Available online at www.sciencedirect.com
ScienceDirect
American Journal of Otolaryngology–Head and Neck Medicine and Surgery xx (2010) xxx–xxx
American Journal of OTOLARYNGOLOGY
www.elsevier.com/locate/amjoto

Minimally invasive endoscopic resection of sinonasal undifferentiated carcinoma☆,☆☆,★

Peter C. Revenaugh, MD[a], Rahul Seth, MD[a], Justin B. Pavlovich, MD[a], P. Daniel Knott, MD[a], Pete S. Batra, MD[b,*]

[a]*Head and Neck Institute, Cleveland Clinic, Cleveland, OH, USA*
[b]*Department of Otolaryngology–Head and Neck Surgery and Comprehensive Skull Base Program, University of Texas Southwestern Medical Center, Dallas, TX, USA*

Received 23 July 2010

Abstract

Purpose: The purpose of the study was to review a single-institution experience with endoscopic resection of sinonasal undifferentiated carcinoma (SNUC).

Materials and methods: Thirteen patients underwent treatment of SNUC between January 2002 and July 2009. Retrospective data were collected including demographics, tumor characteristics, surgical strategy, adjuvant therapies, local and regional recurrence, distant metastasis, overall survival, and disease-free survival.

Results: The mean age was 51.8 years. The most common tumor stage at presentation was T4 (92%). Seven patients (53%) were treated with minimally invasive endoscopic resection (MIER) with negative intraoperative margins. Endoscopic anterior skull base resection was performed in 5 patients, and endoscopic-assisted bifrontal craniotomy was performed in 1 patient to clear the superior tumor margin. Six patients received pre- or postoperative chemoradiation. One patient underwent palliative chemoradiation, and one patient underwent open craniofacial resection. In the MIER group, simultaneous local and regional recurrence was observed in 1 patient (14%) after 30 months. Distant metastases were observed in 2 other patients (28%) without local or regional recurrence. All 3 patients with recurrences died of their disease. The remaining 4 patients were clinically, endoscopically, and radiographically free of disease, resulting in overall and disease-free survival rates of 57% with mean follow-up of 32.3 months.

Conclusions: These preliminary data suggest a potential role for MIER in the comprehensive management algorithm of SNUC in appropriately selected patients. Patient outcomes including local and regional recurrence, distant metastases, and overall and disease-free survival were comparable to a treatment strategy using traditional craniofacial resection.

Level of evidence: 2b.

1. Introduction

Sinonasal undifferentiated carcinoma (SNUC) is a rare and aggressive neoplasm of the head and neck first described as a distinct clinical entity by Frierson et al [1] in 1986. Arising in the paranasal sinuses, this malignancy occurs near critical structures and usually presents with locally advanced disease and carries high rates of regional

☆ Disclosures/conflicts of interest: Pete S Batra: Medtronic (research grant), LifeCell (consultant), NeilMed (consultant), Xoran (research grant), MedInvent (Research grant); P Daniel Knott: none; Justin B Pavlovich: none; Rahul Seth: none; Peter C Revenaugh: none.

☆☆ Financial support: none.

★ Presented at the Combined Sections Triological Society Meeting on February 4, 2010, in Orlando, FL.

* Corresponding author. Department of Otolaryngology–Head and Neck Surgery, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390, USA. Tel.: +1 214 648 3104; fax: +1 214 648 9122.

E-mail address: pete.batra@utsouthwestern.edu (P.S. Batra).

0196-0709/$ – see front matter © 2010 Elsevier Inc. All rights reserved.
doi:10.1016/j.amjoto.2010.09.006

and distant metastases. Because of the rarity of SNUC and paucity of controlled clinical studies, no consensus exists regarding optimal treatment [2-7]. Multimodality therapy, including chemotherapy, radiotherapy, and surgery, has been widely used in an attempt to improve survival and disease control [2-3]. Two-year survival rates among patients treated in this fashion in reported series to date range from 25% to 67% [2-5].

