Endoscopic Resection of Sinonasal Cancers With and Without Craniotomy

Oncologic Results

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Objective: To evaluate the oncologic outcomes of patients with sinonasal cancer treated with endoscopic resection.

Design: Retrospective review.

Setting: Tertiary care academic cancer center.

Patients: All patients with biopsy-proved malignant neoplasm of the sinonasal region who were treated with endoscopic resection between 1992 and 2007 were included in the study, and their charts were reviewed for demographics, histopathologic findings, treatment details, and outcome.

Main Outcome Measures: Oncologic outcomes, including disease recurrence and survival.

Results: Of a total of 120 patients, 93 (77.5%) underwent an exclusively endoscopic approach (EEA) and 27 (22.5%) underwent a cranioendoscopic approach (CEA) in which the surgical resection involved the addition of a frontal or subfrontal craniotomy to the transnasal endoscopic approach. Of the 120 patients, 41% presented with previously untreated disease, 46% presented with persistent disease that had been partially resected, and 13% presented with recurrent disease after prior treatment. The most common site of tumor origin was the nasal cavity (52%), followed by the ethmoid sinuses (28%). Approximately 10% of the tumors had an intracranial epicenter, most commonly around the olfactory groove. Tumors extended to or invaded the skull base in 20% and 11% of the patients, respectively. An intracranial epicenter (P < .001) and extension to (P = .001) or invasion of (P < .001) the skull base were significantly more common in patients treated with CEA than in those treated with EEA. The primary T stage was evenly distributed across all patients as follows: T1, 25%; T2, 25%; T3, 22%; and T4, 28%. However, the T-stage distribution was significantly different between the EEA group and the CEA group. Approximately two-thirds (63%) of the patients treated with EEA had a lower (T1-2) disease stage, while 95% of patients treated with CEA had a higher (T3-4) disease stage (P < .001). The most common tumor types were esthesioneuroblastoma (17%), sarcoma (15%), adenocarcinoma (14%), melanoma (14%), and squamous cell carcinoma (13%). Other, less common tumors included adenoid cystic carcinoma (7%), neuroendocrine carcinoma (4%), and sinonasal undifferentiated carcinoma (2%). Microscopically positive margins were reported in 15% of patients. Of the 120 patients, 50% were treated with surgery alone, 37% received postoperative radiation therapy, and 13% were treated with surgery, radiation therapy, and chemotherapy. The overall surgical complication rate was 11% for the whole group. Postoperative cerebrospinal fluid leakage occurred in 4 of 120 patients (3%) and was not significantly different between the CEA group (1 of 27 patients) and the EEA group (3 of 93 patients) (P > .99). The cerebrospinal fluid leak resolved spontaneously in 3 patients, and the fourth patient underwent successful endoscopic repair. With a mean follow-up of 37 months, 18 patients (15%) experienced local recurrence, with a local disease control of 85%. Regional and distant failure occurred as the first sign of disease recurrence in 6% and 5% of patients, respectively. The 5- and 10-year disease-specific survival rates were 87% and 80%, respectively. Disease recurrence and survival did not differ significantly between the EEA group and the CEA group.

Conclusions: To the best of our knowledge, this is the largest US series to date of patients with malignant tumors of the sinonasal tract treated with endoscopic resection. Our results suggest that, in well-selected patients and with appropriate use of adjuvant therapy, endoscopic resection of sinonasal cancer results in acceptable oncologic outcomes.


During the last decade, there has been increasing adoption of endoscopic approaches for surgical resection of sinonasal cancer. Despite this growing enthusiasm, the oncologic outcomes for endoscopic resection of sinonasal cancer have not been adequately reported. Most published reports include small case series with short follow-up. The majority of these reports focus exclusively on esthesioneuroblastoma, and the results of endoscopic resection of other types of sinonasal cancer are not widely described. The purpose of this study was to determine the oncologic outcomes of patients with sinonasal cancer who were treated with en-
After approval by the institutional review board, a search of the Department of Head and Neck Surgery and sinus cancer databases was performed to identify all patients who underwent endoscopic resection of sinonasal cancer between 1992 and 2007 at the University of Texas M. D. Anderson Cancer Center, a tertiary care comprehensive cancer center. Patients’ medical records were reviewed for information regarding demographics; tumor characteristics, such as mode of presentation and prior treatment; site and extent of tumor; disease stage; histopathologic findings; and treatment details, including adjuvant therapy, complications, and oncologic outcomes, such as disease control, recurrence, and survival.

