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TITLE PAGE

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Outcome of elderly patients undergoing intracranial meningioma resection: a single center experience.

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ABSTRACT

Background: Higher life expectancy and higher mean age in general population created growing interest in medical and surgical management of meningiomas in elderly. It is well known that, due to possible complications, pre-operative status and comorbidities, expecially in aged people, should be carefully considerated in the decision-making process. We described our experience with this kind of patients and analized the influence of complications on the outcome.

Methods: We conducted a monocentric retrospective study to evaluate outcome and complications in elderly patients that underwent intracranial meningioma surgery in our center in a ten year period. Between January 2005 and December 2014, 107 patients - older than 70 years old - were operated for an intracranial meningioma. We excluded patients operated for a recurrent meningioma. We use the Dindo classification modified by Poon to describe complications and the Karnofsky Performance Status Scale and Glasgow Outcome Scale to evaluate the outcome at discharge and after a 6 months period.

Results: 84 patients did not have postoperative complications, 10 patients had mild postoperative complications, while 13 patients suffered severe postoperative complications. As a group, patients with mild complications presented, six months after surgery, an average Karnofsky Performance Status better than preoperative one.

Conclusions: Even though the fragility is considered an important risk factor, surgery for symptomatic intracranial meningiomas should be considered also in elderly patients. The presence of early postoperative mild complications do not seem to worsen the average 6 months- KSP score.

Keywords: meningioma, elderly, outcome, complications

MANUSCRIPT

Introduction

Meningiomas represent more than a third of all primary intracranial tumors[1]. The average age at diagnosis is around 65 years old[2,3]. The incidence of this kind of tumor rises with age[4]. Higher life expectancy and higher mean age in general population created growing interest in medical and surgical management of meningiomas in elderly. This tumors are mostly benign and a gross total resection allows complete biological recovery, although high rate of morbidity and recurrence should be kept in mind. Nowadays, many authors agree that operating meningiomas in elderly patients[5] brings to worse results. Anyway, a careful preoperative evaluation should be done: many comorbidities, such as hypertension, diabetes, respiratory disease, ischemic heart disease, cause increased perioperative risks. Mortality and morbidity in these kind of patients are indeed reported between 0 and 12% and between 2.7 and 29.8%, respectively[6]. Different prognostic grading systems were proposed[7,8]. Poon et al. compared mortality and morbidity between young and old patients undergoing surgery for intracranial meningiomas[9], by outlining that no mortality rate difference between the two groups was found and that, on the contrary, elderly patients had a higher overall complication rate, required longer hospital stay, and were more likely to suffer from added neurological deficits. Moreover, these considerations underline the importance of a proper patient selection for surgical treatment, based on a careful preoperative study of the patient's general status and comorbidities. We report our experience in surgical treatment of intracranial meningiomas in a group of 107 patients of over 70 years of age, who underwent surgery for intracranial meningiomas, focusing our attention to the complications rate and their influence on long-term outcome.

Materials and Methods

We conducted a monocentric, retrospective study on 107 consecutive patients referring at our Institution from January 2005 and December 2014 for an intracranial meningioma. Patients were eligible to surgery if they were symptomatic or they showed a tumor growing at the follow-up imaging determining an asymptomatic mass effect on surrounding brain; they were not eligible if KPS was less than 50 and removal of meningioma would not change preoperative disability surely. Patients operated for recurrence were not included in the study. We recorded for each patient baseline characteristics (gender, age, comorbidities and clinical onset). Pre-operative assessment considered American Society of Anesthesiologist (ASA) score and Karnofsky Performance Status (KPS) at admission. Tumor characteristics analyzed were side (divided in right, left or median), origin and World Health Organization (WHO) histological classification; the origin was divided in two groups: “A” group including convexity, falcine and parasagittal tumors; “B” group made up by skull base, cerebellopontine angle and foramen magnum/tentorium/craniocervical junction. Operative informations considered Simpson grading of tumor resection. Post-operative outcome was evaluated by Glasgow Outcome Scale (GOS) at discharge, length of hospitalization, discharge destination (home discharge vs transfer to rehabilitation ward) and KPS at the discharge. The follow-up analysis was focused on 6 months mortality and KPS.

Follow-up data were all collected by an outpatient interview. We analyzed postoperatory complications according to Dindo et al. classification[10] modified by Poon[9] (table 1), dividing patients into three groups:

- patients with none complications (group 1);

- patients with “mild complications” that was referred to cases with grade 1 or 2 of complications (group 2);

- patients with “severe complications” that was referred to case with grade 3 or 4 of complications (group 3);

In every group we analyzed the difference from the mean KPS at the discharge and the mean preoperative KPS, and the difference from the mean KPS at 6 months and the KPS during the preoperative period.

