

## Health-related quality of life in meningioma

Sameah Haider, Martin J.B. Taphoorn, Katharine J. Drummond, and Tobias Walbert

*Department of Neurosurgery, Hermelin Brain Tumor Center, Henry Ford Health System, Detroit, Michigan, USA (S.H., T.W.); Department of Neurosurgery, Royal Melbourne Hospital, Parkville, Victoria, Australia (K.J.D.); Department of Surgery, University of Melbourne, Parkville, Victoria, Australia (K.J.D.); Department of Neurology, Leiden University Medical Center, Leiden, The Netherlands (M.J.B.T.); Department of Neurology, Haaglanden Medical Center, The Hague, The Netherlands (M.J.B.T.)*

**Corresponding Author:** Tobias Walbert, MD, Department of Neurosurgery, Hermelin Brain Tumor Center, Henry Ford Health System, 2799 West Grand Boulevard, Detroit, MI 48202, USA ([Twalber1@hfhs.org](mailto:Twalber1@hfhs.org)).

### Abstract

**Background.** Meningiomas are the most common primary intracranial tumor in adults. Although frequently histologically benign, the clinical severity of a lesion may range from being asymptomatic to causing severe impairment of global function and well-being. The diversity of intracranial locations and clinical phenotypes poses a challenge when studying functional impairments, however, more recent attention to patient-reported outcomes and health-related quality of life (HRQOL) have helped to improve our understanding of how meningioma may impact a patient's life.

**Methods.** Treatment strategies such as observation, surgery, radiation, or a combination thereof have been examined to ascertain their contributions to symptoms, physical and cognitive functioning, disability, and general aspects of daily functioning.

**Results.** This review explores the multidimensional nature of HRQOL and how patients may be influenced by meningiomas and their treatment.

**Conclusion.** Overall, treatment of symptomatic meningiomas is associated with improved HRQOL, cognitive functioning, and seizure control while tumor size, location, histologic grade, and epileptic burden are associated with worse HRQOL.

### Key Points

- Meningiomas and treatment may cause neurologic symptoms and functional impairment.
- Patients report impaired Health-Related Quality of Life compared to healthy controls.
- Treatment may result in symptom reduction, though HRQOL may remain depressed.

Meningiomas are among the most common primary intracranial tumors, accounting for nearly one-third of all central nervous system tumors.<sup>1–5</sup> Incidence in the general population is 2.3–5.5 cases per 100 000 people, the range inclusive of incidental and autopsy findings.<sup>6,7</sup> While the majority of meningiomas are histologically benign, they nonetheless may contribute to neurologic dysfunction by means of regional mass effect, inducing epileptogenicity or might affect patients' lives by treatment-related sequelae. Meningiomas are frequently asymptomatic and may be found incidentally during diagnostic

workups for alternative indications. Incidental meningiomas without mass effect that are asymptomatic either do not affect quality of life or are inherently challenging to study given that this subgroup evades detection of the underlying lesion.

Health-related quality of life (HRQOL) is a multifactorial concept capturing commonly valued aspects of life and how they contribute to one's overall health functioning and sense of well-being. A patient's level of functioning is influenced by symptoms, physical and cognitive impairments, as well as the downstream activity limitations secondary to neurologic

dysfunction. The World Health Organization further classifies determinants of patient functioning as those that affect daily functioning, disability, or health.<sup>8</sup> The main objective of this review is to characterize HRQOL in meningioma patients as well as how it may be influenced by the disease and its treatments. The overarching categories of HRQOL of meningioma patients covered in this review include physical functioning, cognitive functioning, disability, treatment, and general aspects of daily functioning.

## Health-Related Quality of Life

The natural history of diseases and their treatments have historically been examined by clinical endpoints and objective biomarkers of disease. Over recent decades the concept of HRQOL has emerged as a significant area of interest with a focus on how disease states impact a patient's functioning.<sup>9,10</sup> HRQOL is not merely the perception of how fulfilling one perceives their existence, but is best regarded as a multidimensional framework that incorporates one's physical, psychological, and social functioning as it relates to their disease-specific signs, symptoms, treatment, and sequelae.<sup>9</sup> Given the conceptual complexity of HRQOL, specific and validated tools are required.

HRQOL instruments may be used from both a research perspective and clinical practice. From a research standpoint, these instruments provide patient-perspective insights that can be tied to objective survival rates to ascertain the net utility of a therapeutic modality. In a clinical setting, these questionnaires may enable a provider to track a patient's disease course, identify problem areas, and facilitate communication regarding symptoms and their impact on daily living. The implementation of patient-reported outcome measures in cancer care may simultaneously guide subsequent treatment decisions as well as provide insights for departmental quality improvement initiatives.<sup>11–13</sup>

While symptoms can be ascertained from a healthcare provider, caregiver, or patient, quality of life data is directly reported from the patient themselves via questionnaires. Patient-reported outcome measures are increasingly valued and are felt to reflect the patient's perspective most truthfully. Researchers have identified disparities between provider- and patient-reported outcomes; thus, it is generally accepted that a communicative patient is the best source of information on their own HRQOL.<sup>9</sup>

The most widely utilized questionnaires used to assess HRQOL and symptoms include generic instruments (SF-36, EQ-5D, MDASI), cancer-specific instruments (FACT-G, EORTC QLQ-C30), disease-specific instruments tailored to the brain tumor population (FACT-BR, EORTC QLQ-BN20, MDASI-BT), or instruments that can be adjusted as needed (National Institute of Health Patient-Reported Outcomes Measurement Information System [PROMIS]). The more broadly designed questionnaires have been designed for diverse target populations to measure physical, cognitive, emotional, and social functioning, though not uniquely for central nervous system pathology. As a result, there may be meningioma-specific issues that remain unexplored or unaddressed from these instruments. Others have also employed cancer-specific instruments to assess HRQOL in

meningioma; though these instruments have been historically developed and validated for solid tumor malignancies outside the central nervous system.<sup>14,15</sup> Both the cancer- and brain tumor-specific questionnaires have not been validated for the full spectrum of issues relevant to the meningioma population; though the SF-36 has been validated for brain tumor patients, 40% of whom were meningioma patients.<sup>16</sup> With the aforementioned limitations in mind, these instruments still afford structured insight into HRQOL for this subset of brain tumor patients (Table 1<sup>17–23</sup>).

