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Adult intracranial WHO grade II ependymomas: long-term outcome and prognostic factor analysis in a series of 114 patients†

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Ependymomas account for 2% of all intracranial tumors in adults. Considerable controversy continues to exist with regard to their prognostic factors and therapeutic management due to the rarity and the heterogeneity of series reported so far. The authors report a retrospective study of a homogenous population of 114 adult patients harboring WHO grade II intracranial ependymomas from 32 French Neurosurgical Centers between 1990 and 2004. All clinico-radiological and follow-up data were analyzed, and a central pathologic review was performed by two confirmed neuropathologists. The 5- and 10-year overall survival (OS) rates were 86.1% and 81.0%, respectively; the 5- and 10-year progression-free survival (PFS) rates were 74.6% and 58.9%, respectively. On multivariate analysis, the OS rates were associated with preoperative KPS score ($P = .027$), extent of surgery ($P = .008$), and tumor location (supratentorial vs infratentorial, $P = .012$). The multivariate analysis also revealed that the risk of recurrence was associated with incomplete resection ($P = .001$) and supratentotrial location ($P = .038$). Moreover, adjuvant radiotherapy (RT) for patients with incompletely resected tumors is responsible for a significant improvement of both overall ($P = .005$) and progression-free ($P = .002$) survival. This study clearly supports the major prognostic impact of the extent of surgery in WHO grade II. Interestingly, tumor location also seems to have an actual impact on both OS and PFS. Finally, the prognostic impact of RT was found to be beneficial for incompletely resected tumors.

Keywords: adults, ependymomas, histology, radiotherapy, prognostic factors.

Adult intracranial ependymoma is a relatively rare brain tumor entity, accounting for 2%–5% of all intracranial neoplasms.[1–6] Over the last decades, attempts have been made to isolate factors of prognostic significance for patients with ependymal neoplasms.[2–12] Owing to the extremely low incidence of intracranial ependymal tumors in adults, most reported series of these neoplasms involve childhood tumors, are retrospective, include limited numbers of patients, and have limited statistical power. Furthermore, most series span several decades, thus hampering the interpretation of results, because of the changes in histological grading and in diagnosis and therapeutic tools and policies.[13] As a consequence, these neoplasms continue to generate a considerable controversy with regard to their rational clinical management. However, in virtually all large recent studies, histological grade was identified as a major prognosticator.[1,5,6] WHO grade II intracranial ependymomas are more common than their anaplastic counterparts (WHO grade III). The prognostic significance of various parameters, including patient age, gender, clinical status, tumor location and extension, extent of resection, and adjuvant therapy protocol in this histological subgroup, is still a considerable source of debates.

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To date, no studies assessing specifically these different prognostic factors, in a homogenous histological subgroup of adult intracranial ependymomas (WHO grade II), have ever been conducted. We report herein the results of a multi-institutional retrospective analysis of 114 WHO grade II intracranial ependymomas in adult patients diagnosed between 1990 and 2004. This cohort study was conducted by the French Neurosurgical Society (Société Française de Neurochirurgie, SFNC), the French Speaking Association of Neurologist and Neuro-Oncolgists (Association des Neurologues et Neuro-Oncologues de Langue Française, ANOCEF), and the French Neuropathological Society (Société Française de Neuropathologie, SFNP) to determine whether age, gender, preoperative clinical status, tumor location, extent of surgery, histological features, and postoperative radiotherapy (RT) affect both overall survival (OS) and progression-free survival (PFS).

Materials and Methods

Study Population

A multi-institutional database search on adult intracranial ependymomas including 32 French Neurosurgical University Hospital Centers was conducted by the SFNC, the ANOCEF, and the SFNP. Inclusion criteria were: confirmation by two independent neuropathologists (D.F.B., A.J.) of WHO grade II intracranial ependymoma diagnosis in patients of both sexes, aged 18 years or older, operated on between 1990 and 2004, and with no previous brain irradiation for any intracranial pathology. After central pathological review of 274 cases of intracranial tumors initially diagnosed as ependymomas, 114 patients with confirmed diagnosis of WHO grade II ependymoma were eligible for this multicenter retrospective study. The clinical and radiological treatment and follow-up data were collected by a senior neurosurgeon (P.M.) and a senior neuro-oncologist (M.B.).

