· Clinical Research ·

# Prevalence, risk factors and clinical features of sensory A-V pattern exotropia

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Received: 2023-06-18 Accepted: 2024-04-17

## Abstract
● **AIM:** To investigate the potential mechanisms of A-V pattern and evaluate the surgical outcomes used in the treatment of sensory exotropia.

● **METHODS:** The medical records of patients with sensory A-V pattern exotropia who underwent strabismus surgery between May 2014 to June 2019 was retrospectively reviewed. The control group included sensory exotropia patients without A-V pattern and concomitant A-V pattern exotropia patients with normal vision who undergone strabismus surgery over this same time period. Ocular alignment, best corrected visual acuity, oblique muscle function, and stereopsis records were collected.

● **RESULTS:** Among the 843 eligible patients, 91 (10.79%; 39 males and 52 females) had A-pattern (54, 6.4%) or V-pattern (37, 4.4%). Age at onset of vision impairment was 4±5y and at the time of surgery was 25±9y. Statistically significant negative correlations were present between impaired visual acuity and the pre-operative exodeviation ($r$=-0.198, $P$=0.016) and patterns ($r$=-0.207, $P$=0.015). Age at surgery and exodeviation in patients with concomitant A-V pattern exotropia was significantly earlier as compared with that of sensory A-V pattern exotropia and sensory exotropia (both $P$<0.0001). There were no significant differences in these clinical variables between sensory exotropia with or without A-V pattern. Deviation and pattern were significantly reduced in patients receiving horizontal rectus surgery with or without oblique muscle surgery (both $P$<0.0001).

● **CONCLUSION:** The prevalence of sensory A-V pattern exotropia in our study is 10.79%. Visual acuity represents an important factor contributing to the occurrence and development of A-V pattern. Isolated horizontal rectus surgery can provide a good option for the correction of sensory A-V pattern exotropia.

● **KEYWORDS:** sensory exotropia; A-V pattern; oblique muscle dysfunction; horizontal rectus surgery
**DOI:10.18240/ijo.2025.02.17**

**Citation:** Zhu BB, Tang SY, Wang XJ, Fu LC, Yan JH. Prevalence, risk factors and clinical features of sensory A-V pattern exotropia. *Int J Ophthalmol* 2025;18(2):323-329

## INTRODUCTION

Sensory exotropia is generally defined as a secondary deviation that develops due to partial or complete disruption of fusion resulting from congenital or acquired visual impairments in one eye[1]. As a result of these fusion impairments and relatively large-angle deviations associated with sensory exotropia, surgical treatments for this condition remain a challenge and surgical outcomes are less predictable[2-4]. Similar to that observed in infantile esotropia, A-V pattern, dissociated vertical deviation (DVD) and oblique muscle dysfunction can also occur in patients with sensory exotropia[5]. As the etiology and age at onset of visual impairment of the underlying eye disorders can be well characterized in sensory A-V pattern exotropia, the information derived from this model can provide a good foundation for the understanding and investigation of mechanisms and occurrence of A-V pattern. However, details regarding the etiology, mechanisms and treatment of sensory A-V pattern exotropia have yet to be clearly established.

Therefore, the goal of this study was to evaluate the prevalence, risk factors and clinical features associated with sensory A-V pattern exotropia. To assess the significance of these factors results obtained from sensory A-V pattern exotropia patients were compared with that of patients who had sensory exotropia without A-V pattern (hereafter referred to as sensory exotropia) as well as concomitant A-V pattern exotropia patients with normal vision.

## PARTICIPANTS AND METHODS

**Ethical Approval** This study protocol was reviewed and approved by the Research Ethics Board of Zhongshan Ophthalmic Center (approval number: 2019KYPJ103). Informed written consent for the surgical procedure and use of medical records was obtained from all patients or their parents.

**Participants** The medical records of patients who had undergone strabismus surgery for sensory A-V pattern exotropia over the period from May 2014 to June 2019 were retrospectively reviewed. The control groups randomly consisted of sensory exotropia patients without A-V pattern and concomitant A-V pattern exotropia patients with normal vision who also had undergone strabismus surgery over this same time period.

