ORIGINAL ARTICLE

RESULTS OF ENDOSCOPIC RESECTION FOLLOWED BY RADIOTHERAPY FOR PRIMARILY DIAGNOSED ADENOCARCINOMAS OF THE PARANASAL SINUSES

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Abstract: *Background.* Adenocarcinoma is the most frequent histological subtype of paranasal sinus malignancy diagnosed in Belgium. Classical treatment consists of an external surgical approach (lateral rhinotomy with medial maxillectomy or craniofacial resection) followed by radiotherapy. The role, possibilities, and limitations of endoscopic sinus surgery (ESS) are to date unknown.

Methods. We studied 44 patients with primary (not treated previously) adenocarcinoma treated with endoscopic sinus surgery and radiotherapy between 1992 and 2004.

Results. The median follow-up of the patients alive at the end of the study period was 36 months. For the 3-year follow-up, the overall survival, disease-specific survival, and local control rate were 81%, 91%, and 73%, respectively. Corresponding rates for the 5-year follow-up were 53%, 83%, and 62%. Union Internationale Contre le Cancer T classification did not appear to influence these results.

Conclusions. Endoscopic sinus surgery followed by radiotherapy for primary adenocarcinoma of the paranasal sinuses gives oncological results comparable to those of standard external approaches. ©2008 Wiley Periodicals, Inc. *Head Neck* **30:** 728–736, 2008

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Malignancies of the paranasal sinuses and nasal cavity are rare. In Belgium they account for only 3% of the overall head and neck oncology diagnoses.[1,2] Worldwide, squamous cell carcinoma is the most frequently found paranasal/nasal malignancy, mainly occurring in the maxillary sinus (60%). Squamous cell carcinoma and esthesioneuroblastoma are the most frequently reported histologies in North American series.[3] The intestinal type of adenocarcinoma occurs mainly in the ethmoid sinus. Because sinus adenocarcinoma is generally found in areas where there is a flourishing wood or leather industry, organic dust inhalation is thought to be responsible for tumorigenesis. In Belgium, adenocarcinoma of the sinuses is recognized by the Ministry of Health as an occupational disease. The Union Internationale Contre le Cancer (UICC) classification is today the most often used staging system.[4]

Treatment of paranasal sinus tumors has developed empirically. Surgical and radiotherapeutic treatment is difficult because the tumor lies near and has often invaded several vital structures.[5] Surgical resection is generally considered to be the keystone of treatment and can be done

via a transfacial (lateral rhinotomy, midfacial degloving, or Caldwell-Luc approach), craniofacial (associating a craniotomy with the transfacial approach), or transnasal endoscopic approach. Radiotherapy and chemotherapy are usually administered postoperatively.

Draf,[6] Messenklinger,[7] and Stammberger[8] first separately described endoscopic nasal surgery for inflammatory sinusal disease. Later, the endoscopic technique proved valuable in the management of benign and malignant tumors of the paranasal sinuses, mainly as an instrument for diagnosis, preoperative biopsy sampling, and postoperative follow-up.[9,10] Later, endoscopic surgery was described as an alternative to the lateral rhinotomy approach in the extracranial removal of a sinonasal tumor when a craniofacial resection was performed.[11,12] Since 1999, results of series of maxillofacial and skull base tumors treated with endoscopic approach as surgical technique have been published. Cohorts are always very small and often include a diversity of histologies and treatment protocols.[13–19] Postoperative radiotherapy is nearly always arranged. In some French centers, however, the treatment protocol differs; Roux,[20] Brasnu et al,[21] and George et al[22] published their results after treatment with neoadjuvant chemotherapy, followed by resection of the tumor. In Canada, Waldron et al[23] starts the treatment with radiotherapy, followed by surgery.

Within tumors of the paranasal sinuses, disease-related death is mainly caused by local recurrence of the tumor,[5,24,25] and survival is consequently determined by local control of the disease. We tried to clarify this key oncologic outcome in our patient group. In the current study, we analyzed the survival of a large well-defined group of patients with a specific tumor localization and histopathology and undergoing a new treatment technique. We documented long-term follow-up and compared our findings with previously reported results arising from the use of classical treatment strategies, thus characterizing the indications and limits of the endoscopic approach as a resection technique.

PATIENTS AND METHODS

Patients. From 1992 until 2004, 44 patients presenting in our center with a previously untreated adenocarcinoma of the ethmoid sinus underwent an endoscopic resection. This approach was chosen when no invasion in dura, brain, or orbita was shown on preoperative CT or MRI. When such invasion was present, a craniofacial resection was offered. Patients presenting with a T4B tumor showing only limited dural involvement were also eligible for the endoscopic approach. All but 1 of the subjects were male, and the mean age at diagnosis was 62 years.

