

Factors Affecting Visual Field Outcome Post-Surgery in Sellar Region Tumors: Retrospective Study

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Prabu Rau SRIRAM^{1,2,3}, Puliventhan SELLAMUTHU¹, Abdul Rahman IZANI GHANI²

¹ Department of Neurosurgery, Queen Elizabeth Hospital, 88200 Kota Kinabalu, Sabah, Malaysia

² Department of Neurosciences, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

³ Center for Neuroscience Services and Research, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

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Abstract

Background: Despite the broad category of differentials for sellar region, most of them present with similar clinical signs and symptoms. Headache and visual disturbance are among the frequently seen as presenting symptom. Visual field (VF) assessment is one of the crucial component of neuroophthalmologic assessment and mean deviation (MD) value from automated perimetry allows quantification of the visual field defect. We formulated a study to look into the factors that affect the visual field outcome after surgery.

Methods: All patients with sellar region tumor who has underwent surgery in Queen Elizabeth Hospital from July 2010 to July 2016 were retrospectively analysed through hospital notes. VF assessment via Humphrey visual assessment for these patient pre and post-surgery were reviewed for MD value.

Results: Eighty four patients were recruited and out of them, 151 eyes were taken into analysis after excluding eyes with missing data. Mean age of patients were 45.4 years with 70.2% of them were male. Visual disturbance is the commonest presenting symptom with mean duration of symptom prior to surgery is 9.7 months. Majority of them were pituitary adenomas (75%) followed by sellar meningioma (19%), craniopharyngioma (4.8%), and rathke cleft cyst (1.2%). 70.9% of patients showed improvement in VF based on MD outcome. Mean MD for pre surgery and post-surgery were -14.0 dB and -12.4 dB, respectively. Univariate analysis reveals younger age, female sex, shorter duration of symptom, pituitary adenoma, transsphenoidal approach, and transcranial approach favours improvement in VF. Multivariate analysis shows only shorter symptom duration, transphenoidal approach, and transcranial approach are significant for favourable VF outcome when other factors adjusted.

Conclusion: Symptom duration and surgical approach were independent factors that affects the visual field after surgery in patients with sellar region tumors.

Keywords: visual field, perimetry, sellar tumor, pituitary adenoma

Introduction

Sellar region, being a tiny space in the centre of cranial base in human, harbours a complex anatomy (1). It contains various vital

nervous, vascular, and endocrine structures which include optic apparatus, anterior circulation arteries, third part of internal carotid artery, and cavernous sinus and its containing cranial nerves. In addition, pituitary gland,

pituitary stalk, and hypothalamus which also lies in this region could lead to significant neuro endocrinological morbidity when affected (2, 3). All these structures lie in close proximity to each other in the sellar region (3). Anatomical terms like sellar, suprasellar, and parasellar are used very frequently without clear definition of boundaries for each of the term. The anatomical boundaries of sellar and parasellar region includes basisphenoid sinus inferiorly, cavernous sinus laterally on both sides, and suprasellar extension into ventricle walls. Areas of the sellar and parasellar region have anatomical boundaries that extend from the basisphenoid sinus below, laterally to the cavernous sinus, with suprasellar extension to ventricular walls (4). Cavernous sinus is the most clinically relevant para sellar structure. However, all structures surrounding sella turcica is included in the parasellar region (5).

