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Functional outcome after gamma knife surgery or microsurgery for vestibular schwannomas

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Object. Microsurgical excision is an established treatment for vestibular schwannoma (VS). In 1992 the authors used a patient questionnaire to evaluate the functional outcome and quality of life in a series of 224 consecutive patients. In addition, starting with gamma knife surgery (GKS) in 1992, the authors decided to use the same methodology to evaluate prospectively the results of this modality to compare the two alternatives.

Methods. Among the 500 patients who were included prospectively, the authors only evaluated patients in whom GKS was the primary treatment for unilateral VS. Four years of follow up was available for the first 104 consecutive patients. Statistical analysis of the GKS and microsurgery populations has shown that only a comparison of Stage II and III (according to the Koos classification) was meaningful in terms of group size and preoperative risk factor distribution. Objective results and questionnaire answers from the first 97 consecutive patients were compared with the 110 patients in the microsurgery group who fulfilled the inclusion criteria.

Questionnaire answers indicated that 100% of patients who underwent GKS compared with 63% of patients who underwent microsurgery had no new facial motor disturbance. Forty-nine percent of patients who underwent GKS (17% in the microsurgery study) had no ocular symptoms, and 91% of patients treated with GKS (61% in the microsurgery study) had no functional deterioration after treatment. The mean hospitalization stay was 3 days after GKS and 23 days after microsurgery. All the patients who underwent GKS who had been employed, except one, had kept the same professional activity (56% in the microsurgery study). The mean time away from work was 7 days for GKS (130 days in the microsurgery study). Among patients whose preoperative hearing level was Class 1 according to the Gardner and Robertson scale, 70% preserved functional hearing after GKS (Class 1 or 2) compared with only 37.5% in the microsurgery group.

Conclusions. Functional side effects happen during the first 2 years after radiosurgery. Findings after 4 years of follow up indicated that GKS provided better functional outcomes than microsurgery in this patient series.

KEY WORDS • acoustic neuroma • vestibular schwannoma • nerve palsy • ocular symptom • tinnitus • hearing preservation • radiosurgery • microsurgery

DESPITE great advances in microsurgery, morbidity remains an issue after resection for VS. The tumors are now detected much earlier; frequently, patients with newly diagnosed unilateral VS have minimal symptoms, and they often have normal hearing. For these patients, selection of the best management option often presents a therapeutic dilemma.

Gamma knife surgery may be an appealing alternative in terms of reduced morbidity. To determine if this was true, we first evaluated functional outcomes in our patients with VS in whom the microsurgical approach was used.[30,32] This study showed that even in a population with acceptable objective results, the postoperative functional deterioration and the worsening of quality of life reported by the patients were surprisingly high. Conflicting opinions have been expressed concerning the respective roles of and indications for microsurgery and radiosurgery. Reports dealing with this controversy mostly originate from authors who are mainly concerned with either radiosurgery[5,17,18,26] or microsurgery of VS.[20–22,42,46,48] The authors of this paper are part of a multidisciplinary team that includes a group of skull base surgeons and otologists. Our goal was to evaluate the potential improvement of functional outcome after GKS compared with microsurgery for medium-sized VSs and to obtain data to clarify the role of each of these two procedures.

To evaluate the functional outcome in patients with VSs after GKS, we designed a prospective study in which we used a methodology identical to the one for the microsurgery series. Our aim was to take into consideration the evaluations made by the patients themselves of their postoperative outcome in terms of functional status and quality of life. This information was added to the objective evaluation performed by the physicians.

Abbreviations used in this paper: AEP = auditory evoked potential; CSF = cerebrospinal fluid; GKS = gamma knife surgery; MR = magnetic resonance; VS = vestibular schwannoma.

TABLE 1

*Koos neurotopographic grading system**

Grade	Description
I	small intracanalicular tumor
II	small tumor w/ protrusion into CPA
III	tumor occupying cerebellopontine cistern w/ no brainstem displacement
IV	large tumor w/ brainstem & cranial nerve displacement

* CPA = cerebellopontine angle.

TABLE 2

House–Brackmann facial nerve grading system

Grade	Description	Characteristics
I	normal	normal facial function in all areas
II	mild dysfunction	gross: slight weakness noticeable on close inspection; may have very slight synkinesis at rest: normal symmetry and tone motion forehead: moderate to good function eye: complete closure with minimum effort mouth: slight asymmetry
III	moderate dysfunction	gross: obvious but not disfiguring difference between two sides; noticeable but not severe synkinesis, contracture, and/or hemifacial spasm at rest: normal symmetry and tone motion forehead: slight to moderate movement eye: complete closure with effort mouth: slightly weak with maximum effort
IV	moderately severe dysfunction	gross: obvious weakness and/or disfiguring asymmetry at rest: normal symmetry and tone motion forehead: none eye: incomplete closure mouth: asymmetric with maximum effort
V	severe dysfunction	gross: only barely perceptible motion at rest: asymmetry motion forehead: none eye: incomplete closure mouth: slight movement
VI	total paralysis	no movement

Clinical Material and Methods

Patient Population

In our radiosurgical population, all patients were treated by the first author between July 1992 and June 1998. Among the 500 patients who were included, 435 (87%) were undergoing primary treatment for unilateral VS. Four years of follow up was available for the first 104 consecutive patients with unilateral VS. The average age was 61 years (range 17–82 years). Classification by size was based on the Koos grading system[13,14] (Table 1). Five patients had Stage I tumors, 64 had Stage II, 33 had Stage III, and two had Stage IV tumors. A total of 97 patients with Stage II and III tumors who underwent GKS (64 with Stage II and 33 with Stage III lesions) fulfilled all the inclusion criteria for the functional outcome comparison. One hundred ten patients who underwent microsurgery (49 with Stage II and 61 with Stage III tumors) fulfilled the inclusion criteria for the comparative study.

