UNIVERSITE DE LAUSANNE - FACULTE DE BIOLOGIE ET DE MEDECINE

Département des Neurosciences Cliniques
Service de Neurochirurgie

Prognostic factors and role of adjuvant therapies in the management of parasagittal meningiomas

THESE

préparée sous la direction du Docteur Jocelyne BLOCH

et présentée à la Faculté de biologie et de médecine de
l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

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Lausanne

2011

UNIL | Université de Lausanne
Faculté de biologie
et de médecine

Ecole Doctorale
Doctorat en médecine

Imprimatur

Vu le rapport présenté par le jury d'examen, composé de

Directeur de thèse	*Madame le Docteur* **Jocelyne Bloch**
Co-Directeur de thèse	
Expert	*Monsieur le Docteur* **Andrea Rossetti**
Directrice de l'Ecole doctorale	*Madame le Professeur* **Stephanie Clarke**

la Commission MD de l'Ecole doctorale autorise l'impression de la thèse de

Monsieur Jimmy Villard

intitulée

Prognostic factors and role of adjuvant therapies in the management of parasagittal meningiomas

Lausanne, le 17 avril 2012

pour Le Doyen
de la Faculté de Biologie et de Médecine

Madame le Professeur Stephanie Clarke
Directrice de l'Ecole doctorale

RESUME:

Contexte:

L'objectif du présent travail de thèse est d'analyser rétrospectivement la série de méningiomes parasagittaux traités au CHUV, soit par traitements simples ou combinés (chirurgie et / ou radiochirurgie et radiothérapie fractionnée), afin de déterminer les facteurs qui influencent leur pronostic.

Méthode:

Entre Janvier 1999 et mai 2007, 37 méningiomes parasagittaux ont été traités dans notre centre. Nous avons analysé de manière rétrospective les différents paramètres du traitement de ces méningiomes ainsi que leur emplacement le long du sinus sagittal supérieur, leur volume, leur grade histologique et le degré de résection ainsi que le sexe et l'âge du patient afin de comprendre les facteurs qui influencent leur histoire naturelle.

Résultats:

Le suivi médian était de 6,7 ans (2,4 -12 ans). Les grades histologiques et le degré de résection tumorale (Simpson) étaient répartis uniformément le long du sinus sagittal supérieur. Le taux actuariel de contrôle global des tumeurs était de 65,9%. L'analyse de régression montre que le grade tumoral et le degré de résection sont deux facteurs extrêmement importants pour déterminer le contrôle tumoral ($p < 0,002$ et $p < 0,008$). La localisation le long du sinus sagittal supérieur a montré une baisse du taux de contrôle dans le tiers postérieur ($p < 0,002$). Le sexe, l'âge et le volume de la tumeur n'étaient quand à eux pas des facteurs significatifs. Par ailleurs, et de façon inattendue, dans notre série, la proportion du traitement adjuvant a été beaucoup plus élevée que dans les séries décrites jusqu'à maintenant (39% vs 7%) mais avec un taux de contrôle similaire et diminution de la morbidité et la mortalité.

Conclusions:

Dans notre série, le grade histologique et le degré de résection tumorale (Simpson) sont des facteurs indépendants de récidive et de contrôle tumoral. Fait intéressant, l'emplacement dans le tiers postérieur du sinus sagittal supérieur semble être un autre facteur indépendant de récidive. Afin d'éviter les morbidités importantes liées à la chirurgie nous préconisons une utilisation précoce de traitements adjuvants pour les tumeurs grade histologique élevé et pour les tumeurs situées dans la partie postérieure du sinus sagittal supérieur.

Article accepté pour publication dans "Journal of Radiosurgery & SBRT (Stereotactic Body Radiation Therapy)"

Editor-in-Chief: Samuel Ryu

ISSN: 2156-4639 (print)

ISSN: 2156-4647 (online)

80 pages/issue · 8.5" x 11"

Issue Coverage: Volume 1 (2010) – Present

Prognostic factors and role of adjuvant therapies in the management of parasagittal meningiomas

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Sources of Support: None

ABSTRACT:

Background:

The goal of the present study was to retrospectively analyze our series of parasagittal meningiomas, treated by either single or combined therapies (surgery and/or SRS and FSRT), in order to determine the factors that influence patient outcome.

