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Abstract

Purpose: To determine the level of stereopsis in anisometropic children with or without amblyopia using corrective glasses and to investigate the effect of type and magnitude of anisometropia on the level of stereopsis.

Methods: Medical records of 256 children with the diagnosis of non-amblyopic anisometropia, anisometropic amblyopia, and healthy controls were retrospectively reviewed for this study. The anisometropia was categorized into three groups: The spherical equivalent anisometropia alone, the astigmatic anisometropia alone, and combined anisometropia groups. The level of stereopsis was measured with the Titmus stereo test and compared among groups. The correlation of the stereopsis with the magnitude of anisometropia was also analyzed.

Results: Patients in the non-amblyopic anisometropia group had similar stereopsis levels with the control group (55.2±41.03 and 47.2±19.8 sec of arc, respectively, p=0.223). On the other hand, the stereopsis was significantly more reduced in the anisometropic amblyopia group (279.4±120 sec of arc) compared to the non-amblyopic anisometropia (55.2±41.03 sec of arc) and control groups (47.2±19.8 sec of arc) (p=0.008, p=0.006, respectively). Higher spherical equivalent difference between eyes resulted in worsening stereopsis in the anisometropic amblyopia group, and the combined anisometropia subtype was found to be related to worse stereopsis levels in the non-amblyopic anisometropia group.

Conclusion: Non-amblyopic anisometropia patients had a similar level of stereopsis with controls while wearing their corrective glasses. This result provides us that as long as patients have good visual acuity, stereopsis is preserved, and refractive correction with glasses does not interfere with stereopsis in childhood anisometropia.

Key Words: anisometropia; amblyopia; depth perception; children; stereopsis

Introduction

Anisometropia is a status that sphero-cylindrical refractive error varies significantly among
two eyes. It may cause discordant binocular vision in the critical visual development period of life, and this can cause amblyopia (1,2). Increased anisometropia amplitude is related to higher risk and severity of amblyopia, so some guidelines recommend the degree of anisometropia should be corrected to prevent the development of amblyopia (3).

Stereopsis is the ability of depth perception depending on the sensorial fusion of the disparate retinal images from two eyes (4). Good binocular visual acuity and healthy visual pathway are necessary for the development of stereopsis. It has been shown that problems like amblyopia, anisometropia, cylindrical refractive error and aniseikonia may result in reduced stereo acuity (4-7).

While it is evident that amblyopia is associated with reduced stereopsis, the results in anisometropia without amblyopia differ in the literature. Lee et al.(8) reported that the stereopsis was worse, and the ratio of subjects with normal stereo acuity was also lower in the non-amblyopic anisometropic patients while using their anisometropic glasses. Contrary, Jeon et al.(9) found that stereopsis in the non-amblyopic anisometropic group did not vary meaningfully from non-anisometropic control while it was worse in amblyopic anisometropia.

The current study aimed to determine the level of stereopsis in anisometropic patients with or without amblyopia wearing corrective eyeglasses. We also investigated the effect of type and magnitude of anisometropia on the stereopsis level.

Methods

The study was carried out in conformity with the Helsinki Declaration, with the approval by the Institutional Review Board of Istanbul Medipol University (issue number: 10840098-604.01.01-E.64942, approval date:11.12.2019).

Medical records of 256 children (age range: 5-17 years) with the diagnosis of non-amblyopic anisometropia (NA), anisometropic amblyopia (AA), and healthy controls without anisometropia were retrospectively reviewed between January 2017 and January 2020.
**Inclusion Criteria**

For the inclusion criteria, anisometropia was defined as ≥0.5 D of spherical equivalent (SE) or ≥1.5 D cylindrical refractive error difference, and amblyopia was described as the best-corrected visual acuity (BCVA) difference of ≥2 Snellen lines between the eyes (10). The anisometropia was categorized into three groups:

1. **SE anisometropia alone group** includes subjects who have SE difference ≥0.5 D in the absence of astigmatic refractive error difference ≥1.5 D between eyes.
2. **Astigmatic anisometropia alone group** includes subjects who have astigmatic refractive error difference ≥1.5 D in the absence of SE difference ≥1.5 D between eyes.
3. **Combined anisometropia group** includes subjects who have both SE and astigmatic refractive error difference ≥1.5 D between eyes (10).

While evaluating the astigmatic anisometropia, because all patients with significant cylindrical refractive error had a cylindrical axis within 10 degrees of symmetry, the axis was not taken into consideration. Control group included children without anisometropia, and whose visual acuity was 10/10 with Snellen chart with correction of refractive error if needed.

