Endoscopic nasal versus open approach for the management of sinonasal adenocarcinoma: A pooled-analysis of 1826 patients

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ABSTRACT: *Background.* Surgical resection represents the gold standard for the treatment of sinonasal malignancies. This study reviewed the published outcomes on endoscopic surgery or endoscopic-assisted surgery versus open approach for the management of sinonasal adenocarcinomas.

Methods. PubMed, EMBASE, the Cochrane Library, and CENTRAL electronic databases were searched for English language articles on endoscopic surgery, endoscopic-assisted surgery, and open approach for sinonasal adenocarcinomas. Each article was examined for patient data and outcomes for analysis.

Results. Thirty-nine articles including 1826 patients were used for the analysis. The endoscopic surgery and endoscopic-assisted surgery showed low rates of major complications (6.6% and 25.9%, respectively) compared to open approaches (36.4%; $p < .01$). The incidence of local failure was lower in the endoscopic surgery group as compared with open approach patients (17.8% vs 38.5%; $p < .01$, respectively). The multivariate Cox regression model showed a worst overall survival related to advanced T classification and open approach.

Conclusion. From the existing body of data, there is growing evidence that endoscopic nasal resection is a safe surgical option in the management of sinonasal adenocarcinomas. © 2015 Wiley Periodicals, *Head Neck* **38**: E2267–E2274, 2016

KEY WORDS: adenocarcinoma, endoscopy, paranasal sinus, postoperative complications, patient outcome assessment

INTRODUCTION

Sinonasal malignancies pose a diagnostic and therapeutic challenge because of their location, resulting symptoms, and presentation mimicking benign lesions.[1] The incidence of nasal and paranasal cancers in most relevant series is less than 1 per 100,000 per year. The ethmoid sinuses are mostly involved (between 5% and 30%), and adenocarcinoma is the most frequent malignancy of the ethmoid sinuses.[2] Primary adenocarcinomas of the sinonasal tract are a diverse group of malignancies that can be initially classified as salivary (5% to 10%) and nonsalivary types.[3] The World Health Organization classification of nonsalivary gland type sinonasal adenocarcinomas considers the categories: high-grade and low-grade adenocarcinomas of nonintestinal type and intestinal-type adenocarcinoma (ITAC) of colonic and mucinous subtypes.[4] Because symptoms are usually similar to inflammatory sinusitis, the diagnosis may be delayed and tumors are diagnosed at advanced stages. As with other malignancies, the presence of unilateral symptoms, typically obstruction, rhinorrhea, and epistaxis, should serve as a warning sign for the clinician. Men are affected 2 to 6 times more often than women, reflecting occupational factors. In most series, the cohorts are relatively small and often no distinction is made among the several subtypes of adenocarcinomas.[5] Surgical resection with negative margins, followed by adjuvant radiotherapy for advanced lesions, represents the gold standard for the management of sinonasal adenocarcinomas. Inability to control local disease is recognized as the cause of death in sinonasal malignancies, highlighting the importance of complete surgical resection at the primary site.[6] In this light, numerous open surgical approaches were used to deal with the complex anatomy of the paranasal sinuses and adjacent structures. Although traditional surgical management is successful in yielding 5-year survival rates ranging from 40% to 70%, open approaches carry specific complications, functional, and cosmetic risks, even with proper execution.[7–9] Recently, endoscopic techniques gained popularity in the management of benign and malignant sinonasal tumors. However, endoscopic management of malignant neoplasms, such as sinonasal adenocarcinoma, is still under evaluation.[5] Evidence-based guidelines on this topic are lacking because of the absence of randomized