Methods:

Between January 1999 and May 2007, 37 parasagittal meningiomas were treated in our center. We compared the outcome of the parasagittal meningiomas in relation to the treatment and adjuvant treatment given, their location along the SSS, their volume, their histological and resection grade as well as the patient's sex and age to understand which factors influenced their natural history.

Findings:

Median follow-up was 6.7 years (2.4 -12 years). Tumor grades and Simpson resection grade were distributed evenly along the SSS. The actuarial overall tumor control rate was 65.9 %. Regression analysis showed, that the tumor histological grade and the Simpson resection grade were two significant factors in determining the tumor control ($p<0.002$ and $p<0.008$). Location along the SSS showed a lower control rate in the posterior third ($p<0.002$). Sex, age and tumor volume, however, were not significant factors. Moreover, and unexpectedly, the In our series, the proportion of adjuvant treatment was much higher than in former described series (39% vs 7%) but with similar control rate and lower morbidity and mortality.

Conclusions:

In our series, histological grade and Simpson grade are independent factors for recurrence and tumor control. Interestingly, location in the posterior third of the SSS seems to be another independent factor for recurrence. In order to avoid major morbidities related to surgery we advocate earlier use of adjuvant therapies for higher histological grade tumors and for tumors located at the posterior portion of the SSS, but definitive conclusions might warrant a larger series.

Key words: parasagittal meningiomas, neurosurgery, stereotactic radiosurgery, brain radiotherapy, tumor control, prognosic factors

Abbreviations:

FSRT: fractionated stereotactic radiotherapy

SD: standard deviation

SRS: stereotactic radiosurgery

SSS: superior sagittal sinus

INTRODUCTION:

Meningiomas represent 15 to 20% of all primary intracranial tumors. Most of them are benign tumors and can be cured if completely resected. Surgery is the gold standard treatment for the majority of meningiomas, and has been proven to be the best way to achieve tumor control if the tumor is completely removed together with any dural involvement (18). However, stereotactic radiosurgery and fractionated stereotactic radiotherapy are alternative therapeutic strategies when the meningiomas are located in delicate areas or in the case of recurrences. Indeed, tumors associated with significant surgical risks are those located close to vascular structures or cranial nerves. Among them, parasagittal meningiomas are challenging tumors due to their anatomic relation to the SSS. These tumors were defined by Cushing and Eisenhardt (7) as those that fill the parasagittal angle, with no brain tissue between the tumor and the SSS. Their intimate relation with the SSS and with critical bridging veins poses a risk for catastrophic complications. Their tendency of invading the SSS adds another challenge for the surgical resection. It is therefore necessary to find the right balance between aggressive surgical resection and the risk of complications (17). In our center, a multidisciplinary approach was preferred over aggressive surgical treatment for these tumors.

Parasagittal meningiomas comprise between 17 and 31% of intracranial meningiomas (3, 5-7, 11, 13, 21, 22). Their distribution along the SSS has already been reported to range from 14.8% to 33.9% in the anterior third, 44.8% to 70.4% in the middle third, and 9.2% to 29.6% in the posterior third of the sinus respectively (6, 7, 9-11, 17). Despite the improvement in the imaging of these tumors, the involvement of the SSS and surrounding veins make these tumors hard to remove completely, thus their management represents a real challenge due to the relatively high mortality and morbidity. Their rate of recurrence remains high despite the routine use of microsurgery and adjuvant therapy, and previous studies have shown that they tend to recur more often than meningiomas in other locations (4, 16).

The aim of the present retrospective study is to analyze factors that influence the outcome of patients treated for parasagittal meningiomas at the Departments of

Neurosurgery and Radiation Oncology at the Centre Hospitalier Universitaire Vaudois (CHUV), in Lausanne, Switzerland.

