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Multi-Institutional Comparison of Quality of Life Between Open Versus Endoscopic Skull Base Approaches

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ABSTRACT

Objectives: The primary objective of this prospective review was to compare quality of life between patients undergoing endoscopic and open skull base approaches.

Study Type and Design: Prospective Review.

Methods: Five centers recruited consecutive patients treated surgically for skull base neoplasms between 2012 to 2018. The Skull Base Inventory (SBI), Anterior Skull Base (ASB), and Sinonasal Outcome Test (SNOT-22) were administered up to 12 months post-operatively. Mean change from baseline scores were compared with univariable and multivariable analyses.

Results: A total of 180 patients were included: 108 (60%) F and 72 (40%) M, of whom 126 (70%) underwent endoscopic and 54 (30%) underwent open approaches. Patients undergoing endoscopic approaches were more likely to have sellar or clival pathology (68 vs. 15%, $p < 0.001$). Those undergoing endoscopic approaches had better disease-specific quality of life at one year using the SBI and ASB (mean change from baseline = 7.2 vs. 0.69, $p = 0.004$; 5.8 vs. -1.1, $p = 0.002$), respectively. On multivariable analysis, endoscopic approach was associated with greater improvement in overall quality of life (mean difference in change scores from baseline = 6.5, $p = 0.009$), as well as endocrine (mean difference = 8.3, $p = 0.011$), neurologic (mean difference = 8.3, $p = 0.012$), visual (mean difference = 7.9; $p = 0.032$), financial (mean difference = 9.7, $p = 0.03$), and spiritual domain scores (mean difference = 4.0, $p = 0.035$). Subgroup analyses of pituitary and non-pituitary histopathologies

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demonstrated trends towards greater quality of life at 1-year compared to baseline in the endoscopic approach compared to the open group.

Conclusions: Endoscopic approaches are associated with better quality of life compared to open approaches. However, baseline differences in histopathology between the group limit the direct comparison of the open and endoscopic approaches. Future studies with larger and more homogenous samples are required.

Level of Evidence: Level IV evidence.

1 | Introduction

Tumors located at the base of the skull are closely associated with vital sensory and neurovascular structures, often leading to notable effects on patients' well-being. These effects can include both physical and emotional changes, such as diminished senses, identity concerns, and social withdrawal, which can profoundly affect their quality of life [1]. Of the many aspects of physical function that may be affected, domains of physical quality of life may be broadly grouped in to visual, nasal, neurologic, endocrine function, and other miscellaneous areas of quality of life [1].

In the past few decades, the advent of expanded endonasal access has improved outcomes for skull base tumor resections. These approaches are associated with significantly shorter hospital length of stay, fewer complications, and comparable survival [2–7]. Proponents of endoscopic approaches suggest that they may confer a quality-of-life benefit, although this has not yet been clearly demonstrated. In one single-center study, the endoscopic approach was shown to be associated with better scores relating to physical function and emotional domain in comparison to subcranial surgery [8]. Given the lack of large numbers, the need for prospective multi-institutional studies to answer these questions has been identified [9].

Measurement of quality of life after skull base surgery can be complex given the variety of histopathologies, unique anatomic locations, and paucity of tumors. The Anterior Skull Base Quality of Life Questionnaire (ASB) was developed to help measure quality of life in patients undergoing open skull base surgery [10]. Although it has been subsequently administered to patients undergoing endoscopic approaches, with only seven disease-specific items, it may not comprehensively identify quality of life issues in this population. The Skull Base Inventory (SBI) was developed in an effort to measure quality of life for patients undergoing either open or expanded endonasal approaches using patient focus groups, expert opinion, and systematic review of the literature [11–13]. Cross-sectional and prospective psychometric properties have been demonstrated. This instrument has been validated and is comprised of 41 items of which 22 are disease-specific. It is intended to comprehensively measure quality of life for all skull base surgical patients. A prospective international, multi-institutional review study was conducted with administration of validated quality of life instruments in order to assess quality of life changes experienced after surgery for tumors of the skull base in both open and endoscopic approaches.

2 | Methods

2.1 | Participating Centers and Regulatory Approvals

Five international centers participated in the study including 2 in North America, 2 in Israel, and 1 in Australia. All participating sites underwent local institutional research board (IRB) or research ethics board (REB) approvals prior to site approval. Patients were approached by study team members and completed informed consent prior to enrollment.

2.2 | Patients

Patients were recruited between 2012 and 2018. Eligible patients included those (1) age 18 or over, (2) with benign or malignant skull base neoplasms, (3) located in the anterior, antero-lateral or central skull base location, and (4) requiring either an open or endoscopic skull base approach, but not both. Open approaches were defined as those required external facial or scalp incisions with bony disassembly of the craniofacial skeleton to facilitate resection. Endoscopic approaches were defined as approaches done entirely through an expanded endonasal approach with internal transnasal soft tissue and bony resection as needed for tumor resection. Patients were excluded if they (1) were unable or unwilling to consent to surgery or trial participation, (2) were unable to complete the proposed schedule of questionnaires, (3) treated non-surgically as the primary modality, (4) had incurable disease at initial diagnosis, (5) required a combined open and endoscopic approach or had a previous surgical approach that was different than the current approach, (6) had a concurrent malignancy at another site, or (7) required a posterolateral skull base approach through the temporal bone or suboccipital approach defined as Zone 4 tumors in a previous anatomic classification system [14].

