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Therapeutic Strategies of the Intracranial Meningioma in Elderly Patients

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Objective : The apparent increase in the incidence of the intracranial meningiomas in the elderly is due in part to improved diagnostic tools and improved span of life. The authors carried out a retrospective study to validate the use of the Clinical-Radiological Grading System (CRGS) as a clinical tool to orientate surgical decision making in elderly patients and to explore prognostic factors of survival.

Methods : From January 1997 to January 2006, the authors consecutively recruited and surgically treated 20 patients older than 65 years of age with radiologic findings of intracranial meningiomas and a preoperative evaluation based on the CRGS.

Results : High CRGS score was associated with a higher probability of good outcome ($p=0.004$) and a lower probability of postoperative complications ($p=0.049$). Among the different subset items of the CRGS score, larger maximum tumor diameters ($D \geq 4cm$) and the presence of a severe peritumoral edema were associated with incidence rate of postoperative poor outcome and complications ($p<0.05$). Additionally, the critical location of the tumor was also correlated with poor outcome ($p<0.05$).

Conclusion : A CRGS score higher than 13 is a good prognostic indication of survival. The CRGS score is a useful and practical tool for the selection of elderly patients affected by intracranial meningiomas as surgical candidates.

KEY WORDS : Intracranial meningioma · CRGS · Elderly patients · Prognosis.

Introduction

Intracranial meningioma occurs frequently and 14-20% of all brain tumors are meningioma[5,20]. The incidence of meningioma is 1-2.8 per 100,000 people. However, the incidence among the elderly population (aged 80 or more) is extremely high; being 8 per 100,000[23]. Recently, the incidence of meningioma has been increasing not only because the elderly population has grown with the increasing average lifespan but also because diagnostic equipments like computerized tomography (CT) and magnetic resonance imaging (MRI) have been introduced.

The death rate after surgery for meningioma is 1.1% in patients aged under 70, but 4.0% in groups aged 70 and older[3]. Thus, studies on cause analysis and prognosis prediction are essential. When neurological symptoms are serious in elderly patients, surgical treatment is necessary. However, when the symptoms are minor or meningioma is diagnosed incidentally, many studies contradict each other, showing that there is no common consensus on the appropriate medical care. Several studies reported that the American Society of Anesthesiology (ASA) classification and Karnofsky Performance Scale (KPS) are statistically significant with the prognosis, and the diameter and edema are not closely correlated with the prognosis[9,26]. On the other hand, another study suggested that the diameter of meningioma and peritumoral edema should determine whether surgery is performed because they are the important factors which may affect the prognosis[10]. But, there have still been various opinions and arguments on these issues.

In particular, underlying diseases, such as diabetic mellitus or hypertension, are common among elderly patients, and age itself can be a risky factor for elderly patients undergoing general anesthesia. The death rate and prevalence rate of elderly patients are higher and recovery time is longer than for younger patients when postoperative complications occur. Thus, treatment guidelines for the elderly with meningioma are very important.

The aim of this study was to identify various factors that may have an effect on the prognosis of meningioma patients

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aged 65 and over, to verify the causal relation of the factors and the prognosis, and to proper the treatment guidelines for meningioma patients.

Materials and Methods

This study is a retrospective analysis of 20 consecutive patients, aged 65 or older, who underwent the surgical removal of an intracranial meningioma between January 1997 and January 2006. Their ages ranged from 65 to 76 years (mean 68.6 years). Fourteen patients were female, and 4 were male.

The common symptoms and signs experienced by the patients were headache, motor weakness, dizziness and seizure, in descending order of frequency (Table 1). The preoperative neurological status was evaluated according to the KPS score. Eleven patients were were rated 90 and 100, and nine were 60 to 80.

In the neurological examination, 2 patients exhibited unrecoverable dificits four patients showed progressive deficits, and 14 presented no deficits or only seizure (Table 2). General health condition was evaluated according to the ASA classification. Five patients were graded as Class I(healthy), 11 as Class II (having mild systemic disease but no functional limitation), and 4 as Class III (having severe systemic disease and difinite functional limitations) (Table 2). Patients' systemic diseases which could affect anesthesia before and after surgery were surveyed. Hypertension and diabetic mellitus were the most common and whether existing diseases were medically controlled or not are listed in Table 3.

