Endoscopic trans-ethmosphenoid optic canal decompression is an optimal choice to save vision for indirect traumatic optic neuropathy

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ABSTRACT.
Purpose: **To evaluate and compare the effectiveness of endoscopic trans-ethmosphenoid optic canal decompression (ETOCD) and steroid pulse therapy (SPT) for indirect traumatic optic neuropathy (ITON).**
Design: **Prospective interventional case series.**
Methods: **Total 140 monocular ITON patients from January 2017 to June 2019 were recruited, including 100 patients received ETOCD (56 patients received ETOCD only and 44 patients received ETOCD combined with SPT before surgery), and 40 patients received SPT only. Their visual acuity (VA) and visual evoked potential (VEP) were analysed before and after treatments. Initial VA, lag time, causes of injuries and age were analysed for evaluating prognosis of treatment.**
Results: **In contrast with patients received SPT only (15/40 = 38%), the effective rate of patients received ETOCD only and patients received ETOCD combined with SPT were both significantly better (46/56 = 82%, p < 0.001 and 30/44 = 68%, p = 0.005). Whether with SPT before ETOCD or not, after ETOCD, patients with VA improvement showed no significant difference. And 59/76 (77.6%) patients showed improvement within 24 hours. Patients who had residual visions achieved higher effective rate than those with no light perception (56/58 = 97% and 20/42 = 48%; p < 0.001) after ETOCD. For patients with long lag time of 21–90 days, 23/32 (72%) patients presented with vision improvement. Moreover, VEP was significantly improved after ETOCD. No severe complications were observed.**
Conclusions: **Endoscopic trans-ethmosphenoid optic canal decompression (ETOCD) is an effective and safe therapy for ITON, which is more effective than SPT. Even for patients with failure in responding to SPT, the successfully physical decompression is the most effective way to rescue optical nerve from permanent damage.**

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Introduction

Indirect traumatic optic neuropathy (ITON) accounts for 2–5% of facial trauma and 0.5–2% of head trauma and is a severe complication after craniofacial injury (Anderson et al., 1982; aI-Ourainy et al., 1991; Jamal et al., 2009). Indirect traumatic optic neuropathy (ITON) often results from concussive shockwave-induced secondary damages to the optic nerve due to intraneural oedema, occlusion of microvasculature or cerebrospinal fluid circulation, and interruption of direct axoplasmic transport (Lee, 2000; Steinsapir & Goldberg, 2011; Tong et al., 2019). The clinical characteristics include severe acute decrease in visual acuity (VA), impaired visual evoked potential (VEP) and a relative afferent pupil defect (RAPD). The prognosis is usually poor (Wang, 2015; Yu et al., 2016; Lai & Liao, 2018; Ma et al., 2018); loss of eyesight may cause heavy financial burdens to patient families as craniofacial injuries often occur to young and middle-aged working males.

The main therapeutic options for ITON include steroid pulse therapy (SPT), surgical optic canal decompression, the combination of the two and even simple observation (Yang et al., 2004; Entezari et al., 2007; Tandon & Dorrepaal, 2009; Steinsapir & Goldberg, 2011; Samardzic et al., 2012; Soldevila et al., 2013). Endoscopic trans-ethmosphenoid optic canal decompression (ETOCD) is gradually becoming a trend in the recent decade.

Nevertheless, the application of ETOCD for ITON is still debatable among clinicians. Indirect traumatic optic neuropathy (ITON) is a challenging disease, and there are many issues remained to be addressed, including standard regimen for management, prognostic factors, clinical outcomes and the window period for ETOCD surgery, as well as visual function change after the therapy.

In this prospective case series study, we comprehensively evaluated and compared the clinical effectiveness and safety in 140 ITON patients, who were treated with ETOCD, SPT or ETOCD combined with SPT by investigating the visual acuity changes, visual function change and a variety of possible factors related to vision improvement. Our findings demonstrate that ETOCD is an optimal treatment option/choice to improve the vision and quality of life for patients suffering ITON.

Methods

Ethics approval

Ethical approval and patient consent were obtained before surgery, and the procedures adhered to the tenets of the 1964 Declaration of Helsinki. For patients who are under 18 years, consent was obtained from their parents or legal guardians. Protocols were approved by the Institutional Ethics Committee (2019KYPJ155, Medical Ethics Committee, Zhongshan Ophthalmic Center, Guangzhou, Guangdong, China).

Participants

This prospective case series study included 140 consecutive patients who were diagnosed with indirect traumatic optic neuropathy (ITON) and underwent endoscopic trans-ethmosphenoid optic canal decompression (ETOCD) surgery and/or steroid pulse therapy (SPT) in Zhongshan Ophthalmic Center from January 2017 to June 2019. The inclusion criteria were as follows: (1) diagnosed of ITON; (2) underwent ETOCD surgery and/or SPT; (3) followed up for at least 3 months; (4) no history of other ocular disorders or ocular surgery; (5) patients' vital indexes were steady, with good consciousness for assessing visual acuities and other ophthalmic examinations; and (6) no other severe non-ophthalmic complications were found by systemic examination. Details on visual acuity, gender, age, causes of injuries and lag time from injury to surgery were recorded.

The diagnosis of ITON was made by traumatic history and examination, including: (1) a closed head injury with no direct trauma to the optic nerve, (2) decrease in visual acuity (VA) and (3) a positive relative afferent pupil defect (RAPD) and an abnormal visual evoked potential (VEP) with normal fundus examination. All patients had comprehensive systemic and ophthalmic examination.

Intervention

Different treatment options were randomly provided to ITON patients. Doctors have had comprehensively informed the patients about the possible outcomes/risks of treatment options, and the treatment for ITON was performed with the patient's consent. According to different selections of treatments, all of the patients were divided into three groups as follow: (1) ETOCD only ($n = 56$); (2) SPT only ($n = 40$); and (3) SPT + ETOCD, that is high dose steroid pulse therapy was given prior to ETOCD ($n = 44$).

Fifty-six patients received ETOCD surgery only. The surgery was performed in the following four steps: (1) expose the optic canal, (2) open the optic canal, (3) incise the annulus of Zinn and (4) cover the optic nerve with nerve growth factor.

Patients with contraindications for high dose steroid were excluded, and there were forty patients received SPT treatment alone. Intravenous high dose steroid (1 g methylprednisolone per day for adults or 15 mg/kg/d methylprednisolone for children) was given to patients daily for 3 days.

