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PEDIATRICS

Quantitative measurement of passive duction force tension in intermittent exotropia and its clinical implications

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Abstract

Purpose To evaluate the passive duction force (PDF) in extraocular muscles (EOMs) in patients with intermittent exotropia (IXT) using a quantitative tension-measuring device.

Methods This prospective, case–control study enrolled 25 patients with IXT and 26 age- and sex-matched controls. PDF was measured under general anesthesia as the eyeball was rotated medially or laterally away from the direction of the force being tested. The preferred eye for fixation was determined using a cover–uncover test.

Results The PDF in the IXT and control groups were 60.9 g and 52.1 g, respectively, for the lateral rectus (LR) ($p = 0.046$) and 53.0 g and 48.8 g for the medial rectus (MR) ($p = 0.293$). When the eyes were examined separately in the IXT group, the PDF of LR was larger in the nonpreferred eye for fixation than in the control group ($p = 0.039$), whereas there was no difference in the preferred eye for fixation ($p = 0.216$). Additionally, the relative PDF of LR in the nonpreferred eye compared to the ipsilateral PDF of MR was positively associated with the duration of manifest deviation ($p = 0.042$) and the average angle of the near and far deviations ($p = 0.023$).

Conclusions The PDF in the LR in patients with IXT in the nonpreferred eye for fixation was larger than normal and could increase with the duration of manifest deviation and the angle of deviation. Evaluating the PDF in EOMs could provide information that is useful for managing strabismus and understanding its pathophysiology.

Keywords Exotropia · Extraocular muscles · Tension · Quantitative measurement · Passive duction force

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Key messages

- Intermittent exotropia (IXT) is most common form of strabismus, with surgery being the mainstay of treatment. The forced duction test (FDT) was used to assess the PDF or laxity of the lateral rectus (LR) in IXT surgery. However, the results from the FDT are variable and highly dependent on the experience and skill of clinicians.
- The authors have designed a simple and compact device for quantitatively and continuously measuring the passive duction force (PDF) in extraocular muscle (EOM). The PDF in the LR in the patient with IXT in the nonpreferred eye for fixation was larger than in the age matched control group, and could increase with the duration of manifest deviation and the angle of deviation.
- Quantitative evaluating the PDF in EOMs could be considered when planning strabismus surgery in IXT. Also it could provide useful information for understanding its pathophysiology.

Introduction

Intermittent exotropia (IXT) is the most common form of strabismus, with surgery being the mainstay of treatment [1]. The prevalence of IXT is especially high in Asia, comprising half of all cases of primary horizontal strabismus [2, 3]. Although the pathophysiology of IXT is poorly understood, the mechanical properties of the extraocular muscles (EOMs) have been suggested as one of the important factors affecting the disease course and treatment outcome [4]. Multiple structural changes are seen in long-standing cases of IXT in EOMs, including in myofilaments and sarcomeres, the axonal supply, the proprioception apparatus, and the surrounding extracellular matrix and collagen [5–7].

The forced duction test (FDT) is a simple and easy method for clinically evaluating the mechanical properties of the EOMs. Clinicians can assess the tightness of an EOM by grasping the limbal conjunctiva with toothed forceps and moving the eyeball away from the direction of force being tested. However, this manual test is usually performed in a subjective manner by perceiving the resistance while the clinician grips and moves the eyeball with forceps [8, 9]. Thus, the results from the FDT are highly dependent on the experience and skill of clinicians, and also, this test cannot be used to detect small pathological changes [10, 11]. This qualitative nature of the testing can lead to inaccuracy and variability in assessments of the passive duction force (PDF) in EOMs and therefore might adversely affect the management of IXT.

A method for quantitatively analyzing the passive forces acting on EOMs is required to allow more accurate and objective assessments. We have therefore previously developed a novel device for performing quantitative measurements and demonstrated the reliability of our tension-measuring device in normal subjects [12, 13]. The aim of this study was to present qualitative data of the PDF in EOMs in patients with IXT using our novel device and compare these results with those obtained in healthy control eyes.

Materials and methods

This prospective, case–control study was conducted at the Department of Ophthalmology, Konkuk University Medical Center, Seoul, Korea, between March 2019 and February 2020. This clinical study was approved by the Institutional Review Board/Ethics Committee of Konkuk University Medical Center (registration number: KUH1100071). The study was conducted according to the principles expressed in the Declaration of Helsinki. Informed consent was obtained from all of the included participants and their parents/caregivers.

