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Intraoperative Visual Evoked Potential Monitoring in Endoscopic Endonasal Surgery for Nonpituitary Adenoma Suprasellar Tumors

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Background and Purpose Intraoperative visual evoked potential (VEP) monitoring has been studied mainly in pituitary adenoma, while its role in nonpituitary suprasellar tumors has remained unclear. This study evaluated the predictive usefulness of intraoperative VEP monitoring during endoscopic endonasal surgery (EES) and aimed to identify optimal alarm criteria for visual outcomes.

Methods We retrospectively analyzed a cohort of 87 patients who underwent EES with intraoperative VEP monitoring between April 2021 and September 2023. Visual outcomes were evaluated preoperatively and at short-term (≤3 months) and long-term (12 months) follow-ups, with visual deterioration at these time points defined as worsening of either visual acuity or the visual field. Reductions in the VEP amplitude were quantified using both the maximum intraoperative decrease and the final amplitude after recovery. Receiver operating characteristic (ROC) curve analyses were performed to identify the optimal alarm thresholds, and the sensitivity, specificity, positive predictive value, and negative predictive value were calculated for short-term and long-term visual deteriorations.

Results Short-term and long-term visual deteriorations were detected in 12 (9.2%) and 5 (3.8%) of the 130 analyzed eyes, respectively. ROC curve analyses identified ≥40% and ≥30% reductions in the N75−P100 amplitude as optimal alarm criteria for short-term and long-term visual deteriorations, respectively. A 30% reduction without intraoperative recovery demonstrated markedly higher sensitivity than the conventional 50% alarm threshold for short-term (58.3% vs. 33.3%) and long-term (80.0% vs. 20.0%) outcomes, while maintaining acceptable specificity (82.2% and 80.8%, respectively).

Conclusions A 30% reduction in amplitude represents a more-sensitive and clinically relevant alarm threshold than a 50% reduction for intraoperative VEP monitoring during EES for nonpituitary suprasellar tumors. Incorporating both the magnitude and recovery pattern of VEP amplitude changes may improve the accuracy of predictions of long-term visual deterioration. However, the potential for false positives warrants cautious interpretation, and further studies are needed to validate the impact of intraoperative VEP monitoring on visual outcomes.

Keywords intraoperative neurophysiological monitoring; visual evoked potential; suprasellar tumor; endoscopic endonasal surgery; optic nerve.

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INTRODUCTION

Preserving the function of the optic nerve during transsphenoidal endoscopic endonasal surgery (EES) is crucial since it directly affects the postoperative visual acuity (VA) and visual field (VF).[1] Intraoperative neurophysiological monitoring has been used to protect neurophysiological functions during surgery. The visual pathway can be monitored in real time during surgery by measuring visual evoked potentials (VEPs) using a light-emitting diode (LED) flashlight and electroretinography (ERG).[2] While VEP monitoring has been reported to be correlated with postoperative visual outcomes, the accuracy of such monitoring has varied across studies.[3-8]

Previous studies have mainly focused on pituitary adenoma surgeries, with the reported sensitivity of VEP monitoring for visual deterioration ranging from 25% to 100%.[9] A few studies have specifically assessed the prognostic accuracy of VEP monitoring in craniopharyngioma surgeries.[5,10] Differences in the location and characteristics of suprasellar tumors with the type of tumor mean that the risk of optic nerve damage also varies. A postoperative decline in visual function is more common in craniopharyngioma and meningioma than in pituitary adenoma,[11] and so the usefulness of VEP monitoring should be analyzed separately for suprasellar tumors other than pituitary adenoma.

In this study we aimed to determine the short-term and long-term predictive usefulness of intraoperative VEP monitoring for visual outcomes in transsphenoidal surgeries other than for pituitary adenoma and to propose appropriate alarm criteria for the application of such monitoring.

METHODS

Participants

This single-center retrospective cohort study included all consecutive patients who underwent EES with intraoperative VEP monitoring at Severance Hospital between April 2021 and September 2023, excluding those with pituitary adenoma. To analyze long-term visual outcomes, the final cohort included only patients with at least 12 months of follow-up, excluding those for whom baseline VEP waveforms could not be obtained in either eye (Fig. 1A).