Traditionally, malignancies involving the paranasal sinuses and the adjacent anterior skull base (ASB) have been treated with craniofacial resection (CFR). This approach offers wide exposure, but is associated with significant morbidity and even mortality [8]. Furthermore, CFR involves external incisions, with potential to alter physical appearance and affect patient quality of life [9]. Endoscopic approaches facilitate diagnosis and evaluation of pathologies affecting the ASB and paranasal sinuses. Increasingly, endoscopic techniques are being adapted for resection of both benign and malignant tumors involving the paranasal sinuses and ASB [10-14]. With accrued experience, indications for endoscopic resection of skull base neoplasia have been expanded with improved outcomes [13,15-19]. The objective of this study is to evaluate the role of minimally invasive endoscopic resection (MIER) in the multimodality treatment paradigm of SNUC.

2. Materials and methods

Retrospective chart review was performed on all patients undergoing treatment of SNUC between January 2002 and July 2009 at the Cleveland Clinic Head and Neck Institute. The Cleveland Clinic's Institutional Review Board approved this study. Data collected included patient demographics, tumor characteristics (primary site, TNM staging), treatment modalities including surgical management (intraoperative findings, surgical margins, complications), as well as the use of adjuvant and neoadjuvant therapy. Individualized treatment regimens were formulated based upon recommendations from the institutional head and neck multidisciplinary tumor board. Patient outcomes were assessed, including recurrence rates, survival (overall and disease-free), and long-term status (disease-free, alive with disease, dead of disease, dead from other causes).

Thirteen patients with SNUC were managed in the study period. Two patients were excluded from survival analyses because they did not fall into 1 of the 2 treatment groups studied (MIER/chemoradiation or definitive chemoradiation only). One of these was treated with palliative radiation, and the other patient underwent CFR and postoperative chemoradiation.

2.1. Statistical analysis

Kaplan-Meier curves were used to calculate overall and disease-free survival at 2 years for all patients and were also stratified based upon treatment type. For all estimates, 95% confidence intervals were calculated. Analyses were performed using R software (version 2.8; Vienna, Austria).

3. Results

3.1. Patient demographics

The mean age for the 13 patients was 51.8 years (range, 16–78). The male to female ratio was 1.2:1. The mean follow-up time was 23.3 months (range, 3–62 months).

3.2. Tumor characteristics

Diagnosis was based on histopathologic review by dedicated head and neck pathologists at the Cleveland Clinic. No specimens had evidence of neuroendocrine, squamous, or glandular differentiation. Table 1 reviews tumor site, stage, therapy, and survival status. Using the American Joint Committee on Cancer criteria for tumor staging, 12 of 13 patients had T4 lesions, whereas 1 patient was staged as T1 tumor limited to the maxillary sinus. Six tumors (46%) were primarily left sided, 3 (23%) were primarily right sided, and the remaining 4 (31%) were bilateral at presentation.

The most common sinuses affected in descending order were the ethmoid in 11 of 13 tumors (85%), sphenoid in 8 (62%), frontal in 6 (46%), and maxillary in 5 (38%). Eight tumors (62%) involved the cribriform plate, with dural involvement in 5 cases (38%) and brain involvement in 3 (23%) of these cases. Seven patients (54%) had involvement of the lamina papyracea, with 4 (31%) of these patients having periorbital involvement and 2 (15%) with orbital involvement at presentation. Three tumors (23%) involved both the pterygomaxillary fossa and infratemporal fossa. Two patients (15%) had involvement of the clivus, and 1 patient (8%) had nasopharyngeal extension.

At presentation, 2 patients had distant disease in the form of liver metastases; and 1 of these 2 patients also had regional disease with bilateral cervical adenopathy.