Descriptive statistics for scaled values and frequencies of study patients within the categories for each of the parameters of interest were enumerated with the assistance of commercial statistical software. Correlations between parameters and end points were assessed by a Pearson χ² test or, when there were fewer than 10 subjects in any cell of a 2×2 grid, by a 2-tailed Fisher exact test. Curves describing overall and disease-specific survival were generated by the Kaplan-Meier product limit method. The statistical significance of differences between the actuarial curves was tested by the log-rank test. These statistical tests were performed with the assistance of Statistica (StatSoft Inc, Tulsa, Oklahoma) and SPSS (SPSS for Windows, SPSS Inc, Chicago, Illinois) statistical software applications.

### RESULTS

#### PATIENTS AND TYPE OF ENDOSCOPIC SURGERY

Of a total of 120 patients, 93 (77.5%) were treated with an exclusively endoscopic approach (EEA) and 27 (22.5%) were treated with a cranioendoscopic approach (CEA) in which the surgical resection involved the addition of a frontal or subfrontal craniotomy to the transnasal endoscopic approach. The details are summarized in Table 1.

The patients’ median age was 52.6 years (age range, 11.7-91.8 years). Fifty-five patients (45.8%) were female and 65 (54.2%) were male. The mean follow-up time was 37 months.

#### DISEASE PRESENTATION AND PRIOR TREATMENT

Of the 120 patients, 50 (42%) presented with previously untreated disease, 55 (46%) presented with persistent disease that had been partially resected elsewhere, and 15 (13%) presented with recurrent disease after prior treatment elsewhere. A higher percentage of patients in the CEA group presented with their initial disease (17 of 27 [63.0%]) than in the EEA group (32 of 93 [34.4%]). Notably, the EEA group had a higher percentage of patients who presented with persistent disease (50 of 93 [53.8%]) than the CEA group (5 of 27 [18.5%]). The distributions were significantly different (P=.01).

#### SITE OF ORIGIN AND EXTENT OF TUMOR

The most common site of origin (epicenter) of the tumor was the nasal cavity (52%) and the ethmoid sinuses (28%). Tumors originating from the sphenoid sinus (8%) or frontal sinus (2%) were less common. Approximately 10% of tumors had an intracranial epicenter, most commonly around the olfactory groove. Tumors extended to or invaded the skull base in 20% and 11% of patients, respectively. An intracranial epicenter (P<.001) and extension to (P<.001) or invasion of (P<.001) the skull base were significantly more common in patients treated with CEA than in those treated with EEA. Tumor extension to the following sites was also more common in patients treated with CEA (Table 2): anterior ethmoid sinus (P=.01), posterior ethmoid sinus (P<.001), cribiform plate (P<.001), fovea ethmoidalis (P=.005), orbit (P<.001), pterygoïd plates (P=.05), and nasopharynx (P=.03).

#### TUMOR STAGE

The primary T stage was evenly distributed across all patients as follows: T1, 25%; T2, 25%; T3, 22%; and T4, 28%. However, the T-stage distribution differed significantly between the CEA and the EEA groups (P<.001).

### METHODS

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The primary T stage was evenly distributed across all patients as follows: T1, 25%; T2, 25%; T3, 22%; and T4, 28%. However, the T-stage distribution differed significantly between the CEA and the EEA groups (P<.001).
Approximately two-thirds (63%) of patients treated with EEA had a lower (T1-T2) disease stage, while 95% of patients treated with CEA had a higher (T3-T4) disease stage. Overall, on presentation, only 3 patients had nodal disease (2 patients, N1; 1 patient, N3), and 1 patient had distant disease.

HISTOPATHOLOGIC FINDINGS AND SURGICAL MARGINS

The most common tumor types were esthesioneuroblastoma (17%), sarcoma (15%), adenocarcinoma (14%), melanoma (14%), and squamous cell carcinoma (13%). Other, less common tumors included adenoid cystic carcinoma (7%), neuroendocrine carcinoma (4%), and sinonasal undifferentiated carcinoma (2%). There was no significant difference in the distribution of histopathologic types between the CEA and the EEA surgical groups (P = .22). Microscopically positive margins were reported in 15% of patients.

ADJUVANT TREATMENT

Of the 120 patients, 60 patients (50%) were treated with surgery alone, 44 patients (37%) received postoperative radiation therapy, and 15 patients (13%) were treated with surgery, radiation therapy, and chemotherapy. Conformal radiation therapy, particularly intensity-modulated radiation therapy, was used in the majority (92%) of patients receiving radiotherapy. Twenty-one patients (18%) received chemotherapy, of whom one-third received it as neoadjuvant (induction) therapy and two-thirds as adjuvant (postoperative) therapy.

