ORIGINAL ARTICLE

Quality of Life Following Surgery for Anterior Skull Base Tumors

Ziv Gil, MD, PhD; Avraham Abergel, MD; Sergei Spektor, MD; Jacob T. Cohen, MD; Avi Khafif, MD; Esther Shabtai, MSc; Dan M. Fliss, MD

Objectives: To evaluate patients' quality of life (QOL) after surgical extirpation of anterior skull base tumors, to elucidate different QOL domains, and to define possible predictors of functional outcome postoperatively.

Design: Retrospective survey.

Setting: University-affiliated medical center.

Participants: Sixty-nine patients (76 consecutive cases) who underwent subcranial surgery between 1994 and 2002 for extirpation of anterior skull base tumors.

Main Outcome Measure: A multidimensional, disease-specific questionnaire with 39 items was used. Six relevant domains of QOL were assessed: role of performance, physical functioning, vitality, pain, specific symptoms, and impact on emotions.

Results: The response rate for completing the questionnaire was 98% (40/41) after excluding patients who died (n=13), were lost to follow-up (n=10), and were operated on within 3 months of commencement of the study (n=5). Thirty patients (74%) reported a significant improvement or no change in overall QOL within 6 months after surgery. The worst impact of surgery on the patients' QOL was on their financial status and emotional state. The most influential factor on QOL was malignancy leading to a significant decrease in the overall score. Radiotherapy, old age, comorbidity, and wide resection also significantly worsened QOL scores of specific domains.

Conclusion: After subcranial extirpation of anterior skull base tumors, the overall outcome of the patients is good. Old age, malignancy, comorbidity, wide resection, and radiotherapy are negative prognostic factors for these patients' QOL.

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From the Department of Otolaryngology–Head and Neck Surgery and the Skull Base Surgery Unit (Drs Gil, Cohen, Khafif, and Fliss), the Department of Neurosurgery (Dr Spektor), and The Statistical Service, (Ms Shabtai), Tel-Aviv Sourasky Medical Center, Sackler Faculty of Medicine (Dr Abergel), Tel-Aviv University, Tel-Aviv, Israel.
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THE IMPORTANCE of topics addressing quality of life (QOL) of patients with cancer is now being more and more acknowledged. Quality of life is assessed in an effort to improve treatment modalities, to promote restoration of patients' daily function, and to accelerate their return to normal life. Estimation of the influence of surgical procedures on QOL can serve as a means by which the most appropriate surgical approach can be selected for a given patient. Detailed understanding of the different aspects of QOL may help surgeons improve assessment and management of patients, identify specific impediments as early as possible during follow-up, and direct specific medical interventions to patients with increased risk and poor outcome.[1] Furthermore, early access of patients to detailed information about their disease can yield better adjustment to an imminent medical condition.[2] A multidimensional evaluation of QOL involves retrieving information on the physical, emotional, social, and economical aspects of patients' lifestyle, as well as on specific symptoms associated with their disease. Valid interpretation of the data requires disease-specific instruments that cover the morbidity associated with the site of cancer and its treatment.[3]

The technical development of anterior skull base surgery has had a major positive impact on the long-term survival of patients with lesions involving the anterior cranial fossa and adjacent paranasal sinuses and orbits.[4] Nevertheless, this procedure may carry a considerable risk as well as serious morbidity.[5] The extended subcranial approach was developed for cases of traumatic injuries to the anterior skull base and was later adopted for surgical extirpation of tumors in this anatomical area.[6,7] Subsequent reports have established this approach as a reliable treatment for anterior skull base tumors,[8,9] but

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Table 1. Demographic Characteristics of the Patients*

Demographic Features	Patients (N = 40)
Sex	
Male	23 (57)
Female	17 (43)
Age, y	
≤60	30 (75)
>60	10 (25)
Mean age	45
Comorbidity†	
Yes	10 (25)
No	30 (75)
Radiotherapy	
Yes	10 (25)
No	30 (75)
Months after surgery	
3-6	10 (25)
6-24	10 (25)
>24	20 (50)
Type of surgery‡	
A	14 (29)
B	26 (71)

