Three-muscle surgery for large-angle esotropia in chronic sixth nerve palsy: comparison of two approaches

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ABSTRACT

Aims To report the effect of two three-muscle surgeries, inferior rectus belly transposition plus augmented superior rectus transposition plus medial rectus recession (ISM) and modified vertical rectus belly transposition plus medial rectus recession (VM), in the management of large-angle esotropia in Chinese patients with chronic sixth nerve palsy.

Methods Twenty-eight consecutive patients with large-angle esotropia ≥50Δ were prospectively enrolled and underwent either ISM or VM. Main outcomes included preoperative and postoperative deviation in primary position, abduction limitation and complications. Follow-up was at least 6 months.

Results Of the included patients, 13 underwent ISM and 15 underwent VM. Preoperatively, ISM group displayed larger esotropia and more severe abduction limitation. 27 patients completed the follow-up. The postoperative horizontal deviation and abduction limitation were similar in both groups. At the last follow-up, ISM group demonstrated greater improvement of horizontal deviation and abduction limitation than VM group (p=0.003). Three patients (30%) patients revealed an induced adduction limitation ≤−1. Of the 22 patients with unilateral palsy, eight (36%) developed torsional diplopia. Unexpectedly, keratitis was observed in 4 of 27 (15%) patients, all with concurrent fifth and/or seventh nerve palsy. Three patients (14%) developed vertical diplopia and three (14%) developed torsional diplopia. Unexpectedly, keratitis was observed in 4 of 27 (15%) patients, all with concurrent fifth and/or seventh nerve palsy. Three patients aggravated to corneal ulceration.

Conclusions Two three-muscle surgeries, ISM and VM were both effective for large-angle esotropia in Chinese patients with chronic sixth nerve palsy. However, attention should be paid to potential complications.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Inferior rectus belly transposition could be performed simultaneously with augmented superior rectus transposition and medial rectus recession to correct large esotropia in patients with chronic sixth nerve palsy without increasing the risk of anterior segment ischaemia. However, the real effect of inferior rectus belly transposition plus augmented superior rectus transposition plus medial rectus recession (ISM) needs to be elucidated.

WHAT THIS STUDY ADDS

⇒ Two three muscle surgeries, ISM and modified vertical rectus belly transposition plus medial rectus recession (VM), could effectively manage large esotropia in patients with chronic sixth nerve palsy, despite an indeterminate relative effectiveness of ISM to VM.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ We recommend both ISM and VM for large esotropia ≥50Δ in patients with chronic sixth nerve palsy to reduce the possibility of residual esotropia.

INTRODUCTION

Sixth nerve palsy is one of the common cranial nerve palsies. Complete or partial vertical rectus transposition (VRT) to the lateral rectus is recommended to correct esotropia and improve abduction limitation on the failure of the eye to rotate beyond the midline, thus relieving diplopia and head posture.1–3 Of these procedures, superior rectus transposition (SRT) can be simultaneously performed with ipsilateral medial rectus recession (MRC), and shows superiority in chronic cases with medial rectus contracture.1–3 Regardless of the procedure, residual esotropia continues to be a challenge, particularly for patients with large-angle esotropia and severe abduction limitation. Ipsilateral MRC4–9 following full tendon VRT and inferior rectus transposition5–8 following augmented SRT plus MRC have been reported to manage residual esotropia. However, tenotomy of three or more rectus muscles would increase the risk of anterior segment ischaemia (ASI).10 Even implementation of these additional procedures after at least 2 months cannot avoid this risk.

To reduce the risk of ASI, we have developed a novel method, inferior rectus belly transposition, for treating residual esotropia simultaneously or subsequently following augmented SRT plus MRC.11 This procedure does not require tenotomy or muscle splitting, and can correct residual esotropia of up to 25Δ while least likely to disturb the circulation in the inferior rectus. This three-muscle surgery, namely inferior rectus belly transposition plus augmented SRT plus MRC (ISM), is suggested for patients with large-angle esotropia (≥60Δ). Nonetheless, its real
effect needs to be elucidated. We have also developed another three-muscle surgery, namely modified vertical rectus belly transposition plus MRC (VM), for chronic sixth nerve palsy. Compared with augmented SRT plus MRC, VM shows better effect in correcting esotropia and similar effect in improving abduction limitation. Nonetheless, its effect for large esotropia is unknown. In this prospective observational study, we aim to determine the outcomes of ISM and VM for large esotropia in Chinese patients with chronic sixth nerve palsy.