Clinical and Radiological Data

The following clinico-radiological data were collected: patient's age at surgery, sex, presenting symptoms, pre- and postoperative KPS score, quality of surgical resection based on postoperative MRI scans and complementary treatment protocol (RT and chemotherapy) if performed. The extent of surgery based on the 3-month postoperative MRI scan was defined as complete if no residual tumor was found on pre- and postcontrast T1- and T2-weighted images, as incomplete on the contrary. Tumor location was divided into two groups: infratentorial and supratentorial ependymomas. Contrast enhancement as well as associated pre- and postoperative hydrocephalus was analyzed. Patients were considered metastatic if MRI scans demonstrated intracranial or spinal tumor dissemination and/or if CSF analysis revealed abnormal cells. Outcome measures included: OS and PFS. All variables used in the univariate analysis were tested in the multivariate model.

Treatment Modalities

Except for patients who died in the perioperative period the extent of surgery was evaluated by postoperative MRI scans. Perioperative mortality was defined as death occurring within 3 months postsurgery and included neurosurgical complications and systemic complications such as pulmonary embolism, sepsis, or cardiac failure. Only for these 9 patients, the extent of surgery was evaluated by a single neurosurgeon (P.M.) according to an extensive review of all operative protocols. For all remaining patients (105 patients), surgical resection was classified as complete (patients with no residual tumor on postoperative MRI) or incomplete.

Regarding irradiation, the following data were collected: doses, time to surgery (adjuvant, at recurrence or progression), and location (cranial [focal or panencephalic]) or craniospinal. For patients who received chemotherapy or radiosurgery treatments, no data were collected concerning protocol or doses but precise time to surgery was noted.

Pathological Examination

For all patients, slides used for diagnosis, colored by hematein–eosin, and/or paraffin-embedded blocks were sent to the same neuropathologist. Pathological examination was conducted centrally by two senior neuropathologists (D.F.B., A.J.). Subependymomas and ependymoblastomas were excluded according to the WHO classification. Only ependymomas that fulfilled WHO grade II criteria were analyzed.[7] Ki67-labeling index was performed in 36 cases (paraffin-embedded blocks and specimen fixed in formalin).

In doubtful cases, immunohistochemistry (immunoperoxydase with avidin biotin complex after antigen retrieval on Ventana Devices) was performed to reach diagnosis. Expression of the following antigens was searched for with appropriate antibodies: GFAP (polyclonal Dakopatts), EMA (clone E29), synaptophysin (polyclonal Dakopatts), keratin (clone AE1/AE3/PCK26 and KL1), and vimentin (clone V9).

Statistical Analysis

Categorical variables are expressed as percentage. Survivals were estimated by using the Kaplan–Meier method, and curves were compared by using the log-rank test. The effect of potential risk factors on the disease-free survival and OS were evaluated with Cox proportional hazards models. All statistical tests were two-sided, and the threshold for statistical significance was $P = .05$. Analyses were performed with SPSS for Windows version 15.0 (SPSS, Inc., Chicago, Illinois).

Results

Clinical Data

Demographic data are summarized in Table 1. Mean age was 48 years ($\pm$18 year) and the age range was 18–82 years. Impairment of cranial nerves and cerebellovestibular symptoms was predominantly seen in infratentorial tumors. Supratentorial tumors were more likely associated with hydrocephalus when located in the ventricles and with epilepsy, focal deficit, and behavioral changes (such as personality changes or changes in mood) when located within brain parenchyma. Hydrocephalus requiring shunting or endoscopic ventriculostomy was present in the intraventricular location only. No correlation was found between age, sex, and clinical status. However, patients with better clinical status (KPS $>$ 80) significantly benefited from gross total resection compared with patients with poorer KPS score (Pearson χ^2 test, $P = .006$). Also, intriguingly a significant correlation between sex and tumor location (Pearson χ^2 test, $P = .015$) was found. Patients with infratentorial tumors were significantly more frequently of male gender than patients with supratentorial locations (Table 2).