Visual assessments

The best-corrected VA expressed on a decimal scale, visual field index (VFI), and mean deviation (MD) using a Humphrey visual-field analyzer (HVF) were assessed in all patients at ≤1 month before surgery. For patients who devel-

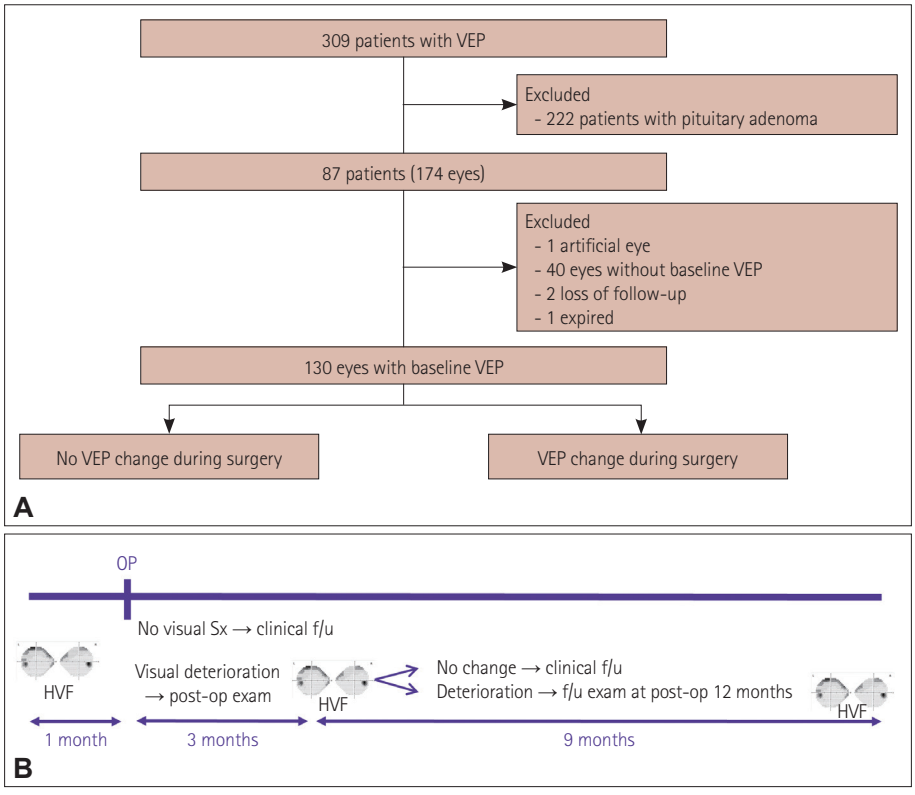

Fig. 1. Flowchart of all participants (A) and the protocol for visual assessments (B). exam, examination; f/u, follow-up; HVF, Humphrey visual-field analyzer; OP, operation; Sx, symptom; VEP, visual evoked potential.

oped new visual symptoms postoperatively, VA and VF tests were performed at ≤3 months postoperatively (short-term visual outcome). All of the tests were conducted by trained optometrists under standard illumination and distance conditions. Worsening of either VA or VF at ≤3 months postoperatively was defined as short-term visual deterioration and at 12 months postoperatively as long-term visual deterioration. VA deterioration was defined as an increase of 0.2 or more in the logMAR value relative to the preoperative value, with decimal-scale measurements converted to logMAR values.[12] In cases where VA could not be measured using the decimal scale, this was categorized into counting fingers, hand motion, light perception, and no light perception, which were scored as logMAR values of 2.1, 2.4, 2.7, and 3.0, respectively.[13] VF deterioration was defined as a decrease of ≥3 dB in the MD value on HVF testing.[14] In participants with short-term postoperative deterioration of VA or VF (i.e., at ≤3 months) compared with preoperative findings, further evaluations were performed at 12 months postoperatively to determine the presence of long-term deterioration (Fig. 1B). Patients were considered to have a decline in visual function if they exhibited deterioration in either VA or VF.