Preparation of Patients

All radiosurgical procedures were performed in the same center (Hôpital Timone), by using the Leksell 201-source Cobalt 60 Gamma Knife (Elekta Instruments, Stockholm, Sweden). The patients were admitted to the hospital the night before the operation to undergo preoperative evaluation procedures consisting of a clinical examination with House–Brackmann grading[11] (Table 2), tonal and vocal audiometry, AEP readings, caloric and pendular tests, and a Schirmer test. We performed radiosurgery after application of local anesthesia, and the patients were discharged from the hospital within 24 hours posttreatment. Patients returned to their preoperative level of functioning or employment within 3 to 10 days posttreatment.

On the morning of the treatment, we secured a neuroimaging-compatible Leksell stereotactic coordinate frame (Elekta Instruments) to the patient's head after application of local anesthesia. We then performed high-resolution contrast-enhanced computerized tomography scanning with 3-mm axial cuts and sagittal/coronal reconstruction to localize the target, define its boundaries, and localize surrounding radiosensitive structures. Nowadays, MR imaging is always required, but for our first patients it was used only for tumors close to the brainstem.[13]

The total radiation dose, number of isocenters, and treatment time were initially calculated using the Kula System on a MicroVax II computer, and more recently with GammaPlan software. The 50% isodose line was used to match the tumor margin in most patients. We use peripheral doses according to the method described by Norén.[26] The choice of the dose to the tumor margin is mostly determined by the treatment volume: 14 Gy for Stage I and small Stage II, and 12 Gy or less for larger tumors.

Follow-Up Review

At 6 months and at 1, 2, 3, 5, 7, and 10 years post-GKS, the patients made follow-up visits and their progress was reviewed with MR imaging and with tonal and vocal audiometry (in cases in which they were not deaf before surgery). After 3 years had passed, a complete evaluation was performed that was identical to the preoperative one described earlier. The functional evaluation questionnaire proposed by Pellet and colleagues[32] (Table 3) was completed by patients after more than 3 years post-GKS.

The microsurgical sample group, which served as a reference for this comparison, consisted of 178 surviving patients in whom unilateral VSs were treated between June 1983 and December 1990 by the second author (W.P.).[32] The translabyrinthine approach was used for 85% and the middle fossa approach for 15% when preservation of hearing was considered feasible. A detailed questionnaire (Table 3) was sent to the patients to assess their complaints.

