



Universiteit
Leiden
The Netherlands

Vestibular schwannoma treatment : patients' perceptions and outcomes

Godefroy, W.P.

Citation

Godefroy, W. P. (2010, February 18). *Vestibular schwannoma treatment : patients' perceptions and outcomes*. Retrieved from <https://hdl.handle.net/1887/14754>

Version: Corrected Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/14754>

Note: To cite this publication please use the final published version (if applicable).

Chapter 1

Introduction and outline of the thesis

The most common benign tumor of the cerebellopontine angle is variously known as acoustic neurinoma, acoustic neuroma or acoustic schwannoma and accounts for 6% to 8% of all intracranial neoplasms. The nomenclature of the tumor, however, changes over time. Because the tumor most commonly arises from the superior vestibular nerve instead of the acoustic division of the eighth cranial nerve and is composed of the Schwann cells in the neurilemma, the more adequate term “vestibular schwannoma” (VS) has been proposed and will therefore be used throughout this thesis (1,2).

The incidence rate of VS now varies between 1-1.5 per 100,000/ year, although the widespread use of magnetic resonance imaging (MRI) may lead to detection of more tumors and an increase of the incidence rate (3-5). VS are usually found in adults with a mean age ranging from 46 to 58 and with female predilection in several series (6-8). They occur in two different clinical presentations. The unilateral sporadic vestibular schwannomas, which are not hereditary, consist of about 95% of cases. Approximately 5% of all patients with vestibular schwannomas have neurofibromatosis type two (NF2), which occurs in 1 per 50,000 of the general population and which is generally found in children or young adults (9). NF2 is autosomal dominant and is characterized by the development of bilateral vestibular schwannomas, peripheral schwannomas, meningiomas and presenile lens opacities. The NF2 gene has been mapped to chromosome 22 and is thought to be a ‘tumor suppressor gene’. Like other tumor suppressor genes (such as p53), the normal function of the NF2 gene is to stall cell growth and division, ensuring that cells do not divide uncontrollably. A mutation in the NF2 gene impairs its function, and accounts for the clinical symptoms observed in NF2 patients. There are major differences in both clinical presentation as well as choice of treatment between the unilateral and bilateral tumors and therefore this thesis will be limited to the unilateral sporadic vestibular schwannomas.

Vestibular schwannomas usually cause unilateral hearing loss, tinnitus and sometimes dizziness or vertigo. In larger tumors unsteadiness, trigeminal symptoms and long tract symptoms may arise. However, symptoms due to affected lower cranial nerves are rarely seen. In very large tumors, brain stem compression, obstructive hydrocephalus and increase of intracranial pressure can also be observed. For many years, VS was diagnosed using standard audiometry together with auditory brain stem evoked responses (ABRs), which is a sensitive indicator of retrocochlear pathology, and computer tomography of the internal auditory canal. This method could demonstrate a widening of the porus or when contrast enhanced, a VS

extending into the cerebellopontine angle (CPA). Nowadays, contrast enhanced MRI using T1-weighted images, is the gold standard for diagnosing VS and tumors as small as 2-3 mm can be detected (10).

Vestibular schwannoma treatment

Microsurgery

More than a century after Eduard Sandifort (1742-1814), professor of anatomy at the University of Leiden, described the first presumptive case of VS, Sir Charles Balance (1856-1936) successfully operated on a VS for the first time in 1894 (11,12). In his surgical report, he described the difficulties of getting his index finger around the tumor to achieve removal. But the patient was still alive after surgery albeit with a fifth and seventh nerve palsy.

Several decades later, the treatment of VS had been further developed, but still with high operative mortality: for instance, at the 1913 International Conference of Medicine in London, the perioperative mortality in the major centers was reported at 78% and most survivors experienced significant postoperative morbidity (13). However, surgical techniques continued to evolve with the introduction of different surgical approaches, better anesthesia and use of antibiotics. One of the greatest improvements of that time was probably the introduction of the operating microscope by the otologist William House in 1961. As of that time, the VS field was no longer dominated by neurosurgeons like Harvey Cushing or Walter Dandy. Together with William Hitselberger, also a renowned neurosurgeon, House could further develop surgical approaches like the translabyrinthine (TL) and middle fossa (MF) approach. They became a unique surgical team and were thereby the founders of the close cooperation between otologists and neurosurgeons in the treatment of VS, a cooperation which still exists today. In 1968, House reported on 141 patients with a 72% facial nerve preservation rate. In 1978, in a subsequent series of 500 VS patients, the facial nerve was anatomically preserved in 96.6% of these patients (14,15). With the use of new surgical approaches and more recently intraoperative facial nerve monitoring, it was not only possible to save the life of a patient suffering from VS, but the tumor could now be removed more radically. Moreover, important structures such as the facial nerve and inner ear could also be saved.

Nowadays, the perioperative mortality has become less than 1%, with favorable cranial nerve outcomes reported by the major centers (16-22). However, despite these advances, considerable risk still exists to both facial nerve functioning and hearing. Furthermore, microsurgery may lead to complications such as postoperative intracranial haemorrhage, cerebrospinal fluid (CSF) leak and meningitis.