The pathology that can present in the sellar region is very diverse which could be neoplastic, congenital, vascular, inflammatory, and infective processes. The unique of lesions in this region are most of the pathologies present with similar clinical signs and symptoms, thus making differentiating the etiologies clinically could be challenging (3, 6). Pathological lesions in this region are common and tumors of sellar region consist of 20% of intracranial neoplasm. Population prevalence for masses in the sellar region reported as 0.1% in a recent study (7). The commonest tumor is pituitary adenoma accounting for 50%–93% of them (7–12). Saeger et al. in their review of 10 years of pituitary tumor registry containing 4122 cases, has found various non adenomatous pathology including craniopharyngioma (3.2%), meningioma (0.9%), metastases (0.6%), chordomas (0.5%), pituitary carcinoma (0.1%), non neoplastic cystic lesion (2.8%), and inflammatory lesions (0.1%) (9). Besides the cases mentioned, there is wide range of possible pathological diagnosis for tumor in the sellar region which carries much less than 1% in Saeger et al. studies. These includes gangliocytoma, chondrosarcoma, suprasellar germinoma, hemangioma, fibroma, hamartoma, and lymphocytic hypophysitis only naming a few (9). Petrakakis et al. in their studies of rare lesions in this region, out of 223 cases only 20 diagnosed with histopathology other than pituitary adenoma, craniopharyngioma, meningioma, and Rathke cleft cyst (13).

Despite the broad category of differentials for sellar region, most of them present with similar clinical signs and symptoms. Headache and visual disturbance are among the frequently seen as presenting symptom. Headache is frequently seen in sellar tumors although being a non specific symptom when it comes to localisation. It accounts for 34%–57% as presenting symptom (10, 14). Close anatomical proximity of sellar region with optic apparatus causes significant number of tumors to present with visual disturbance which vary from mild visual field (VF) defect to blindness (3). Cause for this symptoms are due to the compression of afferent pathway of vision mainly at the region of optic chiasm which lies in this anatomical region (19).

VF assessment is one of the crucial component of neuroophthalmologic assessment particularly in sellar region tumor (SRT) as defect in VF occurs in 92.9% of pituitary adenoma, 34.8% of meningioma, and 75% of craniopharyngioma (20). Often the principle indication for surgical intervention is progressive worsening of the VF defect (21–23). We cannot emphasise more on its importance. Besides, VF defect has significant effect on daily activities including driving, reading, and personal hygiene. VF testing is crucial for diagnostic, follow up, and planning daily living activities (24).

AP being the standard of practise for VF assessment is an automated testing which uses computer algorithm (25). AP is independent of the examiner and conducted by computer in a standard manner making it ideal to follow up patients VF with this method. It also allows quantification of the VF defect through the mean deviation (MD) value given unique for each eye in the result. This value is crucial to see the changes of VF defect over time and signifies overall abnormality of a single VF. One of the factor that was found to be correlated with preoperative severity of the VF deficit is tumor volume (25).

Thus, we decided to formulate a study to look into the factors that affects the improvement of the VF that gives rise to the varying results in previous study. Visual acuity as stated earlier gives idea of the vision subserved by only a small area called macula. VF on the other hand gives a better idea of an overall abnormality of the vision. This is best depicted by MD value through automated perimetry (25).

Methodology

Research Design

This is a cross sectional study with retrospective review of medical records to determine factors associated with VF improvement after surgery in patients who underwent surgical treatment for SRT in Queen Elizabeth Hospital, Kota Kinabalu. The patient population are those with diagnosed SRT and has been subjected to surgery for tumor excision with any surgical approach between July 2010 to July 2016. The study was approved by the Malaysian Medical Research and Ethics Committee (MREC). [NMRR ID: NMRR-15-588-24738]

Research Location and Duration

This study was conducted in a single centre in Queen Elizabeth Hospital, Kota Kinabalu, the only tertiary centre with neurosurgical facility in entire state of Sabah. Thus, this centre receives referral from all over the state for neurosurgical consultation. Patients who fulfill the inclusion and exclusion criterias will be selected and included in this study. The total study duration was over a span of 2 years , from June 2014 till June 2016.

Patients selected for this study must fulfil the inclusive criteria which is all patients who underwent surgery for tumor in sellar region, age 18–65 years old, with SRT of any pathology, and formal automated perimetry VF assessment was done before and after surgery. Those who meets the exclusion criteria including patient without proper visual assessment prior to surgery and after surgery, lost to follow up, has VF assessment done with method other than Humphrey, unreliable Humphrey perimetry test, or treated non surgically for the SRT.

