

# The clinical course of recurrent intermittent exotropia following one or two surgeries over 24 months postoperatively

WJ Kim and MM Kim

CLINICAL STUDY

## Abstract

**Purpose** The aim of this study is to investigate the difference of the clinical course in recurrent intermittent exotropia after second surgery compared with both recurrent intermittent exotropia after its first of two surgeries and intermittent exotropia after only a single surgery.

**Methods** We retrospectively reviewed the medical records of patients diagnosed with intermittent exotropia who underwent lateral rectus recession and medial rectus resection (R&R) between January 1992 and January 2011 at Yeungnam University Hospital. Repeated measure ANOVA (rmANOVA) was used to compare the clinical course of recurrent intermittent exotropia before and after a second surgery with that of intermittent exotropia with a single surgery.

**Results** A total of 352 intermittent exotropia patients who underwent one R&R procedure and 77 recurrent intermittent exotropia patients who underwent a second R&R in the contralateral eye were included in this study. Although exodrift of recurrent intermittent exotropia was observed at 24 months of follow-up even after a second surgery, it was significantly lower than both intermittent exotropia with a single surgery and after its first of two surgeries ( $P < 0.001$ , rmANOVA).

**Conclusion** The clinical course of recurrent intermittent exotropia after a second surgery was improved compared with both recurrent intermittent exotropia after its first of two surgeries and intermittent exotropia after a single surgery.

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## Introduction

Intermittent exotropia is the most common type of strabismus among Asians, especially Koreans. Although surgical treatment results in a better outcome than nonsurgical treatment, such as orthoptics or occlusion therapy, many studies have reported postoperative exodrift and recurrence of intermittent exotropia over time after surgical treatment.<sup>1–5</sup> Regarding a second surgery for recurrent intermittent exotropia, we are often asked by patients or their parents whether a second surgery will improve the outcome following the first surgery. Some studies using survival analysis have found a lower recurrence rate after a second surgery.<sup>6,7</sup> However, few studies have conducted longitudinal comparisons of the clinical course of recurrent intermittent exotropia after a second surgery and intermittent exotropia that showed good ocular alignment after a single surgery. Moreover, we were also interested in the difference of clinical course in recurrent intermittent exotropia before and after a second surgery. Therefore, we investigated the clinical course of recurrent intermittent exotropia after a second surgery, and compared it with not only the clinical course after a single surgery but also the clinical course after the first surgery when a second was performed.

## Subjects and methods

### Patient selection criteria

We reviewed retrospectively the medical records of intermittent exotropia patients who underwent lateral rectus recession and medial rectus resection (R&R) between January 1992 and January 2011 at

Department of Ophthalmology, Yeungnam University College of Medicine, Daegu, South Korea

Correspondence: MM Kim, Department of Ophthalmology, Yeungnam University College of Medicine, 317-1 Daemyung-dong, Nam-gu, Daegu 705-717, South Korea.  
Tel: +82 53 620 3441;  
Fax: +82 53 626 5936.  
E-mail: mmk@med.yu.ac.kr

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Yeungnam University Hospital. For inclusion in this study, the required follow-up period after surgery was 24 months. Intermittent exotropia patients included in this study were first divided into two groups: primary surgery group: those who had good ocular alignment after a single surgery; resurgery group: those who had recurred intermittent exotropia after first surgery and underwent a second surgery. To compare the difference between clinical course of recurrent intermittent exotropia after first surgery and after second surgery, resurgery group was divided into two subgroups: resurgery 1 group: the clinical course of recurrent intermittent exotropia during postoperative follow-up after the first surgery until before the second surgery; resurgery 2 group: the clinical course of recurrent intermittent exotropia during postoperative follow-up after the second surgery. The division of patients into three groups is summarized graphically in Figure 1a. Patients with any other types of strabismus such as oblique muscle dysfunction, dissociated vertical deviation, A-V pattern, and nystagmus were excluded from this study. Patients with previous intraocular surgery, any neurological impairment such as cerebral palsy, or unilateral amblyopia were also excluded.