Participants

This study enrolled 25 patients who were scheduled to receive elective strabismus surgery under general anesthesia for correcting IXT. All of the patients had a basic pattern of IXT, ranging from 10 to 50 prism diopters (PD) with objective control scale 1 or 2 according to the Newcastle Control Score [14] and without (1) dissociated vertical deviation, (2) > 2 PD of vertical deviation, (3) lateral incomitance, (4) an A or V pattern, (5) superior oblique or inferior oblique under-/over-action, or (6) simulated divergence excess/convergence insufficiency. Twenty-six age- and sex-matched patients who underwent epiblepharon surgery under general anesthesia, were within 2 PD of being orthophoric, and did not have limitation of eye movement on duction/version testing were included as a control group. The following exclusion criteria were applied in both groups: (1) presence of other ocular diseases (e.g., prior history of strabismus, nystagmus, ptosis, or orbital diseases), (2) anisometropia or amblyopia, (3) eyes with spherical equivalents of > 3.00 or < −4.00 diopter, (4) thyroid disorder or muscular or neurological diseases (e.g., cerebral palsy or myasthenia gravis), (5) history of ocular trauma or previous ocular or periocular surgery, or (6) history of receiving medications known to affect muscle tension (e.g., botulinum toxin). Lateral incomitance was defined as a change of > 5 PD in the lateral gaze from the primary position. Anisometropia was defined as a spherical or cylindrical difference of > 1.5 PD between the two eyes. Amblyopia is defined as a difference in the best-corrected visual acuity between the eyes of more than two Snellen lines (0.2 logMAR).

Ophthalmological evaluation

The preoperatively recorded patient characteristics included the sex, age at surgery, and refractive error in both groups, and the duration of intermittent eye misalignment, preferred eye for fixation, and angles of deviation at far (6 m) and near (1/3 m) distances in only the IXT group. These variables were defined and examined according to previous researches [15–18]. Refractive errors were determined by first inducing cycloplegic refraction using 1% cyclopentolate hydrochloride and then analyzing the error as the spherical equivalent value, calculated as spherical + cylinder/2.

The duration of manifest deviation was divided into two categories: ≤ 24 months and > 24 months. The duration of intermittent eye misalignment was determined from parental/caregiver and patient reports and from the medical records of the referring ophthalmologist. Because the age at onset was not known precisely for some patients, the duration could not be considered as a continuous variable [16]. In the dominancy test, the preferred eye for fixation was determined using repeated examinations of the cover–uncover test as well as from parental/caregiver and patient reports of the more frequently deviating eye [17, 18].

Passive duction force measurement procedure

PDF measurements were made of each horizontal rectus muscle on both eyes under general anesthesia, as described previously [12, 13]. All participants were confirmed as being at the American Society of Anesthesiologists (ASA) physical status classification I. Anesthesia was induced by administering 5 mg/kg thiopental sodium. Rocuronium (Esmeron®, MSD Korea, Seoul, Korea) 0.6 mg/kg was administered for muscle relaxation under the guidance of peripheral neuromuscular transmission (NMT) monitoring (TOF-watch SX®, Organon, Dublin, Ireland). After performing tracheal intubation, anesthesia was maintained by administering sevoflurane with 40% oxygen in the air and the anesthetic depth was monitored by using a bispectral index which was maintained for a range from 40 to 60. Additional rocuronium was administered under the guidance of peripheral monitoring of NMT and the train-of-four (TOF) count was maintained at 1 to 2 during the operation.

Castroviejo locking forceps were attached to the eyeball just posterior to the limbus perpendicularly at the 3- and 9-o'clock positions. Ten-millimeter medial and lateral rotations (away from the direction of force to be tested) from the primary position were performed for measuring the PDF in the lateral rectus (LR) and the medial rectus (MR), respectively (Fig. 1a and b). The maximum PDF in each rectus was recorded. To compensate for any changes in the eye position before the measurement of PDF, if the eyes were not in their primary position, PDF was measured after they were placed in the primary position. Also, calibration was done for the sensing unit and the measurement device was zeroed every time just after attaching the Castroviejo locking forceps to the globe and before rotating the forceps. The full description of PDF measuring device and calibration curve was described in our previous articles [12, 13]. The measurements were performed by a single masked examiner (H.J.S.).