Intraoperative VEP monitoring

An intraoperative monitoring system (Neuromaster MEE-2000 Intraoperative Monitoring System, Nihon Kohden) was used for intraoperative VEP monitoring. The VEP was stimulated using an LED flashlight at 10,000–15,000 lx, and recordings were performed using active electrodes placed at positions Oz, O1, and O2 of the 10–20 EEG system, with reference electrodes at Cz, A1, and A2 (Fig. 2). All obtained waveforms were averaged from 200 stimulations at a frequency of 1.1 Hz and a duration of 10 ms, with bandpass filtering at 10–500 Hz. ERG was performed by measuring the peak-to-peak amplitude, while VEPs were monitored by measuring the N75–P100 amplitude. All patients underwent surgery under total intravenous anesthesia to ensure the reliability of the intraoperative VEP monitoring.

Alarm criteria

Baseline VEPs were measured 20 min after anesthesia induction and the intraoperative VEPs were monitored in real time throughout the surgery. As reported previously any reduction in the N75–P100 amplitude of ≥50% observed at least twice relative to the baseline was communicated to the surgeon. Suspected amplitude reductions were confirmed only if consistent results were observed during at least two separate averaging trials (Fig. 3). An amplitude recovery to ≥50% of the baseline value by the end of surgery was defined as intraoperative recovery, whereas recovering to <50% of the baseline value was defined as intraoperative nonrecovery. All reductions in the VEP amplitudes were rounded to 10% decrements from 20% to 100%.

Statistical analyses

Descriptive statistical analyses were primarily used in this study. Age is presented as median and interquartile range (IQR) values, while sex and diagnoses are described using numbers and proportions. We performed receiver operating characteristic (ROC) curve analyses to determine the most-appropriate alarm thresholds; these analyses were applied to both the maximum VEP reduction and the final VEP amplitude reflecting intraoperative recovery. Separate analyses were performed for short-term and long-term visual outcomes. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were reported for each alarm criterion and outcome measure. Eyes without baseline VEP waveforms were compared with those with measurable baselines, and group differences were analyzed using Student's *t*-test. All tests were two-sided with a significance level of 0.05. Statistical analyses were performed using the SPSS (version 26 for Windows, IBM Corp.) and R software

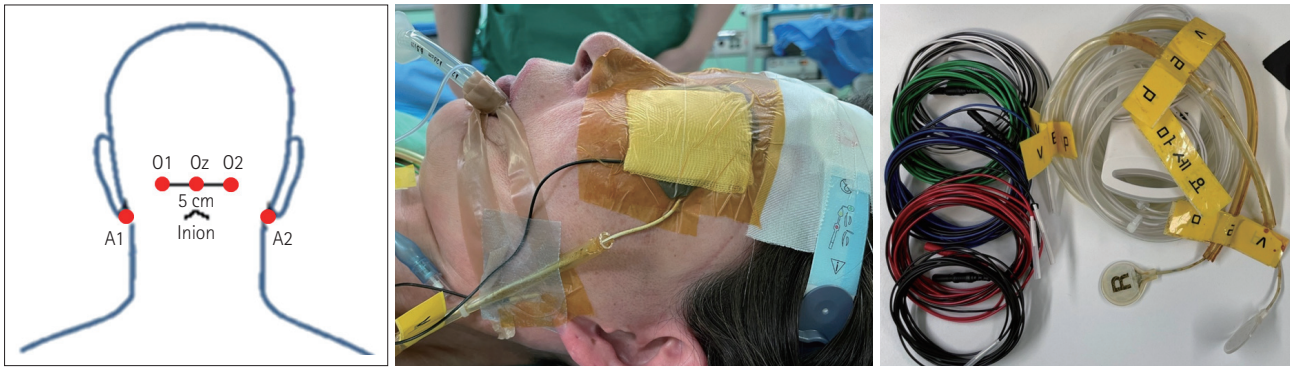

Fig. 2. Procedure used for intraoperative VEP monitoring. The VEP was stimulated using LED flashlight and recordings were performed using active electrodes placed at positions Oz, O1, and O2 of the 10–20 EEG system, with reference electrodes at Cz, A1, and A2. EEG, electroencephalography; LED, light-emitting diode; VEP, visual evoked potential.