3.3. Surgical management

Eight patients (62%) underwent surgical treatment. Seven patients underwent MIER for definitive tumor management. Image guidance was used in all 7 cases. One patient in this group required bifrontal craniotomy to clear the superior tumor margin because of intracranial extension. One additional patient underwent open CFR consisting of extended maxillectomy, open sphenoidotomy, and ethmoidectomy with orbital exenteration.

Six (86%) of 7 patients treated with MIER underwent formal endoscopic ASB resection. Reconstruction was performed based on the preference of the attending surgeon in a multilayered fashion in all cases [20]. Three patients were noted to have cerebrospinal fluid leaks intraoperatively, with 2 patients having subarachnoid lumbar drain placement for 3 to 5 days. Neurosurgical assistance was required during

Table 1
Detailed patient characteristics

Pt	Age	Tumor site	TNM stage	Surgical therapies	Adjuvant therapies	Recurrence	Additional procedures	Follow-up (mo)	Status at last follow-up
1	77	Left orbitoethmoid with cribriform plate and dural involvement	T4bN0M0	None	Palliative XRT	None	None	5	DOD
2	39	Left orbitoethmoid with infratemporal fossa and pterygopalatine fossa involvement	T4N0M0	MIER	Preop cisplatin and etoposide, postop XRT	Local recurrence	None	34	DOD
3	34	Left orbitoethmoid with dural and brain involvement	T4bN0M0	MIER with bifrontal craniotomy	Preop cisplatin and etoposide, preop XRT	Distant recurrence	None	7	DOD
4	39	Left frontal, orbitoethmoid with cribriform plate and dural involvement	T4bN0M0	None	Definitive cisplatin and etoposide, XRT	Regional recurrence	None	33	AWOD
5	73	Right sphenoethmoid with lamina papyracea and cribriform plate involvement	T4bN0M0	MIER	Preop cisplatin and etoposide, XRT	None	None	62	AWOD
6	78	Right maxillary, orbitoethmoid, with orbital, dural, infratemporal fossa involvement	T4bN0M0	CFR with orbital exenteration	Postop cisplatin and etoposide, XRT	None	None	5	AWD
7	49	Left sphenoid, frontal, and orbitoethmoid with dural and cribriform plate involvement	T4bN0M0	MIER	Postop cisplatin and etoposide, XRT	None	None	24	AWOD
8	16	Bilateral ethmoid with dural and brain involvement	T4bN0M0	MIER	Preop cisplatin and etoposide, XRT	None	None	17	AWOD
9	51	Bilateral sphenoid, ethmoid	T4N0M0	MIER	Postop cisplatin and etoposide, XRT	Distant recurrence	None	28	DOD
10	51	Bilateral frontal, ethmoid with dural and brain involvement	T4bN0M1	None	Definitive cisplatin and etoposide, XRT.	None	None	8	DOD
11	76	Left maxillary	T1N0M0	MIER	Postop XRT	None	None	54	AWOD
12	47	Bilateral sphenoid with cribriform, dural and brain involvement	T4bN2cM1	None	Definitive cisplatin and etoposide, XRT	None	None	21	AWD
13	44	Right maxillary, ethmoid	T4N0M0	None	Definitive cisplatin and etoposide, XRT	None	None	9	AWOD

2 cases, including patient 3 requiring bifrontal craniotomy. Orbital decompression was necessary in 4 patients, and optic nerve decompression with subtotal resection of the clivus was performed in 1 patient. There were no perioperative complications or delayed cerebrospinal fluid leaks.

3.4. Chemotherapy and radiation therapy

All patients treated in this study received chemotherapy (CTX) and/or radiation therapy (XRT). The most common chemotherapeutic regimen consisted of cisplatin (60 mg/m^2 given once) usually concurrently with etoposide (120 mg/m^2 for 3 days repeated every 3 weeks for 2–5 total cycles).

