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Extent of Resection and Long-Term Survival of Pineal Region Tumors in Helsinki Neurosurgery

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■ BACKGROUND: **Pineal region tumors represent challenging surgical lesions with wide ranges of survival reported in different surgical series. In this article, we emphasize the role of complete microsurgical resection (CMR) to obtain a favorable long-term outcome of pineal region tumors.**

■ METHODS: **We report a retrospective study of pineal region tumors operated on in Helsinki Neurosurgery between 1997 and 2015. Information was obtained from the hospital records, and an evaluation of the Finnish population register was conducted in July 2018 to determine the current status of the patients.**

■ RESULTS: **A total of 76 pineal region tumors were operated on. The survival was 62% at a mean follow-up of 125 ± 105 months (range, 0–588 months), and the disease-related mortality was limited to 14 patients (18.4%). Up to July 2018, 29 patients had died. Two patients died 1 and 3 months after surgery of delayed thalamic infarctions, 12 patients of disease progression, and 15 had non–disease-related deaths. Only 1 patient was lost in the long-term follow-up. Ten of 14 disease-related deaths occurred during the first 5 years of follow-up: 5 diffuse gliomas, 3 germ cell tumors, 1 grade II–III pineal parenchymal tumor of intermediate differentiation, and 1 meningioma. CMR was linked to better tumor-free survival and long-term survival, with the exception of diffuse gliomas.**

■ CONCLUSIONS: **CMR, in the setting of a multidisciplinary management of pineal region tumors, correlates with favorable survival and with minimal mortality. Surgically treated grade II–IV gliomas constitute a particular group with high mortality within the first 5 years independently of the microsurgical resection.**

INTRODUCTION

The pineal region or the so-called posterior incisural space/quadrigeminal cistern is a deep intracranial structure that may harbor a variety of neurosurgical diseases such as benign pineal cysts, a wide range of pineal region tumors, vascular malformations, and aneurysms.[1-7]

The pineal region represents a microsurgical challenging location. Since the introduction of the operative microscope and, later, of the endoscope, the surgical outcome of these diseases has improved dramatically. On the other hand, in the last decades, the development of radiochemotherapy has made possible, in selected

Key words
- Microneurosurgery
- Multidisciplinary management
- Pineal region lesions
- Pineal tumors
- Radiochemotherapy
- Sitting position
- Supracerebellar infratentorial approach

Abbreviations and Acronyms
CMR: Complete microsurgical resection
CSF: Cerebrospinal fluid
GCT: Germ cell tumor
HN: Helsinki Neurosurgery
MRI: Magnetic resonance imaging
mRS: Modified Rankin Scale
OIH: Occipital interhemispheric approach
PPT: Pineal parenchymal tumor
PPTID: Pineal parenchymal tumor of intermediate differentiation
PTPR: Papillary tumor of the pineal region
SCIT: Supracerebellar infratentorial
STR: Subtotal resection
WHO: World Health Organization

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cases, less invasive therapeutic modalities, in particular for germinomatous tumors.[8-12] However, in opposition to all these therapeutic developments, the diagnostic imaging of pineal region tumors still lacks precision, and histopathologic and immunohistochemical examination is required for the definitive diagnosis.

Even although these technical advances have improved the surgical outcome of pineal region lesions and different surgical series have reported wide ranges of survival, long-term follow-up data are still scarce in the literature.[8-12]

We present the long-term surgical outcome of patients with pineal region tumors operated on in Helsinki Neurosurgery (HN) between 1997 and 2015. Moreover, we aim to emphasize the importance of complete microsurgical resection (CMR) in the setting of a multidisciplinary management of pineal region lesions (microneurosurgery and radiochemotherapy), to obtain a favorable long-term outcome.

METHODS

Population

After institutional ethics board approval (number HUS/2772/2017), we retrospectively reviewed the patients with pineal region tumors who were consecutively operated on in our department between 1997 and 2015. Few previously treated patients underwent surgical removal of a persistent or recurrent pineal lesion during the study period. Definitive histologic diagnoses were recorded and, in cases of unclear diagnosis, the histologic samples were re-revised by our neuropathologist. IMPAX version 6.5.5.1608 (Agfa, Mortsel, Belgium) was used for the presurgical radiologic evaluation and for the postoperative imaging and evaluation of the extent of tumor resection as well. We examined the medical records to determine the preoperative status of the patients, the immediate and long-term clinical follow-up of the patients, and one of the coauthors (R.R.) revised the Finnish population register in July 2018 to determine their current status.

The modified Rankin Scale (mRS) was used to categorize and compare the preoperative, immediate postoperative, and long-term postoperative functional status of the patients. The correlations between the grade of microsurgical resection and mortality, pineal tumor-free outcome, and volume of the lesion were analyzed using the χ^2 and Mann-Whitney U test. P values <0.05 were considered significant. SPSS version 22 (IBM Corp., Armonk, New York, USA) was used.

CMR of Pineal Region Lesions

CMR was introduced as a key component of the protocol for the management of the pineal region lesions when the senior author (J.H.) became the chairman of the Department of Neurosurgery in Helsinki in 1997. Thus, the term subtotal resection (STR) of the tumor was conveniently coined to refer to only a very small and usually firmly adhesive residual piece attached to the venous walls or infiltrating critical structures, after a procedure aiming at complete removal of the lesion. A few biopsies were performed by other colleagues as a part of the initial management of the lesions.

As mentioned earlier, the pineal region is a challenging surgical location because it is surrounded by critical neurovascular structures. Thus, the microsurgical principle "Simple, clean, fast and safe" under high operative magnification is imperative for efficient surgery.[13-16]

General Approach for Pineal Region Lesions During the Study Period

In HN, most patients harboring pineal region tumors associated with subacute or chronic symptoms are transferred from primary centers, the Department of Neurology, or from some other hospitals across Finland or from abroad. Moreover, few cases are diagnosed as incidental findings after diagnostic imaging for unrelated symptoms.

All patients harboring a pineal lesion underwent the following examinations: tumor markers in blood and cerebrospinal fluid (CSF), endocrine assessment, basal pituitary hormone tests, CSF sampling for cytology, computed tomography studies, and magnetic resonance imaging (MRI) (T1-weighted imaging, T2-weighted imaging, T1 with gadolinium enhanced/fat suppression, fluid-attenuated inversion recovery, and diffusion-weighted sequences). Moreover, proton density, spectroscopy, tractography, CSF flow studies, and magnetic resonance angiography/venography may also be required in addition. In general, the preoperative evaluation of the deep venous system is the most valuable factor in planning the surgical strategy of pineal region tumors.

The therapeutic decision after all preliminary studies is recommended by the neuro-oncologic team composed of a neurosurgeon, an oncologist, a neuropathologist, a radiologist, and a neurologist. Once the histologic diagnosis is confirmed, the neuro-oncologic team determines all further management and the required adjuvant treatment.