2.3 | Demographic, Clinical, and Treatment Details

Demographic, clinical, and treatment related details were collected using case report forms. Demographic questions related to age, gender, education, income, occupation, ethnicity, and household supports. Relevant clinical details including histopathologic diagnosis, tumor location, any medical comorbidities, surgical approach, extent of surgery, type of reconstruction, whether orbital exenteration was performed, margin status,

complications, adjuvant therapies, as well as follow-up status were collected.

2.4 | Quality of Life Questionnaires

Three questionnaires including the Skull Base Inventory (SBI), the Anterior Skull Base (ASB), and the Sinonasal Outcome Test (SNOT-22) were completed by all participants prior to surgery (baseline), and at 2 weeks, 3, 6, and 12 months post-operatively.

2.4.1 | Skull Base Inventory

The SBI is a validated disease-specific quality of life instrument with established content validity for patients undergoing either endoscopic or open skull base approaches [11–13]. The instrument is composed of 41 items divided into 6 non-physical domains (cognitive, emotional, family, financial, social, and spiritual) and 5 physical domains (nasal, neurologic, endocrine, visual, and other). Twenty-two of 41 items are disease-specific items. Scoring can be reported as domain-specific scoring or composite/overall scoring. Domain scores are calculated by summing all scores across the relevant items and dividing by the maximum possible score multiplied by 100. The total instrument score is the average of all domain scores with a range from 0 (minimum) to 100 (maximum). Higher scores represent better quality of life.

2.4.2 | Anterior Skull Base Quality of Life Questionnaire (ASB)

The ASB is also a validated disease-specific quality of life instrument. It was originally designed to measure quality of life in patients with open skull base approaches prior to the advent of endoscopic techniques [10]. There are 35 items, of which seven items are disease-specific items. The instrument is scored by taking the mean across all items and multiplying by 20. Scores range from 0 (minimum) to 100 (maximum). Higher scores represent better quality of life.

2.4.3 | Sinonasal Outcome Test (SNOT-22)

The SNOT-22 is a validated instrument used to measure nasal related quality of life particularly as it relates to inflammatory sinonasal disease and endoscopic sinus surgery [15]. The instrument consists of 22 items, each of which is scored from 0 to 5. The total instrument score ranges between 0 and 110. Higher scores reflect higher burden of disease.

2.5 | Analysis

Descriptive summary statistics were used to summarize the data with medians and ranges for non-parametric data, means and standard deviations for parametric data, and counts and relative frequencies for categorical data. Demographic and treatment variables were compared between groups using

t-test for continuous variables and Fisher tests for categorical variables. Differences in quality of life between groups were compared as changes in scores from baseline for each respective instrument and were compared with *t*-tests. For the primary analysis, total instrument scores for the SBI were calculated and differences from baseline to the 1-year time-point were compared between patients undergoing “open” and “endoscopic” approaches using a linear regression model adjusting for confounding variables. Univariable and multivariable models were used to compare changes in quality of life scores from baseline to 1-year post-treatment using linear regression models. In multivariable models, variables from univariable regression were selected with *p*-values < 0.1. Comparison of domain scores between surgical approaches were similarly performed by determining change from baseline scores. To determine changes in quality of life for all patients over time, paired *t*-tests were used. *p*-values of 0.05 were used to determine statistical differences. Minimal clinically important clinical (MCID) for the SBI were applied to determine clinically important differences in groups. The MCID for the SBI was previously determined to be 6 [13]. Subgroup analyses were performed to assess differences in change from baseline scores between endoscopic approaches and open approaches for patients with sella/pituitary lesions and nonpituitary lesions.

2.6 | Sample Size Calculation

An a priori sample size was determined to be 63 patients per group based on an assumed pooled standard deviation of 20 points for the SBI, an assumed MCID of 10 points, and thus a moderate effect size of 0.5, with an alpha of 0.05. At the time of the sample size calculation, the MCID of the instrument was not determined. After 6 years of accrual (*n* = 126 endoscopic, *n* = 54 open), a post hoc power calculation based on observed means and standard deviations indicated 83% power to detect a significant difference in mean SBI scores (observed mean difference = 6.51), standard deviations 12.8 (open) and 15.1 (endoscopic) and as such accrual was stopped.

3 | Results

3.1 | Patients

A total of 187 patients were recruited for the study from five participating centers. Seven patients were excluded due to “combined” surgical approaches. 180 patients were eligible for study inclusion, of whom 54 underwent open surgical approaches and 126 underwent endoscopic approaches. The majority of patients undergoing endoscopic approaches had pituitary adenomas (51%), while the majority of patients undergoing open approaches had meningiomas (70%) (*p* < 0.001). The majority of patients who underwent endoscopic approaches underwent reconstruction with vascularized nasoseptal flaps (56%) while many patients undergoing open approaches had either simple closures without flaps (65%), regional flaps (26%), or free flap (7%) (*p* < 0.001). Patients in the open group were more likely to have comorbidities at presentation (35% vs. 20%, *p* = 0.05) and were more likely to develop a post-operative complication (43% vs. 25%, *p* = 0.025) (Table 1).