*Data are number (percentage) of patients unless otherwise specified.
†Comorbidity includes myocardial infarction, chronic lung disease, heart failure, peripheral vascular disease, cerebrovascular accident, liver dysfunction, chronic renal failure, diabetes mellitus, and other malignancies.
‡Type A surgery: osteotomy and removal of the anterior frontal sinus wall and the nasal frame in one block. Type B surgery: osteotomy and removal of the anterior and posterior frontal sinus wall and the nasal frame.

tumor control should not be the only goal of patient care. During the last decade, numerous studies have assessed QOL issues in patients with head and neck cancer[10,11]; however, to our knowledge, the physical and psychological sequelae of anterior skull base surgery in general and of the subcranial approach in particular have not been systematically evaluated.

The aims of the present study were to assess the influence of surgery for extirpation of anterior skull base tumors on patients' QOL and to investigate possible predictors of functional outcome after surgery. Since skull base surgery differs from other head and neck procedures, the psychological, social, and physical well-being of the this group of patients were assessed using a disease-specific multidimensional questionnaire.

METHODS

PATIENTS

This study is based on a review of the hospital medical records of 69 patients (76 consecutive cases) operated on between 1994 and 2002 for extirpation of anterior skull base tumors at Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel. All operations were performed via the subcranial approach to the anterior skull base and carried out by the same interdisciplinary team.

Inclusion criteria dictated that at least 3 months had to have passed since surgery. Of the 69 potential study candidates, 13 died of various causes, 5 did not reside in Israel, 5 were lost to follow-up, 5 patients were operated on less than 3 months before commencement of the study, and 1 patient was noncompliant. Thus, a total of 40 questionnaires were completed and analyzed. All the candidates who agreed to fill out a QOL questionnaire also gave a full medical history and underwent a physical examination on the same day. The demographic data of the patients are given in **Table 1**. Comorbidity was defined according to the Charlson Comorbidity Index.[12] An independent physician conducted all the interviews to avoid any bias that could stem from surgeon-patient interaction.

The patients were at least 18 years old, were able to read and write, had no severe psychopathological or cognitive impairment, and gave their informed consent to participate in this survey. The study was approved by the Institutional Helsinki Committee.

QUESTIONNAIRE

The development of the questionnaire, including its reliability and validity, are described elsewhere.[13,14] Six relevant domains were identified by factor analysis: role of performance (6 items), physical function (7 items), vitality (7 items), pain (3 items), specific symptoms (7 items), and impact on emotions (5 items). **Table 2** summarizes the 6 categories of QOL, each category representing 1 domain. Internal consistency of each of the 6 domains was evaluated using Cronbach α coefficient. Cronbach α values for each domain were greater than .8. Construct validity demonstrated that the direction of differences for each domain was as hypothesized (paired *t* test, $P<.05$).

After a review of the literature, questions were generated from a pool of questions related to general QOL (Medical Outcomes Study Short Form 36-Item Health Survey [SF-36], Glasgow Benefit Inventory, and The Center for Epidemiologic Studies Depression Scale)[15-17] and from questionnaires related to head and neck cancer (European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire [EORTC QLQ-C30]).[18] Additional questions were included to cover symptoms specifically associated with anterior skull base tumors and its postoperative morbidity. These questions were derived from (1) interviews with head and neck surgeons, nurses and social workers, (2) interviews with patients, and (3) interviews with caregivers.

Seven more questions were included to cover aspects of altered taste, smell, and appearance, as well as of epiphora, nasal secretions, and visual disturbances, all of which were frequently found in our patients. All questions were phrased to detect differences in QOL between the preoperative and postoperative periods. Four general questions were also included to provide cross-sectional values of the different domains of QOL. The answers were given on an ordinal scale with either 5 levels (35 specific questions) or 3 levels (4 general QOL questions) that indicate the QOL change relative to the period before surgery. All questions had an identical level of importance. An example of this questionnaire is provided on our Web site (http://www.skullbase.dot.co.il).

