# Instruments for Estimation of Health-Related Quality of Life in Patients with Skull Base Neoplasms

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## ABSTRACT

With advances in treatment of patients with tumors of the skull base and associated improvement in length of survival, the need for assessment of quality of life (QOL) is becoming increasingly apparent. A thorough assessment of QOL, including functional, physical, social, and emotional status, as well as disease-specific symptoms, allows for comparison of treatments and informs treatment decisions. In addition, it allows for problems following intervention to be identified and addressed, thereby assisting patients in their pursuits of returning to their normal activities and level of functioning. Although health care providers and researchers are increasingly aware of the need to assess patients' QOL, few standardized measures exist with which to perform a comprehensive assessment of QOL in patients with skull base neoplasms. Further research is needed, including prospective trials using reliable and valid measures tapping various aspects of QOL and specific symptoms unique to patients with tumors of the skull base.

**KEYWORDS:** Skull base tumor, quality of life

Advances in multimodal treatment and surgical approaches have led to increased survival for patients with skull base tumors; however, patients may experience significant morbidity following intervention. Serious side effects can include problems with eating, sleeping, speaking, anosmia, facial deformity, and visual disturbance.[1] Additionally, neurocognitive impairment may develop as skull base tumors grow and involve proximal brain structures. Treatment of these tumors may also lead to the development of cognitive symptoms through disruption of frontal-subcortical networks.[2] Although the World Health Organization has long defined health as not only the absence of disease, but as "complete physical, mental, and social well being," reports of surgical outcome for patients with skull base lesions have often been limited to length of survival or the presence or absence of disease.[3] More recently, there has been greater recognition of the importance and feasibility of including quality of life (QOL) indices as additional clinical end points.[4] Although there is no universally accepted definition for QOL, it is generally agreed that QOL is a multidimensional construct encompassing patient perception of overall well-being. It is necessary to differentiate QOL from symptom assessment, as the perceived impact of a given symptom may vary significantly between individuals and over time.[5] QOL data may serve to increase awareness regarding variables impacting patient well-being, inform treatment decisions, and identify

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targets for intervention.[6] As this review will highlight, such measures are increasingly incorporated into research trials and clinical care, and although still in early stages are already bearing useful information.

Many studies have made inroads toward assessment of QOL through reliance on informal measures. Although this represents an improvement beyond length of survival, caution is warranted when utilizing nonstandardized methods. One study examining outcome following skull base procedures included data regarding speech, oral intake, cosmetic results, resumption of social activities, and pain. However, the assumption of "good" posttreatment QOL may be faulty, as it was based on only some of the above variables. For example, pain, which was not well controlled in the majority (67%) of patients, may have engendered poor QOL despite gains in other areas.[7] Another study evaluating patients with petroclival meningiomas broadened the postoperative outcome data by including informal questions regarding work status and "disability," which was defined narrowly by physical symptoms such as diplopia, partial hearing loss, and trigeminal neuropathy.[8] However, although such impairments may not prevent return to work, they might have a significant impact on a patient's perceived QOL; thus, although an improvement over mortality alone, data regarding the presence or absence of physical symptoms are insufficient.[9,10]

Other studies have attempted to garner greater outcome data by including standard measures completed by health care providers. However, this approach is problematic, as evidence suggests that physicians' ratings of patient QOL may be inaccurate. In one study, surgeons overrated patients' QOL in the majority (24/35) of cases ($p < 0.07$), and there was no significant correlation between patient and surgeon ratings at the individual level. The authors suggested these results underscore the need for increased communication between health care providers, patients, and caregivers regarding expected treatment outcomes.[6] This is of particular note as numerous studies have employed the Karnofsky Performance Scale (KPS), a rating of functional status determined by health care providers, as a proxy for QOL.[8,11,12] Additionally, the KPS, although valuable as a gross estimate of functional status, measures only one facet of the broader concept of QOL. Thorough assessment extending beyond functional status alone can enrich physicians' understanding of patient QOL by increasing awareness of other key factors contributing to this outcome.

## INSTRUMENTS UTILIZED TO ASSESS QOL IN PATIENTS WITH SKULL BASE TUMORS

An ideal QOL measure demonstrates reliability and validity and taps patient perception of all relevant domains, including functional status, social well-being, cognitive symptoms, physical functioning, and emotional health. Although no perfect or universally applicable measure exists, numerous instruments have been developed in an effort to meet the need for QOL data in medical patients, and several have been applied in patients with skull base neoplasms. Additionally, specific measures have been developed to address the symptoms unique to this patient population. The following review will focus on the most frequently employed measures used to assess QOL in adults with tumors of the skull base and the information that has been garnered from those assessments to date. Greater detail regarding the characteristics and psychometric properties for these instruments is provided in Table 1.

