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Changes in choroidal blood flow and choroidal thickness after treatment in two cases of pediatric anisohypermetropic amblyopia

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A B S T R A C T

Purpose: We aimed to examine the changes in choroidal blood flow (CBF) and central choroidal thickness (CCT) in children with anisohypermetropic amblyopia using laser speckle flowgraphy (LSFG) and enhanced depth imaging optical coherence tomography (EDI-OCT).

Observations: The patients were both 6-year-old Japanese male children with complaints of worsening right visual acuity and were diagnosed with anisohypermetropic amblyopia. The decimal best-corrected visual acuities (BCVAs) in cases 1 and 2 were both 0.5. In both cases, LSFG results demonstrated CBF impairment in amblyopic eyes compared with fellow eyes. EDI-OCT results also showed that the CCTs of amblyopic eyes were greater than those of fellow eyes at the initial visit. Several months after the first visit, the decimal BCVAs in both cases had improved to 1.0 because of treatment. Further, the CBF gradually increased along with a decrease in the CCT of the amblyopic eye. The axial lengths and spherical powers of the amblyopic eyes in the two cases were not different during follow-up.

Conclusions and importance: We have determined the changes in CBF and CCT in two children with anisohypermetropic amblyopia for the first time. CBF impairments may be involved in the pathogenesis of anisohypermetropic amblyopia, and LSFG may be useful in examining CBF in pediatric anisohypermetropic amblyopia.

1. Introduction

Amblyopia is a quite common vision disorder in children and causes visual acuity impairment despite normal structural findings in the eye. Previously, amblyopia has been reported to be related to several factors such as strabismus, anisometropia, and from deprivation.[1] Among these factors, anisohypermetropia was thought to be the most frequent risk factor for amblyopia.[2] However, the cause of the visual acuity reduction in anisohypermetropic amblyopia has not been elucidated. Considering these findings, early diagnosis and treatment of anisohypermetropic amblyopia are very important to improve visual acuity in children. Further, it is important to clarify the mechanism by which amblyopia is caused by anisohypermetropia.

Recently, several authors have investigated the choroid in children with anisohypermetropic amblyopia.[3–5] Nishi et al. demonstrated that central choroidal thickness (CCT) was greater in amblyopic eyes than in fellow eyes in children.[6] However, to the best of our knowledge, a long-duration time course of choroidal blood flow (CBF) in anisohypermetropic amblyopia before and after treatment has not yet been investigated. In the present case series, we describe the CBF changes in two cases of anisohypermetropic amblyopia in children.

1.1. Findings

1.1.1. Case 1

A 6-year and 1-month-old Japanese male child presented at the initial visit with a complaint of worsening visual acuity in his right eye. He visited the department of ophthalmology at a local hospital and was diagnosed with anisohypermetropic amblyopia. He was referred to Toho University Sakura Medical Center in Sakura, Japan (referred to hereafter as “our hospital”) to undergo a detailed examination and treatment for anisohypermetropic amblyopia in the right eye. At the initial visit to our hospital, the patient's decimal best-corrected visual acuity (BCVA) of the right eye was 0.5 and that of the left eye was 1.2.

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The refractive status of the patient was measured using an autorefractometer (Kowa Co., Ltd.; Tokyo, Japan) under cycloplegia. One percent atropine eye drops were prescribed twice per day for 1 week before the initial visit. The refractive errors of the amblyopic eye and the fellow eye after the application of a drop of atropine were +4.00 diopters (D) and +1.5 D. Anisometropia was defined as an interocular cycloplegic spherical equivalent difference or astigmatism difference of 1.5 D or greater. We measured axial length using IOL Master® (Carl Zeiss Meditec; Jena, Germany).

The axial length of the amblyopic eye (22.16 mm) was shorter than that of the fellow eye (23.38 mm). Findings related to binocular vision and amblyopia due to strabismus were normal. Slit-lamp and fundus examinations of both eyes were normal. Subsequently, we measured the CBF in the macular region by using laser speckle flowgraphy (LSFG-NAVI™; Softcare Co., Ltd.; Fukuoka, Japan).