Statistical Method

Several issues needed to be clarified to assess if a com-

TABLE 3

*Translation of the questionnaire sent to the patients**

Have you any vertigo? ☐ yes ☐ no if yes, does it turn as if ☐ in a waltz ☐ you were the worse for drink ☐ you were on a boat ☐ you were falling down a hole?
can you stand up? ☐ alone ☐ w/ a cane ☐ w/ someone's aid ☐ not at all
can you walk? ☐ alone ☐ w/ a cane ☐ w/ someone's aid ☐ not at all
can you run? ☐ yes ☐ no
do you have to catch hold not to fall? ☐ never ☐ rarely ☐ sometimes ☐ often
How do you hear?
on the treated side? ☐ nothing ☐ less than preop ☐ as before ☐ better than before
on the other side? ☐ nothing ☐ less than preop ☐ as before ☐ better than before
is your hearing worse in a crowd? ☐ yes ☐ no
can you locate from which direction a sound comes? ☐ yes ☐ no
Do you have tinnitus? ☐ yes ☐ no
on the treated side? ☐ yes ☐ no if yes, please specify: ☐ in silence ☐ constantly ☐ unbearable
on the other side? ☐ yes ☐ no if yes, please specify: ☐ in silence ☐ constantly ☐ unbearable
is it ☐ high ☐ low ☐ continuous ☐ intermittent?
was it ☐ triggered ☐ stopped ☐ worsened ☐ improved ☐ unchanged by the operation?
Facial motion on the treated side
can you move the corner of your mouth? ☐ normally ☐ a little ☐ not at all
can you raise your eyebrow? ☐ normally ☐ a little ☐ not at all
can you close your eye? ☐ normally ☐ a little ☐ not at all
how many millimeters does it remain open? _____ mm
when you are whistling, is your mouth: ☐ symmetrical ☐ slightly crooked ☐ very crooked ☐ or does it leave your teeth visible?
is your face symmetrical at rest? ☐ yes ☐ no
is your face symmetrical when smiling? ☐ yes ☐ no
does your face contract unintentionally? ☐ yes ☐ no if yes, how much?_____
do you need facial rehabilitation? ☐ yes ☐ no if yes, how much? _____
does your eye close when you smile? ☐ yes ☐ no
Eye on the treated side
does it cry? ☐ yes ☐ no if yes, does it cry only when eating? ☐ yes ☐ no
is it dry? ☐ yes ☐ no
does it smart? ☐ yes ☐ no
is its vision worse? ☐ yes ☐ no
do you have vision problems? ☐ yes ☐ no
do you have double vision? ☐ yes ☐ no
current treatment for this eye: ☐ none ☐ ointments ☐ eye drops ☐ taping shut overnight ☐ other
Sensitivity of your face on the treated side
when touching it, do you feel it less than on the other side? ☐ yes ☐ no if yes: ☐ on the forehead ☐ on the cheek ☐ on the chin
w/o touching it, do you feel numbness? ☐ yes ☐ no if yes: ☐ on the forehead ☐ on the cheek ☐ on the chin
have you any pain? ☐ yes ☐ no if yes: ☐ on the forehead ☐ on the cheek ☐ on the chin
when? ☐ all the time ☐ sometimes ☐ when touching face
Have you any pain? ☐ yes ☐ no if yes: ☐ headache ☐ pain in the ear ☐ behind the ear ☐ in the neck ☐ in the jaw ☐ in the rt eye ☐ in the lt eye ☐ in both eyes ☐ in the scar behind the ear ☐ in the abdominal scar
Do you have difficulties when swallowing? ☐ yes ☐ no if yes, please specify: _____
do you swallow normally? ☐ yes ☐ no
do you lose your food in your mouth? ☐ yes ☐ no
does your food unintentionally fall back out of your mouth? ☐ yes ☐ no
do liquids go the wrong way when swallowing? ☐ yes ☐ no
solids? ☐ yes ☐ no
Have you become awkward? ☐ w/ your rt hand ☐ w/ your lt hand
did your writing change? ☐ yes ☐ no if yes, what has changed? _____
Did you undergo other ops in connection w/ the one for the neuroma? ☐ yes ☐ no if yes: ☐ tarsorraphy (suturing of eyelids) ☐ facial nerve anastomosis ☐ plastic surgery (describe) _____ ☐ other (describe) _____
Have you resumed a normal life?
social ☐ yes ☐ no
family ☐ yes ☐ no
sexual ☐ yes ☐ no
professional ☐ yes ☐ no
intellectual ☐ yes ☐ no
sport ☐ yes ☐ no
specify the nature of your troubles:_____
Has your character changed? ☐ yes ☐ no if yes, please specify: _____
are you more anxious? ☐ yes ☐ no
more tired? ☐ yes ☐ no
more irritable? ☐ yes ☐ no
depressed? ☐ yes ☐ no
do you have problems w/ dreaming? ☐ yes ☐ no
problems w/ speaking? ☐ yes ☐ no
memory problems? ☐ yes ☐ no
concentration problems? ☐ yes ☐ no
Did you work before the operation? ☐ yes ☐ no
how many days did you stay in the hospital postop? _____
did you return to work? ☐ yes ☐ no ☐ if yes, how many days postop? _____
is it the same work? ☐ yes ☐ no ☐ if no, why? _____
What has been your most troublesome problem since the operation (among those already noted or other)? _____

* Patients who underwent surgery for an acoustic neuroma were asked to fill out this questionnaire to ascertain any trouble they may have suffered from since the operation. They were asked to comment on some of their answers if it seemed useful.

TABLE 4

*Comparison of the functional outcome after microsurgery and after GKS**

Functional Complaint	After Microsurgery (%)	After GKS (%)	p Value
facial palsy	47	0	0.00005
hemispasm	27	3	0.002
loss of functional hearing	62.5	30	0.000001
tinnitus	40	50	NS
hypesthesia	29	4	0.0009
vertigo	68	63	NS
imbalance	22	26	NS
ocular problems	83	27	0.000001
feeding problems	16	9	0.004
no return to work	34	1	0.00016

* Percentages correspond to frequency of onset of a new permanent complaint (evaluated at ≥ 3 years). For the rate of loss of functional hearing, the patients in Class 1 according to the Gardner and Robertson scale who underwent "conservative" microsurgical treatment are compared with the ones who underwent GKS. Abbreviation: NS = not significant.

parison between the groups of patients who underwent microsurgery and those treated with radiosurgery was valid. An analysis of tumor size distribution in the two samples was performed to match the cases. This study demonstrated that because of differences in the sizes of the populations in the microsurgical and radiosurgical samples, Stages I and IV could not be compared; individuals whose tumors were Stage II or III were analyzed. The observed proportion of Stage III tumors was overrepresented in the microsurgery group (55%) and underrepresented in the GKS group (34%). The possible influence of this difference between GKS and microsurgery on any of the outcome variables was analyzed (interaction effect between stage and surgery in the multiple logistic regression model) but no statistically significant effect was found.

Preoperative functional status in the microsurgery and GKS groups was compared by including preoperative values in the logistic regression modeling. No statistically significant differences were found except for the discovery that the prevalence of tinnitus before surgery in the GKS group was higher than in the microsurgery group and that there were more patients in the microsurgery group who were employed before treatment.

Demographic factors in the microsurgery and GKS groups were compared in the same way. The proportion of men was 35% for the microsurgery group and 46% for the GKS group. There was a difference in the mean age: 52 years for patients in the microsurgery group compared with 61 years for the GKS group. Nevertheless, it was shown that this did not influence the outcome variables.