**Exclusion Criteria**

The exclusion criteria for the present study were; ocular surgery or trauma history, abnormal eye alignment at a distance or near fixation or other types of amblyopia, corneal abnormality, and optic disc or retinal diseases.

**Study procedures**

All participants underwent an ophthalmic examination (visual acuity testing with Snellen charts, orthoptic screening, slit-lamp, and dilated fundus evaluations). The subjects’ BCVA was transformed into the LogMAR scale. The cycloplegia was performed by applying cyclopentolate 1% three times and thirty minutes later, autorefraction was done by using an auto keratorefractometer (KR-8900; Topcon Co, Tokyo, Japan). Stereopsis was tested using the Titmus stereo test (Stereo Optical Co., Inc., Chicago, IL, USA). Gross stereopsis was evaluated by asking to patients to pinch the tip of the wing of fly. Then, fine stereopsis was evaluated with circle patterns. Patients were asked to tell the
one which seems to come out nearer to them. Patients wore polarized glasses over their appropriated refractive corrections and all subjects were asked to be wearing their best refractive corrected glasses for at least 16 weeks. Refractive corrections were based on the cycloplegic refraction. Myopia and astigmatism were corrected in full, whereas hypermetropia was usually under-corrected by up to 1.5 D. Patients, who were prescribed glasses for the first time, were re-evaluated after 16 weeks refractive adaptation period. The stereopsis level after this period was used in the analysis.
Stereacuity was compared among groups (NA, AA and, healthy controls), and the effects of SE and cylindrical power difference, BCVA, and type of anisometropia on stereopsis were also evaluated.

Statistical Analysis
All statistical analyses were done using SPSS 19 (SPSS for Windows, Chicago, IL, USA). Pearson’s chi-square test was used to compare differences in gender. The normality between samples was assessed with the Kolmogorov-Smirnov test. Because the data distribution was not normal Kruskal-Wallis tests and then for post-hoc analysis, Mann-Whitney U tests with Bonferroni correction were used to compare groups in terms of age, BCVA, refractive error, anisometropia magnitude, and stereopsis level. The correlation of the stereopsis with SE and cylindrical power differences and BCVA were evaluated with Spearman’s correlation coefficient. P<0.05 was set up statistically significant.

Results
The baseline characteristics and the stereopsis level for the 256 subjects (124 females, 132 males) divided into the NA (n=100), AA (n=52), and healthy controls (n=104) are provided in Table 1. The patients’ mean age was 9.6±2.9 years (range 5-17 years). There was no remarkable difference in terms of gender and age distributions among the groups (p=0.492 and p=0.060, respectively). Worse eye describes the eyes with higher refractive error for the AA and NA group.
The mean SE of the better eye in the AA group was higher than the control group (p<0.001). However, SE values of the better eyes were not importantly different between the NA group and the AA and control groups (p=0.401 and p=0.048, respectively). The mean SE of the worse eyes in the NA and AA groups were significantly higher than that in the control group (p=0.009 and p<0.001 respectively), while SE in the AA group was higher than the NA group (p=0.041). The SE difference between the eyes was remarkably greater in the AA group compared to the NA group (p<0.001). The cylindrical refractive error of the better eye in the AA group was significantly higher than the control group (p=0.025). There was no important difference between the NA group and the AA and control groups (p=0.696 and p=0.147, respectively). The cylindrical refractive error of the worse eyes in the NA and AA groups were significantly higher than the control group (p<0.001 for both), while it did not vary between the NA and AA groups (p=0.325). There was no differentiation between the NA and AA groups in terms of cylindrical refractive error difference (p=0.411).

The mean level of stereopsis was significantly worse in the AA group compared to the NA and control groups (p=0.008 and p=0.006, respectively). However, the NA and control groups had similar stereopsis results (p=0.223).

When the results of stereopsis were compared among three subtypes in the NA group, combined anisometropia group had significantly lower stereopsis levels compared to the astigmatic anisometropia and spherical anisometropia groups (p=0.012 and p=0.036 respectively). Still, there was no important difference between the spherical anisometropia and astigmatic anisometropia groups (p=0.707). On the other hand, the difference was not significant among the three subtypes in the AA group (p=0.164) (Table 2).