Table 1. Clinical symptoms of patients

Symptoms	No. of pts.
Headache	9
Motor weakness	5
Dizziness	3
Seizure	2
Memory disturbance	2
Syncope	2
Personality change	1
General weakness	1
Incidental finding	1

Table 2. Clinical characteristics of patients

Score	KPS Description	No. of pts.
100	Normal; no complaints, no evidence of disease	11
90	Able to carry on normal activity; minor symptoms	
80	Normal activity with effort; some symptoms	9
70	Cares for self; unable to carry on normal activity	
Category	**ASA classification Description**	**No. of pts.**
I	Healthy pt.	5
II	Mild systemic disease. No functional limitation	11
III	Severe systemic disease. Definite functional limitation	4
Classification	**Neurologic condition Description**	**No. of pts.**
Unrecoverable deficits	Deficits complete and stabilized (hemiplegia or amaurosis, etc.)	2
Progressive deficits	Deficits incomplete or worsening (hemiparesis or impairment of visual acuity, etc.)	4
No deficits, only seizure	–	14

KPS : Karnofsky Performance Scale, ASA : American Society of Anesthesiology, pts : patients

Table 3. Systemic concomitant diseases of patients

Disease	Response to medical Tx.	Unresponse to medical Tx.
HTN	8	2
DM	2	2
Angina	2	0
Pulmonary ds.	1	1
CRF	0	1
Hepatic ds.	0	1
Cerebral infarction	0	1

HTN : Hypertension, DM : Diabetes mellitus, CRF : Chronic renal failure, ds. : disease

All patients underwent the CT scan and MRI of the brain, and 8 patients underwent angiography. The localization of the tumor was cortical convexity in 14 patients, parasagittal falx in 3, sphenoidal ridge in 2, and tuberculum sella in 1. In 11 patients, the maximum diameter of the meningioma was less than 4 cm and 4 patients had a maximum diameter of 6cm or over (Table 4). Using CT scan, MRI, and angiography, we classified the location of the tumor into three categories (Fig. 1); highly, moderately, and not critical, according to the proximity to major cerebral vessels, cranial nerve, or the brain stem and eloquent areas. Four patients were classified into highly, 9 moderately, and 7 not critical (Table 4).

Peritumoral edema was classified as severe, moderate, and absent (Fig. 2). Severe peitumoral edema was found in 3 patients, and moderate peritumoral edema was observed in 11. We observed no edema in 6 patients (Table 4). With regards to the different clinical and neuroimaging prognostic factors, we analysed retrospectively using the Clinical-Radiological Grading System (CRGS) composed of several subset items including the patient's neurological status, the preoperative KPS score, and the presence of concomitant diseases, the size and the location of the tumor, and the presence of peritumoral edema (Table 5).

Table 4. Characteristics of tumor according to radiologic findings

Classification	Location / Charact.†	Conveixity	Parasagittal falx	Sphenoid	Tuberculum sella
Size (cm)	<4	7	2	1	1
	4≦D<6	3	1	1	0
	6≦	4	0	0	0
Whether location	not critical	4	3	0	0
is critical*	moderately	8	0	1	0
	highly	2	0	1	1
Edema†	absent	2	2	1	1
	moderate	10	1	0	0
	severe	2	0	1	0

*A critical location is present if the tumor is attached to a primary vascular or nervous structure (such as the cranial or an eloquent area). †Peritumoral edema is classified as moderate (only peritumoral) and severe (with a shift of midline structures). †Characteristics. D : diameter

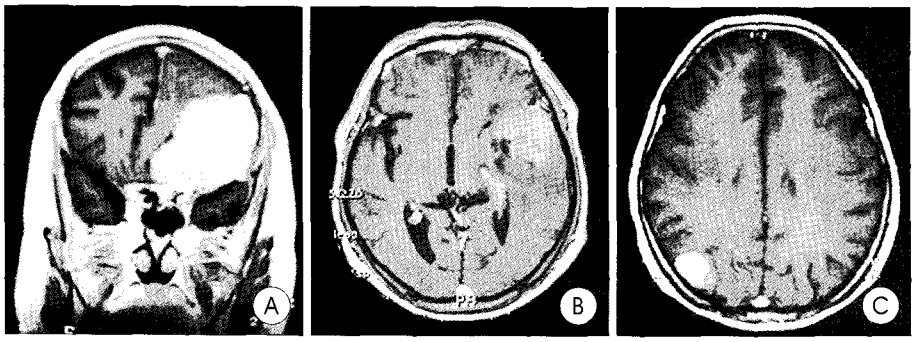

Fig. 1. Location of tumors are classified into three types according to the proximity to main blood vessel, nerve, or brain stem is A : High, B : moderate, C : not critical.

