Predictive Factors for Vision Recovery after Optic Nerve Decompression for Chronic Compressive Neuropathy: Systematic Review and Meta-Analysis

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Abstract

Objectives Surgical optic nerve decompression for chronic compressive neuropathy results in variable success of vision improvement. We sought to determine the effects of various factors using meta-analysis of available literature.

Design Systematic review of MEDLINE databases for the period 1990 to 2010.

Setting Academic research center.

Participants Studies reporting patients with vision loss from chronic compressive neuropathy undergoing surgery.

Main outcome measures Vision outcome reported by each study. Odds ratios (ORs) and 95% confidence intervals (CIs) for predictor variables were calculated. Overall odds ratios were then calculated for each factor, adjusting for inter study heterogeneity.

Results Seventy-six studies were identified. Factors with a significant odds of improvement were: less severe vision loss (OR 2.31 [95% CI = 1.76 to 3.04]), no disc atrophy (OR 2.60 [95% CI = 1.17 to 5.81]), smaller size (OR 1.82 [95% CI = 1.22 to 2.73]), primary tumor resection (not recurrent) (OR 3.08 [95% CI = 1.84 to 5.14]), no cavernous sinus extension (OR 1.88 [95% CI = 1.03 to 3.43]), soft consistency (OR 4.91 [95% CI = 2.27 to 10.63]), presence of arachnoid plane (OR 5.60 [95% CI = 2.08 to 15.07]), and more extensive resection (OR 0.61 [95% CI = 0.4 to 0.93]).

Conclusions Ophthalmologic factors and factors directly related to the lesion are most important in determining vision outcome. The decision to perform optic nerve decompression for vision loss should be made based on careful examination of the patient and realistic discussion regarding the probability of improvement.

Keywords

- ▶ optic nerve
- ▶ optic nerve decompression
- ▶ skull base meningioma
- ▶ skull base surgery
- ▶ vision loss

Introduction

Vision loss related to skull base pathology can be a disabling symptom for patients. Surgical decompression is usually the preferred method of treatment, given that the tumor adjacent to

the optic nerve cannot be irradiated without putting the nerve at risk (especially if nonfractionated). Significant disagreement exists in the surgical literature regarding rates of improvement in vision and factors that may predict outcome, likely due to small sample sizes and variations between institutions.

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Surgical series of optic nerve decompression have been described since the very earliest days of neurosurgery.¹ More recent advances over the past several decades in terms of anatomic imaging and surgical technique have dramatically increased the surgeon's ability to plan surgical approaches. Magnetic resonance imaging (MRI) and multidetector high-resolution computed tomography (CT) in particular have allowed for resolution of fine details around the anterior skull base, sella, and optic apparatus. In addition, surgical advances have allowed the ability to tailor an approach based on the lesion characteristics using image-guided or endoscopic techniques—likely contributing to increased safety of these sometimes-complex operations. The most commonly encountered pathologies in this region causing optic nerve compression include pituitary tumors,^{2,3} meningiomas,^{4,5} and craniopharyngiomas.^{6–8} Other less common pathologies that can cause vision loss include aneurysms,⁹ Rathke's cleft cyst,¹⁰ sinus mucocele,¹¹ fibrous dysplasia,¹² and rare skull base tumors. Other acute compressive pathologies such as trauma and pituitary apoplexy likely have different recovery characteristics than chronic compression¹³ and so were omitted from this analysis. The surgical literature is inconsistent with regard both to which factors should be considered as well as the effect of them when counseling patients regarding likelihood of vision recovery.^{5,13–15} This is important information, especially for patients who may be at higher risk from surgical intervention. For benign lesions with a low chance of vision recovery, the risks of surgery may not be acceptable to many patients. Patients with a high chance of improvement could also be prioritized for surgical decompression if these factors were better understood.

We performed a systematic review and meta-analysis to better assess these discrepancies in likelihood of improvement.^{16–18} Using this technique we sought to better determine factors which overall affect vision outcome after optic nerve decompression for vision loss from chronic compressive neuropathy.

Methods

Data Collection

A standardized approach to meta-analysis was used according to PRISMA guidelines.¹⁶ There is no online review protocol or registration for the current study. A MEDLINE search was performed for the period 1990 to 2010 for articles reporting preoperative and postoperative vision data in the following categories: tumor (meningioma, craniopharyngioma, pituitary, "skull base tumor"), aneurysm, mucocele, and fibrous dysplasia. See ►**Table 1** for complete search strategy. This search was performed by the first author with the assistance of a professional medical research librarian. These years (1990 to 2010) were used to include series that were reported in the era of MRI availability. Abstracts were screened for the following inclusion and exclusion criteria: chronic compression, surgical intervention, linked preoperative and postoperative data, and English language. Excluded trials were other compressive neuropathies (trauma, endocrine, acute compression), other types of decompression (i.e., optic nerve sheath fenestration for pseudotumor

cerebri), radiation therapy only, case reports, no surgical intervention, cadaver or anatomic studies, or previously reported data (to the extent that this could be identified). Abstracts meeting these criteria were then screened with full text in all cases by the reviewer. The last full search was completed August 3, 2010. References and similar citations (as listed on PubMed) were further reviewed for potential additional citations. Authors were contacted for data clarification either for determining entry or for data abstraction. No abstracts with unpublished studies were included.