Forty-four patients received combined treatment of SPT and ETOCD, where high dose steroid (same dose as SPT only group) was given prior to ETOCD.

Postoperative management

Intravenous broad-spectrum antibiotics were given to patients daily for 3 days postsurgery. Patients were advised not to blow their noses and avoid strenuous activity for three months after ETOCD surgery. Endoscopic examination of the ethmoidal–sphenoidal sinus and wound surface check was performed for each patient within 2 weeks after surgery. Postoperative examinations were required for the first 3 days and followed by week 1, week 2, month 1, month 2, month 3 and month 6, while subsequent examinations were upon patients' requests.

Measurements

To evaluate the vision changes after ETOCD, VA was measured before and after the surgery at various time-points: 1 day (D1), 2 days (D2), 3 days (D3), 1 week (W1), 2 weeks (W2), 1 month (M1) and 3 months (M3). Several measurements and indexes were used: (1) logMAR VA: VA was recorded with the decimal visual acuity chart, and it was converted to logMAR VA (Supplemental Table 1); (2) the improved degree of VA (IDVA): IDVA = (logMAR VA after treatments – logMAR VA before treatments)/(0.12* – logMAR VA before treatments), and *20/15 (logMAR = 0.12) was considered to be the perfect vision (Chen et al., 2007; Yan et al., 2017); (3) the effective rate: the percentage of patients with any VA improvement after treatments.

Visual evoked potential (VEP) was measured before and 1 week, 1 month and 3 months after ETOCD (RETI-Port, Roland Consult, Brandenburg, Germany).

We investigated the possible affecting factors of ETOCD, including initial VA, lag time from injury to surgery, causes of injuries, age and gender of the patients.

Statistical analysis

All personnel who performed measurement for visual acuity and VEP, and data analysis were masked. All patients were labelled by numbers instead of their real names.

Statistical analysis was performed with statistical software (SPSS version 20; IBM Corp., Armonk, NY, USA). Continuous variables were described as means ± standard deviation (SD); t-tests for comparisons and correlation analysis were performed where appropriate. Statistical significance was defined with p-value of less than 0.05.

Results

Baseline characteristics of patients

A total of 140 patients with monocular indirect traumatic optic neuropathy (ITON) were treated with endoscopic trans-ethmosphenoid optic canal decompression (ETOCD) surgery and/or steroid pulse therapy (SPT). Among them, 56 patients received ETOCD only and 40 patients received SPT only, as well as 44 patients had previously received SPT before ETOCD. Patient characteristics were listed in Table 1: 125 were male (89.3%), and 15 were female (10.7%); the mean age was 26.9 ± 14.1 years (range 5–62). Before treatments, 61 patients had no light perception (NLP), and 79 patients had residual vision (RV), and all visual acuity (VA) was measured with decimal visual chart (ranged from NLP to 0.3). Lag time from injury to treatment ranged from 1 to 80 days, with a mean time of 15.6 ± 21.9 days. The most common cause of ITON in our study was traffic accident (83/140 = 59.3%), followed by accidental falls (39/140 = 27.8%) and fights/assaults (18/140 = 12.9%).

ETOCD present better therapeutic effects than SPT in ITON patients

In order to analyse the effect of ETOCD more objectively, we compared 3 groups of patients according to the 3 different treatments, including ‘ETOCD only’ (56 patients), ‘SPT only’ (40 patients) and ‘ETOCD + SPT’ (44 patients; Table 1). The results showed ETOCD, disregarding SPT was given, could help more patients improving VA.

To evaluate the effectiveness of these different treatments, several measurements were performed, including the effective rate (i.e. the percentage of patients with VA improvement after treatments), the mean logMAR VA and improved degree of VA (IDVA). The effectiveness was defined by an increase in logMAR VA, wider visual fields, brighter visual fields or any VA nuances even the same logMAR VA (e.g. FC/10 cm to FC/20 cm).

In contrast to ‘SPT only’ (15/40 = 37.5%), the effective rate of ‘ETOCD only’ and ‘ETOCD + SPT’ were both significantly better (46/56 = 82.1%, $p < 0.001$ and 30/44 = 68.2%, $p = 0.005$; Fig. 1A). The effective rates showed no significant difference between ‘ETOCD only’ and ‘ETOCD + SPT’ patients ($p = 0.105$; Fig. 1A).

Before treatments, logMRA VA of ‘ETOCD only’, ‘ETOCD + SPT’ and ‘SPT only’ were −3.34 ± 1.60, −3.33 ± 1.69 and −3.55 ± 1.57, respectively, and there was no significant statistical difference among pre-treatment logMRA VA of three groups ($p > 0.05$). However, after treatments, logMAR VA were all significantly better than those before treatments for all three groups. Notably, there was no significant difference between the post-treatment logMAR VA of ‘ETOCD only’ group (−2.48 ± 1.51) and ‘ETOCD + SPT’ group (−2.52 ± 1.77), and they were both significantly higher than that of ‘SPT only’ group (−3.18 ± 1.74; both $p < 0.05$; Fig. 1B).

Meanwhile, there was no significant difference between the improved degree of visual acuity (IDVA) of ‘ETOCD only’ group (0.25 ± 0.21) and ‘ETOCD + SPT’ group (0.24 ± 0.28). Similarly, IDVA of these two groups were both significantly greater than IDVA of ‘SPT only’ group (0.13 ± 0.23, both $p < 0.01$; Fig. 1C).

From above, we found that compared with SPT only, the ETOCD surgery, whether or not SPT was given, is helpful to improve VA and achieving greater degree of VA improvement, togethering suggesting that ETOCD was more effective than SPT for ITON.

ETOCD may further improve vision in patients with previous treatment of SPT, even for the cases who had no response to SPT treatment

Forty-four patients had previously received SPT before ETOCD, and 16 of them presented with improved VA after SPT. Following subsequent treatment with ETOCD, further VA improvement was observed in all the 16 SPT-effective patients. Whilst in those 28 patients who responded poorly to SPT, 14 patients (50%) achieved VA improvement (Fig. 1D). Our results suggested that regardless SPT effective or not, ITON patients may respond well with good vision improvement to ETOCD surgery.

As all VA improvement measurements (the effective rate, post-treatment VA and IDVA) after ‘ETOCD + SPT’ in 44 patients were similar to those 56 patients treated with ‘ETOCD only’ ($p > 0.05$), we combined the ‘ETOCD + SPT group’ and ‘ETOCD only group’ together as ‘ETOCD group’ (100 patients), to analyse the effect, safety and possible affecting factors of ETOCD surgery for ITON as below.

