ISSN: 2688-8238
DOI: 10.33552/OJOR.2019.01.000520
Online Journal of Otolaryngology and Rhinology
Iris Publishers

Review Article

Functional Outcomes in Endoscopic Endonasal Surgery of the Skull Base, A rising challenge

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Received Date: June 05, 2019

Published Date: July 09, 2019

Abstract

Since the introduction of endonasal endoscopic skull base surgery in the management of skull base neoplasms the exclusive purpose has been to increase survival rates. Recently, given the improved of the survival rates, more attention has been focused on other aspects such as nasal symptoms and quality of life. The purpose of this review is to assess the current evidence of functional outcomes after endoscopic skull base surgery.

Keywords: Endoscopic surgery, Skull base, Quality of life, Nasal symptoms

Introduction

Extended endonasal endoscopic approaches (EEEA) for skull base lesions have been increasing over the last decade. Determinants for this development are the enhanced understanding of the endoscopic anatomy, improvement of imaging systems and specific instruments, and the use of vascularized flaps for reconstruction [1]. This EEEA can cause postoperative morbidity related to the reconstruction, like crusting and posterior rhinorrhea, especially in those cases requiring an endonasal flap [2,3]. The healing process start the first week with a reepithelization by stratified epithelium, then hair cells appear in the third week and complete recovery of the sinus epithelium occurs within 6-8 weeks [4]. Given this, [5] conclude that one must wait at least three months to assess the clinical and postoperative symptoms. Regarding quality of life (QOL) after EEEA evidence have shown that the morbidity is related to the extension of the approach. [6] reported a negative impact in QOL after the use of nasoseptal flap which is commonly associated to extended approaches. The latter was mainly due to an increased tendency to headaches and reduced smell; however, recovery occurs over time especially in those patients with secreting pituitary tumors.

Since the use of endoscopic skull base surgery, there have been great efforts to develop specific QOL questionnaires for EEEA and pituitary surgery (Table 1) Until now, the following tests have been applied in English literature; Quality of Life-Assessment of Growth Hormone Deficiency in Adults [7], Hypopituitarism Quality of Life Satisfaction (QLS-H) [8], Previous Skull Base Quality of Life (ASB-QOL) [9], Hormone Deficiency-Dependent Quality of Life (HDQOL) [10], Acromegaly Quality of Life (ACROQOL) [11], Pituitary Adenoma Quality of Life (PA-QOL) [12], Cushing Quality of Life [13], Addison Quality of Life (AddiQOL) [14], or ASK nasal inventory [15]. Handicaps for these tests are that they do not include specific areas about quality of life and cancer, visual defects, hormonal deficiency or sinonasal symptoms. Here, we will discuss the impact of EEEA regarding the following topics:

1. Sinonasal symptoms.
2. Mucociliary clearance.
3. Quality of life.
4. Imaging findings.

Table 1: Publications about Quality of Life and Nasal Symptoms in Surgery ESBC.