Diagnosis was made by histological examination of a preoperative biopsy specimen, with confirmation after surgery. The tumor extent was preoperatively assessed using imaging studies. After 1998, all patients had a preoperative CT with an MRI scan. Four patients treated before 1998 had only a preoperative CT scan. A total of 40 patients had both CT and MRI. On the basis of these imaging studies, all tumors were staged using the UICC 2002 TNM classification.[3]

Patients were evaluated for the presence of regional and distant metastasis. Routine blood tests, chest X-ray and an abdominal ultrasound examination were performed. Every patient was informed about the surgical technique and the possible complications. Informed consent was obtained in all cases.

Treatment and Follow-up. An endoscopic resection of the tumor was performed with cold instruments under general anesthesia by 1 of the senior staff surgeons. For T1 tumors, the technique used can be described as an "en bloc" resection. After removal of the surrounding nondiseased structures for optimal approach, the small tumor was mobilized to allow a view of its insertion site and then removed in 1 piece. Middle-sized (T2) tumors were removed by a "phased" resection. This method consisted of a preparatory phase in which the tumor bulk was visualized. Using atraumatic suction, the insertion site of the tumor was defined as precisely as possible. The next step consisted of removing the tumor bulk using cold instruments and, lately, a microdebrider. In the last step, the tumor origin was broadly circumscribed by standard complete and radical fronto-spheno-ethmoidectomy, including a large middle meatal antrostomy and a resection of the upper third of the septum with a margin of about 1 cm where possible. For larger tumors (T3-T4), there was no option other than "piecemeal" removal, followed by an "en bloc" resection of the paranasal sinuses and nasal septum. The septum was never completely resected, nor was the inferior turbinate. If the tumor was unilateral, no contralateral radical surgery was undertaken.

Table 1. TNM classification according to the Union Internationale Contre le Cancer (UICC).

T status	Nasal cavity and ESS	No. of patients in this study
T1	One subsite	1
T2	Two subsites or adjacent nasoethmoidal site	26
T3	Medial wall/floor orbit, maxillary sinus, palate, cribriform plate	5
T4A	Anterior orbit, cheek skin, anterior cranial fossa, pterygoid plate, sphenoidal/frontal sinus	9
T4B	Orbital apex, dura, brain, middle cranial fossa, cranial nerves other than V2, nasopharynx, clivus	3

Abbreviation: ESS, ethmoidal sinus tumor.

After surgical treatment, follow-up every 2 months was scheduled. The oncological status was followed by clinical endoscopic examination of the nasal cavity and paranasal sinuses. Radiographic follow-up was only done when a clinically suspicious lesion was detected.

All patients had postoperative radiotherapy planned. The dosage of radiotherapy given was usually 60 Gy, given in fractions of 2 Gy. The dosage varied from 50 to 70 Gy. Radiotherapy generally started 5 weeks after surgery.

Statistical Methods. All information was collected retrospectively and processed with the Statistical Package for Social Sciences (SPSS version 12.0, SPSS, Chicago, Illinois) in the laboratory of Physics and Audiology of the University Hospital St. Raphael, Leuven, Belgium. The overall survival, disease-specific survival, and the local control rates were calculated using the Kaplan-Meier method.[26]

The time interval for calculating overall survival was determined as the time between the date of surgery and the day of death, regardless of the cause of death. For calculating disease-specific survival, the time interval between the date of treatment and the date of death was calculated only if death was considered as being causally related to the tumor. The time interval for calculating the local control rate was determined as the time between the day of surgery and the date of diagnosis of the first recurrence.

The log-rank test for a trend was used to estimate the prognostic influence of the T classification on the incidence of local recurrence and the prognostic influence of both on survival.

RESULTS

It is interesting to note that, after exclusion of 16 patients for whom no information was available, 25 (89%) of the remaining 28 patients had an intense exposure to wood dust in their history.

Table 1 shows the patient distribution according to T classification. All T4A tumors showed sphenoidal sinus involvement, whereas all T4B tumors showed perforation of the cribriform plate with dural involvement. Metastatic disease in the neck or at distant sites was not diagnosed at first diagnosis.