The criterion for inclusion of sensory A-V pattern exotropia consisted of: 1) patients with unilateral visual impairment resulting from anisometropic amblyopia or organic congenital or acquired disorders; 2) an A-pattern with a difference of at least 10 prism diopters (PD) between upgaze and downgaze and a V-pattern with a difference of at least 15 PD between upgaze and downgaze. Patients with bilateral visual impairments, intermittent, paralytic or restrictive exotropia, incomplete records and/or previous strabismus surgery were excluded.

All patients underwent a comprehensive ophthalmic evaluation and the following data were recorded: sex, age at surgery, age at onset of vision impairment, medical history, visual acuity, cycloplegic refraction, intraocular pressure, slit-lamp biomicroscopy and fundus examination, ocular alignment, ocular motility, stereopsis at near and distance, surgical procedures and surgical outcomes. Ocular alignment was measured in primary gaze at distance and at 25° of upgaze and downgaze with the best corrected visual acuity assessed using the prism alternate cover test, or the Krimsky test if ocular fixation was poor. Oblique muscle function was graded on a 9-point scale from -4 underaction to +4 overaction, with 0 being normal. Stereopsis was measured with the Titmus stereoacuity test at near and random dot stereograms, and the synoptophore at distance. As our goal was to evaluate the relationships among visual acuity and other clinical variables, the patients were classified according to visual acuity of the deviated eye as follows: no light perception; light perception; hand movement; counting fingers; better than counting fingers, but less than 20/200; and ≥20/200.

**Surgical Techniques and Follow-up** All surgeries were performed through a fornix conjunctival incision under general anesthesia. Various surgical techniques and surgeons were used in the treatment of these patients. A unilateral recess-resect of the deviated eye was performed when visual acuity of deviated eye was relatively poor, even if the ocular motility showed oblique muscle dysfunction; while a unilateral lateral rectus recession was the preferred choice in patients with an exotropia of <25 PD. If the deviated eye was relatively unimpaired, horizontal rectus surgery and simultaneous inferior oblique surgery (such as inferior oblique myectomy and recession) were performed in patients with an obvious inferior oblique muscle overaction (IOOA); while in those with an obvious superior oblique muscle overaction (SOOA) and A-exotropia, a horizontal rectus surgery and simultaneous superior oblique surgery (such as superior oblique tenotomy and tendon expander) were performed. If an obvious coexistence of DVD and IOOA were present, an inferior oblique anterior transposition was the preferred choice, while for the presence of an obvious coexistence of DVD and SOOA a superior rectus recession was performed.

Post-operative assessments were performed at 1d, 1wk, 2, 6mo, and 1y after surgery. Data from the last follow-up visit were used for performing the final analyses. Outcome measures included the angle of deviation in primary position at distance and amount of A-V pattern. A successful outcome was defined as a final horizontal deviation of ≤10 PD and a vertical deviation of ≤5 PD in the primary position at distance.

**Statistical Analysis** Statistical analyses were performed using the SPSS version 24.0 (IBM Corp., Armonk, NY, USA) and Graphpad Prism version 8.2 (GraphPad Software, LLC) programs. Data were expressed as the means±standard deviations. Results were analyzed using paired *t*-test, Chi-square test, Wilcoxon signed rank test or Pearson's correlations as appropriate. A $P$ value <0.05 was required for results to be considered as statistically significant.

## RESULTS

**Demographic Features** Of the 843 patients with sensory exotropia, 91 (39 males and 52 females) had a pattern deviation. Among these 91 cases, 54 showed an A pattern and 37 with V pattern. The age at onset of visual impairment was 4±5y and that at surgery was 25±9y (Tables 1 and 2).

As shown in Table 1, the most common etiology of visual impairment was anisometropic amblyopia (33/91, 36.3%), followed by structural abnormalities due to ocular injury (31/91, 34.1%), unilateral optic nerve and retinal dysplasia (14/91, 15.4%), unilateral congenital cataract (11/91, 12.1%) and corneal opacity due to keratitis (2/91, 2.2%).