TABLE 1 | Baseline demographic, pathologic, and treatment details.

Covariate	Full sample (n = 180)	Endoscopic (n = 126)	Open (n = 54)	p
Age	—	—	—	0.051
Mean (SD)	52.2 (14.5)	53.6 (14.4)	49 (14.4)	—
Median (Min, Max)	53 (18, 81)	55 (18, 81)	50 (26, 76)	—
Missing	1	0	1	—
Gender	—	—	—	0.715
F	108 (60)	74 (59)	34 (63)	—
M	72 (40)	52 (41)	20 (37)	—
Education	—	—	—	0.335
High school or less	12 (9)	10 (12)	2 (5)	—
College	115 (91)	76 (88)	39 (95)	—
Missing	53	40	13	—
Ethnicity	—	—	—	0.607
Other	50 (28)	33 (26)	17 (31)	—
Caucasian	129 (72)	92 (74)	37 (69)	—
Missing	1	1	0	—
Lives alone	—	—	—	0.212
Yes	19 (12)	16 (15)	3 (6)	—
No	140 (88)	94 (85)	46 (94)	—
Missing	21	16	5	—
Income	—	—	—	0.896
<\$40,000	52 (36)	35 (37)	17 (34)	—
\$40–80,000	33 (23)	22 (23)	11 (22)	—
\$\$> \$80,000	60 (41)	38 (40)	22 (44)	—
Missing	35	31	4	—
Subsite	—	—	—	<0.001
Missing	6 (3)	4 (3)	2 (4)	—
Anterior skull base	48 (27)	29 (23)	19 (35)	—
Lateral approaches	32 (18)	7 (6)	25 (46)	—
Clivus/petroclivus	11 (6)	9 (7)	2 (4)	—
Sella	83 (46)	77 (61)	6 (11)	—
Histopathology	—	—	—	<0.001
Adenoma	62 (36)	60 (51)	2 (4)	—
Other	59 (35)	45 (38)	14 (26)	—
Meningioma	49 (29)	12 (10)	37 (70)	—
Missing	10	9	1	—
Surgical approach	—	—	—	—
Endoscopic	126 (70)	126 (100)	0 (0)	—
Open	54 (30)	0 (0)	54 (100)	—

(Continues)

TABLE 1 | (Continued)

Covariate	Full sample (n = 180)	Endoscopic (n = 126)	Open (n = 54)	p
Reconstruction	—	—	—	<0.001
Simple closure	81 (45)	46 (37)	35 (65)	—
Regional flap	15 (8)	1 (1)	14 (26)	—
Septal flap	72 (40)	71 (56)	1 (2)	—
Free flap	4 (2)	0 (0)	4 (7)	—
Missing	8 (4)	8 (6)	0 (0)	—
Benign or malignant	—	—	—	0.757
Benign	141 (81)	96 (80)	45 (83)	—
Malignant	33 (19)	24 (20)	9 (17)	—
Missing	6	6	0	—
Comorbidities	—	—	—	0.050
No comorbidity	130 (76)	97 (80)	33 (65)	—
Comorbidity	42 (24)	24 (20)	18 (35)	—
Missing	8	5	3	—
Preop or postop RT CRT	—	—	—	0.942
No	129 (72)	91 (72)	38 (70)	—
Yes	51 (28)	35 (28)	16 (30)	—
Postop complications	—	—	—	0.025
No	126 (70)	95 (75)	31 (57)	—
Yes	54 (30)	31 (25)	23 (43)	—
Site	—	—	—	0.348
Adelaide	4 (2)	4 (3)	0 (0)	—
Israel 1	15 (8)	13 (10)	2 (4)	—
Israel 2	20 (11)	15 (12)	5 (9)	—
Pittsburgh	59 (33)	41 (33)	18 (33)	—
Toronto	82 (46)	53 (42)	29 (54)	—

3.2 | Comparing Quality of Life Between Approaches

As measured by the SBI at 1 year, patients undergoing an endoscopic approach had significantly higher mean change from baseline scores compared to patients undergoing an open approach (mean change from baseline = 7.2 vs. 0.7, $p = 0.004$) (Figure 1A). At 1 year, the differences between the open approaches and endoscopic approaches exceeded the MCID for the SBI (i.e., 6 points), suggesting that these differences are both clinically and statistically different [13].

As measured by the ASB, patients undergoing endoscopic approaches had significantly better quality of life compared to those undergoing open approaches at 1 year (mean change from baseline = 5.8 vs. -1.1, $p = 0.002$) (Figure 1B).

There were no significant differences in change from baseline scores to 1 year post-treatment in nasal function as measured by the SNOT-22 between endoscopic and open approaches (mean change from baseline -2.13 vs. 2.35, $p = 0.173$) (Figure 1C).