COMPLICATIONS AND MORBIDITY

The overall surgical complication rate was 11% for the whole group. Postoperative cerebrospinal fluid (CSF) leakage occurred in 4 of 120 patients (3%) and was not significantly different between the CEA (1 of 27) and the EEA (3 of 93) groups. The CSF leak in 3 patients resolved spontaneously, and the fourth patient underwent successful endoscopic repair. One patient had meningitis, which resolved with antibiotic therapy. Other less common complications included epiphora in 2 patients and dacryocystitis in 1 patient. In the CEA group, 1 patient had mild brain concussion and 1 patient had postoperative pneumocephalus. Both patients had no neurologic deficits and had complete resolution without intervention.

DISEASE CONTROL, RECURRENCE, AND SURVIVAL

Of the 120 patients, 18 (15%) experienced local recurrence, with local disease control of 85%. Regional and distant failure occurred as the first sign of disease recurrence in 7 (6%) and 6 (5%) patients, respectively. The 5- and 10-year disease-specific survival rates were 87% and 80%, respectively. There was no statistically significant difference in disease-specific survival (P = .92) or overall survival (P = .79) between the EEA and the CEA groups (Figure 1). Survival was better for patients who presented with previously untreated disease than for patients who presented with persistent disease after incomplete surgical resection (Figure 2).

COMMENT

The oncologic outcomes of patients with sinonasal cancer have been steadily improving over the last 4 decades. This progress is probably attributable to more effective surgical treatment, which has been made possible by the advent and subsequent refinements of craniofacial resection, more effective reconstruction using vascularized flaps, and more effective adjuvant therapy, particularly conformal radiation therapy. New ap-
proaches in the treatment of patients with sinonasal cancers will have to “hold the gains” made over the last 40 years, and their efficacy will have to be measured against time-tested approaches.

Endoscopic approaches to the skull base and sinonasal regions offer several advantages. In addition to excellent visualization, endoscopic approaches eliminate or significantly reduce the need for craniofacial soft-tissue dissection, skeletal disassembly, and brain retraction for tumor access and resection. These advantages are probably the impetus for the increasing adoption of endoscopic approaches for surgical management of sinonasal and skull base tumors. However, while there have been many reports describing its use in benign neoplasms, the efficacy of endoscopic resection of sinonasal cancer has not been adequately described in the literature. There have been several recent reports of relatively small case series reporting favorable outcomes of endoscopic resection of esthesioneuroblastoma. Given the better prognosis of esthesioneuroblastoma compared with other sinonasal cancers, these results cannot be extrapolated to more ominous types of sinonasal cancers.

To the best of our knowledge, this is the largest US series reported to date of patients with malignant tumors of the sinonasal tract treated with endoscopic or endoscopically-assisted resection. A previous large series from Italy reported by Nicolai et al., which combined a 10-year experience (1996-2006) of 2 surgical teams at the University of Brescia and the University of Pavia/Insubria-Varese in Italy, included 134 patients who were treated with EEA and an additional 50 patients who were treated with CEA. Interestingly, the Italian series, like most European reports on sinonasal cancers, included a relatively large number of patients with adenocarcinoma (37%), which is less common in the United States and has a relatively better prognosis than squamous cell carcinoma, melanoma, and sinonasal undifferentiated carcinoma.

The excellent overall and disease-specific survival reported in our study suggests that, for well-selected cases and with the appropriate use of adjuvant therapy, endoscopic resection of sinonasal cancer results in acceptable oncologic outcomes. These findings are consistent with those described by Nicolai et al., who reported a 5-year disease-specific survival of 82%. It is noteworthy, however, that, in their study, the 5-year disease-specific survival was only 59% for the subgroup of patients who underwent CEA compared with 91% for those who underwent EEA (P < .001). In contrast, our study showed no statistically significant difference in disease-specific survival between these 2 groups (P = .92), despite the higher disease stage in the CEA group (Figure 2). The reason for this is not entirely clear but may be attributable to a difference in the indications of CEA between these studies. In our practice, EEA is reserved for patients with relatively earlier disease stage and no or limited skull base invasion. When there is significant invasion of the fovea ethmoidalis or the cribriform plate, and particularly if there is dural involvement or transdural spread, we usually perform CEA. In their report, Nicolai et al. described a shift in their selection of the surgical approach in the latter part of their study, extending the indications of EEA to include selected patients with skull base invasion and “local” dural infiltration. We do acknowledge that there are significant limitations of retrospectively comparing 2 groups of patients with different disease burdens among different studies. However, our low threshold for adding a craniotomy to the endoscopic approach is based on the significant negative impact that dural involvement has on prognosis in patients with sinonasal cancer and the frequent need for wide dural resection to achieve negative margins to improve disease control. Using this policy, our study showed excellent disease control and survival rates in patients treated with CEA despite their advanced stage of disease.