Radiosurgery

During the evolution of microsurgical treatment, others were working to develop new concepts for tumor management. In 1969, Lars Leksell was the first to treat vestibular schwannomas with Gamma Knife radiosurgery at the Karolinska Hospital in Stockholm, Sweden (23). He proposed the technique of focusing multiple beams of external radiation on the stereotactically defined intracranial tumor. The average of these intersecting beams results in very high doses of radiation in the tumor, but very low doses to non-target tissues along the pathway of each beam. The modern Gamma Knife consists of 201 fixed cobalt radiation sources in a fixed hemispherical array, such that all 201 photon beams are focused on a single point. The patient is stereotactically positioned in the Gamma Knife so that the intracranial tumor coincides with the isocenter of radiation. The radiation target volume is shaped conform to the intracranial tumor using beam blocking, variable collimation and multiple isocenters.

Another radiation alternative for the treatment of VS is conventional radiotherapy (24). This technique, by contrast, delivers the dose to the tumor in fractions. The dose can be targeted using stereotaxy as well as conformal techniques.

This thesis will discuss the results of radiosurgical treatment of VS using the linear accelerator (LINAC) system. In 1984, an alternative radiosurgical option, the LINAC, was first described by Betti et al (25). Since then, the precision and accuracy of the LINAC systems have been further improved and modified for the required radiosurgical application (26, 27) Most LINAC systems rely on the following basic principles: a collimated photon beam is focused on the stereotactically identified intracranial tumor. The gantry of the LINAC rotates around the patient, producing an arc of radiation focused on the tumor. The patient couch is then rotated in the horizontal plane and another arc is performed. In this manner, multiple non-coplanar arcs of radiation intersect at the target volume and produce a high target dose, with minimal radiation dose to surrounding tissue. The dose concentration method is analog to the multiple intersecting beams of cobalt radiation in the Gamma Knife

system. Again the target dose distribution can be shaped according to the tumor using variable collimation, multiple isocentres or changing the arc angles. Dose distributions are the same for LINAC based and Gamma Knife systems.

In the past, results from radiosurgical studies showed relatively impaired cranial nerve functions, which were probably caused by the higher dose of radiation to the tumor margin and higher target volumes. Moreover, at that time, radiosurgery was planned with early generation CT scans with relatively poor quality, making it more difficult to dose planning to the tumor margin. At the present time, advances in dose planning software and MR imaging together with a gradual decline in the prescribed dose of radiation have significantly improved cranial nerve outcomes, have reduced complication rates and have resulted in promising long term tumor control (28-34). However, there are some limitations to the treatment. For instance, the goal of treatment is to achieve tumor control and not removal, which means that with this technique there is no ability to relieve the mass effect of the tumor. Moreover, in order to avoid complications, lower and potentially less effective doses are required for higher tumor volumes. This limits the use of radiosurgery to the treatment of smaller tumors. Furthermore, the evidence regarding long term tumor control after low dose radiosurgery is only recently becoming available. Another limitation is the need for lifelong follow-up even after successful treatment. Despite these limitations, there is increasing evidence that radiosurgery is a safe and effective alternative therapy for vestibular schwannomas (28-30).

Observation

Technical advances such as the advent of magnetic resonance imaging (MRI) also made it possible to detect small tumors early in patients with minimal or no symptoms. With the widespread use of MRI, the relative incidence of smaller tumors has risen significantly. Moreover, increased knowledge on the natural history of these tumors shows that most VS are slow growing or do not grow at all (35,36). In a recent meta-analysis Smouha et al. found a mean growth rate of 1.9 mm/year during an observation period of 3.2 years (37). Some reports also describe spontaneous involution or rather rapid growth (38,39). As a result, experts in the field of skull base surgery have questioned the need for major skull base surgery in every case of VS. Despite advances in microsurgical treatment, patients may be left with deficits, which are not insignificant and outcomes may not automatically equate improved QoL. Other factors might also influence the decision to refrain from treatment such

as advanced age or severe comorbidity or the fact that the tumor is located at the only hearing ear. Therefore, in many centers, a more conservative approach has been proposed for small and medium-sized tumors, in which no treatment is offered to the patients, but an initial wait and scan surveillance until there is evidence of tumor progression or significant increase of symptoms (40-44). This approach has been increasingly supported in the literature and obviously has great appeal for patients. However, there are some limitations to this kind of approach of VS. The natural course of the tumor is still uncertain, for instance there are no predictive factors for tumor growth or progression of symptoms and delayed treatment in case of growth may impose greater morbidity (44). Furthermore, a wait and scan policy offers no definite treatment and necessitates a prolonged and probably lifelong follow-up.

Treatment decisions

As described above, VS patients have several treatment options including observation, microsurgery and stereotactic radiosurgery. However, the treatment of VS patients is still controversial with advocates and opponents of each modality. There is a large amount of literature supporting these three modalities, which are often separately assessed and only sometimes compared to each other. Despite this abundance, the evidence is generally no better than class III in the Cochrane classification of the quality of evidence (45). Thus, it appears that well-designed, randomized controlled studies (RCTs) are required in order to improve the quality of the evidence and compare the different modalities. However, the difficulty of such a study is that the three methods of VS management have totally different goals. The aim of microsurgery is complete tumor removal whereas radiosurgery aims to control tumor growth assuming that patients will not need additional treatment. Wait and scan offers patients tumor surveillance under the assumption that most tumors do not grow. Until now, there is no hard evidence for any of these approaches. First, there should be some consensus on the goals and success criteria of treatment of VS before RCTs can be undertaken.