Vision was efficiently improved in ITON patients after ETOCD

In all 100 patients received ETOCD, 76% (76/100) patients achieved surgical effectiveness. The surgical effective rate was very high (56/58 cases, 97%)

Table 1. Clinical characteristics of 140 enrolled subjects and included eyes

		Treatment		
Variables	Total	ETOCD only	SPT only	ETOCD + SPT
Patients	140	56	40	44
Sex, male	125 (89.3%)	51 (91.1%)	36 (90.0%)	38 (86.4%)
Age (years)	26.9 ± 14.1 (5–62)	26.7 ± 15.1 (5–62)	27.0 ± 14.2 (9–53)	26.9 ± 13.9 (8–53)
Side, right	69 (49.3%)	28 (50.0%)	20 (50.0%)	21 (47.7%)
Lag time (days)	15.6 ± 21.9 (1–80)	19.3 ± 18.5 (3–60)	3.2 ± 1.7 (1–7)	22.2 ± 21.7 (3–80)
Visual acuity				
Range	NLP to 0.3	NLP to 0.3	NLP to 0.2	NLP to 0.2
No light perception	61 (43.6%)	23 (41.1%)	19 (47.5%)	19 (43.2%)
Residual vision	79 (56.4%)	33 (58.9%)	21 (52.5%)	25 (56.8%)
Causes of injuries				
Traffic accidents	83 (59.3%)	35 (62.5%)	23 (57.5%)	25 (56.8%)
Falls	39 (27.8%)	14 (25.0%)	12 (30.0%)	13 (29.5%)
Fights/assaults	18 (12.9%)	7 (12.5%)	5 (12.5%)	6 (13.6%)

ETOCD = endoscopic trans-ethmosphenoid optic canal decompression, SPT = steroid pulse therapy, Lag time = lag time from the injury to treatment.

