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[Intervention Review]

Surgical interventions for vertical strabismus in superior oblique palsy

Melinda Y Chang[1], Anne L Coleman[1], Victoria L Tseng[1], Joseph L Demer[2]

[1]Stein Eye Institute, UCLA, Los Angeles, California, USA. [2]Ophthalmology, Stein Eye Institute, UCLA, Los Angeles, California, USA

Contact: Melinda Y Chang, Stein Eye Institute, UCLA, 100 Stein Plaza, Los Angeles, California, 90025, USA. melinda.y.wu@gmail.com.

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ABSTRACT

Background

Superior oblique palsy is a common cause of vertical strabismus in adults and children. Patients may be symptomatic from binocular vertical diplopia or compensatory head tilt required to maintain single vision. Most patients who are symptomatic elect to undergo strabismus surgery, but the optimal surgical treatment for vertical strabismus in people with superior oblique palsy is unknown.

Objectives

To assess the relative effects of surgical treatments compared with another surgical intervention, non-surgical intervention, or observation for vertical strabismus in people with superior oblique palsy.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Trials Register) (2016, Issue 12), MEDLINE Ovid (1946 to 13 December 2016), Embase Ovid (1947 to 13 December 2016), Latin American and Caribbean Health Sciences Literature Database (LILACS) (1982 to 13 December 2016), the ISRCTN registry (www.isrctn.com/editAdvancedSearch); searched 13 December 2016, ClinicalTrials.gov (www.clinicaltrials.gov); searched 13 December 2016, and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en); searched 13 December 2016. We did not use any date or language restrictions in the electronic searches for trials.

Selection criteria

We included randomized trials that compared at least one type of surgical intervention to another surgical or non-surgical intervention or observation.

Data collection and analysis

Two review authors independently completed eligibility screening, data abstraction, 'Risk of bias' assessment, and grading of the evidence.

Main results

We identified two randomized trials comparing four different surgical treatments for this condition, two methods in each trial. The studies included a total of 45 children and adults. The surgical treatments were all procedures to weaken the ipsilateral inferior oblique muscle. One study compared inferior oblique myectomy to recession of 10 mm; the other study compared inferior oblique disinsertion to anterior transposition (2 mm anterior to the temporal border of the inferior rectus insertion).

We judged both studies to be at unclear risk of bias due to incomplete reporting of methods and other methodological deficiencies.

Neither study reported data on the primary outcome of this review, which was the proportion of participants with postoperative surgical success, defined as hypertropia less than 3 prism diopters (PD) in primary gaze. However, both studies reported the average reduction

in hypertropia in primary gaze. One study found that at 12 months' postoperatively the average decrease in hypertropia was higher in participants who underwent inferior oblique myectomy than in those who underwent recession, however data were not available for statistical comparison. The other trial found that after at least six months of follow-up, the mean decrease in primary position hypertropia was lower in participants who underwent inferior oblique disinsertion than in those who underwent anterior transposition (mean difference (MD) -5.20 PD, 95% confidence interval (CI) -7.76 to -2.64; moderate-quality evidence).

Both trials also reported the average postoperative reduction in vertical deviation in adduction. One study reported that the average reduction in hypertropia in adduction was greater in participants who underwent inferior oblique myectomy than in those who underwent recession, but data were not available for statistical comparison. The other study found a lower decrease in hypertropia in contralateral gaze in participants who underwent inferior oblique disinsertion than in those who underwent anterior transposition (MD -7.10 PD, 95% CI -13.85 to -0.35; moderate-quality evidence).

Secondary outcomes with sufficient data for analysis included proportion of participants with preoperative head tilt that resolved postoperatively and proportion of participants who underwent a second surgery. These outcomes were assessed in the trial comparing inferior oblique anterior transposition to disinsertion; both outcomes favored anterior transposition (risk ratio 7.00, 95% CI 0.40 to 121.39 for both outcomes; very low-quality evidence). None of the participants who underwent inferior oblique anterior transposition or disinsertion developed postoperative hypotropia or reversal of the vertical deviation. All participants who underwent inferior oblique anterior transposition developed elevation deficiency, which the authors deemed to be clinically insignificant in all cases, whereas no participants who underwent inferior oblique disinsertion experienced this complication. Additionally, the trial comparing inferior oblique myectomy to recession reported that no participant in either group required another strabismus surgery during the postoperative period.

Authors' conclusions

The two trials included in this review evaluated four inferior oblique weakening procedures for surgical treatment of superior oblique palsy. We found no trials comparing other types of surgical procedures for this disorder. Both studies had enrolled a small number of participants and provided low-quality evidence due to limitations in completeness and applicability. We therefore found no high-quality evidence to support recommendations for optimal surgical treatment of superior oblique palsy. Rigorously designed, conducted, and reported randomized trials are needed to identify the optimal surgical treatment for vertical strabismus in this disorder.

PLAIN LANGUAGE SUMMARY

Surgical treatments for vertical eye misalignment (strabismus) in superior oblique palsy

Review aim
The aim of this Cochrane Review was to determine whether surgery for vertical strabismus in people with superior oblique palsy works better than other surgical or non-surgical interventions. We searched for all relevant studies and identified two clinical trials.

Key messages
There is no high-quality evidence regarding the effects of surgery on vertical strabismus in people with superior oblique palsy. Consequently, we were unable to determine the best surgery for this disorder. Carefully designed studies are needed to enable treatment recommendations for this common problem.

What did we study in this review?
We compared different types of surgery to reduce vertical strabismus in children and adults with a diagnosis of superior oblique palsy. Superior oblique palsy occurs when there is weakness of one of the muscles (superior oblique) involved in eye movement, causing a characteristic pattern of strabismus, or misalignment of the eyes, that usually varies with head positioning. Superior oblique palsy is a common cause of vertical strabismus, and can lead to double vision or abnormal head positioning in order to maintain single vision.

Main results
Each of the two included trials compared two different surgical procedures to weaken the inferior oblique muscle, and thus balance the weakness in the superior oblique muscle. A total of four different inferior oblique muscle-weakening surgeries were studied: myectomy (removing part of the muscle), recession (moving the muscle to a position where it exerts less force), anterior transposition (moving the muscle to a position where the direction of force is altered), and disinsertion (detaching the muscle from the sclera).

Neither of the trials examined the main outcome we wished to study, that is the proportion of participants deemed to have successful eye realignment after surgery. Additionally, we judged the quality of the data in both studies to be low.

How up-to-date is this review?
We searched for trials with outcome data published by 13 December 2016. The included trials were published between 2001 and 2003.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Inferior oblique myectomy versus recession for vertical strabismus in superior oblique palsy

Inferior oblique myectomy compared with inferior oblique recession for vertical strabismus in superior oblique palsy

Patient or population: people with symptom-producing and/or socially noticeable unilateral overacting inferior oblique muscle; all participants had longstanding unilateral superior oblique underaction

Settings: eye hospital

Intervention: inferior oblique myectomy

Comparison: inferior oblique recession

Outcomes	Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
Proportion of participants with postoperative surgical success (hypertropia less than 3 PD in primary gaze)	N/A	23 (1 study)	N/A	This outcome measure was not reported in the study included in this comparison. However, median hypertropia in primary gaze at 12 months was 3 PD in the myectomy group and 1 PD in the recession group. The average reduction in hypertropia in primary position was 14 PD in the myectomy group and 8 PD in the recession group (P = 0.042).
Proportion of participants with anomalous head position preoperatively with residual head tilt postoperatively	N/A	23 (1 study)	N/A	This outcome measure was not reported in the study included in this comparison.
Proportion of participants with postoperative hypertropia less than 3 PD in down gaze	N/A	23 (1 study)	N/A	This outcome measure was not reported in the study included in this comparison.
Proportion of participants with postoperative hypertropia less than 3 PD in contralateral gaze	N/A	23 (1 study)	N/A	This outcome measure was not reported in the study included in this comparison.
Proportion of participants who received additional strabismus surgery	N/A	23 (1 study)	N/A	None of the participants in either group required a second strabismus surgery during the follow-up interval.
Proportion of participants with reversal of vertical deviation postoperatively	N/A	23 (1 study)	N/A	This outcome measure was not reported in the study included in this comparison.
Proportion of participants with postoperative orbital cellulitis	N/A	23 (1 study)	N/A	This outcome measure was not reported in the study included in this comparison.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of the effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of the effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

CI: confidence interval; **N/A:** not applicable; **PD:** prism diopters

Summary of findings 2. Inferior oblique disinsertion versus anterior transposition for vertical strabismus in superior oblique palsy

Inferior oblique disinsertion compared with inferior oblique anterior transposition for vertical strabismus in superior oblique palsy

Patient or population: people with unilateral superior oblique palsy

Settings: eye hospital

Intervention: inferior oblique disinsertion

Comparison: inferior oblique anterior transposition

Outcomes	Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
Proportion of participants with postoperative surgical success (hypertropia less than 3 PD in primary gaze)	N/A	22 (1 study)	Moderate	This outcome measure was not reported in the study included in this comparison. However, the mean reduction of hypertropia in primary position was 13.3 (SD 1.9) PD in the disinsertion group and 18.5 (SD 3.9) PD in the anterior transposition group (mean difference -5.20 PD, 95% CI -7.76 to -2.64). This difference favors inferior oblique anterior transposition.
Proportion of participants with anomalous head position preoperatively with residual head tilt postoperatively	RR 7.00 (0.40 to 121.39)	22 (1 study)	Very low	This outcome favors inferior oblique anterior transposition.
Proportion of participants with postoperative hypertropia less than 3 PD in down gaze	N/A	22 (1 study)	N/A	This outcome measure was not reported in the study included in this comparison.
Proportion of participants with postoperative hypertropia less than 3 PD in contralateral gaze	N/A	22 (1 study)	Moderate	The mean reduction of hypertropia in adduction was 20.6 (SD 6.2) PD in the disinsertion group and 27.7 (SD 9.6) PD in the anterior transposition group (mean difference -7.10 PD, 95% CI -13.85 to -0.35). Anterior transposition resulted in a greater decrease in hypertropia in contralateral gaze, but it was unclear whether this difference favored the anterior transposition group, since the authors did not report the num-

				ber of participants overcorrected in contralateral gaze.
Proportion of participants who received additional strabismus surgery	RR 7.00 (0.40 to 121.39)	22 (1 study)	Very low	This outcome favors inferior oblique anterior transposition.
Proportion of participants with reversal of vertical deviation postoperatively	N/A	22 (1 study)	N/A	None of the participants in either group developed postoperative reversal of vertical deviation.
Proportion of participants with postoperative orbital cellulitis	N/A	22 (1 study)	N/A	This outcome measure was not reported in the study included in this comparison.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of the effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of the effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

CI: confidence interval; **N/A:** not applicable; **PD:** prism diopters; **RR:** risk ratio; **SD:** standard deviation

BACKGROUND

Description of the condition

Superior oblique palsy is considered to be the most common cyclovertical muscle palsy (Plager 1999). A recent epidemiological study found the annual incidence of adult-onset superior oblique palsy to be 6.3 cases per 100,000 people, but significantly higher in men than women (Martinez-Thompson 2014). In children younger than 19 years of age, the annual incidence was 3.4 cases per 100,000 (Tollefson 2006), with 31% of vertical strabismus in children attributed to superior oblique palsy, of equal incidence by gender.