As shown in Table 2, the age at surgery and exodeviation in patients with concomitant A-V pattern exotropia was significantly earlier as compared with that of sensory A-V pattern exotropia and sensory exotropia (both $P$<0.0001). However, no statistically significant differences between sensory exotropia and sensory A-V pattern exotropia were obtained for age at surgery ($P$=0.964), age at onset ($P$=0.309), duration ($P$=0.572) and etiology ($P$=0.591) of visual

**Table 1 Comparison of demographic profile of sensory A- and V-pattern exotropia**

| Parameters | A-pattern | V-pattern | *P* |
|---|---|---|---|
| Number of patients, *n* | 54 | 37 | - |
| Gender (male/female), *n* | 27/27 | 12/25 | 0.096 |
| Age at surgery, mean±SD (range), y | 28±10 (8-68) | 23±7 (5-38) | 0.299 |
| Age at visual impairment, mean±SD (range), y | 4±5 (0-25) | 3±4 (1-18) | 0.052 |
| 0-5y, n (%) | 38 (70.4) | 31 (83.8) | 0.314 |
| 6-12y, *n* (%) | 9 (16.6) | 4 (10.8) | |
| ≥13y, *n* (%) | 7 (13.0) | 2 (5.4) | |
| Duration of visual impairment, mean±SD (range), y | 22±10 (7-67) | 21±7 (3-37) | 0.343 |
| Causes of visual impairment, *n* (%) | | | 0.473 |
| Structural abnormalities due to ocular injury | 22 (40.7) | 9 (24.3) | |
| Anisometropic amblyopia | 16 (29.6) | 17 (46.0) | |
| Unilateral congenital cataract | 7 (13.0) | 4 (10.8) | |
| Optic nerve and retinal dysplasia | 8 (14.8) | 6 (16.2) | |
| Corneal opacity due to keratitis | 1 (1.9) | 1 (2.7) | |
| Visual acuity in the deviated eye, *n* (%) | | | 0.161 |
| NLP | 4 (7.4) | 3 (8.1) | |
| LP | 2 (3.7) | 0 | |
| HM | 12 (22.2) | 2 (5.4) | |
| CF | 11 (20.4) | 6 (16.2) | |
| CF to <20/200 | 16 (29.6) | 16 (43.3) | |
| ≥20/200 | 9 (16.7) | 10 (27.0) | |
| Exodeviation, mean±SD (range), PD | 51±15 (15-90) | 47±8 (25-66) | 0.001 |
| Pattern, mean±SD (range), PD | 18±7 (1-40) | 20±6 (15-40) | 0.421 |
| Vertical deviation, mean±SD (range), PD | 2±4 (0-15) | 4±6 (0-25) | 0.083 |
| Oblique muscle dysfunction, *n* | 40 SOOA | 24 IOOA | - |

CF: Counting fingers; HM: Hand movement; IOOA: Inferior oblique muscle overaction; NLP: No light perception; LP: Light perception; PD: Prism deviation; SOOA: Superior oblique muscle overaction.

impairment, visual acuity of the deviated eye (*P*=0.447) and exodeviation (*P*=0.522).

**Clinical Features** Exodeviation of V-pattern exotropia was significantly less than that of A-pattern exotropia (*P*=0.002). However, there were no differences in pattern or vertical deviation between these two conditions. Forty patients (74.1%) with A-pattern exotropia had SOOA, while 24 patients (64.9%) with V-pattern exotropia had IOOA.

There were 40 patients with visual acuity ranging from no light perception to counting fingers. Among these 40 cases, 19 showed A-pattern and 11 with V-pattern (Table 1). Mean horizontal deviation, vertical deviation and pattern were -52±13, 2±5, and 19±6 PD, respectively. There were 51 patients with a visual acuity above counting fingers, with 25 of these cases showing A-pattern and 26 with V-pattern. Mean horizontal deviation, vertical deviation and pattern were -47±12, 3±6, and 18±7 PD, respectively. Statistically significant differences between the A- and V-pattern patients were obtained for horizontal deviation (*P*=0.044) and type of pattern (*P*=0.007).

**Surgical Outcomes** Surgical outcomes of patients with sensory A-V pattern exotropia who underwent different surgical procedures were summarized in Table 3. Isolated horizontal rectus surgery was performed in 69 patients, with the surgical success rate of the 45 patients within the A-pattern group being 40% (18/45) while the 24 patients in the V-pattern group showed a 54.2% (13/24) success rate. Horizontal rectus surgery combined with oblique surgery was performed in 22 patients, and the surgical success rate in the 9 patients within the A-pattern group was 77.8% (7/9) and 84.6% (11/13) in the 13 V-pattern patients. In the remaining 26 patients, success rates were 7/11 (63.6%) for the A-pattern and 13/15 (86.7%) for the V-pattern groups. The oblique surgery was performed as follows: inferior oblique myectomy in 8 patients, inferior oblique tenotomy in 1, inferior oblique tendon expander in 2, inferior oblique anterior transposition in 2, superior oblique tenotomy in 6 and superior oblique tendon expander in 3. A significant reduction in the amount of deviations and pattern was observed in both A- and V-pattern groups (*P*<0.05 for both).