The populations with Stage II and III tumors were compared in the microsurgery and GKS groups. We demonstrated that belonging to the Stage II or III subgroup did not influence the probability of incidence of a new complaint. No effect was found in the logistic regression analysis for sex or age. On the other hand, in both samples these patients were completely comparable in terms of age, size of population, sex, and preoperative incidence of cranial nerve impairment. Patients with Stages II and III tumors were comparable in terms of functional outcome in the microsurgery and GKS groups. In conclusion, this preliminary statistical study allowed us to establish that a comparison of the results after microsurgery or radiosurgery could be done globally by mixing patients with Stage II or III tumors.

TABLE 5

*Gardner and Robertson hearing classification**

Hearing Class	Clinical Description	Min SDS (%)	Max PTA (decibels)
1	good	70–100	0–30
2	serviceable	50–69	31–50
3	nonserviceable	5–49	51–90
4	poor	1–4	91–max
5	none	0	not testable

* Max = maximum; min = minimum; PTA = pure tone average; SDS = speech discrimination score.

Inclusion/Exclusion Criteria

Because neurofibromatosis was an exclusion criterion, only unilateral Stage II or III tumors with no previous microsurgical resection were studied. Among the GKS cases, we selected the first 100 consecutive patients who fulfilled inclusion criteria. Among the microsurgical reference population, 110 patients fulfilled the inclusion criteria for the comparative study.

Statistical Analysis

We estimated the influence of different variables on the probability of the occurrence of objective complications or functional complaints by using logistic regression modeling.[43] We used a multivariate approach to predict this proportion, assuming that more than the surgery factor (GKS or microsurgery) may influence the outcome variables. We also checked for possible interactions. Survival analysis was used on the outcome variables measuring the time to an event. Data were illustrated with Kaplan–Meier curves and analyzed using the log-rank test. The hearing variable was divided into four categories (improved, stable, deteriorated, deaf) and was analyzed using a chi-square test. With logistic regression modeling we estimated the influence of the type of surgery on the probability of the occurrence of a complaint and calculated an estimation of the relative difference between the two surgeries (microsurgery divided by radiosurgery), by odds ratio estimates.[47]

Results

At the end of the procedure, tumor removal appeared to be total in 99% of cases and anatomical facial nerve continuity was preserved in 94% of cases; results are summarized in Table 4. The median maximum tumor diameter was 16.5 cm for Koos Stage II tumors (GKS group 16.25 cm, microsurgery group 17 cm) and 21 cm for Koos Stage III tumors (GKS group 21.5 cm, microsurgery group 20.7 cm).

The facial motor function evaluation was based on the House–Brackmann grading scale.[11] In the GKS group the following results were seen at preoperative examination: 90 patients were Grade I (86.5%), 12 were Grade II (11.5%), and two were Grade III (2%); at 3 years of follow up 99 patients were Grade I (95%) and five were Grade II (5%). At preoperative examination, three patients had hemifacial

spasm; at 3 years, it had disappeared in all three patients. Two other patients had a transient hemifacial spasm, one at 8 and one at 11 months. In the microsurgery group, 52.5% of patients kept or recovered Grade I function and 14% kept or recovered Grade II function. Thus, the facial motor function was normal or almost normal in 66% of cases. The postoperative House–Brackmann grade was III in 20% and IV in 4% of cases. Patients who underwent microsurgery needed a hypoglossal–facial nerve anastomosis in 10% of cases. In all cases, this anastomosis restored good facial motion (close to Grade III).

Meanwhile, 100% of patients who had undergone GKS reported that they had no facial motor disturbance, compared with only 53% in the group treated with microsurgery ($p = 0.00005$). Although no patient reported facial palsy 2 years after GKS, in fact two of our patients experienced a transient slight facial palsy. Only 8% of patients reported hemifacial spasm after GKS, whereas one third (29%) suffered it after microsurgery ($p = 0.002$).

Facial Sensation. In the GKS group at preoperative examination, four patients had facial numbness and 14 had hypesthesia. At 3 years of follow up, the trigeminal nerve function was normal for all patients except one, who was only improved. Seven other patients presented with a transient numbness or hypesthesia. In the GKS group, 20% of the patients had subjective trigeminal symptoms. This rate was significantly higher for the microsurgical group, in which patients reported trigeminal symptoms in 55% of cases. Twenty-nine percent of the patients without preoperative trigeminal nerve deficit who underwent microsurgery, compared with 4% who received GKS, complained of a facial sensory disturbance. This represents a distinctly higher risk associated with microsurgery when compared with GKS ($p = 0.0009$). These trigeminal complaints included facial hypesthesia, facial swelling, and facial pain.

Ocular Symptoms. Among the patients who underwent GKS, 49% reported they had no ocular symptoms, compared with only 17% in the group who underwent microsurgery. Even when there was no postoperative facial palsy there was a high risk of ocular symptoms after microsurgery. Eleven percent of patients experienced hypersecretion of tears, and up to 75% of the patients who underwent microsurgery with no postoperative facial palsy suffered subsequent ocular problems (sensation of sand in the eye, double vision, dry eye or crying, smarting eye, vision deterioration, and/or permanent ocular treatment including ointments, eye drops, or taping shut at night). In contrast, only 27% of those who underwent GKS with no postoperative facial palsy experienced such side effects ($p < 0.000001$).