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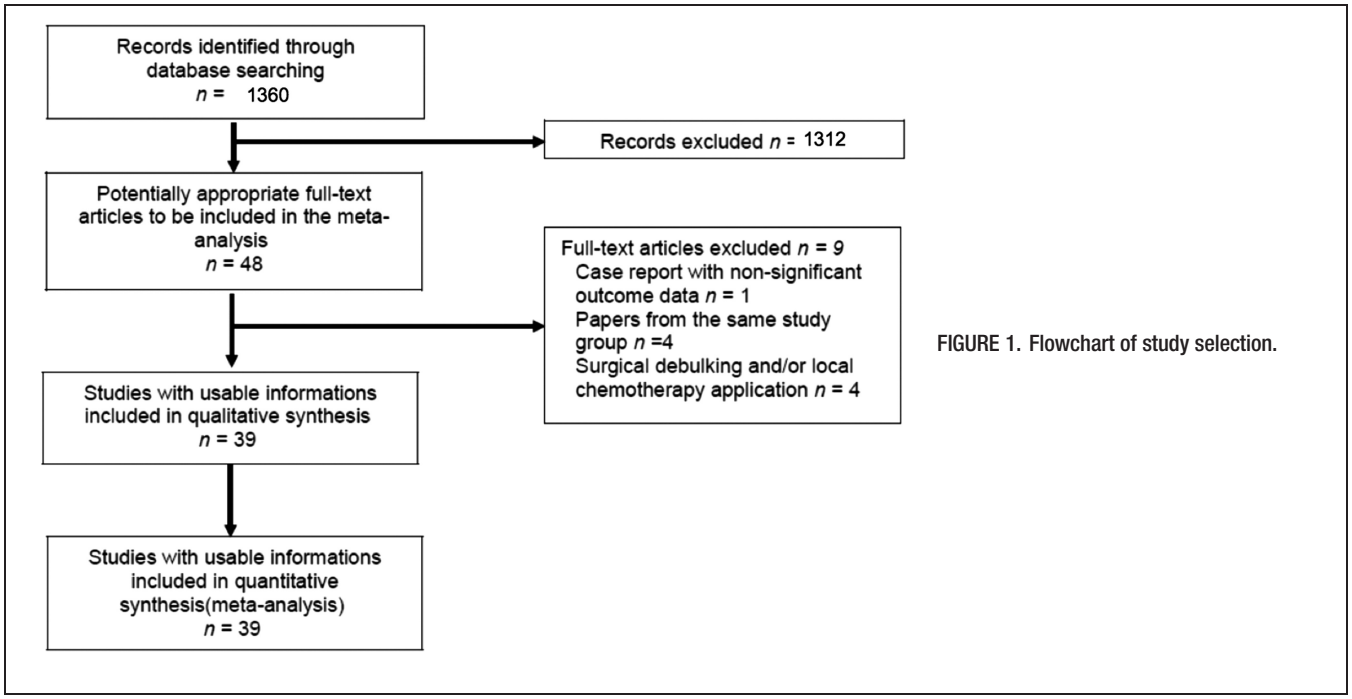

FIGURE 1. Flowchart of study selection.

control trials, the low incidence of sinus adenocarcinoma that renders prospective studies difficult, and because of the widely variable reporting methods used with data from various histopathological types often aggregated together. Consequently, the purpose of this study was to compile and analyze outcome data in patients who received surgical treatment (endoscopic or open surgery) for sinonasal adenocarcinoma taking into account the variety of reporting methods for outcomes and tumor characteristics found across the literature on this entity.

MATERIALS AND METHODS

Literature search protocol

A comprehensive review of the English language literature on the surgical management of sinonasal adenocarcinomas was performed using PubMed, EMBASE, the Cochrane Library, and CENTRAL electronic databases (see Figure 1). Three searches using the keywords (1) surgery OR endoscopic OR craniofacial OR open approach, (2) adenocarcinoma OR malignancy OR tumor, and (3) paranasal OR sinonasal OR nasal were performed. These searches were combined with the AND function to find all relevant articles. The following inclusion criteria were applied to each article: (1) available information on outcome data with survival statistics related to the treatment of sinonasal or skull base adenocarcinomas, and (2) data concerning the type of surgical resection: endoscopic, or endoscopic assisted, or open approaches/craniofacial resection.[7,9–46] When multiple articles were published by a single institution[8,47–49] with updated follow-up on their patient populations, the most recent publication was used for analysis to maximize accuracy of follow-up data and reduce the risk of redundancy.[9,35,41] Articles not meeting the inclusion criteria were excluded. Further exclusion criteria were: case reports without significant outcome data,[50] reports on surgical debulking, and studies regarding local 5-fluorouracil applications.[51–54] To further reduce the risk of an incomplete literature search, a manual search through the references of the included articles was performed.

