Quality of life in sinonasal tumors: an up-to-date review

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Purpose of review
To assess the impact of benign and malignant sinonasal tumors and their management on patients' Quality of Life (QOL) as measured by Patient Reported Outcome Measures (PROMS).

Recent findings
Although there is a growing consensus that endoscopic surgical management in carefully selected patients with sinonasal tumors is at least as (and probably more) effective than open resection, it is not clear to what extent this translates to better QOL outcomes. Earlier studies reported better outcomes in the emotional and physical function domains after endoscopic resection, and it seems that postsurgical morbidity is less in endoscopic compared to open approaches. QoL after endoscopic surgery for sinonasal and anterior skull base tumors seems to improve within several months of surgery in both benign and malignant tumor groups. However, patients with benign sinonasal tumors have a higher QOL pre and post operatively compared to those with malignancy mainly due to absence of (neo) - adjuvant radiotherapy and/or chemotherapy. Factors that seem to be associated with worse QoL include $>$ 60 years, less than 6 months from surgery, prior and adjuvant chemo and radiotherapy, smoking history, advanced staging and malignancy.

Summary
There is not a universally accepted PROM for use in patients with sinonasal benign and malignant tumors: A variety of different PROMs have been used with different degrees of effectiveness. Most likely a combination of disease-specific (such as SNOT 22 and anterior skull base questionnaire) and generic (such as Short Form health survey questionnaire (SF-36) and Karnofsky Performance Status) health outcome measures provide the most insight into QOL of patients with sinonasal tumors. QOL of these patients appears to undergo a bimodal impact with patients experiencing an initial dip in QOL after surgical treatment followed by a slow improvement over time. However, while patients with benign tumors' return to their status quo ante QOL, this is not the case for patients with malignant tumors who stabilize at a lower than initially QOL. To a large extent this seems to be the effect of (neo) adjuvant chemo radiotherapy.

Keywords
ASBQ, quality of life, sinonasal tumours, skull base tumours, SNOT 22

INTRODUCTION

Sinonasal tumors occur in the paranasal sinuses or nasal cavity, with malignancy accounting for approximately 3–5% of all head and neck cancers and less than 1% of all malignancies [1]. The annual incidence of sinonasal papillomas is 0.74–2.3 per 100 000 population and comprises of 0.5–4% of all primary nasal tumours [1,2]. Sinonasal inverted papilloma (SNIP) is the most common subtype significantly differing from the other subtypes in its invasiveness, high tendency to recur, and its well-recognized relation to squamous cell carcinoma (SCC) [2,3]. Symptoms are similar to those of inflammatory sinonasal diseases and thus diagnosis may delay significantly. Poor prognosis with approximately 50–60% 5-year survival rate is mostly attributed to the advanced stage at presentation [1,2,4].

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KEY POINTS

- Sinonasal tumors are uncommon tumors associated with significant impairment of patients' QOL.
- There are specific symptoms that may accompany sinonasal tumors and their treatment regimen.
- There is only a small body of literature addressing the QOL in patients with sinonasal tumors and comparison is difficult between studies due to the heterogeneity of the tumors, patient demographics and various QOL tools used by physicians.
- QOL after endoscopic surgery for sinonasal and anterior skull base tumors appears to improve within several months of surgery in both benign and malignant tumor groups.
- The key to improving patient's QOL is to identify patient's needs by implementing QOL measurements and conducting long-term studies.

Sinonasal tumors are divided into epithelial and nonepithelial tumors and accurate confirmation of histopathology is imperative to define the management plan [2,5]. The potential for malignant transformation and propensity of recurrence and local aggressiveness of benign sinonasal tumors along with local extension of sinonasal malignancies (SNM) to adjacent structures such as the brain, orbit and cranial nerves, may lead to extended resections and aggressive adjunct therapy, with significant impact on health-related quality of life (HRQoL) [6–9].

There are several studies focusing on the clinical aspects of populations who underwent skull base surgery [10]. Evaluation of postoperative complications, treatment response and survival rate are the most popular objectives. However, clinical observations about patient's daily quality of life (QOL) due to sinonasal tumors are limited. Patients with sinonasal tumors are often confronted with a unique set of biopsychosocial challenges. Therefore, evaluation of their HRQoL over a duration of time can only be achieved by vigilant awareness and appropriate assessment of these challenges in a comprehensive fashion.

This paper aims to explore the recent relevant literature pertaining to the QOL of individuals with sinonasal tumors.