Method of Research

In this retrospective study, we aim to study the factors that associated with outcome of VF improvement after surgery in SRT of any aetiology. We recruited list of patient suitable for the study from operation theatre log book of Queen Elizabeth Hospital. All cases of SRT which were operated between July 2010 to July 2016 were chosen. Case records were then traced from record office. We then filter our patient list based on our inclusion and exclusion criteria. Those who meet the criteria as mentioned above underwent detailed screening of the case record which includes patients demographic, doctors

entry, operative note, MRI report, histopathology report, and perimetry report. Data collected using a data collection sheet.

Pre-operative and post-operative visual assessment for these patients are done which include perimetry with Humphrey visual field analyser (HVFA). Post-operative assessment are done routinely at about 3 months post-surgery. Perimetry was conducted according to Swedish Interactive Threshold Algorithm (SITA) 24–2 of the Humphrey Field Analyser program (Carl Zeiss Meditec Inc, Dublin, CA, USA). This VF test done by requiring patient to respond to a flashing light by pressing button when he or she is able to see it. The flashing light are of variable intensity and test done while patient fixates his eye on a centre target. The entire procedure is conducted by optometrist who will be instructing the patient on the test process. We then look for reliability of the Humphrey test looking at false positive, false negative, and fixation losses whose values are obtained in HVFA report. We accept reliable test as less than 20% of fixation losses and less than 33% of false positive and false negatives (21). Only reliable test study are included. In HVFA, the Mean Deviation (MD) result is used to quantify the VF defect and the improvement or worsening of this value post-surgery is taken as outcome of VF for each eye individually and each eye is analysed.

Tumor volume was estimated assuming all the tumor takes an ellipsoid pattern. Based on Cavalieri principle, the formula used is $\frac{4}{3} \pi (A/2 * B/2 * C/2)$ and p assumed to take the value of 3, thus simplifying the equation to $(A * B * C)/2$. A is tumor height, B is tumor width, and C is tumor length (Gondim, Tella Jr. (32) Lee, Park (25)).

Statistical Analysis

The obtained data was keyed into the computer software Statistical Package for Social Sciences (SPSS) for Mac version 24.0. Data generally contains demographic information, predictors, and VF assessment. Demographic information are expressed in table form as mean and standard deviation for numerical variables and number and percentage for categorical variable. The predictors of VF analysed with univariable logistic regression and multiple logistic regression to report on crude and adjusted odd ratio respectively. In these study predictors were entered as covariates and the dependent variable is VF outcome based on difference of MD pre and post-

surgery (categorised into no improvement and improved). The outcome is unique to each eye and thus univariate and multivariate analysis done with the number of eyes after exclusion of eyes with missing data. Purposeful variable selection based on univariable result and clinical significance were done to achieve the final model in multivariable analysis.

Results

Data from 84 patients who met the study requirement have been collected from their case records for this study. However, out of 168 eyes of this patients, only 151 satisfies the inclusion and exclusion criteria and suitable for analysis. The patient and tumor characteristic for all 84 patients are depicted in Table 1. Mean (SD) age of the patients was 45.4 (11.3). The youngest is 19 years old while the eldest is 65. Fifty nine (70.2%) of our patients were male. Majority of them are from ethnic group Kadazan ($n = 26$) who are natives in this region, followed by Malay ($n = 14$) and Chinese ($n = 10$). Other ethnic group which include all other minority in this population makes 34 of them.

Initial symptom to appear among our patients were visual disturbance ($n = 48$), headache ($n = 25$), and hormonal symptom ($n = 11$). Visual disturbance include loss of VF, blurring of vision, and diplopia. Duration of visual symptom prior to surgery ranges from two weeks to four years with mean (SD) of 10 (7) months. Histopathological diagnosis which was obtained from surgical specimen consist of pituitary adenoma ($n = 63$), sellar meningioma ($n = 16$), craniopharyngioma ($n = 4$), and rathke cleft cyst ($n = 1$). Other sellar tumors were not seen in our study sample. Average mean volume of the tumor in cubic centimeters was 14.7 (16.4).