At the initial visit, we set the measurement circle at the center of the macula in both the amblyopic eye and the fellow eye. We manually determined the circle's position by comparing infrared reflectance fundus images obtained using optical coherence tomography (OCT) (Spectralis OCTR; Heidelberg Engineering Inc.; Heidelberg, Germany) (Fig. 1A and B) and LSFG color map images. LSFG images from both eyes are shown in Fig. 1C and D. LSFG findings indicated that the fundus image of the amblyopic eye contains cooler colors than that of the fellow eye. LSFG uses the mean blur rate (MBR) as an indicator of blood flow.[7] In this case, the CBF of the amblyopic eye (5.8) was lower than that of the fellow eye (14.5).

CBF is generally influenced by ocular perfusion pressure (OPP) fluctuations.[8] To investigate alterations in OPP over time, we measured the patient's intraocular pressure (IOP) and systolic and diastolic blood pressures (SBP and DBP, respectively) at each measurement point. We used this information to calculate mean blood pressure (MBP) and OPP.

MBP was calculated from the SBP and DBP measurements using the following equation: $MBP = 1/3 \cdot (SBP - DBP) + DBP$. Subsequently, OPP was calculated as the weighted difference between the MBP and IOP using the following equation: $OPP = 2/3 \cdot MBP - IOP$. The difference in OPP between the amblyopic eye (30.3 mmHg) and fellow eye (32.3 mmHg) at the initial visit was not significant.

An OCT examination had normal findings and the central retinal thickness (CRT) was not different between the amblyopic eye (209 μm) and the fellow eye (204 μm). However, enhanced depth imaging OCT (EDI-OCT) indicated that the CCT of the amblyopic eye (387 μm) was greater than that of the fellow eye (250 μm) (Fig. 1E and F). All examinations were performed between 12:00 p.m. and 3:00 p.m. to avoid circadian variations in CCT.[9] Three examiners (J.K., A.H., and M.O.) performed the measurements using LSFG, OCT, and EDI-OCT.

We diagnosed the patient with anisohypermetropic amblyopia based on the above clinical findings and began treatment, which included asking the child to wear glasses full-time and patching the eye for 6 hours per day. Seven months after treatment, the decimal BCVA of the amblyopic eye had gradually improved to 0.8. Fig. 2 shows the time course of the CBF and CCT changes in the amblyopic eyes. LSFG findings indicated that the distributions of warm colors and MBR (8.6) were gradually increased when compared to those obtained at the initial visit (5.8). Moreover, there was a decrease in CCT (377 μm) (Fig. 2A and B). One year after treatment, the decimal BCVA of the amblyopic eye remained at 1.0 and complaints of worsening visual acuity had disappeared. CBF was more greatly increased (9.6) and CCT was decreased (354 μm) (Fig. 2C and D) in the amblyopic eye. The axial lengths and refractive errors of the amblyopic eye after treatment were 22.22 mm and +4.0 D. These values were not different than the values obtained at the initial visit.

The CRTs of the amblyopic and fellow eyes were not different from baseline at the seven-month (214 and 206 μm, respectively) and twelve-month (189 and 183 μm, respectively) visits. Furthermore, neither the CBF nor the CCT of the fellow eye was different during the follow-up period. The OPP of the amblyopic eye remained unaltered during the follow-up period, and had values of 32.8 and 32.2 at 7 and 12 months after the initial visit, respectively.

1.1.2. Case 2

A 6-year and 4-month-old Japanese male child presented at the first visit with complaints of worsening visual acuity in his right eye. He was referred to our hospital from a local hospital to undergo treatment for anisohypermetropic amblyopia. At the first visit to our hospital, the decimal BCVA of the amblyopic eye was 0.5 and that of the fellow eye was 1.2. The refractive errors of the amblyopic and fellow eye following a drop of atropine were +6.25 D and +1.75 D, respectively. The axial length of the amblyopic eye (21.87 mm) was shorter than that of the fellow eye (23.46 mm). There were no abnormal findings from the slit-lamp examination or fundus examination. Fig. 3A and B shows infrared reflectance fundus images; LSFG images of both eyes are shown in Fig. 3C and D. As in case 1, the MBR in the macular region of the amblyopic eye (10.7) was lower than that of the fellow eye (17.9). The difference in OPP between the amblyopic eye (33.8 mmHg) and fellow eye (35.4 mmHg) was not significant at the initial visit. An OCT examination showed normal findings and that the CRT was not significantly different between the amblyopic eye (214 μm) and fellow eye (206 μm). EDI-OCT showed that the CCT of the amblyopic eye (316 μm) was larger than that of the fellow eye (233 μm) (Fig. 3E and F).