SURGERY

Extirpation of anterior skull base tumors was performed via the subcranial approach in all patients. The surgical technique, complications, and outcome have been described in detail elsewhere.[6-9] Fourteen patients underwent a type A osteotomy in which the anterior frontal sinus wall as well as the nasal frame are osteotomized and removed in 1 block. This approach is used for relatively small and anteriorly located tumors. Twenty-six patients underwent a type B osteotomy in which burr holes are made and the posterior frontal sinus wall is resected after the dura has been detached. Type B osteotomy was used for large and posterior tumors. The patients were followed up every 1 to 3 months for an average of 26 months.

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Table 2. Summary of Domain Questions in the Skull Base Quality of Life Questionnaire

Role of performance
General performance
Performance at work
Performance at home
Participation in social activities
Communication with people
Effect of health on performance
Physical functioning
Climbing stairs
Leaning and standing
Walking long distances
Walking short distances
Preferring to stay in bed
Carrying out routine activities
Reducing extent of physical activity because of disease
Vitality
Feeling weak
Feeling tired
Achieves what is desired
Feeling enthusiastic
Feeling motivated
Feeling energetic
Relationships with spouse
Pain
Experiencing pain
Effect of pain on activity
Use of painkillers
Specific symptoms
Change in appetite
Altered sense of taste
Altered sense of smell
Altered appearance
Nasal secretions
Eye secretions
Affect of surgery on vision
Impact on emotions
Feeling tense
Problems falling asleep
Feeling worried or frustrated
Feeling relaxed and calm
Worrying about finances

STATISTICAL METHODS

The *t* test, Spearman correlation coefficient, Cronbach α coefficient, and the Mann-Whitney test were applied as appropriate. We considered a *P* value less than .05 to be significant and a *P* value less than .1 to be of borderline significance. The Ryan-Einot-Gabriel-Welsch multiple-range test was used to determine significant differences between pairs of groups. Multiple comparisons for the adjusted means were carried also using the studentized maximum modulus method.

RESULTS

Of the 69 patients operated on by us, 40 were enrolled in this study. The response rate for completing the questionnaire, after excluding the patients who died, were lost to follow-up, and were operated on within 3 months of the commencement of this study was 98% (40 of 41 patients). The tumors were malignant in 13 patients (33%) and benign in 27 (68%). There was no significant difference in age or sex between these 2 groups. The study population was divided into 2 groups according to the extent of the tumor: (1) confinement of the tumor to the paranasal sinuses and (2) intracranial extension of the tumor. In the group of patients with benign tumors, 21 (78%) of 27 had intracranial extension of the tumor. In the group of patients with malignant tumors, 12 (92%) of 13 had intracranial involvement. **Table 3** provides a summary of the underlying pathologic conditions of the patients.

Table 3. Tumor Distribution in the Study Population

Pathologic Condition	No. (%) of Patients (N = 40)
Malignant tumors	
Adenoid cystic carcinoma	1 (3)
Adenocarcinoma	1 (3)
Esthesioneuroblastoma	2 (5)
Malignant melanoma	1 (3)
Malignant schwannoma	1 (3)
Sarcoma	2 (5)
Squamous cell carcinoma	3 (8)
Plasmocytoma	1 (3)
Undifferentiated carcinoma	1 (3)
Benign tumors	
Mucocele	7 (18)
Meningioma	9 (23)
Inverted papilloma	3 (8)
Osteoma	3 (8)
Fibrous dysplasia	1 (3)
Epidermoid cyst	1 (3)
Angiofibroma	1 (3)
Meningoencephalocele	2 (5)

The study population was divided into the following subgroups: age, sex, type of surgery (osteotomy A or B), time from surgery, type of tumor, perioperative radiotherapy, and comorbidity. In the first section of the questionnaire, patients were asked to grade their overall postoperative QOL relative to their preoperative QOL. **Figure 1** shows the overall results of 4 general questions relating to the effect of surgery on overall QOL, social activity, financial status, and emotional state. The results show that 15 patients (37%) reported a significant improvement in overall QOL and 15 (37%) reported no change in QOL after surgical removal of their tumor. The minority of our patients (10 [26%]) answered that the surgical procedure worsened their QOL. The scores of the social, financial, and emotional state domains were lower relative to the overall QOL score (Figure 1).