There was a significant correlation between the level of stereopsis and SE difference, cylindrical power difference, and BCVA of the worse eye in the total anisometropic patients (NA+AA groups) (r=0.381, p<0.001; r=0.176, p=0.030; r=0.642, p<0.001, respectively). In the AA group, increasing SE difference between eyes and decreasing BCVA resulted in worsening stereopsis (r=0.328, p=0.017; r=0.608, p<0.001, respectively). However, there was
Discussion

In the current study, the stereopsis level of anisometropic patients using their corrective glasses was evaluated with the Titmus stereo test. The results showed that patients in the NA group had similar stereopsis levels with the control subjects. On the other hand, the stereopsis was remarkably poorer in the AA group compared to the NA and control groups. Increased SE difference between eyes and decreased BCVA resulted in worsening stereopsis in the AA group, and the combined anisometropia subtype was found to be related to worse stereopsis levels in the NA group.

Anisometropia may lead to amblyopia secondary to a defocusing image at the fovea or active suppression mechanism (11). It has also been shown that anisometropia, even in the absence of amblyopia, may affect binocular vision and cause decreased stereopsis (8-15). Since decreased visual acuity may cause difficulty in the differentiation of stereo acuity test targets, it is expected to find that the level of stereopsis correlates with the amount of anisometropia and depth of amblyopia. Chen et al. (12) evaluated the stereopsis level of previously untreated anisometropic amblyopia patients using the Lang stereo acuity test, and they found that larger degrees of anisometropia induce poorer stereopsis. They also noticed that when anisometropia magnitude less than 3D, 80% of patients retain stereopsis smaller than 1200 sec-arc, but when anisometropia magnitude between 3 to 6D, 80% patients have an absence of stereopsis function.

Wallace et al. (10) included 633 subjects from Pediatric Eye Disease Investigator Group studies with moderate anisometropic amblyopia to determine the factors associated with pre-treatment and post-treatment stereo acuity. They used the Randot Preschool Stereoacuity test to evaluate the stereopsis level, and they reported that better stereo acuity was associated with less anisometropia and better visual acuity. On the other hand, Jeon et al.(9) reported no
important relation between the anisometropia degree and stereopsis level using the Titmus stereo test in their study with thirty-five amblyopic anisometropia patients. Similar to Chen et al.’s (12) and Wallace et al.’s (10) studies, we found that increasing SE difference between eyes and decreasing BCVA resulted in worsening stereopsis in the AA group. Wallace et al. (10) reported that anisometropia due to astigmatism alone was associated with better stereovision in their anisometric amblyopia patients. But, in the current study, no significant difference was shown among the three types of anisometropia.

In the literature, the results of the studies about the effect of NA on stereopsis are conflicting. Jeon et al. (9) evaluated 72 NA patients using the Titmus stereo test, and they reported that the NA patients had a similar level of stereopsis with the patients in the control group. Still, they noticed that the increased anisometropia magnitude caused worsening in stereopsis. Lee et al. (8) reported a stereopsis level of 106 non-amblyopic patients wearing glasses for anisometropia using the Titmus-fly and Randot stereo test. Although they found better stereopsis levels in the isometric patients compared to anisometric patients, they thought that anisometric patients wearing their glasses had clinically near-normal stereopsis level and they reported no significant association between the anisometropia magnitude and stereopsis (8). Also, in the Pediatric Eye Disease Investigator Group study, even if their visual acuity deficit resolved, many children with AA had worse stereopsis compared to non-amblyopic age-matched group (10). Similar to Jeon et al.’s study (9), we didn’t show a difference in the stereopsis level of non-amblyopic anisometropia and isometric patients and similar to Lee et al.’s (8) study there was no significant relationship between the stereopsis level and SE difference. Lee et al. (8) also analyzed the effect of type of anisometropia on stereopsis and, they found that the stereopsis did not significantly vary among the subtypes of anisometropia (spherical, astigmatic, or mixed type). Contrary, the combined anisometropia group had the worst stereopsis result in the present study.

Aniseikonia, the difference in recognized retinal image size between eyes, is thought as an issue that should be considered while prescribing anisometric glasses by many practitioners. Studies showed that higher than 3-5% magnification difference between eyes
begins to disrupt binocular vision and decrease stereopsis (16,17). Both anisometropia itself and its optical correction can induce aniseikonia, and it is shown that contact lens usage instead of glasses may end with less image size difference (18). The result of the present study showed us that non-amblyopic anisometropia with corrective glasses did not interfere with binocular functions and stereopsis. It might be thought that the existence of good stereopsis mostly depends on good visual acuity, and aniseikonia created by corrective eyeglasses is clinically well tolerated under normal viewing conditions.