Quality of life

WHO defines QOL as a multidimensional reflection of an 'individual's perception of their position in life in the context of their culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.'[11]. Measuring one's QOL enables clinicians to align their treatment approach to the patient's goals and priorities. Extension of one's life span does not necessarily lead to improvement in QOL, whereas treatments that do not increase overall survival may in fact enhance one's QOL [12,13].

There are factors that may lead to a shift from measuring general QOL to measuring one's HRQoL, which focuses on a patient's specific illness and treatment response [8▪]. Both in literature and in clinical practice QOL and HRQoL are often interchangeable. The fundaments of accessing HRQoL lies in its multidimensionality and commonly categorised into two broad domains, physical and nonphysical (Table 1) [8▪].

Quality of life instruments used to assess sinonasal malignancies

QOL in patients with sinonasal tumors has been assessed through Patient Reported Outcome Measures (PROMs), instruments that 'measure outcomes reported directly from patients about how they function or feel in relation to a health condition and its therapy, without interpretation of the

Table 1. Physical and Nonphysical health domains commonly evaluated in skull base malignancies [8▪]

	Non-physical health				
Physical health	**Psychological**	**Level of independence/ function**	**Social**	**Environment**	**Spirituality**
Nasal Visual Neurological Endocrine Systemic (Pain Fatigue Sleep)	Depression Anxiety Stress Mood Memory/Cognitive abilities Physical body image	Basic daily activities Work capacity Mobility and Accessibility	Work Family and Friends Relationships Sexuality	Finance Transportation Safety	Religion Personal beliefs and values

Table 2. Instruments that can be used to measure quality of life in patients with skull base malignancies [8▪,17]

General Health	Site-Specific	Disease-specific	Domain-specific	Treatment-specific	Symptom-specific
EuroQoL 5D	UWQOL	ASBQ	MDADI	UWQOL	BFI
SF-36	FACT-HN	SBI		QOL-RTI/H&N	BPI-SF
SIP	MDASI-HN	FACT-G		Liverpool Oral Rehabilitation Questionnaire	
KPS	SNOT-22				

EuroQoL 5D: European Quality of Life Five Dimension; SF-36: 36-item Short Form Survey; KPS: Karnofsky performance status scale; UWQOL: University of Washington Quality of Life; FACT-HN:Functional Assessment of Cancer Therapy – Head and Neck; MDASI-HN: MD Anderson Symptom Inventory Head and Neck Cancer; SNOT-22: Sinonasal Outcome Test; ASBQ: Anterior skull base questionnaire; SBI: Skull Base Inventory; Functional Assessment of Cancer Therapy; MDADI: MD Anderson Dysphagia Inventory; QOL-RTI/H&N: Quality of Life Radiation Therapy Instrument Head and Neck Module; BFI: Brief Fatigue Inventory; Brief Pain Inventory- short form.

patients' responses by a clinician or anyone else' [14]. This is vital because a surgeon's perception is not always accurate in assessing a patient's QOL as previously shown by a study in which poor correlation was found between a patient's self-rating and the surgeon's perception of patient's QOL [15].

Tools are assessed for their validity, reliability, sensitivity, clinical relevance, administration efficiency, patient relevance, and comprehension and ease of scoring and interpretation [16]. PROMs that have been used to record patient's perspective in sinonasal tumors are seen in Table 2 [8▪,17]. It is important to note that many of these questionnaires were used in patients with skull base malignancies and not benign sinonasal tumors specifically.

Generic QOL tools have been broadly used in the assessment of sinonasal and skull base malignancies. A systematic review pertaining to QOL assessment in adults undergoing anterior skull base surgery showed that the most common generic QOL tool used was the Karnofsky Performance Status (KPS) [18]. The KPS is a rating scale of functional status evaluated by healthcare providers, ranging from 0 to 100 with 100 indicating better functional status. Included studies reported an increase in average KPS scores following skull base surgery. Despite being a valuable tool, KPS has the drawback of measuring only one aspect of the broader concept of QOL [18]. A valid and reliable generic tool frequently used in otolaryngology and neurosurgery is the validated 36-item Short Form health survey questionnaire (SF-36) which comprises 36 questions covering eight domains of health. General health QOL outcomes following endoscopic pituitary surgery for adenomas were assessed in a recent retrospective study. Authors reported that, initially, patients had lower QOL in six of eight domains preoperatively, however, returned to baseline values after the early postoperative period in seven of eight domains highlighting the restorative role of minimally invasive pituitary surgery in QOL [19].