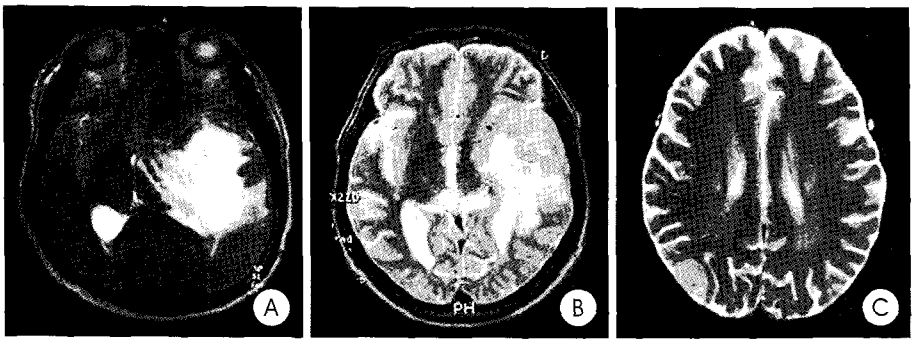

Fig. 2. The scale of peritumoral edema was categorized categories; A : severe, B : moderate, C : absent.

The significance of CRGS, ASA classification, KPS score, neurological condition, tumor size, tumor location, edema and concomittant disease on postoperative outcome and complications were analysed by the Chi-Square. A p-value below 0.05 was considered as being statistically significant.

Results

In order to assess the risk factors for a poor outcome and postoperative complications, we evaluated the values of ASA classification and the different subset items of the CRGS score (Table 6, 7).

Preoperative American Society of Anesthesiology (ASA) classification

Of the 5 patients graded as ASA Class I, 4 patients had good results and one patient had poor outcome as a result of postoperative intracranial hematoma (ICH).

Of the 11 patients graded as ASA Class II, 10 patients had good results, and 1 patient had poor result due to wound infection. Among 10 patients with good results, 3 patients experienced postoperative problems resulting from wound infection, cerebrospinal fluid (CSF) leak, and toxic hepatitis. Two of the 4 patients graded as ASA Class III had good results without postoperative complication. In remaining 2 patients, 1 patient died in the postoperative period as a result of postoperative ICH and diffuse cerebral edema. The other patient had poor result because of additional postoperative medical complication.

The group of patients graded as ASA Class III showed higher incidence rate of postoperative comlications and poor outcome than the other two groups, but there were no statistically significant differences ($p>0.05$). Also, the overall incidence rate of postoperative complications and poor outcome were not significantly different among several ASA classes ($p>0.05$).

Preoperative Karnofsky Performance Scale (KPS) ratings

Of the 9 patients who received preoperative KPS ratings of 70 or 80, 6 had good results, and the other 3 patients had poor results owing to postoperative ICH, wound infection, and toxic hepatitis. Of the 11 patients who received KPS ratings of 90 or 100, 10 had good results, and 1 had poor result due to postoperative ICH. The incidence rate of postoperative comlications and poor outcome was not significantly different among several KPS scores ($p>0.05$).

Table 5. Clinical-Radiological Grading System (CRGS) of patients

Factor	Score					
	1		2		3	
KPS	≦50	(0)	60-80	(9)	90-100	(11)
Neurological condition*	Unrecoverable deficits	(2)	Progressive deficits	(4)	No deficits, only seizure	(14)
Concomitant disease†	Uncontrolled	(1)	Controlled	(10)	Absent	(9)
Size (cm)	≧6	(4)	4≦Ø<6	(5)	<4	(11)
Whether location is critical‡	Highly	(4)	Moderate	(9)	Not critical	(7)
Peritumoral edema§	Severe	(3)	Moderate	(11)	Absent	(6)