**METHODS**

Chinese patients with large-angle esotropia suffering from chronic sixth nerve palsy were prospectively enrolled. The inclusion criteria included preoperative esotropia ≥50 Δ, abduction limitation ≤−4 and a stable deviation angle for at least 6 months. Patients who had undergone previous strabismus surgery on the affected eye or a prior botulinum toxin injection to the antagonist medial rectus within 6 months were excluded. Patients who had concurrent third or fourth nerve palsy were excluded. All surgeries were performed by a single surgeon (CZ). The choice of the approach was dictated by the experience of the surgeon. All patients underwent a complete ophthalmic evaluation at baseline. Follow-up was scheduled at 1 month and 6 months. However, some patients were unable to finish the follow-up at 6 months on schedule because of COVID-19. Therefore, the actual last follow-up time was recorded. Except special annotation, the postoperative outcomes were reported according to the last follow-up. Preoperative and postoperative deviation were measured using reverse Krimsky test and prism alternating cover test, respectively. Ductions were graded from 0 (normal) through −4 (inability to move beyond the midline) and −5 (inability to reach midline) to a maximum of −8 (fixed in an extreme adducted position). Furthermore, a self-designed ruler was used to quantify the abduction limitation (Figure 1). The photograph was accepted for quantitation only when the contralateral eye was adducted to the inner canthus. Torsional deviation was subjectively and objectively assessed by double Maddox rod test and fundus photograph (evaluating the position of the fovea relative to the optic disc), respectively. Stereoview was measured using Titmus (Stereo Optical, Chicago, Illinois, USA). Surgical success was defined as a postoperative deviation in primary position within 10 Δ at the last follow-up. Patients were assigned to exo-drift, no-drift or eso-drift according to the horizontal deviation in primary position from 1 month to the last follow-up. The postoperative drift of abduction limitation was defined as the difference in abduction quantitation by subtracting the last follow-up from 1 month: >0.2 mm as improvement, <−0.2 mm as regression and −0.2 to 0.2 mm as no change. To avoid the bias, all the tests were conducted by study-certified examiners masked to the treatment.

At the beginning of the surgery, forced duction test was performed. If medial rectus contracture was confirmed, an ipsilateral hang-back MRC with an adjustable suture was simultaneously performed. The amount of recession was measured from the original insertion, which was primarily based on the deviation in primary position and the tightness of the medial rectus. As for patients under topical anaesthesia, the amount of MRC was adjusted during operation while the adjustment was performed on the subsequent day in patients under general anaesthesia. All surgeries were performed using a fornix incision and minimal dissection of the surrounding connective tissue.

**Augmented SRT**

It was performed as described previously. Following the isolation of the superior rectus, it was secured using a double armed 6–0 polyglactin 910 suture, disinserted and then reattached adjacent to the superior border of the lateral rectus along the spiral of Tillaux. Augmentation was performed by anchoring the temporal one-fourth of the width of the superior rectus belly to the sclera 8 mm posterior to the insertion of the lateral rectus using 5–0 polyester suture.

**Inferior rectus belly transposition**

After exploring the inferior rectus, a non-absorbable 5–0 polyester suture was passed through its temporal one-fourth of the belly width at a distance of 8 mm behind its insertion and was tied there to avoid muscle breakage during transposition. Subsequently, the temporal margin of the inferior rectus was temporally transposed and anchored onto the sclera, 2 mm adjacent and 6–8 mm posterior to the inferior pole of the lateral rectus using the same suture.

**Modified vertical rectus belly transposition**

The representative steps were demonstrated in our previous study. Both the superior and inferior rectus muscles were transposed. Briefly, after exploring the superior or the inferior rectus, a non-absorbable 5–0 polyester suture was passed through the temporal one-fourth width of the superior rectus belly or the inferior rectus belly at a distance of 8 mm behind its insertion and then transposed the temporal margin of the superior rectus or the inferior rectus to 2 mm adjacent and 6 to 8 mm posterior to the superior or inferior pole of the lateral rectus.