3.3 | Predictors of Quality of Life Following Skull Base Surgery

In univariable analysis using the SBI, several variables were significantly associated with changes in quality of life from baseline to 1-year post-surgery. These included age (mean difference in change from baseline = -0.15 over 1 year, $p = 0.047$), the presence of co-morbidity (mean difference = -5.6, $p = 0.031$), histopathology (mean difference = -7.0

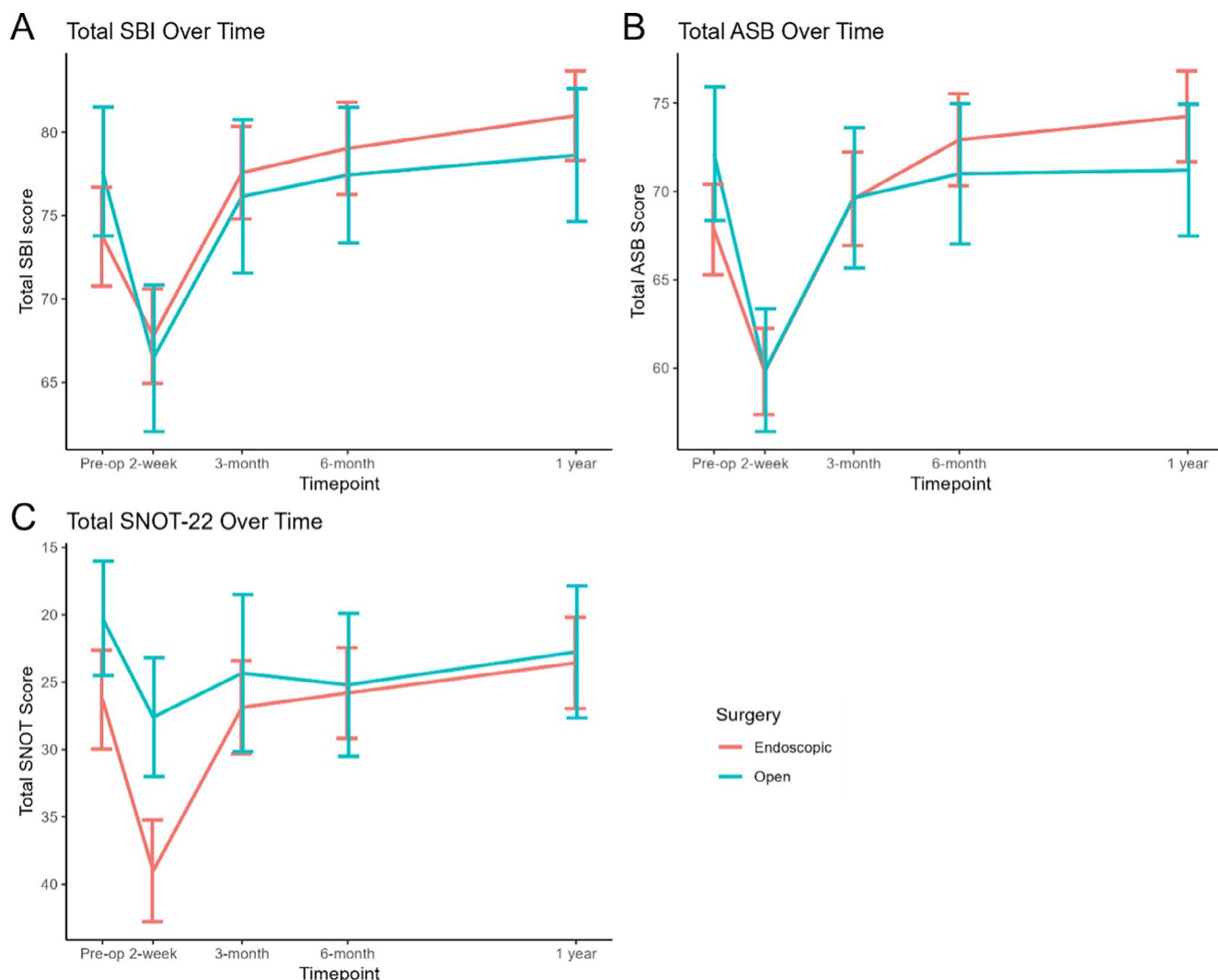


FIGURE 1 | Comparisons of quality of life between open and endoscopic approaches using (A) the SBI, (B) the ASB, and (C) the SNOT-22.

for meningioma compared to pituitary adenoma, $p=0.01$), and surgical approach (mean difference = -6.5 for open compared to endoscopic approaches, $p=0.006$) (Table 2). In multivariable analysis, open compared to endoscopic approaches remained significantly associated with change in quality of life, independent of age, comorbidity, and post-operative complications (mean difference = -6.5 for open compared to endoscopic; $p=0.009$) (Table 3).