One patient refused radiotherapy. Radiotherapy was discontinued in 1 patient who showed lung metastases and in a second patient who suffered from a cerebrovascular accident. No information was available for 3 patients who had radiotherapy in another hospital. Three patients had a boosting dosage, which was 10 or 20 Gy. In 1 patient, the neck was also treated. The mean overall treatment time was 55 days. Overall, 31 patients were treated with a conventional technique using 3-field photons, and 8 patients received intensity-modulated radiotherapy.

Median follow-up, as well as follow-up of the patients alive at the end of follow-up, was 36 months. The 3-year overall survival was 81% (±7% standard error). The 5-year overall survival was 53% (±10%), with 57% (±13%) for T2 tumors and 37% (±19%) for T4 tumors (Figures 1A and 1B). The 3-year disease-specific survival was 91% (±5%). The 5-year disease-specific survival was 83% (±7%), with 83% (±10%) for T2 tumors and 83% (±15%) for T4 tumors (Figures 2A and 2B). The 3-year recurrence-free survival was 73% (±8%). The 5-year recurrence-free survival was 62% (±10%), with 66% (±14%) for T2 tumors and 67% (±16%) for T4 tumors (Figures 3A and 3B).

Following primary treatment, 12 (27%) of 44 patients presented with a local recurrence. Six of them, following salvage, presented with a second recurrence later on. The first recurrences were treated by surgery. Three patients received a craniofacial resection because of intracranial extension of the recurrence, and the others underwent another endoscopic resection of their tumor.

The overall and disease-specific survival rates were not statistically significantly determined by

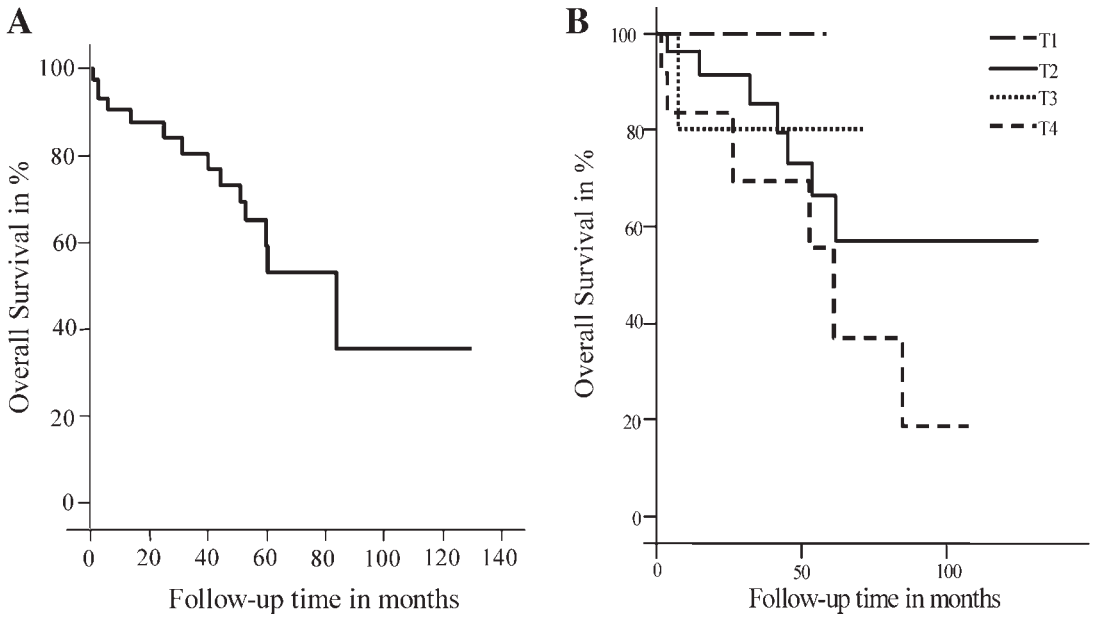

FIGURE 1. (**A**) Overall survival of the whole group. (**B**) Overall survival of the T subgroups.

occurrence of local recurrence (log-rank test, $p = .21$ and $p = .09$, respectively) or by the T classification (trend log-rank test, $p = .18$ and $p = .09$, respectively). There was no statistically significant influence of T classification on local control (trend log-rank $p = .86$).

By evaluating time and location of recurrence after treatment, we could observe a difference between early and late recurrences. Two patients presented a recurrence earlier than 12 months after treatment, and another 6 presented recurrence before 24 months of follow-up had passed.