All our patients were subjected to surgery of various approaches in our hospital. Mean (SD) duration of onset of visual symptom to surgery was 9.7 (7.1) months. They were broadly categorised into 3 group of surgical approaches which were transphenoidal surgery, transcranial, and supraorbital approach consisting of 56.0%, 28.6%, and 15.5% of patients, respectively. The duration of surgery ranges from 140 to 430 minutes with mean (SD) of 259 (78) minutes. Intraoperative finding of these tumors has found the tumor was soft in 61.9% and firm in the remaining.

Table 1. Patient and tumor characteristics of 84 patients

	<i>n</i>	%
Age, mean (SD)	45.48 (11.39)	years
Sex		
Male	59	70.2
Female	25	29.8
Race		
Malay	14	16.7
Chinese	10	11.9
Kadazan	26	31
Others	34	40.5
Presenting symptom		
Visual field loss	48	57.1
Headache	25	29.8
Hormonal symptoms	11	13.1
Diagnosis		
Pituitary adenoma	63	75
Sellar meningioma	16	19
Craniopharyngioma	4	4.8
Rathke cleft cyst	1	1.2
Symptom duration, mean (SD)	9.7 (7.1)	months
Tumor volume, mean (SD)	14.7 (16.4)	cm ³
Surgical approach		
Transsphenoidal	47	56.0
Transcranial	24	28.6
Supraorbital	13	15.5
Surgery duration, mean (SD)	259 (78)	minutes
Tumor consistency		
Soft	52	61.9
Firm	32	38.1

SD = Standard deviation

Visual Assessment

The visual assessment for the 151 eyes that were taken into account for analysis are illustrated in Table 2. Seventeen eyes were excluded because of missing or incomplete data on eye assessment. Automated perimetry results for all the 151 eyes shows pre-operative MD with mean (SD) of -14.0 (9.0) dB and post operation MD with mean (SD) of -12.4 (9.4) dB. 107 (70.9%) eyes have showed improvement in VF in terms of mean deviation and 44 showed no improvement.

Univariate logistic regression analysis was done for predictive factors of VF improvement as shown in Table 3. Younger age (P-value < 0.001), female sex (P-value 0.037), and shorter duration of visual symptom prior to surgery (P-value < 0.001) has significantly higher odds to

VF improvement. In comparison to supraorbital approach, transphenoidal (P-value 0.001) and transcranial (P-value 0.020) approach has tendency for improvement in VF. In terms of histopathological diagnosis, pituitary adenoma has 4.15 times the odds for VF improvement compared to others (95% CI 1.10, 15.73, P-value 0.036) when other confounders not adjusted. Tumor volume and tumor consistency has no significant effect on VF improvement after surgery in SRT.

Table 2. Visual field assessment of 151 eyes

	n	%
Pre-surgery MD, mean (SD)	-14.0 (9.0) dB	
Post-surgery MD, mean (SD)	-12.4 (9.4) dB	
MD Outcome		
Improved	107	70.9
Not Improved	44	29.1

MD = Mean deviation, SD = Standard Deviation, dB = Decibel

On multivariate analysis which is tabulated in Table 4, an increase of 1 month in the duration of symptom prior to surgery has 0.79 times the odds of having VF improvement (95% CI 0.70, 0.89, P-value < 0.001) when adjusted

for age, sex, tumor consistency, and surgical approach. Transphenoidal approach compared to supraorbital approach has 5.56 times the odds of having VF improvement (95% CI 1.52, 20.26, P-value 0.009) when adjusted for age, sex, tumor consistency, and symptom duration. Transcranial approach has 4.42 times the odds of having VF improvement in comparison with supraorbital approach (95% CI 1.06, 18.52, P-value 0.042) when adjusted for age, sex, tumor consistency, and symptom duration.