3.4 | Individual Changes in Domain Scores by Surgical Approach

For the following individual SBI domain scores, patients in the open group compared to the endoscopic group experienced a significantly smaller increase, but less than MCID, in quality of life comparing 1-year post-treatment to baseline in the spiritual domain (mean difference = -4.0 , $p=0.035$). For the following individual SBI domain scores, patients in the open group compared to the endoscopic group experienced significantly worse improvement in quality of life: endocrine (mean difference in change

scores = -8.3 , $p=0.011$), neurologic (mean difference = -8.3 , $p=0.012$), financial domain (mean difference = -9.7 , $p=0.03$), and visual (mean difference = -7.9 ; $p=0.032$) (Figure 2).

3.5 | Temporal Changes in Quality of Life Following Skull Base Surgery

Both the SBI and ASB instruments demonstrated temporal changes in quality of life following surgery with transient worsening of quality of life 2 weeks following surgery (mean change from baseline for SBI = -8.1 , $p<0.001$; for ASB = -10.1 , $p<0.001$) with gradual recovery at up to 1 year post-treatment using the SBI (mean change from baseline at 12 months = 5.3 , $p<0.001$) and ASB (mean change from baseline at 6 months = 3.1 , $p=0.004$; and at 12 months = 3.7 , $p=0.001$) respectively. Using the SNOT-22, there was a transient reduction in nasal-related quality of life at 2 weeks compared to baseline (mean change from baseline = -11.9 , $p<0.001$). The reduction in nasal related quality of life paralleled the reduction in overall QOL (Figure 3).

TABLE 2 | Univariable linear regression analysis of changes in quality of life at 2 weeks and 1 year post treatment using the SBI.

Covariate	N	Estimated difference in SBI change scores from pre-op to 1 year		
		Estimate (95% CI)	p	Global p
Age	—	−0.15 (−0.30, −0.00)	—	0.047
Gender	—	—	—	0.934
Female	108	Reference	—	—
Male	72	−0.19 (−4.57, 4.20)	—	—
Ethnicity	—	—	—	0.758
Caucasian	129	Reference	—	—
Other/unknown	51	0.75 (−4.03, 5.53)	—	—
Education	—	—	—	0.901
College	115	Reference	—	—
High school or less	12	−0.53 (−8.88, 7.82)	—	—
Comorbidities	—	—	—	0.093
Comorbidity absent	130	Reference	—	—
Comorbidity present	42	−5.61 (−10.66, −0.57)	0.031	—
Unknown	8	−1.13 (−11.45, 9.20)	0.831	—
Histopathology	—	—	—	0.041
Adenoma	62	Reference	—	—
Meningioma	49	−7.04 (−12.50, −1.58)	0.012	—
Other/unknown	69	−3.06 (−8.05, 1.94)	0.232	—
Lives alone	—	—	—	0.957
No	140	Reference	—	—
Yes	19	−0.20 (−7.54, 7.13)	—	—
Income	—	—	—	0.721
< \$40,000	52	Reference	—	—
\$40–80,000	33	−0.47 (−6.82, 5.87)	0.884	—
> \$80,000	60	−2.15 (−7.61, 3.31)	0.441	—
Benign or malignant	—	—	—	0.683

(Continues)

TABLE 2 | (Continued)

Covariate	N	Estimated difference in SBI change scores from pre-op to 1 year		
		Estimate (95% CI)	p	Global p
Benign	141	Reference	—	—
Malignant	33	−1.97 (−7.52, 3.59)	0.488	—
Unknown	6	−3.60 (−15.55, 8.34)	0.555	—
Postop complications	—	—	—	0.095
No	126	Reference	—	—
Yes	54	−3.98 (−8.64, 0.69)	—	—
Preop or postop RT/CRT	—	—	—	0.915
No	129	Reference	—	—
Yes	51	0.26 (−4.50, 5.01)	—	—
Subsite	—	—	—	0.499
Sella	83	Reference	—	—
Anterior skull base	48	1.33 (−3.91, 6.58)	0.619	—
Lateral approaches	32	−4.02 (−10.06, 2.01)	0.193	—
Clivus/ petroclivus	11	−4.09 (−13.27, 5.10)	0.385	—
Unknown	6	−2.15 (−14.25, 9.95)	0.728	—
Reconstruction	—	—	—	0.821
Simple closure	81	Reference	—	—
Regional flap	15	1.69 (−6.90, 10.28)	0.701	—
Septal flap	72	1.62 (−3.07, 6.31)	0.498	—
Free flap	4	−0.52 (−15.24, 14.20)	0.945	—
Missing	8	6.08 (−4.57, 16.73)	0.265	—
Open vs. endoscopic	—	—	—	0.006
Endoscopic	126	Reference	—	—
Open	54	−6.51 (−11.14, −1.88)	—	—

3.6 | Subgroup Analysis

In the pituitary subgroup, 62 patients were treated with an endoscopic approach and 2 patients with an open approach. There was no difference in change in SBI baseline to 1 year scores between the open and endoscopic approaches on univariate analysis (mean difference in change from baseline scores = -9.3; 95% CI (-30.0, 11.4), $p=0.38$). In the non-pituitary subgroup, there were 62 patients treated endoscopically and 50 patients treated with an open approach. Open approaches were associated with significantly worse SBI scores 1-year post-treatment compared to baseline in univariable analysis (mean difference in change from baseline scores = -6.0; 95% CI -11.3, -0.7, $p=0.03$), and approached statistical significance on multivariable analysis accounting for age, comorbidities, post-op complications (mean difference in change from baseline scores = -4.9, 95% CI -10.4, 0.58, $p=0.08$).