Reference	Method	Type of Pathology	Items	No. of Items	No. of Answers	Results	Valoration Time
Georgalas 2012 [6]	RSOM-31	Benign tumors of the skull base	General, Nose, Ocular, Hearing, Sleep.	31	5	Secreting tumors are a negative factor in the quality of life.	142-1104 Days
McKenna 1999 [7]	QOL-AGH-DA	Patients with growth hormone deficiency		25	2		
Herschbach 2001 [8]	QLS-H	Patients with growth hormone deficiency/hypopituitarism		9	5		
Gil 2004 [9]	ASB-QOL	Patients with anterior skull base cancer	Performance physical function, vitality, pain, specific symptoms, influence on emotions, Physical, emotional	35	5	Malignancy, RT and comorbidity is associated with a lower score.	More than 3 months
McMillan 2006 [10]	HDQOL	Patients with hypopituitarism	Work, family, social, sex, appearance, self-confidence, physical capabilities, leisure, travel, motivation, spiritual, society's reaction, future worries,	20	7		
Kan 2006 [12]	Pituitary adenoma	Patients with pituitary adenoma	General health, emotional, social, family, health problems, physician relations	54	7		
Webb 2008 [13]	Cushing QoL	Patients with Cushing's Disease		12	5		
Lovas 2010 [14]	AddiQoL	Patients with Addison's Disease	Physical, emotional	36	5		
Martinez-Devesa 2006 [43]	UoW-QOL HAD	Patients with anterior skull base cancer	Specific symptoms, physical, emotional. Depression and anxiety	12 14	100 4	The worst domains are humor, activity, taste and. 1/3 had psychiatric risk.	
Castelnuovo 2013 [45]	ASB-QOL	Malignant tumors of the skull base	Pain, physical function, vitality, specific symptoms, performance.	32	5	The radical endoscopic resection needs at least a year to recover ll or part of QoL	1-12 Month
McCoul 2013 [46]	SNOT 22 ASB-QOL	Tumors of the skull base	Diverse symptoms related.	22 35	5	Initial deterioration with long-term improvement	12 months
Diaz 2014 [50]	SF-36 PHQ-9	Skull Base Chordomas	Health, pain, social, mental health, limitations, relationships, vitality, personal perception. Depression.	36	6-Feb	Worse quality of life	
Abergel 2012 [51]	ASB-QOL	Tumors of the skull base	Pain, physical function, vitality, specific symptoms, performance.	32	5	Some domains of QoL are better with endoscopic than open approach.	12 Months
Palme 2009 [52]	FACT CES-D ALHR MDS	Patients with anterior skull base cancer	Physical, social, physical function, emotional, social, family. Depression and happiness Sight, hearing, taste, touch	38 20 1 4	5 4 11 5	Recurrence RT and MDS presented lower QOL scores	
Badia 2004 [53]	Acro-QOL	Patients with acromegaly	Physical, psychological apparence, psychological relations	22	5		
Patel 2015 [55]	ASBS – Q SNOT 22	Craniopharyngiomas	Diverse symptoms related	35 22	5 5	Overall maintenance during postoperative	> 9 months

Bernal Sprekelsen 2016 [57]	VAS, BAST – 24, saccharin test, SF 36, RSOM	Pituitary adenomas and other benign parasellar tumours	Sinonasal Symptoms, mucociliary clearance time, olfactometry, QOL	Diverse	Diverse	no significant difference between preoperative and long-term postoperative	12 months
Wu V, 2018 [61]	SNOT 22	Pituitary adenomas and other midline anterior skull base lesions	Diverse symptoms related.	22	5	Temporal worsening with complete recovery after 5 months.	> 5 months
Kuan 2018 [62]	SF 36	Pituitary adenomas	physical functioning, emotional role functioning, energy/fatigue, emotional well-being, social functioning, pain, and general health	36	6-Feb	no significant difference between preoperative and long-term postoperative	>2 weeks after surgery
Glicksman 2018 [63]	SNOT 22	Malignant and benign sinonasal tumors	Diverse symptoms related.	22	22	Improvement from baseline to 2 years	2 years
Riley 2019 [66]	SNOT 22 Lund Mackay	Malignant and benign pituitary and skull base tumors	Diverse symptoms related. Radiological findings.	22	5	Increase in radiological findings without significant difference between preoperative and long-term postoperative QOL	>5 years
Seo 2019 [68]	SNOT 20	Malignant and benign pituitary and skull base tumors	Diverse symptoms related.	20	5	Significantly worsening in extended procedures and NSF usage	6 months
Ahn 2019 [69]	SNOT 22	Malignant and benign pituitary and skull base tumors	Diverse symptoms related.	22	5	QOL was recovered within 6 months	6 months

Sinonasal symptoms

In the last decade, endoscopic skull base surgery has had a massive development in terms of surgical experience and technological advancement. Nowadays is it possible to address larger and more complex tumors, as so, patients suffer large anatomical and functional changes of the sinonasal cavity postoperatively. It is in the first postoperative period (2-4 weeks) when nasal symptoms are more evident, usually patients refer thick anterior and posterior rhinorrhea, nasal congestion, facial pain and headaches [16]. Currently nasal symptoms are measured according to the visual analogue scale and/or by different questionnaires such us the Sinonasal Outcome Test 22 (SNOT-22), Rhinosinusitis outcome measure (RSOM-31) and the Rhinosinusitis Disability Index (ISDN).