KPS : Karnofsky Performance Scale. * Unrecoverable deficits: deficits complete and stabilized (for example hemiplegia or amaurosis); progressive deficits : deficits incomplete or worsening (for example hemiparesis or impairment of visual acuity). † Concomitant diseases were evaluated as being compensated (controlled by medical therapy) or decompensated (uncontrolled despite medical therapy). ‡ A critical location is present if the tumor is attached to a primary vascular or nervous structure (such as the cranial or an eloquent area). § Peritumoral edema is classified as moderate (only peritumoral) and severe (with a shift of midline structures). ( ) : No. of operated patients

Table 6. Statistical correlation between various factors and surgical results

Factors	Outcome			Surgical	related	complication
	Good	Poor	p-value	none	occur	p- value
ASA						
1	4	1		1	3	
2	10	1	>0.05	7	4	>0.05
3	2	2		4	1	
KPS						
1	0	0		0	0	
2	6	3	>0.05	3	6	>0.05
3	10	1		9	2	
Neurologic condition						
1	0	2		0	2	
2	3	1	>0.05	1	3	>0.05
3	13	1		11	3	
Size						
1	1	3		1	4	
2	4	1	0.023	2	3	0.016
3	11	0		9	1	
Peritumoral edema						
1	0	3		0	3	
2	10	1	0.004	7	4	0.049
3	6	0		5	1	
Location						
1	1	3		1	3	
2	9	0	0.013	7	2	>0.05
3	6	1		4	3	
Concomittant disease						
1	2	2		1	3	
2	9	0	>0.05	7	2	>0.05
3	5	2		4	3	

ASA : American Society of Anesthesiology, KPS : Karnofsky Performance Scale

Neurological condition

Of the 2 patients who exhibited unrecoverable deficits, all had poor results with postoperative complications. Of the 4 patients who showed progressive deficits, 3 patients had postoperative complications, including one patient who exhibited a poor result. Among the 14 patients who presented normal neurologic findings, there were 3 patients with postoperative complications and of these, one patient had poor outcome. The impairment of the preoperative neurological condition was not significantly correlated with outcome and postoperative complications ($p>0.05$).

Tumor size

Of the 11 patients whose tumor were less than 4cm in diameter, all patients showed good results and of these, only 1 patient experienced postoperative problem resulting from a CSF leak. Nine patients had tumor size of more than 4cm with postoperative complications (including postoperative ICH in 2 patients, wound infection in 2, toxic hepatitis in 2, and hydrocephalus in 1). Of them, 4 patients with postoperative complications had poor results; 3 patients were required reoperation due to postoperative ICH and wound infection. The tumor sizes of these 3 patients were 6cm or more. The incidence rate of postoperative complications ($p=0.016$) and poor outcome ($p=0.023$) seem higher with larger maximum tumor diameters ($D\geqq 4cm$).

Peritumoral edema

Three patients who exhibited severe peritumoral edema had postoperative complications and all patients had poor results. Of the 17 patients who experienced either moderate or no edema, only 1 patient had poor result. Of the 11 patients who experienced moderate peritumoral edema, 4 patients had postoperative complications including postoperative ICH, wound infection, hydrocephalus, and toxic hepatitis. Statistically, the presence of a severe peritumoral edema was only associated with high

Table 7. Results of operated cases

CRGS	No. of pts.	No. of Cx.	Surgical related Cx. (p=0.049)		GOS
			Surgical	Medical	(p=0.004)
7	1	1	ICH	-	1 D
9	2	2	Hydrocephalus	Toxic hepatitis	1 SD 1 GR
10	1	1	Wound infection, Recur	-	1 MD
13	4	2	Wound infection, Recur	Toxic hepatitis	4 GR
14	1	0	-	-	1 GR
15	4	2	CSF leakage ICH	-	3 GR 1 MD
16	4	0	-	-	4 GR
17	4	0	-	-	4 GR

GOS : Glasgow Outcome Scale, CRGS : Clinical-Radiological Grading System. D : death, SD: severe disability, MD : moderate disability, GR : good recovery

incidence rate of postoperative poor outcome (p=0.004) and complications (p=0.049).

Location

Of the 4 patients whose tumor were located in the critical area, 3 had poor results due to postoperative ICH in 1, wound infection in 1 and toxic hepatitis in 1. Of the 7 patients whose tumor were not located in the critical area, only 1 patient showed poor results.

The group of patients whose tumor were located in the critical area showed higher incidence rate of poor outcome than the other two groups (p=0.013). But the incidence rate, of postoperative complications has no value showed no statistically significant difference ($p>0.05$).