In general, the choice of treatment for many patients depends on their own specific goals and on the expected results from their treatment. Before this decision, every patient must be provided with information about all available treatment options, including the advantages and disadvantages of each, as this is the basis for informed consent. Traditionally, the primary outcome measures in the evaluation

of treatment have evolved around mortality and morbidity. However, there is an increased interest concerning the impact of interventions on function and quality of life (QoL). QoL assessment may provide valuable information that is not always supplied by traditional outcome measures. It is now well recognized that treatment choices in individual patient care can be positively influenced by QoL assessment (46). QoL can not only help to determine patient preference, or compare well-being after different treatment modalities but also measure minor differences in response to treatment which may be missed by the traditional outcome measures.

Patients' perceptions

During the last 20 years, interest in patient reported outcomes (PROs) research has increased enormously, especially towards health status and health care interventions (46). Quality of life is an operationalization of PROs and represents the sum of an individual's physical, social, emotional, occupational and spiritual well-being. Defining QoL is therefore a complex matter and a comprehensive definition does not exist (47).

The World Health Organization has proposed "the individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals and expectations, standards and concerns" (48). This approach is a more broad and generic conceptualization of QoL and can be differentiated from a more specific 'health-related QoL', which concerns those aspects of people's lives that impact directly their health status or the more economic cost-effectiveness models of QoL. A widely used definition of 'health-related QoL' was proposed by Patrick and Erickson: "the value assigned to the duration of life as modified by the impairments, functional states, perceptions and social opportunities that are influenced by disease, injury, treatment or policy" (49). More recently, Schipper et al. described health-related QoL as: "the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient" (50). These functional effects are divided into three categories: physiological, psychological and social effects, which are thought to adequately represent QoL.

Some of the first aspects of QoL assessment were introduced in 1949 by Karnofsky, who used an index to evaluate treatment success in his patients. The Karnofsky Performance Status is an observer-rated measurement to assess patients on a 0-100 scale (0 for 'dead' and 100 for 'no evidence of disease, able to carry out normal

activity and to work') (51). Since that time, a number of rating scales for clinicians have been developed, especially in the cancer research field. However, over time the ratings on a patient's QoL by others were considered as 'surrogate' and patients themselves were asked to provide information concerning aspects of their QoL (46). At present, PROs are considered as a recognized measure in modern health care research.

In VS, QoL has long been a neglected area, given the quite low incidence compared with other more common diseases such as cancer. In the latter area, QoL is assessed with well-designed and validated measures and QoL has become a major outcome variable, which also affects the choice of medical management (52). However, since the beginning of the 1990s, QoL in VS has received increasing attention. One of the first studies on PRO was performed by Wiegand et al. in 832 VS patients who had joined a patient member organisation, the Acoustic Neuroma Association, after microsurgical treatment between 1973 and 1983 (53). Results showed that microsurgery has a significant impact on a patient's quality of daily life and that facial nerve dysfunction and hearing loss were the most difficult aspects to cope with postoperatively. However, the authors also recognized that one of the major limitations of their study was the patient sample itself, which consisted of operated VS patients who had joined the self-help group. On the other hand, this group may represent the majority of patients that underwent VS surgery in this period and therefore the results may still reflect an average VS population after surgery. The results of this study have led to numerous studies on the effects of microsurgery on QoL (54-63). Most of these were performed using a retrospective design and the QoL measures used were often not reliable or had not previously been used. However, some did use validated questionnaires such as the Short-Form 36 Health Survey (SF-36) or Glasgow Benefit Inventory (GBI) (60-63). They found that QoL was generally impaired after microsurgical treatment. Interestingly, facial nerve function only correlated weakly with impaired QoL whereas balance problems and hearing loss most affected quality of functioning.

Valid and reliable measures are necessary to assess QoL. A widely used and reliable measure of generic QoL is the SF-36, which has proven its reliability in a variety of diseases throughout different patient populations. It assesses QoL in 8 domains and measures physical, psychological and social well-being. However, the sensitivity of such a generic measure to otolaryngologic interventions or audiological or vestibular symptoms has been questioned (64). Disease-specific measures have

been developed, therefore, in order to particularly assess QoL of patients with a specific disease. Unfortunately, a validated disease-specific questionnaire has not been developed specifically for VS patients yet. However, there are some studies that use validated questionnaires addressing symptoms that are typically observed in (treated) VS patients (56-59). Again, most of these studies were performed retrospectively; they generally demonstrated a negative effect of surgery on the subsequent symptoms and on QoL. Still, there is a need for validated disease-specific questionnaires, which might be combined with generic questionnaires in the future.