Analysis protocol

Data from the studies were first extracted and assessed by the principal investigator (M.G.) and thereafter independently by 2 coauthors (D.A. and G.C.) using standardized data forms. Articles were examined for data resolution with the intent to perform a meta-analysis. Different methods of meta-analyses were considered in reviewing the literature to seek results that would provide meaningful analysis with the least risk of introducing biases. The quality assessment of diagnostic accuracy studies (QUADAS-2) tool was used to evaluate relevant study design characteristics of the included articles.[55] A graphical display of QUADAS-2 results is shown in Figure 2. Based on the surgical treatment, 3 groups were defined: endoscopic surgery, endoscopic-assisted surgery, and open approach. The articles were analyzed to extrapolate all information for each treated patient about age, sex, occupational exposure, smoking, tumor staging, total admission time, adjuvant therapies, disease-free survival (in months), events of local recurrence, regional recurrence, distant metastasis, total follow-up time (in months), and survival. However, survival data were limited in the endoscopic-assisted surgery group; thus, we compared only survival data from endoscopic surgery and open approach groups. The articles were also reviewed for data concerning the occurrence of perioperative and postoperative complications. A major complication was defined as at least one reported event of: cerebrospinal fluid leak, hemorrhage or severe epistaxis, stroke, severe pneumocephalus, meningitis, brain abscess, sepsis, or postoperative death. A minor complication was noted as at least one reported event of: light or moderate epistaxis, light or moderate pneumocephalus, agitation, minor subdural blood collection, central

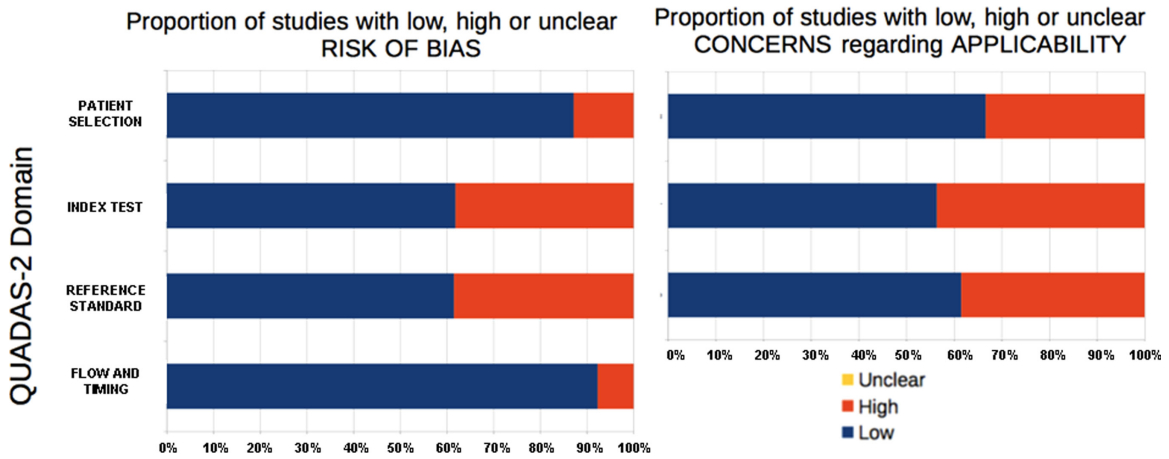

FIGURE 2. Graphical display for quality assessment of diagnostic accuracy studies (QUADAS)-2 results.

venous catheter infection, fever, deep venous thrombosis, epilepsy, headache, pneumonia, hallucinations, cranial nerve palsy, anisocoria, diplopia, or epiphora.

Statistical analysis

To test the differences among groups, the Fisher's exact test was used for categorical data, whereas the *t* test was used for continuous data. The role of each possible prognostic factor (univariate analysis) and their independent effect (multivariate analysis) was explored using logistic regression model or Cox proportional hazard model, as appropriate. Unfortunately, because of discrepancies in the presentation of survival data, including follow-up, it was impossible to calculate Kaplan–Meier curves. Probability values lower than .05 were considered statistically significant. All analyses were performed with STATA 12.0 software (Stata, College Station, TX).