Superior oblique palsy may be congenital or acquired. Possible causes of congenital superior oblique palsy include hypoplasia of the trochlear nucleus or nerve and anatomical defects or absence of the superior oblique tendon or trochlea (Chan 1999; Helveston 1992; Mansour 1986). Acquired cases have been presumed to be most frequently secondary to trauma, although the association is in many cases tenuous. Other causes of acquired superior oblique palsy include inflammation, infection, vascular malformation, infarct, tumor, myasthenia gravis, or iatrogenic denervation of muscle complicating sinus, orbital, or neurologic surgery (Plager 1999; Tamhankar 2013).

Clinical characteristics

The main clinical feature of superior oblique palsy is vertical binocular misalignment (strabismus), which occurs when the vertical angular orientation of one eye differs from that of the other eye. In superior oblique palsy, there is hypertropia (upward deviation) of the eye on the same side as the affected muscle, which may present with diplopia (double vision) or be compensated by an abnormal head position. The head is usually tilted in the direction of the shoulder opposite to the elevated eye, and the chin may be lowered or, less commonly, raised to minimize the vertical strabismus. There may also be excyclotorsion of the hypertropic eye, that is rotation of the eye about the line of sight so that the normally vertical meridian of the eye is tilted away from the midline of the face.

Diagnosis

Superior oblique palsy is typically considered to produce an incomitant strabismus in which the vertical misalignment varies in magnitude with different gaze positions relative to the head. However, there may be individual exceptions. The historical gold standard for diagnosis has been considered to be the Parks-Bielschowsky three-step test. The elements of the three-step test for acute, unilateral (one eye) superior oblique palsy consist of: 1) hypertropia of the eye ipsilateral to the palsied superior oblique muscle; 2) increased magnitude of hypertropia in lateral gaze contralateral to the affected eye; and 3) increased magnitude of hypertropia when the head is tilted towards the shoulder corresponding to the affected eye (Bielschowsky 1935). Investigators of more recent magnetic resonance imaging (MRI) studies of superior oblique structure and function have challenged the three-step test, demonstrating it to be only about 70% sensitive, Manchandia 2014, and 50% specific, Demer 2011, for deficient superior oblique function. Consequently, earlier studies that reported the clinical characteristics of superior oblique palsy as diagnosed by the three-step test probably included a substantial fraction of misdiagnosed alternative causes of vertical strabismus, and also systematically omitted many cases of actual superior oblique weakness.

Historically, it has been hypothesized that when longstanding, as in congenital superior oblique palsy presenting in adulthood, the vertical strabismus may be more comitant, or similar in magnitude in all gaze directions. In general, children more often present with an anomalous head position rather than diplopia, because the developing brain suppresses central perception from one eye when the eyes are not aligned. Older children with acquired superior oblique palsy who see double may be unable to verbalize this symptom. Adults may present with an anomalous head position or diplopia from vertical misalignment or excyclotorsion.

Bilateral superior oblique palsy

Superior oblique palsy may be bilateral, involving both eyes. In this case, patients may have hypertropia that alternates with gaze position and head tilt, as well as crossing of the eyes (esotropia) increasing in down gaze with a V pattern. On right gaze, the left eye is hypertropic, while the right eye is hypertropic in left gaze. In addition, with the head tilted to the right, the right eye is hypertropic, while the left eye is hypertropic on left head tilt. The degree of excyclotorsion is typically larger in bilateral than in unilateral superior oblique palsy (Kushner 1988).

Congenital superior oblique palsy

Congenital superior oblique palsy may manifest in childhood or adulthood. Presentation may be precipitated by inability to sustain the effort required to compensate for the vertical misalignment. Clinical signs associated with a congenital superior oblique palsy include longstanding torticollis and facial asymmetry (Plager 1999), although the relationship between facial asymmetry and superior oblique palsy has been questioned (Velez 2000). People with congenital superior oblique palsy also may have a larger-than-normal vertical fusion amplitude. The vertical fusion amplitude refers to the greatest amount of vertical ocular misalignment that the brain can tolerate without the person experiencing diplopia. The normal vertical fusion amplitude for long-distance viewing is less than or equal to 3 prism diopters (PD) (Bharadwaj 2007; Parks 2005); people with a vertical fusion amplitude greater than this are suspected of having congenital superior oblique palsy.

Acquired superior oblique palsy

Superior oblique palsy may also be acquired in either childhood or adulthood. The trochlear nerve, which innervates the superior oblique muscle, may be compromised anywhere along its long course from the dorsal midbrain to the orbit, traversing intracranial structures including the tentorium cerebelli and cavernous sinus (Plager 1999). The superior oblique tendon itself may also suffer injury, particularly during sinus or orbital surgery. People with acquired superior oblique palsy may present with an anomalous head position or vertical or torsional diplopia. Such patients typically have normal vertical fusional amplitudes and do not have facial asymmetry. Because the normal vertical fusion amplitude is less than or equal to 3 PD, patients may be significantly disabled by small degrees of hypertropia caused by acquired superior oblique palsy.

Challenges to diagnosing superior oblique palsy

Although the Parks-Bielschowsky three-step test has been considered the gold standard for diagnosing superior oblique

palsy, 30% of people with superior oblique palsy confirmed by MRI may not fulfill all three of these criteria (Manchandia 2014). Recent studies utilizing MRI have shown that many cases diagnosed clinically as superior oblique palsy may be related to connective tissue abnormalities rather than dysfunction of cranial nerves (Demer 2011). Specifically, heterotopic extraocular muscle pulleys can cause patterns of incomitant strabismus that may be attributed to oblique muscle dysfunction (Clark 1998; Suh 2016). Because neurogenic atrophy occurs rapidly and reliably after denervation of extraocular muscles (Demer 2010), superior oblique atrophy observed on MRI may be used to confirm the clinical diagnosis of superior oblique palsy (Demer 1995). In cases of head tilt-dependent hypertropia with absence of superior oblique atrophy, MRI demonstrates abnormal shifts of extraocular muscle pulleys during head tilt (Demer 2011). Magnetic resonance imaging studies have also shown that compartmental palsy of the superior oblique can occur, which may account for the heterogeneity of clinical presentation in this disorder (Shin 2015). Notwithstanding this objective evidence that clinical ocular motility patterns are not specifically interpretable for oblique extraocular muscle dysfunction, clinical terminology remains deeply grounded in the belief that underdepression of the eye in adduction is a pathognomonic reflection of “superior oblique muscle underaction,” while overelevation in adduction is a pathognomonic reflection of “inferior oblique muscle overaction.” The studies reviewed here were based upon the historical diagnostic concepts, and employed the historical terminology.

Description of the intervention

People with superior oblique palsy may seek treatment due to symptomatic vertical or torsional diplopia or the anomalous head posture adopted to minimize vertical ocular misalignment. Children with a constant head tilt can develop permanent contracture of the neck muscles, particularly the sternocleidomastoid muscle (Lau 2009). Various non-surgical and surgical treatment options exist. When patients are asymptomatic or minimally symptomatic, observation without treatment may be considered. In cases where the vertical deviation is small and comitant, prisms may be sufficient to improve symptoms. However, the majority of people treated for symptomatic superior oblique palsy undergo surgery (Plager 1999), the main goal of which is to reduce the vertical ocular misalignment such that diplopia or anomalous head position, when present preoperatively, is improved or resolved.

Surgical options for hypertropia in superior oblique palsy include: ipsilateral superior oblique tendon plication ('tucking') (Bhola 2005; Durnian 2011); superior oblique tendon resection and advancement (Luton 1998; Wheeler 1934); procedures to weaken the ipsilateral inferior oblique, including recession (Hendler 2013; Parks 1972), myectomy (Bahl 2013; Lee 2015), myotomy (Lee 2015), marginal myotomy (Mellott 2002), disinsertion (Parks 1972; Yanyali 2001), anterior transposition (Elliott 1981; Farvardin 2002), anterior nasal transposition (Hussein 2007; Stager 2003), and orbital fixation (Ela-Dalman 2007); ipsilateral superior rectus recession (Ahn 2012); and contralateral inferior rectus recession (Mahmoud 2009).

In patients symptomatic from excyclotorsion, surgical options include Harada-Ito advancement of the anterior portion of the superior oblique tendon (Harada 1964; Nishimura 2002), inferior oblique weakening as listed above, and transposition of vertical rectus muscles (Nemoto 2000). We have not included surgical options to address excyclotorsion in this review; we have focused on surgical procedures to address symptomatic hypertropia.

How the intervention might work

Strabismus surgery works by changing the forces or pulling directions of the extraocular muscles, or both, as influenced by their associated orbital connective tissues (pulleys). A variety of surgical approaches are used to treat superior oblique palsy. Advancement, resection, or plication of the superior oblique tendon shorten a lax tendon, which may improve action of the superior oblique muscle. Weakening the superior oblique's opponent, the ipsilateral inferior oblique muscle, decreases the activity of the antagonist. Recession of the ipsilateral superior rectus muscle reduces the upward force elevating the hypertropic eye. Recession of the contralateral inferior rectus reduces the force rotating the contralateral eye downward, shifting it upward to match the position of the eye hypertropic due to the palsied superior oblique muscle.

Why it is important to do this review

Although many people with symptomatic superior oblique palsy undergo surgical treatment, there is no consensus as to which, if any, surgical procedure is most effective for remediating strabismus due to this condition, or whether different surgical approaches may be optimal for differing clinical presentations of superior oblique palsy. Moreover, although certain surgical procedures are subject to particular complications (e.g. iatrogenic Brown syndrome in superior oblique tuck, or anti-elevation syndrome in inferior oblique anterior transposition), there are few data comparing the rates of complications between the various surgical procedures used to treat superior oblique palsy. A comprehensive review was needed to guide practitioners in choosing effective surgical interventions.