Statistical analyses were performed using SPSS V.22.0 software. Data distribution and homogeneity were analysed. Independent sample t-test or Mann-Whitney U test was applied to compare the continuous variables between groups. Moreover, paired t-test or Wilcoxon signed-rank test was performed to analyse the preoperative and postoperative esotropia and
abduction limitation. Categorical variables between groups were compared via Pearson χ² test or Fisher’s exact test for any of the expected values in the contingency table less than 5. Multiple linear regression analysis was used to investigate the associated factors with stereoacuity. A p<0.05 was considered statistically significant.

RESULTS

Of the 28 patients, 13 underwent ISM and 15 underwent VM. Two patients in ISM group were reported in our previous study. The characteristics of patients in both groups were comparable except the time from onset to surgery (table 1). The aetiologies for the patients were as follows: trauma 16/28 (57%), tumour 10/28 (36%) and vascular 2/28 (7%). Of the 10 patients with tumour, 3 suffered from nasopharyngeal carcinoma.

Positive forced duction test was demonstrated in all patients postsurgery. Of the 22 patients with unilateral palsy, the deviation reduced from 81.2° to 0.2° in ISM group, and from

The horizontal deviation in primary position was reduced in all patients postsurgery. Of the 22 patients with unilateral palsy, the deviation reduced from 81.2° to 0.2° in ISM group, and from

Table 1 Patients’ characteristics in ISM and VM groups

| Characteristic                  | Group          | ISM (n=13) | VM (n=15) | P value |
|--------------------------------|---------------|------------|-----------|---------|
| Male, no (%)                   | 8 (62)        | 4 (27)     | 0.13†     |
| Age at surgery, mean±SD (range), year | 54.9±12.0 (38–75) | 45.5±11.2 (19–63) | 0.05    |
| Time from onset to surgery, mean±SD (range), month | 28.3±19.1 (9–60) | 20.1±22.2 (7–72) | 0.03*    |
| Aetiology, no (%)              |               |            | 0.45†     |
| Traumatic                      | 7 (54)        | 9 (60)     |           |
| Tumour                         | 4 (31)        | 6 (40)     |           |
| Vascular                       | 2 (15)        | 0 (0)      |           |
| Eyes affected, left:right:both | 5:5.3         | 5:8.2      | 0.69†     |
| Follow-up, mean±SD (range), month | 9.5±3.8 (6–19) | 8.1±3.4 (6–16) | 0.20     |

*P<0.05.
†Pearson χ² test or Fisher’s exact test.
‡n=11 in VM group due to lateral tarsorrhaphy of 2 patients.

The median follow-up durations are 8 months in ISM group and 6 months in VM group, respectively. The bottom and top of each box represent the 25th and 75th percentiles and lines within the boxes are the medians. The ends of the whiskers represent the minimum and maximum of all the data. MRc, medial rectus recession; ISM, inferior rectus belly transposition plus augmented superior rectus transposition plus medial rectus recession; VM, modified vertical rectus belly transposition plus medial rectus recession.

Table 2 Preoperative and postoperative abduction limitation and adduction limitation in ISM and VM groups

| Preoperative and postoperative abduction limitation | ISM (n=13) | VM (n=14) | P value |
|----------------------------------------------------|------------|-----------|---------|
| Abduction grading, mean±SD (range)                 | Baseline -6.6±0.9 (−5 to −8) | -4.6±1.1 (−4 to −7) | <0.001* |
| 1 month after surgery -2.2±0.7 (−1 to −3) | -2.2±0.5 (−1 to −3) | 0.83 |
| Improvement at 1 month -4.4±1.0 (−3 to −7) | -2.4±1.1 (−1 to −5) | <0.001* |
| The last visit after surgery -2.2±0.7 (−1 to −3) | -2.3±0.7 (−1 to −4) | 0.91 |
| Improvement at the last visit -4.5±1.1 (−3 to −7) | -2.4±1.0 (−1 to −5) | <0.001* |
| Abduction quantitation, mean±SD (range) | Baseline 12.8±2.6 (7.7–18.2) | 10.0±2.0 (7.1–14.9) | 0.003* |
| 1 month after surgery 5.9±2.1 (1.5–9.0) | 4.9±1.5 (3.0–7.6) | 0.14 |
| Improvement at 1 month 6.9±1.4 (4.8–9.8) | 5.1±1.7 (2.6–8.5) | 0.006* |
| The last visit after surgery 5.2±2.2 (1.0–8.0)† | 4.9±1.8 (2.9–9.5) | 0.47 |
| Improvement at the last visit 7.8±1.6 (5.8–10.2)† | 5.2±1.5 (3.4–8.7) | 0.001* |
| Change from 1 month to the last visit | 1:1:91† | 2:5:7 | 0.23† |