#### *Preoperative evaluation*

At the initial visit, all patients underwent a full ophthalmologic examination, including visual acuity testing, ocular alignment status, slit-lamp biomicroscopy, refraction, fundus examination, and stereoacuity test. The angle of deviation was measured by alternate prism cover testing at 6 m and 33 cm fixation in cooperative children both pre- and postoperatively. Best-corrected visual acuity was measured where possible. Amblyopia was defined as an interocular difference in visual acuity of two lines or more. If amblyopia was found, the occlusion therapy was performed to treat amblyopia as soon as possible before surgery. Stereoacuity was measured with Lang I test and Titmus stereotest when the patient was able to cooperate and complete the test.

#### *Surgical plan*

Every surgery was performed by a single surgeon (MMK) under general anesthesia. The unilateral R&R procedure was undertaken using surgical dosage of our clinic (Table 1) based on the patients' angle of deviation measured the day before the surgery. The contralateral R&R procedure was performed as the second surgery in recurrent intermittent exotropia patients who had previously undergone unilateral R&R procedure.

#### *Postoperative evaluation*

The patients were followed-up at 1, 3, 6, and 12 months after the surgery, and every 6 months thereafter. The

postoperative angle of deviation was measured at each visit. Patients who missed any regular follow-up over the 24 postoperative months were excluded from this study.