## Quality of Life of Meningioma Patients Compared With Healthy Controls

Up to one-third of meningiomas are discovered incidentally, and the majority of these patients are asymptomatic at presentation.<sup>24,25</sup> An increased use of diagnostic imaging has paralleled the increased incidence of meningioma while autopsy studies report a prevalence as high as 2%.<sup>26,27</sup> While a subset of meningiomas remain asymptomatic for the duration of follow-up (or absence of discovery), patients with symptomatic lesions report lower health status and functioning compared to normative healthy controls. These impairments can be subtle. One study following patients with suspected meningiomas, reported a decrease in general health and vitality but there were no statistically significant differences within the SF-36 domains of physical functioning, role limitation, bodily pain, social functioning, emotional problems, or mental health.<sup>2</sup> The authors attribute these changes to the simple awareness of an intracranial tumor and the impact it can have on patients by lowering the HRQOL scores in the vitality and general health domains, as this was not explained by neurocognitive test performance comparable to healthy controls.<sup>2</sup> These findings suggest the notion that patients with meningiomas, while not having significant physical detriments referable to their lesions, still may endure psychological distress. Others have similarly reported significant preoperative anxiety and depression scores that generally decrease post resection.<sup>28</sup>

When clinically symptomatic, meningioma patients reported lower scores for physical health, vitality, self-care, cognition, psychomotor speed, verbal memory, working memory, and role limitations compared to age-matched healthy controls.<sup>2,29,30</sup> While scores were lower in 7 out of 8 domains of the SF-36, they might have not been clinically relevant and they were still relatively comparable to healthy controls with the exception of "role limitations caused by physical problems," which was significantly lower in meningioma patients.<sup>30</sup>

## HRQOL and Physical Functioning

Symptomatic meningiomas present with a wide range of clinical severity and symptoms depending on the specific intracranial location. The most common anatomic sites of

**Table 1.** Health-Related Quality of Life Assessment Tools

Instrument Specificity	Instrument(s)	Disease States Evaluated	What Is Measured	Subdomains
Generic	EQ-5D <sup>17</sup>	Widely applicable, common among population health studies, clinical studies, and economic evaluation	Descriptive assessment of 5 subdomains coupled with evaluation of overall health status using the visual analog scale (VAS)	Mobility, self care, usual activities, pain/discomfort, anxiety/depression
	SF-36 <sup>16</sup>	Evaluating health status, commonly used among health economic analyses and calculating cost-effectiveness <sup>18</sup>	36 items, patient reported	Physical functioning, role limitations, pain, general health perception, vitality, social functioning, general mental health
	PROMIS <sup>19</sup>	Widely applicable across a chronic and acute disease states	Patient-reported physical, mental, social functioning assessment	Fatigue, pain intensity, pain interference, physical function, sleep disturbance, anxiety, depression, role limitation
Cancer	EORTC QLQ-C30 <sup>13,20</sup>	Lung, breast, gynecologic, prostate, colorectal cancer. May be used in a variety of cancers and also brain tumors	30 cancer-related items, patient reported	Physical, role, cognitive, emotional, social functioning, fatigue, nausea, emesis, pain
Brain tumor	EORTC QLQ-BN20 <sup>21</sup>	Those undergoing treatment for glioma	20-Item supplement to EORTC QLQ-C30	Future uncertainty, visual disorder, motor dysfunction, communication deficit, headache, seizure, drowsiness, hair loss, itchy skin, weakness of legs, bladder control
	FACT-BR <sup>22</sup>		44 items, patient reported	Physical, emotional, functional well-being, additional symptoms/concerns
	MDASI-BT <sup>23</sup>		22 symptom items, patient reported	General, focal, and treatment-related symptoms over past 24 h
	BN20 <sup>13</sup>		10 items, patient reported	Future uncertainty, visual, motor, communication, emotional distress, signs/symptoms (brain tumor specific)

Adapted from <sup>13,14</sup>. BCM-20, Brain Cancer Module 2.0; EORTC QLQ-BN20, Quality of Life Questionnaire Brain Neoplasm Module 2.0; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Version 3; EQ-5D, EuroQol 5 Dimension; FACT-BR, Functional Assessment of Cancer Therapy Brain Module; MDASI-BT, M.D. Anderson Symptom Inventory—Brain Tumor; PROMIS, National Institute of Health Patient-Reported Outcomes Measurement Information System; SF-36, Short Form Health Survey—36 item.

meningioma include: convexity (35%), parasagittal (20%), sphenoid ridge (20%), infratentorial (13%), intraventricular (5%), tuberculum sellae (3%), and others (4%).<sup>1</sup> These locations serve as important subgroups as they represent distinct pathologic phenotypes of physical symptoms. For example, a meningioma of the tuberculum may affect vision at a relatively small size while an infratentorial meningioma of similar volume can cause myelopathy at the craniocervical junction or hearing loss at the cerebellopontine angle.