Study Classification

General descriptive characteristics, including overall rate of improvement, number of subjects, and factors linked to outcome, were recorded. Only factors identified in > 1 study as potential predictors were used. For determining improvement, only patients with a preoperative deficit were used from the data. If this could not be determined, the article was excluded. To classify whether or not there was improvement, the specific criteria used by the study was used. If there was no specific criteria of improvement, but preoperative and postoperative vision data were included, any change in Snellen lines was considered improvement. If both visual acuity (VA) and visual field (VF) were reported, VA was used for analysis of improvement due to the variable methods in reporting VF data.

Articles were then categorized by data type. Some articles contained data assessing a specific risk factor on outcome divided into dichotomous (or more) categories (such as age > 60 or < 60 years). These articles were required to have enough information on true positives, true negatives, false-positives, and false-negatives to be able to calculate the odds ratio for improvement. Where there was more than one category, the categories and patient outcomes were combined into dichotomous data. The categories were ordered to be consistent between studies, even though the specific threshold varied between studies (e.g., younger category versus older category). Whether each study was evaluating outcome by eye or by patient was recorded.

The second category of articles contained enough patient level data to determine factors and outcome in each patient. These articles, therefore, had continuous data for predictor variables (such as age). Outcome for each patient or eye was then recorded. The third category of article was those with some statistical analysis of risk factors for vision improvement, but without adequate data to fit into one of the above categories. These articles were then reviewed with the statistician (O.M.) to determine if there was any method to use the data for meta-analysis in one of the above categories.

No specific procedures were made to assess bias in individual studies, however the effects of interstudy variability was accounted for in the statistical analysis. Simplifications were made in terms of reporting thresholds for dichotomous data, but the original cutoff points were retained for reference. If the study reported improvement in "visual function," this was used as improvement. If improvement was not explicitly stated, any improvement in reported VA was taken to be improvement. Though all "vision improvement"

Table 1 Search strategies

General search	((“surgical procedures, operative”[MeSH Terms]) AND ((“optic nerve diseases”[MeSH Terms]) OR (“optic chiasm”[MeSH Terms]) OR (“optic nerve”[MeSH Terms]))) AND (“vision” OR “visual”) NOT (“glaucoma” OR “central retinal vein occlusion” OR “pseudotumor cerebri” OR “optic nerve glioma”))
Craniopharyngioma search	(“craniopharyngioma”[MeSH Terms] OR “craniopharyngioma”[All Fields]) AND ((“vision, ocular”[MeSH Terms] OR (“vision”[All Fields] AND “ocular”[All Fields]) OR “ocular vision”[All Fields] OR “vision”[All Fields]) OR “visual”[All Fields])
Meningioma search	(“meningioma”[MeSH Terms] OR “meningioma”[All Fields]) AND ((“vision, ocular”[MeSH Terms] OR (“vision”[All Fields] AND “ocular”[All Fields]) OR “ocular vision”[All Fields] OR “vision”[All Fields]) OR “visual”[All Fields]) AND (“humans”[MeSH Terms] AND English[lang] AND (“1990”[PDAT]: “2010”[PDAT]))
Pituitary search	((“pituitary gland”[MeSH Terms] OR (“pituitary”[All Fields] AND “gland”[All Fields]) OR “pituitary gland”[All Fields] OR “pituitary”[All Fields]) AND ((“vision, ocular”[MeSH Terms] OR (“vision”[All Fields] AND “ocular”[All Fields]) OR “ocular vision”[All Fields] OR “vision”[All Fields]) OR “visual”[All Fields]) AND ((“surgery”[Subheading] OR “surgery”[All Fields] OR “surgical procedures, operative”[MeSH Terms] OR (“surgical”[All Fields] AND “procedures”[All Fields] AND “operative”[All Fields]) OR “operative surgical procedures”[All Fields] OR “surgery”[All Fields] OR “general surgery”[MeSH Terms] OR (“general”[All Fields] AND “surgery”[All Fields]) OR “general surgery”[All Fields]) OR (“surgical procedures, operative”[MeSH Terms] OR (“surgical”[All Fields] AND “procedures”[All Fields] AND “operative”[All Fields]) OR “operative surgical procedures”[All Fields] OR “surgical”[All Fields])) NOT ((“radiation”[MeSH Terms] OR “radiation”[All Fields]) OR (“radiosurgery”[MeSH Terms] OR “radiosurgery”[All Fields]))
Aneurysm search	(“aneurysm”[MeSH Terms] OR “aneurysm”[All Fields]) AND ((“vision, ocular”[MeSH Terms] OR (“vision”[All Fields] AND “ocular”[All Fields]) OR “ocular vision”[All Fields] OR “vision”[All Fields]) OR “visual”[All Fields])
Mucocele search	(“paranasal sinuses”[MeSH Terms] OR (“paranasal”[All Fields] AND “sinuses”[All Fields]) OR “paranasal sinuses”[All Fields] OR “sinus”[All Fields]) AND (“mucocele”[All Fields] OR “mucocele”[MeSH Terms] OR “mucocele”[All Fields])) AND ((“vision, ocular”[MeSH Terms] OR (“vision”[All Fields] AND “ocular”[All Fields]) OR “ocular vision”[All Fields] OR “vision”[All Fields]) OR “visual”[All Fields])
Skull base tumor search	(“skull base neoplasms”[MeSH Terms] OR (“skull”[All Fields] AND “base”[All Fields] AND “neoplasms”[All Fields]) OR “skull base neoplasms”[All Fields] OR (“skull”[All Fields] AND “base”[All Fields] AND “tumor”[All Fields]) OR “skull base tumor”[All Fields]) AND ((“vision, ocular”[MeSH Terms] OR (“vision”[All Fields] AND “ocular”[All Fields]) OR “ocular vision”[All Fields] OR “vision”[All Fields]) OR “visual”[All Fields])
Fibrous dysplasia search	(“fibrous”[All Fields] AND “dysplasia”[All Fields]) AND ((“vision, ocular”[MeSH Terms] OR (“vision”[All Fields] AND “ocular”[All Fields]) OR “ocular vision”[All Fields] OR “vision”[All Fields]) OR “visual”[All Fields])