**Correlations Among Clinical Variables** Statistically significant negative correlations were obtained between impaired visual acuity and pre-operative exodeviation

**Table 2 Comparison of clinical features among the patients with sensory A-V pattern exotropia, sensory exotropia, and concomitant A-V pattern exotropia**

| Parameters | Sensory A-V exotropia | Sensory exotropia | Concomitant A-V exotropia |
|---|---|---|---|
| Number of patients, *n* | 91 | 91 | 91 |
| Age at surgery, mean±SD (range), y | 25±9 (5-48) | 25±10 (6-61) | 17±10 (4-48) |
| Age at visual impairment, mean±SD (range), y | 4±5 (0-25) | 5±6 (1-31) | - |
| 0-5y, *n* (%) | 69 (75.8) | 67 (73.6) | - |
| 6-12y, *n* (%) | 13 (14.3) | 16 (17.6) | - |
| ≥13y, *n* (%) | 9 (9.9) | 8 (8.8) | - |
| Duration of visual impairment, mean±SD (range), y | 22±9 (3-67) | 21±10 (1-52) | - |
| Causes of visual impairment, *n* (%) | | | - |
| Structural abnormalities due to ocular injury | 31 (34.1) | 31 (34.1) | - |
| Anisometropic amblyopia | 33 (36.3) | 26 (28.6) | - |
| Unilateral congenital cataract | 11 (12.1) | 10 (11.0) | - |
| Optic nerve and retinal dysplasia | 14 (15.3) | 19 (20.9) | - |
| Acquired corneal opacity | 2 (2.2) | 2 (2.2) | - |
| Glaucoma | 0 | 2 (2.2) | - |
| Unilateral retinal detachment | 0 | 1 (1.0) | - |
| Visual acuity in the deviated eye, *n* (%) | | | - |
| NLP | 7 (7.7) | 7 (7.7) | - |
| LP | 2 (2.2) | 2 (2.2) | - |
| HM | 14 (15.4) | 13 (14.3) | - |
| CF | 17 (18.7) | 29 (31.9) | - |
| CF to <20/200 | 32 (35.1) | 23 (25.2) | - |
| ≥20/200 | 19 (20.9) | 17 (18.7) | - |
| Exodeviation, mean±SD (range), PD | 49±13 (15-90) | 48±15 (20-100) | 41±13 (12-85) |
| Pattern, mean±SD (range), PD | 19±6 (10-40) | - | 18±6 (10-31) |

CF: Counting fingers; HM: Hand movement; NLP: No light perception; LP: Light perception; PD: Prism deviation.

**Table 3 Surgical outcomes in patients with sensory A-V pattern exotropia** mean±SD, PD

| Parameters | A-pattern | | *P* | V-pattern | | *P* |
|---|---|---|---|---|---|---|
| | Horizontal surgery (*n*=45) | Combined surgery (*n*=9) | | Horizontal surgery (*n*=24) | Combined surgery (*n*=13) | |
| Preop. horizontal deviation | -51±15 | -47±13 | 0.854 | -48±9 | -45±7 | 0.447 |
| Postop. horizontal deviation | 11±9 | -0.4±13 | 0.744 | 7±14 | 4±5 | 0.102 |
| *P* | <0.0001 | <0.0001 | | <0.0001 | <0.0001 | |
| Preop. pattern | 18±7 | 16±7 | 0.682 | 19±6 | 20±6 | 0.359 |
| Postop. pattern | 0.9±3 | 2±4 | 0.068 | 2±4 | 0 | 0.002 |
| *P* | <0.0001 | <0.0001 | | <0.0001 | <0.0001 | |
| Preop. vertical deviation | 2±5 | 3±4 | 0.903 | 4±7 | 3±5 | 0.674 |
| Postop. vertical deviation | 2±4 | 0.5±2 | 0.061 | 0 | 0.7±2 | <0.0001 |
| *P* | 0.545 | 0.059 | | 0.012 | 0.065 | |
| Preop. oblique muscle overaction, *n* | 32 SOOA | 8 SOOA | | 11 IOOA | 13 IOOA | |
| Postop. oblique muscle overaction, *n* | 6 SOOA | 1 SOOA | | 3 IOOA | 3 IOOA | |

IOOA: Inferior oblique muscle overaction; PD: Prism deviation; SOOA: Superior oblique muscle overaction.