Eating Difficulties. In the GKS group, 8% of the patients reported difficulties in chewing. In the microsurgery group, the incidence of problems with chewing was higher (13%). No patient in the GKS group experienced other kinds of eating difficulties as opposed to 16% in the microsurgery group. This is a very significant difference and is clearly related to the higher incidence of facial palsy in the microsurgery group. The risk of experiencing eating difficulties, even in the absence of clinical injury to the fifth of seventh cranial nerve, was high after microsurgery and low after GKS (28% compared with 9%, $p = 0.004$). The patients who had undergone microsurgery reported that liquids went the wrong way when they swallowed (27% compared with only 4% after GKS), that they lost their food in their mouth (70% compared with 0% after GKS), and that their food unintentionally fell back out of their mouth (60% compared with 0% after GKS).

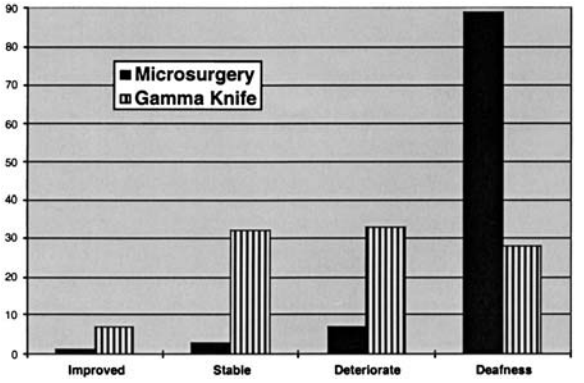

FIG. 1. Bar graph showing hearing preservation evaluated by the patients. In each surgical group, the patients were asked if the hearing on the treated side is completely lost, decreased, stable, or improved. Numbers on the y axis represent the number of patients.

Half of the patients with a balance disturbance before surgery were cured of it afterward, whatever the surgical procedure used (GKS 47% compared with microsurgery 47%). One quarter of the patients with no balance disturbance suffered from it after treatment (GKS 26% compared with microsurgery 22%, nonsignificant difference). Sometimes, patients without vertigo before surgery developed it afterward, regardless of the surgical method used (GKS 37% compared with microsurgery 33%). The probability that vertigo would disappear after treatment was higher after GKS (60% compared with microsurgery 50%, $p < 0.0001$). The risk of experiencing clumsiness seemed to be higher after microsurgery (10%) than after GKS (5%) but did not reach statistical significance ($p = 0.2$).

Hearing Preservation. The audiological classification used (Table 5) was based on that of Gardner and Robertson.[6] At preoperative examination of the GKS group, 19 patients were in Class 1, 29 were in Class 2, 30 were in Class 3, seven were in Class 4, and 12 were in Class 5. After exclusion of patients who were totally deaf preoperatively, 10% of those treated with GKS reported that they lost hearing, 57% reported no change in hearing, 3.5% said their hearing improved, and 29.5% said it deteriorated partially. Taking into account only those patients whose preoperative hearing was useful, that is to say Class 1 or 2 (48 patients; 49% of the GKS population), 50% (24 patients) maintained useful hearing (Class 1 or 2), 38% (18 patients) maintained Class 3 or 4 hearing, 4% (two patients) observed their Class 2 hearing improve to a Class 1, and 7% (four patients) became totally deaf. Taking into account only those patients considered to have subnormal hearing (Class 1 according to Gardner and Robertson), that is to say, 19% of our survey group (19 patients), in 42% their hearing was preserved unchanged (eight patients) and in 68% a useful hearing level was preserved (13 patients). Whatever the grade in terms of hearing status, the risk of total deafness was approximately 10% (Fig. 1).

When the previously mentioned preoperative AEPs were desynchronized, 39% of patients kept effective hear-

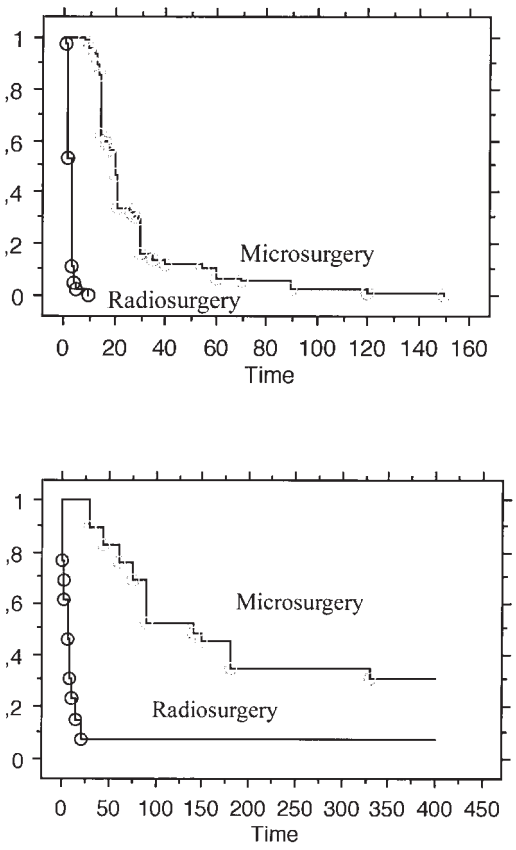

FIG. 2. *Upper:* Graph showing hospital stay; the hospital stay is shorter after radiosurgery compared with microsurgery ($p = 0.000001$). The event is the exit from the hospital, and time is expressed in days. *Lower:* Graph showing the time course of the "return to work" parameter in each of the two groups. Among the GKS group all but one of the patients had returned to work (this patient has no functional complaint). Among the microsurgery group only 66% of the patients had a functional outcome compatible with their previous employment and were able to return to work. The mean period off work was 120 days after microsurgery and 7 days after radiosurgery ($p = 0.00016$). Numbers on the y axis represent percentages of patients remaining in the hospital *(upper)* and returning to work *(lower)*.