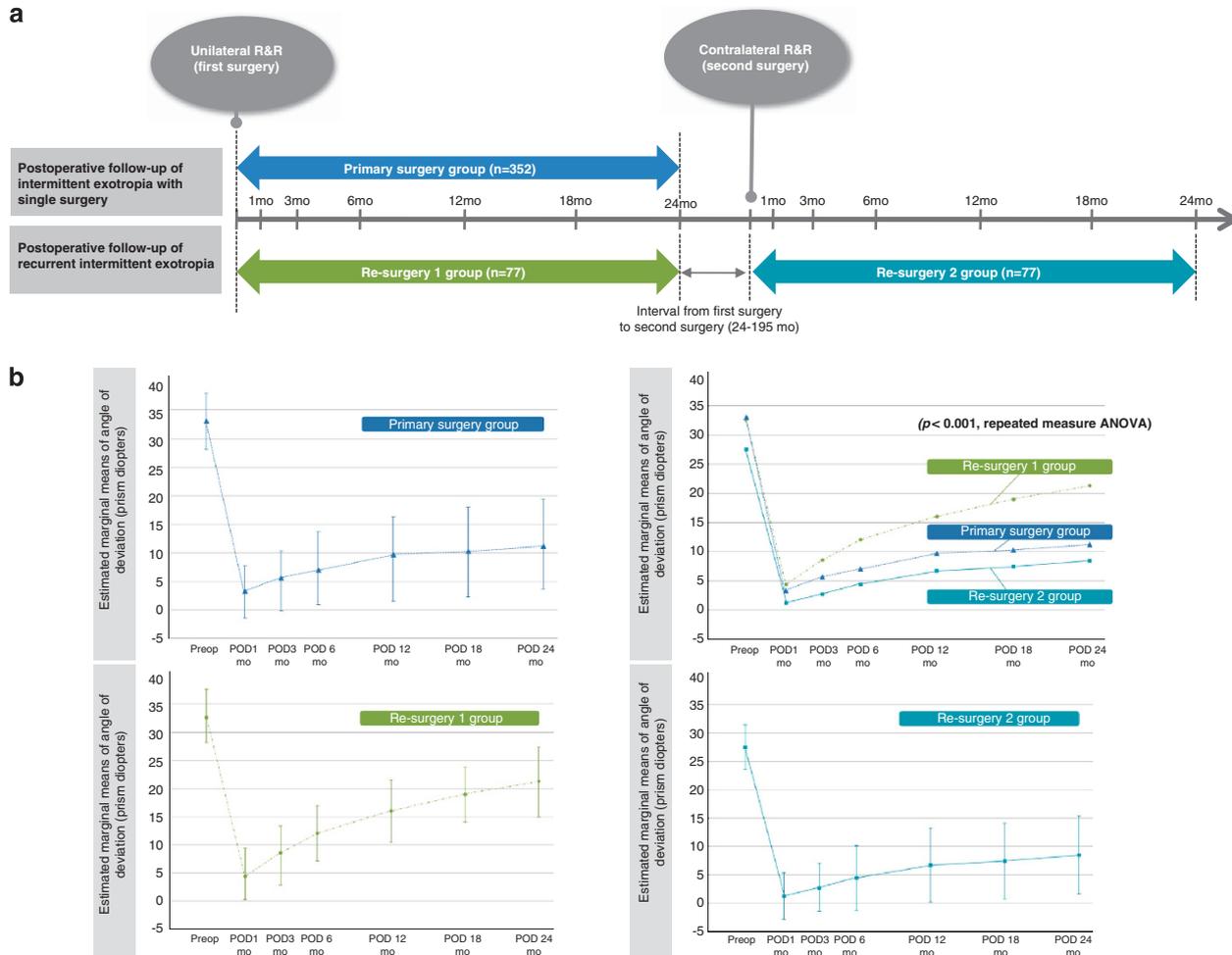
#### *Statistical analysis*

Continuous data are presented as a mean with SD, and categorical data are presented as counts. Comparisons for continuous variables were performed using independent *t*-test. The  $\chi^2$  method was used to test the significance of differences between proportions and categorical variables. We used repeated measures ANOVA (rmANOVA) to analyze the difference in clinical course between the primary surgery group, resurgery 1 group, and resurgery 2 group. Univariate and multivariate logistic regression tests were conducted to evaluate factors associated with the second surgery. The SPSS statistical software, version 20.0 (SPSS, Inc., an IBM Company, Chicago, IL, USA) was used for statistical analyses. A *P*-value of  $<0.05$  was regarded as statistically significant.

#### **Results**

The clinical records of 1618 intermittent exotropia patients who underwent R&R procedure were retrospectively reviewed. Among them, 182 patients underwent contralateral R&R procedure as a second surgery. No patient required an additional surgery for overcorrection after first surgery and one patient underwent a third surgery for overcorrection after second surgery. Of the total 1618 patients, 429 patients met the inclusion criteria for this study. In all, 352 patients were included in the primary surgery group and 77 patients in the resurgery group. The demographic and clinical characteristics of these patients at the first surgery are in Table 2. In the resurgery group, the mean interval from the first surgery to second surgery was  $46.32 \pm 27.87$  (24–195) months. The basic type, which was defined when the difference between distant and near angle was within 10 PD, was the most common in both groups. The pre- and postoperative angle of deviation for each group are shown in Table 3. The postoperative angle of deviation significantly increased in each group at all postoperative follow-ups over 24 months. An rmANOVA analysis revealed statistically significant group-by-time effects for the postoperative angle of deviation (Figure 1b, rmANOVA,  $P < 0.001$ ). The postoperative angle of deviation of resurgery 2 group was lower than that of both the primary surgery group and resurgery 1 group over postoperative 24 months.

The association between the resurgery group and clinical characteristics was assessed by univariate and multivariate logistic regression. Multicollinearity was evaluated by the tolerance and variance-inflation-factor, and the assumption of multicollinearity was not violated with these variables.



**Figure 1** The summarized design and result of study. (a) Intermittent exotropia patients were divided into three groups: primary surgery group, resurgery 1 group, and resurgery 2 group. The difference in the postoperative angle of deviation within and between the three groups was analyzed using repeated measure ANOVA. (b) Postoperative angle of deviation in the three groups: primary surgery group, resurgery 1 group, and resurgery 2 group. Repeated measure ANOVA found significant difference among the groups ( $P < 0.001$ ).

Age at first surgery, gender, spherical equivalent refractive error, the result of Lang I stereotest, and pre- and postoperative angle of deviation were first tested using univariate analysis; variables with  $P < 0.2$  in univariate analysis are shown in Table 4. The preoperative angle of deviation showed little association with the second surgery ( $P = 0.739$ ). Filtered variables with  $P < 0.2$  in univariate analysis were further evaluated to identify association using multivariate analysis. In entry mode of multivariate analysis, age at first surgery (odds ratio: 0.752,  $P < 0.001$ ) showed the strongest association with the second surgery.