Adduction grading at the last visit, mean±SD (range) | -0.6±0.8 (−2 to 0) | -0.6±0.6 (−2 to 0) | 0.91 |

*P<0.05.
†n=11 in ISM group due to lateral tarsorrhaphy of 2 patients.
‡Pearson χ² test or Fisher’s exact test.

ISM, inferior rectus belly transposition plus augmented superior rectus transposition plus medial rectus recession; VM, modified vertical rectus belly transposition plus medial rectus recession.
null hypotheses was not achieved. The patient with residual esotropia of 5° did not achieve success at the last follow-up: one undercorrected and one overcorrected (table 3). The patient with residual esotropia of 20° suffered intermittent diplopia. However, she refused prismatic correction. The other patient with intermittent esotropia of 25° was almost asymptomatic except contralateral diplopia owing to an abduction limitation of −2. Four patients in ISM group developed hypotropia (5°, 8°, 10°, 18°). One patient in ISM group (5°) and three patients in VM group (5°, 10°, 14°) developed hypertropia (table 3). However, only three (14%) complained of a vertical diplopia (2 ISM, 1 VM). Nonetheless, the diplopia could be compensated with a head turn and the patients refused prisms or further surgery.

Double Maddox rod test and fundus photography were performed in all patients. Of the 22 patients with unilateral palsies, no patient demonstrated subjective torsional diplopia preoperatively. Clear preoperative fundus photograph was only performed in all patients. Of the 22 patients with unilateral palsies, no patient demonstrated subjective torsional diplopia preoperatively. Clear preoperative fundus photograph was only obtained in three patients (all normal) in ISM group, and five patients (one extorsion and four normal) in VM group owing to severe abduction limitation. No patient in either group developed intorsion postsurgery. At the last follow-up, seven patients (32%) demonstrated postoperative extorsion, and three (14%) complained of a torsional diplopia (table 3). All the torsional deviation was no more than 5°, which was asymptomatic or could be compensated with a head turn except one patient in VM group. The exceptional patient displayed a hypertropia of 14° and a subjective torsional deviation of 25°. However, her vertical and torsional diplopia could be compensated by an inverse head turn. No further treatment was required.

None of the patients demonstrated measurable stereocuity preoperatively. Ten patients (37%) displayed near stereocuity ≤200 arcsec postsurgery (4 ISM, 6 VM). The proportion was similar in both groups (p=0.69). Multiple linear regression analysis (factors: postoperative spherical equivalence, best-corrected visual acuity, horizontal deviation, vertical deviation, subjective torsional deviation and objective torsional deviation) demonstrated that postoperative best-corrected visual acuity (p=0.02), vertical deviation (p=0.02) and objective torsional deviation (p=0.04) were associated with near stereocuity.

Unexpectedly, two patients in ISM group and one in VM group developed keratitis in the operated eye. One patient with bilateral palsy in VM group developed keratitis in both the operated and the contralateral eyes. Three of them aggravated to corneal ulceration and underwent tarsorrhaphy. The corneal ulceration was ultimately resolved with residual corneal opacity. They demonstrated recovered visual acuity. ASI was not detected at the last follow-up. No other serious intraoperative and postoperative complications were observed.

### DISCUSSION

So far as we know, our study cohort had the largest amount of preoperative esotropia owing to chronic sixth nerve palsy. The two approaches of three-muscle surgery, ISM and VM, effectively corrected esotropia and improved abduction limitation. All unilateral patients achieved success except 1 undercorrected and 1 overcorrected. ISM corrected more esotropia and improved greater abduction limitation than VM. Nonetheless, we could not confirm the relative effectiveness of ISM to VM owing to the differences in their preoperative esotropia and abduction limitation. Therefore, the real clinical superiority of ISM to VM requires further research.