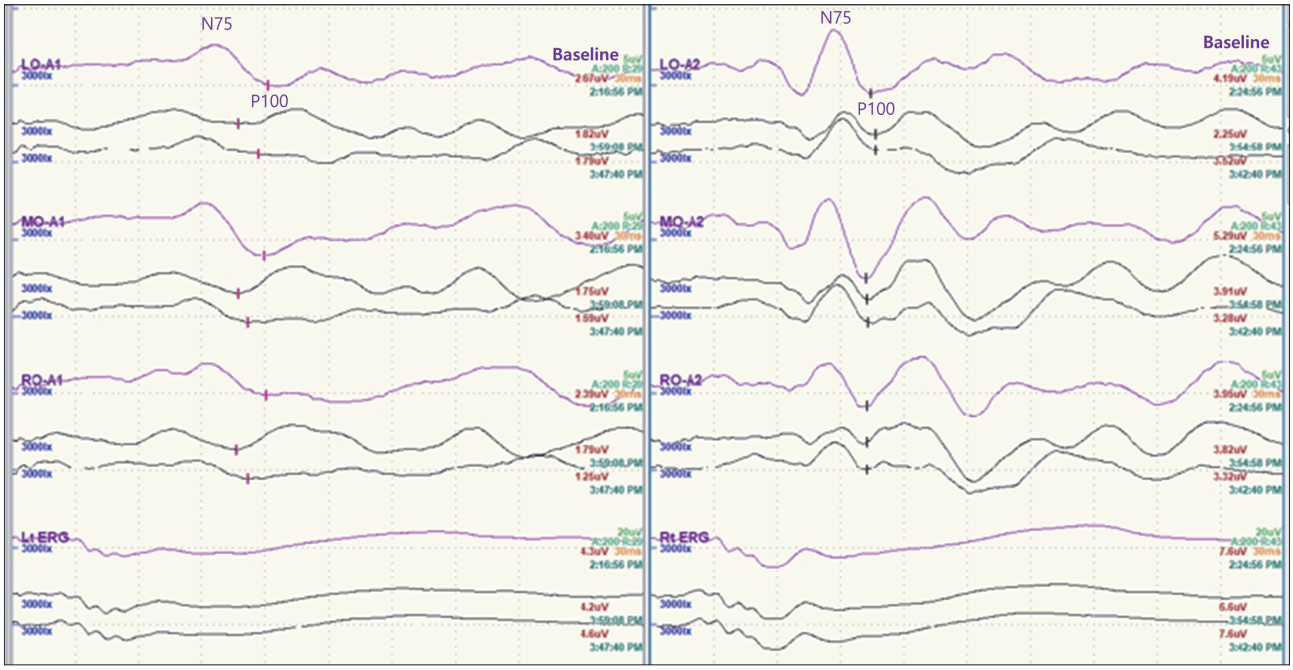

Fig. 3. Illustrative case of a reduction in the N75–P100 amplitude of >50% in both eyes. In each montage, the top purple waveform represents the baseline while the black waveforms below the baseline are the intraoperative VEP signals obtained through averaging. A reduction in the N75–P100 amplitude relative to the baseline waveform is clearly observed. VEP, visual evoked potential.

(version 3.6.3, R Foundation for Statistical Computing).

Ethical considerations

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Severance Hospital (approval number: 4-2025-0481). This study was a retrospective cohort study, and the requirement for informed consent was waived by the Institutional Review Board because of the minimal risk to participants.

RESULTS

Demographics and clinical characteristics of the participants

A cohort of 87 patients with nonpituitary adenoma underwent EES with intraoperative VEP monitoring. Their median age was 54.4 years (IQR=52.3–62.0 years), and they included 61 (70.1%) females. The tumor types included meningioma (54.0%, 47/87) and craniopharyngioma (35.6%, 31/87). One prosthetic eye of the 174 eyes of the 87 patients was excluded, and 40 eyes were excluded due to the absence of a baseline VEP waveform. Consequently, intraoperative VEP monitoring was performed in 133 (76.9%) of the 173 eyes (Table 1). The 40 eyes in which the VEP baseline was not established showed significantly lower VA (logMAR=1.14±0.85 vs. 0.24±0.42 [mean±standard deviation], p<0.001), VFI (33.2±31.4 vs. 85.3±18.8, p<0.001), and MD (-21.42±9.55 dB vs. -5.92±5.95 dB, p<0.001) than the 133 eyes with an established baseline. During the follow-up period, both eyes of one patient were excluded because they were lost to follow-up, and one eye from another patient was excluded because the patient died from an unrelated cause.