OBJECTIVES

To assess the relative effects of surgical treatments compared with another surgical intervention, non-surgical intervention, or observation for vertical strabismus in people with superior oblique palsy.

METHODS

Criteria for considering studies for this review

Types of studies

We included only randomized controlled trials. We did not exclude studies on the basis of publication status or language of publication.

Types of participants

We included studies of adults and children with acquired or congenital vertical strabismus considered compatible with the diagnosis of unilateral superior oblique palsy. We did not limit inclusion based on the angle of deviation, as patients may be symptomatic at different degrees of hypertropia based on their vertical fusional amplitudes. We excluded studies of people who underwent surgical intervention for any strabismus before entering the trial. We also excluded studies of people undergoing surgical interventions primarily for torsion, as this review was focused on vertical strabismus. We also excluded studies of people who

underwent simultaneous concomitant horizontal rectus muscle surgery.

Types of interventions

We included trials that compared any type of surgical procedure to another type of surgical procedure. The types of surgical procedures for comparison included the following.

- Superior oblique plication ('tuck')
- Superior oblique resection
- Superior oblique advancement
- Inferior oblique recession
- Inferior oblique myectomy
- Inferior oblique myotomy
- Inferior oblique marginal myotomy
- Inferior oblique disinsertion
- Inferior oblique anterior transposition temporal to the inferior rectus insertion
- Inferior oblique anterior transposition nasal to the inferior rectus insertion
- Inferior oblique orbital fixation
- Inferior oblique denervation and extirpation
- Superior rectus recession
- Inferior rectus recession
- Posterior fixation suture
- Combinations of any of the above

We included studies that utilized unilateral or bilateral surgical procedures.

Additionally, we included studies that compared any surgical procedure to observation or non-surgical treatment.

Types of outcome measures

Primary outcomes

The primary outcome measure was the proportion of participants with postoperative surgical success, defined as hypertropia at distance and near in primary position (with the head upright and looking straight ahead) of less than 3 PD, as measured by alternate cover testing with prism, without reversal of the direction of hypertropia, at one-year postoperatively. When no one-year outcome data were available, we considered the proportion of surgical success at the longest postoperative follow-up time (minimum six weeks).

Secondary outcomes

We evaluated all secondary outcomes at one-year postoperatively, or at longest postoperative follow-up when no outcome data were available at one year.

The secondary outcome measures were as follows.

1. Proportion of participants with an anomalous head position preoperatively who had a residual head tilt greater than 15 degrees in central gaze postoperatively
2. Proportion of participants with postoperative hypertropia less than 3 PD, as measured by alternate cover testing with prism, in down gaze
3. Proportion of participants with postoperative hypertropia less than 3 PD, as measured by alternate cover testing with prism, in contralateral gaze (adduction of affected eye)
4. Proportion of participants with symptomatic cyclotorsion postoperatively
5. Proportion of participants who received another strabismus surgery
6. Proportion of participants who reported relief of symptoms (e.g., diplopia), assessed by questionnaire or other instrument
7. Scores from vision-specific quality of life instruments, such as the National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25) for adults, Adult Strabismus-20 Questionnaire (AS-20) for adults, and vision-specific pediatric quality of life instruments for children

Adverse effects

Adverse effects documented and compared were as follows.

- Orbital cellulitis
- Endophthalmitis
- Retinal perforation
- Iatrogenic Brown syndrome
- Anti-elevation syndrome
- Reversal of vertical deviation.

Search methods for identification of studies

Electronic searches

The Cochrane Eyes and Vision Information Specialist conducted systematic searches in the following databases for randomized controlled trials and controlled clinical trials. There were no language or publication year restrictions. The date of the search was 13 December 2016.

- Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 12) (which contains the Cochrane Eyes and Vision Trials Register) in the Cochrane Library (searched 13 December 2016) (Appendix 1)
- MEDLINE Ovid (1946 to 13 December 2016) (Appendix 2)
- Embase Ovid (1947 to 13 December 2016) (Appendix 3)
- LILACS (Latin American and Caribbean Health Sciences Literature Database) (1982 to 13 December 2016) (Appendix 4)
- ISRCTN registry (www.isrctn.com/editAdvancedSearch; searched 13 December 2016) (Appendix 5)
- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov; searched 13 December 2016) (Appendix 6)
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp; searched 13 December 2016) (Appendix 7)

Searching other resources

We did not conduct manual searches of conference proceedings or abstracts specifically for this review because proceedings and abstracts from major eye conferences are searched annually by Cochrane Eyes and Vision and trials identified are added to CENTRAL.

Data collection and analysis

Selection of studies

Two review authors independently assessed the titles and abstracts of all reports identified by the electronic search. We classified the studies corresponding to the abstracts as (a) definitely relevant, (b) possibly relevant, or (c) definitely not relevant. For studies classified as (a) or (b) based on review of abstracts, we obtained and assessed the full-text reports. Using the full-text reports, we classified each study as (1) include, (2) awaiting assessment, or (3) exclude. Any disagreements at either stage of screening were resolved by a third review author. We assessed studies identified as 'included' for risk of bias. We documented studies excluded after review of the full-text report with reasons for exclusion. The review authors were unmasked to the report authors, institutions, and trial results during the selection of studies.

Data extraction and management

Two review authors independently extracted data for study methods and characteristics, such as details of participants, interventions, outcomes, and other relevant information for all included studies, and quantitative outcome results onto data collection forms developed by Cochrane Eyes and Vision. We did not pilot test the forms as specified in the protocol for this review as we included only two trials, which was the number of trials recommended for pilot testing the form (Chang 2016). Any discrepancies were resolved by discussion. Wherever possible, and for included trials for which we were unable to obtain data from the investigators, we extracted data from figures in the published papers. One review author entered data into Review Manager 5 (Review Manager 2014), and a second review author verified the data entry.

Assessment of risk of bias in included studies

Two review authors independently assessed each included trial for risk of bias according to methods set out in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We considered the following domains: selection bias (sequence generation, allocation concealment before randomization), performance bias (masking (blinding) of participants and personnel), detection bias (masking of outcome assessors), attrition bias (incompletely reported outcome data), reporting bias (selective outcome reporting), and any other sources of bias. We judged each study for each domain as being at high, low, or unclear risk of bias. A third review author resolved any disagreements in the bias assessments. We recorded our assessments in the Cochrane 'Risk of bias' table.

Measures of treatment effect

For primary and secondary dichotomous outcomes, we calculated risk ratios with 95% confidence intervals. Dichotomous outcomes included the proportion of participants with postoperative surgical success, residual head tilt greater than 15 degrees in central gaze, hypertropia less than 3 PD in down gaze and contralateral gaze, and symptomatic cyclotorsion; the proportion of participants who received another strabismus surgery; and the proportion of participants with adverse effects.

We calculated mean differences with 95% confidence intervals for continuous outcomes including quality of life scores and measures of postoperative change in vertical deviation, which were reported by the included studies but not prespecified as outcomes for this review.

Unit of analysis issues

The unit of analysis was the individual participant; all participants had unilateral superior oblique palsy.

Dealing with missing data

Since the studies included in this review were published 14 or more years ago, we used the data available. We did not impute data for the purposes of this review.

Assessment of heterogeneity

We assessed clinical and methodological heterogeneity by comparing participant characteristics, inclusion/exclusion criteria, and assessments of primary and secondary outcomes. As each included study evaluated different surgeries and outcomes, meta-analysis was not feasible. Had we performed any meta-analysis, we planned to test for statistical heterogeneity using the Chi^2 test and evaluate the I^2 value, with an I^2 value greater than 50% indicating the presence of substantial statistical heterogeneity. We also planned to examine the overlap of effect estimates and confidence intervals among studies, with poor overlap suggestive of heterogeneity.

Assessment of reporting biases

We did not examine funnel plots for asymmetry to identify potential publication (reporting) bias because no meta-analysis was performed. We assessed selective outcome reporting as part of the 'Risk of bias' assessment for individual trials.

Data synthesis

Data analysis followed the guidelines in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011). We planned to use a fixed-effect model when there were fewer than three trials in a meta-analysis, and a random-effects model when there were three or more trials in an analysis. Due to clinical and methodological heterogeneity, we did not perform meta-analysis, and have presented a narrative summary.

Subgroup analysis and investigation of heterogeneity

Data were insufficient to conduct our planned subgroup analyses. We had planned to analyze outcomes within subgroups based on participant age (adults 18 years of age and older versus children); etiology of superior oblique palsy (congenital versus acquired); and clinical presentation (primarily symptomatic due to head tilt versus diplopia in various gaze positions).

Sensitivity analysis

Data were insufficient to conduct our planned sensitivity analyses to examine the impact on effect estimates of exclusion of studies at high risk of bias, industry-funded studies, and unpublished studies.

Summary of findings

We prepared a 'Summary of findings' table that includes relevant outcomes in the included studies. We based the seven outcomes selected for presentation in the table on clinical and patient importance. We reported the following outcomes in the 'Summary of findings' table.

1. Proportion of participants with postoperative surgical success, as defined above
2. Proportion of participants with an anomalous head position preoperatively who had a residual head tilt greater than 15 degrees in central gaze postoperatively
3. Proportion of participants with postoperative hypertropia less than 3 PD, as measured by alternate cover testing with prism, in down gaze
4. Proportion of participants with postoperative hypertropia less than 3 PD, as measured by alternate cover testing with prism, in contralateral gaze (adduction of affected eye)
5. Proportion of participants who received additional strabismus surgery
6. Proportion of participants with reversal of the vertical deviation at distance or near postoperatively
7. Proportion of participants with the postoperative complication of orbital cellulitis.

We used the GRADE approach to grade the overall certainty of evidence for each outcome (GRADEpro 2014). We assessed the certainty of evidence for each outcome as high, moderate, low, or very low according to the following criteria as described in Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2011).