Disease-specific instruments have the advantage that they include domains that are specific to skull base tumors, allowing clinicians to monitor specific changes pre and post operatively, assess treatment responses and compare different treatment approaches [17]. The most widely used tool for patients undergoing skull base surgery is the anterior skull base questionnaire (ASBQ), which encompasses 35 items that cover six domains, including questions from general domains of pain, energy, and mood to specific questions related to smell, taste, and nasal function. The tool has been assessed for psychometric properties among patients undergoing open surgical approaches and was later validated for the endoscopic surgery as well [8▪]. Interestingly, the ASBQ has proved to predict the postoperative QOL of different groups of patients following skull base tumor surgery even prior to surgery [18]. A main limitation of this tool is that it includes only seven disease-specific items as it was primarily designed for open approaches [8▪]. In addition to that, SNOT-22 is commonly used in assessing QOL after endoscopic surgery for benign disease such as chronic rhinosinusitis [8▪,20,21] (Table 3). Although it lacks questions related to skull base, it has been previously used to assess postoperative QOL in patients undergoing endonasal surgery for sinonasal and skull base tumors, showing significant improvement in sinonasal morbidity [22▪,23–25].

The aforementioned generic tools are considered valid and reliable allowing comparisons across different clinical entities, treatment options, and population groups, however, it should be noted that they have not been established to detect changes in clinical status of patients with skull base tumor and, more often than not, they fail to account for specific outcomes considered important for this specific group of patients. On the contrary, disease and site-specific QOL tools are responsive to clinical changes, they are regarded as more clinically relevant, and they are appropriate for clinical trials assessing interventions such as skull base surgery

Table 3. Common instruments used in Sinonasal Malignancy [8▪,17,20–21]

Instrument	Description	Scoring	Notes
Sinonasal Outcome Test -22 (SNOT-22)	Derived from SNOT-20 and two additional items (nasal obstruction and sense of taste & smell), crucial symptoms for CRS, differs SNOT-22 from SNOT-20, thus strengthening the content validity of SNOT-22. Widely applied patient-reported questionnaire used in clinical practice as a measurement of health burdens in patients with chronic rhinosinusitis. EPOS (2012) recommends the usage of SNOT22 and suggests that it is the most adequate tool in the evaluation of CRS surgery.	Consists of 22 questions and recorded on a 6-item Likert scale (0–5). Total score ranges from 0–110 with a higher score indicative of a worse QOL. Four domains: nasal related, ear and facial, functional limitations, psychological.	Validated for CRS and not tailored to patients with malignant sinonasal tumors and/or skull base surgery
Anterior Skull Base Questionnaire (ASBQ)	Originally for assessment of QOL after open craniotomy for anterior skull based tumors. Have also been validated for endoscopic approaches as well.	Consists of 35 questions and recorded on a 5-item Likert scale (1 – 5). Total score ranges from 35–175. Overall scores are recorded as mean item scores that range from 1.0–5.0 with a higher score indicative of a better QOL. Six domains: performance, physical function, vitality, pain, emotional wellbeing, and specific symptoms (appetite, taste, smell, appearance, epiphora, nasal secretions and visual disturbances)	Time sensitive and specific for patients with anterior skull base tumors. Only three questions relating to sinonasal function.

[18]. Table 4 presents the most recent pertinent studies reviewing QOL outcomes in patients with sinonasal tumors.

Trajectory of overall quality of life

In terms of SNM, scattered data and reports suggest a bimodal impact with patients experiencing an initial dip in QOL after surgical treatment followed by a slow progression over time. This trend is seen in older studies, with a worsening of QOL in the first 6 months followed by an improvement at 12 months [23,26–29]. Within these studies, it is important to note that most QOL instruments are comprised of subdomains. A large proportion of patients may identify difficulties that are captured by a single item or subdomain, and although substantial for the patient, it may not be considerable enough to affect the overall QOL scores. This might explain the statistically insignificant overall scores seen in these earlier studies [27,28], where only sleep and psychological domains were found to be statistically significant. Postoperative disturbances in sleep, measured by SNOT-22 were also noted in a recent study in patients who had endoscopic endonasal transsphenoidal surgery [24].