The outcome measures were the PDF in the LR and the MR, and the relative PDF in the LR, which was obtained by subtracting the ipsilateral PDF of MR from the PDF of LR.

Statistical analyses

All calculations and statistical analyses were performed using Minitab software (version 19.2, Minitab, State College, PA, USA). The Anderson-Darling test was used to determine whether the data conformed to a parametric (Gaussian) or nonparametric (non-Gaussian) distribution. Sex differences were analyzed using the chi-square test. The age at surgery

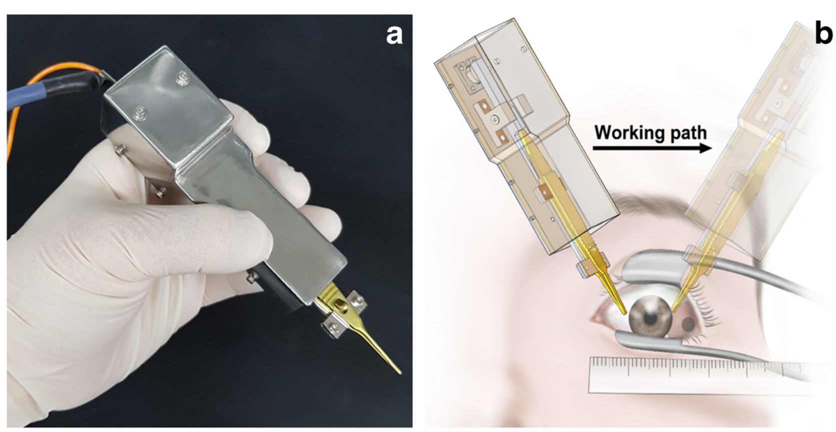

Fig. 1 Photograph of the device and schematic of measuring the passive duction forces (PDF). **a** The compact and simple design of the device. The operation method is similar to the method of the conventional forced duction test using forceps. **b** Measuring the PDF of medial rectus. The locking forceps were attached to the limbus and rotated away from the direction of force to be tested (opposite side of the tested muscle, lateral side)

was analyzed using the Mann-Whitney test. The refractive error was analyzed using the independent-samples *t* test. The two eyes in each patient were compared using the paired-samples *t* test. ANOVA with post hoc analysis was used for comparisons of the PDF among the controls and preferred and nonpreferred eye for fixation. The linearity of relationships between the deviation angle and PDF was evaluated using Pearson's correlation test. The data are presented as mean ± standard deviation values, and the criterion for statistical significance was set as $p < 0.05$.

Results

This study included the 50 eyes of 25 patients with IXT (age, 10.1 ± 6.8 years) and 51 eyes of 26 control patients (age, 9.0 ± 6.1 years). All of the PDF data conformed to a Gaussian distribution in the Anderson-Darling test. The baseline characteristics (sex, age at surgery, and refractive error) did not differ significantly between the two study groups (Table 1). In the IXT group, the average angle of the near and far deviations was 27.4 ± 9.5 PD, and the duration of manifest deviation was 23.0 ± 17.1 months.

The PDF in the LR was significantly larger in the IXT group (60.9 ± 23.9 g) than in the control group (52.1 ± 19.0 g) (p = 0.046), whereas there was no significant intergroup difference in the PDF in the MR (53.0 ± 21.2 g and 48.8 ± 18.9 g, respectively; $p = 0.293$) (Fig. 2). For analyzing each eye separately, we randomly selected right eye or left eye from all in the control group. Table 2 revealed that the PDFs in the LR and MR in the preferred eye for fixation in the IXT group did not differ significantly from those in the control group (all $p > 0.05$). However, the PDF in the LR in the nonpreferred eye for fixation (63.9 ± 26.1 g) was significantly larger than that in the control group ($p = 0.039$). Also, the PDF in the MR in the preferred eye for fixation (56.5 ± 22.2 g) was significantly larger than that in the nonpreferred eye (49.6 ± 20.1 g) in the IXT group ($p = 0.045$). The relative PDF in the LR in the nonpreferred eye (14.3 ± 14.4 g) was significantly larger than that in the preferred eye for fixation (1.4 ± 20.3) ($p = 0.010$).