To obtain estimates on the specific influence of the subcranial approach on various aspects of QOL, each patient was asked to answer 35 questions related to 6 distinct domains: role of performance, physical function, vitality, pain, specific symptoms, and impact on emotions. The results are summarized in **Table 4**. The domains of role of performance, physical function, vitality, and impact on emotions received lower scores than the overall QOL score. The domains of pain and specific symptoms had scores above the overall QOL.

To predict which of the patients may have poorer outcome after surgery, the study population was divided into 7 subgroups according to demographic and clinical characteristics (Table 4). The mean physical function score of patients 60 years or younger was significantly higher than

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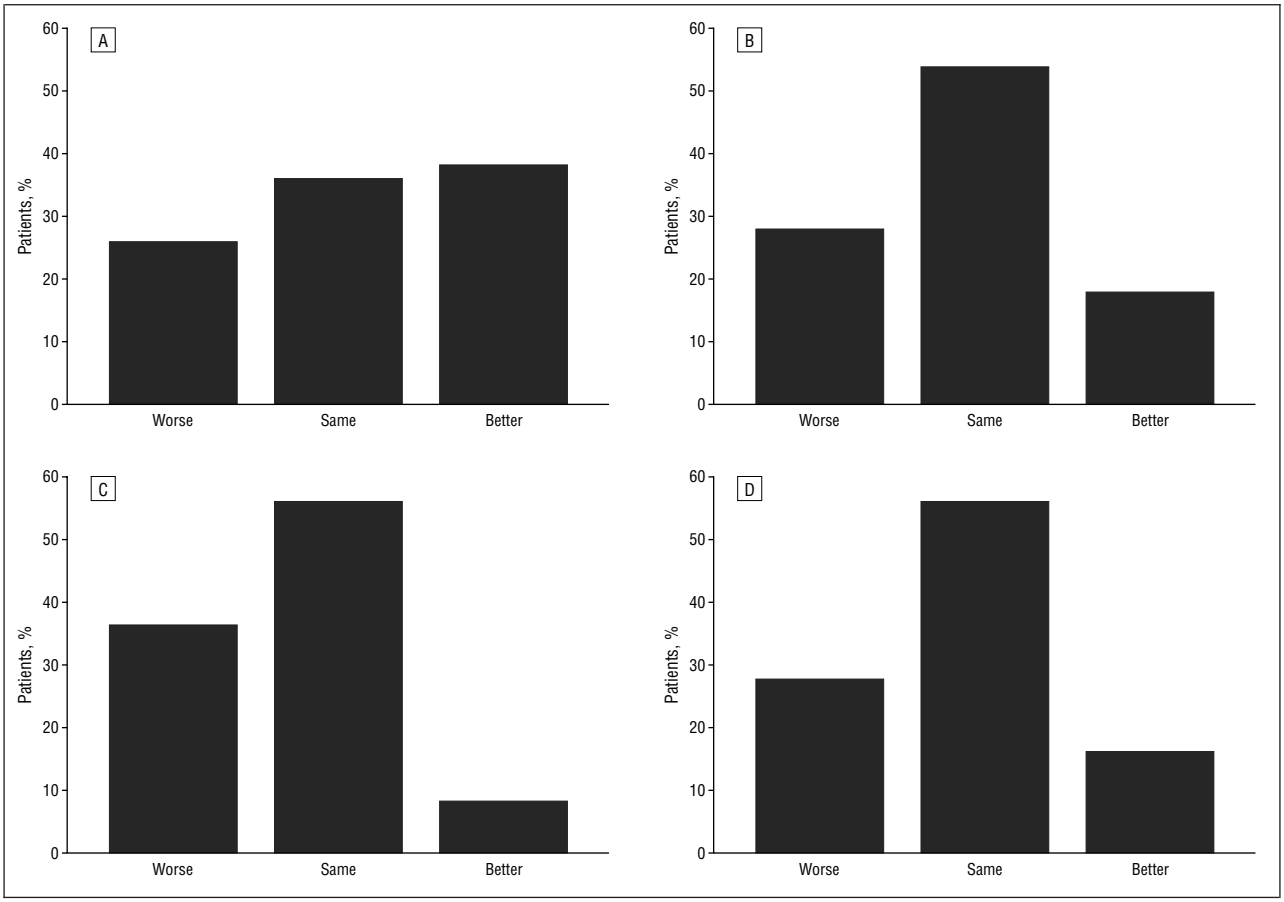

Figure 1. The effect of surgery on different quality of life measures. A, Overall quality of life; B, social activity; C, financial status; and D, emotional state.

that of older patients. Patients with benign tumors reported higher scores in the domains of role of performance, physical function, specific symptoms, and impact on emotions compared with patients with malignant tumors. Interestingly, both groups reported only a minor influence of the aspect of pain on their QOL.