RESULTS

The search was performed in October 2014 and yielded 1360 articles, of which 39 articles met inclusion's criteria,[7,9–46] comprising a total result of 1826 patients for initial analysis. Thirty-six studies[7,9–14,16–20,22,23,25–46] with 1404 cases included at least 3 years of follow-up and were included in the final analysis. All series were retrospective. Most series presented outcome data from heterogeneous histologies,[7,9,14–17,20–22,25–27,31,32,34,37–39,43] at differing stages, of patients who received a variety of treatment strategies over a relatively long timeframe. The largest series of ethmoid adenocarcinomas was published by the French GETTEC group.[30] Table 1 summarizes the extrapolated data from each included study. Palliative treatment was administered in 94 patients (5.1%), 431 patients (23.6%) received endoscopic surgery, 31 patients (1.7%) received endoscopic-assisted surgery, and 1270 patients (69.6%) underwent an open approach. Table 2 shows the patients' characteristics among surgical groups. In 2002 (with implementation starting from 2003), the American Joint Committee on Cancer and the International Union Against Cancer published staging protocols for epithelial tumors arising from sinonasal complex. Of 29 articles published after 2003, 11 studies specifically used the sixth or seventh edition of the TNM staging system.[24,29–31,35–37,41,42,44–46] The remaining articles did not provide any information on the staging of treated adenocarcinomas except for 5 articles published before 2003, which used an earlier version of these guidelines.[13,15–19] All but a few studies mentioned only the classification of the primary tumor (see Table 2), only 8 articles reported N classification at diagnosis, although these studies account for the larger series.[17,19,27,30,35,36,44,46] In total, we had T classification information for 1221 patients. In 937 N classification cases, only 9 N1 (1%), 3 N2a (0.3%), 3 N2b (0.3%), and 1 N3 (0.1%) were recorded, the remaining 921 cases (98.3%) were staged N0. Unfortunately, only 9 studies (364 patients) reported hospital discharge times.[7,9,21,26,33,40,42,44,46] The available data showed a shorter hospitalization in the endoscopic surgery group (4.7 ± 4.6 days) compared to the endoscopic-assisted surgery and open approach groups (9.2 ± 3.7 and 11.5 ± 4.9 days, respectively), which is statistically significant ($p < .01$; Figure 3). Furthermore, 19 published articles recorded perioperative and postoperative complications comprising a total of 938 patients.[13,15,21,23,24,26,27,29,31,33,36,39–46] The endoscopic surgery and endoscopic-assisted surgery showed low rates of major complications (6.6% and 25.9%, respectively) compared with open approaches (36.4%; $p < .01$). Postoperative deaths were recorded in 1 case of endoscopic-assisted surgery and in 7 cases of open approaches, no postoperative death was registered among patients who underwent endoscopic surgery ($p = .04$). Minor complications occurred in 10% of the endoscopic surgery group and in 7.4% of the open approach group, whereas these were recorded in 33.3% of endoscopic-assisted surgery patients who underwent combined endoscopic and open approach (Figure 4). In 9 studies, adjuvant therapy was not documented or impossible to deduce.[9,13,14,21,22,25,31,34,37] According to T classification, adjuvant radiotherapy (RT) was administered in 27.1% of T1 cases, 80% of T2 cases, 92.4% of T3 cases, 90.8% of T4a cases, and 91% of T4b cases. In the endoscopic surgery group, 78.9% of the cases received adjuvant RT, whereas the endoscopic-assisted surgery and open approach patients had adjuvant RT in 73.1% and 85.2%, respectively ($p < .01$).