Concomitant diseases

Of the 4 patients who had medically uncontrolled concomitant diseases, 2 patients had poor results. Of the 16 patients who had medically controlled concomitant disease or no underlying disease, only 2 patients had poor results. The presence of uncontrolled concomitant diseases may be associated with high incidence rate of postoperative poor outcome and complications, but there was no value statistical difference ($p>0.05$).

Clinical-Radiological Grading System (CRGS)

The total CRGS score ranged between 7 and 17 (mean 13.9). In Table 5, average values of the different subset items of the CRGS score in recruited patients was listed the majority of patients tended to cluster on second and third columns. The prognosis of 16 out of the 20 patients in which operations were performed were good, the CRGS scores of the 16 patients were 13 points or higher. The prognosis of the other 4 patients were poor; 1 patient (CRGS score 7) died within 7 days after surgery, 2 patients (CRGS score 9 and 15) showed moderate disability (MD), and 1 patient (CRGS score 9) showed severe disability (SD). Medical and surgical complications are shown in Table 7. The 40% of the patients had surgical related medical or surgical complications. Postoperative hematoma (n=2) and wound infection (n=2) were most frequent and the most severe complication was postoperative hematoma. These complications were directly responsible for poor outcome and in 1 patient, medical complication was significantly associated with poor outcome. Only patients with CRGS score equal to or higher than 13 had significant correlation with higher probability of good outcome (p=0.004) and a lower pro-bability of postoperative complications (p=0.049).

Discussion

In last two decades, life expectancy in the industrial nations has risen, so that more and more elderly patients with intracranial meningiomas come to the neurosurgical clinic, which raises the question of whether to operate or to observe. Papo[21] stated that surgery of intracranial meningiomas in elderly patients over 65 still remains a tremendous challenge despite all the advances in operative technique, neuro-anesthesia and intensive care. Due to the poor results, the author suggested that the surgical indications in these patients be carefully evaluated and that conservative management might be preferred. But later studies have reflected a substantial controversy on the effectiveness of surgical treatment in elderly patients affected with meningiomas[4,9,18,19,26], even in patients older than 80 years of age[17]. All these reports stress the importance of an accurate selection of patients to decrease the incidence of surgery-related mortality and morbidity. However, different scales were used, such as the ASA scale[24] and the KPS grading alone[14]. Djindjian et al.[12] preferred surgery for meningioma in the elderly when the KPS is rated 50 or higher and the physiological condition for anesthesia is good enough (ASA I or II). Umansky et al.[26] reported that those patients with a low KPS (less than 40) on admission present a more complicated postoperative course than those who were in good physical condition before surgery. Mastronardi et al.[17] recommended to attempt total removal of intracranial meningiomas even in very old patients (more than 80 years) if the preoperative ASA Classification is I or II and if the KPS is at least 70.

Results concerning the prognostic relevance of radiological

factors like peritumoral edema and tumor size are still controversial. Some authors emphasized the presence of peritumoral edema as a predictor of poor outcome in elderly patients[1,6,12,17], whereas others did not find any relationship between edema and unfavourable outcome[9,21,22]. Arienta et al.[1] studies 46 cases of intracranial meningioma in patients over 70 years of age, upon which 34 were operated. Severe edema was related to higher operative mortality rate (33%) and morbidity rate (25%) as well. Cornu et al.[9] also mentioned that the risk of postoperative morbidity seemed higher with severe peritumoral edema and most severe complication was a postoperative hematoma, which could be observed in 16%. Their observation was very similar to ours. Similarly, tumor size has been considered as a predictive factor for postoperative outcome by some authors[1,6,17]. In a series of symptomatic and asymptomatic intracranial meningiomas in very elderly patients (aged 80 yr or more), Mastronardi et al.[17] reported that the risk of postoperative morbidity was higher when the maximun tumor diameter of the tumor was 5cm or over. Buhl et al.[6] also reviewed 66 patients older than 70 years old with intracranial meningioma. In 15 patients with meningioma larger than 5cm, eight patients were deteriorated clinically (55%). In our study, there were two cases requiring reoperation due to the occurrence of ICH after the removal of the tumor. The tumor sizes of both cases were 6cm or larger.