Abbreviation: MeSH, Medical Subject Headings; PDAT, Date - Publication.

techniques were combined for analysis, the specific method was recorded for reporting in the forest plots. Specific vision levels were converted to decimal notation where possible for statistical analysis (20/20 Snellen notation = 1.0, 20/400 = 0.05, etc.) By convention, counting fingers is considered 0.014 and light perception or hand motion is 0.0052.

Statistical Analysis

For factors with dichotomous data, and for studies that dichotomized continuous variables in reporting, odds ratios (ORs) and 95% confidence intervals (CIs) for variables from each study were calculated using exact methods as implemented in SAS v9.2 (proc logistic). Overall ORs were then calculated for each factor, adjusting for interstudy heterogeneity using the Breslow-Day test. The hierarchical summary receiver operating characteristic (ROC) curve was then plotted with mean estimates of sensitivity and specificity for the cutoff of the criteria used by each individual study.

For factors with continuous data, logistic regression or linear regression curves were calculated with an overall estimate of difference from 0 slope. Linear as well as binomial and higher-order nonlinear curves were tested to determine the most parsimonious model. ORs were then calculated for a given unit change. For studies with statistical data only or studies that otherwise did not have adequate data to incorporate into further statistical analysis, only descriptive meta-analysis was done. Though it is understood that publication bias may skew data toward higher reported improvement rates, it was considered that the factors affecting such overall bias should not be affected.

Results

The literature search revealed 278 unique citations. **Fig. 1** shows results and screening process for each search. Seventy-six studies reported some analysis of factors (six had multiple types of data analysis). In all 76 studies, 2950 patients were

Fig. 1 Flowchart for literature search. Results for each search strategy are outlined above. Abstracts were reviewed for inclusion and exclusion criteria as listed in the article.

reported. The overall improvement rate for the studies that reported improvement by patient (not eye) ($n = 2469$) was 60%. Factors identified as potential predictive factors included demographic factors (age, gender, and Karnofsky performance score [KPS]), ophthalmologic factors (duration of vision loss, severity of vision loss, pattern electroretinogram [PERG], disc atrophy, and retinal nerve fiber layer thickness [RNFLT] measured by ocular coherence tomography [OCT]), lesion-related factors (size of mass, primary versus recurrent, cavernous sinus extension, optic canal involvement, and pathology), intraoperative factors (consistency and presence of an arachnoid plane), and some potentially modifiable factors (extent of resection, optic canal decompression, and surgical approach.)

All dichotomous predictor study outcomes (forest plots) and sensitivity analysis (ROC curves) are reported in ► **Figs. 2–15**. The differences in vision assessment, length of follow-up, and differences in cutoff points are reported in the forest plots. The continuous data regression curves are summarized in ► **Fig. 16**. The effect of preoperative vision on postoperative vision is reported in ► **Fig. 17**. Data are summarized here by factor.

Patient Demographic Factors

Age

There were nine dichotomous studies^{5,19–26} comprising 413 patients. The overall odds of improvement were 1.29 (95%

CI = 0.86 to 1.94). The cutoff point for young versus old varied from 16²⁶ to 60^{20,22,23,25} years, with most ($n = 4$) being 60. Only one study assessed improvement in eye,¹⁹ and the remainder assessed patients. The ROC analysis revealed a mean sensitivity of 64% and specificity of 49% for young versus old as a predictor of vision improvement (**► Fig. 2**).

There were 21 studies^{12,22,27–47} for which continuous age data was available, comprising analysis of 394 patients. There was a nonsignificant overall trend toward slightly poorer improvement with increasing age (**Fig. 16**). Binomial or quadratic functions did not determine a better fit. The OR for improvement with each 10 years of increased age was 0.92 (95% CI = 0.76 to 1.11). All of these studies assessed patient outcome (rather than eyes).