Until now, only a few studies report on QoL after radiosurgery or conservative treatment and reports comparing different modalities are scarce (61,65-70). When compared to microsurgical patients, patients treated with radiosurgery appear to have a better QoL outcome. For instance, in the study by Régis, a better QoL was reported after Gamma Knife surgery, but the QoL measures were not validated (67). However, Myrseth et al. found better QoL after Gamma Knife treatment when compared to microsurgical treatment using validated questionnaires (68). Surprisingly, little is known concerning QoL in untreated VS patients (71). Generally, impaired QoL is found for the three treatment modalities. However, often one can question whether the reduction is caused by the treatment, by suffering from the tumor, or by both. Both prospective studies with pretreatment QoL data or information from untreated patient samples may be valuable in answering this hypothesis.

Another interesting subject is how patients perceive their illness and how they cope with having an intracranial tumor. Given the quite solid status of QoL as an outcome measure in medicine, researchers and clinicians started examining determinants of QoL. This line of research, and its clinical application, might help to develop interventions that improve QoL. One concept that was found to contribute to variation across patients in their QoL was that of illness perceptions (72). Illness perceptions (IPs) pertain to the idiosyncratic ideas (cognitions) of patients (and physicians) regarding complaints and symptoms. They seem to play a role in the variation in QoL experienced by patients. IPs include the beliefs and attributions patients have regarding their illness and specifically regarding symptoms, causes, consequences, and the time the illness will last (73). They are assessed with questionnaires, drawings or even clay representations of an illness (74). IPs precede coping behavior, and in turn, coping determines QoL (75). IPs have been found to be relevant in virtually any physical disorders, and, increasingly in psychiatric disorders. IPs reflect the relevance and importance of how patients make sense of complaints,

illness and medical treatment – irrespective of objective medical knowledge. In this way, including IPs in QoL research strengthens the biopsychosocial model, which is particularly relevant in medical care for patients with a chronic illness. In patients with VS, IPs have not yet been studied before. Our current study, therefore, explores the relevance of IPs in patients with VS, and their contribution to, hopefully and possibly, an even better quality of care, and QoL.

Overview and aims of the present thesis

In the Netherlands, VS was previously described in a PhD thesis by Jos van Leeuwen, who reported on the diagnostic aspects and results of surgery in particular. The studies were performed at the Department of Otolaryngology at the University Hospital Nijmegen between 1980 and 1993 and van Leeuwen was one of the first who discussed the importance of QoL research after (surgical) treatment for VS (76). A more histopathological approach was described by Ernestine Stipkovits who provided more insight in the natural course of VS (35) in her PhD thesis, entitled “Vestibular schwannomas, aspects of biological behavior” at the University of Utrecht in 2000.

In Leiden, patients with VS have been treated for many years. In the past, VS patients were primarily referred to the Department of Neurosurgery of the Leiden University Medical Centre (LUMC). One of the main reasons was that patients used to be operated either via the retro-sigmoid (RS) or suboccipital approach (SO) and that the experience of the otolaryngologists in our department was generally limited to the translabyrinthine (TL) approach. However, in 1996 the Leiden Skull Base Pathology Meeting (SBP) was founded, which mainly consisted of otolaryngologists, neurosurgeons and neuroradiologists from the LUMC. This multidisciplinary meeting provided the basis for the close cooperation between otolaryngologists and neurosurgeons in VS, which still continues to evolve. Our department was not only increasingly involved in the management of these tumors but also became more skilled in the various surgical approaches such as the TL and middle fossa (MF) approach. As a result, all the three main approaches: TL, RS and MF are now widely used in our center. However, the advantages of the TL approach are increasingly recognized by both our otolaryngologists and neurosurgeons and it has now become the most frequently used approach and ‘workhorse’. Furthermore, relatively new treatment options such as wait and scan or stereotactic irradiation have also made their way into our decision process over time. Nowadays, almost 1000 new VS

patients have been admitted to the LUMC and about 400 have been operated via the TL route.

Over time, our (surgical) treatment also continued to advance, because of improved techniques such as the high resolution MRI, the facial nerve monitor, CUSA aspirator and better perioperative care. As obvious as it may seem, we recognized that the treatment of any condition can only be justified when the results of treatment are better than the natural course of the disease. There is a growing debate on how VS can be best treated as it has become clear that the tumor may remain unchanged for many years. In an effort to contribute to this debate, QoL research was initiated at our department in 2001.

Our study assesses QoL in order to facilitate treatment choices in individual patient care, contributes to the determination of the best use of treatments and evaluates QoL in our VS patient population. It is likely that none of the three treatment modalities on its own is the best option for all individuals. Knowledge of the clinical and QoL effects of each of the different options can help clinicians to outline the choices available to patients and assist them in selecting which is best for them. For instance, if a VS patient has a small tumor with minimal symptoms, reasonable treatment options might be radiosurgery or wait and scan. The treatment choices available depend partly on the patient's age and comorbidity but also, to some extent, on the individual's preferences given the different QoL implications of the two treatments. Some patients may choose radiosurgery with possible surgical risks in the short term. Others will prefer no active treatment or subsequent risks and choose to evaluate their tumor periodically by MR imaging. Information on QoL in this context can be useful to both professionals and patients when considering what to expect, given certain health conditions and treatments. This kind of evidence to inform a clinician or patient comes from studies of populations of patients who are experiencing the condition or treatment (46).

This thesis describes QoL and clinical features in patients with VS at their diagnosis and after treatment with three different modalities: observation, microsurgery or radiosurgery.