In one of the first studies about posterior nasal symptoms in skull base surgery, [3] observed that the most frequent finding were nasal crusts (98%) one month postoperative and at least half of the patients continue with nasal crusts for 3 months post-surgery. The time of disappearance of the crusts was related to the complexity of the surgery but not to the reconstruction of the defect [2] reported that in the postoperative period 28% of patients undergoing transsphenoidal and 64% undergoing extended surgery had posterior rhinorrhea. Interestingly [17] compared the nasal symptoms in patients undergoing endoscopic versus open surgery, they observed that the endoscopic surgery group had a lower score of nasal symptoms compared to the open approaches [18,19] showed that the SNOT-22 total score and the nasal symptoms score increased moderately in the immediate postoperative period but subsequently returned to their preoperative values. The same was reported by [16] who found that nasal symptoms significantly improved over time, although posterior rhinorrhea persisted during the first year after surgery.

Normal sense of smell requires the integrity of the olfactory epithelium for proper functioning. Usually in cases of lateral or anterior skull base surgery (without affecting cribriform plate) is possible to preserve the olfactory mucosa. In cases where the cribriform plate (with or without olfactory bulb resection) must be resected or an EEEA is performed, the integrity of the olfactory mucosa is affected almost entirely with the subsequent olfactory dysfunction for the patient. To almost all the studies regarding olfactory dysfunction after EEEA are made with olfactometry test [20]. used the olfactometry test of the University of Pennsylvania (UPSIT), before and after endoscopic endonasal hypophysectomy in 45 patients. They observed that patients had a lower ability to smell a month after surgery but after three months there were no significant differences compare to preoperative scores [21] did a prospective study with 36 patients and found no significant differences between pre- and post-operative SNOT 20 scores and visual analogue scale scores for nasal obstruction, actually they showed a significant improvement of symptoms [2]. studied

olfaction in 50 patients (36 with transsphenoidal and 14 with extended surgery), they observed that patients undergoing extended approach with nasoseptal flap reconstruction had higher rate of olfactory dysfunction at 3 months compared to patients undergoing transesphenoidal surgery. The same group reported in a prospective study [22] that the smell impairment and the increased posterior nasal discharge is present up to twelve months after surgery. They also reported that the mucociliary clearance time was prolonged after EEEA [23] assessed the long-term olfactory outcomes between cold knife upper septal incision technique compared to monopolar cautery in nasoseptal flap for skull base reconstruction. They found no significant difference in short-term or long-term, assessed by the UPSIT scores 1 year after transnasal skull-base approaches [24], found in a systematic review that endoscopic approach appears to be superior regarding preservation of olfactory outcome when compared with the microscopic approach, especially when the endoscopic approach was performed without harvesting of the nasoseptal flap. Another nasal complaint has been studied [25] in 41 patients undergoing skull base surgery found nasal fossa synechia in 19.5%, internal nasal valve failure in 14.6% and complaints of worsening of the sense of smell in 39%.

Mucociliary clearance

Disruption of the mucociliary clearance (MCC), an important mechanism of the innate immunity of the upper and lower airways, predisposes to airway diseases [26].

The MCC could be altered for two reasons:

1. Misfunction in the movements of the cilia.

2. Dehydration of the mucus, which leads to increased viscosity and therefore the ciliary clearance becomes ineffective.

In the first group we have primary (genetic) and secondary (infection or inflammation) ciliary dyskinesia, while in the second group we found cystic fibrosis, asthma among others. Many factors influence the MCC, some can be derived from the environment, like temperature and humidity, while others are specific to the patient, e.g, trauma, smoking, viral infections, chronic sinusitis, allergic rhinitis, deviated septum, sinus surgery, and cystic fibrosis and asma [27]. At present, there is no gold standard test for MCC analysis, although there are a variety of investigational methods and techniques available.

