements at different meridians, the ICC value was below 0.9 at all nasal meridians, with the exception of nasal angle 10° in operated eyes and higher than 0.8 for all temporal meridians. For the ACD and ACV measurements, repeatability was excellent with ICC > 0.99 and COV < 1.5% in both groups.

TABLE 1: Mean values for each parameter obtained with the Sirius device in unoperated eyes and post-refractive surgery eyes. Values are expressed as mean ± standard deviation.

	Unoperated eyes	Post-refractive surgery eyes	p value*
Parameter			
Average IA (degrees)	40.92±6.07	43.77±8.10	0.17
IA at different meridians (degrees)			
Nasal angle 0°	37.98±7.30	41±9.05	0.21
Nasal angle 10°	36.78±8.22	40.15±9.73	0.21
Nasal angle 20°	36.62±8.88	41.08±9.39	0.12
Nasal angle 30°	36.85±8.76	42.69±8.24	0.04
Nasal angle –10°	37.62±8.29	40.69±9.42	0.25
Nasal angle –20°	38.02±8.21	40.85±9.49	0.29
Nasal angle –30°	38.76±7.57	41.62±10.55	0.27
Temporal angle 0°	44.54±5.08	45±8.32	0.80
Temporal angle 10°	43.98±5.36	45.92±7.97	0.30
Temporal angle 20°	43.64±5.57	46.54±6.88	0.12
Temporal angle 30°	43.96±5.15	48.54±7.01	0.01
Temporal angle –10°	44.2±5.37	45.46±8.17	0.50
Temporal angle –20°	44.45±6.31	46.23±7.41	0.39
Temporal angle –30°	44.66±6.16	46.46±8.08	0.38
ACD (mm)	2.92±0.36	3.11±0.50	0.13
ACV (mm^3)	151.1±31.98	167.7±43.32	0.13

IA: iridocorneal angle; ACD: anterior chamber depth; ACV: anterior chamber volume; *: independent samples t test.

TABLE 2: Relationships between the magnitude of the measured value and within-subject standard deviation for each parameter.

	r	p
Parameter		
Average IA (degrees)	-0.249	0.049*
IA at different meridians (degrees)		
Nasal angle 0°	-0.441	< 0.001*
Nasal angle 10°	-0.369	0.003*
Nasal angle 20°	-0.444	< 0.001*
Nasal angle 30°	-0.273	0.033*
Nasal angle -10°	-0.322	0.01*
Nasal angle -20°	-0.317	0.011*
Nasal angle -30°	-0.293	0.021*
Temporal angle 0°	-0.280	0.026*
Temporal angle 10°	-0.197	0.122
Temporal angle 20°	-0.499	<0.001*
Temporal angle 30°	-0.263	0.039*
Temporal angle-10°	-0.344	0.006*
Temporal angle -20°	-0.262	0.040*
Temporal angle -30°	-0.355	0.004*
ACD (mm)	0.361	0.004*
ACV (mm^3)	0.125	0.330

IA: iridocorneal angle; ACD: anterior chamber depth; ACV: anterior chamber volume; *: independent samples t test.

We did not observe any statistically significant differences in the mean variance of each parameter ($p<0.05$) between unoperated and operated eyes, with the exception of temporal angle 0°, and between subjects in the older group (27 eyes) and younger group (36 eyes). These results indicate that repeatability of the Sirius mostly did not change after myopic refractive laser surgery or with age.

DISCUSSION

To our knowledge, this study is the first to evaluate glaucoma mode of the Sirius device in post-refractive surgery eyes. In this study, we found that refractive laser treatment did not influence the validity of measurements, with the exception of temporal angle 0^0. We revealed that IA (the average of IA values which were measured from different meridians) and temporal IA measurements provided by the Sirius were highly repeatable. Masoud et al. (ICC = 0.94) and Prakash et al. also (ICC=0.995) reported excellent repeatability for IA value in healthy eyes, but they did not evaluate the glaucoma mode of the device (namely, IA values measured from different meridians).[15,17]

TABLE 3: Intrasession repeatability outcomes for measurements obtained using the Sirius device in unoperated eyes.