Outline of the thesis

Chapter two prospectively assesses QoL together with illness perceptions (IPs) and coping behavior in a series of 90 consecutive, untreated VS patients. QoL assessment was performed at the moment of diagnosis, which enabled us to assess the burden of suffering from an (untreated) VS. The results were compared to patients with other serious or chronic illnesses (i.e. head and neck cancer patients or patients with chronic obstructive pulmonary disease) in order to assess what kind of IPs and coping behavior could be expected with these kinds of patients.

Chapter three describes a group of VS patients with small- and medium-sized tumors who were observed for almost four years. Failure of conservative treatment, tumor progression and development of symptoms such as hearing are described. QoL outcomes at baseline and at the end of follow-up are compared in those patients who were still included in our protocol. An initial conservative approach, in which the tumor is watched rather than treated, is an attractive option to many VS patients. However, there is no clarity about the natural course of the disease such as tumor growth, preservation of hearing or QoL.

Until recently, microsurgery was considered the 'gold standard' in the treatment of VS. However, at present stereotactic irradiation is increasingly becoming a first treatment option for VS. Chapter four presents clinical and QoL results of 64 patients with VS after low dose linear accelerator based (LINAC) radiosurgery. This multicenter study is performed in collaboration with the Erasmus University Medical Centre in Rotterdam. Both clinical results and QoL outcome are compared to existing results and norm populations.

Chapter five describes the effect of vertigo on QoL in 18 VS patients using generic and a disease-specific questionnaire for vertigo. Of the cochleovestibular symptoms in VS, vertigo is thought to affect QoL most (71). Vertigo may increasingly cause anxiety, depression and impaired functioning during physical and social activities and may therefore have a severe negative effect on quality of daily functioning of VS patients. Despite the significant impact on QoL, there is little evidence with regard to any interventions in VS patients with these symptoms. In an attempt to relieve patients from their vertigo and improve QoL, we performed translabyrinthine (TL) surgery and preoperative and postoperative results are evaluated.

The effects of postoperative facial nerve impairment on QoL still remain unclear. Some studies report a significant negative effect on QoL, whereas others do not.

However, it is well recognized that patients with facial nerve paralysis experience significant functional and psychological morbidity (77,78). In order to reanimate the paralyzed facial musculature after (surgical) trauma, there are various treatments, which consist of static and non-static procedures (79-83). The technique that is most frequently used involves a variation of the facial-hypoglossal nerve coaptation with or without static procedures. Chapter six presents a new variation to the facial-hypoglossal technique (FHT) to restore facial nerve paralysis as a result of (surgical) trauma. QoL and functional improvements are described and compared to results from other comparable techniques.

Facial nerve function is one of the most important factors defining success of treatment for both the patient and surgeon. In case of microsurgical treatment, the surgeon therefore may decide to leave some of the tumor in situ in order to preserve facial nerve function and maintain QoL, especially in large tumors. Intraoperative assessment of the extent of tumor removal, however, lacks objectivity. Objective assessment of the actual extent of removal documented with postoperative gadolinium enhanced magnetic resonance imaging (MRI) scans is therefore necessary, but is scarcely provided. Chapter seven examines the hypothesis that postoperative facial nerve function should be significantly better when residual tumor is deliberately left behind. We also objectively assess the extent of the removal using gadolinium-enhanced MRI scans and compare results with the extent of the removal as intraoperatively estimated by the surgeon.

Chapter eight discusses our major results and conclusions of the studies in this thesis and presents clinical implications and suggestions for future research.