Eight studies^{4,13,48-53} reported only statistical data for the effect of age on visual outcome. Six of these found no association of age with outcome.^{4,13,49,51-53} One study found a negative correlation (spearman CC $r = 0.34$, $p = 0.000185$),⁴⁸ though interestingly, the long-term follow-up study of many of these patients⁴ did not report a significant outcome. Another study found that the odds of complete recovery were 0.75 ($p = 0.019$) for each one year of increased age.⁵⁰

Overall, all these methods of assessment of the literature support the conclusion that age alone is a poor predictor of vision recovery.

Fig. 2 Effect of younger age on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VIS, visual impairment score.

Gender

There were 25 studies^{5,12,19–23,25,27–31,33–40,43–45,47} reporting gender data with vision outcome, comprising 658 patients. Overall odds of improvement for male versus female were nonsignificant at 1.07 (95% CI = 0.73 to 1.57). Five studies reported outcome by eye^{12,19,37–39} and the remainder by patient. The mean sensitivity was 30% and specificity was 70% for gender in predicting outcome (► **Fig. 3**). One additional study reporting only statistical data reported no significant effect of gender.⁵⁴ Gender is unlikely to be a significant predictor of vision outcome.

Karnofsky Performance Score

Two studies^{32,46} reported preoperative KPS of 40 patients. These were only continuous data but grouped at the high end of the scale, ranging from 60 to 90. The relationship was nonsignificant (► **Fig. 16**). Due to the very small numbers reported, it is impossible to determine the effect of functional independence measured by KPS on vision outcome.

Ophthalmologic Factors

Duration of Vision Loss

There were 11 studies^{5,19–21,23–25,55–58} with dichotomous data, comprising 485 patients. The overall odds of improvement for shorter versus longer duration were significant at 3.65 (95% CI = 2.40 to 5.54). Almost all studies used 12 months as a cutoff, with two studies using shorter intervals of 6¹⁹ or 7²¹ months. All studies reported recovery of vision in patients (not eyes). ROC analysis revealed a mean

sensitivity of 67% and specificity of 62% for shorter versus longer duration of symptoms in predicting recovery (► **Fig. 4**).

There were eight studies^{4,35,36,38–40,43,47} with continuous data for duration of preoperative vision loss, comprising 150 patients. Two studies^{4,39} had outlier data with patients with > 84 months of symptoms (*n* = 3) and were excluded due to the low numbers at the very high end tending to skew the curve and make the upper end unreliable. Linear regression did not reveal a significant association with duration of preoperative vision symptoms (*p* = 0.75) (► **Fig. 16**). The odds of improvement for every 6 months of increased symptoms were nonsignificant at 0.97 (95% CI = 0.79 to 1.19). All of these studies reported vision outcome by patient, not eye. We tested the very short duration data available to determine if there was a better fitting, significant curve at the very early stages of vision loss, but still did not find a significant fit (data not shown).

There were five studies that reported statistical analysis of duration of symptoms. Three found no significant relationship.^{13,30,49} One found that the odds of complete recovery decreased for every month of symptoms (OR 0.085, *p* = 0.05).⁵⁰ Another study found a negative correlation (*r* = −.34, *p* = 0.0006).⁴⁸

There are conflicting data on the effect of the duration of vision loss on vision outcome. Dichotomous data seem to suggest a significant cutoff at 12 months, but with poor sensitivity and specificity, making this likely a poor clinical decision-making tool. The linear regression data did not show a significant effect. The current study did not address the patient group with acute deterioration, such as traumatic

Fig. 3 Effect of male gender on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VF, visual field; VIS, visual impairment score.

neuropathy or pituitary apoplexy, so no comment can be made.

Severity of Vision Loss

There were 18 studies^{4,5,20,21,23,24,51,55-57,59-66} with dichotomous data, comprising 1042 patients. The overall odds of improvement for better versus worse were significant at 2.31 (95% CI = 1.76 to 3.04). Studies varied significantly on the specific cutoff for vision, with many even being qualitative (partial versus severe deficit). Some used VA decimal/Snellen notation, some used visual impairment score (VIS), some used VF. There was a mixture of reporting of eyes and patients in terms of outcomes, partially dependent on the type of measure, since some are for a specific eye and some factor in both eyes. ROC analysis revealed a mean sensitivity of 59% and specificity of 63% for better versus worse vision in predicting recovery (►Fig. 5).

There were 14 studies^{4,22,30,35-39,42,43,45,47,48,67,68} with 323 patients who had both preoperative vision level and postoperative vision level reported, allowing for linear regression to determine the degree of recovery. In patients

where both eyes were considered, inpatient similarity was controlled for. The linear regression curve is shown in ►Fig. 17. Multiple curve types were fit to the data, and the general additive model fitted a B-spline curve as the most parsimonious model. This demonstrated a strong likelihood of improvement in all patients, but with a greater degree of improvement for patients in the very low vision range, which levels off toward the middle of the range, then possibly increases again at the very high end, though the CI expands here significantly.