There are some limitations to this study. First, there was a lack of information about the history of amblyopia treatment in the NA group. After visual acuity deficit resolves with the treatment of amblyopia, subnormal stereopsis may persist, so this may have affected our outcome. Second, we didn't know how old the patients were when they first wore glasses. We selected patients who had been wearing glasses at least 16 weeks for an adaptive refractive period. Still, there might be a relationship between the level of stereopsis and time of first glasses usage. On the other hand Lee et al.8 reported no significant relationship between the age at the time of prescription of the first glasses and the level of stereopsis for anisometropic patients. Third, subgroups based on anisometropia type differed in size, which may have been a source of bias. Fourth, usage of the Titmus stereo test is another limitation. It may overestimate stereoacuity due to some monocular clues.19

Studies with larger patient groups, where patients can be evaluated for a longer period of time before and after wearing glasses, will be more helpful in understanding the relationship between anisometropia and stereopsis. In addition, the evaluation of stereopsis after correction of anisometropia by refractive surgery in appropriate age patients may be the subject of another study.

Conclusion

In conclusion, NA patients had a similar level of stereopsis with isometric controls while wearing their corrective glasses, and the level of stereopsis was not correlated to anisometropia magnitude in the NA patients. This result provides us that as long as patients...
have good visual acuity, stereopsis is preserved, and refractive correction with glasses does not cause aniseikonia, which may interfere with stereopsis in childhood anisometropia. Therefore, we can recommend the use of glasses for the prevention and treatment of amblyopia to our anisometropic patients.

Ethics Committee Approval: This prospective study was approved by the ethics committee of the Istanbul Medipol University, Date:11.12.2019, Number: 10840098-604.01.01-E.64942.

Conflict of Interest: All authors certify that they have no financial conflict of interest.

References


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Table 2. The results of the three types of anisometropia in the non-amblyopic anisometropia and anisometropic amblyopia groups.
Table 3. Correlation between the level of stereopsis and spherical equivalent difference, cylindrical power difference and visual acuity of the worse eye.
Table 1. Demographics and level of stereopsis among groups.

<table>
<thead>
<tr>
<th></th>
<th>NA group (n=100)</th>
<th>AA group (n=52)</th>
<th>Control group (n=104)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (F:M)</td>
<td>47:53 (47%)</td>
<td>29:23 (55.7%)</td>
<td>48:56 (46.1%)</td>
<td>0.492†</td>
</tr>
<tr>
<td>Age (years)</td>
<td>10.1±2.9 (5-16)</td>
<td>9.6±2.7 (6-17)</td>
<td>9.1±2.8 (5-16)</td>
<td>0.060†</td>
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<tr>
<td>BCVA_better (LogMAR)</td>
<td>0.0005±0.005 (0-0.05)</td>
<td>0.0029±0.01 (0-0.05)</td>
<td>0.001±0.006 (0-0.05)</td>
<td>0.172†</td>
</tr>
<tr>
<td>BCVA_worse (LogMAR)</td>
<td>0.0045±0.01 (0-0.1)</td>
<td>0.24±0.18 (0.1-0.8)</td>
<td>0.001±0.006 (0.0-0.05)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>SE_better (D)</td>
<td>0.93±2.41 (-8.0/+6.0)</td>
<td>1.41±3.34 (-2.5/+5.75)</td>
<td>0.23±1.76 (-5.25/+4.5)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>SE_worse (D)</td>
<td>1.41±3.34 (-8.50/+8.25)</td>
<td>2.85±3.40 (-8.75/+7.50)</td>
<td>0.28±1.83 (-5.50/+4.50)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>SED (D)</td>
<td>1.13±0.80 (0.25-5.0)</td>
<td>2.43±1.83 (0.1-0.8)</td>
<td>0.10±0.12 (0.0-0.5)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>C_better (D)</td>
<td>0.72±0.89 (-3.50)</td>
<td>0.89±1.06 (-4.0)</td>
<td>0.50±0.78 (-4.0)</td>
<td>0.016†</td>
</tr>
<tr>
<td>C_worse (D)</td>
<td>1.41±1.43 (-0.475)</td>
<td>1.81±1.55 (-0.525)</td>
<td>0.68±0.95 (-0.4-0.50)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>CD (D)</td>
<td>0.68±0.9 (0-4.75)</td>
<td>0.91±0.9 (0-4.50)</td>
<td>0.17±0.3 (0-1.25)</td>
<td>&lt;0.001†</td>
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</tbody>
</table>