References

1. Murray M and Stout AP: Schwann cell versus fibroblast as origin of specific nerve sheath tumor, observations upon normal nerve sheaths and neurilemmomas in vitro. *Am J Pathol* 1940;16:41-60.
2. Stewart TJ, Liland J, Schuknecht HF: Occult schwannomas of the vestibular nerve. *Arch Otolaryngol* 1975;101:91-95.
3. Tos M, Stangerup SE, Caye Thomasen P, Tos T, Thomsen J. What is the real incidence of vestibular schwannoma? *Arch Otolaryngol Head Neck Surg* 2004;130:216-220.
4. Moffat DA, Jones SE, Mahendran S, Humphriss S, Baguley DM. Referral patterns in vestibular schwannoma – 10 years on. *Clin Otolaryngol Allied Sci* 2004;29:515-517.
5. Mirz F, Jorgensen B, Fiirgaard B, Lundorf E. Incidence and growth pattern of vestibular schwannomas in a Danish country, 1977-1988. *Acta Otolaryngol Suppl* 2000;543:30-33.
6. Mathies C, Samii M. Management of 1000 vestibular schwannomas (acoustic neuromas): clinical presentation. *Neurosurgery* 1997;40:1-9.
7. Myrseth E, Moller P, Pedersen PH, Vassbotn FS, Wentzel-Larsen T, Lund-Johansen M. Vestibular schwannomas: clinical results and quality of life after microsurgery or gamma knife radiosurgery. *Neurosurgery* 2005;56:927-935.
8. Ryzenman JM, Pensak ML, Tew JM Jr. Headache: a quality of life analysis in a cohort of 1657 patients undergoing acoustic neuroma surgery, results from the Acoustic Neuroma Association. *Laryngoscope* 2005;115:703-711.
9. Abaza MM, Makariou E, Armstrong M, Lalwani AK. Growth rate characteristics of acoustic neuromas associated with neurofibromatosis type 2. *Laryngoscope* 1996;106:684-699.
10. Sidman JD, Carrasco VN, Whaley RA, Pillsbury HC 3rd. Gadolinium. The new gold standard for diagnosing cerebellopontine angle tumors. *Arch Otolaryngol Head Neck Surg* 1989;115:1244-1247.
11. Sandifort E. Observaciones anatomico-pathologicae. Lugduni Batavorum: Apud P.v.d. Eyk et D. Vygh, 1777:116-120.
12. Ballance CA. Some points in the surgery of the brain and its membranes. London: Macmillan 1907:249-284.
13. von Eiselsberg A. Ueber die chirurgische Behandlung der Hirntumoren. *Trans Int Congress Med London* 1913;7:203-207.
14. House WF. Case summaries. *Arch Otolaryngol* 1968;88:586-591.
15. House WF, Luetje CM. Evaluation and preservation of facial function: postoperative results. In: House WF, Luetje CM, eds. *Acoustic Tumors*. vol 2. Baltimore: University Park Press, 1979:89-96.
16. Brackmann DE, Cullen RD, Fischer LM. Facial nerve function after translabrynthine vestibular schwannoma surgery. *Otolaryngol Head Neck Surg* 2007;136:773-777.
17. Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): the facial nerve preservation and restitution of function. *Neurosurgery* 1997;40:684-694.
18. Darrouzet V, Martel J, Enee V, Bebear JP, Guerin J. Vestibular schwannoma surgery outcomes: our multidisciplinary experience in 400 cases over 17 years. *Laryngoscope* 2004;114:681-688.
19. Gjuric M, Wigand ME, Wolf SE. Enlarged middle fossa vestibular schwannoma surgery: experience with 735 cases. *Otol Neurotol* 2001;22:223-230.
20. Hardy DG, Macfarlane R, Baguley D, Moffat DA. Surgery for acoustic neurinoma. An analysis of 100 translabrynthine operations. *J Neurosurg* 1989;71:799-804.

21. Tos M, Charabi S, Thomsen J. Clinical experience with vestibular schwannomas: epidemiology, symptomatology, diagnosis, and surgical results. *Eur Arch Otorhinolaryngol* 1998;255:1-6.
22. Sanna M, Taibah A, Russo A, Falcioni M, Agarwal M. Perioperative complications in acoustic neuroma (vestibular schwannoma) surgery. *Otol Neurotol* 2004;25:379-386.
23. Leksell L: A note on the treatment of acoustic tumors. *Acta Chir Scand* 1971;137:763-765.
24. Mendenhall WM, Friedman WA, Amdur RJ, Antonelli PJ. Management of acoustic schwannoma. *Am J Otolaryngol* 2004;25:38-47.
25. Betti OO, Derechinsky VE: Hyperselective encephalic irradiation with a linear accelerator. *Acta Neurochir Suppl* 1984;33:385-390.
26. Winston KR, Lutz W: Linear accelerator as a neurosurgical tool for stereotactic radiosurgery. *Neurosurgery* 1988;22:454-464.
27. Das IJ, Downes MB, Corn BW, Curran WJ, Werner-Wasik M, Andrews DW. Characteristics of a dedicated linear accelerator-based stereotactic radiosurgery-radiotherapy unit. *Radiother Oncol* 1996;38:61-68.
28. Kondziolka D, Lunsford LD, McLaughlin MR, Flickinger JC. Long term outcomes after radiosurgery for acoustic neuromas. *N Engl J Med* 1998;339:1426-1433.
29. Lunsford LD, Niranjan A, Flickinger JC, Maitz A, Kondziolka D. Radiosurgery of vestibular schwannomas: summary of experience in 829 cases. *J Neurosurgery Suppl* 2005;102:195-199.
30. Régis J, Roche PH, Delsanti C. Modern management of vestibular schwannomas. In: Szeifert GT, Kondziolka D, Levivier M, Lunsford LD, eds. *Radiosurgery and Pathological Fundamentals*. Prog Neurol Surg. Basel: Karger, 2007;129-141.
31. Chopra R, Kondziolka D, Niranjan A, Lunsford LD, Flickinger JC. Long term follow-up of acoustic schwannoma radiosurgery with marginal tumor doses of 12 to 13 Gy. *Int J Radiation Oncol Biol Phys* 2007;68:845-851.
32. Friedman WA, Bradshaw P, Myers A, Bova FJ. Linear accelerator radiosurgery for vestibular schwannomas. *J Neurosurg* 2006;105:657-661.
33. Prasad D, Steiner M, Steiner L. Gamma surgery for vestibular schwannoma. *J Neurosurg* 2000;92:745-759.
34. Hasegawa T, Fujitani S, Katsumata S, Kida Y, Yoshimoto M, Koike J. Stereotactic radiosurgery for vestibular schwannomas: analysis of 317 patients followed more than 5 years. *Neurosurgery* 2005;57:257-265.
35. Stipkovits EM, Graamans K, Vasbinder GB, Van Dijk JE, Beek FJ. Assessment of vestibular schwannoma growth: application of a new measuring protocol to the results of a longitudinal study. *Ann Otol Rhinol Laryngol* 2001;110:326-330.
36. Nutik SL, Babb MJ. Determinants of tumor size and growth in vestibular schwannoma. *J Neurosurg* 2001;94:922-926.
37. Smouha EE, Yoo M, Mohr K, Davis RP. Conservative treatment of acoustic neuroma: a meta-analysis and proposed treatment algorithm. *Laryngoscope* 2005;115:450-454.
38. Luetje CM. Spontaneous involution of acoustic tumors. *Am J Otol* 2000;21:393-398.
39. Hwang SK, Kim DG, Paek SH, Kim CY, Kim MK, Chi JG, Jung HW. Aggressive vestibular schwannomas with postoperative rapid growth: clinicopathological analysis of 15 cases. *Neurosurgery* 2002;51:1381-1390.
40. Tschudi DC, Linder TE, Fisch U. Conservative management of unilateral acoustic neuroma. *Am J Otol* 2000;21:722-728.
41. Al Sanosi A, Fagan PA, Biggs ND. Conservative management of acoustic neuromas. *Skull Base* 2006;16:95-100.