MATERIAL AND METHODS :

Patients

A total of 225 patients were treated for intracranial meningiomas in our center between January 1999 and December 2007. Among them, 37 parasagittal meningiomas, including two patients with multiple meningiomas, were treated. Patients with neurofibromatosis were excluded, although representing 9 parasagittal meningiomas. Therefore a total of 28 parasagittal meningiomas were included in our series. Patient data, including surgical records, discharge letters, histological records, follow-up records and MR imaging studies were analyzed retrospectively. Patients with multiple meningiomas were of similar age and sex distribution as the overall population. Follow-up MR imaging studies were obtained at 3 and 9 months and then annually. Moreover, each patient was clinically evaluated 6 weeks after surgery and then following each MR imaging. Median follow up was 6.7 years (2.4 - 12 years). No patient was lost during follow-up.

Treatments

As a primary treatment, surgery was the first line of treatment for all patients for meningiomas over 1cm diameter or $0.5cm^3$. Tumor exposure and removal were performed with standard microsurgical techniques. In patients with complete SSS obliteration in the anterior third of the SSS (2/28) (Sindou grade Type V and VI (19, 20)), ligation and section of the proximal and distal ends of the sinus allowed an "en bloc" removal of the tumor. No attempt at complete sinus resection followed by reconstruction was performed when the tumor was placed in the posterior two thirds of the SSS. A dural patch was then used to reconstruct the dura and the bone flap was then fixed to the cranium using low profile titanium mini plates. The extension of the resection was assessed during surgery and with a postoperative MRI.

Stereotactic Radiosurgery (SRS) and Fractionated Stereotactic Radiotherapy (FSRT) were performed using a 6-MV photon beam provided by a Primus linear accelerator (Siemens®, USA) and a micromultileaf collimator with 3 mm width leaves at isocenter (Brainlab®, Germany).

SRS was performed for meningiomas under 1 cm as a first intention treatment in case of symptomatic meningiomas or radiological proof of progression (2 patients). SRS was also a second intention therapy for recurrences or residual tumor under 3 cm (7 patients) [Figure 1]. Patient immobilization and target volume definition was achieved using the Radionic stereotactic frame (Integra®, USA). After fixation of the stereotactic frame under local anesthesia, a three-dimensional CT data cube generated from continuous 2-mm CT scan slices was performed and was then fused with a previous non-stereotactic MPRAGE gadolinium MRI. When the size was under 1 cm, a dose of 18 Gy at the isodose 80% was delivered in a single fraction. For meningiomas between 1 and 3 cm, a dose of 16 Gy at the isodose 80% was delivered a single fraction.

FRST was used for the same indications as for SRS but for meningiomas larger than 3 cm. Patients were immobilized using a commercially available stereotactic mask (BrainLAB® Mask System) made of thermo-plast material. The main goal of treatment planning was complete coverage of the tumor volume with the prescribed dose and maximal dose limitation to adjacent critical structures. A median dose of 54.6 Gy (range 50.4 Gy - 60 Gy) at the isocenter was delivered, with a dose of 1.8 Gy per fraction, an a median of 31 fractions.

Statistics

A regression analysis was performed examining the influence of sex, age, Simpson resection grade, tumor size, tumor location, type of treatments and adjuvant treatment received and tumor histology at diagnosis. Recurrence-free survival rates (calculated from date of first treatment to date of first recurrence, or last follow-up in patients with no recurrence) were estimated with the Kaplan-Meier method. Additional comparisons used Student T-tests and Chi-square tests as appropriate.

RESULTS:

Epidemiology

There were 14 females (50%) and 14 males, with a mean age at diagnosis of 54.8 ± 13 years. Tumor volumes ranged from 0.5 cm^3 to 113 cm^3, with a median volume of 13.4 cm^3 (0.5-113 cm^3). The location along the SSS was: 8 (28.5%) in the first anterior third, 11 (39.2%) in the middle third and 9 (32.1%) in the posterior third. There was no significant difference in the location for sex and age. [Table 1]