All patients received radiotherapy with curative intent to the primary site, with the exception of patient 1 who underwent palliative XRT only. Daily fractions (200 cGy) were administered to a total dose of 56 to 70 Gy (mean, 59.4 Gy). Three patients (27%) underwent elective radiation to the neck from 46 to 60 Gy (mean, 53.3 Gy), with 1 receiving preoperative and 2 postoperative therapy. The patient undergoing CFR received postoperative intensity-modulated radiation therapy to the primary site.

Four patients underwent concurrent CTX/XRT as definitive treatment without surgical intervention. Two of these patients received planned preoperative CTX/XRT; however, because no evidence of disease was present on posttreatment imaging or diagnostic endoscopy, surgery was deferred. One of these 2 patients was found to have regional recurrence at 10 months, which was treated with radiation and modified radical neck dissection and was alive without evidence of disease at 23 months after recurrence. The other patient is currently under surveillance without evidence of disease at 9 months. Another patient upon completion of planned preoperative CTX/XRT was found to have unresectable local and distant metastases and died of his disease. The last of the 4 patients was started on CTX and XRT because of large, unresectable intracranial disease. Distant and regional metastases were discovered during treatment, and the patient soon thereafter died of disease.

Six of 7 MIER patients had concurrent CTX/XRT, with 3 (43%) of 7 patients receiving preoperative therapy and 3 (43%) receiving postoperative therapy. One of 7 (patient 2) underwent preoperative CTX followed by postoperative XRT. The sole patient with a T1N0M0 tumor (patient 11) underwent only postoperative radiation without CTX because of advanced age, comorbidities, and limited extent of disease.

The only reported complications of chemotherapeutic or radiation treatments were transient myelosuppression in 2 patients.

Table 2
Outcomes by treatment

Treatment modality	2-y OS (%)	2-y DFS (%)	LR recurrence (%)	Distant recurrence (%)	Follow-up (mo)
MIER (n = 7)	85.7	71.4	14.3	28.9	32.3
Nonoperative (n = 4)	66.7	66.7	25.0	0.0	17.8

OS indicates overall survival; DFS, disease-free survival; LR, local and regional.

3.5. Survival data

Survival and recurrence data were compiled for the 11 patients undergoing either definitive CTX/XRT or MIER. Four patients (36%) recurred following definitive treatment. For the entire cohort, recurrences were found to occur locally in 1 case (9%), regionally in 2 cases (18%), and distantly in 2 cases (18%).

Of the MIER group, simultaneous local (left parapharyngeal space) and regional (left level II lymph node) recurrence was observed in 1 patient (14%) after 30 months. This was treated with adjuvant radiation to the primary site and neck following unilateral selective neck dissection. Distant metastases were observed in 2 other patients (28%) without local or regional recurrence. These were observed as bilateral pulmonary metastases in 1 patient (patient 3) at 6 months and right iliac bone metastasis in the other (patient 9) at 10 months. All 3 patients in the MIER group with recurrences died of their disease at an average of 23 months following therapy.

At the time of last follow-up, 6 (54%) of 11 patients were alive without evidence of disease, 3 (27%) were dead from disease, and 1 patient (9%) was alive with disease. Within the subgroups (Table 2), 3 patients treated with MIER had died of disease; and the remaining 4 patients were clinically, endoscopically, and radiographically free of disease, resulting in overall and disease-free survival rates of 57% at mean follow-up of 32.3 months.

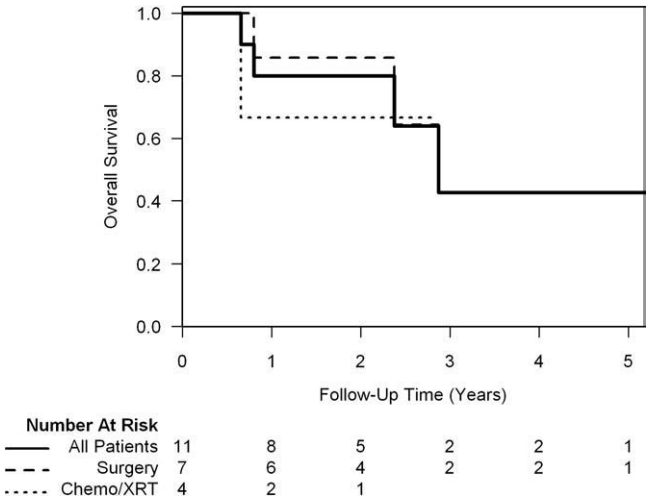

Fig. 2. Disease-free survival by treatment modality.