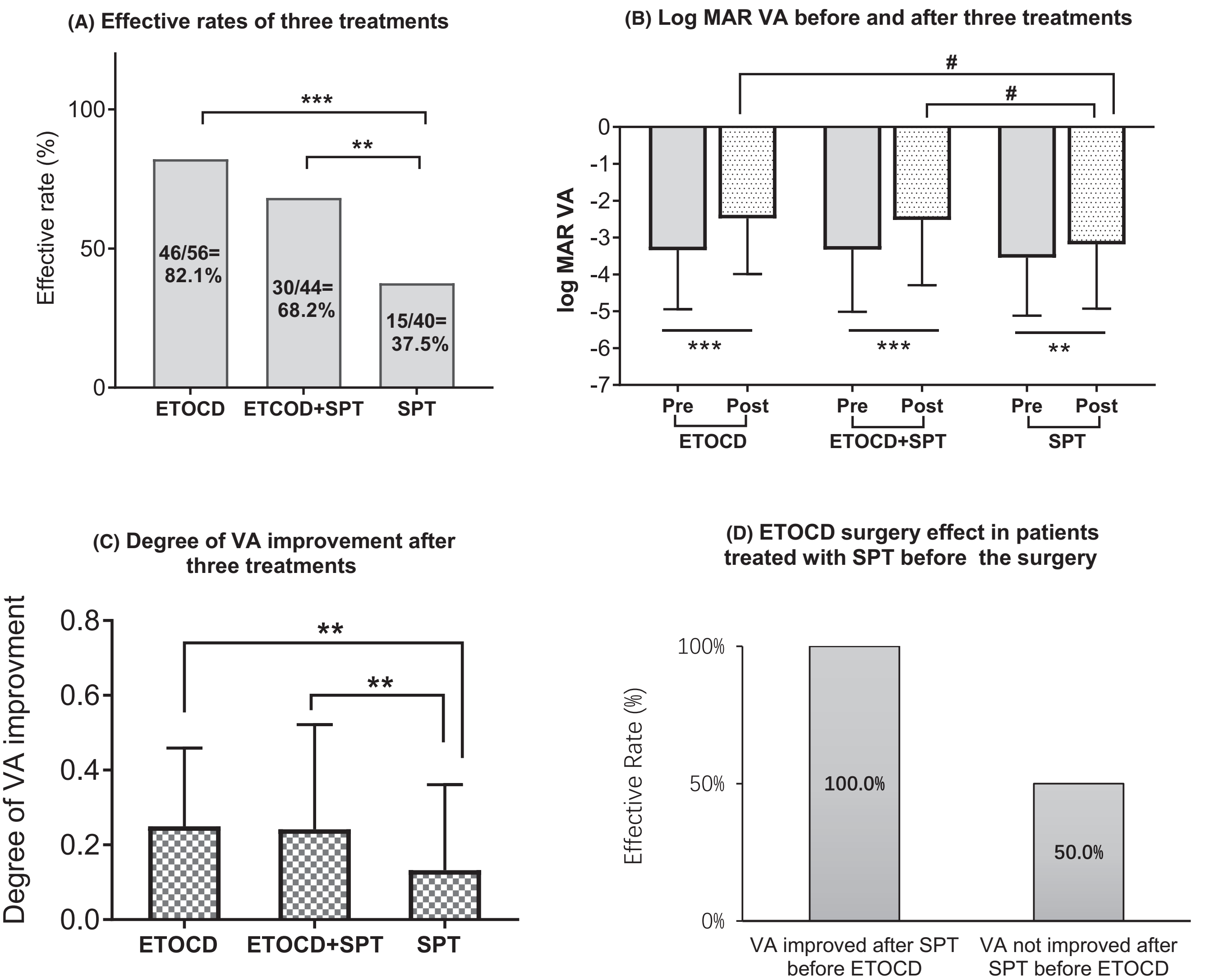

Fig. 1. ETOCD present better treatment effects than steroid pulse therapy (SPT) in ITON patients. (A) The effective rates (refers to the percentages of patients with VA improvement) of three different treatments, including ETOCD only (left), the combination of ETOCD + SPT (middle) and SPT only (right). In contrast with patients treated with SPT only (37.5%), the effective rates of ETOCD only (82.1%) and ETOCD + SPT (68.2%) were both significantly greater (**$p < 0.01$; ***$p < 0.001$). (B) The logMAR VA before and after three different treatments, including ETOCD only, ETOCD+SPT and SPT only. The logMAR VA after three treatments were significantly greater than that before treatments, respectively (**$p < 0.01$; ***$p < 0.001$ between logMAR VA before and after the same treatment). There was no significant difference of logMAR VA before the three different treatments in all ITON patients. However, the logMAR VA after ETOCD only and ETOCD + SPT were significantly higher than that after SPT only. (#$p < 0.05$ between post-treatment logMAR VA of patients treated with different treatments). (C) The improved degree of VA (IDVA) after three different treatments, including ETOCD only, the combination of ETOCD + SPT and SPT only. IDVA = (logMAR VA after treatments – logMAR VA before treatments)/(0.12* - logMAR VA before treatments). There was no significant difference between IDVA after ETOCD only and ETOCD + SPT. Improved degree of visual acuity (IDVA) after ETOCD only and ETOCD + SPT were both significantly higher than that after SPT only. (**$p < 0.01$ between IDVA of patients treated with different treatments). (D) The effective rates of ETOCD in 44 patients who were treated with SPT before ETOCD. For the 16 patients whose VA were improved with SPT before ETOCD surgery, they can all got benefit from ETOCD surgery (16/16 = 100%, left). Even for those 28 patients with failure in responding to SPT, 50.0% (14/28) of them got better VA after ETOCD (right).

in the patients with RV while it was 48% (20/42) in the NLP patients.

The logMAR VA was significantly improved in ITON patients after 3 months of ETOCD, when compared with preoperative VA (Fig. 2A). The logMAR VA was significant between preoperative and postoperative (-3.33 ± 1.63 versus -2.50 ± 1.61, $p < 0.001$) for the 100 patients: -5.00 ± 0 versus -3.97 ± 1.33 ($p < 0.001$) in NLP groups, and -2.13 ± 1.04 versus -1.43 ± 0.72 ($p < 0.001$) in RV group, respectively.

The IDVA was all positive (0.25 ± 0.24) after ETOCD in the 100 patients, among them IDVA was 0.28 ± 0.22 in RV group, slightly better than 0.20 ± 0.26 in NLP patient ($p = 0.062$, Fig. 2B). The case number and percentage of each level of IDVA were clearly presented in Fig. 2C–E, indicating no case had worse IDVA after surgery.

To show vision improvement more visibly, the patients were divided into 6 groups according to their preoperative VA (Pre-Op) (Fig. 2F–K). In NLP group, 48% (20/42) of patients improved after surgery, and one

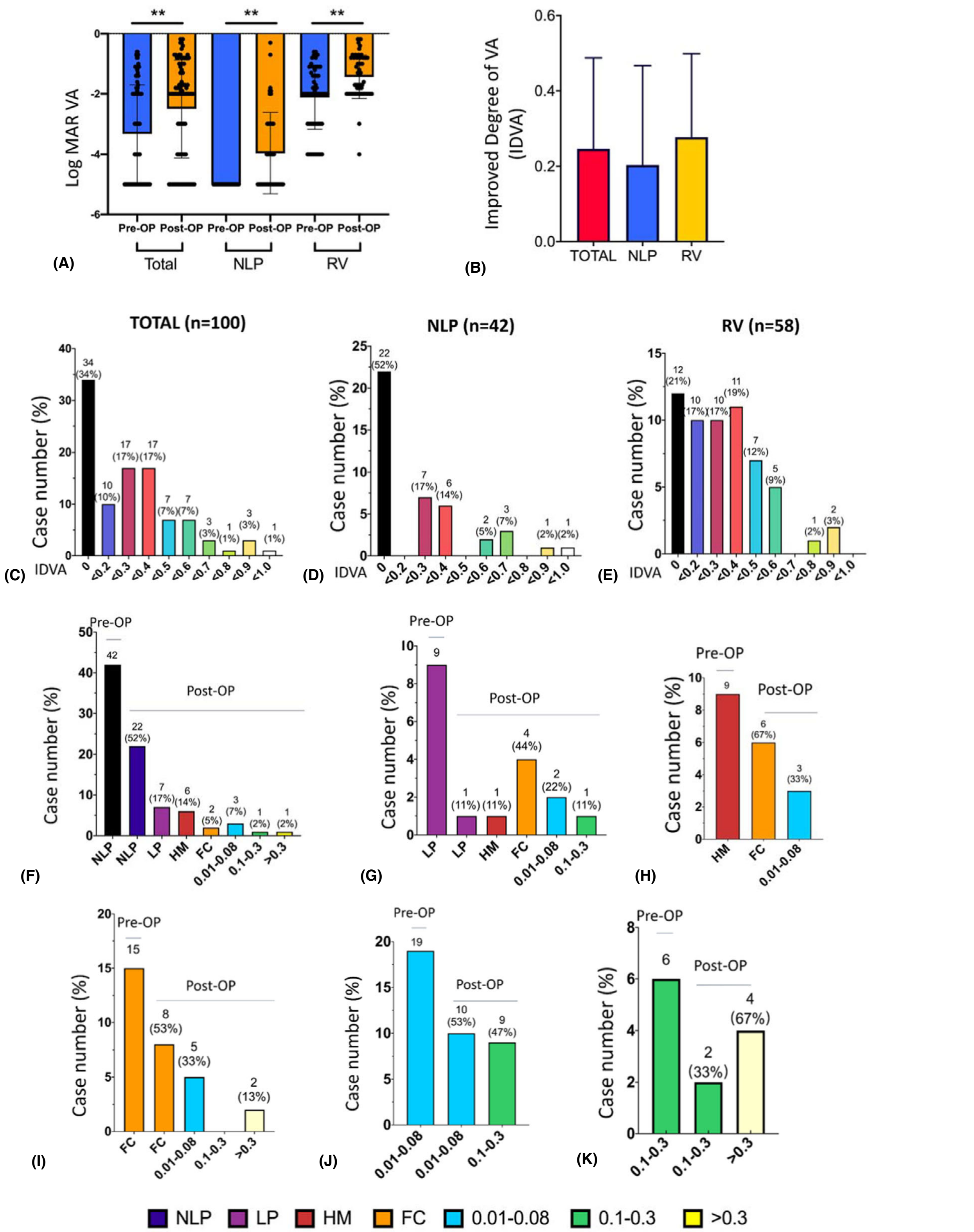

Fig. 2. The visual acuity (VA) of indirect traumatic optic neuropathy (ITON) patients was dramatically improved after endoscopic trans-ethmosphenoid optic canal decompression (ETOCD) surgery. (A) The logMAR VA before and after ETOCD. The postoperative logMAR VA after three months from surgery was significantly higher than that preoperative in all groups. **$p < 0.01$ between VA preoperative and postoperative. (B) The improved degree of VA (IDVA) after ETOCD. No case showed worse IDVA after surgery. IDVA = (logMAR VA after treatments – logMAR VA before treatments)/(0.12 - logMAR VA before treatments). (C–E) The case number and percentage of different IDVA levels of total patients (C), NLP group (D) and RV group (E). (F–K) The case numbers and percentage of different postoperative VA levels in 6 groups according to preoperative VA: NLP (F), LP (G), HM (H), FC (I), 0.01–0.08 (J), and 0.1–0.3 (K). NLP = no light perception, RV = residual vision, LP = light perception, HM = hand movement, FC = finger counting, IDVA = improved degree of visual acuity, Pre-OP = preoperative, Post-OP = postoperative.