Treatments

Two patients had SRS as their sole treatment due to their meningioma size (0.76 cm and 0.75 cm). The other twenty-six patients underwent surgery as the first treatment. Among these, fifteen patients had surgery only (53.57%) and eleven (39.2%) had an adjuvant treatment. Recurrence, as defined by reappearance of a meningioma on MR imaging in the same location as the previously treated and completely removed meningioma, occurred in 8 patients and progression, as defined by progression of a residual tumor on MR imaging, happened in 3 patients who had subtotal resection. Surgery was proposed as a second-intent treatment in our series for two patients with incomplete resection and re-growth that necessitated a second surgery; both had histological grade progression and will be discussed below. Radiosurgery was performed in two cases after incomplete surgery with progression during follow-up and in four cases of recurrence. Three patients had fractionated stereotactic radiotherapy for recurrence (2) or subtotal surgery with progression (1). Two patients had both radiosurgery and fractionated stereotactic radiotherapy for recurrence. These data are summarized in [Figure 1].

Simpson grades

Simpson grade of resection was determined for the 26 patients who underwent surgery. Two patients had complete anterior third SSS obliteration with "en bloc" removal of the parasagittal meningioma and of the invaded sinus. In our series, location along the SSS was not a determining factor for Simpson grade of resection.

The resection grade in the anterior third of the sinus was: Simpson I in seven patients and Simpson IV for one patient. In the middle third of the sinus, the distribution was three Simpson I, seven Simpson II and one Simpson III respectively. Finally, in the posterior third of the SSS there were two Simpson I, one Simpson II, three Simpson III and one Simpson IV respectively. There was no statistically significant difference ($p=0.20$) in the Simpson grade along the SSS. [Table 2]

Histological grades

According to the WHO classification (14), 18 patients presented grade I (benign) meningiomas (7 transitional, 5 meningothelial, 4 fibroblastic, 1 angiomatous, 1 mixed), 6 had grade II (atypical) and 2 had grade III meningiomas. In 2 patients treated with radiosurgery only, histological grade was not available. Their distribution along the SSS is summarized in [Table 2]. Here again, there was no statistically significant difference of histological grade distribution along the SSS ($p<0.09$) but males in our series tended to present higher grade lesions than women ($p<0.01$). Age and tumor size were not related to the histological grades ($p=0.39$ and 0.32 respectively).

Two patients had a histological progression during the course of their disease. The first patient was 34 years old when he presented a second third SSS, frontal parasagittal meningioma with partial sinus obliteration. Partial resection was performed in 1999 and the histology was that of a grade I meningioma. Three years later, the follow-up showed growth of the residual tumor motivating a second surgery. The histology then demonstrated an atypical meningioma with a high mitotic rate and it was decided therefore to perform radiosurgery on the 1.2cm residual tumor that could not be resected during the second surgery. The second patient presented at the age of 65 with a posterior third SSS parasagittal meningioma. He had a first incomplete resection due to the partial sinus obliteration. The histology at that time was that of a menigiomatous WHO grade I meningioma. Two years later, he presented with headaches and was found to have a recurrent 3 cm mass. A second surgery was performed and histology showed an atypical meningioma with a high mitotic rate. The residual tumor was 0.9 cm and the patient was treated with radiosurgery.

Tumor control

When defining the failure of tumor control either by radiological demonstration of tumor growth or by the need of adjuvant treatment for clinical or radiological reasons, the multivariate regression analysis showed that tumor histological grade and Simpson resection grade were significant factors in determining the tumor control ($p<0.002$ and $p<0.008$ respectively), but that the other factors (tumor size ($p=0.09$), sex ($p=0.1$) and age ($p=0.4$)) were not. A chi square analysis supports this [Table 3]: 89% of WHO grade I meningiomas were controlled by treatment, decreasing to 33% for WHO grade II meningiomas and none of the malignant lesions were controlled in our series; 92% of Simpson grade I were controlled, decreasing to 0% with grade IV. In our series, considering that the two smaller meningiomas were treated by radiosurgery only and that their histology was not available, we could not determine within this small group if radiosurgery as the sole treatment was better, or as efficient for tumor control as surgery. Surprisingly, a segmentation of the SSS in three thirds shows that posterior location is a factor of worse prognosis in terms of recurrence and progression when compared to the two anterior thirds ($p<0.002$).