Several authors have pointed out that outcome is less favourable in elderly patients with meningiomas located at the base of the skull, especially the posterior fossa[1,2,6,9,22]. Cornu et al.[9] reported that elderly patients with a tumor located on the skull base or posterior fossa had a relative risk of poor outcome of 3.27 fold by comparison on patients with tumors at other locations. Arienta et al.[1] emphasized that location of the tumor was one of the determing factors for the duration of surgery and therefore indirectly affected mortality, since skull base or posterior fossa meningiomas led to longer surgery and higher mortality rates in elderly patients.

The introduction of gamma knife surgery not only led to change in the treatment of benign tumors but also provided a useful tool for dealing with residual and recurrent tumor[8,11,15,16,25]. Sonoda et al.[25] suggested that the most important treatment aim in elderly meningioma patients was tumor control and the maintenance of their ability to pursue their acitivities of daily life. For there. they developed multimodal treatment strategy comprised of surgery, gamma knife surgery, and careful follow-up. However, we couldn't analyze the natural course of patients with other therapeutic modalities. Meaningful answers in this regard would require a randomized prospective study.

Many elderly patients suffer from underlying diseases like diabetic mellitus or hypertension etc.. Even though a certain disease may not be evident in elderly people, the function of their organs can be decreased. Additionally, the prevalence rates of disease and the death rates are higher and the rehabilitation period is longer because elderly patients' recovery capabilities are poorer than that of young patients, especially when postoperative complications develop. Gijtenbeek, et al.[13] indicated that complications such as wound infection, embolism, brain edema, pneumonia etc., more frequently occurred among elderly patients who had surgery. Hence, it was considered that the occurrence of these should be observed in the greatest detail. Black, et al.[4] revealed, with a study of 417 meningioma patients aged 65 or over, that the mortality and morbidity at the 30th day after surgery were high, at 16% and 39% respectively. Consequently, they showed that precise evaluation of patients' condition, with intensive care, and rehabilitation before and after surgery were indispensable. In our series, the presence of uncontrolled concomitant diseases may be associated with high incidence rate of postoperative poor outcome and complications although there these were not statistically different ($p>0.05$).

Summing up all these studies, Arienta et al.[1,7] showed that CRGS which was concerned with neurological condition, preoperative KPS, tumor size, tumor location, the degree of edema and concomitant diseases, could act as a crucial standard, determining whether or not elderly patients should undergo surgery for meningioma. They established that a score of 10 was the cutoff for the surgical indication; a patient with a score higher than 10 was the best candidate for surgery. Once more, they pointed out that female patients, peritumoral edema and concomitant disease were statistically significant with poor prognosis, but age, location, KPS, and neurological symptoms were not. In our study, we found that a score of 13 was the cutoff for the surgical indication ($p<0.05$). Also, we detected that tumor size ($D\geqq 4$cm), severe peritumoral edema and critical location among the different subset items of the CRGS score showed statistical significance with poor prognosis ($p<0.05$).

Conclusion

We believe that the CRGS score can be a useful and practical tool for the selection of elderly patients harboring intracranial meningiomas. Especially, when CRGS is high, i.e. 13 points or over, aggressive treatment including surgical treatment will be helpful to improve the quality of life, even though patients are older than 65. However, it is to keep in mind that when the tumor is larger ($D\geqq 4$cm), when peritumoral edema is severe, and when tumor is located in the critical area, there is a poor prognosis.

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Commentary

We neurosurgeons not infrequently meet elderly patients with meningiomas for the increasing elderly population together with availability of modern imaging techniques. Some patients are asymptomatic and the others have serious neurological symptoms. According to recent reports, age in general is not a contraindication for operation. The incidentally found small meningiomas are recommended observation with image follow-up. In contrast, symptomatic meningiomas should be removed whenever there is an acceptable risk from an internal or anaesthesiological point of view. To date, we however do not have the exact knowledge about the biological behavior and any common consensus on the management of the meningiomas in elderly persons.

In this paper, the various factors were analyzed to verify the causal relation among them in terms of the prognosis after surgical removal of meningiomas and to seek the proper treatment guidelines for elderly patients with meningiomas. Authors suggest that the CRGS score can be a helpful criteria to evaluate the indications for operative treatment in elderly patients with meningiomas. Although the sample size is not large, this paper contribute to improve our understanding in the management of elderly patients with meningiomas.

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