particular case reached 0.5 (decimal visual chart) a 3 months after ETOCD. In light perception (LP) and hand movement (HM) groups, 89% (8/9) and 100% (9/9) of patients had improved vision after surgery. The proportion of improvement was 47% (7/15), 47% (9/19) and 67% (4/6), in finger counting (FC), 0.01-0.08 and 0.1–0.3 groups, respectively. The FC group had fewer cases with VA improvement because some patients improved VA from FC/10cm to FC/20cm or better but still in FC level.

Vision was rapidly improved as early as 1 day after ETOCD and steady improving during follow-up in 3 months

The proportions of patients with VA improvement in total 100 ITON patients were 59%, 66%, 67%, 70%, 75% and 76% on D1, D2, D3, W1, M1 and M3, respectively (Fig. 3A). Interestingly, among these 76 cases with VA improvement, 78% (59/76) were improved within 24 hr, and 87% (66/76) and 92% (70/76) were improved on D2 and W1, respectively (Fig. 3B). This clinical observation shows the rapid and steady effectiveness of ETOCD in ITON patients.

The logMAR VA was found to increase significantly to -2.98 ± 1.63, -2.92 ± 1.65, -2.85 ± 1.67, -2.71 ± 1.63, -2.55 ± 1.61 and -2.50 ± 1.62 (all $p < 0.001$) on D1, D2, D3, W1, M1 and M3 after surgery when compared with preoperative logMAR VA (-3.33 ± 1.64) (Fig. 3C). As shown in Fig. 3D, the IDVA also increased steadily during follow-up from D1 (0.10 ± 0.14) to M3 (0.24 ± 0.24). Improved degree of visual acuity (IDVA) at each time-points was statistically significant from the previous time-points (all $p < 0.05$).

The lag time from injury to ETOCD plays a role in surgical outcomes, but patients with longer lag time may have benefit from ETOCD

To address whether the lag time from injury to ETOCD was crucial to VA recovery, we divided patients into three groups according to the lag time: group A, 3–10 days; group B, 11–20 days; and group C, 21–90 days (Fig. 4, A1). Overall, there was no significant change in the percentage of patients with VA improvement among three groups in total 100 cases or RV patients. Whilst in NLP patients, 12/21 (57%) Groups A and 7/13 (54%) B patients presented with VA improvement, respectively, and the proportion in Group C NLP patients with VA improvement was low as 1/8 (13%, $p = 0.031$ compared with Group A). The quantitative correlation analysis further showed a statistically significant correlation between the lag time and IDVA ($r = 0.-292$, $p = 0.039$) in total ITON patients (Fig. 4, A2), indicating a decreasing trend of IDVA with prolonging lag time.

Interestingly, a few cases showed impressive response in vision improvement to ETOCD even with very long lag time. Case 1, a 26-year-old young male, whose VA of left eye dropped to FC/50 cm after head trauma, received ETOCD 2 months later. Surprisingly, his best-corrected VA recovered to 0.6 (decimal visual chart) in 3 days after ETOCD (indicated by the arrow-pointing datapoint at the upper right of Fig. 4, A2). Case 2 was not included in this study: a 45-year-old man with binocular NLP after head trauma for more than 4 months received the ETOCD surgeries in our hospital, one after the other in two consecutive days. His left eye VA became LP on the first day after the surgery, and it was gradually getting better at follow-up. By 3 months after ETOCD, the best-corrected VA of his left eye recovered to 0.5 (decimal visual chart), and VA of the right eye was improved to HM/20 cm. These bright examples should encourage surgeons to perform ETOCD surgery for saving the vision of ITON patients who missed early treatment.

Other parameters, such as age, gender and causes of injuries, were not statistically correlated with the effectiveness of ETOCD surgery (Fig. 4B, $p > 0.05$).

The visual evoked potential (VEP) was significantly improved after ETOCD

The latent period of N1, N2 and P1 was significantly decreased, and the amplitude of P1 and P2 was significantly increased after ETOCD in all ITON patients (all $p < 0.05$, Fig. 5A).

To explore whether VEP change was related to VA improvement, we divided 100 ITON patients who received ETOCD into two groups: with or without VA improvement after ETOCD (Fig. 5B). All VEP parameters before ETOCD were similar between these two groups. The latent period of N2 and P1 was observed to decrease significantly (N2, from 111.00 ± 19.75 ms to 81.4 ± 17.01 ms; P1, 89.00 ± 17.01 ms to 65.80 ± 19.18 ms, both $p < 0.01$); meanwhile, the amplitude of P2 was dramatically increased from 4.60 ± 2.53 μV to 7.60 ± 3.02 μV ($p = 0.007$) after surgery in VA improvement group ($n = 76$). However, these three parameters were not significantly improved in the group with no VA improvement ($n = 24$).

Other VEP parameters, latent period of N1 and the amplitude of P1 were significantly improved in both groups disregarding VA improvement, but latent period of P2 was not changed after ETOCD in neither group with nor without VA improvement.

Surgical complications and safety

In all 100 patients who underwent ETOCD surgery, three patients presented with minor complications of nasal bleeding after the operation, which spontaneously stopped within 48 hr. No patient showed VA loss or decrease after ETOCD surgery. There were no other severe complications observed, such as cerebrospinal fluid rhinorrhea, severe bleeding or death.

Discussion

Indirect traumatic optic neuropathy (ITON) often causes severe vision loss of the patients following head injuries. The treatment of ITON remains a great challenge to doctors. Trans-ethmosphenoid optic canal decompression (ETOCD) is one of the most recognizable treatments of ITON in recent years. However, very few publications have comprehensively compared the impact of ETOCD surgery and steroid pulse therapy, and the effectiveness of ETOCD with time course and possible affecting factors.