TABLE 1. Overview of studies on sinonasal adenocarcinoma

Article	Year of publication	No. of patients	Mean age, y	No. of men	No. of adenocarcinomas	No. of patients with high-risk exposure	No. of ITACs	No. of endoscopic surgery	No. of endoscopic-assisted surgery	No. of open approaches	3-y DFS	5-y DFS	3-y OS	5-y OS
Grosjean et al[46]	2014	74	66	72	74	70	74	41	2	31	23%	ND	70.3%	ND
Bhayani et al[45]	2013	66	57.1	47	66	6	35	14	1	28	ND	79.1%	ND	65.9%
Vergez et al[44]	2013	159	68.9	148	159	140	136	159	0	0	84%	74%	74%	62%
Cantù et al[43]	2012	366	58	ND	178	ND	157	0	0	178	ND	ND	ND	ND
Vergez et al[42]	2012	48	ND	ND	48	32	ND	23	0	25	ND	87.5%	ND	75%
Nicolai et al[41]	2011	67	67	63	67	58	64	29	9	39	ND	ND	68%	48.4%
Breheret et al[40]	2011	42	61.5	41	42	36	42	0	1	34	ND	ND	64%	44%
Carta et al[39]	2011	16	58.5	11	11	10	11	11	0	0	ND	71%	ND	ND
Mine et al[38]	2011	32	57.5	ND	3	ND	ND	0	0	3	ND	ND	ND	52%
Luong et al[37]	2010	61	59	ND	6	ND	ND	6	0	0	ND	69.2%	ND	84.6%
De Gabory et al[36]	2010	95	ND	87	95	69	ND	0	0	95	ND	61%	ND	ND
Van Gerven et al[35]	2010	44	62	43	44	42	44	44	0	0	ND	60%	ND	63%
Cohen et al[34]	2009	41	61	ND	2	ND	ND	1	0	1	ND	ND	ND	ND
Jardeleza et al[33]	2009	12	66	10	12	10	10	12	0	0	91.6%	ND	91.6%	ND
Madani et al[32]	2009	84	ND	ND	54	46	ND	0	0	54	ND	ND	ND	57
Hanna et al[31]	2009	120	52.6	ND	13	ND	ND	10	3	0	ND	87%	ND	76%
Choussy et al[30]	2008	418	62.8	307	418	364	359	6	0	373	ND	ND	72%	64%
Llorente et al[29]	2008	79	61	78	79	62	ND	0	0	79	ND	ND	ND	36%
Bogaerts et al[28]	2008	44	62	43	44	25	ND	44	0	0	73%	72%	81%	53%
Podboj and Smid[27]	2007	16	50.2	3	5	ND	ND	5	0	0	100%	100%	ND	100%
Lund et al[9]	2007	49	60	ND	15	ND	ND	14	1	0	ND	72%	ND	83%
Castelnuovo et al[26]	2006	18	60.2	ND	10	ND	ND	0	10	0	ND	ND	ND	61.1%
Buchmann et al[25]	2006	78	55	ND	2	ND	ND	0	2	0	ND	ND	ND	86%
Batra et al[7]	2005	25	58	ND	3	ND	ND	2	0	1	ND	ND	ND	ND
Poetker et al[24]	2005	16	57.3	ND	2	ND	ND	2	0	0	ND	100%	ND	100%
Orvidas et al[23]	2005	24	64	17	24	3	8	3	0	20	87%	73%	76%	58%
Ganly et al[22]	2005	334	57	ND	107	ND	ND	0	0	107	ND	ND	ND	ND
Eviatar et al[21]	2004	6	ND	ND	1	0	0	1	0	0	ND	ND	ND	ND
Roh et al[20]	2004	19	56.9	2	3	ND	0	1	2	0	87%	73%	ND	66.7%
Claus et al[19]	2002	47	59	46	47	38	ND	1	0	46	58%	35%	71%	60%
Lee et al[18]	2002	9	51	5	9	ND	3	0	0	3	ND	ND	ND	ND
Dulguerov et al[17]	2001	220	ND	ND	25	ND	ND	0	0	22	ND	25%	ND	50%
Bridger et al[16]	2000	73	57	ND	27	9	ND	0	0	27	ND	70%	ND	62%
Thaler et al[15]	1999	4	54	1	1	0	0	0	1	0	ND	ND	ND	ND
Shah et al[14]	1997	115	49	ND	17	ND	ND	0	0	17	ND	69%	ND	78%
Brasnu et al[13]	1996	22	58	ND	22	21	ND	0	0	22	65.7%	ND	68.1%	ND
Alessi et al[12]	1988	13	49.2	7	13	ND	4	0	0	9	ND	ND	ND	ND
Klintenberg et al[11]	1984	28	ND	24	28	20	ND	0	0	23	ND	ND	ND	50%
Heffner et al[10]	1982	50	59	24	50	ND	ND	0	0	41	ND	ND	ND	ND

Abbreviations: ITAC, intestinal-type adenocarcinoma; DFS, disease-free survival; OS, overall survival; ND, not defined.

TABLE 2. Patients' characteristics among surgical groups

Characteristics	Endoscopic surgery	Endoscopic-assisted surgery	Open approaches	*p* value
Male:female ratio	360:30	20:3	543:317	<.01
Age (mean ± SD)	64.3 ± 13.3	59.7 ± 12.4	61.1 ± 12.8	<.01
ITAC:non-ITAC ratio	242:35	11:5	612:100	.11
No. of patients with wood dust exposure (%)	292 (67.8)	8 (25.8)	656 (51.7)	<.01
No. of T1 (%)	52 (12.8)	1 (3.7)	56 (7.1)	<.01
No. of T2 (%)	169 (41.4)	2 (7.4)	244 (31)	
No. of T3 (%)	83 (20.3)	4 (14.8)	178 (22.7)	
No. of T4a (%)	68 (16.7)	8 (29.6)	188 (23.9)	
No. of T4b (%)	36 (8.8)	12 (44.4)	120 (15.3)	
No. of N0 (%)	253 (98.8)	2 (100)	603 (98.4)	.25
No. of N1 (%)	3 (1.2)	0 (0)	4 (0.7)	
No. of N2a (%)	0 (0)	0 (0)	2 (0.3)	
No. of N2b (%)	0 (0)	0 (0)	3 (0.5)	
No. of N2c (%)	0 (0)	0 (0)	1 (0.2)	