We began therapy for anisohypermetropic amblyopia as described for the patient in case 1. Two months after treatment, the decimal BCVA of the amblyopic eye had improved to 0.7. The time courses of the CBF and CCT in the amblyopic eye are shown in Fig. 4. LSFG results indicated that the MBR at the macular region (11.4) was slightly increased when compared to that at the initial visit and that the CCT (294 μm) was decreased in the amblyopic eye (Fig. 4A and B). Eight months after treatment, the decimal BCVA of the amblyopic eye had improved to 1.0 and the MBR of the macular region (13.4) was more greatly increased. At the same time, CCT (287 μm) was decreased when compared to the previous visit (Fig. 4C and D). The axial length and refractive error of the amblyopic eye after treatment were 22.08 mm and +5.5 D, respectively, and were not significantly different than those observed at the initial visit. The CRTs of the amblyopic and fellow eyes were not different from baseline at the two-month (214 and 206 μm, respectively) and eight-month (209 and 203 μm, respectively) follow-up visits. Neither the CBF nor the CCT of the fellow eye were different during the follow-up period. The OPP remained unaltered during the study time course, with values of 30.7 and 30.9 at 2 and 8 months after the first visit, respectively.

2. Discussion

We for the first time report changes in choroidal circulation in anisohypermetropic amblyopia after treatment. In both cases, the CBF of the amblyopic eye was reduced compared to that of the fellow eye at the initial visit. Furthermore, the CBF of the macular regions gradually increased along with the improvement in visual acuity and decrease in CCT due to treatment. During the follow-up durations, both the CBF and CCT of the fellow eyes were not different compared to the values at the initial visit. The axial lengths and refractive errors in the amblyopic eyes also were not different compared to those from the initial visit.