Statistical analysis

Continuous numeric variables were summarized as mean and standard deviation for normalized distributed variables and as median and interquartile range for non-normalized variables. Categorical variables were summarized in the form of percentage proportions. The differences in numeric variables were evaluated with ANOVA test for normalized distributed variables or Wilcoxon signed-rank test for non-parametric statistical analysis as appropriate. The differences in categorical variables were compared using chi-square or Fisher exact test when appropriate. All tests were two-tailed and a P-value < 0.05 was determined to represent statistical significance. All statistical analyses were performed using Epi-Info 7.0 (Centers for Disease Control and Prevention, CDC, Atlanta, GA, USA) and JMP ® 10 (SAS Institute Inc., Cary, NC; USA) program for Windows.

Results

This study included 107 patients aged between 70 and 86 years old. We divided them in three groups: 84 (78.50%) without complications (group 1), 10 (10.7%) with mild complications (group 2) and 13 (12.15%) with severe complications (group 3). Women were 78 (72.89 %) and the majority (71.43%) was in the first group. Men were 29 (27.1 %) without any male patient in the second group. Mean age of the group recruited was approximately 75 years with females slightly

older than males. Age range was from 70 to 86 years old, with about the same mean age in each group. As for as comorbidities are concerned, hypertension had the highest prevalence in every group; other common disorders were a tumor history, an heart disease, renal failure, brain disorders, pulmonary disease and diabetes mellitus/dyslipidemia. The main onset symptoms were focal deficit and signs of intracranial hypertension, even if in every group about 20% of patients come to our attention for a seizure. Five patients were asymptomatic before intervention. The prevalent preoperative ASA score was class 2 or 3 for all three groups, while only 2 cases were defined by an ASA score of 4 (one in the group of "none complications" and one in the group of "mild complications"). Preoperative KPS range from 40 to 100 and the median preoperative KPS was 71.9 for patients without complications, 69 for patients with mild complications and 76.92 for patients with severe complications. None patients had a KPS less than 40. Considering all the cases in group A, the origin of the tumor was above all at convexity in 60 cases, at the falx in 9 cases and it was a parasagittal tumor in 3 cases; as for as group B is concerned, we had 22 cases of skull base meningiomas, 8 cases of foramen magnum, tentorium and craniocervical junction tumors, while it originated in pontocerebellar angle in 5 cases. Patients with severe complications presented a midline meningioma in the 23.08%, while tumor was in the left hemisphere in 51.19% and in the right hemisphere in 37.74%. In the first two groups, the tumors were at the convexity/falx/parasagittal region respectively in the 70.24% and in the 70%, while in the group of severe complications the tumor was located at the convexity only in the 46.15% of case. Most lesions were WHO grade I in all three groups. Simpson score was used to evaluate surgical resection of meningiomas: a grade I was reached in the greater part of the patients. 23 patients suffer from at least one complication: 10 were of grade 2, 10 of grade 3 and 3 of grade 4 according to Dindo et al classification modified by Poon (Table 2). Median Glasgow Outcome Scale (GOS) at discharge was 4.15 in the first group, 3.8 in the second group and 3.69 in the third group (the range was from 2 to 5) respectively. None GOS grade 1 was found, so perioperative mortality was 0%

and only 2 patients (1.87%) had a GOS=2. Mean duration of hospitalization has been almost the same in the first two groups (10.7 and 10.6 days), but it was twice longer in the third group (22.23 days). In the first group 51.19% of the patients was discharged at home while in the second and in the third group only the 20% and the 46.15% was discharged at home, respectively. We report 5 deaths in the first postoperative years: 2 in the not-complicated patients and 3 in the patients with severe complications (in each group one exitus was not correlated to the meningioma). Postoperative KPS went from 30 to 100, its mean was 73.69 in the first group, 65 in the second group and 73.3 in the third group. Only in the first group it was higher than preoperative mean KPS (+ 1.78), while in the second and third group it was lower (respectively – 4 and -3.85) than the preoperative mean KPS. Mean KPS at six months was 79.88 in the first group, 80 in the second one and 60 in the third one. So the mean KPS at six month was +6.16 points higher than the postoperative mean KPS for patients without complications; it was +15 points higher than the mean postoperative KPS for patients with mild complications and it was -13.07 points lower compared to the mean postoperative KPS in patients with severe complications. Mean KPS at six months was higher than mean preoperative KPS in the first two groups (respectively +7.98 and +11), but it was lower in the third group (-16.92). Attitudes of study population and patients characteristics according to type of complications are summarized in table 3 and 4, respectively.