Table 1. Population characteristics

Age	
Min–Max	18–82
Mean (years $\pm$ SD)	48 $\pm$ 18
Sex	
Male, *n* (%)	59 (51.7)
Female, *n* (%)	55 (48.3)
KPS score (preoperative)	
$\leq$80, *n* (%)	53 (46.5)
$>$80, *n* (%)	61 (53.5)
Location	
Infratentorial, *n* (%)	92 (80.7)
Lateral extension, *n* (%)	16 (17.4)
Floor extension, *n* (%)	28 (30.4)
Extension (lateral + floor), *n* (%)	28 (30.4)
No extension, *n* (%)	20 (21.8)
Supratentorial, *n* (%)	22 (19.3)
Parenchymal, *n* (%)	6 (27.3)
V3, *n* (%)	11 (50.0)
Lateral ventricle, *n* (%)	5 (22.7)
Extent of surgery (MRI based[a])	
Gross total resection (GTR +), *n* (%)	67 (58.7)
Gross total resection (GTR −), *n* (%)	47 (41.3)
Operative mortality	9 (7.9)
Adjuvant treatment	
RT and/or CT, *n* (%)	35 (30.7)
Cranial alone, *n* (%)	31 (88.6)
Craniospinal, *n* (%)	4 (11.4)
Chemotherapy	0
No RT/CT, *n* (%)	79 (69.3)
Recurrence/progression	
Yes, *n* (%)	38 (33.3)
Local isolated, *n* (%)	37 (97.4)
Metastasis, *n* (%)	1 (2.6)
No, *n* (%)	76 (66.7)
Death during follow-up, *n* (%)	18 (15.8)
Follow-up period (mo)	
Range	24–212
Median	74

Abbreviations: CT, chemotherapy; Max, maximum; Min, minimum; RT, radiotherapy; SD, standard deviation; V3, third ventricle; WHO, World Health Organization.
[a]Except for the 9 patients who died within 3 months postoperatively. For these patients, the extent of surgery was based on the assessment of the neurosurgeon's operative protocol.

Pathological Data

Of the 167 cases, initially diagnosed as WHO grade II ependymomas, only 106 fulfilled diagnostic criteria of WHO grade II tumors. However, 8 cases initially diagnosed as WHO grade III ependymomas were re-classified as WHO grade II tumors leading to an entire population of 114 WHO grade II tumors. On both pathological and immunohistochemical features, the following diagnoses were excluded: glioblastomas, oligodendrogliomas and mixed oligoastrocytomas, pilocytic astrocytomas, subependymomas, papillary tumors of the pineal gland, central neurocytomas, papillary glioneuronal tumors, metastases, and papillary meningioma (Table 3).

Location, Extent of Surgery and Adjuvant Treatment

These data are summarized in Table 2. Infratentorial location was found in 92 patients (80.7%) and supratentorial location in 22 patients (19.3%). No correlation was found between the location and extent of surgery or adjuvant treatment prescription. Gross total resection was performed in 67 cases (58.7%) and incomplete resection in 47 cases (41.3%). A significant correlation was found between the extent of surgery and adjuvant treatment occurrence (Pearson χ^2 test, $P < .0001$).

Follow-up Data and Patterns of Failure

At the endpoint of the follow-up analysis, 98 (85.9%) patients—74 (58.7%) disease free—were still alive after a median duration follow-up of 74 months (range, 24–212 months). Eighteen patients (15.8%) died during the follow-up period. Of these patients, causes of death included ependymoma progression in 6 of 18 patients (33.3%), complications within 3 months after surgery (operative mortality) in 9 of 18 patients (50.0%), or 7.9% of the entire population) and unrelated cause (lung cancer in 1 case, cardiac failure in 2 cases) during disease-free period in 3 of 18 patients (16.7%). All 9 patients who died within the 3-month postoperative course experienced immediate

Table 2. Correlations between prognostic factors in WHO grade II adult intracranial ependymomas

Characteristics	Number of patients	Number of patients (% of patients with specified characteristic)					
		Tumor location		Extent of surgery		Adjuvant RT	
		Infra T	Supra T	GTR (+)	GTR (−)	Yes	No
Age (y)							
<55	74 (65.1)	58 (78.4)	16 (21.6)	44 (59.5)	30 (40.5)	24 (32.4)	50 (67.6)
≥55	40 (34.9)	34 (85.0)	6 (15.0)	23 (57.5)	17 (42.5)	11 (27.5)	29 (72.5)
Sex							
Male	55 (48.2)	50 (90.9)[a]	5 (9.1)[a]	32 (58.2)	23 (41.8)	15 (27.3)	40 (72.7)
Female	59 (51.8)	42 (71.2)[a]	17 (28.8)[a]	35 (59.3)	24 (40.7)	20 (33.9)	39 (66.1)
KPS score (preoperative)							
≤80	53 (46.5)	41 (77.4)	12 (22.6)	24 (45.3)[b]	29 (54.7)[b]	20 (37.7)	33 (62.3)
>80	61 (53.5)	51 (83.6)	10 (16.4)	43 (70.5)[b]	18 (29.5)[b]	15 (24.6)	46 (75.4)
Tumor location							
InfraT	92 (80.7)	NA	NA	55 (59.8)	37 (40.2)	28 (30.4)	64 (69.6)
Supra T	22 (19.3)	NA	NA	12 (54.5)	10 (45.5)	7 (31.8)	15 (68.2)
Extent of surgery							
GTR (+)	67 (58.7)	55 (82.1)	12 (17.9)	NA	NA	8 (11.9)[c]	59 (88.1)[c]
GTR (−)	47 (41.3)	37 (76.6)	10 (23.4)	NA	NA	27 (57.4)[c]	20 (42.6)[c]
Adjuvant RT							
Yes	35 (31.2)	28 (80.0)	7 (20.0)	8 (22.9)[c]	27 (77.1)[c]	NA	NA
No	79 (68.8)	64 (81.0)	15 (19.0)	59 (74.7)[c]	20 (25.3)[c]	NA	NA