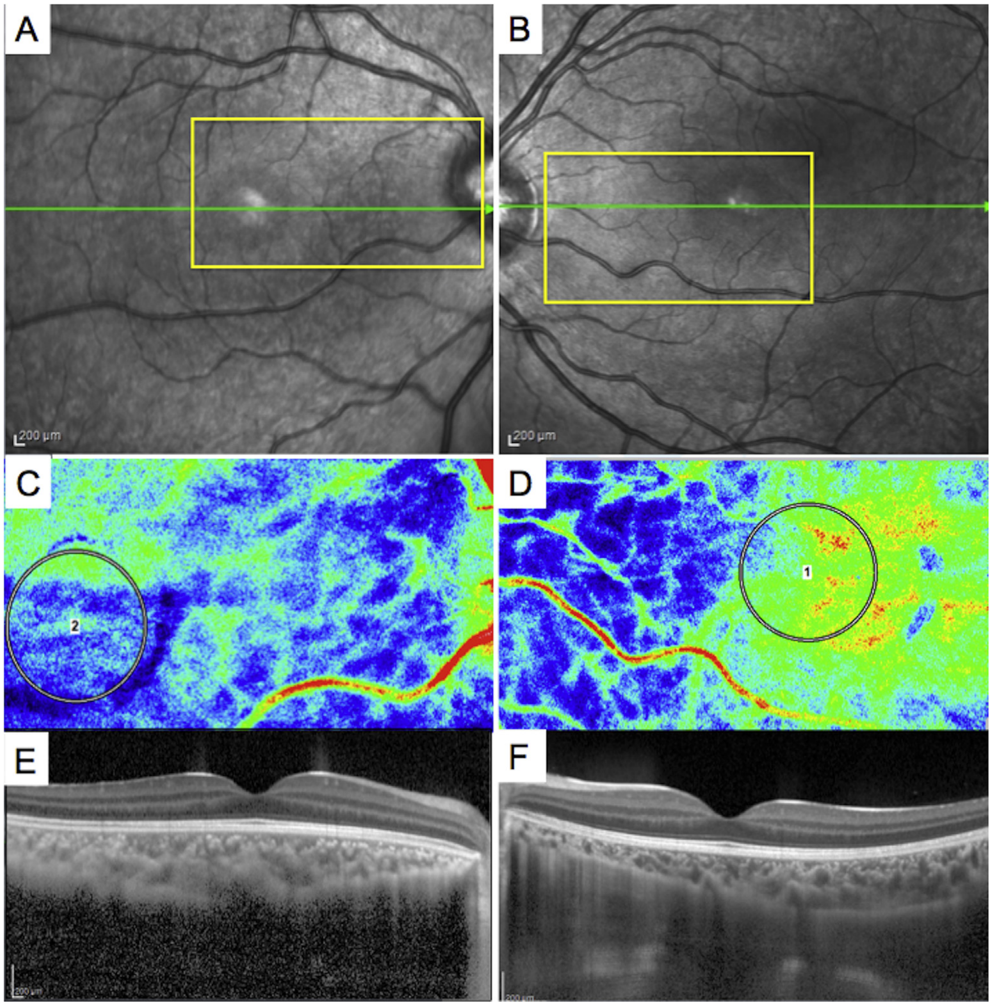

Fig. 1. Infrared reflectance fundus images, laser speckle flowgraphy findings, and enhanced depth imaging optical coherence tomography findings at the initial visit in case 1 Infrared reflectance (IR) fundus images of the right eye (A) and left eye (B) were normal. A laser speckle flowgraphy (LSFG) color map of the right eye is shown in (C), and an LSFG image map of the left eye is shown in (D). Based on IR fundus images, a circle was set on the LSFG color map at the first visit. The circle is located on the fovea. Red colors represent high blood flow and blue colors represent low blood flow. The color in (C) is a cooler than that shown in (D). Enhanced depth imaging optical coherence tomography of the right eye (E) shows that the central choroidal thickness is 387 μm while that of the left eye (F) is 250 μm. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Several researchers have investigated the morphologic features of the choroid in children using EDI-OCT.[3–6,10] Choroidal thickness has been shown to be greater in amblyopic eyes than in fellow and control eyes in children with anisohypermetropic amblyopia.[3,6] Our results agreed with results from previous studies. However, the mechanism responsible for the thickened choroidal area in amblyopic eyes has not yet been clarified. Recently, Nishi et al. described choroidal structure in children with anisohypermetropic amblyopia by binarizing OCT images.[6] Their study demonstrated that the luminal/stromal ratio in the choroidal area was greater in the amblyopic eye than in the fellow eye in children with anisohypermetropic amblyopia.[6] In normal adult subjects, the CBF was reported to be positively correlated with the luminal area and negatively correlated with age.[11] Considering the above findings, the CBF of the amblyopic eye is inferred to have been more greatly increased than that of the fellow eye. However, in the present cases, the CBFs of the amblyopic eyes were lower than those of the fellow eyes at the initial visit. These discrepancies might have resulted from several factors including differences in age or the prevalence of anisohypermetropic amblyopia.

In both cases, the CBF gradually improved along with improvements in visual acuity and decreased CCT during the follow-up period after treatment. In general, intrinsic choroidal neurons have a role in controlling choroidal vasculature and are located in stromal areas of choroidal tissue.[12] In the present cases, focusing on images of the retina using treatments such as glasses and patching of the eye might induce increases in the activity of the neurons in the amblyopic eye and result in parallel improvements in CBF and visual acuity. Taking into account the above-mentioned findings, the elevation of CBF might be an effect of treatment. It is thus hypothesized that CBF impairment might be involved in the pathogenesis of anisohypermetropic amblyopia. However, it is not known whether CBF or visual acuity will recover faster after treatment. This is because we did not perform eye examinations every other month in this study. Further studies with larger numbers of cases and monthly examinations are required to clarify whether CBF or visual acuity recovers faster.