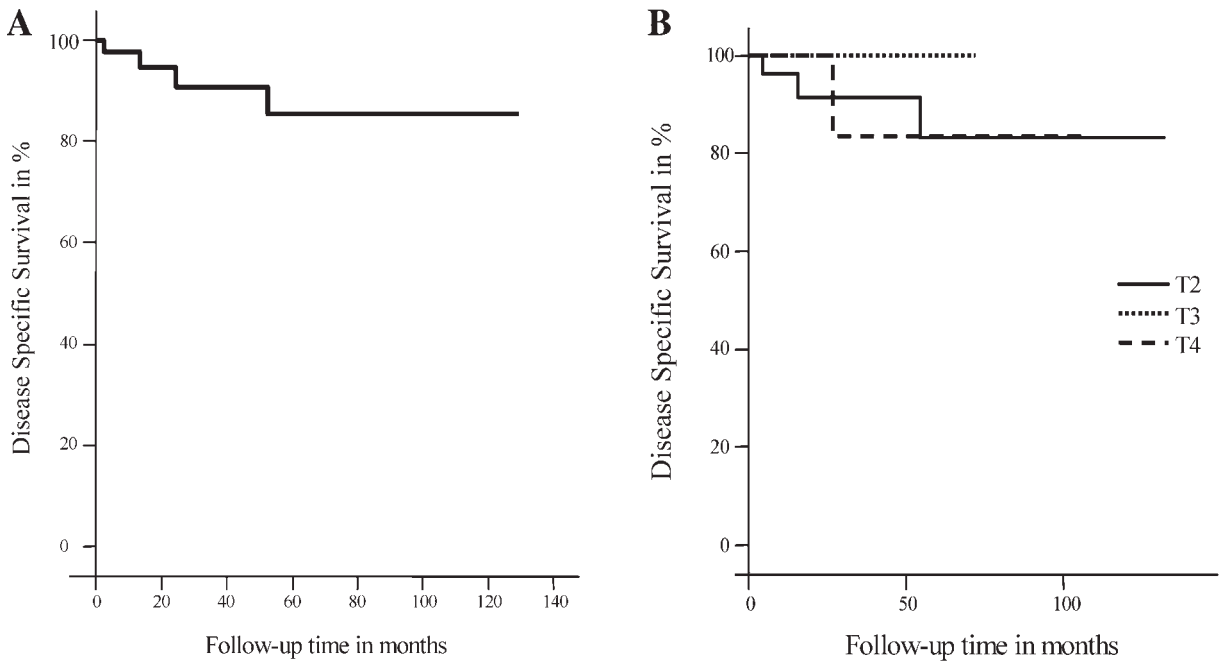

FIGURE 2. (**A**) Disease-specific survival of the whole group. (**B**) Disease-specific survival of the different T subgroups.

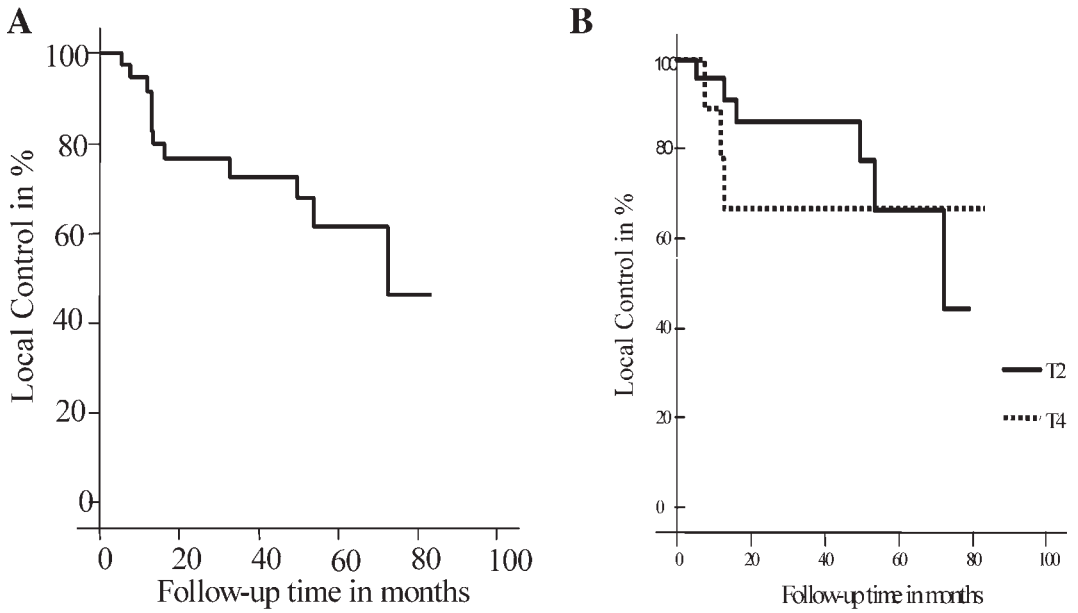

FIGURE 3. (**A**) Local control of the whole group. (**B**) Local control of the T2 and T4 groups separately.