The relative PDF in the LR in the nonpreferred eye was significantly larger in the patients with a manifest duration of > 24 months (21.3 ± 15.0 g) than in the patients with a manifest duration of ≤ 24 months (9.5 ± 11.8) ($p = 0.042$), whereas there was no significant intergroup difference in the relative PDF in the LR in the preferred eye (− 0.3 ± 23.1 g and 3.5 ± 19.1 g, respectively; $p = 0.643$) (Fig. 3). In addition, the relative PDF in the LR in the nonpreferred eye increased with the mean angle of the near and far deviations (Pearson correlation coefficient = 0.459, $p = 0.023$) (Fig. 4).

Discussion

In the present study, we evaluated the quantitative PDF in the horizontal rectus muscles (the LR and the MR) in patients with IXT under general anesthesia and compared these results with those in age- and sex-matched healthy control eyes. Comparing these two groups revealed that the mean PDF of LR in both eyes was larger in the IXT group than in the control group. Specifically, when the eyes in the IXT group were analyzed separately, the PDF of LR in the nonpreferred eye for fixation was larger than that in the control group, while the PDF of LR in the preferred eye for fixation did not differ from that in the control group. In addition, the relative PDF of LR in the nonpreferred eye increased with the duration of manifest deviation and the angle of deviation.

The PDF in the LR in the IXT group—more specifically, in the nonpreferred eye for fixation—was larger than that in the control group. There are several possible explanations for these findings. Previous studies have reported the extraocular muscles to remodel and have structural changes in strabismus [18, 19]. Long-standing strabismus may result in fibrosis of the muscle–tendon and induce a certain degree of restriction, and tension in an EOM may cause the resistance of the eyeball when moving to the opposite direction [20, 21]. Rosenbaum

Table 1 Clinical characteristics of the study subjects in the control and intermittent exotropia (IXT) groups

Characteristic	Control	IXT	*p*
Number of subjects	26	25	
Sex (male/female)	14/12	13/12	0.895[a]
Age at operation (years)	9.0 ± 6.1	10.1 ± 6.8	0.338[b]
Refractive error (SE)*	− 0.95 ± 1.24	− 0.67 ± 1.27	0.459[c]
Duration of manifest deviation (months)	N/A	23.0 ± 17.1	N/A
Average angle of near and far deviations (PD)	N/A	27.4 ± 9.5	N/A

Data are *n*/*n* or mean ± standard deviation values. *SE*, spherical equivalent value; *N/A*, not applicable

*Average SE of both eyes

[a] *p* value from the chi-square test

[b] *p* value from the Mann-Whitney test, [c] *p* value from the independent-samples *t* test

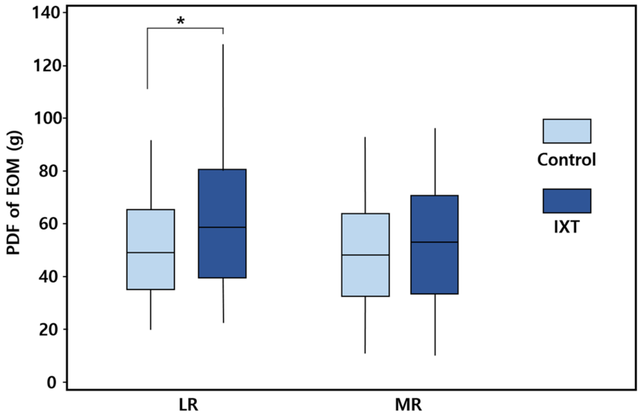

Fig. 2 PDF in the horizontal rectus muscles in the control group (light blue) and the intermittent exotropia (IXT) group (dark blue). The horizontal line indicates the median value, the boxes indicate the interquartile interval (25th and 75th percentiles), and the whiskers indicate the range. LR, lateral rectus; MR, medial rectus; asterisk indicates a statistically significant difference

and Myer reported that a trend toward greater resistance to lateral rotation in patients with esotropia was compatible with the tightness of the MR [22]. Another previous study found that in patients with large-angle IXT, the loss of elasticity, and the resulting tight LR could produce a leash effect [23]. Thus, frequent deviation of the nonpreferred eye and a large deviation angle could be closely associated with increased PDF of LR in IXT.