In patients harboring pineal region tumors associated with hydrocephalus, acute and rapidly progressive hydrocephalus may initially require external ventriculostomy, endoscopic third ventriculostomy, ventriculoperitoneal/ventriculoatrial shunt, or direct removal of the lesions. This neurosurgical decision making is related to the cytology study of the CSF, the presence of tumor markers in blood or CSF, and the preference of the surgeon. On the other hand, slow progressive hydrocephalus is generally treated by direct removal of the lesion.

Premicrosurgical Stage

Positioning and draping the patient are procedures performed under the previously well-described protocol developed in Helsinki for a more ergonomic variant of the classic sitting position: the sitting praying position.[1-5]

The supracerebellar infratentorial (SCIT) approach, which is suitable for infratentorial lesions behind and below the neurovascular structures, is the most frequently used route for pineal region surgery at our institution. Over the years, a modified paramedian approach to the pineal region has been perfected and performed routinely because of complications observed with the classic midline approach.[3,16,17] The occipital interhemispheric (OIH) approach with or without transtentorial opening is more suitable for tumors with large supratentorial segments extending behind and above the corpus callosum and the deep venous system. This approach is the second most frequently used at our institution and was widely described in other studies.[4,5] The transcortical and the subtemporal approach are less frequently

performed for lesions extended laterally to the temporo-occipital gyri. Other approaches might be also used according to specific locations of recurrent or residual tumors.

Microneurosurgery

When a proper premicrosurgical stage is achieved, a good microscopic procedure is more fluent.[16] Efficient microneurosurgery is achieved only after continuous training, adequate knowledge of microsurgical principles, and proper neuroanatomic knowledge.

We summarize our microsurgical strategy for approaching pineal region tumors as follows[13,15]:

1) After a suboccipital craniotomy, the dura is opened under the microscope based on the transverse sinus. An OIH approach requires a superior sagittal sinus-based dura opening. Strong retraction with dural stitches provides an adequate surgical view along the approaches.
2) Under high magnification, we access the quadrigeminal cistern after a SCIT approach and the pericallosal cistern if the OIH approach is performed. In both cases, CSF is continuously released along the access instead of preoperative spinal catheter placement. On the other hand, opening of the cisterna magna is often unnecessary in the SCIT approach.
3) In the SCIT approach, the quadrigeminal cistern is recognized as a dark tight membrane covering its dorsal and superior walls. We open it sharply, uncovering the pineal tumor. After an OIH approach, the tumor may be directly recognized following the falx toward the splenium because no membrane covers the lesion.
4) We coagulate and cut the posterior or superior walls of the tumor, and microsurgical ring forceps help us to obtain a tumor sample for immediate and definitive histologic study.
5) A critical aspect before intending to remove the tumor consists of the proper preoperative evaluation of the MRI to define some degree of differentiation between the tumor and surrounding structures through some cleavage plane. Throughout our intraoperative evaluation, we identified that unlike infiltrative gliomas, most pineal region tumors tend to preserve regular borders without aggressive microscopic infiltration of the surrounding parenchymal structures. This aspect remains a key component for CMR without damage of the neurovascular structures.
6) Internal decompression of the tumor with thumb-regulated suction and bipolar forceps or ring microforceps is followed by a conventional microsurgical dissection aiming to reach the posterior wall of the third ventricle. The tumor is separated from the adjacent neurovascular tissue, under soft but continuous traction using bipolar microforceps or ring microforceps. Cotton dissection and water dissection techniques are useful tools as well, and a microsurgical mirror or an endoscope may find some residual tumor in the inferior hidden area.
7) Another essential aspect of microneurosurgery is closely related to the adherence and infiltration of the tumor into external layers of the deep venous system. The tumor should be carefully and softly dissected by a water dissection technique, cotton dissection, and using microscissors and bipolar microforceps, avoiding any vascular injury, which may produce immediate or delayed complications. The postoperative evaluation of our subtotal resections showed small residual pieces attached to these vessels.
8) Microsurgical dissection of meningiomas follows the same principles. However, extreme caution should be taken while dissecting surrounding arterial and venous vessels. Moreover, falcotentorial attachments of the tumor should be sectioned, aiming at a CMR.
9) Accurate hemostasis with patient observation of any leak under continuous saline irrigation guarantees preventing postoperative hemorrhagic events.
10) Closing under the microscope looks beneficial for better hemostasis, precise wound margin approximation, atraumatic handling of tissues, and improvement of surgical dexterity. All those elements, together with the use of a paramedian SCIT approach, instead of a more traumatic midline approach, associated with new dura sealing agents might be essential in reducing the high risk of postoperative CSF leak and meningitis in pineal region surgery.[3,17]

Neuroanesthesia

The main objective of neuroanesthesia is to maintain optimal perfusion and oxygen delivery to the central nervous system during treatment. Moreover, intraoperatively, neuroanesthesia has to provide good surgical conditions. Some neuroanesthesiologic considerations for pineal region surgery in a sitting position were detailed previously.[1,2]

Adjuvant Therapy

Radiation therapy and chemotherapy represent essential tools in the management of pineal region tumors. They were used as adjuvant therapy a few weeks after microsurgical resection of pineal region tumors with aggressive behavior such as high-grade gliomas, high-grade pineal parenchymal tumors (PPTs), germinomas, mixed germ cell tumors (GCTs), immature teratomas, high-grade ependymomas, papillary tumors of the pineal region (PTPR), microcellular metastases; and also after recurrences of malignant and some more benign tumors such as meningiomas. In a few cases, radiochemotherapy is used as a primary line of treatment. From our study and from the literature, we have noticed new protocols emerging constantly. The different protocols used at our institution according to the definitive diagnosis of the tumor are described in **Table 1**.

RESULTS

A total of 147 pineal regions lesions (pineal cysts, vein of Galen malformations, arteriovenous malformations, cavernous venous malformations, posterior cerebral artery aneurysms, and pineal region tumors) were operated on in HN between 1997 and 2015. Seventy-six patients with pineal region tumors (38 females and 38 males) were operated on during the study period: 23 PPT (30%), 12 GCT (16%), 10 meningiomas (13%), 10 pilocytic astrocytomas

(13%), 6 grade II–IV diffuse gliomas (8%), and 15 other tumors (20%). The mean age of the patients was 38.4 ± 24 years (5 months to 82 years). The average length, height, and width of the lesions were 2.8, 2.5, and 2.6 cm with maximal dimensions of 9 × 7.3 × 5.8 cm, respectively. Detailed information of the study population is summarized in Figure 1 and Tables 2 and 3.

Around 90% of the cases were initially operated on by an SCIT approach and 10% by an OIH approach. These 2 surgical approaches were combined in a few cases, at the same stage or in multiple stages. Other surgical routes (such as the suboccipital midline approach to the fourth ventricle, the anterior interhemispheric approach, the subtemporal approach, the occipital transtentorial approach, and the parietal transcortical approach) were selected in a few cases or combined with the 2 most used approaches mentioned earlier. The senior author (J.H.) performed the microsurgical removal of most of the tumors.