3. Conclusions

In conclusion, this is the first report to demonstrate increases in CBF in amblyopic eyes coinciding with visual acuity improvement in children with anisohypermetropic amblyopia. CBF impairment might be involved in the pathogenesis of anisohypermetropic

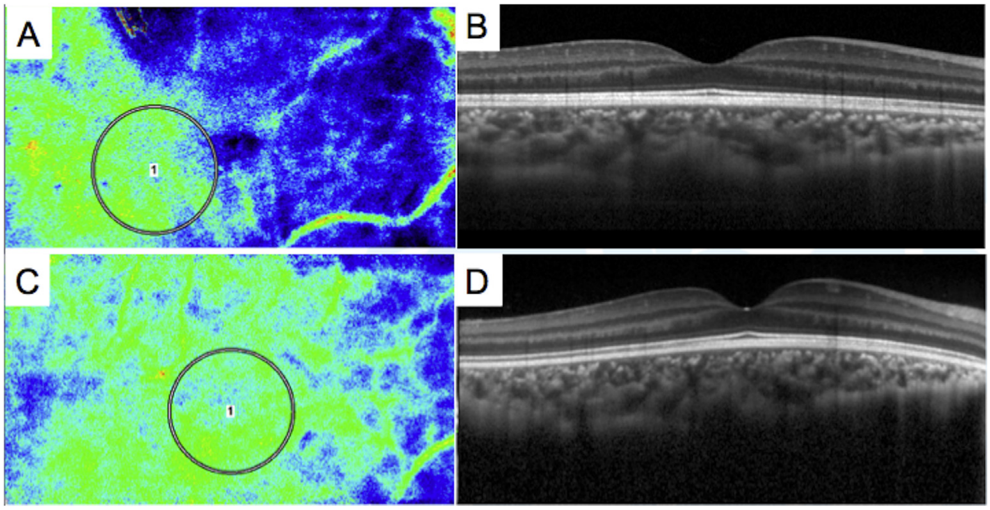

Fig. 2. Change in laser speckle flowgraphy and enhanced depth imaging optical coherence tomography findings in the amblyopic eye in case 1. A laser speckle flowgraphy color map and enhanced depth imaging optical coherence tomography images of the right eye at 7 months (A and B) and 12 months (C and D) after the initial visit are shown. The mean blur rates, which indicate blood flow, were 8.6 and 9.6 at 7 and 12 months after the initial visit, respectively. Central choroidal thicknesses were 377 and 354 μm at 7 and 12 months after the initial visit, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