Discussion

Especially in elderly patients, postoperative complications often frighten the surgeon. According to the literature, postoperative complication rate for an intracranial meningioma removal is between 2.7% and 29.8%[6]. For this reason, we have retrospectively analyzed their effect on 6-month outcomes in elderly patients operated for intracranial meningioma. According to the literature, also our population was composed by a majority of women[9]. As expected, this kind of patients have a lot of comorbidities - the most frequent was hypertension - that determined an ASA score of 2 or 3 in

most of cases. The main onset symptoms were focal deficit, signs of intracranial hypertension and seizure. Preoperative conditions were discrete (mean KPS of about 70), all due to the fact that meningiomas were symptomatic. Considering all the groups, about 70% of patients received a complete resection of the tumor with at least dural coagulation (Simpson grade 2 or higher). Even by comparing the rate of complications and mortality, our results do not deviate from what is reported in the literature[9] . In fact our cases of mortality happened from 4.7 to 6 months after intervention and only the 2.8% of cases was related to the disease; nevertheless no cases of perioperative mortality was reported. As for as complications are concerned, we report them in 21.5% of the patient: in 9.3% mild and in 12.2% severe. Considering the outcome of the three groups we have seen that in the second group (mild complications) the initial worsening is recovered six months away. As expected, in the second group the majority of patients are transferred to a rehabilitation center and this element seems to be an element for the improvement of KPS at 6 months without any doubt. This data confirm the importance of a proper rehabilitation: if adequately followed, the patient after 6 months of treatment can improves his or her KPS beyond the preoperative one. Nevertheless, if we consider data, this inference could be done only for the mild complication group, as the severe one shows a worsening of KPS at 6 months. However, these data should be better evaluated: excluding deceased patients, only 2 patients with serious complications worsened with regard to remote KPS. An adequate rehabilitation period can be therefore recommended also in patients with severe complications. All this indicates that in addition to a good patient selection, by a careful evaluation of preoperative risks, a proper postoperative and rehabilitation management can be crucial. The center where elderly patients with intracranial meningiomas are treated must therefore have a good network of rehabilitation centers to provide adequate post-operative care and recover as much as possible.

The principal limit of our study is the small number of patients and the different distribution of them among the three complication-related groups. For these reasons, our findings has not a statistical power, as confirmed by p-value obtained.

In conclusion, our results show as seniority do not seem to represent a key factor as for as surgery clinical outcome is concerned. Nevertheless, more studies are necessary to confirm this sentence and the role of single adjuvant therapies (for example the rehabilitation program) to determine short- and long-term outcome.

Conclusions

In our view, advanced age can no longer be considered alone as a criterion of exclusion for the surgical treatment of this type of disease. Careful preoperative assessment is essential for proper patient selection; the presence of postoperative mild complications do not seem to affect the outcome at 6 months and even patients with severe complications could improve with time and a correct rehabilitation program; nevertheless, more studies are necessary to confirm it.

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Table 1: Dindo et al. classification modified by Poon et al.

Grade	Description
I	Requiring no treatment other than the 'allowed' therapeutic regimens (antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy), and wound infections opened at the bedside
II	Requiring blood transfusions, total parenteral nutrition, or pharmacological treatment other than the 'allowed' regimens
III	Requiring surgical, endoscopic or radiological intervention
IV	Life-threatening complication (including CNS complications)a requiring IC/ICU management

Table 2: Recorded complications

Complications	Grade	N.	Description
Mild complications	Grade 1	0	
	Grade 2	10	4 hematomas in surgical side treated conservatively; 1 DVT treated pharmacologically; 5 neurological deficits and / or seizures not associated with hematoma in the surgical side
Severe complications	Grade 3	10	3 CSF fistulas treated with ESD; 2 hydrocephalus treated with VPS; 3 wound infections treated with surgical cleaning; 1 acute colecystitis treated with cholecystectomy; 1 DVT treated with vena cava filter
	Grade 4	3	1 massive hematoma of the hemispherical center; 1 empyema and important bleeding;

			1 septic shock

DVT= deep venous thrombosis; CSF= cerebral spinal fluid; ESD= external spinal drainage; VPS= ventriculo-peritoneal shunt

Table 3: Characteristics of study population (N=107)