Of the cases, 90% were operated on with patients in the sitting praying position. Other positions included the prone, supine, semi-sitting, and park bench positions, particularly for biopsies, endoscopic procedures, brachytherapy, and for complementary multistage surgical procedures.

The survival for our surgically treated 76 pineal region tumors was 62% (47/76) at a mean follow-up of 125 ± 105 months (range, 0–588 months). However, the disease-related mortality of our series was limited to 14 patients (18.4%). Up to July 2018, 29 patients had died. No perioperative death was reported, 2 patients had delayed postoperative complications and died after 1 and 3 months since surgery, 12 patients died with disease progression, and the other 15 died with reasons unrelated to the disease. Eleven disease-related deaths occurred during the first 10 years of follow-up: 5 diffuse gliomas, 3 GCTs, 2 grade II–III PPT of intermediate differentiation (PPTID), and 1 meningioma. All except a grade II–III PPTID had died within the first 5 years.

Only 1 foreign patient with grade II–III PPTID was lost at the long-term follow-up after partial resection. Moreover, another foreign patient with a large hemangiopericytoma who was operated on twice in Finland was contacted by e-mail in 2017. She was alive more than 11 years after the initial gross total resection of the lesion, with some dependency for her daily activities after the second surgery for a recurrent tumor in 2014.

Pineal Tumors in Pediatric Patients

Pineal region tumors in 22 young patients (30%) with ages ranging between 0 and 21 years were mainly characterized by GCTs, pilocytic astrocytomas, pineocytomas, pineoblastomas, and diffuse gliomas.

The first group of 10 patients (6 males, 4 females) includes children up to 6 years old with 3 pilocytic astrocytomas and 7 other tumors (ganglioneuroblastoma, GCT, arachnoidal cyst, PTPR, World Health Organization [WHO] grade II glioma, pineoblastoma, and pineocytoma). Six patients (60%) debuted with hydrocephalus, 7 patients (70%) underwent SCIT approach, and 7 patients (70%) were operated on in the sitting position. Three disease-related deaths (30%) were in this group and only 1 patient was dependent at the last follow-up (mRS score 3).

The second group of 15 patients (10 males, 5 females) includes patients ranging between 14 and 21 years old. The tumors were characterized by 7 GCTs, 2 pineocytomas, 2 pilocytic astrocytomas, 1 pineoblastoma, 1 choroid plexus papilloma, 1 WHO grade II–III PPTID, and 1 glioblastoma multiforme. Ten patients (67%) debuted with hydrocephalus, 14 patients (93%) underwent SCIT approach, and the sitting position was used in 14 patients (93%). Four disease-related deaths (27%) were in this group and only 1 patient was dependent at the last follow-up (mRS score 4).

Hydrocephalus and Pineal Tumors

Of the 76 studied patients, 53 (70%) presented with preoperative obstructive hydrocephalus (information about preoperative hydrocephalus was unavailable in 2 cases) (Table 2).

Twenty-four patients underwent initial shunt surgery before tumor removal, 2 patients had initial endoscopic third ventriculostomy, and direct removal of the lesion was performed in 27 patients. Most of the patients received initial shunt surgery during the first half of the study period. This group of patients underwent an average of >2 (2.3) shunt-related surgeries during the follow-up. Seven patients undergoing initial shunt surgery had shunt removal for different reasons and did not require a shunt device at the last radiologic follow-up.

Three patients (2 pediatric and 1 adult) with large pineal region pilocytic astrocytomas had the higher number of shunt-related surgeries, with 10, 6, and 5 procedures, respectively. All underwent initial shunt surgery with multiple shunt dysfunctions during the follow-up. The patient with the 10 shunt-related surgeries was a 2-year old boy with a giant tumor, initially considered inoperable, who underwent shunt surgery and radiotherapy in 1985, brachytherapy in 1995, and microsurgical removal of the tumor only in 2000.

Only 1 of the 27 patients undergoing direct removal of the lesion required further endoscopic third ventriculostomy for persistent hydrocephalus caused by a blood clot in the aqueduct. A ventriculoperitoneal shunt, still present at the last radiologic follow-up, was implanted in this patient. Regarding the 2 patients undergoing initial endoscopic ventriculostomy, one did not require any further treatment after complete resection of the lesion. However, the other patient underwent stereoscopic biopsy, shunt surgery because of persistent hydrocephalus, and brachytherapy. One more patient required endoscopic third ventriculostomy because of shunt dysfunction after initial shunt surgery and removal of the tumor. At the last radiologic evaluation, 49 patients (64%) of our study population did not require shunts.

Microsurgical Management of Pineal Region Tumors

Table 4 describes the differences between the CMR, STR, and partial resection of our pineal tumors series.

CMR. A CMR during treatment was possible in 70% of the cases (53 patients). Only 3 (4%) showed recurrences in the pineal region at the last follow-up. A patient with PPTID II–III and one with meningioma are alive and have very small controlled recurrences 178 and 135 months after surgery. The third patient, with a locally recurrent germinoma and panventricular metastasis, died as a result of the progression of the disease 46 months after surgery and radiotherapy-based adjuvant therapy.

Table 1. Different Adjuvant Therapy Protocols Used at Helsinki Neurosurgery According to the Definitive Diagnosis of the Tumor