Meningiomas of the skull base carry an intrinsically higher risk of surgical morbidity given the narrow working corridors, proximity to critical neurovascular structures, and the relative fragility of lower cranial nerves with respect to tolerating surgical manipulation.<sup>31,32</sup> Karsy et al. utilized the EQ-5D tool to follow 52 patients with skull-base meningiomas from presentation to long-term follow-up; outcomes were categorically classified as improved, worsened, or unchanged. Patients that improved by 1-month postoperatively continued to improve at 1-year follow-up, however, those with unchanged or worsened scores did not improve, implying fixed deficits conferred a persistent decrement

in HRQOL scores.<sup>33</sup> Preoperative symptoms in this cohort included vision changes, cranial nerve deficit, ambulation difficulties, tinnitus, and cognitive decline. Of note, visual symptoms had the strongest impact on lowering HRQOL with optic nerve decompression and lack of proptosis correlating to improved scores.<sup>33</sup> This relationship highlights the importance of vision preservation as a goal of management for meningiomas near the optic apparatus.

## HRQOL and Cognitive Functioning

Neurocognitive function is a major component of HRQOL. Changes to cognitive function can be related to the tumor itself or treatment. Unfortunately, not much is known about the neurocognitive implications on HRQOL prior to surgery. Several studies have examined untreated, radiographically suspected meningioma patients with standardized neurocognitive testing and patient-reported outcome scales.<sup>2,34,35</sup> These studies uniformly detected deficits in working memory, fluency, attention, processing speed,

longer reaction times, and increased error rates when compared to healthy controls. All studies were restricted to supratentorial meningiomas and there were no significant associations with tumor volume or lesion laterality.<sup>2,34,35</sup>

While it remains difficult to establish when meningioma patients have preoperative cognitive dysfunction, there is a greater compendium of work investigating cognitive impairments in those with meningiomas warranting treatment. In the largest prospective, cross-sectional cohort study of HRQOL by Nassiri et al., 291 meningioma patients were assessed using the validated EORTC QLQ-C30 questionnaire in annual intervals up to 120 months and beyond. In comparison to a normative population, meningioma patients exhibited reduced global HRQOL scores at nearly every 12-month interval. While there was a demonstrable reduction in each subdomain of HRQOL (physical, role, emotional, cognitive, social, fatigue, sleep), a clinically meaningful difference was particularly appreciated in the cognitive domain. The limitations in cognitive, emotional, and social functioning persisted for more than 120 months after initial treatment.<sup>4</sup> Of note, this study examined perceived cognitive impairment and did not objectively measure this domain.

Despite the persistence of neurocognitive impairments well after treatment, most meningioma patients experience improved HRQOL after surgery.<sup>5,29</sup> Sixty-eight meningioma patients evaluated with a battery of neuropsychological tests right after surgery demonstrated lower scores across all cognitive domains; memory, psychomotor speed, reaction time, complex attention, cognitive flexibility, processing speed, and executive functioning. When reexamined 3 months later with the same battery of tests, the scores revealed improvements across all domains with the exception of psychomotor speed and reaction time.<sup>5</sup> In similar studies linking patient-reported outcomes to objective neuropsychological testing, most patients with WHO Grade 1 meningiomas had similar HRQOL compared to that of healthy controls in 7 out of 8 domains of the SF-36, however, those with impaired cognitive functioning reported significantly lower HRQOL scores as well.<sup>4,30</sup>

## HRQOL and Patient Perspective

With the subjective nature of HRQOL assessments, personality-related determinants may also paint the perceived experience of living with and undergoing treatment for a brain tumor. When personality tests and psychological distress scales were linked to the SF-36 assessment tool, researchers found that emotional stability was independently associated with SF-36 emotional well-being and general health scores. Additionally, anxiety and depression scores among meningioma patients were the strongest determinants of 7 out of 8 SF-36 domains (with the exception of physical functioning).<sup>36</sup> In the realm of resilience research, the theory of hedonic adaptation refers to the tendency of humans to vacillate around a “set point” of happiness over time, despite positive and negative life events.<sup>37,38</sup> Given that degree of oscillation or change around this “set point” of happiness is dependent on the

individual’s ability to adapt, it is thought that higher scores for emotional stability and consciousness are linked to better HRQOL while cognitive impairment and functional disability reduced HRQOL.<sup>36</sup> The biopsychosocial perspective on brain tumor survival and adjustment/coping remains an important avenue for continued research.

## QOL and Epilepsy in Meningioma

Epilepsy has been reliably shown to have a negative impact on HRQOL in meningioma patients.<sup>30</sup> Seizures represent a common presenting symptom for meningiomas and 10%–50% of individuals with supratentorial meningiomas present with concurrent localization-related epilepsy.<sup>39,40</sup> Up to one quarter of patients may present with seizure as their initial symptom.<sup>30,39,41</sup>

Researchers from the National Health Service Foundation Trust in the United Kingdom further investigated the impact of epilepsy in surgically treated meningiomas using the SF-36 and Functional Assessment of Cancer Therapy subscale for brain cancer (FACT-BR, [Table 1](#)) and a cohort of epilepsy patients without brain tumors. After matching for age, sex, and duration of epilepsy, patients with meningioma and comorbid epilepsy had consistently lower HRQOL scores as evidenced by statistically significant declines in FACT-BR scores. A hierarchical regression analysis of participant and demographic variables further indicated that antiepileptic drug (AED) use consistently predicted lower SF-36 and FACT-BR scores.<sup>42</sup> Waagemans et al. similarly found that postoperative meningioma patients on AEDs had significant impairment on 5 out of 8 domains of the SF-36. Further subgroup analysis of the meningioma patients on AEDs, showed no difference in HRQOL measures when stratified by those with ongoing seizures versus those with complete seizure freedom.<sup>30</sup> This supports the conclusion that AED use negatively impacts HRQOL independent of seizure frequency—this notion is supported in the general neurology literature as well.<sup>43,44</sup>