4 | Discussion

In the present multi-institutional prospective study, we demonstrated that the endoscopic approach for skull base tumors is associated with significantly better quality of life outcomes compared to open approaches. Although surgical treatment of these tumors is associated with a transient decline in quality of life, there is a subsequent improvement in comparison to pre-operative scores that is durable as long as one-year post-treatment. In the present study, surgical approach is a major determinant of outcome. Although this study does not provide randomized comparative data, these data indicate that when both treatment options exist, an endoscopic approach provides improvement in quality of life scores.

Perhaps the greatest challenge in evaluating quality of life between different surgical approaches is the fact that not all tumors are amenable to both surgical approaches. The choice of surgical approach is not only limited by the availability of surgical expertise but also by the extent and location of the tumor which may preclude either approach. Nicolai et al. delineated contra-indications to the endoscopic approach for sinonasal malignancy including extensive dural or brain parenchymal involvement, erosion of the nasal bones, erosion of the nasal floor or hard palate, orbital invasion, extensive nasolacrimal involvement, and infiltration of anterior or lateral maxillary sinus walls [16]. These factors generally necessitate an open approach. As a general rule, more extensive tumor involvement is more likely to require an open approach for access and complete extirpation, thus complicating the interpretation of comparative quality of life analyses. As endoscopic techniques continue to advance, accesses to surgical expertise improves globally, and the role of neoadjuvant/adjuvant therapy evolves, there may be more areas of clinical equipoise when selecting the optimal surgical approach for certain skull base lesions.

It is important to note that the overall quality of life of all patients who undergo skull base surgery returns to normal, after a short-term decline immediately after surgery, and may even improve compared to baseline pre-treatment scores at 1 year following surgery. We observed these improvements using two separate disease-specific instruments, the SBI as well as the ASB. Gil et al. previously demonstrated that from 3 months to 2 years following treatment, patients may experience an improvement in quality of

TABLE 3 | Multivariable predictors of quality of life changes from baseline to 1 year post treatment using the SBI.

Covariate ^a	N	Estimate (95% CI)	p	Global p
Open vs. endoscopic	—	—	—	0.009
Endoscopic	124	Reference	—	—
Open	51	-6.48 (-11.32, -1.65)	—	—
Age	—	-0.16 (-0.31, 0.00)	—	0.051
Comorbidities	—	—	—	0.576
Comorbidity not present	126	Reference	—	—
Comorbidity present	41	-2.69 (-8.00, 2.61)	0.321	—
Unknown	8	0.89 (-9.75, 11.53)	0.870	—
Postop complications	—	—	—	0.518
No	123	Reference	—	—
Yes	52	-1.65 (-6.65, 3.35)	—	—

^aHistopathology was excluded in multivariable analysis because of strong collinearity with surgical approach.

life [17]. Previous assertions of significant impairment of quality of life after skull base surgeries is not supported in the current study.

The proposed benefits of an expanded endonasal approach are the potential to decrease complications and reduce traumatic manipulation of the brain. These data support multiple other studies showing a reduction in complications with an expanded endonasal approach [5, 18, 19]. Previous literature has demonstrated that endoscopic approaches are associated with improvements in post-treatment MRI compared to open approaches [20]. However, there has been little data previously to confirm improved functional outcomes or quality of life. When examining specific quality of life domains that may be preserved by minimizing brain retraction, the expanded endonasal approach was associated with significant improvements in neurologic domain scores and a trend towards improvements in cognitive domain scores. Further larger studies with homogeneous disease populations and formal neurologic or neuropsychiatric testing are required to validate these findings.

With respect to nasal related quality of life, we did not observe any long-term decline following skull base surgery. These findings confirm previous reports demonstrating gradual improvement after a transient decline [17]. Previous studies have demonstrated that nasal related quality of life following skull base surgery may stabilize over time and usually this is achieved within 6 months of surgery. In a meta-analysis, Bhenswala et al. demonstrated that patients with impaired