Tumor	Radiotherapy	Chemotherapy
Glioblastoma multiforme	54 Gy of focal fractionated external radiotherapy	Multiple doses of temozolomide 150mg/m^2
Pineoblastoma	Fractionated external radiotherapy with 36 Gy craniospinal radiation and additional 18 Gy boost of radiation on the tumoral bed after gross total resection	Medulloblastoma protocol: initially, vincristine 1.5 mg/m^2 once a week for 6 weeks is set. Six weeks after this initial treatment, a new scheme of chemotherapy is administrated every 6 weeks with 8 cycles of lomustine: 75mg/m^2 × 1; cisplatine: 75mg/m^2 × 1; and vincristine: 1,5 mg/m^2 × 3 on days 0, 7, and 14 It is used for children and patients with high risk of metastases such as incomplete resection or tumor recurrences
Grade II–III pineal parenchymal tumor of intermediate differentiation	Fractionated external radiation therapy with 54 Gy divided in a daily dose of 1.8–2 Gy was delivered in selective cases, such as high-grade pineal parenchymal tumor of intermediate differentiation with pleomorphic histology including pineoblastoma features, after partial resection of the lesion, and after recurrence of the tumor at the follow-up Brachytherapy with 125 iodine seeds was used in a case	No chemotherapy was administered in our series, but we recommend to use it in case of a pediatric presentation
A large recurrent grade III papillary tumor of the pineal region in a pediatric case	Fractionated external radiotherapy of 54 Gy divided in a daily dose of 1.8 Gy after gross total resection	High-grade ependymoma protocol: cisplatin-cyclophosphamide-vincristine-etoposide, delivered in 4 intravenous cycles, each lasting 21 days: 1) days 1, 8, and 15 for the first 3 cycles: vincristine, 1.5 mg/m^2, 2) days 1, 2, 3: etoposide, 100 mg/m^2, 3) day 1: cisplatin, 100 mg/m^2, and 4) days 2, 3: cyclophosphamide, 1000 mg/m^2
Ependymoma	Fractioned radiation therapy with 54 Gy was used for a small remnant in a grade I–II	Recommended in high-grade ependymomas as mentioned above
Germinoma	Fractionated radiotherapy of 45 Gy (30.6 ventricular area and a booster of 14.4 Gy to the hypophysis-pineal region) divided in a daily dose of 1.8 Gy	Postradiation chemotherapy with etoposide 100 mg/m^2 days 1–5, cisplatin 20 mg/m^2 days 1–5, and bleomycin 30,000 IU days 1, 8, and 15
Mixed germ cell tumors	Fractionated radiotherapy. Variable doses of craniospinal radiotherapy or whole-ventricular radiation therapy are applied according to the poor or intermediate prognosis of the lesion based on the histopathology (poor: yolk sac tumor-choriocarcinoma-embryonal carcinoma; intermediate: germinoma-teratoma) and serum markers (poor >2000 UI) of α-fetoprotein and β-human chorionic gonadotropin	Chemotherapy after gross total resection based on the above etoposide-cisplatin-bleomycin protocol
Immature teratoma	Requires radiochemotherapy. However, the unique case in our series had a bad neurologic outcome and did not receive any complementary treatment	
Microcellular metastases	30 Gy of whole brain external radiation therapy	Chemotherapy according to the primary tumor
Small recurrent meningiomas or pilocytic astrocytomas	Mainly treated by focal external radiation therapy	

A patient with anaplastic meningioma and one with diffuse grade II glioma had died 1 and 3 months after surgery with delayed postoperative infarctions. A patient with a pineoblastoma had multiple intracranial and spinal metastases without recurrence of the pineal tumor and died 173 months after surgery. A patient harboring a glioblastoma multiforme died 9 months after the initial surgery; nevertheless, the lesion did not recur in the pineal region, but in the cerebellum with multiple foci and important edema. A patient with mature pineal teratoma, who initially had concomitant small intraventricular and interhemispheric tumors, was still alive 229 months after the initial surgery, free of recurrence, with very slowly growing concomitant lesions. Fifteen patients died in this CMR group, with 5 disease-related deaths (2 gliomas, 1 germinoma, 1 pineoblastoma, and an anaplastic meningioma).

STR. STR was achieved in 14 patients (18.4%) and, after adjuvant radiochemotherapy, only 2 were disease free at the last follow-up: one with ependymoma and one with mixed GCT who were alive 165 and 86 months after surgery. Five patients (1 with grade III glioma, 1 with glioblastoma, 1 with mixed GCT, 1 with giant immature teratoma, and 1 with giant grade II–III PPTID) died 52, 5, 11, 1, and 39 months after the initial surgery, respectively, and a proper adjuvant therapy. The last 3 tumors had spinal metastases.

Another PPTID II–III with very small controlled disease died of pneumonia a few weeks after a suicide attempt. A patient with a

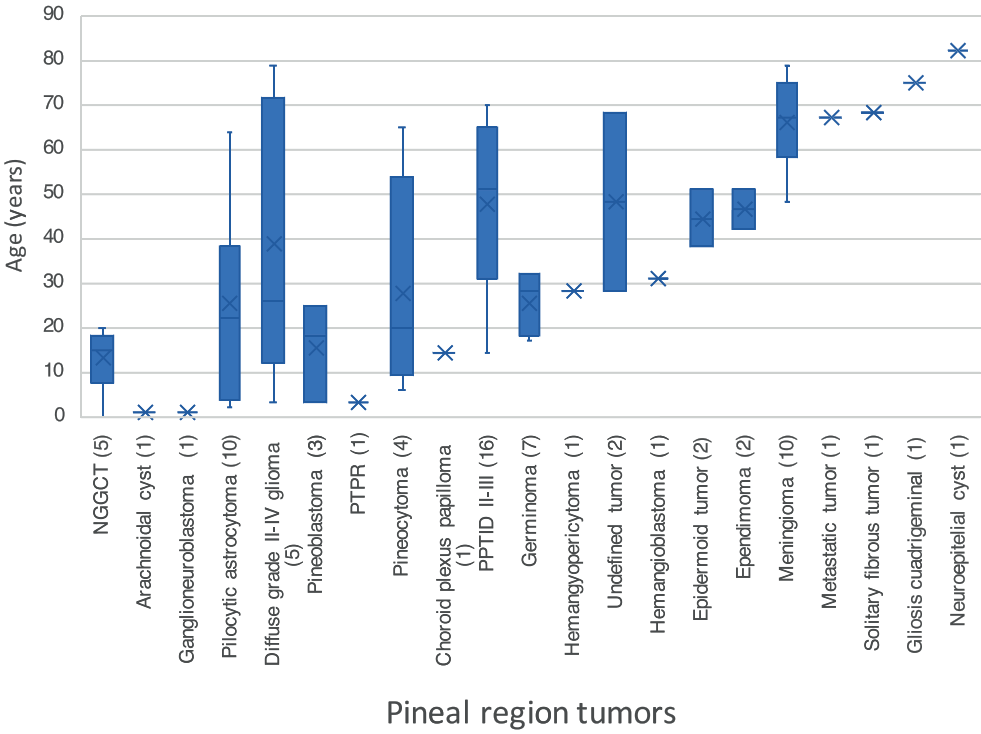

Figure 1. Age distribution in patients with pineal region tumors in the Department of Neurosurgery, Helsinki University Hospital. NGGCT, nongerminomatous germ cell tumor; PPTID, pineal parenchymal tumor of intermediate differentiation; PTPR, papillary tumors of the pineal region.

gliosis/glioma died 2 months after surgery; the reason of death was unavailable. Four patients (3 with pilocytic astrocytoma and 1 with epidermoid tumor) were alive with very small controlled lesions 231, 136, 139, and 376 months after the initial surgery. Seven patients died in this STR group, with 5 disease-related deaths (2 with gliomas, 1 with mixed GCT, 1 with teratoma, and 1 with PPTID II–III).

Partial Resection. A partial resection was carried out in 5 cases (6.6%): the resection of the cystic component of a germinoma initially treated by radiation therapy 6 years previously, a grade III glioma with thalamic infiltration, a pineal meningioma associated with a lymphoma of the splenium, a giant pilocytic astrocytoma (that initially was unsuccessfully treated with external radiation therapy 15 years before and later with brachytherapy 5 years before surgery), and a large PPTID II–III. The first 4 patients died 223, 12, 77, and 324 months after the initial surgery. The last PPTID was operated on in a foreign patient, who was lost to follow-up. Thus, we had 3 disease-related deaths in this group.