Between 24 and 48 months of follow-up, only 1 patient showed a local recurrence. After 48 months, 3 patients presented with a local recurrence (for these late recurrences, the mean tumor-free interval was 52 months). The site of recurrence was often the nasal septum or the roof of the ethmoid sinus if the recurrence occurred early (before 24 months after treatment). Late recurrences presented with multiple tumor sites, tumor growth distant from the primary site, or even situated on the contralateral side (Table 2). Regional recurrence (neck metastasis) did not occur. Distant metastasis occurred in 3 patients: 1 patient presented with metastasis to the lungs; 1 patient presented with metastasis to the brain; and 1 patient had multiple metastases.

At the moment of finalising this report, 29 (66%) of 44 patients were tumor free and alive.

Table 2. Time and localisation of recurrences.

	T classification	Year of primary treatment	Year of local Recurrence	Months disease free	Localization of recurrence	Treatment of recurrence
Patient 1	2	1999	1999	6	Roof of ethmoid sinus	CFR
Patient 2	4A	2003	2004	8	Septum	ESS
Patient 3	3	2003	2004	13	Septum	ESS
Patient 4	2	1994	1995	13	Superior concha Roof of ethmoid sinus Septum	ESS
Patient 5	4B	2001	2002	13	Intracranial	CFR
Patient 6	1	1999	2001	14	Roof of ethmoid sinus	ESS
Patient 7	2	1999	2002	16	Septum	ESS
Patient 8	4B	1995	1996	24	Intracranial	CFR
Patient 9	3	2000	2003	33	Sphenoidal sinus	ESS
Patient 10	2	1993	1997	50	Middle concha Posterior ethmoid	ESS
Patient 11	2	1998	2003	54	Roof of ethmoid sinus	ESS
Patient 12	2	1998	2004	73	Anterior ethmoid Lamina papyracea Lamina cribrosa Septum	ESS

Abbreviations: CFR, craniofacial resection; ESS, endoscopic sinus surgery.

There was 1 patient alive with active local recurrent disease. The median follow-up for patients alive at the end of follow-up was 36 months, and the mean follow-up was 42 months. In total, 4 patients died of their adenocarcinoma. Two of these patients had both a local recurrence and a distant metastasis, 1 died of local disease without metastasis, and 1 died of distant metastasis but with local control. Ten patients died from causes unrelated to the tumor: cerebrovascular accident ($n = 2$); encephalitis, suicide, pneumonia, car accident, cardiac pathology, pancreatic carcinoma, intestinal carcinoma with distant metastasis, and unknown ($n = 1$ for each). The recurrence-free interval varied from 6 to 73 months, with a mean of 25 months.

For the group of 12 patients with a T4 tumor, at the time of analysis, 6 were alive without tumor, 5 patients had died of another disease, and 1 had died of local recurrence and distant metastasis. Of the 3 patients initially presenting with a T4B tumor, 2 presented with a local recurrence after 12 and 13 months, respectively (1 of these also presented with a distant metastasis), and 1 showed no recurrence.

A systematic or standard scoring of morbidity was not performed after treatment. All patients complained of crusting in the nose, and all had regular visits to their ENT surgeon for local cleaning and care. There was no case of posttreatment eye or vision damage. One patient reported persistent severe facial pain that was resistant to all pain treatments and without evidence of residual or recurrent disease. This patient unfortunately committed suicide.

DISCUSSION

The low morbidity and mortality rates, the low risk of complications, the absence of facial incisions as well as the short hospital stay are clear advantages of the minimal invasive aspect of the endoscopic approach. Considering this, we would like to open the debate about the impact on survival of en bloc versus a piecemeal resection in the treatment of this particular tumor. In endoscopic sinus surgery, only small tumors can be removed en bloc, larger tumors have to be excised in fragments. As this seems contradictory to one of the main rules of oncological surgery that focuses on a maximal en bloc resection with margins wherever possible, there are some observations and reflections to be made.

First, piecemeal resection could involve the risk of tumor spilling, causing an iatrogenic tumor implantation. There are currently no data supporting this hypothesis in malignant paranasal sinus disease. Nevertheless, Cantu et al[27] describes an unfavorable prognosis of previously treated patients compared with primary cases treated with an anterior craniofacial resection of malignant ethmoid tumors, which he attributes to possible seeding of neoplastic cells by previous surgery and selection of more malignant clones by radiotherapy.