Of the 4 patients treated with CTX/XRT, 1 was currently undergoing treatment. Of the remaining 3 patients, 1 had died of disease, 1 was alive with disease, and 1 was alive without disease, resulting in overall and disease-free survival of 66% and 33%, respectively, with mean follow-up time of 21 months.

Kaplan-Meier curves for overall and disease-free survival are illustrated in Figs. 1 to 3. Five-year estimates were not calculated because of limited number of patients. Calculated overall survival for all 11 patients included in the survival analyses was 80% at 2 years, and disease-free survival was 70% for all patients. For the patients treated with MIER, overall survival and disease-free survival estimates were 85% and 71.4% at 2 years. The patients treated with CTX/XRT had an overall survival of 66.7% and disease-free survival of 66.7% at 2 years.

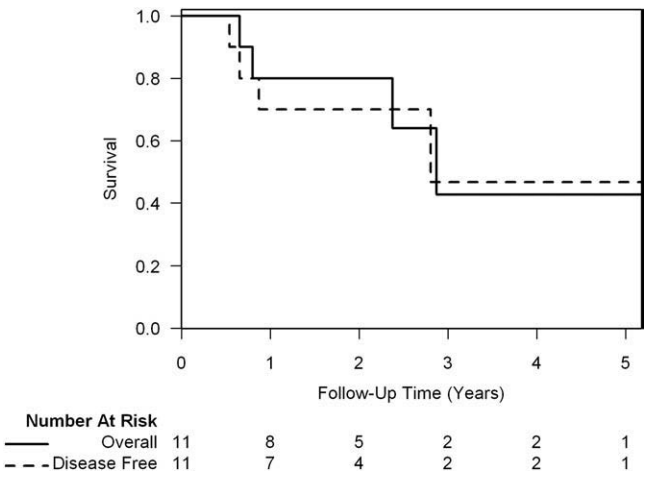

Fig. 1. Overall and disease-free survival for all patients.

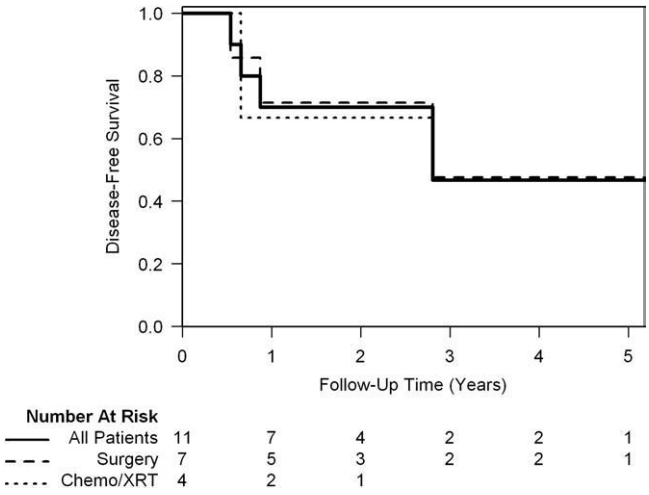

Fig. 3. Overall survival by treatment modality.

4. Discussion

The results of the present study represent the only series to date highlighting the role of MIER as part of multimodality treatment regimen for SNUC. Since its initial description 1986, management of SNUC has remained a significant challenge, with survival reported to be 25% to 65% and 38% to 62% at 2 and 5 years, respectively, among larger published series [3-5,21]. The rarity of the tumor, coupled with varied treatment strategies and use of different staging systems across the literature, underscores the difficulty in interpreting and generalizing outcomes from the previous studies.