Biopsy and Adjuvant Therapy

Two grade II–III PPTIDs followed biopsy and radiotherapy. One of the patients died with poor neurologic condition and well-controlled tumor, 8 years after brachytherapy. The other patient was alive 368 months after the initial procedure, without evident tumor on imaging.

We could not determine the grade of removal of the lesion in 2 patients harboring a ganglioneuroblastoma and an undefined tumor. They died 23 and 35 months after surgery, respectively. The reason for death was unavailable as well.

Survival and Surgical Features of Different Type of Tumors

Throughout our analysis, we determined 3 well-differentiated groups of tumors. The first has a very good survival outcome after surgical treatment and is composed of arachnoid cysts, ependymomas, epidermoid tumors, hemangioblastomas, mature teratomas, PTPRs, choroid plexus papilloma, pilocytic astrocytomas, pineocytomas, and solitary fibrous tumors/hemangiopericytomas. All represent 33% of the pineal region tumors and had an overall survival of 90%–100% at an average follow-up of 182 ± 121 months (range, 45–588 months). Only 2 patients died after a long follow-up: a patient with epidermoid tumor died 246 months after gross total resection without recurrence of the tumor, and a patient with pilocytic astrocytoma died 324 months after multiple combined therapies. The histologic phenotype of some patients with tumors who underwent ≥2 surgeries, such as a patient with WHO grade I pilocytic astrocytoma, a patient with WHO grade II papillary tumor of a pineal region, and a patient with WHO grade II hemangiopericytoma, evolved into more aggressive WHO grade II, III, and III tumors, respectively, between surgeries.

Grade II–III PPTID, pineoblastomas, germinomas, and nongerminomatous GCTs with the exception of mature and immature

Table 2. Characteristics of the 76 Patients with Surgically Treated Pineal Region Tumors

Population	76 patients; age, 38.4 ± 24 years (0.4–82 years); 38 females and 38 males
Symptoms of presentation	Symptoms: anosmia, ataxia, balance disturbances, cognitive deficits, disorientation, facial and corporal sensory deficits, headache, memory deficits, nausea, psychomotor disturbances, seizures, tremor, vomit, unconsciousness, urinary incontinence, vertigo, walking difficulties, motor deficits Visual and oculomotor abnormalities: anisocoria, double vision, Parinaud syndrome, visual field defects, and unspecific visual disturbances Rare presentations: apoplectic hemorrhage, asymptomatic germ cell tumor with diabetes insipidus and hormonal imbalance
Hydrocephalus in pineal tumors: 53 patients (70%)	Initial treatment: initial shunt surgery before tumor removal: 24 patients. Mean, 2.3 (1–10) shunt-related surgeries Endoscopic third ventriculostomy: 2 patients Direct removal of the tumor: 27 patients
Pineal tumor size (cm)	Mean (maximal): length: 2.8 (9) cm; height: 2.5 (7.3) cm; width: 2.6 (5.8) cm
Surgical approach	Supracerebellar infratentorial approach: ± 90% Occipital interhemispheric approach: ± 10% Other approaches: combined supratentorial and infratentorial approaches, anterior interhemispheric approach, telovelar approach, subtemporal approach, transcortical approach
Surgical position	Sitting position: 90%; others (supine, park bench): 10%
Microsurgical resection	Complete: 53; subtotal: 14; partial: 5; biopsy: 2; UI, 2
Preoperative functional status (mRS score) (n)	0, 4; 1, 3; 2, 8; 3, 17; 4, 28; 5, 14; UI, 2
Immediate postoperative evaluation (mRS score) (n)	0, 3; 1, 22; 2, 30; 3, 8; 4, 7; 5, 3; UI, 3
Functional status at the last clinical evaluation, 125 ± 105 (0.5–588) months (mRS score) (n); and deaths in July 2018	0, 20; 1, 15; 2, 13; 3, 7; 4, 3; 5, 2; 6, 14; UI, 2 Deaths in July 2018: 29 (14 disease related, 8 unrelated to the disease, 6 unknown reason of death)
Final status at the last clinical evaluation	Improved, 54 (20 symptom free) patients No change in mRS, 4 patients (2 patients were dependent due to other comorbidities) Worsened, 17 patients (14 disease-related deaths) UI, 2

mRS, modified Rankin Scale; UI, unavailable information.

teratomas represent 38% of tumors in the pineal region and had a moderate survival between 60% and 70% at an average follow-up of 132 ± 86 months (0–368 months). Germinomas, the most radiosensitive tumors, were diagnosed in 7 patients. CMR was achieved in 71% of cases. We had 2 deaths in our series. A patient underwent CMR of a local germinoma and adjuvant pineal-panventricular radiotherapy without chemotherapy. One year after the initial treatment, the patient had a metastatic spinal recurrence controlled by radiochemotherapy. However, 2 years after the initial treatment, the patient presented with small recurrences in the left frontal horn and in the third ventricle with no response to adjuvant therapy and with posterior multiple large panventricular metastases. The patient died 46 months after surgery. Another patient was treated initially with radiation therapy after a biopsy in 1992. In August 1998, the patient returned to the department with a residual tumor and a large cystic component in the pineal region. The patient underwent partial resection with removal of the cystic component. In 2010, the patient had a stroke event and MRI showed a spinal metastatic tumor that required radiochemotherapy. This patient with multiple intracranial and spinal metastases died in 2011, 223 months after the initial treatment.

Ten meningiomas of the pineal region represent 13% of the tumors with 50% of overall survival at an average follow-up of 94.5 ± 56 months (1–205 months). Even although this group has a high mortality, only 1 patient had a delayed postoperative thalamic infarction and died 1 month after surgery. Two patients had died because of multisystemic atrophy and an intractable lymphoma of the corpus callosum, respectively, and the other 2 patients died at 91 and 83 years old without recurrence of the lesion and without postoperative complications. All underwent CMR except a patient with a lymphoma of the corpus callosum, who underwent partial resection. Two falcotentorial meningiomas included in this series had superior and anterior location with a minimal tentorial component.

Gliomas, immature teratomas, ganglioneuroblastomas, microcytic cancer metastases, and neuroepithelial cysts are lesions with very bad prognoses in our series. They represent 13% of the tumors, and all patients died after between 1 and 68 months (mean, 18 ± 23 months). The patients with neuroepithelial cyst and microcytic metastasis died of reasons unrelated to the intracranial lesion. The median survival for the rest of these tumors was 5 months.