($r$=-0.198, $P$=0.016) and pattern ($r$=-0.207, $P$=0.015). The preoperative pattern was negatively correlated with postoperative exodeviation ($r$=-0.243, $P$=0.002) and positively correlated with postoperative pattern ($r$=0.214, $P$=0.020). The preoperative exodeviation was positively correlated with the age at surgery ($r$=0.166, $P$=0.029). The post-operative vertical deviation was positively correlated with preoperative vertical deviation ($r$=0.324, $P$=0.001) and duration of visual impairment ($r$=0.223, $P$=0.009). The age at onset of visual impairment was positively correlated with age at surgery ($r$=0.242, $P$=0.003) and negatively correlated with duration of visual impairment ($r$=-0.172, $P$=0.033).

## DISCUSSION

**Visual Acuity and Occurrence/Development of A-V Pattern** The overall prevalence of A-V pattern in concomitant strabismus can range from 12%–50%, while that in infantile strabismus is 50%[6]. In our previous study, 10.36% of patients who received strabismus surgery had pattern strabismus[7]. Accordingly, salient differences exist between concomitant and sensory A-V pattern strabismus. While the former condition may be associated with the neurological involvement, the latter is clearly associated with the visual impairment. Any abnormal visual experience during the critical period of visual development may lead to anatomical/functional abnormalities in the visual system, eventually resulting in strabismus. Das *et al*[8] successfully produced pattern strabismus in a primate model by using the occlusion method during the critical period of visual development. With this approach, the A-V pattern induced in these monkeys was similar to the sensory strabismus with A-V pattern in humans. Abnormal supranuclear circuits have been proposed to explain the basis for this A-V pattern. In this primate model of pattern strabismus, the interstitial nucleus of Cajal (INC) receives abnormal eye position signals, and it has been reported that the cause of A-V pattern appears to involve an abnormal cross-talk within the INC[9-10]. Cetin *et al*[11] reported that a cat with malignant peripheral nerve sheath tumor had a right-sided head tilt accompanied by ipsilateral ventral strabismus, which also suggesting the association between central nervous system and pattern strabismus. In our study, 75.8% (69/91) of our patients experienced visual impairment in the first five years of their life. As described above, an early abnormal visual experience within these patients may produce a similar developmental sequence as that observed in strabismic monkeys, suggesting the possibility of a neural mechanism involvement. Our current results do not allow us to identify a precise neurological mechanism, thus further studies on brain structures and functions in patients with pattern strabismus are recommended for future investigations.

Several studies[2,12-13] have reported that visual acuity might be a predictor for long-term surgical success of sensory strabismus. Kim *et al*[14] reported that no significant differences were observed between the age at onset of visual impairment and the type of strabismus. Havertape *et al*[15] reported that esotropia occurred more frequently in patients with congenital vision loss, while exotropia was more common in those with acquired vision loss. However, in the other study, the duration or extent of visual impairment had no relation to surgical success[16]. Recently, Raouf and Kodsi[17] reported case series of patients with high ratio of accommodative convergence to accommodation who experienced a spontaneous conversion from a sensory exotropia to a sensory esotropia without the management of strabismus surgery. In our current study, patients with visual acuity ranging from no light perception to counting fingers showed larger horizontal deviations, and a significant difference in the type of pattern was present between the two visual acuity groups with the A-pattern being more prevalent in patients with lower visual acuity. Moreover, the negative correlations, as obtained between impaired visual acuity and preoperative exodeviation and pattern, suggested that the presence of enhanced visual acuity may have an effect upon the control of eye position (including horizontal deviation and pattern). When collating the findings of multiply clinical variables among the three types of strabismus it appeared that patients with concomitant A-V pattern showed a smaller degree of exodeviation and underwent strabismus surgery at a younger age. In this way, our results demonstrated that visual acuity contributes to the occurrence and development of A-V pattern. Unfortunately, the factor of accommodation was not included in our study.