The negative impact of comorbid seizures, as well as AED use, on patient-reported outcome measures persists when analyzed with standardized neuropsychological tests. A study of 89 postsurgical meningioma patients focusing on epilepsy burden (defined by seizure frequency and AED regimen) found that higher epilepsy burden and AED use was significantly related to lower executive functioning.<sup>45</sup>

For meningioma patients with preoperative seizures, surgical resection is often effective in improving seizure control and reducing AED use.<sup>46,47</sup> In a single center series of supratentorial meningiomas with preoperative seizures, 187 patients were followed longitudinally demonstrating approximately 90% seizure freedom by 1 year postoperatively. Independent predictors of poor seizure control included the presence of peritumoral edema greater than 1 cm, higher WHO grade, incomplete extent of resection (Simpson III–IV), and tumor progression during surveillance.<sup>3</sup> In a systematic review on postoperative seizure outcomes in meningioma patients with preoperative epilepsy, postoperative seizure freedom ranged from 38% to 90% of resected meningiomas.<sup>3</sup>

Epilepsy with an earlier age of onset and AED use have both been related to cognitive impairment and lower quality of life in patients with seizures. Regardless of seizure etiology, treatment with antiepileptics and polypharmacotherapy are strong negative predictors of cognitive performance in the domains of processing speed, verbal comprehension, and visuospatial abilities.<sup>48</sup> The decision to discontinue AEDs is a complex one shared between clinicians and patients and depends on factors such as disease severity, medication side effects, and risk tolerance for a breakthrough seizure. In a single center series of 169 brain tumor patients, postwithdrawal seizure rates were similar between meningioma and primary brain tumor patients among those in whom AEDs were discontinued. Factors favoring AED continuation included the presence of preoperative seizures, temporal tumor location, recurrent disease, and subtotal resection. There were no independent risk factors identified among those with seizures after discontinuing AEDs.<sup>49</sup> Patient preferences, medication side effects, and risk tolerance for a breakthrough seizure all play a part in the complex discussion between provider and patient when weaning antiepileptics. For example, some locales prohibit driving an automobile for a duration of time after a breakthrough seizure, which can have profound implications on employment status and independence.

## HRQOL After Meningioma Treatment

Treatment for meningioma can often preserve or even improve function and HRQOL. Most patients are treated with surgical resection and/or radiation therapy. The degree of HRQOL improvement generally varies according to pretreatment symptom burden.<sup>39</sup> For instance, symptomatic skull-base meningiomas are associated with greater deficit at presentation, lower gross-total resection rates, and shorter retreatment-free intervals than their nonskull-base counterparts.<sup>31</sup> Studies have shown that the degree of symptom severity before treatment has implications for the quality of life experienced after treatment. Meningioma features that have been tied to a greater degree of symptom burden include tumor volume >25 cc, frontal lesions, recurrent lesions, subtotal resections, and skull-base lesions where gross-total resection is commonly not feasible.<sup>3,29,33,50</sup>

Overall, surgical resection is tied to improvements in HRQOL in those with symptomatic meningiomas, with half of patients reporting benefit.<sup>51</sup> One prospective study found that the improvements in HRQOL after surgery were largely attributable to improvements in the EQ-5D domains of usual activities, pain/discomfort, and anxiety/depression.<sup>51</sup>

Perhaps the strongest evidence for clinical predictors of HRQOL comes from Miao et al., who examined 147 meningioma patients with a 25-item questionnaire tailored to the brain tumor population.<sup>29,52</sup> The HRQOL assessment tool was administered pre- and postoperatively to meningioma patients as well as age-matched healthy controls. HRQOL scores of meningioma patients improved with treatment, however still lagged behind the baseline HRQOL scores of normal controls. Univariate analysis of clinical factors

showed histologic grade (RR = 3.83), recurrent tumor (RR = 1.33), tumor size (RR = 1.13), and location (RR = 1.09) to be significant predictors of HRQOL scores.<sup>29</sup>

A cross-sectional multicenter study examining determinants of HRQOL, showed that patient-specific demographic characteristics, surgical complications, recurrent disease, radiotherapy, and presence of edema were significant predictors of the patients' HRQOL. A complex treatment course involving radiotherapy and reoperations to control the disease portends a higher risk of decreased HRQOL. The presence of edema and large tumor diameter has also been correlated to higher histological grade with decreased executive and physical functioning.<sup>3,53</sup>

The largest longitudinal cohort study of HRQOL in meningioma found that patients continue to report limitations in HRQOL for more than 120 months after surgery—most notably in the domains of cognitive, emotional, executive, and social functioning.<sup>4</sup> It is worth noting that the majority of the HRQOL literature represents findings from grade 1 and 2 meningiomas. Survival in this patient group is routinely greater than 10 years and therefore it should be considered as a chronic disease. When comparing these patients with long-term glioma survivors, meningioma patients tend to report better HRQOL. When compared to healthy controls, however, meningioma patients consistently demonstrate worse HRQOL in both the short and long term. Features such as edema, brain invasion, and tumor size affect meningioma patients in a way analogous to that of intramedullary brain tumors. Patients with minimal brain compression or those with tumor growth near noneloquent cortices are more likely to be minimally symptomatic or asymptomatic.