Abbreviation: ITAC, intestinal-type adenocarcinoma.

For what concerns the outcome and survival, statistics varied among the articles, and, in some studies, data were not amenable for meta-analysis.[24,25,30–32,34] The mean follow-up time was 51.9 ± 45.8 months (range, 1–360 months), with 46.4 ± 37.6 months (range, 2–180 months) in the endoscopic surgery group and 53.6 ± 47.6 months (range, 1–360 months) in the open approach group ($p = .09$). Within the available data, 536 failure events were reported: 424 local (31.5%), 15 regional (1.1%), and 97 distant (7.2%) failures, resulting in crude disease-free survival (DFS) of 60.7% and local recurrence free survival of 67.6%. The crude DFS, locoregional relapse-free survival, and overall survival (OS) according to T classification between endoscopic surgery and open approach groups is shown in Table 3. Univariate and multivariate logistic regression analysis demonstrated that advanced T classification and open approach are statistically related to a high rate of major complications (odds ratio [OR] = 6.1; $p < .01$ and OR = 3.5; $p < .01$, respectively). Univariate and multivariate Cox regression model showed that advanced T classification and open approach are statistically related to the high rate of local relapses (see Table 4). Regarding the OS, the univariate Cox regression model highlighted the relationship among non-ITAC, advanced T classification, and bad prognosis, albeit the statistical significance persisted only for advanced T classification and open approach in a multivariate model (see Table 5).

DISCUSSION

Endoscopic surgery is increasingly and effectively used for sinonasal inflammatory diseases, even showing intracranial extension, and benign tumors[56]; nevertheless, for malignant tumors, this approach is in its relative infancy. A comprehensive analysis of the existing evidence would help to serve as a barometer for the state-of-the-art and to suggest future directions. Given that different types of tumors have several treatment survival implications for patients, we focused this analysis on the surgical management of sinonasal adenocarcinomas comparing outcomes between endoscopic surgery and traditional open approaches. The potential benefits of endoscopic resections in sinonasal adenocarcinomas are numerous, including lack of facial incisions, excellent visualization and illumination of the surgical site, minimal trauma, shorter hospital stay, and lower costs.[57] However, any treatment in sinonasal malignancies must be primarily judged by its efficacy. In that respect, our study is not conclusive. This is indeed a pooled analysis of patient data, rather than a comparative meta-analysis. This is inevitable, as, up to now, there are no comparative studies (and certainly no randomized controlled trials) comparing endoscopic with external approaches for adenocarcinomas.

The main problem in comparing different interventions is Simpson's paradox (ie, the effect of case mix); in our case, the proportion of patients with T1/T2 versus T3/T4 tumors in the endoscopic versus the open approaches, which could erroneously lead to false conclusions regarding their efficacy.

It is true that smaller tumors are more likely to be treated endoscopically, and this is indeed what we found within our data. However, comparing results by T classification, we found that endoscopic management was associated with better OS and DFS across almost all tumor classifications.

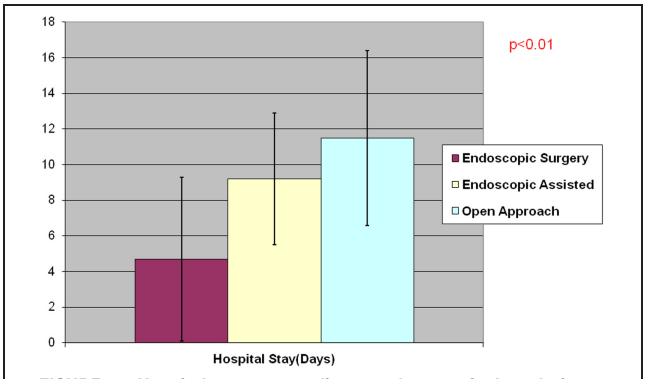

FIGURE 3. Hospital stay according to the surgical techniques ($p < .01$).