There were four studies that reported statistical data only regarding severity of vision loss. Two reported no significant association^{50,69} and two reported significant association. One of these showed $r = 0.656$ ($p < 0.001$),¹³ and the other described a “significant correlation”⁴⁹ with no further description of the analysis.

It seems that there is likely to be an effect of preoperative vision loss on outcome, though with a complex relationship. Broad classification of better vision versus worse vision (the dichotomous data) suggests that there is a significant, statistically sound effect. The fact that the thresholds varied

Fig. 4 Effect of shorter duration of vision symptoms on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VIS, visual impairment score.

significantly makes this data more difficult to interpret, except in saying that there is an effect of the degree of vision loss making the chances of recovery worse with worse loss. On the other hand, the continuous data suggest that there is a more rapid rise along the very low preop vision level, which then flattens out toward the middle of the spectrum in terms of the *degree* of vision improvement (as opposed to the *probability* of vision improvement we report for the other parameters and in the dichotomous data.)

Pattern Electoretinogram

Two studies assessed the predictive value of PERG on visual outcome, but neither qualified for statistical analysis due to the discrepant reporting systems used. Parmar⁷⁰ reported data from 72 eyes of 36 patients and found a significant association of postoperative improvement with the PERG N95:P50 ratio, with 65% improvement with a normal ratio compared with 27% improvement with abnormal. There was no effect on visual acuity. Ruther⁶⁸ showed that in 19 patients, all PERG variables (P50, N95, and steady-state amplitude) had predictive value for vision outcome. This may represent a useful adjunct to preoperative evaluation, but no comment can be made from this analysis regarding the overall predictive value.

Disc Atrophy/Pallor

There were six studies^{42,43,47,51,67,71} assessing optic disc atrophy or pallor preoperatively, comprising 152 patients.

The overall odds of improvement with no pallor or atrophy were significant at 2.60 (95% CI = 1.17 to 5.81). Three studies assessed specific eye,^{47,51,67} whereas the others assessed patients.^{42,43,71} Atrophy and pallor were considered together in this analysis as “abnormal.” ROC analysis revealed a sensitivity of 57% and specificity of 60% for presence of disc atrophy or pallor (→ Fig. 6).

One study²² reported “improvement or normalization was observed with normal or some pallor of the optic discs, some improvement with more severe pallor, and no improvement in optic disc atrophy,” though no specific analysis was reported.

Retinal Nerve Fiber Layer Thickness

Two studies^{50,72} assessed the value of retinal nerve fiber layer thickness (RNFLT) as measured by ocular coherence tomography (OCT) but did not qualify for statistical analysis due to differences in outcome reporting. Jacob⁵⁰ reported that the odds of complete recovery were 1.29 for each increase in one micron of RNFLT in 19 patients with pituitary tumors. Darnesh-Meyer⁷² found a cutoff of around 85 microns where patients did not improve below and tended to improve above in patients with a variety of perichiasmal tumors. Furthermore, they demonstrated odds of improvement of 11.5 (95% CI = 1.2 to 108.8) for thick versus thin RNFL. These two studies suggest that there may be a strong predictive value for vision recovery using RNFLT, but since these outcome measures are not standardized or compared with other

Fig. 5 Effect of severity of vision loss on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VF, visual field; VIS, visual impairment score.

Fig. 6 Effect of optic nerve atrophy or pallor on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VF, visual field.

Fig. 7 Effect of smaller size on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VIS, visual impairment score.

predictive factors, it is difficult to determine the relative predictive value.

Lesion Factors

Size of Mass

There were 12 studies^{5,19–21,23,25,55,57,58,73–75} with dichotomous size data, reporting 467 patients. The overall odds of improvement for smaller versus larger mass was significant at 1.82 (95% CI = 1.22 to 2.73). The size of cutoff ranged from 2 cm²³ to 4 cm,^{74,75} with most (n = 7) being 3 cm. Most studies used only the single maximum dimension, but one used a volumetric analysis²⁰ and one evaluated “parasellar extension.”¹⁹ Only one study¹⁹ assessed outcome by eye, and the remainder were by patient. The ROC analysis revealed a mean sensitivity of 64% and sensitivity of 50% for small versus large size as a predictor of recovery (►Fig. 7).

There were 12 studies^{22,27,29,31,34,39–41,44,45,47} with continuous data for size, comprising 239 patients for analysis. There was a significant negative linear correlation of size with visual outcome (p = 0.002) (►Fig. 16). The odds of improvement for every 1 cm of increased size was 0.6 (95% CI = 0.43 to 0.82). Size was converted to maximum linear dimension for homogeneity, or mean diameter if the study reported volumetric data.^{41,45} All of these studies assessed outcome by patient.

There were five studies that reported only statistical data for improvement by size. Three studies did not find a statisti-

cal difference.^{24,30,69} One study⁴⁹ found that size remained related to outcome even after controlling for preoperative VA (p = 0.03), and another⁷⁶ found a significant association by linear regression (slope = − 0.21, p = 0.006).