## HRQOL After Radiotherapy

While surgical resection has long been foundational to the treatment of meningioma, radiation therapy provides a formidable adjunct or primary treatment with excellent local control. A subgroup of meningioma patients, unresectable lesions or surgically high-risk patients, are appropriate candidates for treatment with radiotherapy; a treatment option with a comparatively lower risk-profile than surgery and high rates of local tumor control.<sup>54–57</sup> Nonetheless, treatment-related toxicity includes neurological deficits related to reactive edema in the short term and neurocognitive sequelae as a delayed effect. In a one-armed, prospective nonrandomized study on the quality of life after stereotactic radiosurgery (SRS), investigators followed 67 patients with symptomatic or progressive meningiomas. Patients underwent weekly follow-up during treatment followed by SF-36 assessments at 6, 12, 18, and 24 months. Radiated patients experienced clinically meaningful declines across all 8 domains of the SF-36 tool immediately after treatment (25%–50%), however these domains were subsequently normalized near baseline values by the 12-month follow-up. Local control was excellent at 98% with a singular event of disease progression at 18 months observed in a patient with WHO III meningioma.<sup>58</sup> It is important to note that radiotherapy does not address neurologic symptoms due to extrinsic compression. Fifty-two of the 67 patients experienced some

degree of low-grade treatment-related toxicity—9 showed improvements in their initial complaints while 43 remained stable regarding deficits/symptoms.<sup>58</sup> Debilitating treatment-related symptoms are generally attributable to transient cerebral edema and occur in 2.5% of patients undergoing SRT (Common Toxicity Criteria Grade 3 or 4).<sup>59</sup> Fatigue is the most common ongoing grievance among patients undergoing treatment; this global symptom may negatively contribute to every subdomain of HRQOL.

The most commonly encountered low-grade treatment toxicities include local alopecia and radiodermatitis, though half of patients remain completely asymptomatic. Clinically moderate symptoms such as headache and ataxia may be addressed with a short course of corticosteroids, while severe acute toxicity requiring urgent intervention is rare (<1%). When urgent surgical intervention is warranted, it is often related to mass effect from edema. Therefore, patient selection for radiotherapy candidates considers the volume and location of the lesion as well as appraisal of the patient's ability to tolerate local mass effect.<sup>59,60</sup> In a systematic review of radiosurgical toxicity, grade 3 toxicity or greater (Common Terminology Criteria for Adverse Events) was  $3.4\% \pm 2.9\%$  with the majority of toxicities occurring before 9 months.<sup>61</sup> While SRS and fractionated radiation therapy both exhibit good local control rates for meningioma, fractionated radiotherapy is associated with a lower risk of treatment-related edema.<sup>62</sup>

A common pattern within the radiotherapy literature supports that HRQOL decreases initially after treatment, followed by a period of normalization or improvement from baseline on long-term follow-up.<sup>58,59,63,64</sup> A prospective, longitudinal analysis of HRQOL of meningioma patients demonstrated radiographic treatment response rates >68%, stable cognitive function at 1 year, and decreased QOL-BN20 scores attributable to future uncertainty and headaches.<sup>63</sup> Henzel et al. reported an identical pattern in a similar prospective series of meningioma patients. An initial decrease of functional outcomes with SRS was followed by a period of normalization at 12 months when headache frequency and severity scores decreased.<sup>58</sup>

While not commonly used after gross-total resection of grade 1 meningioma, adjuvant radiation is often added to the surgical management of grade II and III meningioma or in the instance of recurrent disease.<sup>60</sup> Up front primary radiosurgery for radiographically suspected meningiomas demonstrates excellent local control rates,<sup>62</sup> however, the literature is scarce when it comes to comparing HRQOL among the different treatment populations of surgery, surgery followed by RT, and RT alone for meningioma. Despite short-term impairments in verbal memory, working memory, and executive functioning, long-term stabilization or improvements in HRQOL have been noted after skull-base meningioma resection<sup>65</sup> and radiosurgery for brain metastasis.<sup>66</sup>

Few studies have examined the differential effect of adjuvant radiotherapy over primary SRS with respect to HRQOL. In a historical cohort study comparing patients with WHO I meningioma undergoing adjuvant radiotherapy after resection with patients having had surgery alone, those undergoing surgery plus radiation had lower HRQOL scores than those treated with surgery alone. Those

undergoing surgery plus radiotherapy had decreased HRQOL scores particularly in the domains of physical performance, memory, processing speed, and psychomotor speed. When matched for demographics and disease duration, however, these differences disappeared suggesting radiotherapy after surgery does not have additional prolonged negative effects on HRQOL.<sup>67,68</sup> The dearth of information available highlights the importance of future study of long-term HRQOL changes related to various meningioma treatments.

## Socioeconomic Impact of Meningioma

Meningioma patients afflicted during their working years may endure declines in quality of life related to loss of employment or concerns over financial security. A cross-sectional survey of 249 WHO grade 1 meningioma patients evaluating socioeconomic parameters and HRQOL, revealed that a significant fraction experienced a decrease in employment after surgical resection. Despite improvements in the HRQOL domains of global health (21%, 95% CI 15%–26%), headaches (19%, CI 13%–24%), and seizures (12%, CI 8%–17%), one-fifth of patients became unemployed, 22% transitioned from full- to part-time, and an additional 10% of respondents became dependent on professional care for activities of daily living. Those in a higher income bracket did not experience a large shift in monthly income, but 7% of respondents in the lower income bracket shifted into the lowest income segment.<sup>69</sup> It is important to note this study took place in Switzerland, a country with relatively generous social safeguards and a universal, comprehensive healthcare system for all citizens.<sup>70</sup> While the external validity of this work is limited, the authors hypothesize that both the strength and magnitude of associations between HRQOL and socioeconomic status would be magnified in countries without the same social and healthcare standards. Binary regression analysis of this cohort revealed that occupational status (OR 0.41, 95% CI 0.17–0.98,  $P = .045$ ) and subjective ability to work (OR 0.37, 95% CI 0.15–0.92) were associated with a clinically meaningful decline in quality of life.<sup>69</sup> Other studies have also reported that 19%–35% of posttreatment meningioma patients are unable to return to their prior level of work.<sup>71</sup>