In the past, CFR was offered to appropriate patients as the surgical therapy of choice. However, with recent advances in endoscopic therapy and demonstrated efficacy in skull base neoplasm management, MIER may provide a potential alternative for surgical extirpation of SNUC [17]. Irrespective of the preferred surgical technique, the advanced stage at presentation and the propensity for involvement of critical structures exemplify the surgical dilemma in these patients [22]. Twelve (92%) of the 13 patients in this series presented with stage T4 disease, with high rates of orbital (23%), dural (38%), and intracranial (23%) involvement. Musy et al [4] described similar rates of orbital and dural involvement at 33% and 53%, respectively. Interestingly, despite the locally advanced presentation, Chen et al [3] did not find dural involvement to predict overall survival. In our series, among those treated with MIER for complete resection, 2 of 3 patients with dural involvement (one of whom had intracranial extension) were alive without disease at follow-up.

Improvement in overall and disease-free survival has been the foremost goal in treatment of SNUC, with variety of treatment strategies used over time. This study presents a series of patients with overall 2-year survival estimates at 80%. Historically, 2-year survival rates have been lower. In 1996, Righi et al [7] reported on 7 patients treated with combination CFR and XRT, with 2 patients receiving concurrent CTX. Three (42.9%) of the 7 patients were alive with a mean survival time of only 12 months. Miyamoto et al [23] described similar outcomes in 14 patients treated predominantly with XRT and CFR, yielding 57.3% and 38.2% in 2- and 5-year survival rates, respectively. In 2002, Musy et al [4] reported treatment using preoperative multidrug CTX plus radiation followed by CFR in 11 of 20 diagnosed patients. Survival rate of 47% was reported at 2 years. Survival rates were higher for patients undergoing surgery and radiation vs those treated nonsurgically (64% vs 25%), suggesting a role for surgical intervention.

The necessity for surgical intervention was questioned by Rischin et al [5]. Induction, multiagent CTX was given, followed by full-course radiation and single-agent platinum-based concurrent therapy. The 2-year survival was roughly equivalent to prior studies at 64%, suggesting the role of concurrent chemoradiation in the management of SNUC. A high proportion of patients in the present series underwent concurrent chemoradiation, with or without surgery, with acceptable survival. The role of surgery should however not be discounted. It is instrumental in clearing any residual disease after definitive chemoradiation. Interestingly, 2 cases underwent MIER after chemoradiation given abnormal signal in the tumor bed by magnetic resonance imaging. No tumor was present in the specimen on final pathology.

Despite the high rate of regional metastasis at presentation (30%) and regional failure at 3 years (60%), there is no consensus on the treatment of the neck. Tanzler et al [2] suggested irradiation of the N0 neck based upon their experience of 13 patients with clinically N0 necks. Regional control was obtained in 7 (100%) of 7 patients treated with elective neck irradiation vs 4 (66%) of 6 patients who did not receive radiation [2]. Only 2 of our patients underwent elective treatment of the neck, with neither patient recurring at mean follow-up of 9 months. However, a 9% rate of regional recurrence in our series may skew these results.

Distant metastasis has been reported to occur in 13% to 43% of patients [2-4,21]. Analysis performed by Chen et al [3] did not identify factors predictive of distant metastasis. In our study, distant metastases occurred in 9% of patients. Despite 6 of 7 patients receiving CTX, there were more distant recurrences in the MIER group vs the CTX/XRT group (28.9% vs 0%). However, this could be attributed to the shorter follow-up time for the CTX/XRT group (21 vs 32 months). On the other hand, the rate of locoregional recurrence was lower in the MIER group (14.3% vs 25%) despite longer follow-up.