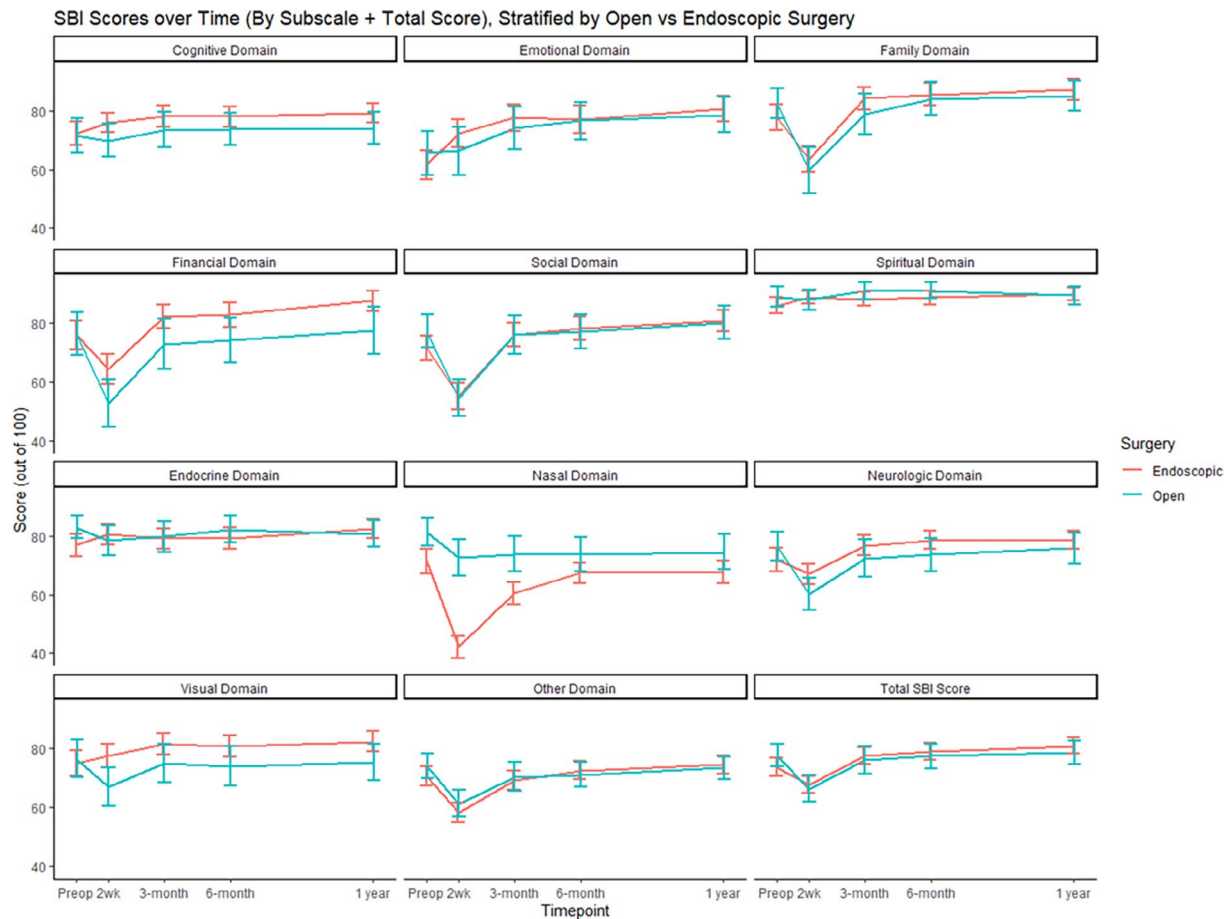


FIGURE 2 | Differences in individual domain scores between open and endoscopic approaches.

sinonasal quality of life improve following surgery and that those with normal pre-treatment scores remain unimpaired post-treatment [21]. We confirmed the stability of nasal quality of life using both the SNOT-22 as well as the nasal domain of the SBI.

We noted that open approaches may be associated with poorer visual outcomes. Other groups have also demonstrated improvements in the visual domains with endoscopic approaches compared to open surgery [22]. In the absence of a randomized trial, it is difficult to know if improvements in visual function with an endoscopic approach are due to improved visualization of neural structures such as the optic nerve or other cranial nerves, or due to case selection with more favorable tumor involvement. In a previous meta-analysis, Lu et al. demonstrated lower likelihood of worsening vision ($OR=0.31$, $p=0.04$) in patients with olfactory groove or tuberculum sellae meningiomas treated with an endoscopic approach compared to transcranial approaches [23]. Similarly Shetty et al., demonstrated that for anterior skull base meningiomas, expanded endonasal approaches are associated with improved ability to restore vision in patients with pre-operative disturbance (81% vs. 12.8%, $p<0.0001$) [24]. The authors concluded, that if visual restoration was the primary goal, one may consider an endoscopic approach, but otherwise transcranial approaches are still a good option.

We observed that open approaches were also associated with poorer non-physical domains including financial and spiritual

domain scores, and with trends towards lower emotional and family scores. Previous studies have corroborated the fact that open approaches may affect emotional well-being [8]. The findings of the current study demonstrate the importance of the non-physical aspects of quality of life as defined by the World Health Organization [25]. Qualitative research studies with patient focus groups have shown that surgery for skull base tumors may affect spirituality, alter family dynamics, and increase social isolation [1]. These challenges are particularly concerning for patients undergoing open approaches and should be discussed with patients while counseling them about the impacts of surgery.