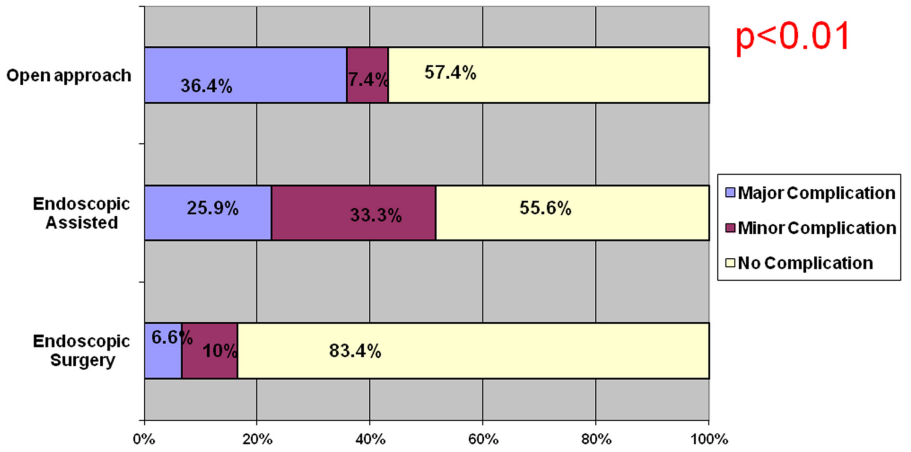

FIGURE 4. Distribution of complications.

An issue is the possible reporting bias. It is true that the most experienced surgeons with the best results would be the first to publish their results. Unfortunately, this is true in all surgical series, and we can only acknowledge it.

In our analysis, we found a statistically lower rate of major and minor complications in endoscopic surgery (16.6%) compared with open approaches (43.8%; $p < .01$). Postoperative deaths were recorded only within patients who underwent either endoscopic-assisted surgery or open approach. Of note, the open craniectomy might represent a risk factor in itself for the development of postoperative complications; in fact, the higher rate of complications in endoscopic-assisted surgery and open approach groups is mainly related to this external approach. Furthermore, the hospital stay in the endoscopic surgery group was statistically shorter compared with the endoscopic-assisted surgery and open approach groups ($p < .01$). Almost all series largely used postoperative RT in the majority of the cases, and its use is reasonable in a district surrounded by noble structures where wide clear margins are often difficult to obtain[7,10–12,15–20,23,24,26–30,32,33,35,36,39–46]; nevertheless, no randomized or even controlled trials of its precise role for sinonasal adenocarcinomas are available. This does not mean that RT plays no role in the management of sinonasal adenocarcinomas, but highlights the importance of a complete surgical resection. Outcomes are reported as combined results with and without RT. Patients treated with adjuvant RT are more likely to have locally advanced tumors and to be high-grade and/or to have positive margins, and are not comparable with those treated with surgery alone. Because of this understandable bias a conclusion cannot be drawn on its precise role. The overall local recurrence rate was reported as 32.5% with a rate of 17.8% for the endoscopic surgery group and 38.5% in the open approach group. Nevertheless, a recurrence can occur even 10 years or more after the initial treatment. The application of endoscopic techniques for the management of malignant sinonasal tumors is still controversial. The primary concern worries about the adherence to the oncologic principle of en bloc excision with adequate margins. However, many sinonasal tumors have a small area of tissue invasion despite filling the nasal cavity and paranasal sinuses; furthermore, tumor growth into sinuses and skull

TABLE 3. The crude survivals according to T classification

T classifications	Endoscopic surgery group	Open approach group	*p* value
T1			
DFS (no. of survivals)	81% (34)	80% (28)	.57
Local recurrence-free survival (no. of survivals)	81% (34)	77.1% (27)	.45
OS (no. of survivals)	81.3% (39)	76.4% (42)	.36
T2			
DFS (no. of survivals)	83.2% (134)	64.4% (139)	<.01
Local recurrence-free survival (no. of survivals)	84.5% (136)	66.7% (144)	<.01
OS (no. of survivals)	84.2% (139)	71.4% (162)	<.01
T3			
DFS (no. of survivals)	80.8% (63)	61% (94)	<.01
Local recurrence-free survival (no. of survivals)	85.9% (67)	66.7% (102)	<.01
OS (no. of survivals)	79.5% (62)	66.5% (111)	.03
T4			
DFS (no. of survivals)	70% (86)	41% (187)	<.01
Local recurrence-free survival (no. of survivals)	77.2% (95)	57% (305)	<.01
OS (no. of survivals)	66.4% (81)	47.1% (254)	<.01

Abbreviations: DFS, disease-free survival; OS, overall survival.