## Conclusion

Meningiomas are the most commonly diagnosed primary brain tumors in adults. Even though most are histologically benign, meningiomas and their treatment are associated with notable neurologic symptoms and oftentimes functional impairment. Patients with meningiomas, even those who are minimally symptomatic, report significantly impaired HRQOL compared to healthy controls. The domains affected include a range of concerns pertaining to physical functioning, neurocognitive and psychosocial functioning, as well as role limitations attributed to the tumor and its treatment. Known risk factors for worse HRQOL include tumor size, location, histologic grade, seizure burden, and

recurrent tumor. Patients typically experience some degree of improvement after treatment, though HRQOL scores may remain depressed indefinitely.<sup>4</sup> Treatment often results in increased seizure control and decreased use of antiseizure medications. This is important as the side effects of these medications are known to affect HRQOL. Radiotherapy may be accompanied by transient symptoms related to cerebral edema, but mostly appear to resolve in the long term. Recognizing at-risk patients, that is, those with histologically high-grade lesions,<sup>29</sup> frontal location,<sup>28,35</sup> skull-base location,<sup>33,50</sup> and size greater than 25 cc,<sup>72</sup> may aid in counseling patients and outlining expectations, as well as identifying those that may benefit from targeted supportive therapy.

## Keywords

epilepsy | health-related quality of life | meningioma | patient-reported outcome measures | quality of life | radiotherapy | socioeconomic

## Funding

There was no funding for this study.

**Conflict of interest statement.** None declared.

**Authorship Statement.** Manuscript composition, interpretation of data, and study oversight: S.H., M.J.B.T., K.J.D., and T.W.; data collection: S.H. and T.W.

## References

- Winn HR, Youmans JR, eds. *Youmans Neurological Surgery*. 5th ed. Philadelphia: ff. Saunders; 2004.
- van Nieuwenhuizen D, Ambachtsheer N, Heimans JJ, Reijneveld JC, Peerdeman SM, Klein M. Neurocognitive functioning and health-related quality of life in patients with radiologically suspected meningiomas. *J Neurooncol*. 2013;113(3):433–440.
- Schneider M, Güresir Á, Borger V, et al. Preoperative tumor-associated epilepsy in patients with supratentorial meningioma: factors influencing seizure outcome after meningioma surgery [published online ahead of print October 2019]. *J Neurosurg*. 2019;1–7. doi:10.3171/2019.7.JNS19455
- Nassiri F, Price B, Shehab A, et al.; International Consortium on Meningiomas. Life after surgical resection of a meningioma: a prospective cross-sectional study evaluating health-related quality of life. *Neuro Oncol*. 2019;21(suppl 1):i32–i43.
- Meskal I, Gehring K, van der Linden SD, Rutten GJ, Sitskoorn MM. Cognitive improvement in meningioma patients after surgery: clinical relevance of computerized testing. *J Neurooncol*. 2015;121(3):617–625.
- Johnson MD, Abu-Farsakh S. Clinicopathologic features of incidental meningiomas: a review of the literature and the University of Rochester autopsy experience. *Clin Neuropathol*. 2019;38(3):118–121.
- Rohringer M, Sutherland GR, Louw DF, Sima AA. Incidence and clinicopathological features of meningioma. *J Neurosurg*. 1989;71(5 Pt 1):665–672.
- Weltgesundheitsorganisation, ed. *International Classification of Functioning, Disability and Health: Children & Youth Version; ICF-CY*. Switzerland: World Health Organization; 2007.
- Zamanipour Najafabadi AH, Peeters MCM, Dirven L, et al. Impaired health-related quality of life in meningioma patients—a systematic review [published online ahead of print December 29, 2016]. *Neuro-Oncology*. 2017;19(7):897–907.
- Dirven L, Armstrong TS, Taphoorn MJ. Health-related quality of life and other clinical outcome assessments in brain tumor patients: challenges in the design, conduct and interpretation of clinical trials. *Neurooncol Pract*. 2015;2(1):2–5.
- Zamanipour Najafabadi AH, Peeters MCM, Lobatto DJ, et al. Health-related quality of life of cranial WHO grade I meningioma patients: are current questionnaires relevant? *Acta Neurochir (Wien)*. 2017;159(11):2149–2159.
- Scheibe M, Herrmann A, Schmitt J, Einhart N, Sedlmayr B, Kowalski C. Implementation of patient-reported outcome assessment in routine cancer care: a systematic review of multicentric programs in Europe. *Z Evid Fortbild Qual Gesundheitswes*. 2020;156–157:11–23.
- Schiestel C. Quality of life in patients with meningiomas the true meaning of benign. *Front Biosci*. 2009;E1(2):488–493.
- Salas M, Henderson M, Wientzek-Fleischmann A, et al. Validated instruments of quality of life (QOL) in patients with acute myeloid leukemia (AML) and other cancers. *Front Pharmacol*. 2020;11:1109.
- van Roij J, Fransen H, van de Poll-Franse L, Zijlstra M, Raijmakers N. Measuring health-related quality of life in patients with advanced cancer: a systematic review of self-administered measurement instruments. *Qual Life Res*. 2018;27(8):1937–1955.
- Bunevicius A. Reliability and validity of the SF-36 Health Survey Questionnaire in patients with brain tumors: a cross-sectional study. *Health Qual Life Outcomes*. 2017;15(1):92.
- Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med*. 2001;33(5):337–343.
- Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. *J Health Econ*. 2002;21(2):271–292.
- Romero MM, Flood LS, Gasiewicz NK, Rovin R, Conklin S. Validation of the national institutes of health patient-reported outcomes measurement information system survey as a quality-of-life instrument for patients with malignant brain tumors and their caregivers. *Nurs Clin North Am*. 2015;50(4):679–690.
- Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85(5):365–376.
- Taphoorn MJ, Claassens L, Aaronson NK, et al.; EORTC Quality of Life Group, and Brain Cancer, NCIC and Radiotherapy Groups. An international validation study of the EORTC brain cancer module (EORTC QLQ-BN20) for assessing health-related quality of life and symptoms in brain cancer patients. *Eur J Cancer*. 2010;46(6):1033–1040.
- Lien K, Zeng L, Nguyen J, et al. FACT-BR for assessment of quality of life in patients receiving treatment for brain metastases: a literature review. *Expert Rev Pharmacoecon Outcomes Res*. 2011;11(6):701–708.
- Armstrong TS, Mendoza T, Gning I, et al. Validation of the M.D. Anderson Symptom Inventory Brain Tumor Module (MDASI-BT). *J Neurooncol*. 2006;80(1):27–35.
- Buerki RA, Horbinski CM, Kruser T, Horowitz PM, James CD, Lukas RV. An overview of meningiomas. *Future Oncol*. 2018;14(21):2161–2177.