Statistically significant improvements in the rhinologic, psychological and sleep domains were seen at 3 months with overall improvements in the rhinological and ear/facial domains at 6 months as measured by SNOT-20 [27]. A longer-term study showed patients with inverted papilloma to have statistically significant improvements in postoperative overall QOL scores and in the rhinologic and sleep domains at 6 months but not at the 1 or 2 year time point [28]. Results may be due to the smaller sample size at 1 and 2 years [28]. A following study in 2016, investigated Inverted Papilloma (IP) after endoscopic resection using SNOT-22 and showed no statistically significant impairment to patients' QOL after 5 years [3]. With this study as well, the sample size was too small to draw generalised conclusions.

Specific postoperative symptoms in patients with sinonasal tumors

As seen in Table 2, there are specific symptoms that may accompany sinonasal tumors and their

Table 4. Most recent pertinent studies reviewing QoL outcomes in patients with sinonasal tumors

Author (Year)	Country	Study Design	n	Age in years	Study population	Data Capture	Intervention	Follow-up time points in months	QoL Assessment tool	Main findings
Alshammari *et al.* (2021) [24]	Saudi Arabia	Single-center retrospective cross-sectional study	96	39.5	pituitary adenoma (46.9%), CSF-related leak (41.7%), Craniopharyngiomas (2.1%), clival mass (5.2%) meningiomas (4.2%)	March 2010 to March 2020	Endoscopic endonasal transsphenoidal surgery	3,6	SNOT-22	Statistically significant improvement in overall SNOT-22 scores postoperatively at 3 and 6 months with no long-term effects. Increase in discomfort in the sleep domains after surgery.
Philips *et al.* (2021) [50▪]	USA	Single-center retrospective study	81	60	Sinonasal Malignancy Extension into the skull base (44.4%) Into the orbit (29.6%) in the ITF (4.9%) and in the PPF (9.9%)	2006 to 2019	Surgery (87.7%) Endoscopic (62%) Open/ combined (38%) Concurrent neck dissection (22.2%), and orbital exenteration (6.2%)	24 (median)	HADS FACT-NP	Advanced Tumor stage and single relationship status were found significantly predict anxiety and depression (HADS) A worse social support survey score was related to worse anxiety, depression, and QOL (HADS and FACT-NP)
Tyler *et al.* (2020) [53▪]	USA	Single-center cross-sectional study	114	55	Malignancy originating from: Nasopharynx (54%) Paranasal sinus (25%) Nasal Cavity (21%)	2001 to 2013	RT (all patients) CMT (76%) Surgery (33%)	65	EQ-5D VAS MDASI-HN ASBQ	HRQoL in based on EQ-5D VAS was similar to that of the general population. MDASI-HN and ASBQ showed unique symptoms, underscoring the complex symptom burden in these patients.
Shah *et al.* (2020) [22▪]	USA	Single-center retrospective study	83	55	Benign or malignant tumors with both sinonasal and skull base involvement (excluding osteomas or inverted papillomas)	2004 to 2017	Endoscopic resection (59% intradural dissection) Additionally: RT (51.8%) CMT (26.5%) RT and CMT (25.3%)	1, 1.5	SNOT-22	Pre and post skull base surgery SNOT-22 scores showed significant improvement in sinonasal symptoms (32.6 vs. 24.5, $p = 0.030$).
Sharma *et al.* (2020) [60▪▪]	Denmark	Two-center cross-sectional study	27	67	Recurrence-free patients previously treated with RT for sinonasal malignancy	January 2008 to December 2016	RT	76.8 (median)	EORTC-QLQ-C30 EORTC-QLQ-BN20 HADS PSQI PAOFI	The most affected outcomes were 'fatigue', 'insomnia', and 'drowsiness'. A total of 59% reported significantly impaired sleep quality. 'Memory' was the most affected cognitive domain.

Table 4 (*Continued*)

Author (Year)	Country	Study Design	n	Age in years	Study population	Data Capture	Intervention	Follow-up time points in months	QoL Assessment tool	Main findings
Pacalic *et al.* 2020 [62]	USA	Single-center prospective observational study	64	55	Sinonasal Malignancy	2011 to 2019	PBT Most commonly surgery followed by either concurrent RT and CMT (33%) or RT alone (23%) or induction CMT followed by concurrent CMT and RT (11%)	33 (median)	XeQoLS MDADI FACT	Significant worsening from baseline in the XeQoLS acute-subacute physical functioning, pain, personal/psychological distress, and social function; acute-subacute MDADI physical function; and acute-subacute FACT head/neck subscale. PROs indicated significant changes in the acute-subacute period but no chronic effect.
Glicksman *et al.* (2018) [23]	USA	Single-center prospective cohort study	145	58.6 (Malignant) 51.8 (Benign)	Both malignant and benign sinonasal tumors	January 2011 to June 2015	Endoscopic tumor resection Additionally: Preoperative CMT and/or RT (3.1%) Adjunctive CMT and/or RT (75%) in malignant tumors	3,6,12,24	SNOT-22	Patients with both malignant and benign tumors experienced a statistically significant improvement across all subdomains of the SNOT-22 questionnaire at 3 months post operatively, sustained over the course of 2 years of follow-up.