In this study, we assessed the percentage of patients with visual acuity (VA) improvement, logMAR VA, improved degree of visual acuity (IDVA) and other clinical data of 140 ITON patients who received ETOCD only, SPT only and ETOCD combined with SPT before

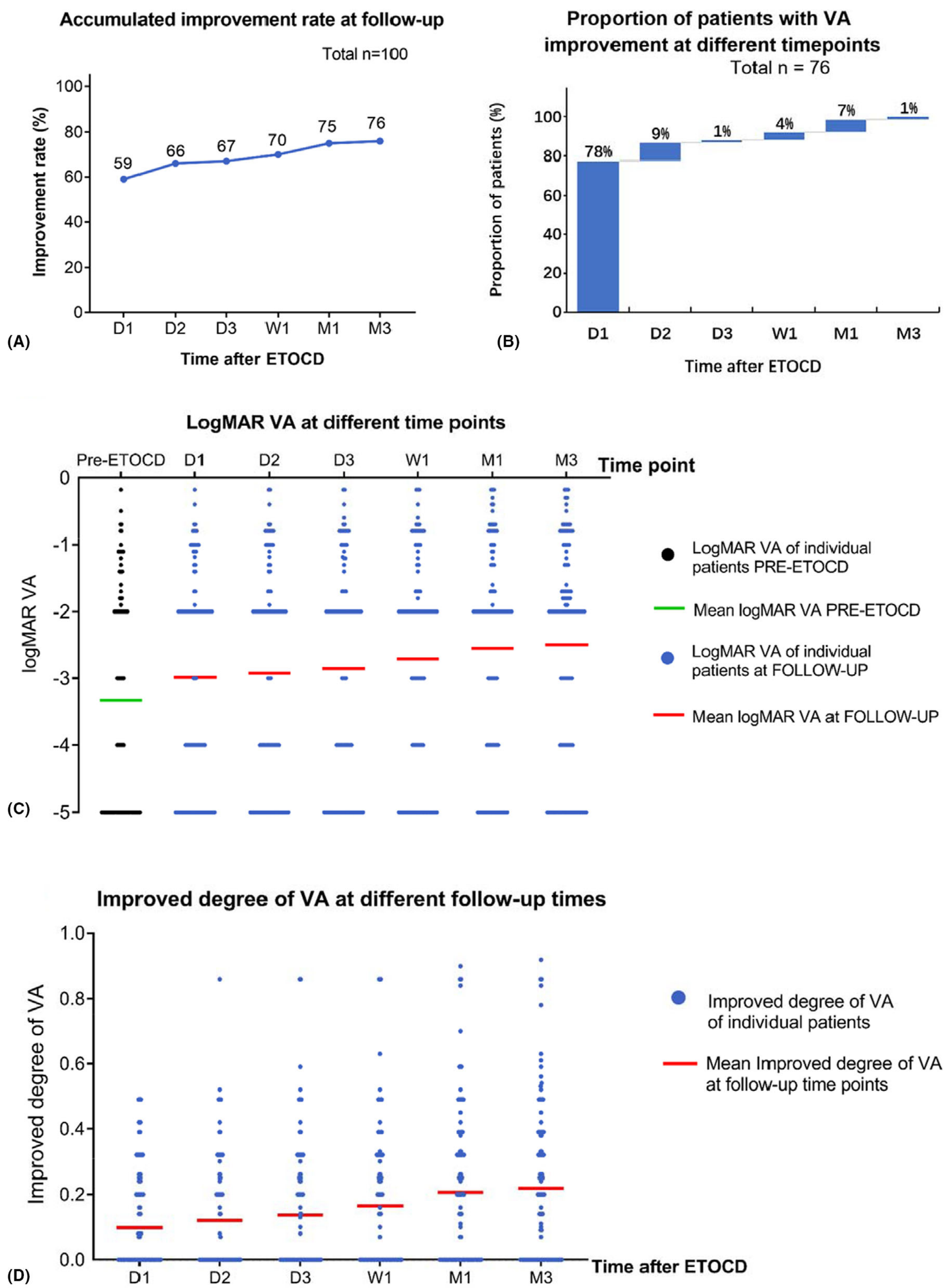

Fig. 3. The postoperative visual acuity (VA) was rapidly and steadily improved after endoscopic trans-ethmosphenoid optic canal decompression (ETOCD) surgery. (A) The accumulated percentage of VA improvement cases among total 100 patients though different follow-up time-points. (B) The proportions of VA improvement at different follow-up time-points among all 76 cases with VA improvement after ETOCD surgery. (C) The mean logMAR VA increased steadily during follow-up time-points and all had statistical significantly compare with logMAR VA preoperative (all $p < 0.001$) and also significantly increased compare with previous follow-up time-points (all $p < 0.05$). (D) The improved degree of VA (IDVA) increased steadily during follow-up from 1 day to 3 months after ETOCD and were statistically significant from the previous VA check at each time-point (all $p < 0.05$). Postsurgery time-points were as follows: after 1 day (D1), 2 days (D2), 3 days (D3), 1 week (W1), 1 month (M1) and 3 months (M3).