Abbreviations: GTR (+), gross total removal; GTR (−), incomplete tumor resection; InfraT, infratentorial; RT, radiation therapy; SupraT, supratentorial.
[a]$P = .015$; [b]$P = .006$; [c]$P < .0001$

Table 3. Results of the Central Pathological Review of 167 adult primary brain tumors initially diagnosed as grade II ependymoma

	Number of patients (%)	Repartition among initial misdiagnosis, *n* (%)
Confirmed diagnosis of WHO grade II ependymoma among presumed WHO grade II tumors	106/167 (63.5)	–
Misdiagnosis/differential diagnosis	61/167 (31.7)	61 (100)
Ependymoma WHO grade III	13 (7.8)	21.3
Glioblastomas	11 (6.6)	18.0
Oligodendrogliomas and mixed oligoastrocytomas	12 (7.2)	19.7
Pilocytic astrocytoma	4 (2.4)	6.6
Subependymomas	10 (5.9)	16.4
Papillary tumor of the pineal gland	3 (1.8)	4.9
Central neurocytomas	3 (1.8)	4.9
Papillary glioneuronal tumors	3 (1.8)	4.9
Metastasis	1 (0.6)	1.6
Papillary meningiomas	1 (0.6)	1.6
Confirmed diagnosis of WHO grade II ependymoma initially misclassified as WHO grade III tumors	8/49 (16.3%)	–

postsurgical complications responsible for a prolonged hospitalization in intensive care unit. All these patients remained with a KPS score of <70 until death.

Thirty-eight patients (33.3%) presented with recurrence or progressive disease during follow-up. Disease progressed as an isolated local recurrence in 37 patients (32.5% of patients; 97.4% of failures). Disseminated disease within the central nervous system was found in only 1 patient (0.9% of patients; 2.6% of failures). In this patient, metastatic progression was associated with focal progressive disease.

Survival Analysis

Overall Survival.—The 5- and 10-year OS rates for the entire cohort were $86.1 \pm 3.5\%$ and $81.0 \pm 4.4\%$,

Table 4. Overall survival rates in WHO grade II adult intracranial ependymomas

Variables	No. of deaths/ no. of patients (%)	Univariate analysis			Multivariate analysis		
		5 y ([%] ± SE)	10 y ([%] ± SE)	Log-rank	*P*	HR	95% CI
Overall	18/114 (15.8)	86.1 ± 3.5	81.0 ± 4.4	–	–	–	–
Age (y)							
<55	9/74 (12.2)	92.0 ± 3.5	84.8 ± 5.1	.050	.218	1	–
≥55	9/40 (22.5)	75.0 ± 7.3	75.0 ± 7.3			1.913	0.682–5.362
Sex							
Male	11/59 (18.6)	78.3 ± 5.8	78.3 ± 5.8	.176	.269	1	–
Female	7/55 (12.7)	93.3 ± 3.8	84.0 ± 6.2			1.8	0.634–5.110
KPS score (preop)							
>80	4/61 (6.6)	94.8 ± 2.9	92.0 ± 4.0	.007	.027	0.264	0.081–0.859
≤80	14/53 (26.4)	76.8 ± 6.3	69.9 ± 7.3			1	–
Extent of surgery							
GTR (+)	6/67 (8.9)	91.7 ± 3.6	88.5 ± 4.6	.016	.008	1	–
GTR (−)	12/47 (25.6)	78.1 ± 6.7	70.0 ± 8.1			5.335	1.534–18.552
Location							
InfraT	12/92 (13.0)	88.2 ± 3.5	86.0 ± 4.1	.068	.012	0.172	0.044–0.675
SupraT	6/22 (27.3)	75.1 ± 11.5	54.7 ± 15.0			1	–
Adjuvant RT							
No	14/79 (17.7)	83.4 ± 4.4	78.3 ± 5.4	.273	.503	1	–
Yes	4/35 (11.4)	92.1 ± 5.4	87.3 ± 6.9			0.653	0.188–2.270