Following VRT, different rates of residual esotropia have been reported: 6/8 (75%) cases in Lee’s study and 9/26 (35%) cases in del Pilar Gonzalez’s study following full tendon VRT, 2/13 (15%) cases in Patil-Chhablani’s study, 1/7 (14%) cases in Mehendale’s study, and 7/13 (54%) cases in Liu’s study following SRT plus MRc. This difference may be attributed to the diverse procedures, preoperative esotropia, and preoperative abduction limitation. Patil-Chhablani’s study demonstrated that residual esotropia easily occurred in patients with large preoperative esotropia of ≥50°. However, ISM group had a larger patient number and all had preoperative esotropia ≥50°. Nonetheless, only one patient had residual esotropia of 20°. Multivariable linear regression analysis conducted by Liu et al revealed that preoperative abduction limitation was the only factor associated with residual esotropia. The fact of our cohort did not support it. The only undercorrected patient had an abduction limitation of −7. However, other patients with an abduction limitation ≤−7 achieved success. At present, we could not identify the factor predisposed to residual esotropia. Nevertheless, an effective procedure appears feasible to avoid residual esotropia.

Full tendon VRT is an effective procedure and transposition with resection of the vertical rectus or augmentation sutures could increase the surgical effect from 36.0° to 46.4° or to 41.3° respectively. Addition of MRc could achieve a larger effect. However, transposing both the vertical rectus muscles and MRc are fraught with the risk of ASI, and even partial VRT or rectus muscle union without tenotomy cannot avoid this risk. Addition of MRc could achieve a larger effect. However, transposing both the vertical rectus muscles and MRc are fraught with the risk of ASI, and even partial VRT or rectus muscle union without tenotomy cannot avoid this risk. Therefore, MRc has to be performed as an additional procedure, which is associated with additional direct and indirect costs. To reduce the risk of ASI, vertical
recusus belly transposition, which does not require tenotomy or muscle splitting, has been developed. It can be simultaneously performed with ipsilateral MRc without increasing the risk of ASI, which displays priority in chronic cases associated with medial rectus contracture. VM as described by Muraki et al. corrected an average esotropia of 46.3°. With the modification of the anchoring position, VM increased the correction amount of esotropia to 37.8° in our previous study. In this study, the correction amount in VM group was 66.2°.

Besides vertical rectus belly transposition, SRT (Johnston SC, et al. IOVS 2006;47:ARVO E-Abstract 2475) transposes the superior rectus alone, and can be simultaneously and safely performed with ipsilateral MRc. Previous studies reported that SRT plus MRc could correct esotropia up to 40.6°. Compared with full tendon VRT, SRT plus MRc displayed similar effect in the correction of esotropia and fewer additional procedures in Lee’s study. However, it’s correction amount of esotropia was less than VM in our previous study. If there is residual esotropia following SRT plus MRc, some researchers have attempted inferior rectus transposition, which may predispense the patients to an increased risk of ASI. Inferior rectus belly transposition introduced in our previous study could treat residual esotropia with the least risk of disturbing the circulation in the inferior rectus. In this study, ISM effectively managed large esotropia caused by chronic sixth nerve palsy. It could correct esotropia of 81.0° in one-step surgery, greater than VM. The indeterminate relative effectiveness of ISM to VM can be attributed to larger preoperative esotropia and relatively greater amount of MRc in ISM group. However, both ISM and VM are suggested for large esotropia ≥50° to reduce the possibility of residual esotropia and additional procedures.

