Chapter 8

General discussion and conclusion
The overall aim of this thesis was to examine the outcomes of current treatment options for vestibular schwannoma (VS) with an emphasis on patient reported outcomes (PROs). First, we described quality of life (QoL) outcome, illness perceptions (IPs) and coping behavior in patients with VS at diagnosis. Secondly, we investigated QoL and important clinical aspects in patients with VS who were treated either with wait and scan, microsurgery or radiosurgery.

Nowadays, major technical advances have ensured that the treatment of VS no longer involves life saving surgery but rather prophylactic management of future morbidity in most patients. As part of these advances, relatively new treatment options have evolved such as a wait and scan policy or stereotactic irradiation (1-12). However, the diversity in available options does not necessarily facilitate the choice of treatment. Microsurgery implies that a patient has to undergo major skull base surgery for tumor removal with significant risk of morbidity including facial nerve palsy and hearing loss, while radiosurgery is non-invasive and aims at tumor control. Radiosurgery further carries less risk of cranial nerve deficit, while conservative treatment generally implies tumor surveillance until tumor progression is observed. As a result, all current options have completely different treatment goals and criteria of success. Moreover, VS patients increasingly have their own priorities regarding treatment. Each treatment therefore, may have entirely different consequences for the life of VS patients. From this point of view, PROs such as QoL may provide valuable information in addition to the traditional outcome measures. Recently, it was also recognized that besides these conventional measures, psychological factors could play an important role in determining the patient’s QoL (13-15).

In this thesis, we could not identify significant relationships between conventional measures and QoL outcomes.

For instance, deterioration of hearing loss was most reported, but this did not seem to meaningfully interfere with QoL (Chapters three and four). This could be explained by the fact that the majority of symptoms were already present before treatment or that patients gradually adjusted to them over time due to response shift (16).

Although dizziness and especially vertigo are not a common symptom in VS, they are recently thought to be predictive in QoL perception (17). We did not observe such strong relationships, but results from Chapter five showed that QoL was impaired in VS patients with vertigo to such a degree that finally microsurgery was chosen. This study has very well displayed that impaired QoL can be a decisive factor in
VS treatment. Hence, in VS patients with disabling symptoms such as vertigo, QoL assessment is crucial to further optimize VS treatment.

Tinnitus is the second most frequent symptom in VS and its development after treatment is generally thought to be unpredictable, but a slight overall increase has been observed. Tinnitus developed in a small number of conservatively treated patients, but without significant impact on QoL (Chapter three). After radiosurgical treatment, inverse correlations were found between tinnitus and the physical domains of QoL (Chapter four). Apparently, tinnitus may affect QoL in VS patients to some degree, but it is limited to daily physical tasks. Patients did not experience any emotional handicap from tinnitus, as frequently has been described (18).

In patients with facial nerve deficit or trigeminal symptoms, reduced QoL scores were observed compared to other VS patients, but differences were not significant (Chapter three and four). There has been some inconsistency with regard to the effects of facial nerve impairment on QoL after treatment for VS. Some studies report a significant negative effect on QoL, whereas others do not (19-21). A possible explanation might be the use of the SF-36 which has slight limitations with respect to otolaryngologic interventions (22,23). The use of an additional disease- or symptom-specific questionnaire could prevent these kinds of problems.

In Chapter six, we demonstrated that patients with facial nerve palsy actually experienced significant functional and psychological morbidity. A disease-specific measure, the Facial Disability Index (FDI) was used to rate impact of patients’ facial function on QoL, which was significantly impaired. After facial-hypoglossal nerve transfer surgery, most patients experienced functional oral sphincter musculature and sufficient eye closure to prevent any eye problems. In addition, tongue function was preserved in all patients and no tongue atrophy was observed. Despite the small number of patients, we found significantly better QoL afterwards. It was the first report in which QoL was assessed after rehabilitative facial-hypoglossal nerve surgery.

Although it is generally known that patients with larger tumors experience increased tumor-related morbidity, we found that QoL did not differ between patients with small or large tumors. For instance, in the microsurgical treatment of large VS, tumor excision carries increased risk of facial nerve paralysis. To preserve facial nerve function and maintain patients’ QoL, the surgeon may therefore leave some tumor in situ. In Chapter seven we hypothesized that postoperative facial nerve function should be significantly better when tumor is deliberately left behind.
We found that when residual tumor was left behind, facial nerve outcome was more favorable. This relationship, however, was not statistically confirmed, probably due to the small sample. In our center, facial nerve outcomes after surgery were favorable and comparable to the results from renowned clinics (24-27).