The most commonly used method is the saccharine test [28]. Although it depends on a subjective factor, it gives a well-defined time of MCC, since subjects clearly described the perception of sweet taste. There are some who criticize the use of saccharin particles as a measure of mucosal transport [29,30] but there are studies that show a good correlation between the time of MCC measured by saccharine test and ciliary beat frequency determined by photometry [31,32] as well as, a significant negative correlation with the transport speed measured by resin particles labeled with 99Tc [33]. The saccharine test is performed at ambient temperature, where the patient is requested not to perform forced inspiration. A 1 mm saccharin particle is applied in the 1 cm of the anterior portion of the inferior turbinate. Patients are asked to report any change in taste without advising them that they will receive a sweet flavor. The time required by the patient to perceive sweetness is the defining time of the test.

Few studies have assessed the impact of EEEA in the MCC [2] studied the MCC in patients undergoing EEEA, they found that patients had a prolonged MCC time until three months after surgery. They also showed that the more extended the approached was the MCC time was higher. On the other hand, several studies have evaluated the effect of nasal surgery in MCC [34] showed that the MCC improved in patients who had a septoplasty, with no significant difference between the blocked nasal cavity and the opposite side [35] evaluated MCC by saccharin test in three groups of patients (septoplasty, endoscopic polypectomy and turbinectomy) and observed that patients with preoperative mucociliary dysfunction didn't improve its function after surgery [36] studied the improvement of MCC in 43 patients undergoing endonasal endoscopic surgery for chronic rhinosinusitis with or without polyposis, they noted that the MCC measured by the saccharin test improved following endoscopic sinus surgery.

Quality of life

QOL is a multidimensional concept that measures the relationship of a series of physical and psychosocial factors. It describes the ability of an individual to make his life and get satisfaction from it. As so, QOL assessments provide a patient-reported estimate of well-being and show their degree of comfort and satisfaction [37]. The analysis of QOL is based on the patient's opinion about different aspects of his life that may have been modified after the treatment. These dimensions or domains include physical activity, psychological state, social interaction and somatic perception [38,39]. The advantages and limitations of endoscopic skull base surgery have been extensively studied [40,41]. Based on the latter results often the surgical success is defined as the balance between of maximal tumor resection and minimal functional impact. In 2013, [42] developed and validated the Anterior Skull Base Nasal Inventory-12 (ASK Nasal-12), a site-specific nasal morbidity instrument to assess patient-reported outcomes following endonasal skull base surgery [43] designed a multidimensional, disease-specific instrument, the Endoscopic Endonasal Sinus and Skull Base Surgery Questionnaire (EES-Q), they proved the importance of a multidimensional health related QOL assessment in a prospective cohort study with 100 patients showing how inconveniences in social functioning had the greatest negative impact on postoperative health status rating 64.

Few studies have evaluated the organ specific functional impairment and QOL; this is mainly due to the low prevalence of the disease, high variability of localization of the tumors, and the different surgical approaches and reconstruction methods [44] were the first that used a generic questionnaire of QOL to

study patients undergoing endoscopic pituitary surgery and showed no difference in QOL when compared with patients who underwent mastoidectomy [45] compared patients with pituitary pathology with the healthy population. They found that patients with acromegaly had impaired physical function while patients with Cushing syndrome showed deterioration in all the evaluated parameters except for one domain. Patients with prolactinoma had mental deterioration, but patients with a non-functioning adenoma presented impairments in the physical and mental spheres [45,46] studied the QOL in patients undergoing pituitary adenoma resection by endonasal endoscopic surgery; they showed that these patients had mild postoperative deterioration on the SF-36 [6] observed that patients with hormone-secreting tumors had greater postsurgical impairment of QOL [2] observed similar results to those previously mentioned; however, they did not find differences between functioning and non-functioning adenomas. Consistent with the latter study, [47] used the Rhinosinusitis Disability Index and observed no differences between preoperative and postoperative scores in patients with or without functioning pituitary pathology [48] found lower QOL in six of eight domains of SF 36 preoperatively but improved to baseline values on the long run after surgery in seven of eight domains [47] used ASBS-Q and SNOT 22 for evaluating the impact of ESBS for craniopharyngiomas resection and shows an overall maintenance of postoperative compared with preoperative QOL, better in patients with gross-total resection and radiation therapy, and worse in patients with visual or endocrine deficits. Nevertheless, patients with craniopharyngiomas still had worse QOL than those undergoing similar surgery for pituitary macroadenomas.