Perioperative radiotherapy was associated with significantly lower scores in the domains of specific symptoms and impact on emotions. Type B surgery, which involves osteotomy and en bloc removal of the anterior and posterior frontal sinus wall (see "Methods" section) was also associated with lower scores in the impact on emotions domain. As expected, patients with an additional illness reported lower scores of QOL in the physical function domain. There was no significant association between recurrent surgery and impaired QOL. **Figure 2** summarizes the overall change in QOL among the different subgroups.

Another aspect of QOL is the length of recovery after surgery and the stability of scores over time. Although we did not estimated the QOL of patients at different points over the course of treatment, we tried to estimate the recovery time by comparing QOL scores among patients who were operated on 3 to 6 months, 6 to 24 months, and more than 24 months before commencement of the study. **Figure 3** depicts the change in QOL relative to the time after surgery. The data show improvement in QOL measures 6 to 24 months following surgery relative to 3 to 6 months after the operation. Figure 3 also demonstrates stability of the overall QOL scores for a period of more than 6 months after surgery.

Twenty patients (50%) reported that they experienced anosmia, but only 9 (22%) claimed not to enjoy eating. Eleven patients (28%) had recurrent nasal secretion, 8 (20%) had epiphora, and 14 (35%) developed visual disturbances as result of their operation. While 17 patients (43%) reported being concerned about their appearance, only 11 (28%) indicated that the operation interfered with their social activity. Impaired performance at work was reported by 15 patients (38%), and 14 (35%) had a poorer financial status since their operation. Finally, 8 patients (20%) reported that the operation changed their relationships with their spouse.

COMMENT

Surgical procedures for resection of neoplasms of the anterior skull base can carry significant morbidity.[4] We had previously found that 44% of the patients may experience anosmia following surgery.[9] Other significant complications that may have influence on the functional outcome of patients are meningitis, cerebrospinal fluid leak, osteoradionecrosis and fistula, mucocele, and visual disturbances.[8,19] Although various surgical techniques for extirpation of anterior skull base tumors have been established during the past 30 years,[4-9] to our knowledge, the impact of surgery on patient's QOL has not been delineated to date.

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Table 4. Association of Demographic and Clinical Variants With Quality of Life Domains*

Variant	Role of Performance	Physical Function	Vitality	Pain	Specific Symptoms	Impact Emotions	Overall
Total	2.64	2.55	2.61	2.82	2.80	2.47	2.66
Age, y							
≤60	2.71	2.68†	2.63	2.83	2.86	2.51	2.71
>60	2.41	2.14†	2.55	2.80	2.64	2.33	2.45
Pathologic condition							
Benign	2.86‡	2.72‡	2.64	2.76	2.94‡	2.60‡	2.77‡
Malignant	2.28‡	2.24‡	2.52	2.95	2.38‡	2.23‡	2.45‡
Time after surgery, mo							
3-6	2.28	2.34	2.48	2.85	2.32	2.37	2.43
6-24	2.73	2.70	2.62	2.93	2.94	2.55	2.81
>24	2.77	2.78	2.64	2.76	2.87	2.48	2.70
Radiotherapy							
No	2.68	2.60	2.66	2.77	2.98‡	2.55†	2.71
Yes	2.48	2.30	2.45	3.00	2.15‡	2.18†	2.41
Recurrent surgery							
No	2.64	2.56	2.51	2.80	2.67	2.50	2.63
Yes	2.63	2.53	2.71	2.86	2.88	2.45	2.67
Craniotomy type							
A	2.93	2.74	2.64	2.93	2.88	2.65†	2.80
B	2.48	2.43	2.57	2.86	2.76	2.37†	2.68
Comorbidity							
Yes	2.32	2.24‡	2.68	2.75	2.80	2.33	2.49
No	2.76	2.84‡	2.58	2.84	2.78	2.51	2.71

*Data are average scores for quality of life domains by patients (N = 40) according to demographic and clinical variants. A higher score indicates a better quality of life.
†$P<.1$.
‡$P<.05$.