- High risk of bias among included studies
- Indirectness of evidence
- Unexplained heterogeneity or inconsistency of results
- Imprecision of results (i.e. wide confidence intervals)
- High probability of publication bias

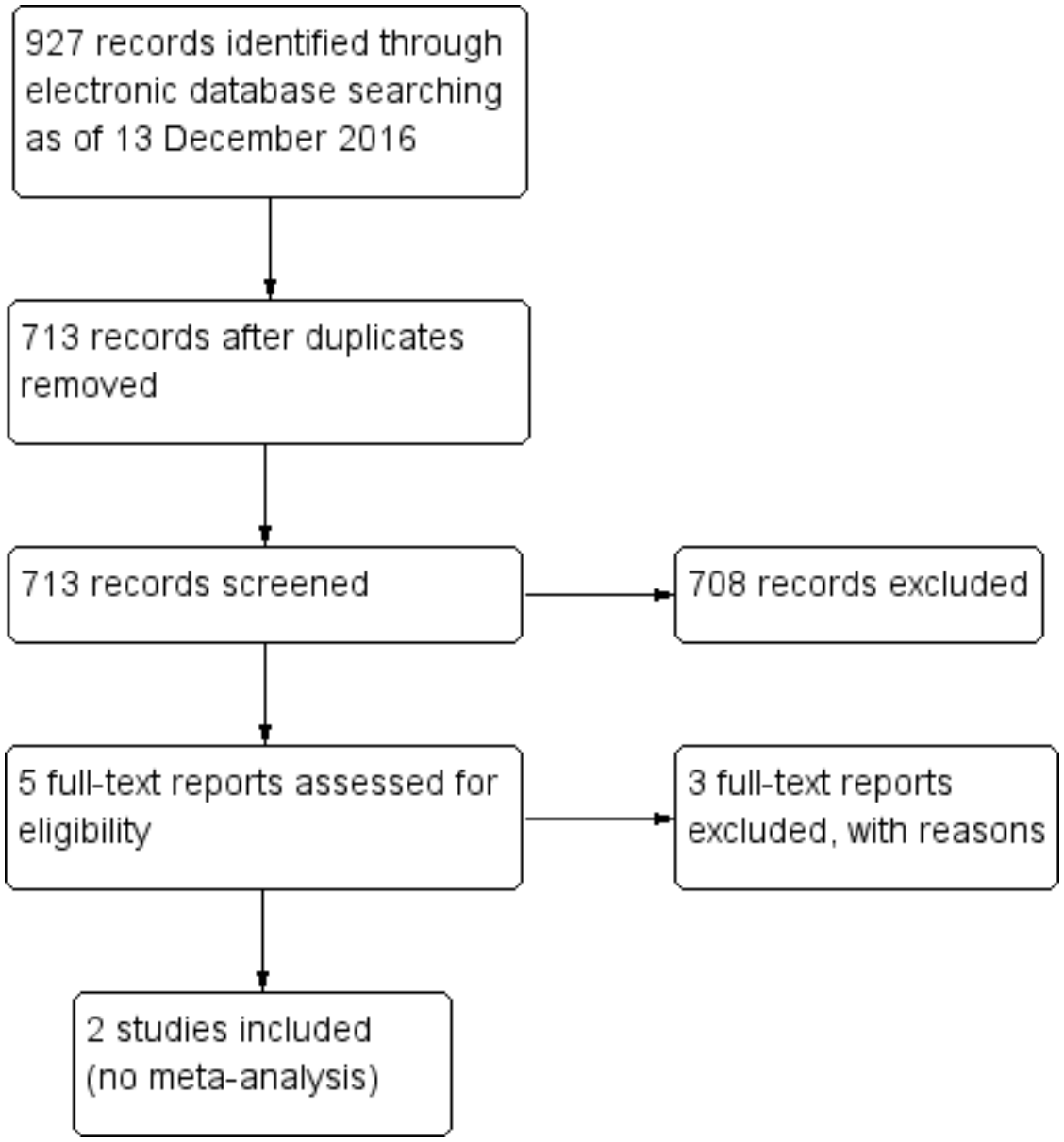
RESULTS

Description of studies

Results of the search

The electronic searches yielded a total of 927 records (Figure 1). The Cochrane Information Specialist scanned the search results and removed 214 duplicate records. We screened the remaining 713 reports and obtained five full-text reports for further assessment. We identified two studies that met the inclusion criteria for this review (Shipman 2003; Yanyali 2001), and excluded the remaining three studies (Bahl 2013; Muchnick 1998; Ziffer 1993). Our searches of clinical trials registries did not yield any ongoing studies.

Figure 1. Study flow diagram.



Included studies

We have described the characteristics of each of the two included studies in detail in the Characteristics of included studies tables. Neither study had been registered in a clinical trial registry, likely because registration was uncommon at the time of publication of the trial reports.

Types of participants

The two included studies involved a total of 45 children and adults of both genders. One study was conducted in the UK, and the other in Turkey. Both studies included people diagnosed with unilateral superior oblique palsy with ipsilateral overelevation in adduction ("inferior oblique overaction"). The surgical procedures were all performed on the inferior oblique muscle, and included 12 myectomies, 11 recessions, 11 disinsertions, and 11 anterior transpositions.

Shipman 2003 recruited 24 adults and children with symptom-producing and/or socially noticeable unilateral overelevation in adduction. The inclusion criteria did not specify superior oblique palsy, but all participants had decompensated longstanding unilateral underdepression in adduction. Exclusion criteria were prior or simultaneous extraocular muscle surgery, inability to co-operate with testing, and visual acuity of 20/60 or worse in either eye. An additional post hoc exclusion criterion was failure to attend any postoperative visit. Participants were randomized to undergo inferior oblique myectomy or recession. Twelve participants were randomized to each group, but one participant who underwent recession failed to complete one-year follow-up, so a total of 23 participants were analyzed. The average age was 30.8 years (range 12 to 77 years) in the myectomy group and 28.5 years (range 13.7 to 69 years) in the recession group. The study authors reported that preoperative hypertropia in the primary position was 15 PD and 10 PD in the myectomy and recession groups, respectively;

preoperative hypertropia in contralateral gaze, "inferior oblique overaction," and "superior oblique underaction" were balanced between the groups.

Yanyali 2001 enrolled 22 adults and children with unilateral superior oblique palsy diagnosed based on ipsilateral hypertropia in the primary position that was greater on contralateral gaze and ipsilateral head tilt, in addition to ipsilateral underdepression in adduction ("superior oblique underaction") and overelevation in adduction ("inferior oblique overaction"). Candidates who had prior extraocular muscle surgery or hypertropia less than 8 PD in primary position were excluded. Participants were randomized to undergo inferior oblique disinsertion or anterior transposition. Eleven participants were assigned to each group, and all completed at least six months of follow-up, thus all 22 participants were included in the analysis. The groups were similar in preoperative characteristics including age, gender, and percentage of participants with head tilt and diplopia, and vertical deviation in primary and contralateral gaze positions.

Types of interventions

The two included studies each compared two different surgeries for overelevation in adduction ("inferior oblique overaction") and hypertropia in people who had unilateral underdepression in adduction ("superior oblique underaction"). All surgeries were procedures to weaken the ipsilateral inferior oblique muscle. Shipman 2003 compared inferior oblique myectomy at the temporal border of the inferior rectus muscle to 10-millimeter inferior oblique recession, with the muscle sutured 3 mm posterior and 2.5 mm lateral to the temporal pole of the inferior rectus muscle insertion. Total follow-up time was 12 months. Yanyali 2001 compared inferior oblique disinsertion to inferior oblique anterior transposition, with the muscle sutured 2 mm anterior to the temporal border of the inferior rectus muscle insertion. The entire muscle, anterior and posterior, was "bunched up" and anteriorized at this location. Participants were expected to complete at least six months of follow-up, and outcomes were assessed at the last follow-up visit rather than at a specific follow-up time point.

Types of outcomes

The studies reported different outcome measures. Shipman 2003 reported the average postoperative reduction in vertical deviation in ipsilateral, primary, and contralateral gaze positions, in addition to median postoperative vertical deviations in these positions. The study authors also reported the change in vertical deviation in these gaze positions between 2 weeks and 12 months postoperatively. Additionally, the median postoperative improvement in overelevation in adduction ("inferior oblique overaction") and undepression in adduction ("superior oblique underaction") were reported. All outcomes were assessed at 2 weeks, 4 months, and 12 months postoperatively. Subgroup analyses were performed on participants with large preoperative vertical deviations, that is those with primary gaze hypertropia of 15 PD or more and those with ipsilateral gaze hypertropia of 10 PD or more. The study did not report adverse events.

Yanyali 2001 reported the reduction of vertical deviation in primary and contralateral gaze positions after surgery. Secondary outcomes included the proportion of participants who had postoperative resolution of preoperative diplopia, the proportion of participants with postoperative resolution of head tilt, and the proportion of participants requiring a second surgery. Adverse outcomes assessed included postoperative development of clinically significant or insignificant elevation deficiency, and postoperative hypotropia in primary position (reversal of vertical deviation). Outcomes were assessed at the last follow-up visit; the mean follow-up time was 18.8 months (range 6 to 40 months).

Neither study reported data for the following outcome measures that were specified in our review: the primary outcome of proportion of participants with surgical success (defined as hypertropia of less than 3 PD in primary position), and secondary outcomes including proportion of participants with postoperative hypertropia less than 3 PD in down gaze and contralateral gaze, proportion of participants with symptomatic cyclotorsion postoperatively, proportion of participants who reported relief of symptoms, quality of life scores, and proportion of participants with adverse events of orbital cellulitis, endophthalmitis, retinal perforation, or iatrogenic Brown syndrome.

Funding sources

Neither group of investigators reported funding sources for their trials (Shipman 2003; Yanyali 2001).