Patients with extended endonasal approaches are a challenge, since they are usually oncological patients with a significant physical, cognitive, emotional or social deterioration [49]. It is possible that these findings correlate more closely with adjuvant treatments and oncological disease than the surgery itself. A meta-analysis confirmed that patients undergoing oncologic disease have a lower QOL compared to patients with benign tumors independent of the type of surgical technique [42,50]. Assessed the QOL in patients with sinonasal carcinomas after surgery and observed that they had a significant deterioration in the domains of anxiety, physical activity and emotional state [51] studied a cohort of 153 patients who received adjunctive therapy and found that they had a worsening of their QOL which was more related to the adjuvant therapy. Regarding the last point, [2] compared the impact of nasal symptoms and QOL using the sinonasal symptoms test RSOM-31 and QOL test SF-36. They found that patients undergoing extended endoscopic skull base surgery showed higher sinonasal symptoms that patients undergoing pituitary surgery, and both had mild impairment QOL assessed by the SF-36 questionnaire [52] showed a temporary worsening during the first year of postoperative ESBS, after which QOL recovers and returns almost to normal [53] in a single-center prospective cohort study of patients with endoscopic transsphenoidal skull base surgery conclude that sinonasal quality of life worsened after 1 month postoperatively but returned to preoperative levels after the second month and remained stable after 5 months of follow up [54] also reported a recovery of QOL after 6 months of ESBS [55] in a prospective cohort study with 145 patients with both malignant and benign sinonasal tumors, found a statistically significant improvement in SNOT-22 score from baseline to 2 years [56] observed that extended procedures and NSF usage was significantly associated with poor outcomes.

Radiological findings

Postoperative imaging evaluation is one of the keystones studies for monitoring patients undergoing skull base pathology. In order to detect residual lesions, recurrence and/or complications, the use of postoperative MRI is one of the fundamental pillars for following patients undergoing skull base pathology.

Correct interpretation of radiological findings implies to know how the healing process occurs in the sinonasal cavity, especially the radiological differentiation of the nasoseptal flap healing process and the differentiation between inflamed mucosa and mucosa infiltrated by tumor. In general, MRI distinguishes normal and inflamed soft tissues, and differentiates between these tissues and tumor. The latter is primarily based on the fact that inflamed mucosa is associated with increased submucosal oedema and increased mucus secretions [57] used MRI to evaluate the viability of the nasoseptal flap in the postoperative setting, they found that flap is healthy when is hypo intense on both T1 and T2. Regarding inflammatory tissue differentiation from tumor recurrence [58] observed that the inflamed sinus mucosa is characterized by hypo intensity on T1 and hyper intensity on T2. In contrast, the tumor tissue is characterized by hypo intensity on both T1 and T2, but to assess tumor tissue/recurrence, is better to assess images on T2 sequence [59,60], found Increased sinus opacification between the mean overall pre and [61-63]postoperative SNOT-22 scores after 67.4 months. Regarding other imaging tests such as PET-CT, one must keep in mind that inflamed cells also show increased glycolytic activity [64-67], consequently inflamed areas cannot be distinguishing with tumor tissue.

Conclusion

The endoscopic endonasal skull base surgery has evolved dramatically, emerging as the treatments of choice in addressing skull base pathology. While the main objective is tumor resection, there is a growing interest on studying the functional outcome in relation to the in QOL and nasal symptoms. Unfortunately, there are still few studies to perform a standardization of methods that measure functional outcomes after endoscopic skull base surgery. In a future, longitudinal studies are needed to standardize the measurement instruments of quality of life, nasal symptoms and general symptoms suffered by these patients after surgery.

Acknowledgement

None.

Conflict of Interest

No conflict of interest.

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