Clinical Follow-Up and Mortality

Preoperatively, 15 patients (19.7%) harbored independent functional status with an mRS score of 0–2, and 59 patients (77.6%) had some degree of dependency, with an mRS score of 3–5. Information

Table 3. Pineal Region Tumors Operated in Helsinki University Hospital Between 1997 and 2015

Diagnosis	Cases	Survival (%)	5-year Survival (%)	10-year Survival (%)	Follow-Up (months)
Pineal parenchymal tumors	23	70	95	88	160 ± 89 (0–368)
16 pineal parenchymal tumors of intermediate differentiation*		63	92	71	143 ± 100 (0–368)
3 pineoblastomas		67	100	100	161.3 ± 13 (147–173)
4 pineocytomas		100	100	100	224.5 ± 18 (204–246)
Germ cell tumors	12	67	72	57	106 ± 81 (1–229)
7 germinomas		71	86	75	113,7 ± 75 (46–223)
1 mature teratoma		100			229
1 immature teratoma		0			1
3 mixed germ cell tumors		67			11, 86, and 148
Pilocytic astrocytomas†	10	90	100	100	143.7 ± 88 (52–324)
Meningiomas	10	50	89	75	94.5 ± 56 (1–205)
Diffuse gliomas (WHO grade II, III, and IV)	6	0	—	—	13.8 ± 19 (2–52)
1 WHO grade II gliomas					3
2 WHO grade III gliomas					12–52
2 glioblastoma multiforme					5–9
1 quadrigeminal glioma/gliosis					2
Solitary fibrous tumor—hemangiopericytoma	2	100			45, and >132
Ependymoma	2	100			122–165
Epidermoid	2	50			246–376
Arachnoid cyst‡	1	100			172
Ganglioneuroblastoma	1	0			23
Hemangioblastoma	1	100			78
Microcytic cancer metastasis	1	0			8
Neuroepithelial cyst	1	0			68
Papillary tumor of the pineal region	1	100			54
Choroid plexus papilloma	1	100			588
Undefined tumors	2	0			3–35
Total	76	62	84	76	125 ± 105 (0–588)

WHO, World Health Organization.
*A pineal parenchymal tumor of intermediate differentiation case did not have a histology report.
†Three cases were reported as atypical, diffuse type, and a tumor change from a grade I astrocytoma to grade II 1 year after partial resection. One case was an anterior vermis region tumor.
‡Wide microsurgical fenestration of the cyst with complete obliteration observed at the follow-up.

was unavailable in 2 patients. Regarding the immediate postoperative follow-up, 55 patients (72.4%) achieved an mRS score of 0–2, and 18 patients (23.7%) had an mRS score ≥3. Information was unavailable in 3 patients; however, no perioperative mortality was reported. At the last clinical evaluation, 14 disease-related deaths (18.4%) (mRS score 6) were reported. Forty-eight patients (63.2%) had an mRS score of 0–2, and 12 (15.8%) patients had an mRS score of 3–5. Information was unavailable in 2 patients (Table 2). Moreover, evaluation of the Finnish population register in July 2018 showed another 15 patients who had died without disease-related complications. Eight patients died of reasons unrelated to the disease, and the information regarding death in patients with good operative outcome was unavailable in 6 patients. A patient harboring an undefined apoplexic tumor who died 3 months after surgery did not register a specific reason of death. However, we highly suspect a death related to the course of the disease.

Table 4. Differences Between the Complete Microsurgical Resection, Subtotal Resection, and Partial Resection of 76 Pineal Tumors Operated in Helsinki Neurosurgery Between 1997 and 2015

Grade of Surgical Resection*	Complete Microsurgical Resection 70% (n = 53)	Subtotal Resection 18% (n = 14)	Partial Resection 7% (n = 5)	*P* Value
General mortality	28 (15/53)	50 (7/14)	80 (4/5)	<0.05
Mortality of the disease	9 (5/53)	36 (5/14)	60 (3/5)	<0.01
Pineal tumor free at last follow-up	94 (50/53)	14 (2/14)	0 (0/5)	<0.001
Pineal tumor volume (mm^3)	9773 ± 11,952 (500–53,261)	25,660 ± 33,764 (392–122,500)	31,387 ± 34,255 (5750–90,000)	0.2
Mortality of the disease	2 diffuse gliomas, 1 germinoma, 1 pineoblastoma, 1 anaplastic meningioma	2 diffuse gliomas, 1 mixed germ cell tumor, 1 teratoma, and a pineal parenchymal tumor of intermediate differentiation II–III	Germinoma, a diffuse glioma, and a giant pilocytic astrocytoma	

P value calculated between complete microsurgical resection and subtotal resection + partial resection as no complete microsurgical resection.
*4 cases (2 patients who underwent biopsies, and 2 patients with unavailable information) were excluded from the analysis. The absolute number of cases is written in parentheses.

CMR and Mortality of the Disease

As mentioned earlier, 14 disease-related deaths were found in our series. Two of these patients (one with anaplastic meningioma and one with a diffuse grade II glioma) had delayed postoperative thalamic infarctions and died 1 and 3 months after surgery, respectively. A patient with a giant immature teratoma had a good postoperative recovery; however, postoperative MRI a week after surgery showed spinal metastasis. The patient died at home 1 month after surgery. A patient with WHO grade II–III PPTID, neurologically disabled, died 39 months after surgery. Eight patients with diffuse grade II–IV gliomas (n = 4), GCTs (n = 3), and a pineoblastoma (n = 1) died of disease progression. A patient with PPTID with very small controlled tumor after biopsy and brachytherapy died 8 years after the procedure with slowly progressive neurologic impairment. A patient with giant pilocytic astrocytoma, who initially underwent biopsy and radiotherapy followed by brachytherapy a few years later and multiple surgeries after the senior author (J.H.) became the chairman in Helsinki Neurosurgery, died >27 years after the initial treatment.

Table 5 summarizes the characteristics of those 14 disease-related deaths. Two patients died of delayed postoperative complications, 7 patients had a progressive tumor growth with intracranial and/or spinal metastases, and 5 patients died without or with very small controlled pineal region tumor, but with intracranial or spinal metastases in 4. The most aggressive tumors were diffuse grade II–IV gliomas followed by nongerminomatous GCT. Overall, at 5 years follow-up, the mortality of both gliomas plus nongerminomatous GCT represents 50% of the entire mortality related to the disease. Moreover, the mortality of diffuse gliomas did not correlate with the degree of surgical resection; different from the 2 patients with nongerminomatous GCTs, who underwent subtotal resection and died as a result of progressive disease. A patient with anecdotal glioblastoma underwent CMR without local recurrence during follow-up. However, multiple cerebellar foci with important peritumoral edema appeared at the last stage of the disease and were the cause of death. Another illustrative case is represented by a patient with a germinoma who died 46 months after surgery, despite a CMR and a successive pineal-panventricular radiotherapy.