### Global QOL Measures

The Medical Outcome Study 36-Item Short Form (SF-36)[13] was developed for use in healthy individuals as well as medical populations and has been utilized on numerous occasions to assess postsurgical outcomes. In 19 patients with petroclival meningiomas, physician ratings of functional outcomes were within normal limits at 1 year postresection. In contrast, patient ratings on the SF-36 reflected problems in all domains.[14] Similarly, in a study of 42 patients who underwent resection of acoustic neuroma, patient responses on the SF-36 revealed reduced ratings of physical functioning, role limitations secondary to physical and emotional factors, bodily pain, general health, and social functioning relative to normative standards.[15] Another study of 72 patients with vestibular schwannoma who were at least 18 months postresection showed reduced ratings on the SF-36 for seven of eight domains relative to normative standards. The clinical significance of this reduction is questionable, however, as standardized scores remained in the average range, and there was no information regarding whether or not the difference between groups was statistically significant.[16]

The SF-36 has also been used to compare treatment outcomes. One study investigated QOL in 70 patients with skull base tumors following interval scans, surgery, or radiosurgery. Those patients who underwent surgery ($n = 19$) reported reduced social functioning and role limitations secondary to physical functioning; in contrast, no significant difference was observed between patients managed with interval magnetic resonance imaging scans ($n = 29$) and the normal population. In patients treated surgically, there was no QOL difference based on tumor type; therefore, it was concluded that the surgery, rather than a specific pathology, impacted QOL.[17]

### Cancer-Specific QOL Measures

Additional instruments have been developed specifically for use in patients with cancer. The European Organization for Research into the Treatment of

**Table 1 Characteristics of Commonly Utilized QOL Measures**

| | Instrument Characteristics | | | | Psychometric Properties | | |
|---|---|---|---|---|---|---|---|
| **Instrument** | **Target Population** | **No. of Items** | **Response Format** | **Areas of Functioning Assessed** | **Internal Consistency** | **Test-Retest Reliability** | **Validity** |
| Medical Outcome Study 36-Item Short Form | Healthy and medical populations | 36 | Likert scale, yes/no | Physical, role limitations, social, general health, mental health, bodily pain, vitality | ≥0.70 | 0.79–0.82 | Good item discriminate validity |
| European Organization for Research and Treatment of Cancer Quality of Life Questionnaire | Clinical cancer research | 30 | Likert scale, yes/no | Physical, role, cognitive, emotional, social, specific symptoms, global QOL | ≥0.70 | 0.80–0.90 | Good sensitivity to between-group differences and change over time |
| Functional Assessment of Cancer Therapy | General cancer (additional disease-specific modules, including brain, head, and neck) | 27 | Likert scale | Physical, social, emotional, functional | 0.89 | 0.82–0.92 | Good convergent and discriminate validity |
| University of Washington Quality of Life Questionnaire | Head and neck cancer | 12 | Likert scale | Pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder, taste, saliva, mood, anxiety, global QOL | 0.86 | 0.94 | Good convergent validity |
| Anterior Skull Base Surgery Quality of Life Questionnaire | Patients undergoing surgical resection of anterior skull base tumors | 35 | Likert scale | Performance, physical function, vitality, pain, influence on emotions, specific symptoms | 0.8 | 0.90 | Strong association between some subscales and relevant clinical variables (malignancy, radiotherapy, etc.) |

QOL, quality of life.

Cancer Quality of Life Questionnaire (EORTC QLQ-C30)[18] is one such instrument that has been applied patients with skull base tumors. Overall postoperative QOL ratings in 227 patients with vestibular schwannoma were ~80% of optimal, with only a minority (15%) reporting their functioning at or less than 50% of ideal levels.[19] An additional measure developed specifically for use in cancer patients, the Functional Assessment of Cancer Therapy (FACT)[20] has been also been utilized to investigate postoperative QOL in patients with skull base tumors. Postoperative responses from 16 patients who underwent anterior craniofacial resection for paranasal sinus malignancies revealed suboptimal ratings of QOL in ~33%. This did not reflect neurological symptoms, disease-specific symptoms, or objectively measured functional status, but rather appeared to reflect problems with psychosocial functioning.[21,22]

The University of Washington Quality of Life Scale[23,24] was developed specifically for use with patients with head and neck cancers and has been applied to evaluate QOL in patients with malignant tumors of the skull base. Results of one study found that patients with anterior skull base tumors (ABSTs) reported lower QOL following treatment than those who had lateral skull base tumors. However, it was noted that the measure does not include some symptoms that are specific to skull base tumors, such as vision, hearing, and olfaction, and the authors called attention to the need for specific questions assessing these symptoms to make the measure more relevant for skull base cancer patients.[25]