ing, whereas 66% of them kept effective hearing when they were not desynchronized. Preservation of hearing was attempted in 11 cases (10%). Hearing preservation was achieved after microsurgery in 45% of these cases (five patients) when it was attempted (via a suprapetrous approach). The hearing thus preserved, however, was functional (Gardner and Robertson Class 1 or 2) in only 36% of cases (four patients), and only 61% of these patients kept or recovered a normal or almost normal facial motor function. The total rate of functional hearing preservation after microsurgery was 5%, which is significantly lower than the 40% rate after radiosurgery ($p = 0.000001$).

The prevalence of tinnitus after treatment in individuals with no preoperative tinnitus was 50% for the GKS group and 40% for the microsurgery group. The corresponding prevalence in patients with preoperative tinnitus was 84% for GKS and 67% for the microsurgery group. The latter values can be interpreted as a reduction of tinnitus of approximately 16% for the patients in the GKS group and approximately 33% for the patients in the microsurgery group. None of these differences was statistically significant ($p = 0.01$).

Other Complications. In the microsurgery group the surgery-related mortality rate was 1%, whereas no deaths were directly linked to radiosurgery. After microsurgery, varying, often severe, complications were observed. There was CSF leakage in 7.5% (eight patients; leakage was through the surgical wound in two thirds of cases), which was caused by raised pressure due to meningitis or CSF circulatory obstruction. This was usually cured by lumbar punctures and, if needed, by antibiotics. In one third of cases, the CSF leakage was through the eustachian tube because of a defect made by drilling of the petrous bone; this usually required reintervention. Postoperative hematomas occurred in two patients, and one of these was fatal. Brain trauma occurred in two patients and meningitis in one. None of these complications arose in the GKS group. In the GKS group three patients had hydrocephalus (that required a shunt) and one had hydrocephalus secondary to tumor growth after treatment. Sixty-six percent of the patients in the microsurgery group experienced some pain, which consisted of headache in half of the cases but also included pains in the scar tissue during yawning, in the mastoid, and in the ear. No patient in the GKS group reported pain.

As far as tumor control was concerned, three patients treated with GKS (3%) had to undergo microsurgery because of tumor progression (two with Stage II and one with Stage III lesions) at 6, 35, and 36 months post-GKS. The operation presented no particular difficulty. In the microsurgery group, the recurrence rate at 5 years was 9% (10 patients).[45]

Other Quality of Life Parameters. Among the patients in the GKS group, 91% reported no change in their daily life, compared with only 61% in the microsurgery group ($p = 0.00017$). After microsurgery, 69% reported psychobehavioral problems (tiredness, anxiety, depression, and so on) compared with only 24% after GKS. The mean hospital stay of patients in the GKS group was 3 days, compared with 23 days for the microsurgery group (Fig. 2 *upper*), which is a significant difference ($p = 0.000001$). After GKS, all patients who had held jobs, with one exception, returned to their previous occupation, compared with only 66% in the microsurgery group (Fig. 2 *lower*), which is a significant difference ($p = 0.00016$). The patient in the GKS group who did not return to work did not experience any kind of side effect or discomfort. Time lost from work after treatment with GKS was a mean of 7 days, whereas it was 130 days after microsurgery.

Discussion

Improvement in Microsurgical Outcomes

The mortality rate is now reduced after resection to between 0.4[1] and 2.9%.[3] At present, preservation of facial function (House–Brackmann Grades I or II) is frequently achieved, attaining 37 to 66% (mean 52%) and 61[2] to 74%[9] for medium-sized tumors. Moreover, some highly special-

ized teams treating a small subgroup of selected patients have attained 30 to 40% of functional hearing preservation (Gardner and Robertson Class 1 or 2 with a follow up > 2 years). Despite this dramatic improvement in the published results from some centers of excellence,[1,2,28,34,40] some risks remain; these are associated with craniotomy, general anesthesia, and tumor removal. Leakage of CSF was observed in 3[3] to 13%,[7] postoperative hemorrhage in 2.2%,[40] meningitis in 0.8[2] to 2.5%,[49] permanent lower cranial nerve deficit in 1.5[2] to 5.5%,[40] and hydrocephalus in 1 to 3%.[40] The Pellet team's results were comparable with the best objective results in the literature as assessed in Table 6. Very few reports in the literature[32,49] have taken into account the perspective of patient opinion. Obviously, there is a clear discrepancy between objective results and the individual patient's evaluation of the functional results and consequences for their quality of life.[32,49]