Overall, it seems that there is indeed a statistical association of size with likelihood of improvement based on several types of reported data. This ranges from probability of improvement about 85% for 1-cm masses to about 30% for 8-cm masses. The wide confidence interval, however, is reflected in the poor sensitivity and specificity and relatively flat ROC, making it difficult to apply this discriminator to clinical practice.

Primary versus Recurrent

There were nine studies^{8,22,27,28,31,44,46,77,78} that assessed the effect of primary versus recurrent tumor in predicting vision outcome, comprising 343 patients. The overall odds of improvement with primary were significant at 3.08 (95% CI = 1.84 to 5.14). All studies assessed patient outcome. The ROC analysis revealed mean sensitivity of 72% and specificity of 58% in predicting outcome (►Fig. 8). Overall, the data available suggest a significant effect of primary versus recurrent resection with moderately good sensitivity (72%), suggesting that patients will have a better chance of improvement with a primary tumor, but the low specificity suggests that recurrent tumor does strongly predict poor outcome.

Fig. 8 Effect of primary versus recurrent surgery on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VF, visual field; VIS, visual impairment score.

Cavernous Sinus Extension

There were four studies^{44,46,56,79} assessing extension of tumor into the cavernous sinus, comprising 228 patients. The overall odds of improvement for no cavernous sinus extension versus cavernous sinus extension were significant at 1.88 (95% CI = 1.03 to 3.43). All studies assessed recovery of patients (not eyes). ROC analysis revealed a mean sensitivity of 57% and specificity of 62% for no cavernous sinus extension versus cavernous sinus extension in predicting recovery (► Fig. 9).

Optic Canal Involvement

There were six studies^{5,23,31,43,80,81} assessing optic canal involvement, comprising 128 patients. The overall odds of improvement with no optic canal extension were nonsignificant at 1.15 (95% CI = 0.46 to 2.88). All studies assessed patients only. ROC analysis revealed a sensitivity of 56% and specificity of 47% for presence of optic canal involvement (► Fig. 10). Both analyses support a lack of predictive value of optic canal involvement in predicting vision recovery.

Pathology

The effect of pathology type on vision outcome may be important; however, the available literature makes any attempt at analysis misleading since there are few studies that compare pathology types in a consistent way. There were six studies^{19,21,27,28,33,44} that reported the effect of pathology type on vision outcome; however, given the different types of tumor reporting, no attempt at statistical meta-analysis was

made. One additional study with statistical analysis only reported nonsignificant difference in odds of improvement between meningioma and nonmeningioma.¹³

Intraoperative Factors

Tumor Consistency

There were four studies^{5,19,23,25} that assessed tumor consistency, comprising 165 patients. Overall odds of improvement for soft tumor versus firm were 4.91 (95% CI = 2.27 to 10.63). One study assessed eyes,¹⁹ and the rest assessed patients. All were reported as soft versus firm. ROC analysis showed sensitivity of 70% and specificity of 65% for soft tumor (► Fig. 11). One additional study²² reported that there was no correlation of consistency with vision outcome, but no analysis was reported. The pooled data suggest a significant association of tumor consistency with vision improvement.

Arachnoid Plane

There were three studies^{20,21,23} reporting the presence of an arachnoid plane in 124 patients. Overall odds of improvement with intact arachnoid plane versus without were significant at 5.60 (95% CI = 2.08 to 15.07). All studies assessed patients. The presence of arachnoid plane was either specifically defined or "adhesion to optic nerve" was interpreted as lack of arachnoid plane. ROC analysis revealed a sensitivity of 90% and specificity of 41% (► Fig. 12). In addition, one study⁵³ reported no significant association without further data. Though very low numbers comparatively, these data suggest that the

Fig. 9 Effect of cavernous sinus extension on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VF, visual field; VIS, visual impairment score.

presence of an intact arachnoid plane is likely a strong predictor of vision recovery.

Potentially Modifiable Factors

Extent of Resection

There were 20 studies^{5,19–23,25,27–34,37,39,41,46,82} assessing extent of surgical resection, comprising 576 patients. The overall odds of subtotal versus total resection was significant

at 0.61 (95% CI = 0.4 to 0.93), indicating higher odds of improvement with total or near total resection. Three studies^{19,37,39} assessed eyes, and the remainder assessed patients. Some studies reported Simpson grade of resection, but almost never had complete data for each grade, sometimes combining grades. For that reason, all data were dichotomized, with subtotal being Simpson III or IV and total being Simpson I or II. ROC analysis revealed a sensitivity of 22% with specificity of 91%

Fig. 10 Effect of optic canal involvement on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VF, visual field; VIS, visual impairment score.

Fig. 11 Effect of tumor consistency on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VIS, visual impairment score.

63% for subtotal versus total resection (►Fig. 13). One additional study⁵³ reported no significant association with extent of resection.