A trend toward a larger relative PDF in the LR in the nonpreferred eye was noted when the duration of manifest deviation was longer in the patients with IXT. Our results are also consistent with a histopathological study by Yao et al. revealing the remodeling of EOMs [7]. Those authors documented that greater abnormal changes in the EOMs such as sarcomere destruction and myofilament disintegration occurred in the adult group than in the adolescent group.

Our results lend some evidence for the paradigm that evaluating the PDF in the LR could be considered when planning strabismus surgery in IXT. This is supported by previous studies that have applied FDT results to IXT surgery aimed at preventing recurrence. These studies have found that the amount of muscle displacement required for surgery or choosing which eye to operate should be determined while considering the PDF in the LR [20, 21]. For example, increased PDF of LR may cause the resistance of the eyeball when moving to the opposite direction, and in such cases, decreasing the tension by recessing the muscle might be beneficial in reducing recurrence and improving success rates. Kim et al. reported that unilateral lateral rectus recession–medial rectus resection performed on the eye with more PDF of the LR resulted in better successful alignment and lower recurrence [20].

One particularly interesting finding of the present study was that the PDF of MR in the preferred eye for fixation was larger than that in the nonpreferred eye in patients with IXT. It can be hypothesized theoretically that the preferred fixating eye will require more tightening of the MR for maintaining its primary position compared to the MR of the nonpreferred eye. Consequently, this increased innervation flow to the yoke muscle (the contralateral LR) might affect the increased PDF of LR in the nonpreferred eye for fixation.

For the quantitative and objective analysis performed in this study, we deployed a tension-measuring device based on the compression weighing of force sensors. The FDT was used to assess the tension or laxity of the LR in previous IXT studies [20, 21], but interpreting the results obtained when applying this subjective test is highly dependent on the examiner. Thus, there has been a need for objective measurements of the PDF of LR in IXT. We previously published a separate paper establishing the device as a reliable instrument for measurements in normal subjects before reporting the results from a group of patients with strabismus [12, 13]. The measurement

Table 2 Comparison of passive duction force (PDF) between the control and IXT groups

	Control*	IXT		Between eyes in IXT	Preferred vs. control	Nonpreferred vs. control
		Preferred**	Nonpreferred	*p*		
LR	51.6 ± 13.7	57.9 ± 21.4	63.9 ± 26.1	0.111[a]	0.216[b]	*0.039*[c]
MR	50.7 ± 15.9	56.5 ± 22.2	49.6 ± 20.1	*0.045*[a]	0.290[b]	0.822[c]
LR-MR	0.89 ± 12.7	1.41 ± 20.3	14.3 ± 14.4	*0.010*[a]	0.912[b]	0.001[c]

LR-MR, relative PDF in the lateral rectus

*Randomly selected single eye of control subjects

**Preferred eye for fixation in patients with IXT; nonpreferred is the contralateral eye

[a] *p* value between the eyes in the same patient with IXT for the related paired-samples *t* test

[b] *p* value between the preferred eye for fixation in the IXT group and control (right and left eyes) for the independent-samples *t* test

[c] *p* value between the nonpreferred eye for fixation in the IXT group and control (right and left eyes) for the independent-samples *t* test

Significant *p* values are indicated in italics

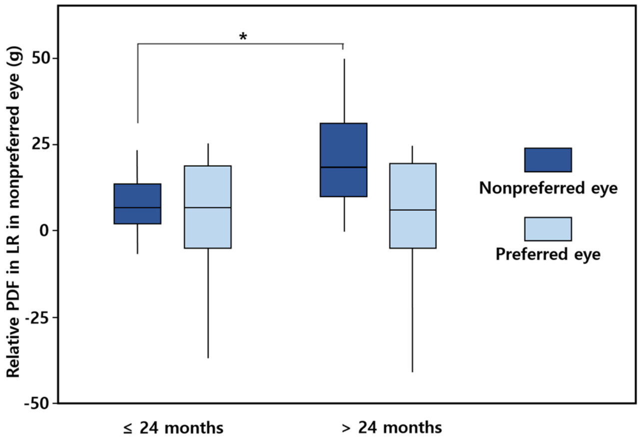

Fig. 3 Relative PDF in the LR in the nonpreferred eye for fixation in the IXT group according to the duration of manifest deviation. The horizontal line indicates the median value, the boxes indicate the interquartile interval (25th and 75th percentiles), and the whiskers indicate the range. The asterisk indicates a statistically significant difference