From the abovementioned results, it appears that QoL is not merely determined by the size of the VS or concomitant symptoms but may also be influenced by the burden of suffering from the disease itself. Therefore, we also explored whether psychological factors may contribute to QoL in VS patients (Chapter two). In an untreated VS patient sample, a poor active and passive coping style was observed compared to other patient groups. In general, patients were shown to perceive their tumor as an acute and life-threatening illness. Consequently, in this patient sample QoL was found to be impaired compared to norms and other comparable patient populations, which corresponds to previous data (17). However, QoL was measured before treatment and patients might not yet have been able to understand the consequences of their illness. Nevertheless, the results are important and have implications for clinicians as well as for the patient’s caretakers.

Now, we can conclude that QoL in VS patients mostly depends on how they perceive their illness and to what extent they cope with it. The effects of conventional measures such as tumor size and symptoms on QoL are limited, which is in line with previous published data (28-38).

For future research, we may be able to improve QoL by an intervention in the field of IPs, as recently described in cardiac patients (39). Our patients could be referred to a medical psychologist, who could then assist them in adapting to their VS.

The results of Chapter two are highly relevant when exploring QoL for current treatment in VS, because baseline data were provided for comparison of QoL outcomes between patients either treated conservatively or with microsurgery or radiosurgery. When compared to the untreated patient sample from Chapter two, improvement of QoL was observed for all three treatment modalities. We hypothesize that after treatment, VS patients experienced their illness as being ‘controlled’ or cured and without significant morbidity. In contrast, the tumors of the patients in Chapter two were not treated yet.

The results of our observational study (Chapter three) were encouraging, because in the past, the presumed impact of a wait and scan policy on QoL has generally been used as an argument to proceed to microsurgery. So far, there has been a paucity on the QoL subject in conservative treatment of VS. Our data were prospectively
collected over a period of almost four years, which is unique when reviewing the current literature. However, follow-up is still short given the slow growing character of VS. Our study failed to assess QoL in the entire observed cohort, which may limit the interpretation of these data. However, in a recent study, QoL was not found to be further impaired in VS patients who had failed conservative treatment (40). As in our study, others also reported on stable QoL in observed VS patients, but without the use of baseline and posttreatment data (41). In our opinion, therefore, we have provided strong evidence that a wait and scan policy does not adversely affect QoL in VS patients.

Despite the favorable outcome of our radio- and microsurgical samples, QoL of these patients was still impaired when compared to their control samples. While radiosurgical treatment of VS is less invasive than microsurgery, it may still induce several complaints such as hearing loss, tinnitus, decrease of facial nerve function, facial pain and dysbalance. Complications of radiosurgery have also been reported, although the consequences for patients are often less serious compared to complications after microsurgical treatment. In those patients who experienced complications in our studies, a significant QoL impairment was not observed. One possible explanation might be that complications were often transient and in a small number of patients. Moreover, QoL was generally assessed some time after treatment.

The QoL outcomes of the operated patients were comparable to the radiosurgically as well as the conservatively treated VS patients. From a QoL point of view, the three patient groups did not seem to differ significantly, although there are major differences in terms of patient and tumor characteristics. Our results were confirmed by a recent prospective study using the SF-36 measure at regular intervals, which also concluded that there were no QoL differences between the three current modalities (42).

Throughout our studies, we have used validated generic questionnaires to measure QoL. However, for optimal QoL assessment, we recommend the use of generic measures in combination with disease- or symptom-specific measures as described in Chapter five. Our methods consisted of solid QoL instruments, but for future research, it would be preferable to use a VS-specific questionnaire in addition to those currently used. Such a questionnaire could focus more on the particular problems encountered when suffering from VS. However, no validated VS-specific measure exists so far.
The results of this thesis have led to a more conservative approach for VS patients in our department. Nowadays, an initial wait and scan policy for our patients with small- or medium-sized tumors is increasingly adopted. In case of tumor progression or increase of symptoms, active treatment is offered to these patients. At the LUMC, microsurgery is generally offered to patients with growing tumors depending on patient and tumor factors. As recognized by others, microsurgery is also our first choice in the treatment of large tumors. However, from our research and from published reports world-wide, we are convinced that radiosurgery has become a well-established treatment option for VS next to microsurgery.

Our study did not aim to compare outcomes of the different modalities in order to claim ‘the best treatment option for VS’. In our opinion, there is no clear option of what would be best for all individuals and it would not even be possible to conclude this from our studies. Given our results, and the state-of-the-art with regard to the medical management of patients with VS, it can be concluded that future research should focus on a number of issues. First, the development of a specific QoL measure for patients with VS would be helpful. Secondly, a head to head comparison of the treatment modalities for patients with VS would shed light on crucial questions about which treatment is best for which patients, taking QoL into account. Thirdly, further research should focus on developing self-management interventions in patients with VS, most likely with the inclusion of partners of the patients, and with QoL as the central outcome measure. VS is an area with exciting research and clinical challenges. This thesis has attempted to contribute to the area.
References