	ICC	Sw	Test-retest repeatability	Coefficient of variation
Parameter				
Average IA (degrees)	0.916	1.71	4.74	4.18
IA at different meridians (degrees)				
Nasal angle 0°	0.727	4.15	11.50	11.29
Nasal angle 10°	0.781	3.98	11.03	11.06
Nasal angle 20°	0.794	3.79	10.51	10.52
Nasal angle 30°	0.726	4.20	11.63	11.53
Nasal angle −10°	0.789	3.68	10.18	9.87
Nasal angle −20°	0.861	3.16	8.75	8.41
Nasal angle −30°	0.797	3.56	9.85	9.25
Temporal angle 0°	0.883	1.85	5.13	4.16
Temporal angle 10°	0.933	1.40	3.88	3.17
Temporal angle 20°	0.937	1.39	3.84	3.17
Temporal angle 30°	0.912	1.60	4.44	3.66
Temporal angle −10°	0.882	1.88	5.21	4.26
Temporal angle −20°	0.968	1.08	2.98	2.41
Temporal angle −30°	0.851	2.68	7.43	6.03
ACD (mm)	0.994	0.03	0.08	0.93
ACV (mm^3)	0.996	2.03	5.63	1.35

ICC: intraclass correlation coefficient; Sw : within-subject standard deviation; IA: iridocorneal angle; ACD: anterior chamber depth; ACV: anterior chamber volume.

TABLE 4: Intrasession repeatability outcomes for measurements obtained using the Sirius device in post-refractive surgery eyes.

	ICC	Sw	Test-retest repeatability	Coefficient of variation
Parameter				
IA (degrees)	0.963	1.45	4.01	3.30
IA at different meridians (degrees)				
Nasal angle 0°	0.813	3.62	10.01	8.78
Nasal angle 10°	0.906	2.77	7.68	6.80
Nasal angle 20°	0.857	3.07	8.51	7.54
Nasal angle 30°	0.842	2.73	7.57	6.48
Nasal angle −10°	0.845	3.18	8.81	7.69
Nasal angle −20°	0.742	4.45	12.33	10.78
Nasal angle −30°	0.725	4.67	12.94	10.93
Temporal angle 0°	0.931	2.21	6.11	4.93
Temporal angle 10°	0.947	1.82	5.03	4.0
Temporal angle 20°	0.934	1.89	5.24	4.12
Temporal angle 30°	0.938	1.72	4.76	3.60
Temporal angle −10°	0.961	1.68	4.64	3.70
Temporal angle −20°	0.942	1.95	5.41	4.28
Temporal angle −30°	0.920	2.42	6.71	5.29
ACD (mm)	0.997	0.03	0.07	0.84
ACV (mm^3)	0.996	2.43	6.73	1.46

ICC: intraclass correlation coefficient; Sw : within-subject standard deviation; IA: iridocorneal angle; ACD: anterior chamber depth; ACV: anterior chamber volume.

On the other hand, repeatability of nasal IA measurements were lower than temporal measurements in both groups. Similarly, Ruiz-Belda et al. found that the repeatability of nasal IA measurements of the Sirius was lower than temporal IA measurements in healthy subjects (for the nasal angle 30°, ICC = 0.778 and test-retest variability = 9.07°; for the nasal angle 20°, ICC = 0.865 and test-retest variability = 10.92°).[16] In this study, for most of the nasal meridians, test-retest variability of the device was more than 10°. Ruiz-Belda et al. hypothesised that the lower repeatability of nasal measurements of the device might be related to the interfered nasal angle scanning due to the nose, eyelid, or supercilium.[16] We hypothesise that the reason for higher variability in nasal angle measurements is that the device has lower ability to measure narrow angles. In the present study, angle width and the corresponding S_w value were inversely correlated, and the nasal angles were narrower than temporal angles at the same meridian. Consistently, Kurita et al. found that the difference between the IA measurements of the Pentacam device -another Scheimpflug device- and the ultrasound biomicroscopy was greater in eyes with a narrower IA.[10] They speculated that this discrepancy is owing to the lower ability of the Pentacam device to scan the most peripheral part of the iris and the base of the IA in eyes with a narrow angle.