In the current study, survival was significantly better for patients who were previously untreated than for those who underwent an incomplete resection and presented for treatment of persistent disease (Figure 3). It is interesting to note that the latter group of patients was more likely to have had their initial disease confined to the nasal cavity and paranasal sinuses without obvious skull base invasion or intracranial extension. Commonly, these
patients were thought to have benign conditions such as polyposis or papillomas and underwent attempted resections elsewhere only to discover that they had sinonasal cancer and were then referred for definitive management after undergoing an incomplete resection. Postoperative changes such as altered anatomy, edema, and fibrosis may make accurate delineation of the extent of disease and definitive surgical resection more difficult and may be responsible for the worse outcome in these patients. Ideally, patients with sinonasal masses should undergo a diagnostic biopsy to firmly establish the diagnosis even in the absence of obvious sinister signs of cancer on imaging or clinical examination. Once the diagnosis of cancer is established, definitive oncologic resection should, whenever possible, achieve complete cancer excision with tumor-free surgical margins regardless of the approach.

Endoscopic resections of sinonasal cancers should be performed by surgeons who have extensive experience in 2 areas: endoscopic techniques and surgical oncologic principles. Lack of expertise in either arena should alert the surgeon to an alternative management strategy, such as an open approach for surgical oncologists with limited endoscopic experience or referral to a surgical oncologist by endoscopic surgeons with limited oncologic training. Also, while surgery is the mainstay of treatment in the majority of sinonasal cancers, the use of appropriate adjuvant or neoadjuvant therapy is critical to achieving good oncologic outcomes. In the current study, postoperative radiation therapy with or without chemotherapy was used in patients with high-grade tumors, advanced T stage, bone invasion, perineural spread, intracranial extension, dural or brain involvement, or positive margins. The majority of patients (90%) received intensity-modulated radiation therapy to optimize the radiation dose to the tumor and to reduce the toxic effects to normal structures, particularly the eyes and the brain, as previously reported by our group.11 Neoadjuvant chemotherapy was used for neuroendocrine carcinoma, sinonasal undifferentiated carcinoma, and most high-grade sarcomas. Given the heterogeneous histopathologic findings, biologic features, and natural history of sinonasal cancers, treatment should always be carried out by an expert multidisciplinary team that is well versed in the management of these rare tumors.

While endoscopic resection of sinonasal and skull base tumors is gaining popularity, there are valid concerns regarding the adequacy and reliability of endonasal reconstruction of major skull base and dural defects. Although fascial or mucosal grafts in combination with tissue sealants may provide adequate reconstruction for small defects resulting from trauma or resection of benign lesions, their success in preventing a CSF leak after wide dural resection in patients with malignant tumors is less clear. A layered reconstruction of the dura with inlay and onlay fascial grafts covered with fat grafts has been described as an effective technique for repair of large dural defects.16 The CSF leak rate with these techniques is significantly higher than rates reported with standard craniofacial resection.10 In a recent study reporting the combined experience of the University of Miami, Miami, Florida, and the University of Pittsburgh, Pittsburgh, Pennsylvania, with endoscopic endonasal resection of esthesioneuroblastoma, 4 of 23 patients (17%) had a postoperative CSF leak.6 Our current policy is to perform CEA in patients who require large dural resections and, because of the high likelihood of delivering postoperative high-dose radiation therapy in these patients, our preference is to use vascularized flaps for reconstruction of the skull base. In addition to allowing wider dural resection, CEA in our hands allows more reliable reconstruction of larger defects using water-tight suture duraplasty reinforced with a well-vascularized pericranial flap. For small defects in the skull base and a minimal intraoperative CSF leak, we use vascularized nasoseptal or turbinate flap through an EEA.17,18 Following these principles, the postoperative CSF leak was rare (3%) in the current study, which compares favorably with results obtained with standard open craniofacial resections.10

In summary, the results of this study suggest that endoscopic resection of sinonasal cancer may yield good oncologic outcomes in well-selected patients. The addition of a craniotomy to an endonasal endoscopic approach may improve tumor resection and dural reconstruction in patients with significant intracranial disease. The surgical principles of adequate oncologic resection and meticulous skull base reconstruction that are the basis for the progress that has been made over the last 40 years should be strictly adhered to, regardless of the approach.

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Author Contributions: Dr Hanna had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Hanna, Levine, and Kupferman. Acquisition of data: Hanna, DeMonte, and Ibrahim. Analysis and interpretation of data: Hanna and Roberts. Drafting of the manuscript: Hanna and Ibrahim. Critical revision of the manuscript for important intellectual content: Hanna, DeMonte, Roberts, Levine, and Kupferman. Statistical analysis: Roberts. Administrative, technical, and material support: Hanna, DeMonte, and Kupferman. Study supervision: Hanna and Levine.

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