FACTORS AFFECTING VISUAL FIELD OUTCOME POST SURGERY IN SELLAR REGION TUMORS: RETROSPECTIVE STUDY

by

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LIST OF ABBREVIATIONS

	Abbreviation	**Description**
1.	VF	Visual Field
2.	SRT	Sellar Region Tumor
3.	HVFA	Humphrey Visual Field Analyser
4.	MD	Mean Deviation
5.	SD	Standard Deviation
6.	SE	Standard Error
7.	CI	Confidence Interval
8.	n	Total Number

ABSTRAK

Latar Belakang Kebanyakan ketumbuhan di bahagian sellar memiliki simptom dan tanda yang sama walaupun kemungkinan diagnosis ketumbuhan tersebut adalah berlainan. Sakit kepala dan gangguan penglihatan adalah antara simptom yang paling kerap ditemui sebagai sebab pesakit menemui doctor. Penilaian medan penglihatan adalah antara komponen utama dalam penilaian neuroophtalmik dan nilai Mean Deviation (MD) yang didapati daripada ujian perimetri automatik membolehkan kecacatan dalam medan penglihatan dikuantifikasi. Kami telah membuat formulasi kajian untuk melihat faktor yang memberi kesan terhadap keputusan medan penglihatan selepas pembedahan bagi ketumbuhan bahagian sellar.

Kaedah Semua pesakit dengan ketumbuhan di bahagian sellar yang telah menjalani pembedahan di Hospital Queen Elizabeth dari bulan Julai 2010 hingga Julai 2016 dianalisis secara retrospektif melalui rekod hospital. Penilaian medan penglihatan melalui penilaian penglihatan Humphrey untuk pesakit tersebut sebelum dan selepas pembedahan disemak untuk nilai MD.

Keputusan Seramai 84 orang pesakit telah dilibatkan dalam kajian ini. Seratus lima puluh satu mata dimasukkan dalam analisis daripada jumlah pesakit tersebut setelah menolak data yang tidak mencukupi. Min umur pesakit adalah 45.4 tahun dan 70.2% darpada pesakit tersebut adalah lelaki. Gangguan penglihatan adalah simptom yang paling kerap dijumpai dan min tempoh simptom sebelum pembedahan adalah 9.7 bulan. Kebanyakan daripada mereka adalah Pituitary Adenoma (75%), diikuti dengan Sellar Meningioma (19%), Craniopharyngioma (4.8%), dan Rathke Cleft Cyst (1.2%). Sebanyak 70.9% pesakit menunjuk peningkatan dalam medan penglihatan berdasarkan nilai MD. Min MD untuk sebelum pembedahan adalah -

14.0dB dan -12.4dB untuk selepas pembedahan. Analisis univariate menunjukkan umur yang muda, jantina perempuan, tempoh simptom yang singkat, ketumbuhan Pituitary Adenoma, pembedahan transphenoidal, dan pembedahan transkranial memihak kepada peningkatan dalam medan penglihatan. Manakala, dalam analisis multivariate, hanya tempoh simptom yang singkat, pembedahan transphenoidal, dan pembedahan transkranial adalah ketara untuk peningkatan medan penglihatan apabila faktor lain diselaraskan.

Kesimpulan Tempoh simptom dan kaedah pembedahan adalah faktor yang memberi kesan terhadap peningkatan medan penglihatan selepas pembedahan dalam pesakit dengan ketumbuhan bahagian sellar.

ABSTRACT

Background Despite the broad category of differentials for sellar region, most of them present with similar clinical signs & symptoms. Headache & visual disturbance are among the frequently seen as presenting symptom. Visual field (VF) assessment is one of the crucial component of neuroophtalmologic 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 -14.0dB and -12.4dB, 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.

1. INTRODUCTION & LITERATURE REVIEW

Sellar region (SR), 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 lies 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. Tang et al in their study of thin sectional anatomy proposed the SR to be divided into suprahypophysial area, hypophysial area, and infrahypophyseal area (1). The anatomical boundaries of sellar & 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 & 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). Other studies have quoted rathke cleft cyst as the commonest non adenomatous lesion of this anatomical location. Valassi et al has classified non adenomatous lesion into cystic lesion, benign neoplasms, malignancies, and inflammatory lesions with frequency of 53%, 22%, 16%, and 9% respectively (10).

Despite the broad category of differentials for sellar region, most of them present with similar clinical signs & symptoms. Headache & 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 localization. It accounts for 34 – 57 % as presenting symptom (10, 14). Levy et al in their study of pituitary tumor and headache recorded 70 % of their pituitary patients has headache. Nature of headache can vary from migraine, trigeminal autonomic cephalgias, such as cluster headache, and neuralgiform headache attacks. They are not related to tumor size nor cavernous sinus invasion and thus might not be just a structural problem. On the other hand, pathophysiology of headache particularly in pituitary tumor might have a neuroendocrine and biochemical basis (15). 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 defect to blindness (3). Visual disturbances from chiasmal tumors can present as visual field defects, visual loss, diplopia, nystagmus and visual hallucinations and among them visual field defect are commonest (16). Valassi et al quoted 22% of the non pituitary sellar mass presented with visual disturbances (10). A review of 57 sellar & suprasellar meningiomas found 58% of them has visual disturbance while only 16% with headache (17). Visual disturbance in sellar tumors are due to the compression or mass effect exerted on optic apparatus and it is one of earliest presenting symptom in craniopharyngiomas (18). Optic chiasm is an important component of optic apparatus in the sellar region. Neuroophtalmologic symptoms seen in these tumors include defect in visual field, central acuity, colour vision, optic nerve head, and pupillary function. The later could also be due to involvement of oculomotor nerve in the parasellar region. Being a major presenting symptom in SRT tumors of varying pathology, visual disturbances is an important indication for surgery of these tumors. 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).