Reflecting the impact of censored observations, actuarial control rates were less good but show the same trend. The 5-year actuarial overall tumor control rate for the entire series was 65.87 % +/- 0.10 [Figure 2a]. For patients who underwent radiosurgery (n=2) or surgery (n=15) as unique treatment, the actuarial 5-year control rate was 100%. Those who underwent surgery as a primary treatment, followed by radiosurgery as adjuvant treatment, had an actuarial 5-year control rate of 45.35 %. The control rate was even lower for those who had fractionated stereotactic radiotherapy as adjuvant treatment (14.96 %).

The factors that influenced negatively the tumor control in our series were the high Simpson resection grade, the high histological grade as well as, more surprisingly, the posterior location of the meningioma along the SSS.

Indeed, Simpson resection grade had an impact on the tumor control rate, Simpson grades 1 had a 5-year control rate of 86 % and higher Simpson grades had an overall control rate of 47 % (Log-rank test P=0.001) [Figure 2b].

Moreover, the 5-year actuarial control rate for typical meningiomas was 89% and 33% for atypical meningiomas. The malignant meningiomas had all progressed by 19 months (Log-rank test P=0.001) [Figure 2c].

Furthermore, there was a trend toward a lower tumor control for meningiomas located in the posterior portion of the SSS (5-year control actuarial control rate was 37.5% in the last third, 80% and 90% for the first and second third respectively) (Log-rank test P=0.07) [Figure 2d].

Although sex was not a statistically significant parameter of tumor control ($p<0.16$), there was also a trend toward better tumor control in females.

Clinical outcome

Most of the patients tolerated their treatment well and their clinical status was either stable (57%) or improved (28%). Two patients had a transient neurological worsening of their clinical status after surgery with a transient hemiparesis that resolved within a few days for one patient and within a few weeks for the other. Both had frontal parasagittal meningioma located at the second third of the SSS. Four patients (14%) had a worsening of their clinical status, either transient due to surgical complication (wound infection and epidural hematoma) in two patients or progressive due to their high grade meningioma progression. Seven patients had a complication related to their treatment. One was due to radiosurgery with the formation of a post actinic cystic lesion of 2cm in a non-eloquent region, and two were indirectly related to surgery: 1 pulmonary embolism and 1 superficial thrombophlebitis.

DISCUSSION:

Epidemiology

In our series, 28 (12.4%) of 225 patients with a radiological diagnosis of intracranial meningioma had parasagittal meningioma. We excluded from our study 9 (4%) parasagittal meningiomas associated with neurofibromatosis since their genetic behavior is different. The parasagittal meningiomas in our series reprensent 16.4% of operated meningiomas, which is a little below their ratio found in the literature (17-

31%) (3, 5-7, 11, 13, 21, 22). The gender distribution was also somewhat different from that of other larger series (6, 8, 15) with a female to male ratio was 1:1. Interestingly, we have noted that men had higher grade meningiomas than women, which corroborates the description made in other larger studies (6).

Tumor control and recurrence

Previous studies have shown that parasagittal meningiomas are known to recur more often compared to those found in other locations (4, 16). The aim of this paper was to evaluate the factors that could influence this different behavior. Complete surgical removal together with any dural involvement, which is proven to be the best way to achieve tumor control, is often not possible due to the close relation between the meningiomas and the SSS.

Tumor control is in itself difficult to define since radiological growth control is not sufficient in assessing the clinical outcome. Therefore, we combined the results of growth demonstrated on the radiological follow up and the need for adjuvant treatment, either for clinical or radiological reasons. Many studies have used simple percentages of these results but an actuarial calculation based on the length of follow-up seems to be mandatory for these slow growing tumors. A limitation of this is, of course, that events can occur after a large number of patients have been censored and might have an excessive effect on the final percentage of control rate, and therefore we chose a 5-year actuarial control rate.

In the present study, the control rate could not be predicted by the tumor volume at the time of diagnosis. This observation is in contrast to a former study (15) in which a tumor volume greater than 13.4 cm^3 (which was the median volume) was correlated with higher recurrence rates. In our series, there was a strong trend toward lower control for bigger tumors but due to the smaller number of meningiomas analyzed in our series, this trend was not statistically significant.