25. Näslund O, Skoglund T, Farahmand D, Bontell TO, Jakola AS. Indications and outcome in surgically treated asymptomatic meningiomas: a single-center case-control study. *Acta Neurochir (Wien)*. 2020;162(9):2155–2163.
26. Vernooij MW, Ikram MA, Tanghe HL, et al. Incidental findings on brain MRI in the general population. *N Engl J Med*. 2007;357(18):1821–1828.
27. Wiemels J, Wrensch M, Claus EB. Epidemiology and etiology of meningioma. *J Neurooncol*. 2010;99(3):307–314.
28. Wagner A, Shiban Y, Kammermeier V, et al. Quality of life and emotional burden after transnasal and transcranial anterior skull base surgery. *Acta Neurochir (Wien)*. 2019;161(12):2527–2537.
29. Miao Y, Lu X, Qiu Y, Jiang J, Lin Y. A multivariate analysis of prognostic factors for health-related quality of life in patients with surgically managed meningioma. *J Clin Neurosci*. 2010;17(4):446–449.
30. Waagemans ML, van Nieuwenhuizen D, Dijkstra M, et al. Long-term impact of cognitive deficits and epilepsy on quality of life in patients with low-grade meningiomas. *Neurosurgery*. 2011;69(1):72–78; discussion 78.
31. Meling TR, Da Broi M, Scheie D, Helseth E. Meningiomas: skull base versus non-skull base. *Neurosurg Rev*. 2019;42(1):163–173.
32. Magill ST, Lee DS, Yen AJ, et al. Surgical outcomes after reoperation for recurrent skull base meningiomas. *J Neurosurg*. 2018;130(3):876–883.
33. Karsy M, Jensen MR, Guan J, Ravindra VM, Bisson EF, Couldwell WT. EQ-5D quality-of-life analysis and cost-effectiveness after skull base meningioma resection. *Neurosurgery*. 2019;85(3):E543–E552.
34. Tucha O, Smely C, Lange KW. Effects of surgery on cognitive functioning of elderly patients with intracranial meningioma. *Br J Neurosurg*. 2001;15(2):184–188.
35. Tucha O, Smely C, Preier M, Becker G, Paul GM, Lange KW. Preoperative and postoperative cognitive functioning in patients with frontal meningiomas. *J Neurosurg*. 2003;98(1):21–31.
36. Bunevicius A, Tamasauskas S, Deltuva V, Tamasauskas A, Radziunas A, Bunevicius R. Predictors of health-related quality of life in neurosurgical brain tumor patients: focus on patient-centered perspective. *Acta Neurochir (Wien)*. 2014;156(2):367–374.
37. Fujita F, Diener E. Life satisfaction set point: stability and change. *J Pers Soc Psychol*. 2005;88(1):158–164.
38. Diener E, Lucas RE, Scollon CN. Beyond the hedonic treadmill: revising the adaptation theory of well-being. *Am Psychol*. 2006;61(4):305–314.
39. Wu A, Garcia MA, Magill ST, et al. Presenting symptoms and prognostic factors for symptomatic outcomes following resection of meningioma. *World Neurosurg*. 2018;111:e149–e159.
40. Englot DJ, Magill ST, Han SJ, Chang EF, Berger MS, McDermott MW. Seizures in supratentorial meningioma: a systematic review and meta-analysis. *J Neurosurg*. 2016;124(6):1552–1561.
41. Lieu AS, Howng SL. Intracranial meningiomas and epilepsy: incidence, prognosis and influencing factors. *Epilepsy Res*. 2000;38(1):45–52.
42. Tanti MJ, Marson AG, Jenkinson MD. Epilepsy and adverse quality of life in surgically resected meningioma. *Acta Neurol Scand*. 2017;136(3):246–253.
43. Nabukenya AM, Matovu JK, Wabwire-Mangen F, Wanyenze RK, Makumbi F. Health-related quality of life in epilepsy patients receiving anti-epileptic drugs at National Referral Hospitals in Uganda: a cross-sectional study. *Health Qual Life Outcomes*. 2014;12:49.
44. Modi AC, Ingerski LM, Rausch JR, Glauser TA. Treatment factors affecting longitudinal quality of life in new onset pediatric epilepsy. *J Pediatr Psychol*. 2011;36(4):466–475.
45. Dijkstra M, van Nieuwenhuizen D, Stalpers LJ, et al. Late neurocognitive sequelae in patients with WHO grade I meningioma. *J Neurol Neurosurg Psychiatry*. 2009;80(8):910–915.
46. Hwang K, Joo JD, Kim YH, et al. Risk factors for preoperative and late postoperative seizures in primary supratentorial meningiomas. *Clin Neurol Neurosurg*. 2019;180:34–39.
47. Li X, Wang C, Lin Z, et al. Risk factors and control of seizures in 778 Chinese patients undergoing initial resection of supratentorial meningiomas. *Neurosurg Rev*. 2020;43(2):597–608.
48. Giménez DeGeorge E, Fullen C, Gess J, Kleiner J, Larson-Prior L. Effects of age of onset and medication on cognitive performance and quality of life in patients with epilepsy. *Epilepsy Behav*. 2021;121(Pt A):108008.
49. Das RR, Artsy E, Hurwitz S, et al. Outcomes after discontinuation of antiepileptic drugs after surgery in patients with low grade brain tumors and meningiomas. *J Neurooncol*. 2012;107(3):565–570.
50. Pintea B, Kandenwein JA, Lorenzen H, et al. Factors of influence upon the SF-36-based health related quality of life of patients following surgery for petroclival and lateral posterior surface of pyramid meningiomas. *Clin Neurol Neurosurg*. 2018;166:36–43.
51. Jakola AS, Gulati M, Gulati S, Solheim O. The influence of surgery on quality of life in patients with intracranial meningiomas: a prospective study. *J Neurooncol*. 2012;110(1):137–144.
52. Miao Y, Qiu Y, Lin Y, Lu X. Assessment of self-reported and health-related quality of life in patients with brain tumours using a modified questionnaire. *J Int Med Res*. 2008;36(6):1279–1286.
53. Zamanipoor Najafabadi AH, van der Meer PB, Boele FW, et al.; Dutch Meningioma Consortium. Determinants and predictors for the long-term disease burden of intracranial meningioma patients. *J Neurooncol*. 2021;151(2):201–210.
54. Pollock BE, Stafford SL. Results of stereotactic radiosurgery for patients with imaging defined cavernous sinus meningiomas. *Int J Radiat Oncol Biol Phys*. 2005;62(5):1427–1431.
55. Hasegawa T, Ishii D, Kida Y, Yoshimoto M, Koike J, Iizuka H. Gamma Knife surgery for skull base chordomas and chondrosarcomas. *J Neurosurg*. 2007;107(4):752–757.
56. Hamm K-D, Henzel M, Gross MW, Surber G, Kleinert G, Engenhart-Cabillic R. Stereotactic radiotherapy of meningiomas compressing optical pathways. *Int J Radiat Oncol Biol Phys*. 2006;66(4):S7–S13.
57. Milker-Zabel S, Zabel-du Bois A, Huber P, Schlegel W, Debus J. Fractionated stereotactic radiation therapy in the management of benign cavernous sinus meningiomas: long-term experience and review of the literature. *Strahlenther Onkol*. 2006;182(11):635–640.
58. Henzel M, Fokas E, Sitter H, Wittig A, Engenhart-Cabillic R. Quality of life after stereotactic radiotherapy for meningioma: a prospective non-randomized study. *J Neurooncol*. 2013;113(1):135–141.
59. Henzel M, Gross MW, Hamm K, et al. Stereotactic radiotherapy of meningiomas: symptomatology, acute and late toxicity. *Strahlenther Onkol*. 2006;182(7):382–388.
60. Lubgan D, Rutzner S, Lambrecht U, et al. Stereotactic radiotherapy as primary definitive or postoperative treatment of intracranial meningioma of WHO grade II and III leads to better disease control than stereotactic radiotherapy of recurrent meningioma. *J Neurooncol*. 2017;134(2):407–416.
61. Patel A, Dong T, Ansari S, et al. Toxicity of radiosurgery for brainstem metastases. *World Neurosurg*. 2018;119:e757–e764.
62. Morgan TM, Zaenger D, Switchenko JM, et al. Fractionated radiotherapy is associated with lower rates of treatment-related edema than stereotactic radiosurgery in magnetic resonance imaging-defined meningiomas. *World Neurosurg*. 2019;121:e640–e646.
63. Bitterlich C, Vordermark D. Analysis of health-related quality of life in patients with brain tumors prior and subsequent to radiotherapy. *Oncol Lett*. 2017;14(2):1841–1846.
64. Bahrami N, Seibert TM, Karunamuni R, et al. Altered network topology in patients with primary brain tumors after fractionated radiotherapy. *Brain Connect*. 2017;7(5):299–308.