In our study, the most common etiology of sensory A-V pattern strabismus was anisometropic amblyopia, along with structural abnormalities due to ocular injury in sensory exotropia. The lack of differences in the causes of visual impairment between sensory exotropia with or without A-V pattern indicated that underlying ocular diseases were not associated with A-V pattern.

**Implications of Horizontal Rectus Surgery and Sensory A-V Pattern Exotropia** The efficacy of various treatments for pattern strabismus, such as oblique muscle weakening, vertical transposition of horizontal rectus, horizontal transposition of vertical rectus and slanting of horizontal rectus insertions have been assessed in a number of studies[18-21]. In patients with sensory exotropia, a monocular procedure is strongly recommended[22]. As a result, when compared with that of other concomitant types of pattern strabismus, the choice of surgical techniques for patients with sensory A-V pattern exotropia is relatively limited. Yin and Chen[5] reported an effective outcome after vertical transposition of horizontal rectus muscle in patients with sensory exotropia with oblique muscle overaction. More recently, there have been a few studies which have concentrated on the effect of isolated horizontal rectus surgery on pattern strabismus[23-24]. For example, Lee *et al*[23] reported a collapse of pattern after horizontal rectus surgery only for intermittent exotropia with the sub-A- or sub-V-pattern, and Shen *et al*[20] reported that mild V-pattern was effectively corrected by upward transposition. These findings call into question the necessity for performing a combination of horizontal rectus surgery and oblique muscle surgery for correction of sensory A-V pattern exotropia. In our study, both isolated horizontal rectus surgery and combined surgeries were effective for the correction of A-V pattern.

Such findings suggested the possibility that collapse of A-V pattern might be a secondary change resulting from insertions of new muscles[24]. Although the surgical success rate of the combination of horizontal rectus and oblique muscle surgery was greater than that obtained in patients receiving horizontal rectus surgery only, there were no differences in post-operative deviations when comparing the two surgical options. As no much potential for fusion exists in patients with sensory exotropia after strabismus surgery, residual horizontal deviation and pattern would seem to exert little impact on the quality of daily life. When considering all of the factors as described above, isolated horizontal rectus surgery may provide a good option for the correction of sensory A-V pattern exotropia in patients with oblique muscle dysfunction.

There are some limitations in this study. 1) The study was retrospective in nature, and the surgical procedures were not performed by the same surgeon. 2) Follow-up periods were relatively short. 3) As all patients had undergone strabismus surgery, no data analysis on outpatients who usually show a small angle of exodeviation were performed. 4) Patients with incomplete records were excluded in our study, which has the potential of introducing some selection bias. 5) Although patients with sensory exotropia without A-V pattern and concomitant A-V pattern exotropia with normal vision were selected at random, there remains a possibility for a sampling error. 6) Most patients in our study were Han Chinese who came from south China, which may introduce some ethnic and/or geographical bias. 7) As there did not seem to be sufficient data to support the role of an A-V pattern in stabilizing eye position some of the evidence for such a relationship remains speculative. A long-term prospective study of sensory exotropia on changes of eye position in both groups with and without A-V pattern will be required to substantiate the conclusions of this report.

In conclusion, we report here that the occurrence of A-V pattern sensory exotropia in present study was 10.79%. Abnormal visual experience resulting from vision impairment during the critical period of visual development might be associated with the occurrence of A-V pattern. Visual acuity appears to be an important factor contributing to the occurrence and development of A-V pattern. As isolated horizontal rectus surgery presented favorable surgical results, it may serve as a good option for the correction of sensory A-V pattern exotropia in patients with oblique muscle dysfunction.

**ACKNOWLEDGEMENTS**

**Authors' contributions:** Yan JH initially designed the concept of this work, Zhu BB, Tang SY, Wang XJ, and Fu LC collected and analyzed the data, Zhu BB and Yan JH authored the manuscript. All authors have read and approved the manuscript.

**Data Availability Statement:** The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Conflicts of Interest: Zhu BB,** None; **Tang SY,** None; **Wang XJ,** None; **Fu LC,** None; **Yan JH,** None.

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