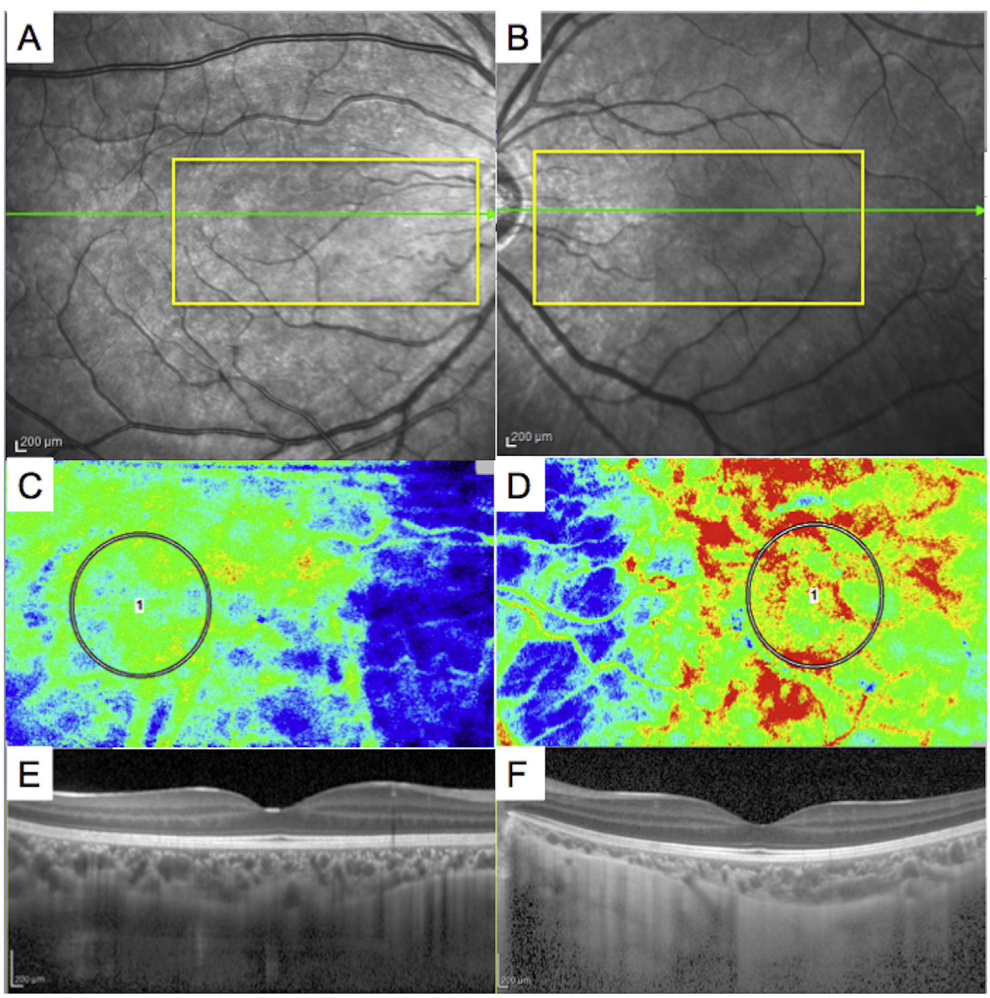

Fig. 3. Infrared reflectance fundus images, laser speckle flowgraphy findings, and enhanced depth imaging optical coherence tomography findings at the initial visit in case 2. Infrared reflectance fundus images of the right eye (A) and left eye (B) were normal. A laser speckle flowgraphy image map of the right eye (C) demonstrates much cooler colors than that of the left eye (D). The central choroidal thickness of the right eye (316 μm) (E) was greater than that of the left eye (233 μm) (F). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

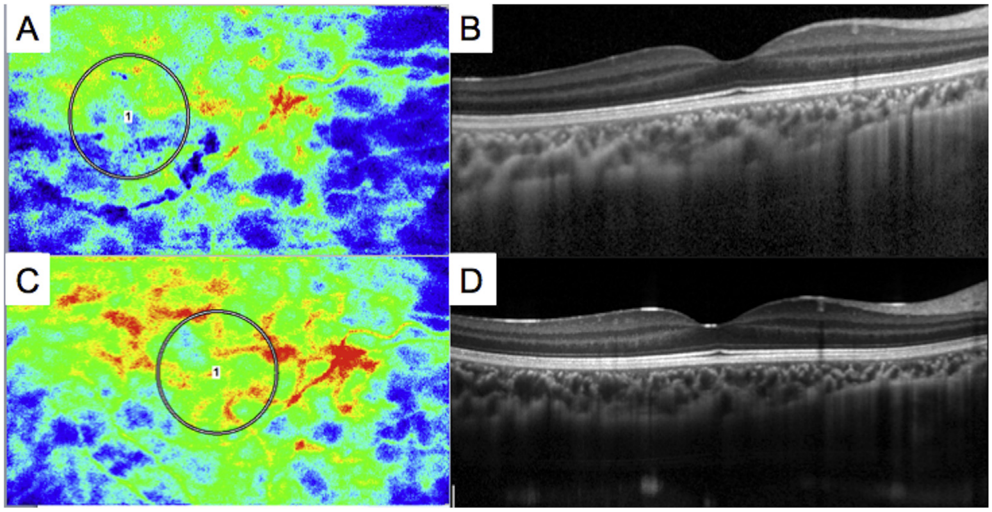

Fig. 4. Changes in laser speckle flowgraphy and enhanced depth imaging optical coherence tomography findings in the amblyopic eye in case 2. A laser speckle flowgraphy color map and enhanced depth imaging optical coherence tomography images of the right eye at 2 months (A and B) and 8 months (C and D) after the first visit are shown. The mean blur rates were 11.4 and 13.4 at 2 and 8 months after the first visit, respectively. The central choroidal thickness of the right eye was 294 μm and 287 μm at 2 and 8 months after the first visit, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

amblyopia. LSFG may be useful in evaluating changes in CBF in patients with pediatric anisohypermetropic amblyopia.

Patient consent

Informed consent was obtained in writing from the parents of patients for the use of their information and external photographs for the purpose of this report.

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None.

Conflicts of interest

None.

Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

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