The present study confirmed the previously reported high repeatability of the ACD measurements of the Sirius device in healthy eyes and in operated eyes.[11,15,18] We found values of 0.07 mm and 0.08 mm test-retest repeatability in this study for unoperated and operated eyes, respectively, and those values were very close to those in previous works which used the Sirius device. For example, Savini et al. found a value of 0.03 mm test-retest repeatability for the post-refractive surgery eyes.[18] For the unoperated eyes, Savini et al. revealed a value of 0.04 mm and Wang et al. and Chen et al. found a value of 0.07 mm test-retest repeatability.[13,14,18] Similarly, Masoud et al. and De la Parra-Colin showed values of 0.03 mm and 0.018 mm S_w for the ACD measurements of the Sirius, respectively (in this study, S_w = 0.03 mm for ACD measurements).[11,15]

According to the results of this study, repeatability of the Sirius device for ACV measurements was high, and it did not change after refractive laser surgery. These results are consistent with the results of Savini et al.'s study which reported an ICC of 0.995 for unoperated eyes and 0.994 for operated eyes and a COV of 1.62% for unoperated eyes and 0.96% for operated eyes.[18] The results were also consistent with Prakash et al.'s study which reported an ICC of 0.988 for healthy eyes.[17] On the other hand, Masoud et al. reported a lower repeatability for the ACV measurements of the device (ICC=0.58 and COV = 3.52%) in a study with 50 healthy eyes.[15] The reason for this disparity is not clear because the designs and study populations of these three studies were very similar but might be related to software versions of the devices used in these studies (version 2.0 in Savini et al.'s study, Phoenix version 2.1 in Prakash et al.'s study, unspecified in Masoud et al.'s study).[15,17,18] Previous studies which evaluated the ACV measurements of the device did not verify the relationship between the ACV magnitude and variability of the devices' ACV measurements.[15,17,18] Impressively, the magnitude of the ACV measurement does not limit the reliability of the ACV measurements. Harmoniously, ACV measurements of the Pentacam device have been found to have the highest discriminative ability for the detection of narrow angles and primary angle closure in the respective studies of Grewal et al. and Kurita et al.[10,22]

Moreover, the IA, ACD, and ACV measurements of the Sirius device are not negatively affected by age. Ruiz-Belda et al. reported results similar to ours for the IA measurements and Savini et al. or the ACD and ACV measurements.[16,18]

Limitations of the present study are as follows. First, this study did not investigate the agreement between the glaucoma summary mode of the Sirius system and the gonioscopy, which is the golden standard of iridocorneal angle examination. Second, we primarily included healthy eyes and post-refractive surgery eyes. Therefore, prospective studies including eyes with different types of glaucoma are still needed to assess the validity of the device in this condition. Finally, we evaluated the patients who underwent LASIK or PRK in the same study group. This might be criticized but similar studies investigated repeatability of ACD and ACV measurements of the Sirius device and IA, ACD, and ACV measurements of the Galilei (Ziemer group, Port, Switzerland) device used similar methodology.[18,23]

In conclusion, iridocorneal angle measurements of the Sirius device at temporal meridians showed high or moderate repeatability, whereas at nasal meridians, it showed poor or moderate repeatability in both normal and post-refractive surgery eyes. Considering the poor repeatability of the device in nasal meridians, which we observed in both groups, the glaucoma mode of the device should not be used alone in the iridocorneal angle examinations. On the other hand, ACD and ACV measurements of the Sirius showed excellent repeatability and, therefore, can be confidently used in clinical practices as well as for research purposes.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

***Idea/Concept:** Ertugrul Tan Yassa, Cihan Ünlü, Tugba Kurt; **Design:** Ertugrul Tan Yassa, Cihan Ünlü, Tugba Kurt; **Control/Supervision:** Ertugrul Tan Yassa, Cihan Ünlü, Tugba Kurt; **Data Collection and/or Processing:** Ertugrul Tan Yassa, Cihan Ünlü, Tugba Kurt; **Analysis and/or Interpretation:** Ertugrul Tan Yassa, Cihan Ünlü, Tugba Kurt; **Literature Review:** Ertugrul Tan Yassa, Cihan Ünlü, Tugba Kurt; **Writing the Article:** Ertugrul Tan Yassa, Cihan Ünlü; **Critical Review:** Ertugrul Tan Yassa, Cihan Ünlü, Tugba Kurt; **References and Fundings:** Ertugrul Tan Yassa; **Materials:** Ertugrul Tan Yassa, Cihan Ünlü, Tugba Kurt.*

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