Despite the data accrued to date, definitive recommendations for optimal management strategy remain elusive. Tanzler et al [2] suggest treating patients with CFR and postoperative radiation, whereas Rischin et al [5] have recommended induction platinum- and 5-fluorouracil–based CTX followed by concurrent platinum-based CTX and XRT. In our study, all of the patients were offered concurrent chemoradiation, in addition to surgical resection based upon the recommendation of a multidisciplinary tumor board. Of the patients undergoing MIER (n = 7), the 2-year overall survival and disease-free survival were 85% and 71.4%, respectively. This is considerably higher than the larger reported series [2-6,21,23]. At present, patients with surgically resectable disease are offered surgery followed by adjuvant chemoradiation. Patients with advanced disease not deemed resectable are given preoperative chemoradiation, followed by surgery if the disease becomes resectable. If surgery is offered, MIER is preferred to CFR if feasible. Although the timing of CTX is not clear, its addition should be seriously considered in all cases without medical contraindications, given the high rate of regional and distant disease.

The emergence of endoscopic techniques, including image-guided technology and sophisticated instrumentation, has revolutionized the treatment of sinonasal and skull base pathology. These technologies can offer significant advantages in selected cases when used alone or in combination

with more conventional open techniques [10,13-14,24]. Superior visualization, avoidance of facial incisions, low complication rates, decreased morbidity, and acceptable disease-free survival in patients are all possible advantages of endoscopic or endoscopic-assisted techniques [17,18]. In the present series, patients did not have any intra- or postoperative complications, in contrast to higher complication rates associated with CFR [9].

The limitations of the endoscopic techniques should be acknowledged as well. Performance of safe and effective endoscopic skull base surgery requires specialized equipment, personnel expertise, and a comprehensive skull base team. It is also suggested that an incremental approach to complex skull base techniques can improve outcomes and decrease risk [25]. The limitations of endoscopic skull base surgery are still being defined; but in the setting of this study, contraindications to endoscopic approaches to SNUC include extensive intracranial or dural involvement, facial soft tissue involvement, frontal sinus anterior table involvement, extension far laterally over the orbital roof, or tumor location limited by critical neurovascular structures [15,17].

Further studies are necessary to fully elucidate the optimal treatment regimen in SNUC given its rarity and heterogenous treatment across institutions. Long-term outcome studies, prospective data, and multi-institutional evaluations will be critical in reducing bias and providing meaningful data to define the optimal approach to improve outcomes for this aggressive malignancy.

5. Conclusions

This single-institution study reports outcomes of 13 patients with SNUC. Seven patients were treated with MIER along with chemoradiation, whereas 4 were treated with definitive chemoradiation. Results suggest comparable or improved outcomes in those patients treated with MIER plus chemoradiation therapy compared with patients treated with chemoradiation therapy alone. Thus, MIER of SNUC may be considered as part of a multimodality treatment regimen in properly selected patients with SNUC treated at centers experienced in endoscopic skull base surgery.

References

[1] Frierson Jr HF, Mills SE, Fechner RE, et al. Sinonasal undifferentiated carcinoma. An aggressive neoplasm derived from schneiderian epithelium and distinct from olfactory neuroblastoma. Am J Surg Pathol 1986;10:771-9.

[2] Tanzler ED, Morris CG, Orlando CA, et al. Management of sinonasal undifferentiated carcinoma. Head Neck 2008;30:595-9.

[3] Chen AM, Daly ME, El-Sayed I, et al. Patterns of failure after combined-modality approaches incorporating radiotherapy for sinonasal undifferentiated carcinoma of the head and neck. Int J Radiat Oncol Biol Phys 2008;70:338-43.

[4] Musy PY, Reibel JF, Levine PA. Sinonasal undifferentiated carcinoma: the search for a better outcome. Laryngoscope 2002;112(8 Pt 1): 1450-5.

[5] Rischin D, Porceddu S, Peters L, et al. Promising results with chemoradiation in patients with sinonasal undifferentiated carcinoma. Head Neck 2004;26:435-41.