QoL, Quality of Life; n, number; CSF, cerebrospinal fluid; SNOT-22, 22-item Sino-Nasal Outcome Test; ITF, infratemporal fossa; PPF, pterygopalatine fossa; HADS, Hospital Anxiety and Depression Scale; FACT-NP, Functional Assessment Cancer Therapy – Nasopharynx score; RT, radiotherapy; CMT, chemotherapy; EQ-5D VAS, EuoQol Group-5 Dimension Visual Analogue Scale EuroQol5D; MDASI-HN, MD Anderson Symptom Inventory–Head and Neck; ASBQ, Anterior Skull Base Questionnaire; HRQoL, health-related quality of life, EORTC-QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Version 3.0; EORTC-QLQ-BN20; European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Brain Cancer Module, PSQI, Pittsburg Sleep Quality Index; PAOFI, Patient's Assessment of Own Functional Inventory; Hospital Anxiety, PBT, proton beam therapy; Xerostomia Related Quality-of-Life Scale (XeQoLS), MD Anderson Dysphagia Inventory (MDADI), and Functional Assessment of Cancer Therapy (FACT); PROs, patient reported outcomes.

treatment regimen. They are evaluated in the different instruments seen in Table 3.

Nasal Complications

Nasal symptoms typically include nasal obstruction, nasal discharge, anosmia, and persistent epistaxis [1,4,17,30]. In specific cases, malignant tumors can erode facial bones and nasal septum causing malformation of the nasal bridge and protrusion into the nasal cavity floor can cause palate compression [4,30,31]. Postoperative complications include acute olfactory loss, nasal crusting/discharge, epistaxis and postnasal drip [3,4,17,21,23,24,27–29,32–34]. Need to blow nose and thick nasal discharge was reported after endoscopic resection of IP, possibly due to postsurgical scarring contributing to the mucociliary epithelium disruption [3]. Tumors that affect the maxillary infrastructure most likely require endoscopic or open maxillectomy [9,31,35–37], and persistent long term with a median time of 45.9 months, significant postmaxillectomy symptoms include hypoesthesia of the upper incisors [36].

A study by Rowan and Mukherjee (2020) outlining the present understanding of endoscopic endonasal skull base surgery notes that olfactory impairments and symptomology to be one of the most crucial sinonasal specific morbidities in those who had EESBS [21]. Patients experiencing olfactory complications often are also associated with decreased socializing, increased mental health, weight loss and higher risk of injury [21]. It has been hypothesized that the extent of EESBS-associated olfactory disturbance are likely associated with the degree of the disease and surgical involvement of the olfactory tract [21]. A physician's interpretation of imaging is therefore crucial in the context of evaluating different surgical techniques that attempt to preserve olfactory function [21,38].

Ocular outcomes

Orbital infiltration results in ocular complications both at presentation and throughout the course of treatment. Direct tumor extension through the lamina papyracea may present as visual acuity disturbances, diplopia, ocular pain, proptosis, and eyelid fullness [4,30,31,39–41]. Soft tissue infiltration requires orbital exenteration. Visual complications due to surgery involve diplopia, globe malposition, enophthalmos, chronic epiphora, iterative dacryocystitis and decrease in visual acuity [31]. Postoperative radiation could lead to keratopathy, visual field defect and visual acuity disturbances [4,39–41]. Sinonasal tumours involving the orbit are common [39,42], however it is vital for physicians to be aware and prepared for such cases due to the difficulty of access and the aggressiveness of these tumours to offer the appropriate therapy and multidisciplinary team to minimise complications and optimise patient's QOL [39,41,43,44]. The importance of accurately staging the extent of orbit involvement as well as taking into account the histology of underlying malignancy has been demonstrated by Castelnuovo *et al.* and has led to a new pathway focusing on orbital preservation when possible while improving oncological outcomes [39].

Endocrine impairment

Inadvertent irradiation of the hypothalamic-pituitary axis may result in endocrinal impairment [45]. An earlier study found that around 60% of irradiated patients with SNMs experienced a deficiency of at least one hypothalamic-pituitary hormone axis hormonal, whereas around 20% of them had definitive hypopituitarism with multiple hormonal deficiencies [46].