Table 1. Demographics and clinical information

Variable	Value
Sex, female	61/87 (70.1)
Age (yr)	54.4 [52.3–62.0]
VEP monitoring, eyes	133/173 (76.9)
Diagnosis	
Meningioma	47/87 (54.0)
Craniopharyngioma	31/87 (35.6)
Angioleiomyoma	3/87 (3.4)
Clival chordoma	1/87 (1.1)
Low-grade glial tumor	1/87 (1.1)
Orbital cyst	1/87 (1.1)
Granular cell tumor	1/87 (1.1)
Arachnoid cyst	1/87 (1.1)
Hemangioblastoma	1/87 (1.1)

Data are *n*/*n* (%) or median [interquartile range] values.
VEP, visual evoked potential.

Short-term visual deterioration

Among the 130 eyes that were evaluated at ≤3 months post-

operatively, 12 (9.2%) showed deterioration in VA (6/130, 4.6%) or VF (11/130, 8.5%) immediately after surgery. When applying the conventional alarm threshold of a 50% reduction in the N75–P100 amplitude, 23 eyes showed a VEP amplitude decrease, with a sensitivity of 58.3% (7/12, 95% confidence interval [CI]=32.0%–80.7%) and a specificity of 86.4% (102/118, 95% CI=79.1%–91.5%). For intraoperative nonrecovery only, the sensitivity was 33.3% (4/12, 95% CI=13.8%–60.9%), specificity was 92.4% (109/118, 95% CI=86.1%–95.9%), PPV was 30.8% (4/13, 95% CI=12.7%–57.6%), and NPV was 93.2% (109/117, 95% CI=87.1%–96.5%).

ROC curve analyses showed that for predicting postoperative visual deterioration, the maximum VEP reduction had an area under the curve (AUC) of 0.752 (95% CI=0.579–0.925, p=0.004), with a ≥40% reduction being the optimal criterion. When using the final VEP amplitude to assess visual deterioration, AUC was 0.705 (95% CI=0.529–0.880, p=0.020), and a ≥30% reduction was identified as the most-appropriate criterion (Fig. 4A and B). The optimal cutoff values remained consistent when VA and VF deterioration were eval-