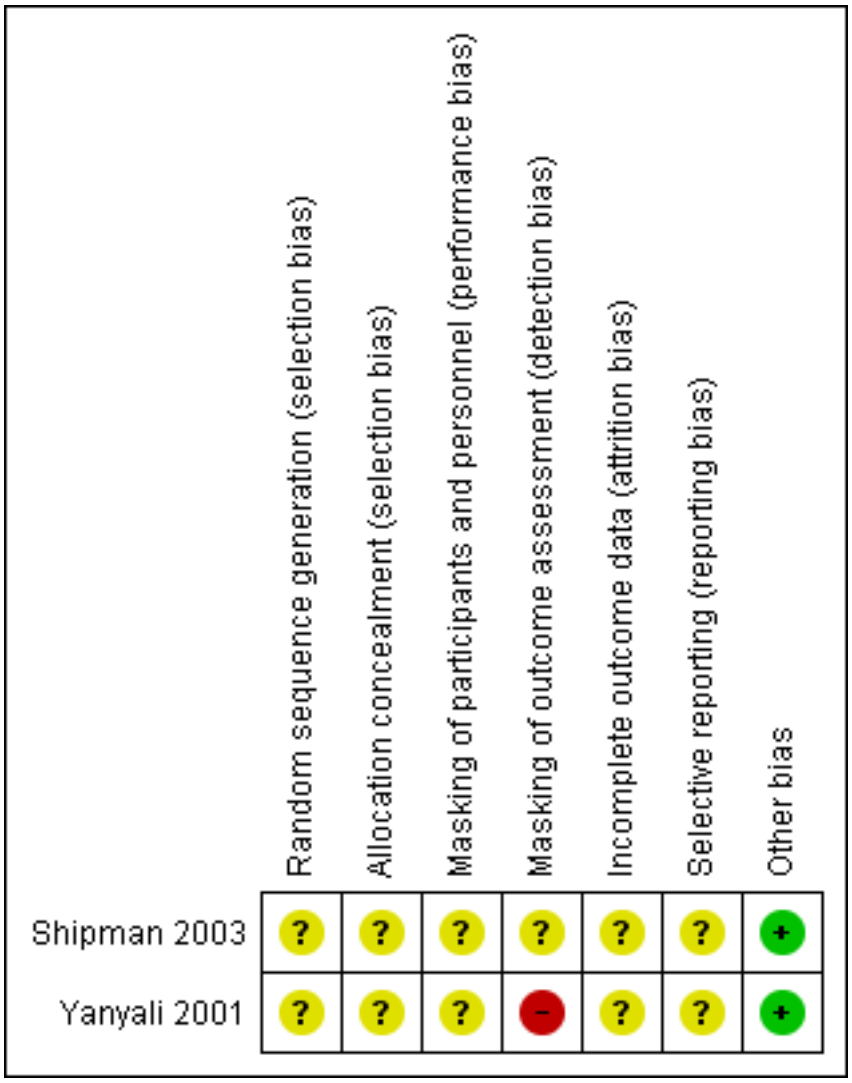
Excluded studies

We excluded three studies for reasons shown in the Characteristics of excluded studies table. We excluded two studies because they were retrospective reviews of cases rather than randomized controlled trials (Bahl 2013; Ziffer 1993). We excluded the third study, Muchnick 1998, because the authors did not state whether the design was retrospective or prospective and did not specify the method of assigning participants to the two different surgeries being evaluated.

Risk of bias in included studies

See Figure 2.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Neither study reported methods of randomization or allocation concealment, therefore we judged the risk of selection bias to be unclear.

Masking (performance bias and detection bias)

Surgeons could not be masked to random assignments in these trials. Neither study reported whether participants were masked to treatment group, so we judged both studies to have an unclear risk of performance bias.

Shipman 2003 reported that outcomes were assessed by an orthoptist, but did not specify whether this orthoptist was masked. We therefore judged this study to have an unclear risk of detection bias.

Yanyali 2001 reported that the same surgeons performed the surgery and assessed preoperative and postoperative measures. This lack of masking led to a judgement of high risk of detection bias for this study.

Incomplete outcome data

We judged both studies to have an unclear risk of attrition bias. Shipman 2003 reported that one participant randomized to the recession group failed to complete one year of follow-up and was excluded from analysis. However, the characteristics of this participant were not described, other than reporting that the participant was “asymptomatic in the early postoperative period.” Yanyali 2001 reported no participants lost to follow-up, but outcomes were not assessed at standardized postoperative times, which would have been necessary for complete and accurate comparison. The last follow-up visit was used, which ranged from 6 to 40 months postoperatively.

Selective reporting

Neither study reported that outcomes had been specified prior to study initiation, therefore we judged both studies to have an unclear risk of reporting bias.

Other potential sources of bias

We identified no other potential sources of bias for either study.

Effects of interventions

See: **Summary of findings for the main comparison** Inferior oblique myectomy versus recession for vertical strabismus in superior oblique palsy; **Summary of findings 2** Inferior oblique disinsertion versus anterior transposition for vertical strabismus in superior oblique palsy

Four different surgical techniques were compared, two in each of the two included studies. The Shipman 2003 study compared inferior oblique myectomy (at the temporal border of the inferior rectus) to recession (of 10 mm); the Yanyali 2001 study compared inferior oblique disinsertion to anterior transposition (2 mm anterior to the temporal border of the inferior rectus insertion). Shipman 2003 reported outcomes at 2 weeks, 4 months, and 12 months, data for the last of which we used for our analysis. Yanyali 2001 reported data at last follow-up (6 to 40 months postoperatively). The follow-up time was not reported separately for the two surgical groups, and the authors did not specify whether follow-up time differed significantly between the groups.

Inferior oblique myectomy versus recession

See Summary of findings for the main comparison for comparison between inferior oblique myectomy and recession. These two surgeries were compared in the Shipman 2003 study. At 12-month follow-up, data were available for 12 participants in the myectomy group and 11 participants in the recession group.

Surgical success

The Shipman 2003 study did not report the proportion of participants with surgical success, as defined in this review by hypertropia less than 3 PD in primary gaze. However, data extracted from the published graphs indicated that the median hypertropia in primary gaze at 12 months was 3 PD in the myectomy group and 1 PD in the recession group. The authors also reported that the average reduction in hypertropia in primary position was 14 PD in the myectomy group and 8 PD in the recession group (P = 0.042). No additional data were available for analysis.

In a subgroup analysis of six participants with preoperative primary position hypertropia of 15 PD or more, the median postoperative vertical deviation in primary gaze at 12 months was 1 PD hypertropia (range orthotropia to 6 PD hypertropia). The study authors did not specify whether these participants had undergone inferior oblique myectomy or recession.

Head tilt

The Shipman 2003 study did not report preoperative or postoperative data on head positioning.

Hypertropia in down gaze

The Shipman 2003 study did not report preoperative or postoperative data on vertical deviation in down gaze.

Hypertropia in contralateral gaze

Although the Shipman 2003 study did not specify the proportion of participants with hypertropia less than 3 PD in contralateral gaze, the study authors did report that the median vertical deviation in adduction at 12 months' postoperatively was 1.75 PD hypertropia (range 5 PD hypotropia to 16 PD hypertropia) in the myectomy group and 3 PD hypertropia (range orthotropia to 9 PD hypertropia) in the recession group. The average reduction of vertical deviation in contralateral gaze at 12 months' postoperatively was 18.5 PD in the myectomy group and 16 PD in the recession group (P = 0.05).

Cyclotorsion

The Shipman 2003 study did not report preoperative or postoperative data on cyclotorsion.

Second surgery

The Shipman 2003 study reported that no participant in either group required a second strabismus surgery during the follow-up period.

Relief of symptoms

The Shipman 2003 study did not report the proportion of participants who reported relief of symptoms.

Quality of life

The Shipman 2003 study did not evaluate quality of life with any standard instrument or method.

Adverse effects

The Shipman 2003 study did not evaluate any of the adverse effects specified for this review. However, tables in the study report indicated that the vertical deviation in contralateral gaze at 12 months' postoperatively ranged from 5 PD hypotropia to 16 PD hypertropia in the myectomy group, and from orthotropia to 9 PD hypertropia in the recession group. These data suggest that there may have been some participants with hypotropia (reversal of vertical deviation) in primary gaze in the myectomy group. The total number of participants, if any, who developed reversal of the vertical deviation, anti-elevation syndrome, orbital cellulitis, endophthalmitis, and retinal perforation was not reported. The final adverse effect to be evaluated by this review, iatrogenic Brown syndrome, was not discussed in the study report, but would not be expected to have been discussed because surgery was not performed on the superior oblique muscle.

Inferior oblique disinsertion versus anterior transposition

See Summary of findings 2 for comparison between inferior oblique disinsertion and anterior transposition. These two surgical techniques were compared by the Yanyali 2001 investigators. Data were available for 11 participants in the disinsertion group and 11 participants in the anterior transposition group at final follow-up visit (range 6 to 40 months).

Surgical success

The Yanyali 2001 study did not specify the proportion of participants with surgical success, as defined in this review by hypertropia less than 3 PD in primary gaze. However, the authors reported that the mean reduction of hypertropia in primary position was 13.3 (standard deviation (SD) 1.9) PD in the disinsertion group and 18.5 (SD 3.9) PD in the anterior transposition group (mean difference (MD) -5.20 PD, 95% confidence interval (CI) -7.76 to -2.64). This difference favors the anterior transposition group, since no participant in either group was overcorrected postoperatively. We rated the quality of the data for this outcome as moderate due to risk of bias in the study design.

Head tilt

The Yanyali 2001 study reported that all participants had head tilt preoperatively. Postoperatively, three of 11 (27%) participants who underwent inferior oblique disinsertion had residual head tilt, and all participants who underwent anterior transposition had resolution of head tilt (risk ratio (RR) 7.00, 95% CI 0.40 to 121.39). However, the authors did not report the angle of head tilt preoperatively or postoperatively. We rated the quality of the data for this outcome as very low due to bias in the study design as well as imprecision, reflected by the large confidence interval.

Hypertropia in down gaze

The Yanyali 2001 study did not report preoperative or postoperative data on hypertropia in down gaze.

Hypertropia in contralateral gaze

The Yanyali 2001 study did not specify the proportion of participants with a hypertropia of less than 3 PD in contralateral gaze. However, the study investigators reported that the mean reduction of hypertropia in adduction was 20.6 (SD 6.2) PD in the disinsertion group and 27.7 (SD 9.6) PD in the anterior transposition group (MD -7.10 PD, 95% CI -13.85 to -0.35). Anterior transposition resulted in a greater decrease in hypertropia in contralateral gaze, but it was unclear whether this difference favored the anterior transposition group, since the authors did not report the number of participants overcorrected in contralateral gaze. We rated the quality of the data for this outcome as moderate due to bias in the study design.

Cyclotorsion

The Yanyali 2001 study did not report preoperative or postoperative data on cyclotorsion.

Second surgery

In the Yanyali 2001 study, none of the participants who underwent anterior transposition required reoperation during the follow-up period. However, three of 11 (27%) participants who underwent disinsertion of the inferior oblique muscle required a second surgery, which was a recession of the contralateral inferior rectus muscle in all cases (RR 7.00, 95% CI 0.40 to 121.39). We rated the quality of the data for this outcome as very low due to bias in the study design as well as imprecision, as indicated by the large confidence interval.

Relief of symptoms

The Yanyali 2001 study reported that one of 11 (9%) participants who underwent inferior oblique disinsertion had diplopia in primary position preoperatively. Two of 11 (18%) participants who underwent inferior oblique anterior transposition had preoperative diplopia. All three participants with preoperative diplopia had resolution of diplopia postoperatively.