Discussion

Visual disturbance is a common presenting symptom in SRT due to the close proximity of this tumors with optic apparatus and the disturbances seen include visual field (VF) defects, visual loss, diplopia, nystagmus and visual hallucinations (3, 16). Among them, VF defect is commonest (16). Progressive worsening of VF defect guides the principle behind the indication for surgery in these tumors (21–23). In our study, we found 58% of our patients presented with visual disturbance making it the commonest presenting symptom followed by headache, 30%. Valassi et al. reported 22% of their non pituitary sellar masses presented with visual disturbances (10). Kwancharoen

Table 3. Univariate logistic regression analysis of the factors affecting visual field outcome

	Univariate Analysis		
	B (SE)	Crude OR (95% CI)	P-value
Age	-0.065 (0.018)	0.94 (0.90–0.97)	< 0.001
Sex			
Male	-0.882 (0.423)	0.41 (0.18–0.95)	0.037
Female		1	
Symptom duration	-0.241 (0.051)	0.79 (0.71–0.87)	< 0.001
Tumor volume	-0.002 (0.011)	1.00 (0.98–1.02)	0.858
Diagnosis			
Pituitary adenoma	1.423 (0.680)	4.15 (1.10–15.73)	0.036
Sellar meningioma	1.322 (0.769)	3.75 (0.83–16.94)	0.086
Others		1	
Tumor consistency			
Firm	-0.625 (0.384)	0.54 (0.25–1.14)	0.103
Soft		1	
Surgical approach			
Transphenoidal	1.667 (0.509)	5.30 (1.95–14.35)	0.001
Transcranial	1.269 (0.544)	3.56 (1.22–10.33)	0.020
Supraorbital		1	

SE = Standard error, OR = Odd ratio, CI = Confidence interval

Table 4. Multivariate logistic regression analysis of the factors affecting visual field outcome after purposeful variable selection

	Multivariate Analysis		
	B (SE)	Adjusted OR (95% CI)	P-value
Age	-0.018 (0.021)	0.98 (0.94–1.02)	0.392
Sex			
Male	-0.470 (0.616)	0.63 (0.19–2.09)	0.446
Female		1	
Symptom duration	-0.232 (0.061)	0.79 (0.70–0.89)	< 0.001
Tumor consistency			
Firm	0.540 (0.536)	1.72 (0.60–4.90)	0.314
Soft		1	
Surgical approach			
Transphenoidal	1.715 (0.660)	5.56 (1.52–20.26)	0.009
Transcranial	1.487 (0.731)	4.42 (1.06–18.52)	0.042
Supraorbital			

SE = Standard error, OR = Odd ratio, CI = Confidence interval

et al. studied features of sellar and suprasellar meningioma and found 58% of them have headache while only 16% had headache (17). On the other hand, in a study of pituitary tumors by Levy et al., 70% of their patients had headache (15). 88% of pituitary tumor patients who underwent transphenoidal surgery in Gnanalingham et al. study presented with visual disturbance (21). Although visual disturbance and headache has been quoted in various studies as the presenting symptom, the mechanism for this 2 symptoms in SRT is totally different. Visual disturbance in sellar tumors are due to the compression or mass effect exerted on optic apparatus mainly at optic chiasm (18, 19). Levy et al. has proposed the headache particularly in pituitary tumor patients is not mere structural problem but rather might have neuroendocrine and biochemical basis to it (15).

In our study, 70.9% of the eyes we analyse has showed improvement in VF after surgery. This figure is comparable with other studies published where the figure varies based on the pathology. In general, VF recovery after surgery for the major common pathology of SRT ranges from 30% to 98% in pituitary adenoma, 56% in meningioma, and 29% to 79% for craniopharyngiomas (18, 21–23, 27–30). Most of the studies of SRT has focused on pituitary tumors since it consist 50%–93% of the tumors in this region. In a more recent study by Ali Mahmoud and Salah (2) has reported improvement in MD in all patients and their study includes all SRT but their sample

size was only fifteen. Sven Berkmann, Javier Fandino (33) quoted 87% improvement in VF after one month of surgery in sellar tumors but their study only on transsphenoidal surgeries. Comparison among these results is limited when it comes to improvement in VF because of differences in methodology and population group. Methodology of the studies especially the technique used for VF assessment differs significantly. Some are qualitative, while the rest gives a quantitative assessment. All our patients had their VF assessed using AP with Humphrey Field Analyser Programme which conducted based on a computer algorithm and ideal for follow up assessment. Though traditional AP is time consuming, SITA has overcome this problem.