The objective of the present study was to assess the long-term QOL of patients undergoing anterior skull base tumor resection via the subcranial approach. Since available instruments for estimation of QOL in patients with head and neck cancer do not encompass the condition of anterior skull base tumors, we have used a novel instrument for QOL assessment that was validated using standard psychometric criteria.[13,14] The response rate in our study was 98%. This high rate may be directly associated with the fact that most of our patients are located in 1 region within driving distance from the medical center and undergo regular outpatient follow-up at our institution. The high response rate may also be attributed to the method of interview (ie, a face-to-face interview), which ensures compliance and decreases errors and missing items due to misunderstanding. Nevertheless, to diminish a possible bias, the interviewing health professional was not one of our clinical staff.

The overall results of this study show that the resection of tumors of the anterior skull base by the subcranial approach has a positive impact on the patients' QOL. Most of our patients (30 [75%]) reported that the surgical procedure improved or did not interfere with their overall QOL. The relatively good scores recorded for the role of performance, pain, and specific symptoms domains further demonstrate this positive impact of surgery on different aspects of QOL.

Most of the studies on QOL after skull base surgery were performed on patients with acoustic schwannoma. Nikolopoulos et al[20] used a disease-specific questionnaire for evaluating patients' QOL after resection of acoustic schwannoma and showed that more than 53% of their patients reported an overall decline in QOL—worse than the 24% in our study. They also showed that 29% of their patients had declined financial status as a consequence of the operation. Similar results were reported by da Cruz et al.[21] A negative impact of surgery on these patients is expected, since the preoperative health-related QOL is hardly affected by their clinical condition. In contrast, our patients presented with major symptoms such as nasal obstruction and secretion, diplopia, epiphora, epistaxis, headache, visual disturbances, and facial deformities. Most of these symptoms are relieved following tumor extirpation, so it can be expected that patients with anterior skull base tumors experience some degree of improvement in their QOL following surgery.

An interesting comparison could also be made between our patients and patients who have had meningiomas removed through various neurosurgical approaches. Mohsenipour et al[22] have recently shown that most patients after meningioma resection had mild to moderate impairment of QOL. Severe impairment was found in the physical handicap and energy level domains. Similar results were reported for meningiomas involving the cavernous sinus.[23] In another study that looked at the outcome of patients after excision of petroclival meningioma in which a standard lateral skull base approach was used,[24] 76% of the patients reported good to moderate recovery at 1 year after the operation, but 43% to 75% of these patients were still functioning below accepted norms.

Studies on patients with malignant intracranial tumors have demonstrated severely deteriorating QOL measures, with marked decline in cognitive, physical, emotional, and social functioning after surgery.[25] In accordance