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NA: non-amblyopic anisometropia; AA: amblyopic anisometropia; F: female; M: male
BCVA_better: best-corrected visual acuity of the better eye; BCVA_worse: best-corrected visual acuity of the worse eye
SE_better: spherical equivalent of the better eye; SE_worse: spherical equivalent of the worse eye
D: dioptr; SED: spherical equivalent difference between eye; C_better: cylindrical refractive error of the better eye; C_worse: cylindrical refractive error of the worse eye
CD: cylindrical refractive error difference
* Pearson’s chi-square test; † Kruskal-Wallis test; ‡ result of right eye; § result of left eye

<table>
<thead>
<tr>
<th>Stereopsis</th>
<th>55.2±41.03</th>
<th>279.4±120.0</th>
<th>47.2±19.8</th>
<th>&lt;0.001†</th>
</tr>
</thead>
<tbody>
<tr>
<td>(second of arc)</td>
<td>(40-400)</td>
<td>(40-3552)</td>
<td>(40-200)</td>
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Table 2. The results of the three types of anisometropia in the non-amblyopic anisometropia and anisometropic amblyopia groups

### Non-amblyopic anisometropia group

<table>
<thead>
<tr>
<th></th>
<th>SE Anisometropia (n= 81)</th>
<th>Astigmatic Anisometropia (n=14)</th>
<th>Combined Anisometropia (n=5)</th>
<th>p value</th>
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<tbody>
<tr>
<td>Gender(F:M)</td>
<td>43:38 (53%)</td>
<td>3:11 (21.4%)</td>
<td>1:4 (20%)</td>
<td>0.043*</td>
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<tr>
<td>(Female %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>10.2±2.9</td>
<td>9.3±2.6</td>
<td>9.8±4.3</td>
<td>0.599†</td>
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<tr>
<td>BCVA_worse (LogMAR)</td>
<td>0.00±0.01</td>
<td>0.00±0.01</td>
<td>0.01±0.02</td>
<td>0.369†</td>
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<tr>
<td>Stereopsis (second of arc)</td>
<td>55.8±44.2</td>
<td>44.2±7.5</td>
<td>76±37.8</td>
<td>0.015†</td>
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### Anisometropic amblyopia group

<table>
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<tr>
<th></th>
<th>SE Anisometropia (n=41)</th>
<th>Astigmatic Anisometropia (n=8)</th>
<th>Combined Anisometropia (n=3)</th>
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<tr>
<td>Gender(F:M)</td>
<td>21:20 (51.2%)</td>
<td>5:3 (62.5%)</td>
<td>3:0 (100%)</td>
<td>0.245*</td>
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<tr>
<td>(Female %)</td>
<td></td>
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<tr>
<td>Age (years)</td>
<td>10.0±2.7</td>
<td>8.7±3.0</td>
<td>7.0±1.0</td>
<td>0.057†</td>
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<td>BCVA_worse (LogMAR)</td>
<td>0.25±0.18</td>
<td>0.14±0.15</td>
<td>0.33±0.31</td>
<td>0.228†</td>
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Table 3. Correlation between the level of stereopsis and spherical equivalent difference, cylindrical power difference and visual acuity of the worse eye

<table>
<thead>
<tr>
<th>NA+AA groups</th>
<th>SED</th>
<th>CD</th>
<th>BCVA_worse</th>
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<tr>
<td>Stereopsis</td>
<td>r= 0.381</td>
<td>r= 0.176</td>
<td>r= 0.642</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.001*</td>
<td>p=0.030*</td>
<td>p&lt;0.001*</td>
</tr>
</tbody>
</table>

SE: spherical equivalent; F: female; M: male; BCVA: best-corrected visual acuity
* Pearson’s chi-square test; † Kruskal-Wallis test

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<table>
<thead>
<tr>
<th>NA group</th>
<th>SED</th>
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<th>BCVA_worse</th>
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<tr>
<td></td>
<td>r= 0.126</td>
<td>r= 0.147</td>
<td>r= 0.128</td>
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<td>Stereopsis</td>
<td>p= 0.212*</td>
<td>p=0.145*</td>
<td>p=0.206*</td>
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<table>
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<th>SED</th>
<th>CD</th>
<th>BCVA_worse</th>
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<tr>
<td></td>
<td>r= 0.328</td>
<td>r= -0.078</td>
<td>r= 0.608</td>
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<tr>
<td>Stereopsis</td>
<td>p= 0.017*</td>
<td>p=0.581*</td>
<td>p&lt;0.001*</td>
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NA: non-amblyopic anisometropia; AA: amblyopic anisometropia; SED: the spherical equivalent difference between eye; CD: cylindrical refractive error difference; BCVA_worse: best-corrected visual acuity of the worse eye.

* Spearman’s correlation.