## Discussion

When considering a second surgery for recurrent intermittent exotropia, we are usually asked by patient or their parents about the expected prognosis after a second surgery. The two most frequently asked questions are as follows: ‘Is there any possibility of

recurrence even after a second surgery?’ and ‘Will the clinical course after the second surgery be better than after the first surgery?’ Several studies have addressed the first question. Hahm *et al*<sup>6</sup> reported that exotropia did recur even after a repeat surgery, although the recurrence rate was lower than that after a primary surgery. The study of Kim and Kim<sup>7</sup> using survival analysis showed decreasing cumulative probabilities of the surgical success rate after a second surgery for recurrent intermittent exotropia. Addressing the second question, we were not able to find out any previous study of longitudinal comparison of clinical course of recurrent intermittent exotropia after second operation. In addition, we aimed to clarify whether there is any difference in the clinical course of recurrent intermittent exotropia after a second surgery as compared with not only intermittent exotropia after a single surgery but also recurrent intermittent exotropia after the first of two surgeries. These questions led us to investigate the

clinical course of recurrent intermittent exotropia after a second surgery. We analyzed the data of intermittent exotropia patients who underwent an R&R procedure using the rmANOVA method.

This study design was used for the following two main reasons. First, the R&R procedure is one of the most common surgical methods used for correction of intermittent exotropia,<sup>8-10</sup> and we are of the opinion that the surgical data gained by a single surgical procedure performed by a single surgeon will be more valid than that gained by different surgeons performing different procedures. Second, the rmANOVA method is able to analyze the difference over time not only within groups

but also between groups. Moreover, since our clinic opened, postoperative examinations have been conducted using the same follow-up protocol. Therefore, we could use the rmANOVA test for our study.

To enhance the accuracy of the analysis, any patient who missed any regular follow-up in the postoperative 24 months was excluded from this study.

The results showed significant increasing postoperative angle of deviation in all three groups over time. This result is consistent with previous reports of exodrift of intermittent exotropia after surgery.<sup>1,3,8,9,11</sup> Exodrift was also observed after a second surgery in recurrent intermittent exotropia patients. However, the postoperative angle of deviation of the resurgery 2 group was significantly lower than that of both the primary surgery group and resurgery 1 group over 24 months of follow-up. This demonstrates that the clinical course of recurrent intermittent exotropia after a second surgery is better than both intermittent exotropia after a single surgery and recurrent intermittent exotropia after the first of two surgeries.

Why was the incidence of exodrift of the resurgery 2 group lower than that of both the primary surgery group and resurgery 1? In a study of large angle amblyopic exotropia, large resection of the medial rectus using a stay suture was stressed to mechanically prevent an

**Table 1** Surgical dosage of LR recession and MR resection in Yeungnam University Hospital for patients with intermittent exotropia

Prism diopters	Recession amounts of LR	Resection amounts of MR
25	4	3
30	4	4
35	5	4
40	5	5
45	7	5
50	8	5
55	8	6

Abbreviations: LR, lateral rectus muscle; MR, medial rectus muscle.

**Table 2** Demographic and clinical characteristics of the primary surgery group and resurgery group at the first surgery

	Primary surgery group n = 352	Resurgery group n = 77	P-value
Gender (male/female)	166/186	34/43	0.632
Age at first surgery, years	8.27 ± 4.73	5.08 ± 1.68	<0.001
<i>Deviation at first surgery, PD</i>			
Distance	32.75 ± 5.29	32.53 ± 5.17	0.739
Near	33.81 ± 5.90	32.96 ± 5.01	0.244
Operated eye (right/left)	153/199	39/38	0.251
<i>Type of exotropia</i>			
Basic	350	76	0.486
Convergence insufficiency	2	1	
<i>SE refractive error (D)</i>			
Right eye	-0.41 ± 1.93 (-11.50 to +4.25)	-0.29 ± 0.94 (-3.75 to +2.25)	0.433
Left eye	-0.41 ± 1.91 (-11.50 to +5.00)	-0.24 ± 0.93 (-3.00 to +2.25)	0.260
<i>SE anisometropia</i>			
<1.00 D	310	67	0.797
≥1.00 D	42	10	
<i>Result of stereotest</i>			
Lang I test, passed, (%)	308/330 (93.3)	66/75 (88)	0.146
Titmus stereotest, arcsec (n)	334.62 ± 836.16 (158)	776.21 ± 1277.28 (29)	- <sup>a</sup>

Abbreviations: arcsec, arcsecond; D, diopters; PD, prism diopters; SE, spherical equivalent.

Categorical variables are reported using proportions and continuous variables are reported using mean ± SD. P-values for independent t-test,  $\chi^2$ -test.

<sup>a</sup>Statistical analysis was not performed because of missing observation.