Central acuity of vision are tested based on Snellen chart which has been the classical method practised worldwide. Other newer methods include logMAR stratification of test lines which gives more quantitative assessment. The fibres that carries the finest visual resolution which arises from fovea centralis and when affected, will cause impairment in central acuity (19). Colour vision is another sensitive parameter to assess particularly in showing optic nerve dysfunction. They are commonly tested with Ishihara test plates or Hardy Rand Ritter plates. Pupil examination to look for pupillary reflexes will indicate the integrity of the pupillomotor fibres that is carried in the optic nerve. Assymetrical responses of the afferent of the pupillary reflex arc can be detected with swinging flash light test indicating relative afferent pupillary

defect. Fundocopy examination will reveal papilloedema or pale optic disc. In case of SRT, the former is probably due to increased intranial pressure from hydrocephalus or huge tumor mass causing significant mass effect (19).

Visual field (VF) assessment is one of the crucial component of neuroophtalmologic assessment particularly in 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 emphasize 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). Confrontational test, tangent screens, Goldmann kinetic perimetry fields, automated perimetry (AP), and multifocal visual evoked potential (MVEP) are among the commonly utilized assessment method for VF defects (19, 24). The former is crude bedside testing done by clinician or neurologist to get an immediate idea on the degree of defect and small defects may easily be missed with this method. Tangent screen testing are done by moving a stimuli slowly from periphery to center to map the contour of the field. Goldmann perimetry involves manually driven special perimetry machine which is done by trained examiner. MVEP though not commonly available, does not depend on the subjects response, thus eliminating human errors caused by fatigue and stress. However, the use of this tool is only in academic or research setting in most of the centres (19).

AP being the standard of practise for VF assessment is an automated testing which uses computer algorithm (25). It has sensitivity of about 70% for detecting arcuate field defects and better than Goldmann perimetry in quantification of defect and sensitivity (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. Traditionally AP is a time consuming test due to its algorithm stepping up and down the stimulus intensity in staircases. Swedish Interactive Threshold Algorithm (SITA) was introduced to overcome this problem, where the VF tested is limited to 24 to 30 degrees on both sides of the central fixation. Jung et al takes in average 5.87 minutes per patient to test VF of central 24 degree with SITA strategy. 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 visual field (25). One of the factor that was found to be correlated with preoperative severity of the visual field deficit is tumor volume (25).

Bitemporal hemianopia and mixed defect is the commonest presentation of VF defect in chiasm compression due to the arrangement of fibres within (22, 25, 26). These defect account for 42.6 % of VF defect seen in pituitary adenoma and 23.6% of craniopharyngiomas (18, 26). The nasal fibres runs on the lateral of the chiasm without decussating while temporal fibres run medially crossing to other side. Thus, compression on chiasm tend to affect the fibres running medially which carries fibres of the temporal field of the eye (25). However, there is no correlation between pattern of chiasmic distortion and the VF defect (18). Chicani et al documented hemianopic, arcuate, altitudinal, central scotoma, and peripheral constriction defects in suprasellar meningiomas (27).

As stated earlier, worsening visual disturbance is an important deciding factors for surgical treatment in SRT. One of the reason is the improvement shown in VF defect in particular post surgery is the very rapid recovery of the defect after surgery and reported as early as 10 minutes after surgery (23, 28). Early recovery happens due to decompression of physiological block in axonal flow in the neve conduction. Numerous studies has reviewed on

improvement of visual field after surgery in SRT and each of it having different method of assessment, different population of patients studied, different surgical approaches, different apathology, and varying results. In general VF recovery after surgery for the major common pathology of SRT ranges from 30.4% to 98% in pituitary adenoma, 56% in meningioma, and 29% to 79% for craniopharyngiomas (18, 21-23, 27-30). As can be seen, most of the studies have focused on pituitary adenomas given that being the commonest tumor of that anatomical region. Ali Mahmoud and Salah (2) has reported improvement in MD in all patients and their study includes all sellar region tumors.

Thus, we decided to formulate a study to look into the factors that affects the improvement of the visual field 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 visual field. This is best depicted by MD value through automated perimetry (25).

2. STUDY PROTOCOL

This study is a 6 years retrospective study with cross sectional design. The research objective of the study is to determine the factors associated with visual field outcome after surgery in sellar region tumors. The subjects for this study consist of those with diagnosed SRT and has been subjected to surgery for tumor excision with any surgical approach between July 2010 to July 2016 in Queen Elizabeth Hospital, Kota Kinabalu. The study was approved by the Malaysian Medical Research and Ethics Committee (MREC). [NMRR ID : NMRR-15-588-24738]

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 asessment 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, treated non surgically for the SRT, or have other ocular pathology that impairs VF asessment such as cataract.

In this retrospective study, we aim to study the factors that associated with outcome of VF improvement after surgery in SRT of any etiology. We recruited list of patient suitable for the study from operation theatre log book of Queen Elizabeth Hospital. Case records were then traced from record office. We then filter our patient list based on our inclusion & 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.

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.

The sample size for this study was calculated based on the Power Primer table by Cohen (31) for medium population effect size with $\alpha = 0.5$ and power 0.80. Seven independent variables were chosen giving sample size of 102. Taking into account drop out rate of 10%, we estimated sample size for our study as 112.

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6. Ms. Prema, Biostatistician, Clinical Research Centre, Hospital Sultanah Aminah

3.2 Abstract

ABSTRACT

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VF assessment is one of the crucial component of neuroophtalmologic 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 emphasize more on its importance. Besides, VF defect has significant effect on daily activities including

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