Abbreviations: 95% CI, 95% confidence interval; GTR, gross total resection; HR, hazard ratio; InfraT, infratentorial; preop, preoperative; RT, radiotherapy; SupraT, supratentorial.

respectively. On univariate analysis (Table 4), age <55 years (P = .05), preoperative KPS score >80 (P = .007), and GTR (+) (P = .016) were found to be associated with a longer survival while location (InfraT vs SupraT) (P = .06) had a borderline significance (Fig. 1). Ki67 expression did not affect (P = .856) OS on univariate analysis. On multivariate analysis (Table 4), preoperative KPS score (P = .027, HR = 0.264, 95% CI = 0.081–0.859), extent of surgery (P = .008, HR = 5.335, 95% CI = 1.534–18.552), and tumor location (P = .012, HR = 0.172, 95% CI = 0.044–0.675) were confirmed as independent prognostic indicators. Age, sex, and adjuvant treatment exhibited no independent association with OS.

Progression-free Survival.—The 5- and 10-year PFS rates for the entire cohort were 74.6 ± 4.5 and 58.9 ± 6.0, respectively. On univariate analysis (Table 5), preoperative KPS score >80 (P = .018) and GTR (+) (P = .007) were found to be associated with a longer PFS, while location (InfraT vs SupraT) (P = .061) had a borderline significance (Fig. 2). The Ki67-labeling index was not significantly correlated to PFS on univariate analysis (P = .151). On multivariate analysis (Table 5), GTR (P = .001, HR = 0.345, 95% CI = 0.15–0.80) and tumor location (P = .038, HR = 0.283, 95% CI = 0.086–0.930) were confirmed as significant independent prognostic indicators.

Adjuvant RT Impact on OS and PFS.—Among the entire WHO grade II ependymomas population, no significant impact of adjuvant RT was found regarding PFS and OS. However, in the subgroup of incompletely resected tumors, adjuvant RT was significantly associated with a better PFS (P = .002) and OS (P = .005) (Fig. 3).

Discussion

Adult intracranial ependymomas are rare CNS tumors that continue to generate considerable controversy with regard to their clinical management. The lack of widely accepted prognostic factors leads to the absence of standardized therapeutic guidelines. In this study, we analyzed potential clinical and pathological prognostic factors in the most important and homogenous population of adult patients harboring WHO grade II ependymomas treated after 1990.

A critical issue that contributes to the lack of widely recognized prognostic factors in this tumor is the actual difficulty to diagnose and to grade an intracranial ependymoma. As emphasized by this study, in 61 of 167 (36.6%) cases, an initial incorrect diagnosis of WHO grade II ependymoma was made. Four classes of pathological misdiagnoses can be distinguished. The first concerns erroneous diagnosis which would be avoided by a trained pathologist aware of the peculiar histological and immunohistochemical features of ependymomas. This category includes central neurocytomas, medulloblastomas, metastatic carcinomas, and papillary meningiomas. The second concerns confusion between subependymomas and ependymomas. The third class