Gamma knife surgery was developed in the 1950s by Leksell[15,16] and was used for the first time by its inventor in the treatment of a VS in 1968. The longest-term series is that of Norén.[26] During the first part of his experience, this author used an early generation gamma knife with limited means of target localization, before the advent of modern imaging methods.[27] The doses used were relatively high (25–35 Gy marginal dose) and sometimes very low. The tumors treated were most often large in volume. Consequently, the incidence of facial paralysis before 1975 was 38%. With the progressive lowering of doses spread over the tumor periphery, the improvement of dose planning and tumor imaging, this level of postoperative facial palsy has diminished dramatically. Since the advent of modern imaging, which has made smaller peripheral doses (10–14 Gy) possible, the level of facial paresis reported by numerous authors is close to zero.[4,12,26,33] At the same time, the high rate of tumor control has been maintained.[33] Obviously, there is a learning curve evident with micro- and also radiosurgical treatment of VS.[6] This should be taken into account when comparing series from different historical periods.[36]

Long-term control of VS after radiosurgery has been established in other series.[33] In a group of patients followed over several decades, Norén[26] showed that all patients whose tumors were considered to be under control at 5 years remained so after 20 years. Similarly, in a series of patients treated between 1975 and 1980, the rate of tumor control rose from 91.7 to 97.2% when the patients in whom tumors were controlled by a second GKS procedure were taken into account.[26] The rate of control for the team of Flickinger, et al.,[4] is 91% in a group of 161 patients. To date, no clinical study has yet compared the functional outcome after microsurgery with that after radiosurgery. Despite some clear methodological limitations, such as the absence of randomization and contemporaneity of the patient populations, our series is valuable because the size of the populations compared, the homogeneity of the two populations, the demonstration of their comparability, and the patient self-evaluation.

From a methodological point of view, three issues must be discussed. Side effects were delayed after GKS. All previous studies demonstrated that functional deterioration in the fifth, seventh, and eighth cranial nerves occurred before the end of the 2nd year posttreatment.[12,17] In our series, a minimum of 3 years of follow up allowed us to evaluate serious side effects and functional outcome. As far as the secondary effects of microsurgery are concerned, only hearing loss tended to run its course in the months after the operation, with a maximum delay of 2 or 3 years.[7,24,29] Second, large tumors treated with microsurgery cannot be compared with small tumors treated with GKS. Therefore, we excluded from our comparative analysis the subgroups that were not comparable, namely Stage I and Stage IV. Tumor size is frequently considered to be a negative factor in functional outcome.[34] Consequently, we analyzed the influence of the size (according to Koos stages[13]) on the occurrence of a new complaint or side effect and we were able to demonstrate the absence of statistical influence of this parameter. We demonstrated that radiosurgical and microsurgical populations were equivalent in terms of preoperative parameters and that Stages II and III within the two groups had identical functional outcomes. Third, it has already been shown that neurological and otological examination underestimated the importance of the real functional deterioration and the degradation in quality of life after microsurgery.[31,32] The same conclusion can be drawn after GKS.

Actually, interpreting functional self-evaluation performed by the patients is sometimes difficult. All the variables in the logistic regression that were statistically significant depending on type of surgery favored GKS. The risk of experiencing hearing loss, facial palsy, facial hypesthesia, and ocular and feeding problems was much higher after microsurgery than after GKS. The chance of returning to work at the same level of employment and of retaining the same overall quality of life was much higher with GKS than with microsurgery. The duration of the hospital stay was clearly shorter and the comfort of the patient during the hospital stay was very much higher with GKS.

Regarding balance disturbance, vertigo, and tinnitus, however, differences between microsurgery and GKS did not reach statistical significance, although this could perhaps be the case with a larger population. When the symp-

TABLE 6

*Comparison of objective results of microsurgical series with the best and more recent results published in the literature**

Authors & Year	Population (no. of patients)	Preservation (%)		CSF Leak	CN Deficit (%)§	Mortality (%)
		Facial Nerve†	Functional Hearing‡			
Hardy, et al., 1989	100	29	ND	13	5	3
Ebersold, et al., 1992	256	64	24	11	2	1
Fischer, et al., 1992	102	66	29	3	ND	2.9
Glasscock, et al., 1993	161	ND	35	13	ND	0
Pellet, et al., 1993	178	66	37.5	7.5	3	1.8
Gormley, et al., 1997	179	77	38	15	2	1
Samii & Matthies, 1997	1000	59	40	9.2	5.5	1.1

* Only papers with sufficient numbers of patients (> 100) and sufficient follow-up duration were selected; duration is crucial for the evaluation of functional hearing preservation, for example. This comparison demonstrates that our reference series for microsurgery (Pellet, et al.) compares favorably with the best series in the literature in terms of objective results. Abbreviations: CN = cranial nerve; ND = not detailed.

† House and Brackmann Grades I and II.

‡ For functional hearing preservation, results correspond to the subgroup that underwent conservative treatment.

§ Lower cranial nerves nine through 11.