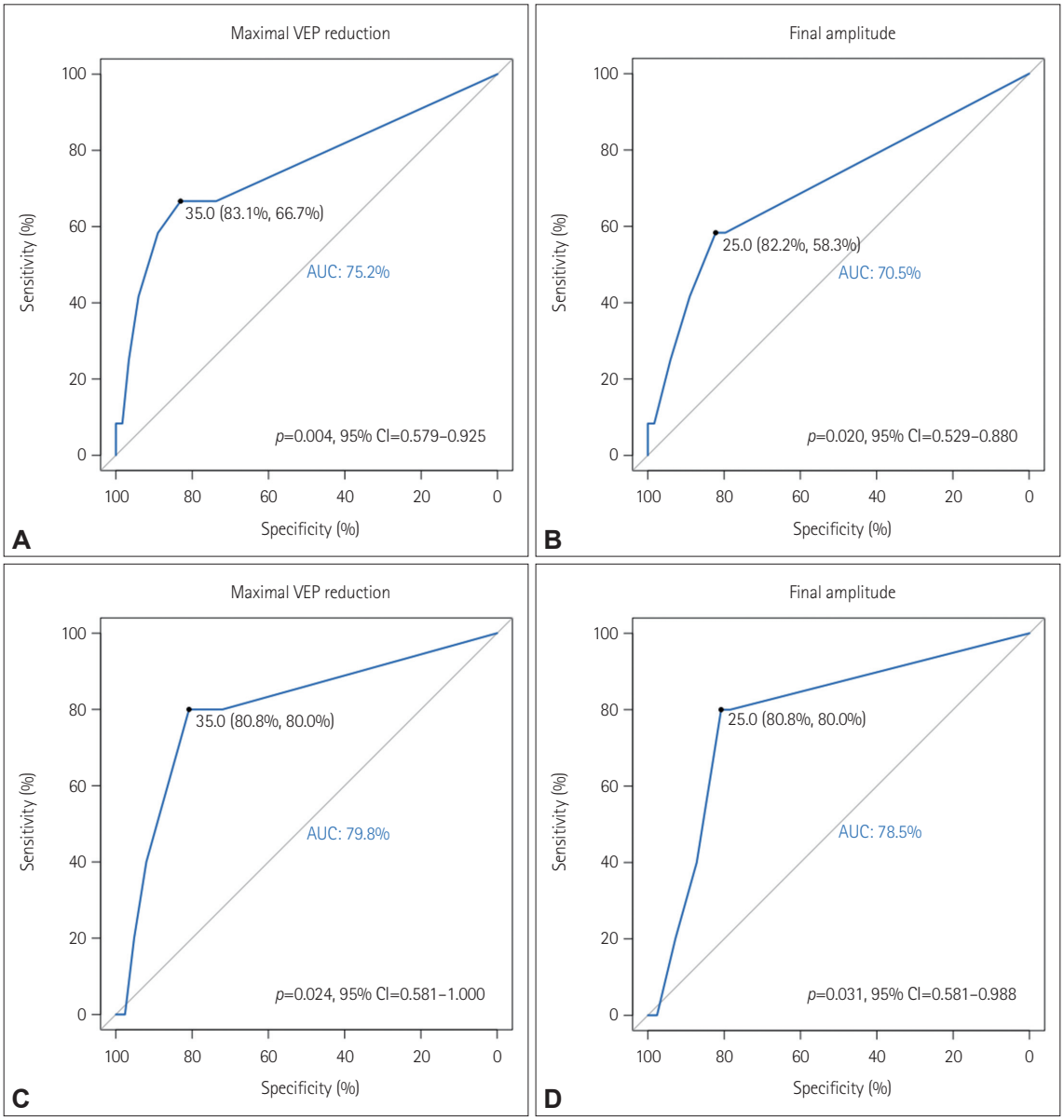

Fig. 4. ROC curves for predicting visual deterioration using intraoperative VEP monitoring parameters. A and B: ROC curves for predicting short-term visual deterioration using the maximum intraoperative VEP amplitude reduction (A) and the final amplitude after intraoperative recovery (B). C and D: ROC curves for predicting long-term visual deterioration using the maximum VEP amplitude reduction (C) and the final amplitude (D). The AUC, optimal cutoff values, specificity, sensitivity, and 95% confidence intervals with p values are indicated in each panel. AUC, area under the curve; CI, confidence interval; ROC, receiver operating characteristic; VEP, visual evoked potential.

uated independently, with significant results observed in both analyses (Supplementary Fig. 1 in the online-only Data Supplement).

For the criterion of a ≥30% reduction, VEP decreased in 38 eyes, with a sensitivity of 66.7% (8/12, 95% CI=39.1%–86.2%) and a specificity of 74.6% (88/118, 95% CI=66.0%–81.6%). For intraoperative nonrecovery only, the sensitivity was 58.30% (7/12, 95% CI=31.95%–80.67%), specificity was 82.2% (97/118, 95% CI=74.3%–88.1%), PPV was 25.0% (7/28, 95% CI=12.7%–43.4%), and NPV was 95.1% (97/102, 95% CI=89.0%–97.9%) (Table 2).

Long-term visual deterioration

Five of the 12 eyes with short-term visual deterioration (representing 3.8% of all 130 eyes) showed persistent long-term visual deterioration at 12 months postoperatively. When applying a 50% amplitude reduction as the alarm threshold, the sensitivity was 60.0% (3/5, 95% CI=23.1%–88.2%) and the specificity was 84.0% (105/125, 95% CI=76.6%–89.4%). For intraoperative nonrecovery only, the sensitivity was 20.0% (1/5, 95% CI=3.6%–62.4%), specificity was 90.40% (113/125, 95% CI=83.97%–94.42%), PPV was 7.7% (1/13, 95% CI=1.4%–33.3%), and NPV was 96.6% (113/117, 95% CI=91.5%–98.7%).