DISCUSSION

We report our results of 76 pineal region tumors operated on between 1997 and 2015 in the centralized Department of Neurosurgery, Helsinki University Hospital, which covers around 1.6 million people from the south of Finland.[18] Of the patients, 62% were alive at the last follow-up; however, the disease-related mortality was limited to 14 patients (18.4%). Up to July 2018, 29 patients had died, with only 1 patient lost in the long-term follow-up. Eleven disease-related deaths occurred during the first 10 years of follow-up: 5 with diffuse gliomas, 3 GCTs, 2 grade II–III PPTID, and 1 meningioma. All except 1 patient with grade II–III PPTID had died within the first 5 years. According to our analysis, the CMR was linked to better tumor-free survival and long-term survival, with the exception of diffuse grade II–IV gliomas.

CMR of pineal region tumors seems effective for the treatment of concomitant hydrocephalus. Initial shunt surgery before removal of the tumor is associated with an increased number of shunt-related surgeries, particularly in those patients who underwent subsequent incomplete removal of the lesion. The number of initial endoscopic third ventriculostomies in our series is small and prevents conclusions. However, 2 of our 4 patients required further shunt surgery for persistent hydrocephalus. We believe that small ostomies associated with reduced experience of the surgeon might play a role in this regard.

The protocol for the management of all pineal tumors during the study period remained similar. A CMR was our primary aim in most cases, with a few cases undergoing initial biopsy and subsequent adjuvant radiochemotherapy. However, the policy for the management of pineal region lesions with hydrocephalus in our department, as in other specialized centers, includes endoscopic third ventriculostomy associated with tumor biopsy and further management, particularly in cases of high suspicion of

Table 5. Mortality Related to Complications of Surgery or Progression of Disease

Tumor (Total Number of Cases)	Mortality During Follow-Up (Cases), % (n)	Mortality in the First 5 Years (Cases), % (n)	Complete Microsurgical Resection	Reason of Death (Surveillance in Months)	Subtotal Resection	Reason of Death (Surveillance in Months)	Partial Resection	Reason of Death (Surveillance in Months)	Biopsy Plus Brachytherapy	Reason of Death (Surveillance in Months)
Grade II—IV glioma (6)	8 (5)	83 (5)	2	Thalamic infarction (3 months), CT + cerebellar infiltration (9 months)	2	PT + ICI (5 and 52 months)	1	PT + ICI (12 months)		
Grade II—III pineal parenchymal tumor of intermediate differentiation (16)	13 (2)	6 (1)			1	CT + SI (39)			1	CT + brain atrophy, rigidity, aphasia (101 months)
Germinoma (7)	29 (2)	14 (1)	1	PT + ICI (46 months)			1	PT + ICI + SI (223 months)		
Nongerminomatous germ cell tumor (5)	40 (2)	40 (2)			2	CT + SI (1 months), PT + ICI (11 months)				
Meningioma (10)	10 (1)	10 (1)	1	Thalamic infarction (1 month)						
Pilocytic astrocytoma (10)	10 (1)	0 (0)					1	PT + ICI (324 months)		
Pineoblastoma (3)	33 (1)	0 (0)	1	CT + ICI (pons) + SI (173 months)						
Total	14	10	5		5		3		1	

CT, controlled tumor; PT, progressive tumor; ICI, intracranial infiltration; SI, spinal infiltration.

radiosensitive germinomas. In this regard, risks of intraprocedural bleeding, inadequate sampling, and inappropriate definitive management should be taken into account.

The approach to pineal region tumors in children did not have substantial changes compared with the adult population. The SCIT approach was the most frequently used. The sitting praying position was also performed as frequently as in adult patients. However, tight elastic bandages in the lower extremities replaced the unavailable antigravity trousers for small children.[2,19] Particular anesthetic considerations for the pediatric population, as described earlier, consist in the use of Ringer solution, saline solution with antibiotics, and mannitol at average volumes of 600 mL, 200 mL, and 125 mL, respectively; and the occasional use of hydroxyethyl starch in bigger volumes than in adult patients.[19]

Sitting Praying Position

The head of the patient, which is tilted beyond the projection of the anterior wall of the thorax, is usually 20°–30° flexed, preserving a distance between the chin and sternum. For this purpose, the table is bent around 90°–100°, elevating the upper torso of the patient. All this sequence maintains the horizontal axis of the tentorium parallel to the floor, with <90° in relation to the axis of the surgeon. The anesthesia team modify the position of the table according to the requirements of the surgeon. In pineal region surgery, other surgical positions such as the prone, semi-sitting, or park bench positions are rarely used when an absolute contraindication for the sitting position exists, or when the lesion is better accessed by a different approach. Inside the operation room, teamwork coordination is essential. Proper teamwork can be clearly exemplified with the immediate reaction of the anesthesiologist in cases of venous air embolism during surgery. The access and compression of both jugular veins by the anesthesiologist is effective in finding the leak, which is repaired by the surgeon using hemostatic agents or direct suturing.[1-3]

The SCIT Approach

The SCIT paramedian approach, a less invasive variant of the midline suboccipital approach, represents an efficient surgical approach to the pineal region that we have developed in recent years because of the relatively high rate of complications with the classic midline approach, as shown in **Table 6**.[3,6,17] Using this approach, the pineal region is accessed over the superior surface of the cerebellar hemisphere. The quadrigeminal cistern is opened laterally without damaging the midline vascular structures. Moreover, because of the gravity effect offered by the praying sitting position, a retractionless approach may be performed.

Outcome and Long-Term Follow-Up

The long-term follow-up in our series allowed us to determine properly the course of the managed pineal region lesions. Thus, recurrences after complete resection, or incomplete removal followed by standard adjuvant therapy and functional outcome, were clearly seen.

Large data analysis about unselected pineal region tumors might be summarized as follows. In the French National Register, which included PPTs, GCTs, gliomas, pineal cysts, and primitive neuroepithelial tumors, patients with pineal tumors had an average survival of 49% within an average follow-up of 5.8 years (1–23 years). Of 452 patients, 328 underwent direct surgery and 164 (50%) had a complete removal (50%), 24% a partial removal, and in 26% of the patients, the quality of removal was not mentioned. The overall mortality was 137 patients (30%), and 20% of the patients were lost to follow-up. The overall postoperative mortality was 1.8%. After 10 years, patients were considered cured and the follow-up ended.[8]

Table 6. Supracerebellar Infratentorial Approach and Postoperative Complications in Surgery of Pineal Region Tumors

Approach	Postoperative Complications Related to the Approach	%
Midline supracerebellar infratentorial approach (number of patients, 28)	Bacterial meningitis, 4 Wound infection, 3 Epidural hematoma, 1 (8 patients)	29
Supracerebellar infratentorial paramedian approach (number of patients, 35)	Wound infection, 2 Cerebrospinal fluid leak, 1 (3 patients)	9

χ^2, $P < 0.05$.