values obtained using the present device in our control group corresponded well to previously reported normative data obtained using different methods [9, 24, 25]. The mean PDF in the horizontal rectus muscles has been previously reported to range from 40 to 65 g. Our data for the average PDF in the horizontal rectus muscles fall within this range, at 50.4 ± 18.9 g. In addition, the mean PDFs in the two horizontal rectus muscles (the LR and the MR) were reported to be similar to each other [22, 26]. Our data showed similar tendencies to these previous reports.

The PDFs measured in EOMs have varied between studies using different methodologies and conditions, which suggests that caution is required when interpreting the overall results. The PDF could be overestimated under local anesthesia since afferent stimuli such as patient anxiety, discomfort, and pain could increase the tensions in EOMs [27, 28]. Even under general anesthesia, the PDF may also vary depending on the depth of anesthesia and type of muscle relaxants administered

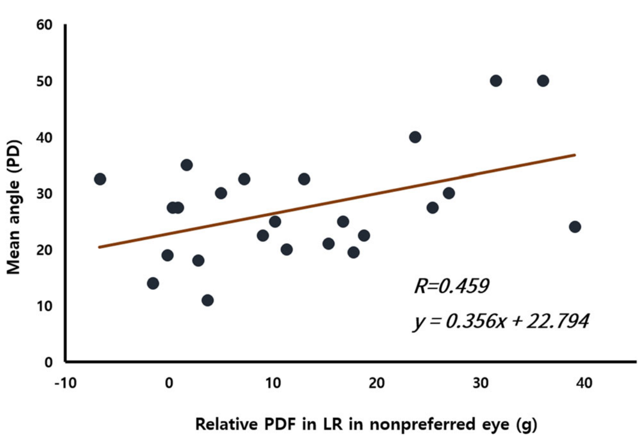

Fig. 4 Correlation between the average angle of the near and far deviations and the relative PDF in the LR in the nonpreferred eye for fixation in the IXT group

[29, 30]. In addition, the tensions in EOMs could increase if there are any mechanical restrictions in the connective tissue, such as due to conjunctival scarring. In our study, we excluded patients with conjunctival scarring and previous ocular surgery. Also, a standardized anesthetic regimen was applied to all patients by a single anesthesiologist to produce a consistent depth of anesthesia.

This study was subject to some limitations. First, the sample was relatively small and so we could not perform various subgroup analyses, such as different types of IXT or degrees of control. Second, we ruled out the A or V pattern, oblique dysfunction, and more than 50 PD of exodeviation. These conditions could be related to ocular torsion, pulley heterotropia, and systemic conditions (e.g., hydrocephalus and facial malformation). Third, we did not assess the grade of fixation preference in patients with IXT. Fourth, we did not investigate the relationship between the PDF and postoperative surgical outcome. Future prospective studies are needed to measure the PDF of EOM in various types of IXT and clarify whether such measurements of PDF could help to predict the surgical outcome of IXT.

In conclusion, the PDF in the LR can be increased in the nonpreferred eye for fixation in patients with IXT. This implies that the PDF of the LR might be considered when planning R&R in IXT and performing the surgery on the nonpreferred eye for fixation with more PDF of the LR might be beneficial. In this regard, evaluating the PDFs in EOMs could allow clinicians to increase the accuracy when planning strabismus surgery and improve the understanding of its pathophysiology. Furthermore, our device for making quantitative measurements is an easily assessable tool and could provide valuable information about the mechanical properties of EOMs that is suitable for use both clinically and in research.

Authors' contributions H.K. Kang developed the instrument and analyzed the data. S.H. Lee designed the study and illustrated figures. C. Oh designed the study and collect the data. H.J. Shin designed the study, collected the data, and wrote the manuscript. A.G. Lee revised the manuscript.

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Data availability Raw data table.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The study protocol was approved by the Institutional Review Board (IRB) of the Konkuk University Medical Center (registration number: KUH1100071).

Consent to participate Informed consent was obtained from all individual participants included in the study.

Code availability Not applicable.

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