Moreover, compared to the study performed by Colli et al where the female gender was a predictive factor for better tumor control rate (6), the female gender, in our

series, was not considered as an independent predictive factor since women had histologically less aggressive menigiomas, which was per se the strongest predictive factor for tumor control.

Most authors agree that recurrence rates for patients with atypical or malignant meningiomas is higher than for patients with WHO grade I (6, 8). In our series, histological grade was also the main determinant of tumor control. No patient with a malignant meningioma had a tumor control longer than two years.

Interestingly, we report for the first time that the posterior site of implantation along the SSS seems to be another independent factor for a worse tumor control. This observation was never reported previously (6, 8). The segmentation of the SSS and the survival curves between anterior, middle and posterior thirds were never analyzed separately. One hypothesis is that a complete resection is more difficult in the posterior two thirds of the SSS, due to the intimate relationship between the tumor and the venous sinus or the critical bridging veins, and due to the increased morbidity in aggressive surgical management in areas of critical brain cortex. The abundant venous drainage in the posterior third of the SSS makes a complete removal more difficult than in other locations, leading therefore to a higher recurrence rate. However, these results need to be interpreted cautiously due to the small sample size of the present study and may warrant further studies.

Finally, the most obvious cause of inability to reach tumor control is the failure to achieve radical resection of the meningioma, which is challenging for parasagittal locations. In our series, Simpson grade was a statistically significant factor for tumor control, which corroborates former studies (1, 8, 12). Only 38% of the patients had a Simpson I resection with a tumor control of 90%. The higher Simpson grades were associated with tumor control rates below 66%. Altogether, 39% of our patients needed adjuvant therapy with similar results to the series focused on parasagittal meningiomas (15). Two patients with small parasagittal menigiomas underwent SRS only, with no tumor progression. SRS as the first treatment should be considered for small parasagittal menigiomas, when complete resection is associated with high morbidity. Nevertheless surgery remains the gold standard procedure for large parasagittal meningiomas and a complete removal should be attempted.

Mortality and Morbidity

Operative mortality for resection of parasagittal meningiomas was formerly reported to range between 1.8% and 7.3%. This has decreased with the use of microsurgical techniques. It has been asserted that complete sinus occlusion allows an en bloc removal of the tumor without significant risk (2, 8, 21). This was confirmed in our series. In fact, we only performed a sinus resection in two patients with complete sinus obstruction and no mortality was observed.

Morbidity, however, remains higher than for other locations. Transient neurological worsening happened in two patients (7.14%) in the immediate postoperative period and were both related to second third SSS location. This has already previously been described (8) and the authors speculate that this transient impairment was caused by venous engorgement and difficulties in venous drainage caused either by sinus stenosis or lesions to collateral veins. The normal conditions of venous drainage are probably restored by the opening of alternative venous outflow pathways leading to neurological recovery.

Other complications were not related to the location along the SSS, and most of them were in close relation to surgery and are comparable with other studies: 3 wound infections (10,7 %), one (3%) epidural hematoma, one deep venous thrombosis and one pulmonary embolism. Radiosurgery had very low morbidity since only one patient (7.9%) had an asymptomatic post-actinic cystic lesion.

Compared to other centers, we tend to be less aggressive in the surgical management of meningiomas with partially invaded SSS. The proportion of adjuvant treatment (39%) is higher than in other series (7%) (8). Nevertheless tumor control based on the recurrence rate described in other series is comparable (71.4% in our series). Morbidity and mortality were somewhat lower in our series.

CONCLUSIONS:

Tumor control in parasagittal meningiomas is challenging. In our series, we confirmed the already well-known fact that histological grade and Simpson grade were two independent and strong factors for recurrence and tumor control, but sexe and size were not independent prognosis factors in our series. Interestingly, we noted that the posterior location along the SSS might as well be a bad prognosis factor and is reported here for the first time. Due to the small number of cases treated, it may warrant further larger studies. In our center, we tend to manage surgically the parasagittal meningiomas less aggressively, compared to other centers, but with an increased use of RSR and FRST as adjuvant treatments; we reach adequate tumor control with lower morbidity and mortality. The practical consequences might be earlier use of adjuvant therapies for higher histological grade tumors and for tumors located at the last portion of the SSS, and even consider SRS as a first treatment for small posterior meningiomas.