Quality of life

The Yanyali 2001 study did not provide any data on quality of life using standard instruments or methods.

Adverse effects

In the Yanyali 2001 study, elevation deficiency was defined as clinically significant when it caused diplopia or restriction of elevation of the abducting eye with secondary upshoot of the contralateral adducting eye. No participant who underwent disinsertion had clinically significant or insignificant elevation deficiency. All participants who underwent anterior transposition had marked elevation deficiency on the first postoperative day, which decreased throughout the follow-up period and was clinically insignificant in all participants at last follow-up.

No participant who underwent inferior oblique disinsertion or anterior transposition developed postoperative hypotropia or reversal of the vertical deviation.

The Yanyali 2001 study did not report rates of orbital cellulitis, endophthalmitis, or retinal perforation. Iatrogenic Brown syndrome, the final adverse effect specified by this review, was not discussed in this study, but would not have been expected to occur because surgery was not performed on the superior oblique muscle.

DISCUSSION

Superior oblique palsy is a common cause of vertical strabismus, and there are a number of surgical treatment options for the condition. However, data comparing these treatments are few or absent. We found only two randomized trials of surgical procedures for this disorder from our search of multiple publication databases and registers of clinical trials. The two trials each compared two different surgical techniques for weakening the ipsilateral inferior oblique muscle, so we analyzed a total of four surgical treatments in this review (inferior oblique myectomy versus recession, and disinsertion versus anterior transposition).

Summary of main results

Because the two studies included in this review compared the effects of two different pairs of surgical procedures, we were unable to combine data in a meta-analysis for any outcome targeted for this review. Furthermore, neither of the studies provided data on our primary outcome, the proportion of participants with postoperative surgical success, defined as hypertropia less than 3 PD in primary gaze. The limited data preclude any conclusion regarding optimal surgical treatment of superior oblique palsy.

Instead of the proportion of participants with postoperative surgical success, both studies reported on the mean postoperative reduction in hypertropia in primary gaze. The Shipman 2003 study reported an average decrease in hypertropia of 14 PD in participants who underwent inferior oblique myectomy, compared to 8 PD after inferior oblique recession. However, the amount of recession performed (10 mm) is considered submaximal, and this study did not address how maximal inferior oblique recession would compare to inferior oblique myectomy. Yanyali 2001 reported that mean reduction in hypertropia in primary gaze was 18.5 (SD 3.9) PD after inferior oblique anterior transposition, compared to 13.3 (SD 1.9) PD after inferior oblique disinsertion.

Similarly, although neither study specifically addressed our secondary outcome of proportion of participants with hypertropia less than 3 PD in contralateral gaze, both studies reported the average postoperative reduction in vertical deviation in adduction. In the Shipman 2003 study, the mean decrease in hypertropia in contralateral gaze was 18.5 PD after myectomy and 16 PD after recession. Yanyali 2001 reported that the average reduction in

hypertropia in adduction was 20.6 (SD 6.2) PD after disinsertion and 27.7 (SD 9.6) PD after anterior transposition. This outcome was similar in each pair of comparisons, and the reduction was large following each type of surgery.

None of the participants in either trial required a second surgery during the follow-up period, except for three of 11 (27%) of those who underwent inferior oblique disinsertion (Yanyali 2001).

The Shipman 2003 study did not address any of the other secondary outcomes specified in this review, including proportion of participants with postoperative resolution of head tilt, postoperative hypertropia in down gaze, cyclotorsion, relief of symptoms, and quality of life.

Of the aforementioned secondary outcomes, the Yanyali 2001 study addressed the proportion of participants with postoperative resolution of head tilt. The Yanyali 2001 study reported that all participants who underwent inferior oblique anterior transposition had resolution of head tilt, in comparison to only eight of 11 (73%) after inferior oblique disinsertion. Additionally, all participants in the Yanyali 2001 study who had preoperative diplopia in primary gaze experienced resolution of diplopia after surgery.

Most of the adverse effects specified for this review (orbital cellulitis, endophthalmitis, retinal perforation, and iatrogenic Brown syndrome) were not addressed by either study. However, the Yanyali 2001 study reported that no participants who underwent inferior oblique anterior transposition or disinsertion experienced clinically significant anti-elevation syndrome or reversal of vertical deviation in primary gaze postoperatively.

Overall completeness and applicability of evidence

Both studies included in this review had limitations in completeness and applicability.

The reporting in the Shipman 2003 study was more complete than the Yanyali 2001 study, due to prespecified time points at which outcomes were evaluated (2 weeks, 4 months, and 12 months). One participant who underwent recession failed to complete 12 months of follow-up and was excluded from analysis. The characteristics of this participant were not described other than indicating that the participant was “asymptomatic in the early postoperative period.” It is therefore unclear whether the exclusion of this one participant could have introduced bias in the study. Because only 12 participants were randomized to inferior oblique recession, the absence of data from one participant could change the final results.

The main problem with applicability of the Shipman 2003 study lies in the subjectivity of the inclusion criteria. Participants were included if they experienced “symptom producing and/or socially noticeable unilateral overacting inferior oblique muscle.” Although the study authors reported that all participants had decompensated longstanding unilateral "superior oblique underaction," this was not stated to have been an inclusion criterion. There were no objective inclusion criteria, such as vertical deviation fulfilling one or more conditions of the Parks three-step test, or evidence of superior oblique atrophy on neuroimaging. It is thus difficult to determine to what patient population the study’s results would be applicable.

Furthermore, the Shipman 2003 study failed to report preoperative data that could be used to compare the two study groups preoperatively, the investigators merely reporting that there was no significant difference in hypertropia in contralateral gaze and degree of "superior oblique underaction."

The reporting of outcomes in the Yanyali 2001 study was incomplete due to varying lengths of follow-up time and absence of specific postoperative time points at which outcomes were assessed. Follow-up of at least 6 months was expected, but follow-up time ranged from 6 to 40 months (average 18.8 months), and outcome data were reported from "final follow-up." The study authors did not specify whether follow-up times differed between the two surgery groups. The Shipman 2003 study demonstrated that postoperative vertical deviation improved with longer follow-up time after inferior oblique muscle surgery, therefore unreported differences in follow-up time between the two surgical groups in the Yanyali 2001 study could confound interpretation of the results.

The inclusion criteria in the Yanyali 2001 study were stringent, requiring that participants demonstrate all three components of the Parks three-step test for diagnosis of superior oblique palsy (hypertropia in primary position increasing on contralateral gaze and ipsilateral head tilt), in addition to ipsilateral overelevation in adduction and underdepression in adduction. Participants were also required to have a hypertropia of at least 8 PD in primary gaze. The study authors included this criterion to avoid postoperative hypotropia, due to the reportedly powerful effect of inferior oblique anterior transposition. The strict inclusion criteria were helpful in reducing the chance of misdiagnosis in the participants, but limit the generalizability of the study findings, as many people diagnosed with superior oblique palsy in clinical practice do not meet all criteria of the Parks three-step test or have a primary position hypertropia of less than 8 PD, or both.

Quality of the evidence

We graded the overall quality of the evidence as low in both of the included studies. Both studies were characterized by poor reporting of methods, which created uncertainty in our assessments of the risk of most types of bias. Additionally, neither study reported data on our primary outcome, the proportion of participants with postoperative surgical success. Furthermore, both studies had a small sample size (22 and 23 participants), which contributed to imprecision in our statistical analysis (e.g. the confidence interval for the risk ratio for reoperation and resolution of head tilt in the Yanyali 2001 study ranged from 0.40 to 121.39). Neither study reported an a priori sample size calculation or computation of post hoc power to detect or rule out differences between surgeries in outcome estimates.

The Shipman 2003 study used a single, subjective inclusion criterion of symptomatic and/or socially noticeable overelevation in adduction. Although the authors stated that all participants had decompensated longstanding unilateral superior oblique palsy, the inclusion criteria are not supportive of this diagnosis. The study authors did not report method of randomization, and did not perform statistical comparisons of the two surgical groups on the measure of interest (vertical deviation in primary gaze) preoperatively. It is therefore unknown whether preoperative differences between the groups could account for the results. Furthermore, there was no indication that the participants or the orthoptist who performed preoperative and postoperative measurements was masked. The authors did not report the proportion of participants with surgical success, but instead

indicated that the mean reduction in vertical deviation in primary gaze was greater in the myectomy group compared to the recession group. This difference was of borderline statistical significance. However, because of the purported self titrating effect of inferior oblique surgery, the absolute decrease in vertical deviation may be less clinically useful than the proportion of participants who achieve postoperative alignment within the vertical fusional range. The authors did report outcomes at prespecified time points, allowing comparisons between groups at 12 months' postoperatively.

In the Yanyali 2001 study, the inclusion and exclusion criteria were well-defined, but there were no prespecified time points for outcome assessment, and the findings at the last follow-up visit were reported. The authors did not report whether the follow-up time differed between groups, therefore it is unknown whether differences in follow-up time confounded interpretation of outcome comparisons. Additionally, the method of randomization was not specified, so the risk of selection and allocation bias is unclear. However, the authors provided statistical analysis showing that basic preoperative characteristics were similar between the groups. The authors did not indicate whether participants were masked, but the surgeons performed all preoperative and postoperative measurements, introducing a high risk of detection bias. Finally, the outcome measure reported in this study was the same as in the Shipman 2003 study, that is mean reduction in hypertropia in primary gaze. As discussed above, this outcome may be of limited clinical applicability as it may be dependent upon the preoperative vertical deviation.

Potential biases in the review process

We did not identify any potential biases in the review process.