Second, there is the debate about obtaining clear margins when resecting a tumor, and subsequently about the limits of an endoscopic approach. After analyzing our results, we can state that, staying on the safe side, the limit for endoscopic treatment should be guided by the dural invasion, and not by the parenchymal invasion, as was previously our policy. The anatomy dictates where adequate margins can be obtained (especially toward the anterior skull base). Attacking the tumor by an open approach from its frontal or its superior boundary is probably the best way to obtain clear margins around the tumoral process; however, because of the structure of the paranasal sinuses, en bloc resection is difficult to achieve even with an open approach. How realistic it is to assume that the en bloc resection can be performed via a craniofacial approach has been questioned, and the need for an en bloc resection has thus been challenged.[12,28] Suarez[29] studied a population of 100 patients with malignancy of the paranasal sinuses (53 cases of adenocarcinoma) treated by combined anterior craniofacial resection and found that spread into the dura had no significant impact on survival; however, involvement of the brain did statistically affect survival. If the tumor is small and well localized under the cribriform plate, a resection using an endoscopic approach seems very safe. If the tumor extends to the cribriform plate, however, a craniofacial resection in combination with an endoscopic approach could offer safer margins because the difficult area is approached from both sides (even if obtaining safe margins at this particular site is difficult with endoscopy as well as with an open technique). There might also be the question whether or not control of the margins by frozen section and biopsy might be useful. Because of the attachment of the mucosa to bone and cartilage, pathologists have difficulties analyzing the specimens of frozen sections.[10,30] Shah et al[1] made frozen sections and found the same local recurrence

rates in patients with positive and negative surgical margins.

Third, by analyzing the occurrence of recurrent disease after endoscopic resection, we think there might be a necessity of removing all of the sinusal mucosa when primarily treating an adenocarcinoma of the ethmoid sinus. However, identifying the morbidity incidence after performing this technique would be important. The recurrence pattern observed in our study showed that, in contrast to late recurrences, early recurrences occurred at the same localization as the primary tumor. Specifically, the roof of the ethmoid sinus, the sphenoid sinus, and the nasal septum were prone to early recurrences. This outcome is probably attributable to the fact that obtaining adequate margins in these locations is difficult for anatomical reasons.[12,28] Recurrences that occurred in a late phase often were multiple, situated in a very different area from the initial presentation or presented on the contralateral side. This outcome is likely the result of the chronic exposure of the entire sinonasal mucosa to the toxic wood dust, leading to a globally diseased upper respiratory mucosa and potential risk of developing malignancy in other areas.[31,32] It is possible that those late recurrences would better be considered as second primaries.

Our series is the largest series of primary adenocarcinoma treated by endoscopic resection (infrequently used and described technique) followed by radiotherapy. This makes it a homogeneous group that can be compared to similar groups described in the literature. Often, studies published on this topic involve more heterogeneous groups differing in pathology as well as in localization of the tumoral process. In addition, not all centers use the same classification. Global results of such series cannot be compared. We found that only 5 studies specifically deal with ethmoidal adenocarcinomas[21,33–36] (Table 3).

Our results for overall, disease-specific, and recurrence-free survival are in the range of published results. After 5 years, the recurrence-free survival was 62%, a value in the published range of 59%[33] and 78%[36]; the disease-specific survival was 83% in our study: situated at the upper end of the range of 36%[33] and 87%.[36] Not only does endoscopic resection seem to be a promising alternative technique to open surgery, but also the low morbidity of endoscopic resection can play an important role in survival figures.

In conclusion, endoscopic resection as a surgical technique for removal of adenocarcinoma of

Table 3. Overview list of published studies on treatment of adenocarcinomas only.

Study	No.of patients	T1/T2/T3/T4, %	5-y OS, %†	5-y DSS, %‡	5-y RFS, %§	Follow-up	Treatment	Treatment period	Kind of Chemotherapy
Brasnu et al[21]	22	45/5/50*	68 (3 y OS%)	NS	66 (3-y RFS %)	NS	Chemo + surg (CFR)	1984–1992	5-fluorouracil and cisplatin
Claus et al[33]	47	4/36/24/36	60	36	59	32 mo	Surg (CFR80%, mentioning ESS) + RT	1985–2001	
Stoll et al[34]	76	3/18/58/21	80	NS	NS	NS	Surg (LR, CFR) ± RT	1975–2000	
Moreau et al[35]	25	4/24/36/36	44	NS	NS	NS	Surg (CFR) + RT	1985–1993	
Knegt et al[36]	62	5/16/39/40	72	87	78	8.2 y	S (CL) + topChemo	1976–1997	5-fluorouracil
This study	44	2/59/11/28	53	83	62	36 mo	Surg (ESS) + RT	1993–2004	