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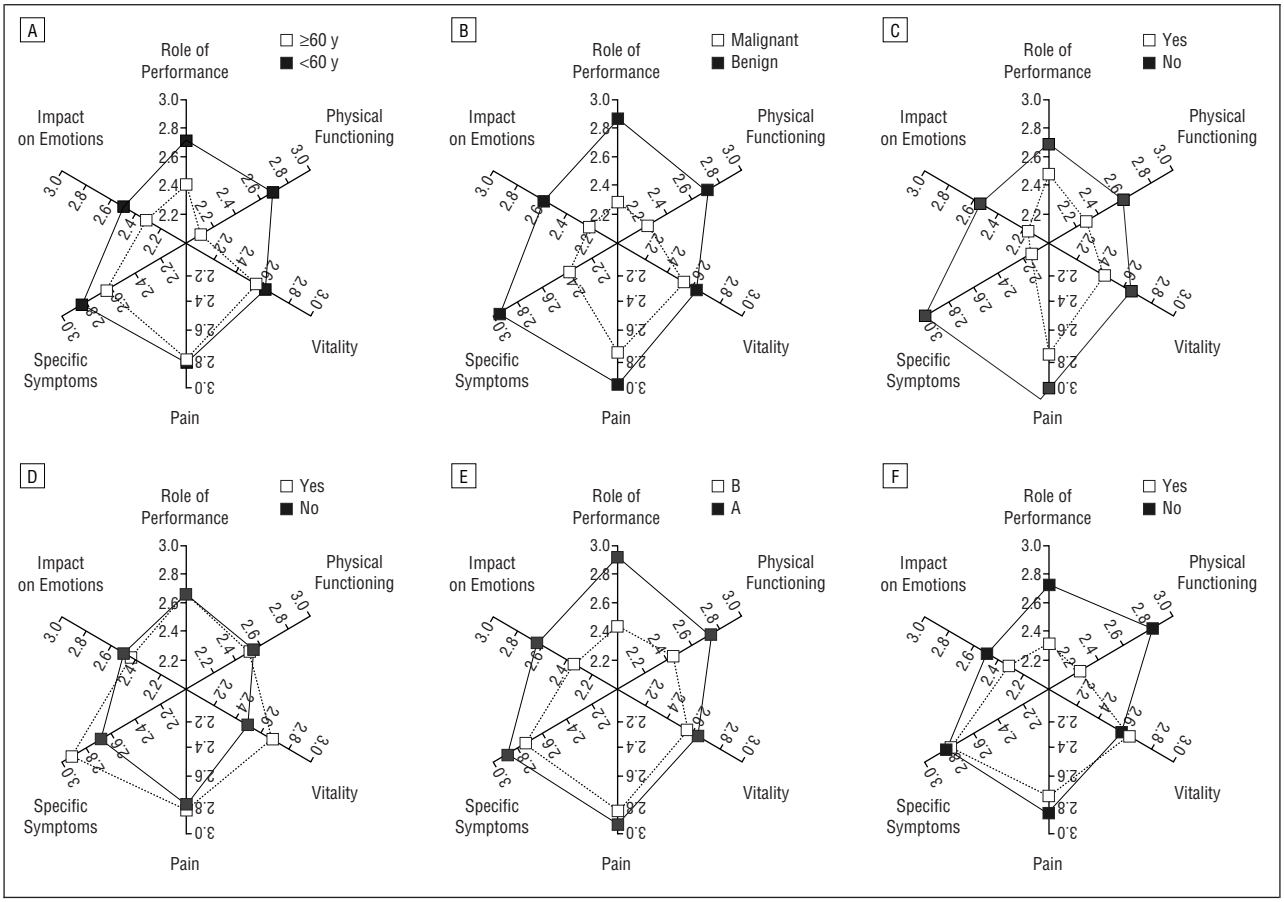

Figure 2. Polar graphs of the quality of life (QOL) questionnaire scores distributed to demographic and clinical variants. Each one of the graphs (A-F) shows the average scores of 6 specific QOL domains represented by each axis. A higher score indicates a better QOL measure. The effect of age (below or above 60 years) (A), type of pathology (malignant/benign) (B), radiotherapy (C), multiple operations (D), type of surgery (type A/B osteotomy) (E), and patients' comorbidity (F) on different QOL measures are shown.

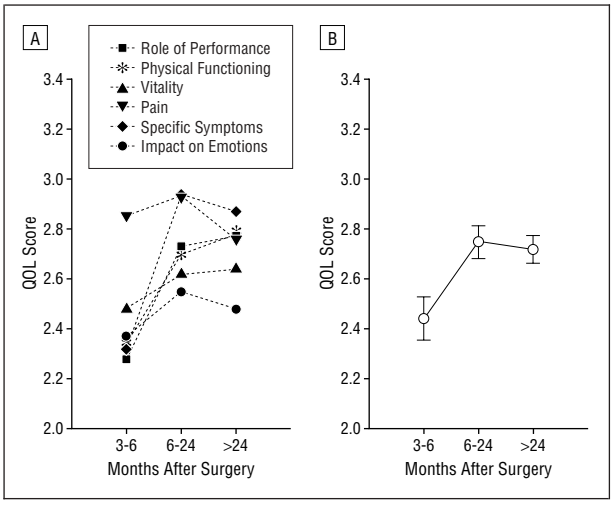

Figure 3. Estimating the recovery period and stability of quality of life (QOL) measures following surgery. A, The average score of the 6 specific domains: 3 to 6 months (n=10 patients), 6 to 24 months (n=10 patients), and more than 24 months (n=20 patients) after surgery. B, Change in overall QOL scores following surgery. Error bars indicate SEM.

with these studies, we also found that patients with malignant tumors have significantly poorer QOL scores compared with patients with benign lesions.