Our study has revealed that younger age, female sex, shorter duration of symptoms, transphenoidal approach and transcranial approach are factors that leads to improvement in VF outcome after surgery based on univariable logistic regression analysis. However, on multivariable analysis, only duration of symptoms and surgical approach remains significant as factors affecting VF outcome. Duration of symptoms is an important factor which has been reported in various studies even those that studied on individual pathology. Duration of symptom could reflect the degree of compression on the optic apparatus. Longer duration of compression could lead to demyelination, prolong suppression of axonal flow, and ischemia of the nerve. This in turn

affects the ability of the nerve to restore axonal flow and remyelination to regain normal function.

Our study identified transphenoidal and transcranial approach has higher odds for VF improvement in comparison with supraorbital approach. Transphenoidal surgery has been the preferred surgical approach for all SRT including those non pituitary in origin (34). This approach also has lesser secondary visual symptoms linked to treatment (22). However, transcranial approaches in this tumors still plays a role while considering factors such as tumor size, consistency, and configuration. In terms of visual outcome, report shows large to giant adenoma has favourable outcome with transcranial approach (34).

Numerous studies were conducted for visual outcome for individual pathology of SRT. On the contrary, only few studies that have looked into factors on visual outcome for all sellar tumors. Suri, Narang, Sharma and Mahapatra (35) has looked into 79 patients with SRT and found blindness for more than 3 months, apoplexy, and suprasellar extension are significant factors on multivariate analysis. However, their study is based only on patient with preoperative blindness and they looked into vision in general. However, Ali Mahmoud and Salah (2) studied VF improvement with AP and quoted temporal field sensitivity measured using Lambert scale as the best predictor of VF outcome.

As we study on the clinical factors of VF outcome in our retrospective study, some authors have looked into investigational and objective factors to prognosticate vision for the tumors in these region. Loo, Tian, Miller and Subramanian (36) measured pretreatment peripapillary retinal nerve fibre layer using optical coherence tomography in anterior pathway meningiomas. They reported improvement in vision post treatment in patients with normal measurements and shorter duration of symptoms. Berkmann, Fandino, Zosso et al. (33) has used intraoperative Magnetic Resonance Imaging finding of optic nerve to prognosticate post operative visual deficits in sellar tumors. A study on preoperative pattern electroretinogram for chiasmal tumors as a prognosticator but found no association with pre and post operation VF (37).

Conclusion

In our study of factors affecting VF outcome after surgery, we found that symptom duration and surgical approach has significant effect on the outcome when other confounders are adjusted. Shorter duration of symptom, transphenoidal approach, and transcranial approaches favours improvement in VF for all SRTs.

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4. Professor Mr (Dr) Zamzuri Idris, Head of Neurosciences Department, Universiti Sains Malaysia, Kubang Kerian, Kelantan
5. Associate Professor Dr Kamarul Imran Musa, Public Health Physician, Universiti Sains Malaysia, Kubang Kerian, Kelantan
6. Ms Prema, Biostatistician, Clinical Research Centre, Hospital Sultanah Aminah, Johor Bahru

Authors' Contributions

Conception and design: PRS
Analysis and interpretation of the data: PRS
Drafting of the article: PRS
Critical revision of the article for important intellectual content: PRS, PS, ARIG
Final approval of the article: PRS, PS, ARIG
Provision of study materials or patients: PS
Statistical expertise: PRS, ARIG
Administrative, technical, or logistic support: PS, ARIG
Collection and assembly of data: PRS

Correspondence

Dr Prabu Rau Sriram
 MD (USM), Master Surgery (Neurosurgery) USM
 Department of Neurosurgery,
 Queen Elizabeth Hospital,
 88200 Kota Kinabalu, Sabah,
 Malaysia.
 Tel: +6012 8331149
 E-mail: praburau@gmail.com

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