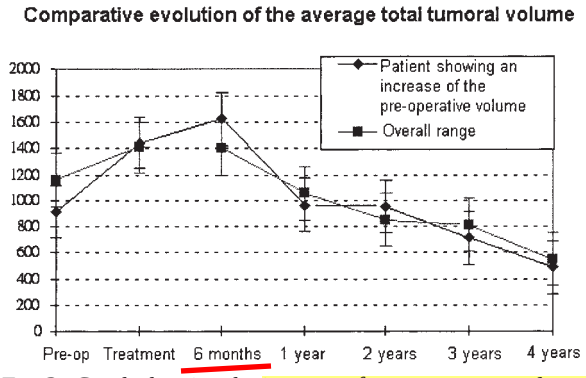

FIG. 3. Graph showing the increase of average tumor volume (y axis) over time. One can deduce from this graph a slow growth in lesion size over the 6 months post-GKS. It is interesting to observe a significant increase in the preoperative average volume. In the subgroup of patients who presented with a marked increase in tumor volume between the moment of diagnosis and the operation (35%), the central necrosis and postoperative growth were even more marked.

tom was present before treatment, the chance that the symptom would disappear after treatment was higher after GKS for vertigo (60%) compared with microsurgery (50%), and higher after microsurgery for tinnitus (33%) compared with GKS (16%). Up to 75% of patients without postoperative facial palsy reported ocular problems after microsurgery and only 27% reported them after GKS. This could indicate that in the absence of facial palsy, the risk of injury to the fibers of lacrymonasal origin was higher with microsurgery than with GKS.

In terms of hearing preservation, we consider as a major bias the fact that the majority of patients were treated via the translabyrinthine approach, which systematically destroys hearing. Comparison of hearing preservation between our GKS and microsurgery groups turned out to be questionable. We can only compare the results of our GKS group with those published in the literature after a conservative approach. With systematic AEP monitoring, and in a small subgroup of selected patients, some highly specialized teams can obtain 30 to 40% functional hearing preservation (Gardner and Robertson 1 or 2 with a follow up $>$ 2 years). This represents no more than 4.4[3] to 15%[39] of the total population that undergoes treatment. In our GKS sample, without preselection of the more treatable cases, patients with normal hearing before radiosurgery preserved functional hearing in 70% of cases. The much better probability of preservation of functional hearing with GKS is a major argument in favor of this technique.[44]

The aim of surgery is to prevent functional consequences brought on by the growth of the untreated tumor and not improvement of preoperative symptoms, which are usually slight, whichever technique is used.[31–33,35,38–43] With microsurgery we endeavor to attain this aim by extirpation of the lesion, whereas with radiosurgery we foresee doing it by stopping tumor growth. Progressive regression of the lesion is only observed after several years. Figure 3 shows the increase of average tumor volume over time in the cases we treated. From this it can be deduced there can be a small expansion of the tumor capsule over the 6 months after GKS. In 72% of cases, a distinct loss of contrast enhancement in the central tumor was noticed; this tended to diminish after 1 year. These two occasional findings at 6 months, namely, loss of contrast enhancement and a slight growth in tumor volume, are factors favoring the efficacy of GKS and should above all not be interpreted as signs of failure and justifications for a microsurgical approach. After this delay, a clear diminution of tumor volume was often observed; after 4 years this represented no more than 39% of the volume calculated on the day of the GKS. In the subgroup of patients in whom an increase of volume of more than 30% of the extracanalicular portion was seen between diagnosis and treatment, we were able to deduce that the average volume had diminished by 50% after 4 years. The stabilization and the diminution of volume of these growing tumors constitutes a more convincing argument in favor of efficacy than simply stabilization after 3 years in lesions that appeared to be stable preoperatively.[35]

The level of long-term tumor recurrence after microsurgery remains insufficiently determined because microsurgical surveys rarely include regular follow up with MR imaging. The so-called conservative microsurgical approaches (middle fossa or retrosigmoid) can preclude adequate removal of the entire neoplasm because of insufficient visualization of certain regions (in contrast to the translabyrinthine approach). In some studies,[23,36,37,41] attempts to preserve hearing did not significantly increase the risk of tumor recurrence, whereas for others[19,25] the risk was higher after this type of approach. Moreover, the fact that 75% of recurrences treated with GKS in our center were lesions occurring after such conservative surgery leads us to believe that this type of surgery almost certainly involves a risk of incomplete extirpation and unexpected regrowth.

Conclusions

Although our follow-up time was too short for a definitive evaluation of tumor control, the results obtained in our series seem to confirm those of the Stockholm and Pittsburgh teams. It must be reemphasized that the limitation of this work consists of the fact that the comparison between GKS and microsurgery was not randomized or even contemporaneous. In our series, however, the sufficient number of patients and the detailed follow up allowed us to propose a serious evaluation of the morbidity and functional effects of GKS. Thus, absence of deaths, greatly reduced objective morbidity, and fewer functional complications strongly favor GKS as the primary treatment for small or medium-sized VSs (Stages II and III) in patients of any age, but particularly in younger patients. It seems to us that radiosurgery for elderly patients should be reserved for tumors that have been shown to have a clear evolution confirmed on neuroimaging. Stage IV tumors should still be treated by microsurgery as the first option. Nevertheless, the range of possible choices to be discussed with the patient includes microsurgical removal, GKS, and conservative management with serial observation. To offer each of these strategies and discuss their indications for each patient requires the competence of several experienced surgeons who specialize in each approach. Vestibular schwannomas should be managed by multidisciplinary surgical teams that include skull base neurosurgeons, neurosurgeons trained in

radiosurgery, and otologists, with the collaboration of physicists and radiation oncologists.

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