Tables:

Parameter	No. (%)
Age [years]	
Median	54.8
Range	29-84
Sex	
Female	14 (50)
Male	14 (50)
Tumor volume [cm^3]	
Median	13.40
Range	0.57-113
Tumor location along the SSS	
First third	8 (28.5)
Second third	11 (39.3)
Last third	9 (32.1)
Follow-up [months]	
Median	80
Range	30-133

Table 1: Patient population and tumor characteristics

	Location along SSS No. (%)			
	1st third	2nd third	3rd third	Total
Simpson Grade				
Simpson grade I	7 (26.92)	3 (11.54)	2 (7.69)	12 (46.15)
Simpson grade II	0	7 (26.92)	1 (3.85)	8 (30.77)
Simpson grade III	0	1 (3.85)	3 (11.54)	4 (15.38)
Simpson grade IV	1 (3.85)	0	1 (3.85)	2 (7.69)
WHO Grade				
WHO Grade I	7 (26.92)	8 (30.77)	3 (11.54)	18 (69.23)
WHO Grade II	0	3 (11.54)	3 (11.54)	6 (23.08)
WHO Grade III	1 (3.85)	O	1 (3.85)	2 (7.69)

Table 2: Simpson grade and WHO grade distribution along SSS

	Tumoral control No. (%)		
	Controlled	Non controlled	p value
Histological grade			< 0.002
WHO grade I	16 (89)	2	
WHO grade II	2 (33)	4	
WHO grade III	0	2	
Simpson grade			< 0.008
Simpson grade I	11 (92)	1	
Simpson grade II	6 (75)	2	
Simpson grade III	1 (25)	3	
Simpson grade IV	0	2	
Location along the SSS			< 0.002
1st third	6 (75)	2	
2nd third	11 (92)	1	
3rd third	3 (37)	5	

Table 3: Tumor histological grade and Simpson grade as the most significant factors for tumor control ($p<0.002$ and $p<0.008$) respectively. In our series, 3rd third SSS location is also a bad prognosis factor for progression / recurrence ($p<0.002$)

Figures:

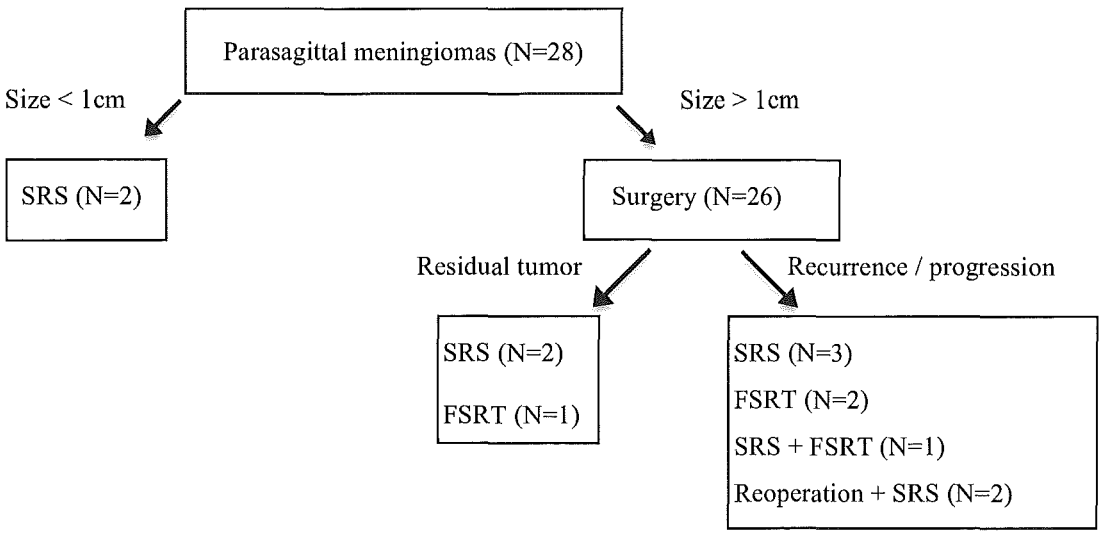

Fig. 1: Treatments

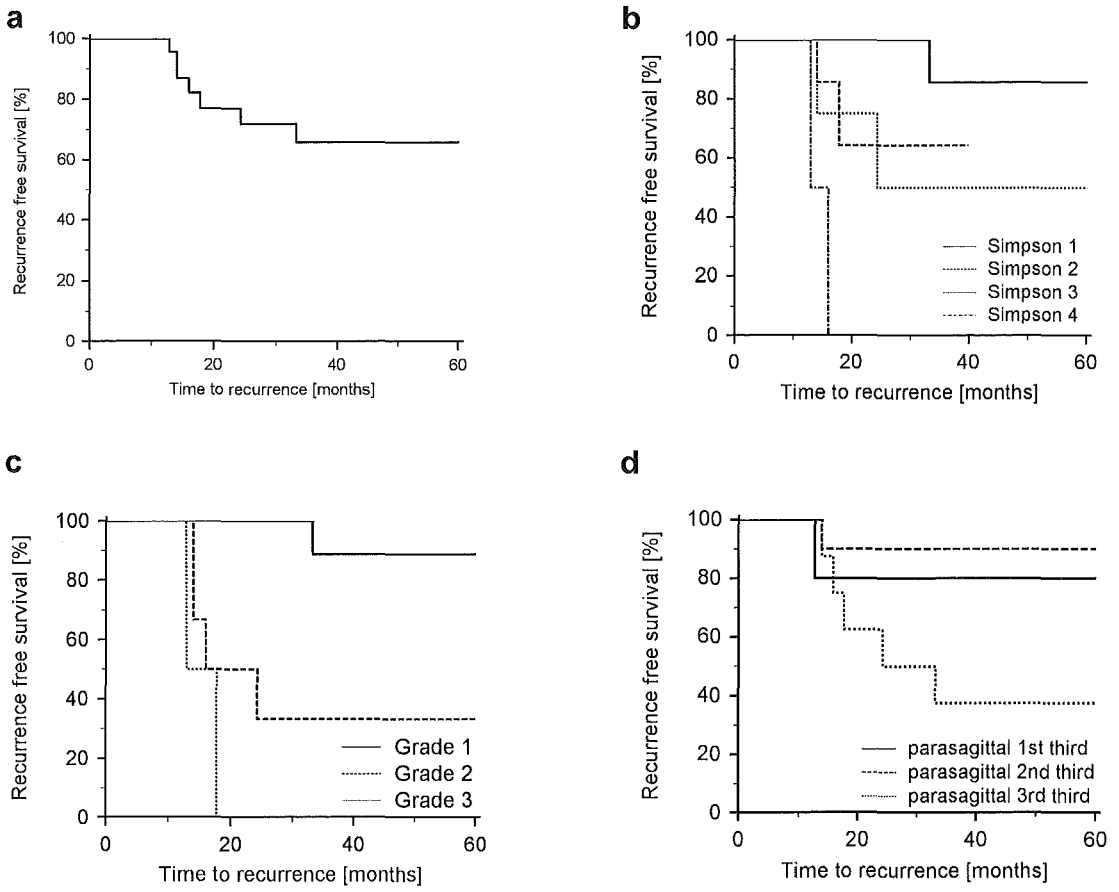

Fig. 2 Kaplan-Meier curves for recurrence-free survival in patients with parasagittal meningiomas. **a** Recurrence-free survival rate in all 28 meningiomas **b** Recurrence-free survival rates for different Simpson grades. Progression-free survival rates differed significantly between groups by log-rank test (P=0.001) **c** Recurrence-free survival rate significantly differs between meningiomas grades by log-rank test (P=0.001) **d** Recurrence-free survival rate shows a trend toward a lower control in 3rd third parasagittal meningioma (log-rank test P=0.07).

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