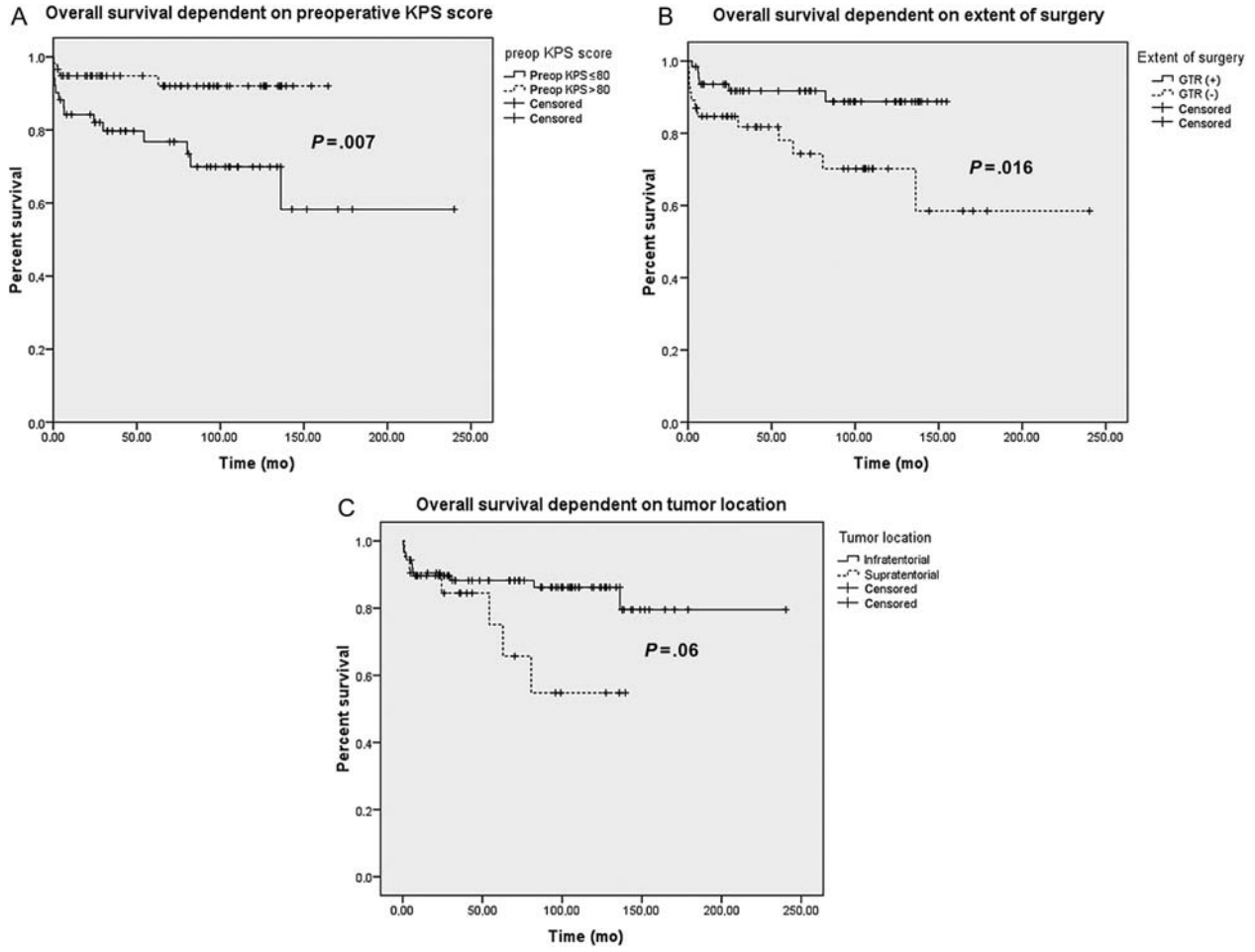

Fig. 1. (A) Comparison of Kaplan–Meier OS curves according to KPS score (log-rank test). (B) Comparison of Kaplan–Meier OS curves according to the extent of surgery (log-rank test). (C) Comparison of Kaplan–Meier OS curves according to tumor location (log-rank test).

results from the emergence of new pathological entities such as papillary tumors of the pineal region, glioneuronal tumors, and oligodendrogliomas with neurocytic differentiation. The fourth and last class corresponds to gliomas that are frequently misdiagnosed as ependymomas. Because *olig2* staining is usually lacking in ependymomas, it might be useful to differentiate true ependymomas from other gliomas based on this molecular marker expression.[14]

Treatment-, tumor-, and patient-related prognostic factors are not clearly defined in adult intracranial ependymomas and few studies have tried to identify them in a homogenous low-grade histological subgroup. The extent of surgery has emerged as one of the most significant predictors of outcome in patients with intracranial ependymomas.[1,4–6,10,11,15–17] Note, however, that some authors have found no correlation between the extent of surgery and prognosis.[3,9,18,19] In our series of WHO grade II ependymomas, the extent of resection was a major prognostic indicator of survival and recurrence both in univariate and multivariate analyses. These results are strengthened by the fact that almost all of our patients benefited from postoperative MRI examination.

Among tumor-related prognostic factors, tumor location has been found to be associated with clinical outcome, although conflicting results have been reported.[1,5,7,11,15,20] Since very few intracranial ependymoma studies have been conducted in adult patients, the role of tumor location in this population is not well known. In the current series, tumor location was significantly correlated to OS and PFS in multivariate analysis. These results contrast with previous reports on mixed WHO grade II and III ependymomas in which tumor location was supposed to be a factor linked to histological grade.[1,5,6,9] In the authors' opinion, tumor location might be an actual parameter that could distinguish two types of WHO grade II ependymomas regarding clinical and biological behaviors. Indeed, recent reports on intracranial ependymomas demonstrated site-related differences in the molecular biology of these neoplasms raising the question of whether infratentorial and supratentorial ependymomas represent molecularly distinct entities.[21,22] These two relevant reports compared intracranial vs spinal ependymomas regarding their gene expression profile.[21,22] However, the actual question of a differential expression profile in supratentorial vs infratentorial ependymomas remains unsolved.