Neurological sequelae

In more advanced cases, intracranial extension through the dura or skull base foramina causes specific neurological deficits and neurological sequelae that often needs neurosurgical intervention [47]. Tumours can also invade the pterygopalatine and infratemporal fossa, which, aside from being potential routes to the brain, host major blood vessels, nerves and muscles [30,31]. Extension into these areas can result in symptoms such as trismus, facial pain, and numbness [30]. Cerebrospinal fluid (CSF) leak is a common postoperative complication in patients that underwent extended resections and has the potential to lead in meningitis or intracranial abscess [30,31]. Other postoperative neurological complications include pneumocephalus, haemorrhage, frontal syndrome and consciousness impairment [31].

Psychological consequences

Psychiatric comorbidities often accompany patients with head and neck cancer [48]. HNCs are associated with depression [48]. This may be due to the profound impact on one's fundamental activities such as limitations in eating, speaking, working and socialising as well as the socioeconomic and financial burden that comes with cancer [48,49]. Furthermore, the location of the tumours and the surgical intervention to manage them including extensive facial resection, maxillectomy or orbital

exenteration may compromise one's sense of identity and mental wellbeing and is associated with adverse aesthetic and functional outcomes [33]. Philips *et al.*, (2021) published a paper focused on the evaluation of patient's anxiety and depression via the Hospital Anxiety and Depression Scale (HADS) and the Functional Assessment Cancer Therapy - Nasopharynx (FACT-NP) score. It was found that those with advanced T-staging, single status and poor social support had worse anxiety and depression scores [50▪]. With relatively increased rates of suicidal ideation and HADS scores in Philip *et al.*'s study, there is an urgent need for further studies, clinician awareness, depression screening, early referral to mental health services and appropriate clinical assessment. Resilience was quantified for HNCa patients in MacDonald *et al.*s (2020) study using QoL scales and found statistically significant results of strong interaction between a patient's resilience and social functioning. It may therefore be useful to access one's preoperative resilient levels to manage future complications post operatively [13]. Another recent study used the Beck Depression Inventory (BDI) to assess depression, Short Form-36 for general HRQOL and Head and Neck Cancer Inventory (HNCI) for Head and Neck Cancer -specific HRQOL (HNCI), to compare quality of health between patients with head and neck cancer- living in rural and urban areas. The rural counterparts were shown to have worst quality of health [51]. Although, this study did not specifically include patients with sinonasal tumours, research in this area could be carried out for sinonasal tumours considering the relatively limited access to mental health services in rural areas.

The importance of quality of life in patients with sinonasal malignancies

Sinonasal tumors have a complex morbidity profile. Their predisposition to recur, their local destructive capability along with the potential of extension into vital adjacent structures, such as cerebellum, pituitary gland, cranial nerves, carotid and vertebral arteries, spinal cord and craniofacial skeleton may lead to symptomatology that affects severely one's physical and mental functioning in varying ways [4,6,30,31].

The important information provided by measuring a patient's QOL is widely acknowledged and accompanied with potential clinical applications [8▪]. It can facilitate better understanding between clinicians and patients, resulting in a more tailored and individualized management plan. A specific line of communication, focused on patient's reported QOL, enables a multidisciplinary team to be more responsive with patient's needs and concerns extending into effective preoperative counselling along with occupational, rehabilitative and educational services [14]. On a larger scale, QOL data can assist in shaping medical institutional protocols and aid in pharmaceutical and treatment-based research [15].

Studies have shown a predictive value in many QOL scales. Poor QOL acts as a surrogate for advanced disease and can predict a high symptom burden and a systemic physiologic cancer burden [51,52]. Questionnaires associated with survival in patients with head and neck cancer include Short Form-36, head and neck QoL scales and General Health Questionnaire (GSQ) sum scores [52]. Tyler *et al.*, (2020) found that T3 and T4 tumors are associated with relatively poor ASBQs compared to those with lower staging. In addition, MD Anderson Symptom Inventory (MDASI) data showed an association between N-classification and teeth and gum symptoms [53▪]. These data can aid in early referral to relevant healthcare professionals. Furthermore, various factors such as smoking history can affect one's QoL and can aid in prediction of a patient's postoperative QOL [28,53▪].