Agreements and disagreements with other studies or reviews

The existing literature on surgical treatment of superior oblique palsy is mainly limited to case reports or retrospective case series, either describing the effects of one surgical treatment or comparing two surgical procedures that were not assigned in a random fashion. For instance, one group published a retrospective review of their results for isolated superior oblique tucking in people with superior oblique palsy over 17 years (Durnian 2011). The authors reported that, among 75 adults with congenital or acquired superior oblique palsy who underwent ipsilateral superior oblique tendon tuck, 71% achieved postoperative success, defined as absence of diplopia requiring reoperation. Similarly, another group published a retrospective non-comparative study of their surgical results after inferior oblique anterior transposition for superior oblique palsy over an 11-year period (Clifford 2015). These authors reported that 82% of 96 patients experienced postoperative success, defined as hypertropia measuring less than 5 PD in primary gaze, with absence of diplopia. These studies, although having the advantage of larger patient numbers since cases were reviewed over a long period of time, are non-comparative and provide lower-quality data due to their retrospective nature. Retrospective studies comparing different surgical procedures for superior oblique palsy have also been published. For example, one study reported the outcomes of 123 patients who underwent one- or two-muscle surgery for superior oblique palsy (Simons 1998). The authors found that oblique muscle surgery (superior oblique tuck or inferior oblique weakening) was more frequently associated with an excellent outcome (hypertropia measuring 3 PD or less in primary gaze and reading position) than vertical rectus muscle surgery or combined oblique-rectus muscle surgery. The authors also found that excellent results were more likely to be achieved with one-muscle surgery when the preoperative vertical deviation measured less than 15 PD; multiple-muscle surgery was more successful in patients with larger deviations. This retrospective study, along with other similar reports, is subject to bias due to lack of randomization, masking, and complete follow-up at prespecified time points.

Additionally, many studies do not provide clear inclusion criteria to establish the diagnosis of superior oblique palsy, which would likely lead to the inclusion of participants with an alternative etiology of vertical strabismus, such as sagging eye syndrome (Chaudhuri 2013). The methodological limitations of these studies preclude meaningful comparison with the current review. We did not identify any prior systematic review or meta-analysis of randomized trials of surgical treatment for vertical strabismus in superior oblique palsy.

Several authors, including the investigators in the Simons 1998 study, suggest performing oblique muscle surgery as the initial surgical procedure for superior oblique palsy. This surgery would consist of superior oblique tendon plication ('tuck') when the superior oblique tendon is found to be lax intraoperatively, or an inferior oblique weakening procedure when the superior oblique tendon is normal. Vertical rectus muscle surgery (contralateral inferior rectus recession or ipsilateral superior rectus recession) has been recommended as a secondary procedure. However, there are no data from randomized trials or well-designed prospective studies to support these recommendations.

Similar to this review, retrospective studies have reported that the risk of elevation deficiency is higher in inferior oblique anterior transposition compared to other inferior oblique weakening procedures. The risk of hypotropia in primary gaze, as well as other adverse effects, varies in the literature.

AUTHORS' CONCLUSIONS

Implications for practice

We found no trials that evaluated our primary outcome, proportion of participants with surgical success, defined as hypertropia less than 3 prism diopters (PD) in primary gaze. Although the average reduction of hypertropia in primary gaze was found to be greater in inferior oblique myectomy than in recession (Shipman 2003), and also greater in inferior oblique anterior transposition than in disinsertion (Yanyali 2001), this outcome measure is problematic because it may depend on the magnitude of preoperative deviation. Additionally, a larger decrease in hypertropia may or may not be desirable, depending on the patient's preoperative vertical deviation. A patient with a small preoperative hypertropia may be significantly symptomatic if overcorrected.

The two included trials both compared two different procedures to weaken the ipsilateral inferior oblique muscle. We did not find any trials comparing other types of surgeries for superior oblique palsy.

Because of the paucity of data, small number of outcomes reported, and methodological limitations causing potential biases in the two studies included in this review, we are unable to identify the optimal surgical treatment for vertical strabismus in superior

oblique palsy. This finding highlights the need for larger, well-designed comparative studies to address this important question.

Implications for research

This review emphasizes the current lack of high-quality evidence to support choice of surgical treatment for people with vertical strabismus due to superior oblique palsy. Future studies should randomly assign participants to surgical procedures of interest, using rigorous inclusion criteria to ensure that all participants carry the correct diagnosis. Consideration of neuroimaging in the inclusion criteria is important due to the lack of sensitivity and specificity of the Parks-Bielschowsky three-step test (Manchandia 2014). The design of randomized trials for this condition is challenging due to the wide spectrum of clinical presentations, because different surgical procedures may be more appropriate in different clinical situations. It may thus be necessary for future studies to perform randomization within subgroups of participants based on clinical features, so that the optimal surgical treatment for each presentation may be identified. For example, the best procedure may be different in people with significant overelevation in adduction versus those with fairly comitant deviations.

Additionally, future studies should use a standard outcome measure to facilitate comparisons of surgeries in future studies and meta-analysis among trials. In this review, the primary outcome specified was proportion of participants with surgical success defined as postoperative hypertropia less than 3 PD in primary gaze, without reversal of hypertropia. We acknowledge that some patients meeting this criterion for surgical success may still be symptomatic; for example, if there is a larger deviation in down gaze, the patient may have diplopia with reading. No single outcome measure will be able to capture all aspects of patient symptomatology in superior oblique palsy, therefore future trials should agree upon an outcome that most patients and their surgeons would consider indicative of surgical success. Secondary outcomes may be used to capture other symptoms related to superior oblique palsy, such as head tilt. The primary outcome measure should enable comparisons of multiple surgical procedures and patients with different clinical presentations. The average reduction in vertical deviation should not be used as the primary outcome, because it may be dependent on preoperative measurements.

Furthermore, outcomes should be assessed at prespecified time points (e.g. one-year postoperatively) in order to facilitate comparison among treatment groups and across studies. Participants should continue to be followed beyond one year, as there may be late effects of surgery such as contralateral overelevation in adduction after ipsilateral inferior oblique anterior transposition, which could affect treatment decisions.

Although this reviewed focused on vertical strabismus and did not address cyclotorsion, future trials should include measurements of cyclotorsion. Other important data to collect include preoperative and postoperative measurements of vertical deviation in all cardinal gaze positions at distance and near, objective measurements of head positioning, and subjective reports of diplopia and quality of life. Adverse outcomes including rates of reoperation, reversal of vertical deviation, procedure-specific complications such as anti-elevation syndrome and iatrogenic Brown syndrome, and surgical complications such as orbital cellulitis, endophthalmitis, and retinal perforation should also be reported. Finally, quality of life should be assessed via patient-reported symptoms and validated questionnaires. Only with complete reporting of these outcomes will future studies be able to capture all aspects of importance to surgeons and patients with vertical strabismus due to superior oblique palsy who wish to undergo strabismus surgery.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Shipman 2003

Methods	**Study design**: parallel-group randomized controlled trial **Number randomized**: 24 total participants, 12 in the unilateral inferior oblique myectomy group and 12 in the unilateral inferior oblique recession group **Exclusions after randomization**: none reported **Losses to follow-up**: 1 participant who underwent recession failed to complete 1-year follow-up **Number analyzed**: 23 total participants, 12 in the unilateral inferior oblique myectomy group and 11 in the unilateral inferior oblique recession group **Unit of analysis**: individual (1 study eye per participant) **How were missing data handled?** 1 participant missing 1-year follow-up excluded from analysis **Power calculation**: none reported
Participants	**Country**: UK **Mean age**: 30.8 years (range 12 to 77 years) in the myectomy group, 28.5 years (range 13.7 to 69 years) in the recession group

Shipman 2003 *(Continued)*

	Gender: not reported **Inclusion criteria**: symptom-producing and/or socially noticeable unilateral overacting inferior oblique muscle **Exclusion criteria**: previous or simultaneous extraocular muscle surgery, strabismus surgery or prisms during follow-up period, inability to co-operate with testing, visual acuity of 20/60 or worse in either eye, failure to attend any postoperative visit **Equivalence of baseline characteristics**: preoperative median hypertropia in primary gaze was 15 PD and 10 PD in the myectomy and recession groups, respectively. Preoperative median hypertropia in contralateral gaze was 26.5 PD and 20 PD in the myectomy and recession groups, respectively. There was no statistically significant difference in hypertropia in contralateral gaze, inferior oblique overaction, or superior oblique underaction preoperatively between groups. **Other participant details**: all participants had decompensated longstanding unilateral superior oblique underaction, although this was not an inclusion criterion
Interventions	**Intervention 1**: unilateral inferior oblique myectomy at the temporal border of the inferior rectus muscle **Intervention 2**: unilateral inferior oblique 10-millimeter recession (3 mm posterior and 2.5 mm lateral to the temporal pole of the inferior rectus muscle insertion) **Length of follow-up**: 12 months
Outcomes	**Main outcomes**: average postoperative reduction of vertical deviation in ipsilateral, primary, and contralateral gaze positions; median postoperative hypertropia in ipsilateral, primary, and contralateral gaze positions; average change of vertical deviation in ipsilateral, primary, and contralateral gaze positions between 2 weeks and 12 months postoperatively; median postoperative reduction in inferior oblique muscle overaction; median postoperative improvement in superior oblique function **Adverse events**: none reported **Intervals at which outcomes assesse**d: 2 weeks, 4 and 12 months postoperatively
Notes	**Publication type**: journal article **Trial registration**: not reported **Study period**: not reported **Funding source**: not reported **Disclosures of interest**: not reported **Subgroup analyses**: participants with preoperative primary position hypertropias of 15 PD or more, participants with preoperative hypertropias of 10 PD of more in ipsilateral gaze **Contact with trial investigators**: none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomization not reported.
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported.

Shipman 2003 *(Continued)*

Masking of participants and personnel (performance bias)	Unclear risk	Surgeons could not be masked. Masking of participants not reported.
Masking of outcome assessment (detection bias)	Unclear risk	Measurements were performed by an orthoptist; masking of the orthoptist not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	1 participant in the recession group withdrew from the study. The characteristics of this participant were not reported, other than indicating that this participant was "asymptomatic in the early postoperative period."
Selective reporting (reporting bias)	Unclear risk	The protocol was not available, so prespecified outcomes are unknown.
Other bias	Low risk	None identified.