Optic Canal Decompression

There were three studies^{23,31,57} that specifically assessed the effect of optic canal decompression or anterior clinoidectomy early in the procedure, comprising 79 patients. The

overall odds of improvement with decompression were nonsignificant at 0.85 (95% CI = 0.35 to 2.10). All studies assessed patients. One study²³ specifically compared early optic canal unroofing to late or no unroofing, whereas the other two assessed the effect of anterior clinoidectomy. ROC analysis revealed mean sensitivity of 49% and specificity of 53% for early decompression (►Fig. 14). One additional study⁴⁹ reported no significant effect with or without canal

Fig. 12 Effect of presence of arachnoid plane on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VIS, visual impairment score.

Fig. 13 Effect of extent of resection on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VF, visual field; VIS, visual impairment score.

decompression without further description. The available literature does not show a benefit to optic canal decompression for vision recovery.

Approach

There were nine studies^{19,32,44,45,51,83–85} that assessed the effect of transcranial versus transsphenoidal surgical approach on visual outcome, with a total of 594 patients. The overall odds of improvement for transcranial approach were significant at 0.36 (95% CI = 0.24 to 0.54). There was a mixture of studies assessing eyes or patients. The specific approach assessed varied. Two studies^{57,86} assessed anterolateral versus subfrontal approach. In this small group, the combined odds of improvement was not significant; the anterolateral versus subfrontal approach was 2.10 (95% CI = 0.84 to 5.27). The overall mean sensitivity of the transcranial approach was 51% and specificity was 35% (→Fig. 15). One additional study without enough data for meta-analysis reported no significant effect of transzygomatic versus transbasal approach in a variety of skull base pathologies.¹³

Discussion

Interpreting the literature with regard to prognosis for vision recovery has historically been difficult. Some factors that

seem intuitive do not show a correlation with improved vision in some studies and show a correlation in others. Possible explanations for this include varying size and quality of studies, heterogeneity of outcome measure (complete recovery versus any improvement), heterogeneity of measurement of predictive factors, and individual institutional variability (surgeon, volume of center, etc.) This disagreement makes counseling a patient with vision loss difficult, especially when considering a sometimes major intervention.

In the current study, we sought to reconcile these differences in several ways. First, the meta-analysis portion was based on patient level outcome data for patients with preoperative vision loss. This overcomes the variability of different statistical methods for analysis. By calculating the odds ratio for each study in the dichotomous data portion and comparing from study to study, we considered the amount of variability between studies when determining the confidence level of the overall OR. For continuous data, all data were pooled into calculating an overall slope of improvement. Combining the various methods used to determine improvement to determine overall statistically significant factors increases the probability that a true “signal” will be detected rather than noise from confounding sources.

In addition to statistical analysis from the published literature, one must consider biological plausibility in terms

Fig. 14 Effect of optic canal decompression on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VIS, visual impairment score.

of explaining the effect of various factors on vision improvement. Based on our meta-analysis, there are likely several factors that affect vision outcome. Basic demographic factors such as age and gender seem to be poor predictors overall. The lack of significant effect of age is somewhat surprising, as it would be plausible to expect poorer recovery in older patients; however, both dichotomous data and continuous data seem to support the lack of overall effect. There may, of

course, be effects of age within certain groups (e.g., different pathology) but no comment can be made regarding these effects here. Advancing age has been linked to increased morbidity and mortality,⁸⁷ so careful consideration of surgical intervention should be made, especially if the surgery is to improve deteriorating vision. The only measure of overall performance status available was the KPS, and this very limited data suggested no effect on vision outcome.

Fig. 15 Effect of surgical approach on vision outcome. CL, (95%) confidence limit; FPR, false positive rate; N, number of patients in study; OR, odds ratio; Pr, positive rate; ROC, receiver operating characteristic; TPR, true positive rate; VA, visual acuity; VF, visual field.

Fig. 16 Linear regression curves for continuously reported variables.

Fig. 17 Spline fitted curve of effect of preoperative vision on postoperative vision (dotted line). There is steeper improvement in vision at the very low initial vision level. Solid line represents theoretical no improvement, dashed lines represent 95% confidence limits.

Certain ophthalmologic features are likely to be predictive of vision outcome, emphasizing the importance of detailed ophthalmologic exam before considering surgery for vision loss. The effect of duration of vision loss is not clear, and this study excluded patients with rapid deterioration such as from apoplexy or traumatic optic neuropathy. A cutoff of 1 year of vision loss seems to portend worse outcome, but the regression analysis did not bear out these results. The severity of vision loss has a complex relationship with outcome. In general, it seems that better preoperative vision is more likely to have any improvement; however, the degree of improve-

ment seems to be higher at the low end of the vision scale. This suggests that even in patients with very poor preoperative vision, some significant improvement is likely. One study even reported improvement of some vision in approximately 30% of patients with complete blindness preoperatively.¹⁹ There was significantly more improvement noted (OR 2.60) in patients who did not have optic disc atrophy or pallor, suggesting the importance of incorporating a detailed fundoscopic examination. Two technologies to further assess functional status of the optic nerve were PERG and RNFLT measured by OCT. Though none of these studies could be included in the formal meta-analysis due to the method the data was reported, they offer some interesting possibilities for assessment. PERG provides functional data of the status of the retinal cells using evoked potentials. There is variability in recording and reporting these data however, making it primarily useful as a research tool currently. RNFLT as measured by OCT likely reflects the preservation of the ganglion cell layer in chronic compressive neuropathy. It is essentially the ophthalmologic equivalent of muscle atrophy after denervation. The preliminary data suggest a very strong predictive value using the mean thickness in patients with vision loss from compression. In addition, it offers the advantage that OCT is widely available, standardized, and used for many other conditions and could be easily adapted to widespread use in preoperative evaluation. More studies are needed to confirm the predictive effects and compare the relative predictive value to the other more widely used parameters.