### Disease-Specific QOL Measures

Assessment of overall QOL and its facets, as attempted by the above-mentioned questionnaires, can be augmented by assessment of symptoms unique to their disease and treatment. Several nonstandardized measures have been created in an attempt to address the unique physical symptoms associated with skull base neoplasms and their treatment, such as hearing loss, facial paralysis, trigeminal neuralgia, and ataxia.[15,19,26]

The Anterior Skull Base Surgery Quality of Life Questionnaire (ASBS QOL-Q) was designed as a standardized tool for assessment of the QOL concerns unique to patients who undergo surgical resection of ABSTs.[1] Questions were phrased to reflect change from preoperative levels and were generated from a review of the literature and interviews with health care professionals, surgeons, patients, and caregivers. No significant correlation was noted between general QOL questions and any of the specific domains, highlighting the importance of disease-specific questions. A retrospective study using the ASBS QOL-Q revealed that of 40 ABST patients who were at least 3 months postresection, the majority reported stable or improved QOL relative to preoperative levels. Patients with benign tumors reported better scores for role of performance, physical function, specific symptoms, and impact on emotions, and patients who underwent perioperative radiotherapy reported significantly more specific symptoms and impact on emotions. Not surprisingly, the presence of an additional illness was associated with lower physical functioning. Comparison of overall QOL scores for revealed an improvement in QOL 6 to 24 months relative to 3 to 6 months after surgery, with relative stability of overall QOL scores thereafter. The authors noted that the change in QOL often depends on level of symptoms experienced preoperatively, as an improvement in QOL may be expected following surgery if preoperative symptoms are present, and a negative impact is not surprising for patients who were asymptomatic prior to treatment.[27]

The ASBS QOL-Q has also been used to compare the differential effects of treatment approaches. In a retrospective comparison of QOL in patients who underwent classic subcranial ($n = 23$) and combined subcranial ($n = 13$) approaches to resection of ABSTs, overall QOL ratings were similar across groups; however, a trend toward lower ratings was observed for the combined group. A significant difference was observed for the specific symptoms domain, with the combined group reporting greater symptoms.[28]

## CHALLENGES IN ASSESSING QOL IN PATIENTS WITH SKULL BASE NEOPLASMS

Although high functional status does not necessarily correlate with high QOL ratings,[22] functional impairment may negatively impact an individual's ability to complete self-report measures; for example, only higher functioning patients (KPS over 60) were able to complete the FACT.[29] In addition, patients with skull base tumors are vulnerable to cognitive dysfunction secondary to mass effect or unfortunate side effects of treatment[2]; this may interfere with the patients' ability to accurately complete self-report measures, especially as the disease progresses and cognitive impairment becomes increasingly problematic.[4] It is important to note that in cancer populations, self-report of cognitive impairment has been shown to correlate more heavily with fatigue and mood disturbance than with objective evidence of cognitive dysfunction, as assessed by standardized neuropsychological tests.[30–33] This again highlights the distinction between objective symptom assessment and patient perception.

Concern has been raised regarding the use of proxy ratings to assess QOL, as it is generally believed to be a subjective experience. However, encouraging data are provided by some studies examining patient-caregiver agreement in QOL ratings. In one study, 35 ABST patients who were at least 3 months postresection and their caregivers completed the ASBS QOL-Q. Results revealed good agreement for overall QOL at the group and individual ratings. At the group level, caregivers tended to overrate the presence of specific symptoms. The strongest agreement was found between patients who had recurrent disease and their caregivers; the authors speculated that this may represent increased knowledge regarding the disease process and the patient's needs.[6] A similar finding was reported in a study utilizing the SF-36; recurrent disease status was associated with significantly higher agreement between patients and their caregivers.[34] An additional study found that substantial discrepancies occurred in only a small minority (5 to 10%) of patient-caregiver pairs using the EORTC QLQ-C30. However, the authors acknowledged that rating agreement decreased as patients' level of physical and cognitive impairment increased, leaving questions regarding the ability to provide proxy ratings for those who may need them most.[35]

## CONCLUSION

The assessment of QOL in patients with skull base neoplasms has become increasingly important in association with advances in treatment and improvements in survival. Merely assessing functional status is not sufficient to assay QOL, as this is only a facet of a larger, complex domain. Ideally, QOL measures should focus on patient self-report, as health care providers have been found to overrate patients' QOL; caution should be used in interpreting caregiver ratings as a proxy for patients whose ability to respond to queries regarding QOL is in question. Measures should have established reliability and validity and should tap the various aspects of QOL, including physical, emotional, and social functioning, as well as functional status and symptoms specific to the disease and treatment. Prospective studies are needed, with longitudinal data including pretreatment and posttreatment ratings. This information will provide valuable insight into the concerns facing patients with skull base tumors, allow comparison of treatments, and inform future treatment decisions, while also identifying patient concerns following treatment, thereby allowing for appropriate interventions to be employed as quickly as possible.

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