Table 5. Progression free-survival rates in adult WHO grade II intracranial ependymomas

Variables	No. of disease progression/no. of patients (%)	Univariate analysis			Multivariate analysis		
		5 y ([%] ± SE)	10 y ([%] ± SE)	Log-rank	*P*	HR	95% CI
Overall	38/114 (33.3)	74.6 ± 4.5	58.9 ± 6.0	–	–	–	–
Age (y)							
<55	25/74 (33.8)	78.5 ± 5.2	62.5 ± 6.8	.264	.505	1	–
≥55	13/40 (32.5)	68.6 ± 8.0	49.4 ± 13.5			1.281	0.619–4.652
Sex							
Male	20/59 (33.9)	71.8 ± 6.5	56.1 ± 8.9	.520	.492	1	–
Female	18/55 (32.7)	77.1 ± 6.2	61.2 ± 8.2			1.337	0.633–2.587
KPS score (preop)							
>80	14/61 (22.9)	81.8 ± 5.6	68.0 ± 8.0	.018	.081	1	–
≤80	24/53 (45.3)	66.7 ± 6.9	48.9 ± 8.8			2.406	0.919–6.295
Extent of surgery							
GTR (+)	15/67 (22.4)	83.8 ± 5.0	66.3 ± 7.7	.007	.001	0.345	0.15–0.80
GTR (−)	23/47 (48.9)	62.1 ± 7.6	50.4 ± 8.7			1	–
Location							
InfraT	28/92 (30.4)	79.2 ± 4.5	63.7 ± 6.6	.061	.038	0.283	0.086–0.930
SupraT	10/22 (45.5)	53.0 ± 13.0	35.4 ± 13.4			1	–
Adjuvant treatment							
No	27/79 (34.2)	69.1 ± 5.7	55.5 ± 7.3	.304	.298	1	–
Yes	11/35 (31.4)	86.9 ± 6.1	68.2 ± 9.6			1.948	0.687–5.525

Abbreviations: 95% CI, 95% confidence interval; Crit., criteria; GTR, gross total removal; HR, hazard ratio; InfraT, infratentorial; preop, preoperative; RT, radiotherapy; SupraT, supratentorial; y, year.

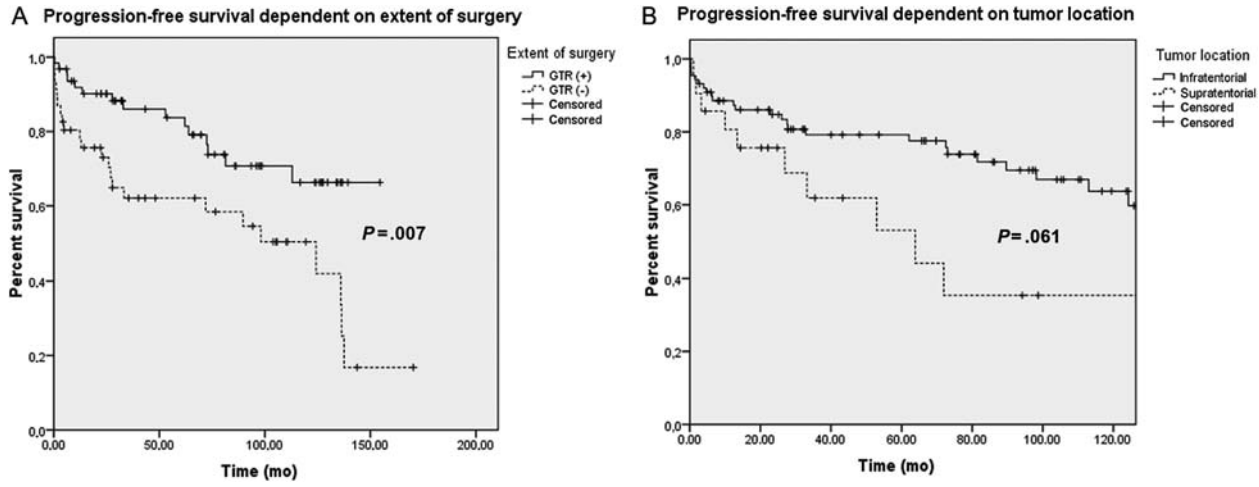

Fig. 2. (A) Comparison of Kaplan–Meier PFS curves according to extent of surgery (log-rank test). (B) Comparison of Kaplan–Meier PFS curves according to tumor location (log-rank test).