Yanyali 2001

Methods	**Study design**: parallel-group randomized controlled trial **Number randomized**: 22 total participants, 11 in the disinsertion of inferior oblique group and 11 in the anterior transposition of inferior oblique group **Exclusions after randomization**: none reported **Losses to follow-up**: none **Number analyzed**: 22 total participants, 11 in the disinsertion of inferior oblique group and 11 in the anterior transposition of inferior oblique group **Unit of analysis**: individual (1 study eye per participant) **How were missing data handled?** no missing data were reported **Power calculation**: none reported
Participants	**Country**: Turkey **Mean age**: 20.6 years in the disinsertion group, 18.5 years in the anterior transposition group **Gender:** 6 men and 5 women in the disinsertion group, 7 men and 4 women in the anterior transposition group **Inclusion criteria**: unilateral superior oblique palsy diagnosed by hypertropia in the primary position, greater hypertropia in contralateral gaze, a positive Bielschowsky head-tilt test with increase of hypertropia on ipsilateral head tilt, underaction of ipsilateral superior oblique muscle, overaction of ipsilateral inferior oblique muscle **Exclusion criteria**: any previous extraocular muscle surgery, primary position hypertropia less than 8 PD **Equivalence of baseline characteristics**: no statistically significant difference between groups in age, gender, etiology (congenital vs acquired), percentage with preoperative diplopia or head tilt, or prism diopters of hypertropia in primary gaze or adduction
Interventions	**Intervention 1**: disinsertion of inferior oblique muscle **Intervention 2**: anterior transposition of inferior oblique muscle (2 mm anterior to temporal border of inferior rectus insertion)

Yanyali 2001 *(Continued)*

	Length of follow-up: at least 6 months (up to 40 months)
Outcomes	**Main outcomes**: reduction of hypertropia in primary position and adduction **Secondary outcomes**: proportion of participants with preoperative diplopia with postoperative resolution of diplopia, proportion of participants with preoperative head tilt with postoperative resolution of head tilt, proportion of participants requiring a second surgery **Adverse events**: primary position hypotropia, clinically significant (causing diplopia or secondary upshoot of the contralateral eye in adduction) or insignificant elevation deficiency **Intervals at which outcomes assessed**: last follow-up (mean 18.8 months, range 6 to 40 months)
Notes	**Publication type**: journal article **Trial registration**: not reported **Study period**: not reported **Funding source**: not reported **Disclosures of interest**: not reported **Subgroup analyses**: none **Contact with trial investigators**: none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomization not reported.
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported.
Masking of participants and personnel (performance bias)	Unclear risk	Masking of participants not reported.
Masking of outcome assessment (detection bias)	High risk	The surgeons performed preoperative and postoperative assessments and were not masked.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No report of incomplete data, but outcomes were assessed at inconsistent time points postoperatively based on follow-up.
Selective reporting (reporting bias)	Unclear risk	The protocol was not available, so prespecified outcomes are unknown.
Other bias	Low risk	None identified.

PD: prism diopters

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bahl 2013	Comparison of 2 different surgical techniques, but the study was retrospective rather than a prospective randomized trial
Muchnick 1998	Comparison of 2 different surgical techniques, but the authors did not specify whether this was a retrospective or prospective study, and also did not describe how participants were assigned to the 2 different surgical groups
Ziffer 1993	Comparison of 2 different surgical techniques, but this was a retrospective review rather than a prospective randomized trial

APPENDICES

Appendix 1. CENTRAL search strategy

#1 [mh ^"Oculomotor Muscles"]
#2 [mh ^"Oculomotor Nerve"]
#3 [mh ^"Trochlear Nerve"]
#4 [mh ^"Trochlear Nerve Diseases"]
#5 superior near/2 nerve* near/2 pals*
#6 superior near/2 oblique near/2 pals*
#7 trochlear near/2 nerve* near/2 pals*
#8 fourth near/2 nerve* near/2 pals*
#9 IV near/2 nerve* near/2 pals*
#10 fourth near/2 cranial near/2 nerve*
#11 IV near/2 cranial near/2 nerve*
#12 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
#13 [mh ^"Ophthalmologic Surgical Procedures"]
#14 MeSH descriptor: [Strabismus] this term only and with qualifier(s): [Surgery - SU]
#15 oblique near/5 (insertion or disinsertion or resection or recession or transposition or myotomy or myectomy or plication or tuck or advancement)
#16 inferior near/4 (transposition or rectus or insertion or orbital or fixation or denervation or extirpation)
#17 Posterior near/2 fixation near/2 suture*
#18 superior near/4 rectus near/4 recession
#19 #13 or #14 or #15 or #16 or #17 or #18
#20 #12 and #19

Appendix 2. MEDLINE Ovid search strategy

1. randomized controlled trial.pt.
2. (randomized or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. exp animals/
10. exp humans/
11. 9 not (9 and 10)
12. 8 not 11
13. Oculomotor Muscles/
14. Oculomotor Nerve/
15. Trochlear Nerve/
16. Trochlear Nerve Diseases/
17. (superior adj2 nerve$ adj2 pals$).tw.
18. (superior adj2 oblique adj2 pals$).tw.

19. (trochlear adj2 nerve$ adj2 pals$).tw.
20. (fourth adj2 nerve$ adj2 pals$).tw.
21. (IV adj2 nerve$ adj2 pals$).tw.
22. (fourth adj2 cranial adj2 nerve$).tw.
23. (IV adj2 cranial adj2 nerve$).tw.
24. or/13-23
25. Ophthalmologic Surgical Procedures/
26. Strabismus/su [Surgery]
27. (oblique adj5 (insertion or disinsertion or resection or recession or transposition or myotomy or myectomy or plication or tuck or advancement)).tw.
28. (inferior adj4 (transposition or rectus or insertion or orbital or fixation or denervation or extirpation)).tw.
29. (Posterior adj2 fixation adj2 suture$).tw.
30. (superior adj4 rectus adj4 recession).tw.
31. or/25-30
32. 12 and 24 and 31

The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville 2006.

Appendix 3. Embase Ovid search strategy

1. exp randomized controlled trial/
2. exp randomization/
3. exp double blind procedure/
4. exp single blind procedure/
5. random$.tw.
6. or/1-5
7. (animal or animal experiment).sh.
8. human.sh.
9. 7 and 8
10. 7 not 9
11. 6 not 10
12. exp clinical trial/
13. (clin$ adj3 trial$).tw.
14. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.
15. exp placebo/
16. placebo$.tw.
17. random$.tw.
18. exp experimental design/
19. exp crossover procedure/
20. exp control group/
21. exp latin square design/
22. or/12-21
23. 22 not 10
24. 23 not 11
25. exp comparative study/
26. exp evaluation/
27. exp prospective study/
28. (control$ or prospectiv$ or volunteer$).tw.
29. or/25-28
30. 29 not 10
31. 30 not (11 or 23)
32. 11 or 24 or 31
33. Extraocular Muscle/
34. Oculomotor Nerve/
35. Trochlear Nerve/
36. Trochlear Nerve Disease/
37. (superior adj2 nerve$ adj2 pals$).tw.
38. (superior adj2 oblique adj2 pals$).tw.
39. (trochlear adj2 nerve$ adj2 pals$).tw.
40. (fourth adj2 nerve$ adj2 pals$).tw.
41. (IV adj2 nerve$ adj2 pals$).tw.
42. (fourth adj2 cranial adj2 nerve$).tw.

43. (IV adj2 cranial adj2 nerve$).tw.
44. or/33-43
45. Eye Surgery/
46. Strabismus/su [Surgery]
47. (oblique adj5 (insertion or disinsertion or resection or recession or transposition or myotomy or myectomy or plication or tuck or advancement)).tw.
48. (inferior adj4 (transposition or rectus or insertion or orbital or fixation or denervation or extirpation)).tw.
49. (Posterior adj2 fixation adj2 suture$).tw.
50. (superior adj4 rectus adj4 recession).tw.
51. or/45-50
52. 32 and 44 and 51

Appendix 4. LILACS search strategy

oculomotor nerve OR trochlear nerve OR superior oblique OR superior nerve OR fourth nerve OR IV nerve OR fourth cranial OR IV cranial and insertion OR disinsertion OR resection OR recession OR transposition OR myotomy OR myectomy OR plication OR tuck OR advancement OR rectus OR orbital OR fixation OR denervation OR extirpation

Appendix 5. ISRCTN search strategy

"(oculomotor nerve OR trochlear nerve OR superior oblique OR superior nerve OR fourth nerve OR IV nerve OR fourth cranial OR IV cranial) AND (insertion OR disinsertion OR resection OR recession OR transposition OR myotomy OR myectomy OR plication OR tuck OR advancement OR rectus OR orbital OR fixation OR denervation OR extirpation)"

Appendix 6. ClinicalTrials.gov search strategy

Interventional Studies | oculomotor nerve OR trochlear nerve OR superior oblique OR superior nerve OR fourth nerve OR "IV nerve" OR fourth cranial OR "IV cranial" | insertion OR disinsertion OR resection OR recession OR transposition OR myotomy OR myectomy OR plication OR tuck OR advancement OR rectus OR orbital OR fixation OR denervation OR extirpation

Appendix 7. WHO ICTRP search strategy

oculomotor nerve OR trochlear nerve OR superior oblique OR superior nerve OR fourth nerve OR IV nerve OR fourth cranial OR IV cranial = Condition AND insertion OR disinsertion OR resection OR recession OR transposition OR myotomy OR myectomy OR plication OR tuck OR advancement OR rectus OR orbital OR fixation OR denervation OR extirpation = Intervention

CONTRIBUTIONS OF AUTHORS

Review co-ordination: MYC

Data collection

- Designing search strategies: MYC, Iris Gordon (CEV Information Specialist)
- Undertaking searches: Iris Gordon
- Screening search results: MYC, VLT
- Organizing retrieval of papers: MYC
- Screening retrieved reports against inclusion criteria: MYC, VLT
- Appraising risk of bias: MYC, VLT
- Extracting data: MYC, VLT
- Obtaining and screening data on unpublished studies: MYC, VLT

Data management for the review

- Entering and verifying data in Review Manager 5: MYC, VLT
- Analyzing data: MYC, VLT

Interpretation of data

- Providing a methodological perspective: MYC, ALC, VLT, JLD
- Providing a clinical perspective: MYC, ALC, VLT, JLD
- Providing a policy perspective: MYC, ALC, VLT, JLD
- Providing a consumer perspective: MYC, ALC, VLT, JLD

Writing the review: MYC, ALC, VLT, JLD

Providing general advice on the review: MYC, ALC, VLT, JLD
Securing funding for the review: JLD
Performing previous work that was the foundation of the current study: JLD
Guarantor for review: MYC

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  The views expressed in this publication are those of the authors and not necessarily those of the NIHR, National Health Service (NHS), or the Department of Health.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

After publication of the protocol (Chang 2016), we modified the outcomes to include the proportion of participants with relief of symptoms. As patients may seek treatment due to symptomatic diplopia and because some patients may still be symptomatic even when meeting objective criterion for surgical success, we added this outcome to assess the patient's experience following surgery.

INDEX TERMS

Medical Subject Headings (MeSH)

*Oculomotor Muscles; Ophthalmoplegia [*complications]; Postoperative Complications; Randomized Controlled Trials as Topic; Strabismus [etiology] [*surgery]

MeSH check words

Adult; Child; Humans