MRc could improve abduction limitation in chronic cases with medial rectus contracture. Greater amount of MRc could theoretically achieve better effect. Our finding of greater improvement in abduction limitation with ISM might be attributed to relatively larger amount of MRc in ISM group. In this study, we introduced abduction quantitation besides abduction grading. The aforementioned two methods generated consistent results, and quantitation appeared better to evaluate the small drift. Nine patients with ISM and seven with VM revealed further improvement in abduction from month 1 to the last follow-up, which was helpful for binocular single vision. However, the large amount of MRc may induce abduction limitation, and a significant compromise in adduction would constrict the gaze field contralateral to the operated eye. The final MRc was 4.5–14 mm in this study. Eighteen patients had a MRc >7 mm, larger than that in previous studies (0–5 mm). Correspondingly, we observed an induced adduction limitation of −2 to −1 in eight patients, while the induced adduction limitation reported in previous studies was no less than −1. Nevertheless, we could not find the association between the amount of MRc and adduction limitation. Small sample size might be one reason. Hangback recession with minimal dissection of the surrounding connective tissue might be another reason. It was reported that the medial rectus would react to the globe closer to the insertion than expected on performing minimal dissection. This may explain the preserved adduction of medial rectus in several patients. How to balance orthophoria and adduction limitation in large esotropia needs to be addressed in further study. Recession of the contralateral medial rectus provides an alternative. Thus, a smaller ipsilateral MRc is needed, which reduces the risk of adduction limitation.

Both asymmetry and symmetry procedures of VRT may induce vertical and torsional deviation. It is proposed that perfect symmetry between the inferior and the superior rectus muscles is difficult to achieve, which can be attributed to the differences in anatomy, mechanical factors, connective tissue and/or attachments to the eyelid. The reported incidence of vertical deviation following full tendon VRT ranges from 10% to 33%, including hypertropia and hypotropia. However, we only observed hypertropia following VM in our previous study and the present study. Both full tendon VRT and VM demonstrate an extorsional shift, consistent with our findings. Considering the function of the superior rectus, SRT may create hypertropia and intorsion. Previous studies have confirmed the intorsional shift following SRT. Nonetheless, hypertropia is also developed following SRT besides hypertropia. In this study, we observed more hypotropia than hypertropia following ISM, which may be attributed to more reduction in elevating force with SRT than that in depressing force with inferior rectus belly transposition. Contrary to SRT, we observed an extorsional shift following ISM. The reported vertical and torsional deviation are small. Nevertheless, preoperative torsion assessment and intraoperative torsion monitoring are suggested to avoid the risk of clinically significant postoperative extorsion.

Refractory keratitis is an unexpected complication. Patients with concurrent fifth and/or seventh nerve palsy are at a high risk of refractory keratitis. Besides topical ischemia and administration of topical medications, induced hypotropia following VRT may contribute to its development. All the aforementioned four patients had concurrent fifth and/or seventh nerve palsy. Two patients with postoperative hypotropia aggravated to corneal ulceration, whereas the one with postoperative hypertropia remained stable. The bilateral case did not reveal vertical deviation. However, keratitis deteriorated post radiotherapy. Fortunately, the corneal ulceration is usually situated on the lower side of the cornea. Rapid treatment can make it resolve with little influence on the visual acuity. Realising the risks of this complication and its instant management would improve the prognosis.

The strengths of our study were as follows: (1) All the surgeries were performed by the identical surgeon, using the same measurement criteria and surgical techniques; (2) Abduction limitation was evaluated by both grading and quantitation; and (3) Despite most patients being unable to finish the 6-month follow-up on schedule owing to COVID-19, the actual last follow-up time was at least 6 months postsurgery, which enabled all patients to reach a relative stable alignment. However, our study had several limitations as follows: (1) It was a small non-randomised prospective study. We identified the differences in the baseline characteristics between the groups (eg, larger esotropia and more severe abduction limitation in ISM group than those in VM group) which would reduce the comparability of the groups. This warrants a randomised clinical trial to compare the effectiveness between these approaches; (2) Owing to severe abduction limitation, we measured preoperative deviation using Krimsky test, which made it difficult to detect the small vertical deviation; (3) A clear fundus photograph could only be obtained in a few patients to evaluate the preoperative objective torsion because of severe abduction limitation; and (4) Abduction quantitation was dependent on the photograph displayed in figure 1. The subjective abducting effort might be a confounder.

Despite the aforementioned limitations, this study highlighted the effectiveness of ISM and VM in the management of large esotropia in Chinese patients with chronic sixth nerve palsy. Both approaches could be used as promising alternatives for large esotropia ≥50° to avoid residual esotropia. Nonetheless, either
approach carries a small risk of induced vertical or torsional diplopia. Added attention to patients with simultaneous fifth and/or seventh nerve palsy is needed owing to the risk of corneal keratitis and ulceration.

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