**Table 3** Preoperative and postoperative angle of deviation in primary surgery group and resurgery group

	Primary surgery group	Resurgery group	
		Resurgery 1	Resurgery 2
Preoperative angle of deviation, PD	32.75 ± 5.29	32.53 ± 5.17	27.22 ± 3.33
<i>Postoperative angle of deviation</i>			
Immediate	0.45 ± 3.71	1.65 ± 3.20	- 1.49 ± 3.42
1 mo	3.00 ± 4.57	4.65 ± 4.56	1.34 ± 3.85
3 mo	5.31 ± 5.64	8.39 ± 5.54	3.18 ± 4.29
6 mo	7.56 ± 6.47	12.08 ± 5.28	4.73 ± 5.91
12 mo	9.26 ± 7.21	16.14 ± 5.75	6.74 ± 6.64
18 mo	10.46 ± 7.55	18.48 ± 5.23	7.00 ± 6.93
24 mo	11.48 ± 7.66	21.01 ± 6.03	8.18 ± 7.10

Abbreviations: mo, months; PD, prism diopters.

**Table 4** Univariate logistic regression results for a second surgery

	Univariate		
	$\beta$ -Coefficient	P-value	OR (95% CI)
Age at first surgery	-0.464	<0.001	0.629 (0.544–0.727)
<i>Postoperative angle of deviation</i>			
Immediate	0.091	0.010	1.095 (1.022–1.173)
1 mo	0.072	0.006	1.075 (1.021–1.132)
3 mo	0.090	<0.001	1.094 (1.048–1.142)
6 mo	0.110	<0.001	1.116 (1.071–1.164)
12 mo	0.138	<0.001	1.148 (1.103–1.196)
18 mo	0.166	<0.001	1.180 (1.128–1.235)
24 mo	0.202	<0.001	1.224 (1.164–1.288)

Abbreviations: CI, confidence interval; mo, months; OR, odds ratio.

exotropic recurrence.<sup>12</sup> The mechanical force caused by resected medial rectus muscles in both eyes after the first and second surgery is postulated to be the main cause of the lower exodrift of recurrent intermittent exotropia after a second surgery. In addition, previous studies reported that immediate postoperative deviation showed significant association with favorable surgical result.<sup>3,8,11</sup> In the present study, recurrent intermittent exotropia after second surgery showed lower immediate postoperative deviation than intermittent exotropia with a single surgery ( $P < 0.001$ ). The difference in immediate postoperative deviation is also considered the reason of the lower exodrift of recurrent intermittent exotropia after a second surgery.

In the analysis of associated factors related to the second surgery using multivariate logistic regression test, age at surgery showed the strongest association with second surgery. The risk of resurgery decreased with increased age at the first surgery. This result agrees with our previous study by Lim *et al.*<sup>8</sup>

There is controversy regarding the association between stereopsis and surgical outcome of intermittent exotropia. Beneish and Flanders<sup>13</sup> reported that poor

preoperation stereopsis does not necessarily preclude, and may enhance, long-term alignment stability postoperatively. However, Yildirim *et al.*<sup>14</sup> reported that better distance stereoacuity and central fusion are frequently associated with better surgical success in intermittent exotropia. In the present study, there was no difference in stereoacuity measured using Lang I stereotest between primary group and resurgery group. The result of Lang I stereotest did not show any association with second surgery. We could not analyze an association between Titmus test and second surgery for missing observations. The limitation of our study was that a small number of recurrent intermittent exotropia patients whose interval from first to second surgery was <24 months were excluded from the study. However, those data would have little influence on the results.

In conclusion, our results demonstrate that the clinical course of recurrent intermittent exotropia after a second surgery is better at postoperative 24-month follow-up compared with both intermittent exotropia with a single surgery and after its first of two surgeries. These results shed light on the prognosis of recurrent intermittent exotropia after a second surgery.

## Summary

### What was known before

- Many studies have reported postoperative exodrift and recurrence of intermittent exotropia over time after surgical treatment.
- However, few studies have conducted longitudinal analysis of the clinical course of recurrent intermittent exotropia after a second surgery.

### What this study adds

- The clinical course of recurrent intermittent exotropia after a second surgery is better at postoperative 24-month follow-up compared with both intermittent exotropia with a single surgery and after its first of two surgeries.

### Conflict of interest

The authors declare no conflict of interest.

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