Among patient-related prognostic factors, we found that KPS score of >80 had positive impact on both OS and PFS. Few reports evaluated the prognostic impact of KPS in ependymomas. All these reports led to conflicting results.[2,3,23,24] However, our results are in keeping with those we recently reported in a population of mixed WHO grade II and III.[6]

There is a widespread opinion that postoperative irradiation should be included in standard care for patients with high-grade ependymomas.[9,11,17,25] However, for patients with low-grade ependymomas, especially when complete tumor excision could be achieved, the role of RT remains controversial. Recently, Rogers et al. reported the impact of RT in a series of 45 patients (25 irradiated) harboring essentially grade II (96%) posterior fossa ependymomas.[11] They concluded that adjuvant RT significantly improves tumor control but not OS and thus recommend the use of postoperative RT regardless of the extent of surgical resection. In our study, we did

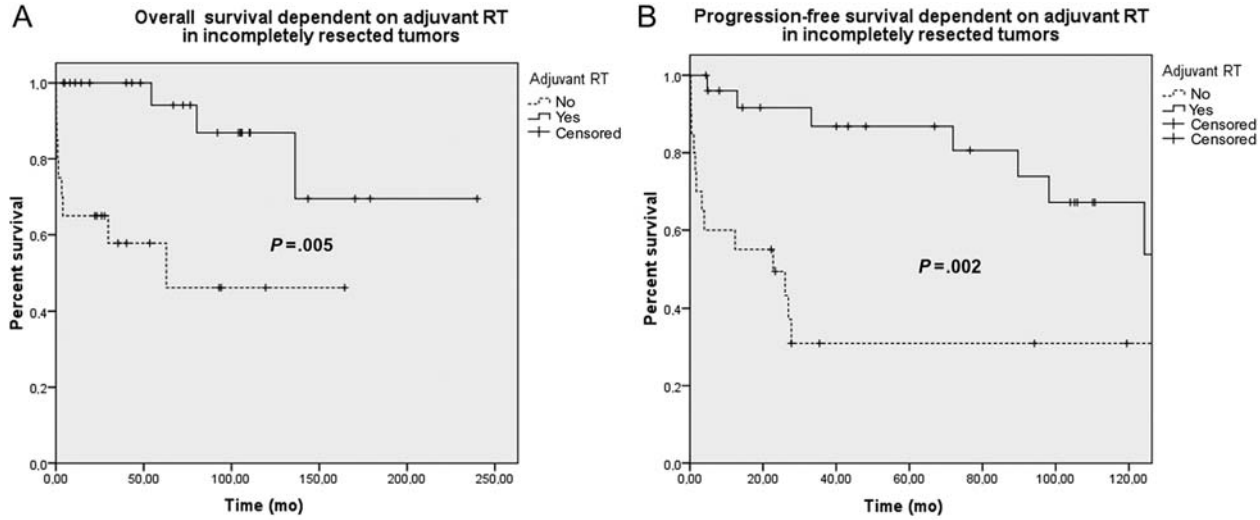

Fig. 3. (A) Comparison of Kaplan–Meier OS curves in patients with incompletely resected tumors according to adjuvant RT prescription (log-rank test). (B) Comparison of Kaplan–Meier PFS curves according to adjuvant RT prescription (log-rank test).

not find any survival benefit to adjuvant RT in completely resected tumors. However, in patients who did not have complete resection, adjuvant RT was associated with significantly better PFS and OS. Even if these findings are interesting, there is not yet enough strong evidence that supports the benefit of RT in incompletely resected low-grade ependymomas to recommend adjuvant RT in this situation. A "wait and see" policy could also be discussed for these cases, reserving RT for recurrent disease.

To our knowledge, the present series represents the largest report on adult intracranial WHO grade II ependymomas treated after 1990. This study further highlights the major role of the extent of surgery on prognosis in adult low-grade ependymomas. Our data also point out the probably important impact of tumor location in the clinico-biological behavior of low-grade ependymomas. Finally, adjuvant RT in incompletely resected WHO grade II ependymomas seems to impact favorably on OS and PFS. However, prospective clinical trials are warranted to ascertain the actual place of postoperative RT in this population.

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