Pineal tumors in the SEER (Surveillance, Epidemiology, and End Results) data of cancer in the United States, mainly based on GCT, PPT, and gliomas, and published in 2010, had a 5-year overall survival of 65% ± 2.1%, and the median survival was 19.3 years. The 5-year overall survival for GCT was 78.9%, 61% for gliomas, and 47.2% for PPT. According to that analysis, non-GCTs and no radiotherapy were factors associated with a negative outcome. The extent of surgical tumor resection did not affect survival in any histologic subgroup. However, the disclosed information showed that surgical data were available for 552 patients: 224 patients had no surgery, only 32 (6%) underwent total excision, and 296 had other surgeries.[9]

Data of the Brain Tumor Registry of Japan showed that the most frequent tumor in the pineal region was germinoma (49.2%) followed by pineocytoma (8.5%), glioma (6.5%), pineoblastoma (5.1%), malignant teratoma (5.2%), and other teratomas (5.1%). The 5-year survival of germinomas, pineocytomas, and pineoblastomas was 89.4%, 84.1% and 46.1%, respectively.[10] Burdenko Neurosurgery Institute in Russia[11] reported the results of 287 patients with histologically verified pineal region tumors from 700 pineal tumors mainly distributed as GCT (31%), PPT (27%), glial tumors (27%), and miscellaneous (15%). Gross total resection was achieved in 148 operations (58%), STR in 74 (29%), and partial in 33 (13%). The projected 5-year and 10-year survival was 95% and 88% for germinomas, 80% and 50% for high-grade gliomas, 44% and 0% for high-grade PPT, and 20% and 0% for malignant GCT.

A report from the International Gamma Knife Research Foundation[12] after stereotactic radiosurgery for pineal region tumors described an actuarial local control and survival of 81% and 76% at 20 years for pineocytomas, 50% and 56% at 5 years for PPTID, 27% and 48% at 5 years for pineoblastomas, 33% and 100% at 5 years for PTPRs, 80% and 80% at 20 years for germinomas, and 61% and 67% at 5 years for tumors of unknown histology.

Our survival was superior to that reported in the literature. Moreover, the evaluation of the Finnish population register to determine the current status of our patients indicates the validity of our study. The analysis of the overall survival of our series uncovered some tumors with bad prognosis, such as metastatic tumors, immature teratomas, ganglioneuroblastomas, and gliomas II–IV. However, the specific mortality analysis determined that grade II–IV gliomas are the unique type of lesion characterized by very aggressive behavior, independently of the degree of resection, and are associated with high mortality during the first 5 years after surgery. The second most aggressive lesion corresponds to some nongerminomatous GCT, particularly immature teratomas and mixed GCT, with a mortality that correlates with the degree of resection. Other patients with tumors with a progressive disease despite CMR were a patient with germinoma who underwent radiotherapy-based adjuvant therapy, and a patient with pineoblastoma with a metastatic recurrence 14 years after surgery.

PPTs except pineocytomas are usually reported as tumors with bad prognosis. Of our patients with pineocytoma and patients with pineoblastoma, 100% were alive after more than 20 and 10 years, respectively. On the other hand, the 5-year and 10-year survival for our grade II–III PPTIDs was 92% and 71%, respectively. On the basis of the literature as well as our data, we strongly believe that the good surgical outcome of patients with PPT is directly related to CMR followed by proper adjuvant radiochemotherapy.[20-22]

Primary glioblastomas in the pineal region are well documented in the literature and show an average survival of 7 months.[23] Similarly, a comprehensive literature review of gliomas in the pineal region showed that grade II and III gliomas have a dismal outcome compared with their hemispheric counterparts. On the other hand, grade I pilocytic astrocytomas have a good prognosis. In this regard, the categorization of pilocytic astrocytomas and nonpilocytic grade II–IV pineal gliomas would better represent the prognosis of this entity.[24]

Our results confirm these findings. Pilocytic astrocytomas had a very good prognosis, with a 5-year and 10-year overall survival of 100%. However, giant tumors requiring multiple surgeries were usually described. CMR was possible in 60% of the cases. Only partial resection was possible after external and internal radiotherapy in a particular giant tumor. On the other hand, and despite our small number of diffuse grade II–IV gliomas, we may conclude that these tumors have a high mortality during the first 5 years after surgery, which does not correlate with the extent of the surgical resection.

Meningiomas of the pineal region might be divided as falcotentorial and velum interpositum meningiomas. Frequent recurrences are observed in patients after STR, and with atypical and anaplastic meningiomas. However, some investigators justify the partial resection of the meningiomas, and the use of radiosurgery for residual tumors or local recurrences attached to the deep venous system, because severe neurologic complications have been reported in the literature after occlusion of the deep venous system.[25-28] Even although, in our series, the mortality related to surgical complications is reduced to 1 patient, we consider extremely important the recognition and preservation of the deep arterial and venous systems, which are commonly involved in the tumor, particularly in large meningiomas. If those structures are insufficiently dissected, radiation therapy might play an important role in the management of residuals or recurrent tumors.

The literature supports radiochemotherapy as the first line of treatment for germinomas. This recommendation is based on the excellent outcomes in the North Asian population series, in whom germinomas account for >40% of the pineal region tumors.[10,29] However, in our population, in whom germinomas represent <10% of pineal tumors, the protocol for their management becomes challenging. Since the senior author (J.H.) introduced CMR as a primary concept for the management of pineal lesions, immediate intraoperative histologic analysis has not offered a consistent diagnosis of the lesions. Moreover, because almost 50% of our GCTs were nongerminomatous and mixed tumors, with less response to radiation and chemotherapy, radical removal of the lesions had to be performed. Based on the development of MRI and serum or CSF tumor markers, we may accomplish a better screening of these lesions that might allow us to perform biopsies followed by radiochemotherapy.

We present our long-term results of tumors of the pineal region. Even although important findings were made, future research is required to determine the impact of adjuvant radiochemotherapy associated with CMR in each specific group of pineal lesions. Diffuse gliomas of the pineal region remain challenging lesions for neurosurgeons and require important research for alternative management. Our internal analysis gave us a clue about the correlation between different protocols of radiation therapy and chemotherapy and the survival of tumors, such as PPT or germinomas. On the other hand, future research is also needed to extend the surveillance analysis of the present series to report longer follow-up outcomes. It is important to determine the treatment modality for these rare and complex lesions, based on the oncologic advisory commission of every neuro-oncologic department.[8]

A limitation of this study is the retrospective approach of the cases. However, because pineal tumors are rare, we still aim to enhance the importance of microneurosurgery as a treatment modality for a favorable long-term outcome.

CONCLUSIONS

CMR, in the setting of multidisciplinary management of surgically treated pineal region tumors in HN, correlates with favorable tumor-free survival and long-term survival with minimal postoperative mortality. Surgically treated diffuse gliomas of the pineal region should be considered a particular group harboring high mortality independently of the microsurgical resection.

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