42. Raut VV, Walsh RM, Bath AP, Bance ML, Guha A, Tator CH, Rutka JA. Conservative management of vestibular schwannomas – second review of a prospective longitudinal study. *Clin Otolaryngol Allied Sci* 2004;29:505-514.
43. Walsh RM, Bath AP, Bance ML, Keller A, Tator CH, Rutka JA. The role of conservative management of vestibular schwannomas. *Clin Otolaryngol Allied Sci* 2000;25:28-39.
44. Bederson JB, von Ammon K, Wichmann WW, Yasargil MG. Conservative management of patients with acoustic tumors. *Neurosurgery* 1991;28:646-650.
45. Nikolopoulos TP, Donoghue GM. Acoustic neuroma management: an evidence based medicine approach. *Otol Neurotol* 2002;23:534-541.
46. McGee H, Ring L. Quality of life. In: D. French, A.A. Kaptein, K. Vedhara, J. Weinman (Eds.), *Health Psychology*, 2nd edition. Chichester/Oxford: Wiley Blackwell British Psychological Society, in press (2010).
47. Kaptein AA, Morita S, Sakamoto J. Quality of life in gastric cancer. *World J Gastroenterol* 2005;11:3189-3196.
48. The WHOQOL Group. The World Health Organization Quality of Life Assessment (WHOQOL): position paper from the World Health Organization. *Soc Sci Med* 1995;10:1403-1409.
49. Patrick DL, Erickson P. Assessing health-related quality of life for clinical decision-making. In *Quality of life assessment. Key issues in the 1990s*. Edited by: Walker SR and Rosser RM. Lancaster, Kluwer;1993:11-64.
50. Schipper H, Clinch J, Olweny LM. Definitions and conceptual issues. In: Spilker B, ed. *Quality of life and pharmacoeconomics in clinical trials*. Philadelphia: Lippincott-Raven, 1996:11-24.
51. Schag CC, Heinrich RL, Ganz PA. Karnofsky performance status revisited: Reliability, validity, and guidelines. *J Clin Oncol* 1984;2:187-193.
52. Bottomley A, Therasse P. Quality of life in patients undergoing systemic therapy for advanced breast cancer. *The Lancet Oncol* 2002;3:620-628.
53. Wiegand DA, Fickel V. Acoustic Neuroma - The Patient's Perspective: subjective assessment of symptoms, diagnosis, therapy, and outcome in 541 patients. *Laryngoscope* 1989;99:179-187.
54. Rigby PL, Shah SB, Jackler RK, Chung JH, Cooke DD. Acoustic neuroma surgery: Outcome analysis of patient-perceived disability. *Am J Otol* 1997;18:427-435.
55. Tos T, Caye-Thomasen P, Stangerup S, Tos M, Thomsen J. Patients' fears, expectations and satisfaction in relation to management of vestibular schwannoma: a comparison of surgery and observation. *Acta Otolaryngol* 2003;123:600-605.
56. Inoue Y, Ogawa K, Kanzaki J. Quality of life of vestibular schwannoma patients after surgery. *Acta Otolaryngol* 2001;121:59-61. Parving A, Tos M, Thomsen J, Møller H, Buchwald C. Some aspects of life quality after surgery for acoustic neuroma. *Arch Otolaryngol Head Neck Surg* 1992;118:1061-1064.
57. Andersson G, Ekvall L, Kinnefors A, Nyberg G, Rask-Andersen H. Evaluation of quality of life and symptoms after translabyrinthine acoustic neuroma surgery. *Am J Otol* 1997;18:421-426.
58. Magliulo G, Zardo F, D' Amico R, Varacalli S, Forino M. Acoustic Neuroma: Postoperative quality of life. *J Otolaryngol* 2000;29:344-347.
59. Betchen SA, Walsh J, Post KD. Self-assessed quality of life after acoustic neuroma surgery. *J Neurosurg* 2003;99:818-823.
60. da Cruz MJ, Moffat DA, Hardy DG. Postoperative quality of life in vestibular schwannoma patients measured by the SF-36 Health Questionnaire. *Laryngoscope* 2000;110:151-155.
61. Kelleher MO, Fernandes MF, Sim DW, O'Sullivan MG. Health-related quality of life in patients with skull base tumors. *Br J Neurosurg* 2002;16:16-20.