Abbreviations: OS, overall survival; DSS, disease-specific survival; RFS, recurrence-free survival; FU, follow-up; NS, not specified; Chemo, chemotherapy; Surg, surgery; CFR, craniofacial resection; ESS, endoscopic sinus surgery; RT, radiotherapy; LR, lateral rhinotomy; CL, calwell luc; topChemo, topical chemotherapy.

**Different classification used.*

†Overall survival measured to death of any cause or end of follow-up.

‡Disease-specific survival measured to death from disease (local, regional, or metastasis) or end of follow-up.

§Recurrence-free survival measured to the first local recurrence or end of follow-up.

the paranasal sinuses, followed by radiotherapy, seems a technically correct approach provided that the indications and limits of the technique are observed. The limits of the technique were defined by the extent of the disease into the brain parenchyma in this series; however, our results suggest that the limit for endoscopic removal should be invasion into the dura. If the invasion reaches the dura, a craniofacial resection approach should be considered, a suggestion that warrants further study. Another element for further investigation is the possible need for removal of all of the sinonasal mucosa to diminish the risk of late recurrence from the known effects of wood dust carcinogen on the whole upper respiratory mucosa. The results of local control of disease and survival after treatment of adenocarcinoma of the ethmoidal sinus by endoscopic resection and radiotherapy are very good and comparable to those published in literature. We conclude that, in experienced hands, endoscopic resection is a valid alternative to open resection in treating adenocarcinoma of the ethmoid sinus.