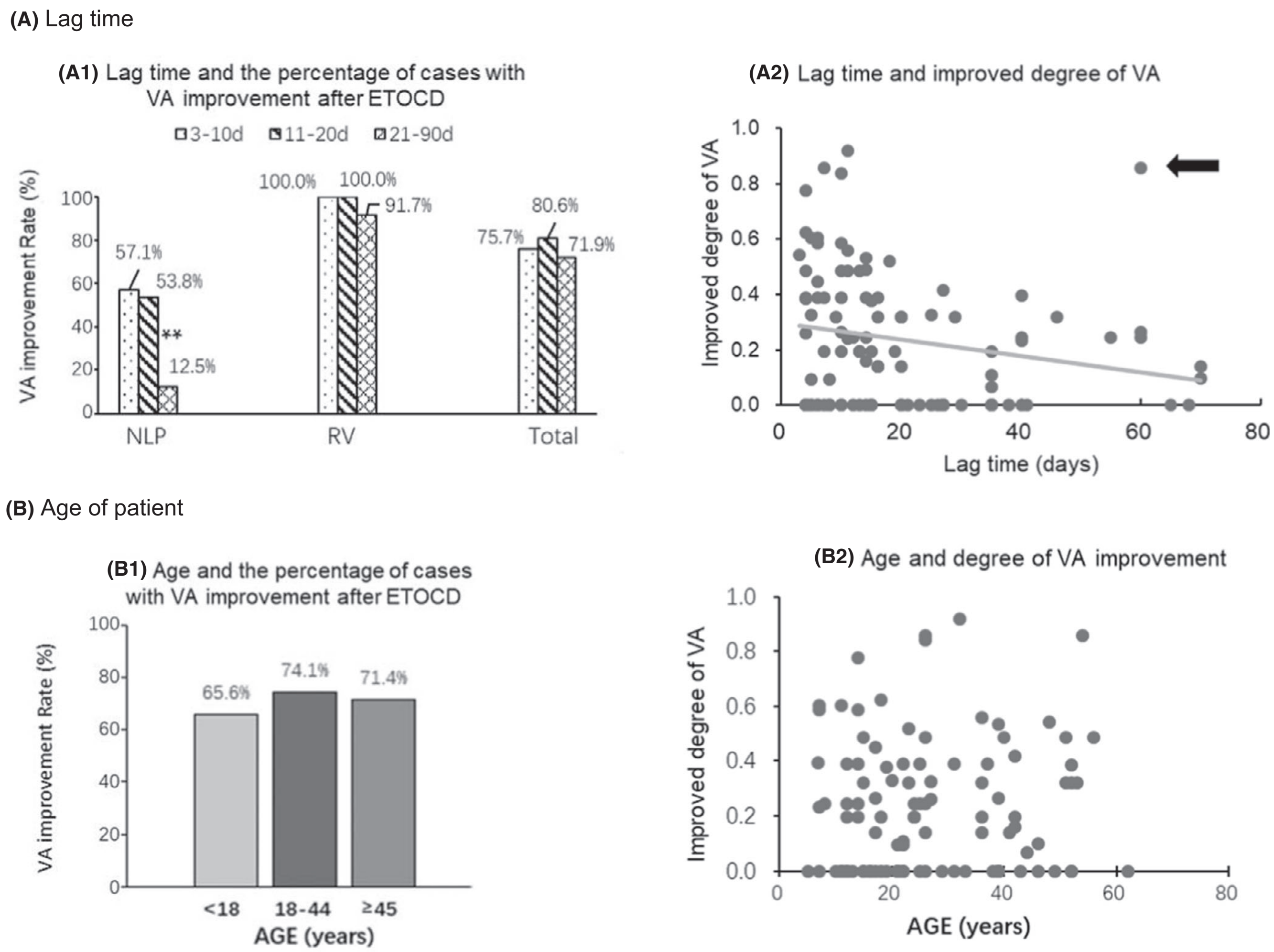

Fig. 4. The influence of the lag time and age to visual acuity (VA) improvement by endoscopic trans-ethmosphenoid optic canal decompression (ETOCD) surgery. (A) Lag time from injury to ETOCD surgery played an important role in VA recovery. In no light perception (NLP) group, the VA improvement rate of shorter lag time achieved better VA improvement than those patients with longer lag time (21–90 days: 12.5%). In total patients and residual vision (RV) group, the improvement rate showed no significant difference among different lag time groups (A1). The scatter diagram showed a negative correlation between the lag time and the improved degree of VA [IDVA = (post-logMAR VA – pre-logMAR VA)/(0.12 - pre-logMAR VA)] (r = 0.-292, p = 0.039) (A2). (B) Age did not relate to VA improvement by ETOCD surgery. The VA improvement rate of ETOCD of different age groups showed no significant difference (B1). The scatter diagram showed there was no correlation between age and the degree of VA improvement (B2).

surgery. Our results provide encouraging outcomes that the ETOCD surgery, one of optimal choice, is an effective and safe therapy for ITON patients to improve and recover vision.

The effectiveness of steroid treatment has been controversial. Some doctors suggested that high dose steroid treatment was as effective as surgical optic canal decompression, or high dose steroid before operation could help the patients to get better results, whilst some doctors suggested that preoperative SPT does not aid significantly better surgical results (Entezari et al., 2007; Wang, 2015). In our study, we analysed the effectiveness of 3 groups of patients: ETOCD only, SPT only, as well as ETOCD combined with SPT. The results showed no statistical different between the 'ETOCD only' and 'ETOCD + SPT' groups, so we combined the data of two ETOCD groups for surgical treatment effect analysis. The effective rate in either of the ETOCD groups (ETOCD group, ETOCD + SPT group, total ETOCD group) was significantly better than the 'SPT only' group, respectively. It suggested ETOCD was more effective than SPT in ITON patients.

Besides, the effective rates and IDVA showed no significant difference between 'ETOCD only' and 'ETOCD + SPT' patients, which indicated that high dose steroid treatment before surgery may not improve the effect of ETOCD.

Moreover, we analysed the effectiveness of ETOCD in 44 patients who had been given SPT ('ETOCD + SPT' group). We found that all SPT-effective patients and those who did poorly with SPT achieved VA improvement after ETOCD, and the logMAR VA also significantly increased after ETOCD. It suggests that the ITON patients with SPT history, regardless effective or not, may respond well with good vision improvement to ETOCD surgery.

Of all 100 ITON patients treated with ETOCD, 76.0% gained vision improvement after ETOCD in our study, in concordance to some reported studies (Yu et al., 2018; Huang et al., 2020; Yan et al., 2020). Among these