Factors regarding the lesion itself also play a role in determining the likelihood of vision improvement. Size

seems to be a consistent effect, with very large lesions less likely to improve than smaller lesions. This makes some biologic sense, especially when considering that larger lesions probably have a much larger degree of anatomical distortion of the optic apparatus, probably at least partially accounting for the effect. In addition, a very large lesion may require more resection of the blood supply to the nerve, and these vascular factors are difficult to quantify. Especially for meningiomas, where the vascular supply to the optic apparatus and nerve sheath may be significantly disrupted due to resection, the fact that larger size is a significant factor is not surprising. The shallow slope of the effect of size, however, does not suggest a specific cutoff for improvement, merely that it should likely be considered as a factor when counseling a patient pre-operatively.

Primary tumors were more likely to recover than recurrent tumors, possibly due to scarring, loss of normal anatomic landmarks, or loss of arachnoid plane, which is also related to vision improvement. This may also be related to vascular effects as described above. Cavernous sinus extension clearly makes complete tumor resection less likely without deficit, but does not seem to affect vision improvement. Interestingly, pooled data do not support the effect of optic canal invasion in vision improvement. We did not assess the effect on whether canal involvement made vision loss more likely, but it seems that there are insufficient data to support decision making with regard to likelihood of improvement based on OC invasion.

Features discovered intraoperatively may have some significant effects. The lack of arachnoid plane portending less chance of improvement is not surprising. This is probably the most direct feature related to the vascular supply to the nerve. Loss of this vascular supply has been hypothesized to be an important feature in recovery apart from direct manipulation of the nerve. Further studies will have to determine the overall benefit of less aggressive surgery intended to preserve this vascular supply versus the loss of total resection in terms of survival and functional status. The effect of softness of a tumor being more likely to result in improvement is also not surprising, since softer tumors likely require less nerve manipulation, or less cauterization or ultrasonic aspiration near the nerve.

Features of the operation itself have also been reported to affect vision outcome. It seems that more aggressive surgical resection is less likely to result in vision improvement, probably as described above, due to loss of vascular supply to the nerve. Though early optic canal decompression seems an intuitive practice to increase the mobility of the nerve and lessen tension around the falciform ligament, the available data do not suggest a statistically significant effect. Approach is a difficult factor to analyze independently, since it is likely related to pathology, size, and other factors. Still, it seemed that a trans-sphenoidal approach was more likely to improve outcome compared with a transcranial approach. Though the most likely reason for this effect is the type of pathology amenable to these approaches, one may consider that perhaps the trans-sphenoidal approach is a less direct approach

to the nerve, potentially limiting surgical manipulation or devascularization.

The limitations of the current study reflect the limitations of the available literature in making decisions regarding interventions for these patients. There is no doubt an effect of publication bias, and high-volume academic centers are more likely to report their results than smaller-volume centers, especially for some of the more rare pathology described here. These data may or may not, therefore, be an accurate reflection of the likelihood of vision improvement in less experienced centers. There was significant variability in how "vision improvement" was reported from study to study. Some studies reported specific, rigorous criteria (such as improvement of two or more Snelling lines, improved visual fields or VIS), whereas some reported only qualitative data (such as the physician or patient's impression of vision status). Some studies did not specifically report improvement or not, so conclusions had to be made based on reported data (such as preoperative and postoperative VA or VF.) Though these differences may have introduced some error into the analysis, it is unlikely that there would be effect modification from this bias.

Because there was significant variability in which factors a specific study reported, we did not feel that there was a statistically sound way to perform a multivariate analysis of the data. Therefore, it is impossible to determine if the effect noted in some of the variables is due to confounding with another variable. There is also a concern that in taking such a large group of heterogeneous patients together, effects that are significant within a specific group may not become significant across all groups. Taking smaller groups, however, runs more risk of not being able to detect an effect due to the much smaller numbers available.

Conclusions

Most patients (60%) will have at least some improvement in vision after optic nerve decompression for chronic compressive neuropathy. Ophthalmologic factors and factors directly related to the tumor or mass are likely most important in determining vision outcome. The decision to perform surgery for optic nerve decompression to improve vision should be made based on careful examination of the patient and realistic discussion regarding the probability of improvement. Future studies are needed to better determine which factors are independently associated with outcome as well as the reliability of emerging diagnostic techniques.

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