Quality of life following treatment of sinonasal tumours

Dependent on the histology and aggressiveness of the tumor, treatment options for sinonasal tumors typically consists of a combination of surgery, chemotherapy, and radiotherapy. Surgery is the treatment of choice for benign sinonasal tumors and although surgery followed by radiotherapy remains the common treatment plan for sinonasal malignancy, there is no consensus for the optimal management algorithm. It is important to note that most sinonasal tumors present late, when infiltration of local structures has already occurred resulting in an increased risk of complications associated with surgical removal [4,37,39].

Surgery

There are two broad strategies to surgical management, open and endoscopic resection. Over time, endoscopic approaches have gained in popularity as they are associated with better visualization of deep sinonasal structures, absence of facial incisions, better morbidity, lower complication rates, and reduced hospital stay [54,55]. QOL in endonasal approaches for skull base tumors seems to be less adversely affected [3,10,18]. The main concern of endoscopic approaches is that tumors are resected in a piecemeal manner and en bloc resection cannot be

performed, thus violating oncologic principles [55]. To date there is a wide consensus on pre-eminence of endoscopic resection, provided that several studies have shown statistically significant lower recurrence rates, comparable survival rates (sometimes greater) as well as postoperative complications including bleeding and CSF leaks with endoscopic as compared with open approaches; therefore, endoscopic resection is currently the preferred modality for sinonasal tumors [56,57]. While postsurgical morbidity in both open and endoscopic seems to be comparable, earlier findings show that contrastingly, QOL of patients operated via an endoscopic approach, as reported by patients using ASBQ, showed to be significantly better in the emotion and physical function domains than those who underwent open surgery [29,58,59]. It is important to note that there is no recent data on the comparison of each surgical modality in reference to sinonasal tumors specifically in the context of patient reported QOL.

Available literature investigating the QOL of patients with inverted papillomas include a long-term study with a median follow up of 6 years which showed patients after endoscopic removal having comparable QOL scores pre and postoperatively, with no significant difference in scores between patients having undergone a wide local excision and those whom had a medial maxillectomy [3]. This study is an effective extension to Harrow & Batra (2013) and Derousseau *et al.*, (2015)'s study which showed QOL improvement at 6 months [27,28].

A recent interesting study by Shah *et al.* (2020), reviewed 83 patients through SNOT-22 and Lund-Mackay scores, and found that a large proportion of patients developed clinically significant chronic sinusitis after endoscopic skull base surgery [22▪]. A key finding in this study was the significant difference of preoperative and postoperative scores in patients who eventually was required to undergo revision endoscopic sinus surgery (rESS). On average the intervention occurred 3.5 years following the initial tumor resection. These recent studies have timelines that indicate (1) how important is to carry out QOL through a long period of time, especially for malignant tumors (2) how implementing QOL questionnaires can identify potential future interventions required.

Radiotherapy

Sinonasal tumors are commonly located in areas whereby delivery of radiation cannot be achieved without damaging adjacent structures. A prospective national study has been initiated with the aim of investigating cerebral toxicity after radiotherapy for SNM following Sharma *et al.*, (2020)'s study which showed significant late neurotoxicity with macroscopic and cognitive impairment present on both hippocampi, both frontal lobes and the right temporal lobe [60▪▪]. High grade radiation toxicity was also found in Patel *et al.* (2020)'s study with a subset of patients requiring endoscopic sinus surgery post radiation due to chronic sinusitis and another group needing operative debridement due to symptomatic nasal obstruction [61].

In view of patient-reported outcomes (PROs), a study, evaluated the QOL of patients who underwent proton beam therapy (PBT) for SNM through physician assessed toxicities and PROs. PROs were evaluated with the Xerostomia Related Quality-of-Life Scale (XeQoLS), MDADI, and Functional Assessment of Cancer Therapy (FACT) for a median time of 33 months [62]. Significant worsening from baseline were seen in the acute – subacute FACT HN subscale, physical function of the MDADI scale, and acute - subacute physical function, pain, psychological distress, and social functioning in the XeQoLS scale. However, no significant findings were seen from baseline to the chronic period.