To our knowledge, the only study on patients with anterior skull base tumors was performed by Fukuda et al.[26] In their study, the authors evaluated the condition of 13 patients who underwent classic craniofacial resection of malignant tumors. Of the patients, 89% had some complaints and 63% of them reported that their QOL worsened after surgery. In contrast, among our 13 patients operated on for extirpation of malignant tumors via the subcranial approach, only 5 (38%) reported deterioration in their QOL following surgery. More studies are required to determine the preferable approach for extirpation of tumors in this anatomical area.

The stability of QOL following the first 6 months after surgery is an important issue in our study. We compared the QOL scores of patients operated on 3 to 6, 6 to 24, and more than24 months before the commencement of the study to estimate the dynamic change in QOL following surgery. We have found that during the first 6 months after surgery there was a gradual improvement in QOL measures, while later on no significant change in QOL was reported by the patients (Figure 3). This dynamic change in QOL measures after skull base surgery was similar to that found by De Jesus et al[23] for meningiomas involving the cavernous sinus but different than that observed for intracranial malignancy.[25]

Our study also indicates that old age has a negative impact on health-related QOL, especially in the physi-

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cal function domain. These results are consistent with the finding of Mohsenipour et al[22] for meningioma resection. In contrast, young patients had a worse overall QOL and financial status after excision of acoustic neuromas.[20] The discrepancy between the studies may emerge from the fact that young patients with acoustic neuromas benefit from a good preoperative QOL compared with young patients with anterior skull base tumors, who experience serious symptoms prior to surgery. It can be also presumed that younger patients cope better with anterior skull base neoplasms and surgery compared with older patients with similar conditions.

Perioperative radiotherapy was also found to predict poor QOL scores. As expected, a worse score was found in the specific symptoms domain. We also found significantly deteriorating emotional functioning in this group. Radiation therapy was used for patients with malignant tumors, and the combination of both factors (malignancy and radiation therapy) probably contributed to the deteriorating emotional states of these patients. Similar effects on the patient's overall QOL and emotional state were found in patients receiving radiation therapy for head and neck cancer[16] or other neoplasms.[27]

We recently reported a retrospective study of 175 skull base operations performed without hair removal.[28] Our results showed that a skull base operation without hair removal does not carry additional risk for wound infection and contamination compared with the rates reported for identical procedures in which the hair was removed. Avoiding hair shaving may have contributed to the improved short-term QOL in our patients by sparing them additional psychological stress, promoting the restoration of their self-image, and accelerating their return to normal life.

Our study involves a single group of patients operated on by 1 group of surgeons in the same medical institute. Therefore, our results may be applicable for this selected population alone, while the impact of other surgical approaches to the anterior skull base on QOL needs to be established. The main limitation of our study is that it involves a retrospective analysis of patients with different types of neoplasms operated on during a period of 8 years. Further prospective, multicenter studies are required to assess more accurately the QOL measures of patients with various anterior skull base tumors. Comparative studies are essential to examine the impact of different surgical modalities with no clear survival advantage on patients' QOL.

CONCLUSIONS

The overall QOL in most patients after anterior skull base tumor extirpation can be classified as good, with significant improvement within 6 months following surgery. The worst impact of surgery was on the patients' financial and emotional QOL domains. Old age, malignancy, comorbidity, radiotherapy, and wide surgery were found to be negative prognostic factors for QOL measures. These findings can be applied for targeting medical resources to improve QOL measures in this group of patients.[29]

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Corresponding author and reprints: Dan M. Fliss, MD, Skull Base Surgery Unit, Department of Otolaryngology, Tel-Aviv Sourasky Medical Center, 6 Weizman St, Tel Aviv, Israel 64239 (e-mail: ziv@dot.co.il).

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