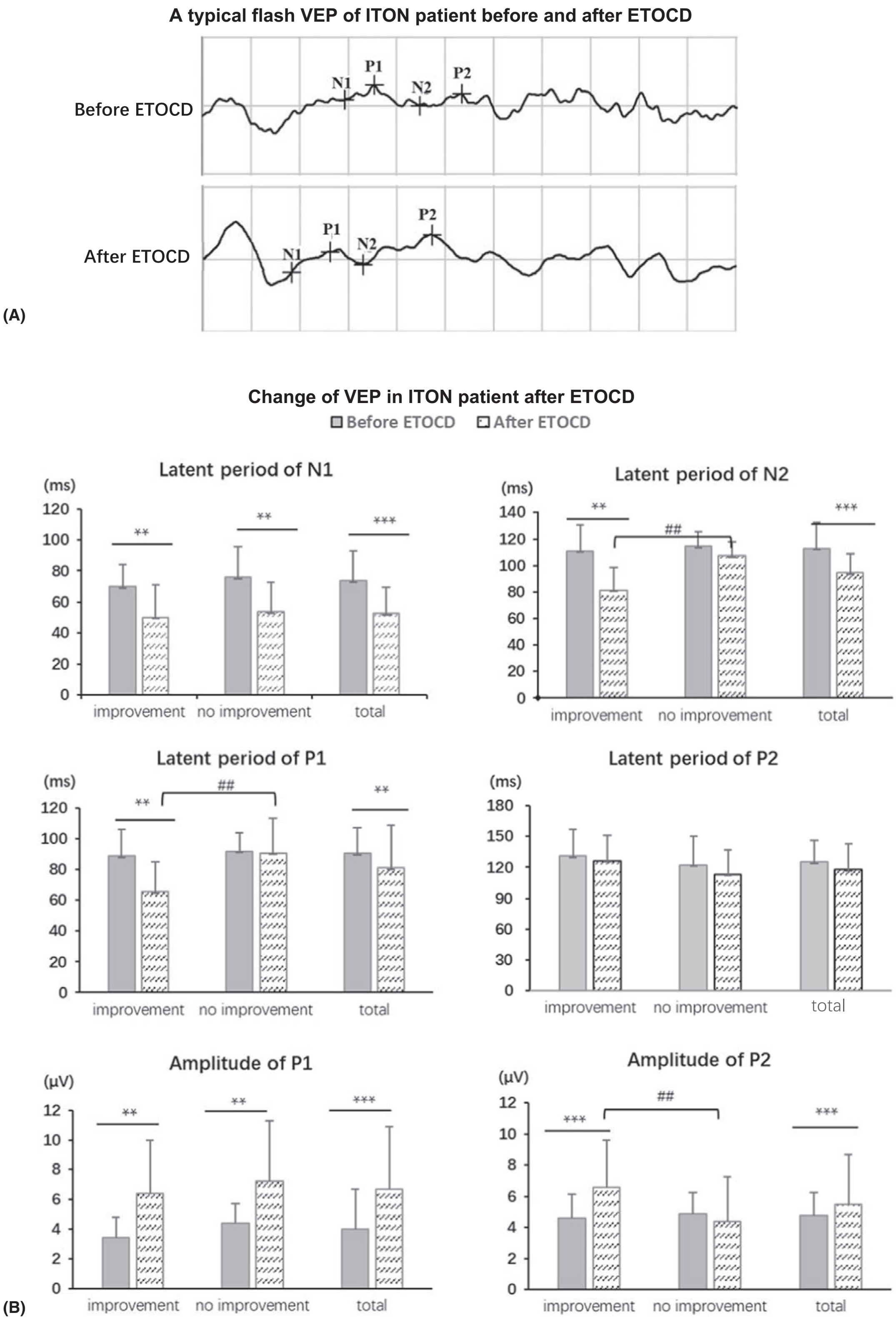

Fig. 5. The flash visual evoked potential (VEP) of indirect traumatic optic neuropathy (ITON) patients was improved after endoscopic trans-ethmosphenoid optic canal decompression (ETOCD). (A) The typical flash VEP before and after ETOCD surgery. (B) Comparison of VEP parameters (latent periods of N1, N2, P1 and P2; and amplitudes of P1 and P2) before and after ETOCD surgery, and between groups of patients with and without VA improvements. In the latter comparison, only latent periods of N2, P1 and amplitude of P2 existed statistical significance between patient groups, suggesting of relation to visual acuity improvement. **$p < 0.01$ between preoperative and postoperative VEP parameters; ***$p < 0.001$ between preoperative and postoperative VEP parameters; $^{##}p < .01$ between the postoperative VEP parameter for two groups of patients with and without VA improvements.

ETOCD-effective patients, the VA could be improved rapidly as early as one day after ETOCD with steady improvement during follow-up in three months. The possible mechanism for rapid vision recovery should attribute to physical decompression to the optic canal by ETOCD, thereby releasing the pressure on swollen optic nerve and alleviating the damage to the optic nerve.

It has been considered that postinjury VA is closely correlated with the severity of optic nerve damage, and severely impaired vision especially NLP may imply the possible degeneration and necrosis of the ganglionic layer of retina (Carta et al., 2003; Ma et al., 2018). In our study, the effective rate of ETOCD was significantly higher in the patients with residual vision (97%) than in the NLP patients (48%) before surgery. The results suggest the preoperative VA may be a crucial factor to prognose for the effectiveness of ETOCD surgery.

Several studies reported that delay to seek treatment is an influencing factor for

A prognosis of ITON patients (Carta et al., 2003; Lai & Liao, 2018; Yan et al., 2020). In this study, we found vision improvement after ETOCD is associated with lag time, especially in NLP patients. No light perception (NLP) was usually considered to be incurable. However, in our study nearly half of our NLP patients benefited from ETOCD, and several cases achieved unexpectedly impressive result of 0.5–0.6. Moreover, patients with long lag time for 60 days or longer may respond well to ETOCD as evidenced by several successful cases. The encouraging effectiveness in these NLP patients with long lag time (up to 4 months) suggests that successful optic canal decompression by ETOCD may be the best therapy to rescue optical nerve from permanent damage even in blinding stages.

To explore the potential mechanism for vision improvement at functional levels, the visual evoked potential (VEP) were examined before and after ETOCD. Visual evoked potential (VEP) was an important parameter of visual function, especially for the function of the optic nerve. In this study, it was found that main VEP values, including the latent period of N1, N2 and P1, as well as the amplitude of P1 and P2, were significantly improved after the ETOCD surgery in ITON patients. Among these main values of VEP, the latent period of N2 and P1 and the amplitude of P2 were specifically correlated with patients who achieved VA improvement, suggesting these parameters of VEP may attribute to vision improvement after decompression by ETOCD.

This study has limitations. Different treatment options were randomly provided to ITON patients, and the treatment was performed with the patient’s consent. Younger patients, or patients with severe injuries, for example, may opt for more aggressive treatments. This may result in patient selection bias due to different severity of the injury or different age. Thus, to avoid this selection bias, we statistically analysed the initial visual acuity before the treatment, genders, age and causes of injuries of these three groups and found these parameters of these groups were matched.

Our findings from ITON patients demonstrated that ETOCD was an effective and safe therapy to improve the vision and quality of life for ITON patients, and it was more satisfactory than SPT. High dose steroid treatment before surgery did not improve the effect of ETOCD. For patients who did not respond well to SPT, or those who missed out the optimal period of treatment, ETOCD may provide an effective treatment alternatively. The visual acuity could be improved or recovered in majority of patients after ETOCD, and many may present rapid improvement.

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