Consistently, when ROC curve analyses were performed for the different parameters, the maximum VEP reduction yielded an AUC of 0.798 (95% CI=0.581–1.000, p=0.024), with a ≥40% decrease identified as the optimal criterion. Similarly, an analysis based on the final amplitude reflecting intraoperative recovery produced an AUC of 0.785 (95% CI=0.581–0.988, p=0.031), with a ≥30% reduction serving as the most-appropriate criterion (Fig. 4C and D). However, in separate analyses of VA and VF, the results for VA were not significant, whereas VF yielded results that were consistent with the overall analysis (Supplementary Fig. 2 in the online-only Data Supplement).

When applying the criterion of a ≥30% reduction, the sensitivity was 80.0% (4/5, 95% CI=37.6%–96.4%) and the specificity was 72.8% (91/125, 95% CI=64.4%–79.8%). For intraoperative nonrecovery only, the sensitivity was 80.0% (4/5, 95% CI=37.6%–96.4%), specificity was 80.8% (101/125, 95% CI=73.0%–86.7%), PPV was 14.3% (4/28, 95% CI=5.7%–31.5%), and NPV was 99.0% (101/102, 95% CI=94.7%–99.8%) (Table 3).

Clinical details of 12 eyes with postoperative visual deterioration

Postoperative VA deterioration was observed in 6 eyes of 5

Table 2. Accuracy of intraoperative visual evoked potential monitoring for predictions of postoperative visual outcomes at ≤3 months

	No visual deterioration	3-month visual deterioration (+)	Total (n=130)
N75–P100 amplitude reduction ≥50%			
No change	102	5	107
Decrease	16	7	23
Intraoperative recovery	6	4	10
Intraoperative nonrecovery	10	3	13
N75–P100 amplitude reduction ≥30%			
No change	88	4	92
Decrease	30	8	38
Intraoperative recovery	9	1	10
Intraoperative nonrecovery	21	7	28

Table 3. Accuracy of intraoperative visual evoked potential monitoring for predictions of long-term visual outcomes at 12 months after surgery

	No visual deterioration	12-month visual deterioration (+)	Total (n=130)
N75–P100 amplitude reduction ≥50%			
No change	105	2	107
Decrease	20	3	23
Intraoperative recovery	8	2	10
Intraoperative nonrecovery	12	1	13
N75–P100 amplitude reduction ≥30%			
No change	91	1	92
Decrease	34	4	38
Intraoperative recovery	10	0	10
Intraoperative nonrecovery	24	4	28

patients, while VF deterioration was observed in 11 eyes of 8 patients. Twelve eyes of nine patients showed deterioration in either VA or VF. Among these, persistent VA deterioration at 12 months was found in four eyes of three patients, persistent VF deterioration was found in five eyes of four patients, and persistent deterioration was found in either modality in five eyes of four patients. Postoperative visual deterioration occurred in 6 (8.3%) of 72 eyes with meningioma and in 4 (9.3%) of 43 eyes with craniopharyngioma. Long-term visual deterioration was observed in three eyes (4.2%) with meningioma and in two eyes (4.7%) with craniopharyngioma. The detailed clinical characteristics and intraoperative VEP changes in these cases are presented in Supplementary Table 1 (in the online-only Data Supplement).

DISCUSSION

In this study we found that intraoperative VEP monitoring during EES for nonpituitary suprasellar tumors showed a low sensitivity when using the conventional alarm threshold of a 50% decrease in the N75−P100 amplitude. However, changing this threshold to 30% improved the sensitivity without significantly compromising the specificity. This advantage was particularly effective for predicting long-term visual deterioration. Excluding cases in which the intraoperative N75−P100 amplitude recovered, the sensitivity and specificity were 80.0% and 80.8%, respectively, for predicting long-term visual outcomes after surgery. Moreover, NPV was particularly high at 99%, indicating that when the VEP P100 amplitude decreased by <30% relative to the baseline value, VA and VF could be safely predicted 12 months postoperatively. However, PPV was very low at 14.3%, highlighting the importance of considering the possibility of false positives.