REFERENCES

1. Shah JP, Kraus DH, Bilsky MH, Gutin PH, Harrison LH, Strong EW. Craniofacial resection for malignant tumors involving the anterior skull base. Arch Otolaryngol Head Neck Surg 1997;123:1312–1317.
2. Mosesson RE, Som PM. The radiographic evaluation of sinonasal tumors: an overview. Otolaryngol Clin North Am 1995;28:1097–1115.
3. Bush SE, Bagshaw MA. Carcinoma of the paranasal sinuses. Cancer 1982;50:154–158.
4. Sobin LH, Wittekind C. TNM Classification of malignant tumours. UICC International Union Against Cancer, 5th ed. New York: Wiley-Liss; 2002.
5. Rosen A, Vokes EE, Scher N, Haraf D, Weichselbaum RR, Panje WR. Locoregionally advanced paranasal sinus carcinoma. Favorable survival with multimodality therapy. Arch Otolaryngol Head Neck Surg 1993;119:743–746.
6. Draf W. Endoscopy of the paranasal sinuses. New York: Springer-Verlag; 1983.
7. Messerklinger W. Endoscopy of the nose. Baltimore: Urban and Schwarzenber; 1978.
8. Stammberger H. Endoscopic endonasal surgery-concepts in treatment of recurring rhinosinusitis. I. Anatomic and pathophysiologic considerations. Otolaryngol Head Neck Surg 1986;94:143–147.
9. Homer JJ, Jones NS, Bradley PJ. The role of endoscopy in the management of nasal neoplasia. Am J Rhinol 1997;11:41–47.
10. Blokmanis A. Endoscopic diagnosis, treatment, and follow-up of tumours of the nose and sinuses. J Otolaryngol 1994;23:366–369.
11. Thaler ER, Kotapka M, Lanza DC, Kennedy DW. Endoscopically assisted anterior cranial skull base resection of sinonasal tumors. Am J Rhinol 1999;13:303–310.
12. McCutcheon IE, Blacklock JB, Weber RS, et al. Anterior transcranial (craniofacial) resection of tumors of the paranasal sinuses: surgical technique and results. Neurosurgery 1996;38:471–479.
13. Goffart Y, Jorissen M, Daele J, et al. Minimally invasive endoscopic management of malignant sinonasal tumours. Acta Otorhinolaryngol Belg 2000;54:221–232.
14. Blockmühl U, Minovi A, Kratzsch B, Hendus J, Draf W. Endonasal micro-endoscopic tumor surgery: state of the art [in German]. Laryngorhinootologie 2005;84:884–891.
15. Roh HJ, Batra PS, Citardi MJ, Lee J, Bolger WE, Lanza DC. Resection of sinonasal malignancies: a preliminary report. Am J Rhinol 2004;18:239–246.
16. Batra PS, Citardi MJ, Worley S, Lee J, Lanza DC. Skull base tumors: comparison of combined traditional and endoscopic techniques. Am J Rhinol 2005;19:521–528.
17. Stammberger H, Anderhuber W, Walch C, Papaefthymiou G. Possibilities and limitations of endoscopic management of nasal and paranasal sinus malignancies. Acta Otorhinolaryngol Belg 1999;53:199–205.
18. Poetker DM, Toohill RJ, Loehrl TA, Smith TL. Endoscopic management of sinonasal tumors: a preliminary report. Am J Rhinol 2005;19:307–315.
19. Lund V, Howard DJ, Wei WI. Endoscopic resection of malignant tumors of the nose and sinuses. Am J Rhinol 2007;21:89–94.
20. Roux FX, Brasnu D, Devaux B, et al. Ethmoid sinus carcinomas: results and prognosis after neoadjuvant chemotherapy and combined surgery—a 10-year experience. Surg Neurol 1994;42:98–104.
21. Brasnu D, Laccourreye O, Bassot V, Laccourreye L, Naudo P, Roux FX. Cisplatin-based neoadjuvant chemotherapy and combined resection for ethmoid sinus adenocarcinoma reaching and/or invading the skull base. Arch Otolaryngol Head Neck Surg 1996;122:765–768.
22. George B, Salvan D, Luboinski B, Boissonnet H, Lot G. [Malignant tumors of the ethmoid sinuses. A homogenous series of 41 cases operated on by mixed approaches]. Neurochirurgie 1997;43:121–124. French.
23. Waldron JN, O'Sullivan B, Warde P, et al. Ethmoid sinus cancer: twenty-nine cases managed with primary radiation therapy. Int J Radiat Oncol Biol Phys 1998;41:361–369.
24. Kraus DH, Sterman BM, Levine HL, Wood BG, Tucker HM, Lavertu P. Factors influencing survival in ethmoid sinus cancer. Arch Otolaryngol Head Neck Surg 1992; 118:367–372.
25. Alvarez I, Suarez C, Rodrigo JP, Nunez F, Caminero MJ. Prognostic factors in paranasal sinus cancer. Am J Otolaryngol 1995;16:109–114.
26. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457–481.
27. Cantu G, Solero CL, Mariani L, et al. Anterior craniofacial resection for malignant ethmoid tumors—a series of 91 patients. Head Neck 1999;21:185–191.
28. Spiro JD, Soo KC, Spiro RH. Nonsquamous cell malignant neoplasms of the nasal cavities and paranasal sinuses. Head Neck 1995;17:114–118.
29. Suarez C, Llorente JL, Fernandez De Leon R, Maseda E, Lopez A. Prognostic factors in sinonasal tumors involving the anterior skull base. Head Neck 2004;26:136–144.
30. Perry C, Levine PA, Williamson BR, Cantrell RW. Preservation of the eye in paranasal sinus cancer surgery. Arch Otolaryngol Head Neck Surg 1988;114:632–634.
31. Bussi M, Gervasio CF, Riontino E, et al. Study of ethmoidal mucosa in a population at occupational high risk of sinonasal adenocarcinoma. Acta Otolaryngol 2002;122: 197–201.

32. Wolf J, Schmezer P, Fengel D, Schoeder HG, Scheithauer H, Woeste Pl. The role of combination effects on the etiology of malignant nasal tumours in the wood-working industry. Acta Otolaryngol Suppl 1998;535:1–16.
33. Claus F, Boterberg T, Ost P, et al. Postoperative radiotherapy for adenocarcinoma of the ethmoid sinuses: treatment results for 47 patients. Int J Radiat Oncol Biol Phys 2002;54:1089–1094.
34. Stoll D, Bebear JP, Truilhe Y, Darrouzet V, David N. Les adenocarcinomes de l' ethmoide: Etude retrospective de 76 patients. Rev Laryngol Otol Rhinol (Bord) 2001;122: 21–29.
35. Moreau J-J, Bessede J-P, Heurtebise F, et al. Adenocarcinoma of the ethmoid sinuses in woodworkers. Retrospective study of 25 cases [in French]. Neurochirurgie 1997;43:111–117.
36. Knegt PP, Ah-See KW, vd Velden LA, Kerrebijn J. Adenocarcinoma of the ethmoidal sinus complex: surgical debulking and topical fluorouracil may be the optimal treatment. Arch Otolaryngol Head Neck Surg 2001;127:141–146.