[6] Kim BS, Vongtama R, Juillard G. Sinonasal undifferentiated carcinoma: case series and literature review. Am J Otolaryngol 2004;25:162-6.

[7] Righi PD, Francis F, Aron BS, et al. Sinonasal undifferentiated carcinoma: a 10-year experience. Am J Otolaryngol 1996;17:167-71.

[8] Ganly I, Patel SG, Singh B, et al. Complications of craniofacial resection for malignant tumors of the skull base: report of an International Collaborative Study. Head Neck 2005;27:445-51.

[9] Fukuda K, Saeki N, Mine S, et al. Evaluation of outcome and QOL in patients with craniofacial resection for malignant tumors involving the anterior skull base. Neurol Res 2000;22:545-50.

[10] Thaler ER, Kotapka M, Lanza DC, et al. Endoscopically assisted anterior cranial skull base resection of sinonasal tumors. Am J Rhinol 1999;13:303-10.

[11] Cannady SB, Batra PS, Sautter NB, et al. New staging system for sinonasal inverted papilloma in the endoscopic era. Laryngoscope 2007;117:1283-7.

[12] Pryor SG, Moore EJ, Kasperbauer JL. Endoscopic versus traditional approaches for excision of juvenile nasopharyngeal angiofibroma. Laryngoscope 2005;115:1201-7.

[13] Batra PS, Citardi MJ, Worley S, et al. Resection of anterior skull base tumors: comparison of combined traditional and endoscopic techniques. Am J Rhinol 2005;19:521-8.

[14] Castelnuovo PG, Belli E, Bignami M, et al. Endoscopic nasal and anterior craniotomy resection for malignant nasoethmoid tumors involving the anterior skull base. Skull Base 2006;16:15-8.

[15] Snyderman CH, Pant H, Carrau RL, et al. What are the limits of endoscopic sinus surgery?: the expanded endonasal approach to the skull base. Keio J Med 2009;58:152-60.

[16] Snyderman CH, Carrau RL, Kassam AB, et al. Endoscopic skull base surgery: principles of endonasal oncological surgery. J Surg Oncol 2008;97:658-64.

[17] Batra PS, Luong A, Kanowitz SJ, et al. Outcomes of minimally invasive endoscopic resection of anterior skull base neoplasms. Laryngoscope 2010;120:9-16.

[18] Lund V, Howard DJ, Wei WI. Endoscopic resection of malignant tumors of the nose and sinuses. Am J Rhinol 2007;21:89-94.

[19] Nicolai P, Battaglia P, Bignami M, et al. Endoscopic surgery for malignant tumors of the sinonasal tract and adjacent skull base: a 10-year experience. Am J Rhinol 2008;22:308-16.

[20] Leong JL, Citardi MJ, Batra PS. Reconstruction of skull base defects after minimally invasive endoscopic resection of anterior skull base neoplasms. Am J Rhinol 2006;20:476-82.

[21] Rosenthal DI, Barker Jr JL, El-Naggar AK, et al. Sinonasal malignancies with neuroendocrine differentiation: patterns of failure according to histologic phenotype. Cancer 2004;101:2567-73.

[22] Suarez C, Llorente JL, Fernandez De Leon R, et al. Prognostic factors in sinonasal tumors involving the anterior skull base. Head Neck 2004; 26:136-44.

[23] Miyamoto RC, Gleich LL, Biddinger PW, et al. Esthesioneuroblastoma and sinonasal undifferentiated carcinoma: impact of histological grading and clinical staging on survival and prognosis. Laryngoscope 2000;110:1262-5.

[24] Hanna E, DeMonte F, Ibrahim S, et al. Endoscopic resection of sinonasal cancers with and without craniotomy: oncologic results. Arch Otolaryngol Head Neck Surg 2009;135:1219-24.

[25] Snyderman C, Kassam A, Carrau R, et al. Acquisition of surgical skills for endonasal skull base surgery: a training program. Laryngoscope 2007;117:699-705.