Variables	N. (%)
Patients characteristics and preoperative features	
Age , mean (SD)	75.1 (3.9)
Gender	
Male	29 (27.1)
Female	78 (72.9)
ASA Score	
I	5 (4.7)
II	58 (54.2)
III	42 (39.2)
IV	2 (1.9)
Comorbidities	
neoplastic disease	15 (14)
hypertension	65 (60,7)
heart disease	25 (23,4)
renal failure	2 (1,9)
brain disorders	13 (12,1)
pulmonary disease	9 (8,4)
DM/dyslipidemia	22 (20,6)
Meningioma and perioperative features	
KPS at admission, mean (SD)	72.2 (13.5)
Side of meningioma	
Midline	10 (9.4)
Left side	44 (41.1)
Right side	53 (49.5)
Location of meningioma	
Convexity/falcine/parasagittal	72 (67.3)
Skull-base	35 (32.7)
Histology	
Grade I	90 (84.1)
Grade II	11 (10.3)
Grade III	6 (5.6)
Simpson score	
I	62 (57.9)
II	25 (23.4)
III	1 (0.9)
IV	19 (17.8)
Postoperative features	
Length of hospital stay, mean (DS)	12.1 (9.5)

Postoperative KPS, mean (SD)	72.8 (17)
Discharge	
At home	51 (47.7)
Long-term care facility	56 (52,3)
GOS at discharge	
1	0 (0)
2	2 (1.9)
3	17 (15.9)
4	55 (51.4)
5	33 (30.8)
Complications	
None	84 (78.5)
Mild	10 (9.3)
Severe	13 (12.2)
KPS at 6 months, mean (SD)	77.5 (23.1)
Related 1-year mortality	3 (2,8)

Table 4: Patients' Characteristics According to type of complications

Variables	Group 1 (N=84)	Group 2 (N=10)	Group 3 (N=13)	p-value
Patients characteristics and preoperative features				
Age , mean (SD)	75.2 (4.1)	75.5 (3.8)	74.3 (3.3)	0.73*
Gender				0.1^
Male	24 (28.6)	0 (0)	5 (38.5)	
Female	60 (71.4)	10 (100)	8 (61.5)	
ASA Score				0.34^
I	3 (3.6)	1 (10)	1 (7.7)	
II	48 (57.1)	5 (50)	5 (38.5)	
III	32 (38.1)	3 (30)	7 (53.8)	
IV	1 (1.2)	1 (10)	0 (0)	
Comorbidities				
neoplastic disease	10 (11.9)	2 (20)	3 (23.1)	0.47^
hypertension	51 (60.7)	4 (40)	10 (76.9)	0.20^
heart disease	21 (25)	2 (20)	2 (15.4)	0.72^
renal failure	2 (2.4)	0 (0)	0 (0)	0.76^
brain disorders	10 (11.9)	1 (10)	2 (15.4)	0.92^
pulmonary disease	5 (5.9)	2 (20)	2 (15.4)	0.20^
DM/dyslipidemia	16 (19)	3 (30)	3 (23.1)	0.70^
Meningioma and perioperative features				
KPS at admission, mean (SD)	71.9 (13)	69 (16.6)	76.9 (13.8)	0.33*
Side of meningioma				0.48^
Midline	6 (7.1)	1 (10)	3 (23)	
Left side	35 (41.7)	4 (40)	5 (38.5)	
Right side	43 (51.2)	5 (50)	5 (38.5)	
Location of meningioma				0.22^
Convexity	59 (70.2)	7 (70)	6 (46.1)	
Basal	25 (29.8)	3 (30)	7 (53.9)	
Histology				0.95^
Grade I	71 (84.5)	8 (80)	11 (84.6)	
Grade II	9 (10.7)	1 (10)	1 (7.7)	
Grade III	4 (4.8)	1 (10)	1 (7.7)	
Simpson score				0.90^
I	49 (58.3)	5 (50)	8 (61.5)	
II	21 (25)	2 (20)	2 (15.4)	
III	1 (1.2)	0 (0)	0 (0)	
IV	13 (15.5)	3 (30)	3 (23.1)	
Postoperative features				
Length of hospital stay, mean (DS)	10.7 (6.8)	10.6 (3.6)	22.2 (18.3)	< 0.001*
Postoperative KPS, mean (SD)	73.7 (15.1)	65 (20.7)	73 (24.3)	0.31*
Discharge				0.03^
At home	43 (51.2)	2 (20)	6 (46.15)	
Long-term care facility	0 (0)	0 (0)	1 (7.7)	
T	41 (48.8)	8 (80)	6 (46.15)	
GOS at discharge				0.02^
1	0 (0)	0 (0)	0 (0)	

2	0 (0)	1 (10)	1 (7.7)	
3	12 (14.3)	3 (30)	2 (15.4)	
4	47 (55.9)	5 (50)	3 (23.1)	
5	25 (29.8)	1 (10)	7 (53.8)	
KPS at 6 months, mean (SD)	79.9 (19.4)	80 (16.3)	60 (39.2)	0.01*
Related 1-year mortality	1 (1.2)	0 (0)	2 (15.4)	< 0.001^

* P-value was obtained with ANOVA test

^ P-value was obtained with Chi-square test