The alarm criteria for intraoperative VEP monitoring typically employ the threshold of a 50% reduction in the N75−P100 amplitude relative to the baseline, while some studies have applied a 25% reduction as the threshold.[1,15] The present study is the first to analyze ROC curves and compare using thresholds of 50% and 30% reductions in the N75−P100 amplitude in nonpituitary adenoma suprasellar tumors, which gave the study particular strength in distinguishing and analyzing short-term and long-term visual deteriorations.

In ROC curve analyses, a ≥40% reduction in VEP amplitude was found to be a more-appropriate criterion for predicting short-term visual outcomes, whereas a ≥30% reduction was more suitable for predicting long-term visual outcomes. One of the five patients who exhibited persistent long-term visual deterioration showed no intraoperative VEP changes, whereas another demonstrated only a 40% reduction, and neither of these cases would have been detected using a 50% reduction as the alarm threshold. Notably, while two of the remaining three patients exhibited an amplitude decrease of >50%, their intraoperative recovery was restricted to within 50%−70% of the baseline. These findings suggest that insufficient recovery of the VEP amplitude following intraoperative reduction is associated with long-term visual deterioration. However, further studies involving larger patient cohorts are required to validate this hypothesis.

Suprasellar tumors can be categorized by cell type, and one of the key differences between pituitary adenoma and other tumors is the presence of direct compression of the optic nerve: pituitary adenoma with suprasellar extension are typically encased by the arachnoid membrane, preventing direct contact with the optic nerve,[16] whereas other tumors such as craniopharyngioma and meningioma directly compress the optic nerve. Moreover, it is known that the prevalence rate of postoperative visual deterioration is higher for craniopharyngioma and meningioma surgery (5%−8%),[11] which is consistent with our findings. Therefore, the impact on the optic nerve during surgery may vary with the tumor type, and changes in VEP should be interpreted separately based on the tumor type.

In this study, 40 (23.1%) of the 173 eyes (i.e., excluding the single prosthetic eye) did not produce recordable baseline VEP waveforms despite the adequacy of the stimulation being confirmed by ERG. Most of these eyes had severe preoperative VF defects, with VFI and MD values that were significantly lower than those of eyes with a VEP baseline waveform. The monitoring of optic nerve function during surgery is currently inadequate for such patients, emphasizing the need for further research in this area to develop methods that can generate meaningful waveforms.

Short-term visual deterioration occurred simultaneously in both eyes of three patients due to bilateral optic nerve injury, and long-term deterioration was observed in one of these patients (Supplementary Fig. 3 in the online-only Data Supplement). The outcomes in such cases were assessed separately for each optic nerve because intraoperative VEP monitoring was performed independently on both sides. This approach made it possible to evaluate whether intraoperative VEP signals and amplitude reductions reflect damage to each optic nerve and thus can be used to predict the prognosis. However, in cases involving a single lesion such as optic chiasmal injury, the damage may have been counted twice (once for each optic nerve), potentially leading to an overestimation of the prevalence of optic nerve injury.

This study was subject to several limitations. First, it had a retrospective design and was performed at a single center. Second, it did not analyze improvements in postoperative visual outcomes. This limitation arose because the long-term

follow-up was conducted only in patients with VA or VA deterioration. Third, 12-month visual deterioration was assessed only in patients who showed early postoperative abnormalities rather than in all patients. Fourth, the exclusion of 40 eyes that did not generate baseline VEP waveforms likely resulted in the omission of individuals with profoundly impaired VA or VF from the final analysis, potentially introducing selection bias. Fifth, because VEP amplitude reductions between 30% and 50% were not communicated to the surgeon intraoperatively, it cannot be ruled out that these missing interventions contributed to unfavorable outcomes. Sixth, the small number of long-term visual deterioration events means that the estimates of diagnostic performance should be interpreted with caution. Further prospective studies are needed to address these limitations.

In conclusion, we propose using a reduction of ≥30% in the N75−P100 amplitude from the baseline as a practical alarm criterion for intraoperative VEP monitoring during EES for nonpituitary suprasellar tumors. This criterion is particularly helpful for predicting long-term visual outcomes; however, the possibility of false-positive results should be considered, and further studies are needed to validate its impact on visual outcomes.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2025.0207.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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