TABLE 4. Univariate and multivariate Cox regression model for local relapses

	Univariate			Multivariate		
	HR	*p* value	95% CI	HR	*p* value	95% CI
ITAC	0.82	.24	0.59–1.14	0.89	.53	0.63–1.27
T3–T4 classification	1.8	<.01	1.44–2.26	1.69	<.01	1.29–2.21
Open approach	1.88	<.01	1.44–2.46	2.57	<.01	1.78–3.69

Abbreviations: HR, hazard ratio; 95% CI, confidence interval; ITAC, intestinal-type adenocarcinoma.

TABLE 5. Univariate and multivariate Cox regression model for overall survival

	Univariate			Multivariate		
	HR	*p* value	95% CI	HR	*p* value	95% CI
non-ITAC	1.46	<.01	0.53–1.88	1.13	.42	0.84–1.52
T3–T4 classification	2.3	<.01	1.87–2.84	2.1	<.01	1.59–2.66
Endoscopic surgery	0.89	.32	0.71–1.12	0.62	<.01	0.47–0.83

Abbreviations: HR, hazard ratio; 95% CI, confidence interval; non-ITAC, nonintestinal-type adenocarcinoma.

base regions often occurs by compression of bony structures rather than by direct invasion. En bloc excision of the entire tumor is not necessary; instead, en bloc resection of the area of invasion is performed with frozen section control confirming clear margins. In order to gain access to the area of invasion, it is frequently necessary to debulk the tumor first. Albeit this clearly violates the tumor, it does not violate normal tissue planes surrounding the malignant proliferation because the tumor is residing in an air-filled cavity, and furthermore there is no evidence that this intraoperative debulking increases the risk of local recurrence. In fact, there are multiple examples of other neoplasms that are removed in a piece-meal fashion without jeopardizing the results: inverted papillomas, and laser resection of laryngeal and pharyngeal carcinomas. Even with an open surgical approach (craniofacial resection), en bloc resection is not always possible because of the fragility and fragmentation of the specimen and the proximity to vital structures. Thus, it is the final resection margin that is crucial, and not the method of tumor removal.[58] Nevertheless, there is no consensus regarding the indication and contraindication for endoscopic surgery as treatment for sinonasal adenocarcinomas. Some authors identified orbital involvement as a contraindication,[28,48] whereas others argued that endoscopic surgery would still be an acceptable method.[27] Dural and intracranial extension, however, served as a nearly universal contraindication to endoscopic surgery,[15,25,26] but this dogma has also been challenged with the constant evolution of techniques, technology, and surgeons expertise.[44,46,59] Histopathologic typing is strictly related to outcome with the poorly differentiated subtypes faring worse. Thus, survival is better in papillary and colonic (ITAC) type than in solid or mucinous type adenocarcinomas.[60] Wood dust exposure as an etiologic factor that confers a better prognosis in the larger, but not all, series.[30,35,36] As ITAC is a subtype of adenocarcinoma showing histological features reminiscent of colonic adenomas and adenocarcinomas, new therapeutic approaches, such as targeted therapy with monoclonal antibodies against epidermal growth factor receptor might, in the future, be helpful in the therapeutic approach of these lesions.[61]

The variability encountered in the reported data was detailed in this study. This variability is partially indicative of the rare nature of this tumor and the changes in staging with time. Another aspect is the difficulty in the interpretation of the oncologic results reported in some studies, given that different histologies with different patterns of behavior and prognosis where mixed. Furthermore, the staging information was not available in all series, thus, this potential bias might distort the results of this study. Nevertheless, for advanced T classifications, surprisingly, the endoscopic surgery showed better outcomes in survival than the traditional open approach.

CONCLUSION

Based on the available published data, endoscopic management of sinonasal adenocarcinomas seems to be a safe and effective treatment modality. Recommendations for future studies include the implementation of prospective multi-institutional studies with detailed data regarding histology, staging, surgical treatment, adjuvant treatment, minor/major complications, and oncologic results.

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