There are several limitations to the current study that are worthy of note. The recruitment period of the study was from 2012 to 2018 which may limit generalizability as this period does not capture more recent advances in the management of skull base lesions in the neoadjuvant setting, endoscopic approaches with broader patient candidacy, as well as adjuvant setting including radiotherapy techniques and systemic therapy. Unlike the SBI, ASB and SNOT-22 are not validated for both endoscopic and open approaches and findings should be interpreted with attention to this. Although this is a prospective study, in the absence of randomization, there is significant selection bias for treatment approach based on histopathology, surgical expertise, and institutional preference. 87% of the study patients were recruited from North American centers and limits generalizability to other geographic regions. The

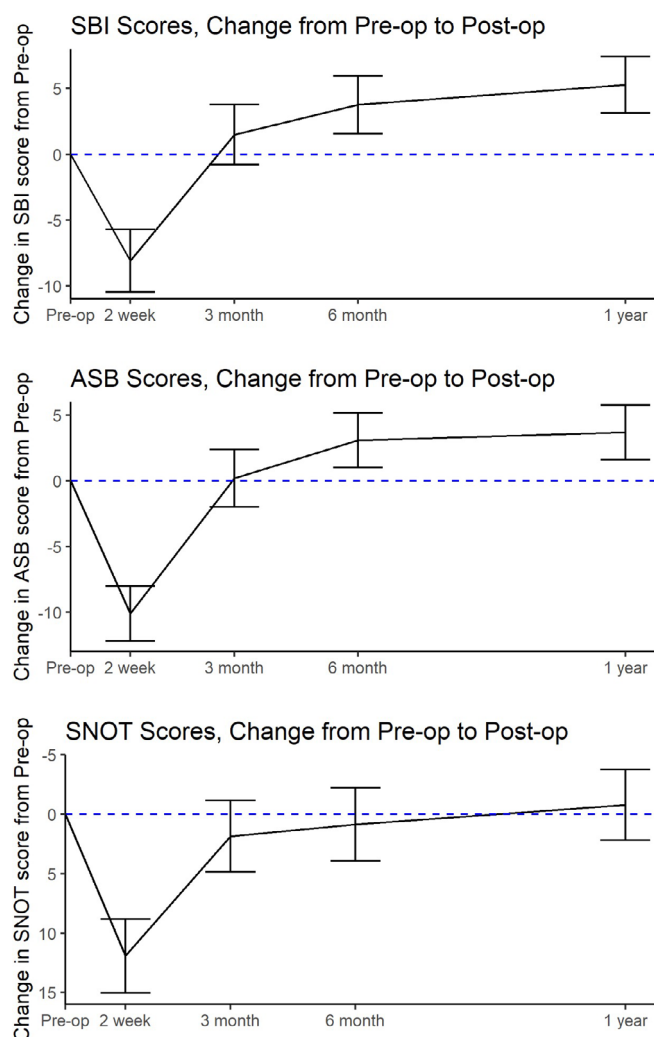


FIGURE 3 | Overall changes in quality of life over time using the SBI, ASB, and SNOT-22.

current study summarized quality of life for all patients with skull base tumors, and as such, there are many heterogeneous comparisons that are made. The open and endoscopic groups had differences in the distribution of histopathologies limiting the findings in this comparative analysis. Pituitary adenomas represented 51% of the endoscopic group and only 2% of the open group, potentially biasing the outcomes in favor of the endoscopic group as the standard transsphenoidal approach is less extensive than other expanded endonasal approaches. The subgroup multivariable analysis showed that when pituitary patients were excluded, a trend towards improved quality of life in the endoscopic group was observed. The authors acknowledge direct comparisons of the non-pituitary group is still limited by heterogeneity in histopathology, tumor location and extent, specific endoscopic/open approach, and candidacy for either surgical approach. However, given the rarity of skull base tumors, studies with large sample sizes with select tumors and locations are very difficult to perform and analyses often require pooling different tumors in various anatomic locations. Further multi-institutional studies capable of pooling various histopathologies in focused locations are needed to make more compelling conclusions.

5 | Conclusions

In the current multi-institutional prospective review, we demonstrate a significant quality of life benefit for patients undergoing endoscopic approaches compared to traditional open approaches after adjusting for confounding variables. These benefits are likely due to improvements in both physical and non-physical aspects of quality of life. However, the conclusions are limited by baseline differences in histopathology between the endoscopic and open groups. Future multi-institutional studies with sufficient sample sizes to focus on specific histopathologies and skull base subsites are required. Clinicians can counsel patients on the relative merits of different approaches when considering surgery for skull base tumors.

Conflicts of Interest

John de Almeida: Grant funding and honoraria from Cardinal Health, honoraria from EMD Serono. Carl Snyderman: Consultant SPIWay LLC. Paul Gardner: Consultant, Peter Latic US Inc; Consultant SPIWay LLC; Consultant, Sutter Medizintechnik GMBH. Katrina Hueniken, Michael Xie, Ian Witterick, Eric Monteiro, Gelareh Zadeh, Ari Kalyvas, Patrick Gullane, Eric Wang, Dan Fliss, Barak Ringel, Ziv Gil, Shorook Na'ra, Eng Ooi, David Goldstein: Declare no conflicts of interest.

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