62. Lynn SG, Driscoll CLW, Harner SG, Beatty CW, Atkinson EJ. Assessment of dysequilibrium after acoustic neuroma removal. *Am J Otol* 1999;20:484-494.
63. Martin HC, Sethi J, Lang D, Neil-Dwyer G, Lutman ME, Yardley L. Patient-assessed outcomes after excision of acoustic neuroma: postoperative symptoms and quality of life. *J Neurosurg* 2001;94:211-216.
64. Ware JE, Sherbourne CD. The MOS 36-item Short Form Health Survey (SF-36). *Med Care* 1992;30:473-483.
65. Pollock BE, Driscoll CL, Foote RL, Link MJ, Gorman DA, Bauch CD, Mandrekar JN, Krecke KN, Johnson CH. Patient outcomes after vestibular schwannoma management: a prospective comparison of microsurgical resection and stereotactic radiosurgery. *Neurosurgery* 2006;59:77-85.
66. van Roijen L, Nijs HG, Avezaat CJ, Karlsson G, Linqvist C, Pauw KH, Rutten FF. Costs and effects of microsurgery versus radiosurgery in treating acoustic neuroma. *Acta Neurochir* 1997;139:942-948.
67. Régis J, Pellet W, Delsanti C, Dufour H, Roche PH, Thomassin JM, Zanaret M, Peragut JC. Functional outcome after gamma knife surgery or microsurgery for vestibular schwannoma. *J Neurosurg* 2002;97:1091-1100.
68. Myrseth E, Moller P, Pedersen PH, Vassbotn FS, Wentzel-Larsen T, Lund-Johansen M. Vestibular schwannomas: clinical results and quality of life after microsurgery or gamma knife radiosurgery. *Neurosurgery* 2005;56:927-935.
69. Sandooram D, Grunfeld E, McKinney C, Gleeson MJ. Quality of life following microsurgery, radiosurgery and conservative management for unilateral vestibular schwannoma. *Clin Otolaryngol Allied Sci* 2004;29:621-627.
70. Macandie C, Crowther J. Quality of life in patients with vestibular schwannomas managed conservatively. *Clin Otolaryngol Allied Sci* 2004;29:215-218.
71. Myrseth E, Moller P, Goplen F, Wentzel-Larsen T, Lund-Johansen M. Untreated vestibular schwannoma: vertigo is a powerful predictor for health-related quality of life. *Neurosurgery* 2006;59:67-76.
72. Leventhal H, Brissette I, Leventhal EA. The common-sense model of self-regulation of health and illness. In LD Cameron & H Leventhal (eds). *The self regulation of health and illness behavior*. London: Routledge, 2003, pp 42-65.
73. Scharloo M, Kaptein AA, Schlösser M, Pouwels H, Bel EH, Rabe KF, Wouters EF. Illness perceptions and quality of life in patients with chronic obstructive pulmonary disease. *J Asthma* 2007;44:575-581.
74. Reynolds L, Broadbent E, Ellis CJ, Gamble G, Petrie KJ. Patients' drawings illustrate psychological and functional status in heart failure. *J Psychosom Res* 2007;63:525-532.
75. Helder DI, Kaptein AA, Van Kempen GM, Weinman J, Van Houwelingen JC, Roos RA. Living with Huntington's disease: illness perceptions, coping mechanisms, and spouses' quality of life. *Int J Behav Med* 2002;9:37-52.
76. van Leeuwen JP, Braspenning JC, Meijer E, Cremers CW. Quality of life after acoustic neuroma surgery. *Ann Otol Rhinol Laryngol* 1996;105:423-430.
77. Coulson SE, O' Dwyer NJ, Adams RD, Croxson GR. Expression of emotion and quality of life after facial nerve paralysis. *Otol Neurotol* 2004;25:1014-1019.
78. de Swart BJ, Verheij JC, Beurskens CH. Problems with eating and drinking in patients with unilateral peripheral facial paralysis. *Dysphagia* 2003;18:267-273.
79. Conley J, Baker DC. Hypoglossal-facial nerve anastomosis for reinnervation of the paralyzed face. *Plast Reconstr Surg* 1979;63:63-72.

80. Gavron JP, Clemis JD. Hypoglossal facial nerve anastomosis: a review of forty cases caused by facial nerve injuries in the posterior fossa. *Laryngoscope* 1984;94:1447-1450.
81. Cusimano MD, Sekhar L. Partial hypoglossal to facial nerve anastomosis for reinnervation of the paralyzed face in patients with lower cranial nerve palsies: technical note. *Neurosurgery* 1994;35:532-534.
82. Arai H, Sato K, Yanai A. Hemihypoglossal-facial nerve anastomosis in treating unilateral facial palsy after acoustic neurinoma resection. *J Neurosurg* 1995;82:51-54.
83. May M, Sobol SM, Mester SJ. Hypoglossal-facial nerve interpositional jump graft for facial reanimation without tongue atrophy. *Otolaryngol Head Neck Surg* 1991;104:818-825.