65. Zweckberger K, Hallek E, Vogt L, Giese H, Schick U, Unterberg AW. Prospective analysis of neuropsychological deficits following resection of benign skull base meningiomas. *J Neurosurg.* 2017;127(6):1242–1248.
66. Verhaak E, Schimmel WCM, Gehring K, Hanssens PEJ, Sitskoorn MM. Cognitive functioning and health-related quality of life of long-term survivors with brain metastases up to 21 months after gamma knife radiosurgery. *Neurosurgery.* 2021;88(5):E396–E405.
67. Meskal I, Gehring K, Rutten GJ, Sitskoorn MM. Cognitive functioning in meningioma patients: a systematic review. *J Neurooncol.* 2016;128(2):195–205.
68. van Nieuwenhuizen D, Klein M, Stalpers LJ, Leenstra S, Heimans JJ, Reijneveld JC. Differential effect of surgery and radiotherapy on neurocognitive functioning and health-related quality of life in WHO grade I meningioma patients. *J Neurooncol.* 2007;84(3):271–278.
69. Wirsching HG, Morel C, Roth P, Weller M. Socioeconomic burden and quality of life in meningioma patients. *Qual Life Res.* 2020;29(7):1801–1808.
70. Biller-Andorno N, Zeltner T. Individual responsibility and community solidarity—the Swiss health care system. *N Engl J Med.* 2015;373(23):2193–2197.
71. Barrash J, Abel TJ, Okerstrom-Jezewski KL, et al. Acquired personality disturbances after meningioma resection are strongly associated with impaired quality of life. *Neurosurgery.* 2020;87(2):276–284.
72. Salo J, Niemelä A, Joukamaa M, Koivukangas J. Effect of brain tumour laterality on patients' perceived quality of life. *J Neurol Neurosurg Psychiatry.* 2002;72(3):373–377.