Chemotherapy

A recent study found an association between receiving prior chemotherapy and teeth and gum symptoms using the MDASI-HN questionnaire, however, did not show other differences in QOL in patients receiving adjunct chemotherapy and those who did not [53▪]. Contrastingly, earlier studies using SNOT-20 showed a decrease in QoL scores in the rhinological domain after endoscopic resection in those who had prior chemotherapy and/or radiation compared to patients with no prior therapy [27]. Other prior studies also showed a worse QOL in those with adjunct chemotherapy compared to their counterparts without [32,63]. A study investigating the QoL using MD Anderson Symptom Inventory and Herth Hope Index among HNC survivors. Five time points from pre - concurrent chemoradiotherapy (CCRT) to 4 months after CCRT completion were measured and showed a decrease in QOL and increased symptom burden which then subsequently improved. It was also found that predictions of QOL change over time correlated with symptom burden and hope [64]. Again, sinonasal tumors were not included in this study, but provides a framework for such studies to be applied to the sinonasal tumor population. Last but not least, Glicksman *et al.* evaluated QOL throughout the 2-year period following endoscopic resection of benign and malignant sinonasal and skull base tumors. They showed that within the

malignant group, a significant difference in SNOT-22 scores was noted between those who underwent adjuvant therapy (radiation or chemoradiation) and those who did not. Specifically, patients who underwent adjuvant therapy experienced worse average sinonasal QOL scores at 6, 12, and 24 months [23].

Comparing quality of life between malignant and benign tumors

Overall, patients with benign sinonasal tumours have a higher QOL pre- and postoperatively as compared to those with malignancy. Harrow and Batra showed that minimally invasive endoscopic resection for sinonasal and skull-base tumors led to an improvement in SNOT-20 scores at 6 months, however, patients with benign histology experienced lower scores. Multivariate analysis proved that prior radiation and/or chemotherapy was the one of the strongest predictors for lack of SNOT-20 improvement [27]. Similarly, Deckard *et al.* reported significantly worse results in ASBQ, SNOT-20, and LKE scores in patients treated for malignant sinonasal tumors as compared with benign ones. The role of postoperative radiation and/or chemotherapy in these unfavorable outcomes was highlighted [32]. I should be noted that the use of adjuvant therapy seems to be an obvious reason for the worse sinonasal QOL scores observed in patients with malignant disease when compared to patients with benign tumors. The detrimental effects of chemoradiation in patients with head and neck cancers has been extensively described. Mucosal dryness, olfactory impairment, and focal osteoradionecrosis may be responsible for worse sinonasal QOL in patients treated with adjuvant therapy. Last but not least, psychological consequences such as depression from the cancer itself should always be kept in mind when one interprets QOL results [23].

Limitations of assessing quality of life in sinonasal malignancies

There is still no universal gold standard for measuring QOL in patients with sinonasal malignancy. Although the establishment of a gold standard would be significant in improving global understanding of how patients with sinonasal tumors are affected, one should keep in mind that there are several factors that inhibit the development of such tool. In the current body of studies available, it is evident that a wide range of diverse methodologies and questionnaires are employed in each study along with patients with different demographic characteristics, comorbidities, stages, and sites affected. Differences in treatment approaches (surgery, radiation, chemotherapy) as well as within each modality (type of surgical resection, chemotherapy regimen, radiation therapy) needs to be considered and assessed individually, despite its wide variety. There are many studies that grouped chemo and radiation therapy together. Only a small handful of sinonasal tumour studies are standalone, while the majority are grouped within skull-based neoplasm literature. One thing to note is that many of these studies have a larger population of Caucasians. There is remarkable anatomic variation in nasal cavities and paranasal sinuses between individuals of different ethnic groups. A systemic review carried out by Papadopoulou *et al.*, (2021), showed the anatomic variations among these groups that is of paramount importance, especially in the context of predicting certain pitfalls and complications when managing sinonasal tumors through endoscopic or surgical means [65]. Thereby, accessing, and distinguishing ethnicity when accessing QOL is crucial due to differences in anatomic variation, genetic and environmental factors [66]. This is especially important as sinonasal tumors are more common in Asia and Africa than in the Western countries [5].

CONCLUSION

Data in the field of sinonasal neoplasm are scattered in terms of QOL tools used and variables measured. Despite the rarity of these tumors, these patients have a unique set of challenges that impacts their QOL which must not be neglected. Although there is a growing consensus that endoscopic surgical management of sinonasal and anterior skull base tumors is at least as (and probably more) effective than open resection, it is not clear to what extent this translates to better QOL outcomes. QOL after endoscopic surgery for sinonasal and anterior skull base tumors seems to improve after surgery in both benign and malignant tumor groups. However, patients with benign sinonasal tumors have a higher QOL pre- and postoperatively compared to those with malignancy mainly due to the prior or adjuvant radiation and/or chemotherapy. The need for a disease- specific, validated gold standard QOL tool for sinonasal and anterior skull base tumors should be highlighted.

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Conflicts of interest

There are no conflicts of interest.

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