A New Risk Score Assessment for Neck Management in T1-T2N0 Sinonasal Squamous Cell Carcinoma Patients: A European Head and Neck Cancer Center Survey Study and Evaluation of 58 Patients with Early Stage Sinonasal Carcinoma

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Abstract

Purpose

The purpose of the present study was to assess whether European head and neck cancer centers perform elective neck dissection (END) in early stage sinonasal squamous cell carcinomas (SCCs) and whether END affects oncological outcome.

Methods

A questionnaire regarding performance of END in T1 - T2 sinonasal SCCs was sent to 38 head and neck cancer centers in Europe. The results were further correlated and compared with clinical data of 58 patients with T1 (n = 37) and T2 (n = 21) sinonasal SCCs, a risk score and a nomogram were generated.

Results

Only 5–10 % of respondents are performing END in T1 and 26–32% in T2 sinonasal SCCs. In our cohort regional recurrence was evident in 10 (17.2%) patients, representing a significant worse prognostic factor for cancer specific survival (HR 8.13; p = 0.016). Particularly, regional recurrence was more frequent in T2 tumors and in patients where the primary tumor originated from nasal septum and vestibule. Based on our clinical and questionnaire data a new risk-score was determined to predict necessity for END. The risk-score, including T-classification and tumor site, assigned T1-classification with 0 points, followed by 1 point for T2; tumor site: nasal septum or vestibule with 1 point and tumors from other subsites with 0 points. Based on these factors we further created a nomogram for predicting the risk of regional recurrence. Patients with a high-risk score showed 9.52-fold higher risk for regional and or distant recurrence (HR 9.52; p = 0.002;) and their 5-year CSS was 44.4% compared to 92.8% in patients with moderate or low risk (p = 0.017).

Conclusions

Our proposed risk-score system in T1-2N0 sinonasal carcinoma is helpful to identify patients who may benefit from END. Although to date END has no value in European head and neck cancer centers for T1-T2 sinonasal SCCs, our study indicates that the neck management in these patients should be reconsidered.

Introduction

Sinonasal squamous cell carcinomas (SCCs) account for less than 3% of malignant tumors of the upper aerodigestive tract and 3% of all head and neck carcinomas [1, 2]. According to the definitions of the American Joint Committee of Cancer (AJCC), sinonasal carcinomas are stratified into tumors originating

form (i) nasal cavity and ethmoidal sinus (nasoethmoidal complex) or (ii) maxillary sinus [3]. The vast majority of SCCs are located in the nasal cavity (43.9–45.7%) followed by the maxillary sinus (33.3–35.9%) [4, 5].

Primary tumor resection followed by adjuvant radiotherapy (RT) in selected cases represents the mainstay of therapy [6, 7]. Scurry et al. reported the risk for regional recurrences in 18.1% of sinonasal carcinomas of the nasal cavity and recommended neck dissection or irradiation especially for high risk tumors presenting perineural spread, lymphovascular invasion and T stage [8]. A more recent meta-analysis (n = 1283) has reported nodal involvement in 14.2% (range, 4–27%) of cases depending on tumor site and extension [2]. We have recently found remarkable differences regarding clinical behavior based on anatomic subsite, such as lymph node involvement and subsequently outcome in patients with SCCs of the nasoethmoidal complex [9].

Nonetheless, elective nodal treatment has no value in the current treatment of sinonasal SCCs. In the NCCN (National Comprehensive Cancer Network) guidelines, nasal cavity stage I and II cancers are recommended to be treated with surgery or radiation or in distinct cases with surgery and adjuvant irradiation [10], while no recommendation is given for elective neck dissection in early stages [10]. However, Scurry and Ahn (2,8) supposed that elective nodal treatment can decrease the risk of nodal recurrence to a 4% rate [2, 8]. Although the risk of regional recurrences can be reduced by incorporating elective nodal treatment [2, 8, 11], elective neck dissection (END) failed to demonstrate significantly better overall survival in T3-T4 sinonasal SCCs of the nasoethmoidal complex and maxillary sinus [12]. Conversely, elective neck treatment was associated with better prognosis in higher stage maxillary sinus SCCs [13, 14, 15].

Hence, one of the purposes of the study was the evaluation of current treatment concepts of stage I (T1N0) and II (T2N0) sinonasal SCCs in Europe and whether or not the anatomic subsites influence treatment decisions and oncological outcome using an online survey (see supplementary material). Additionally, a retrospective analysis of patients with sinonasal carcinomas was performed to create a new risk score for the management of the node negative neck.

Materials And Methods

Questionnaire

We performed an online survey (see supplementary material) based on a questionnaire that was sent to 38 European head and neck cancer centers including Austria (n=11), Germany (n=22), Switzerland (n=2), and Great Britain (n=3). The questionnaire consisted of 7 questions evaluating whether or not END would be performed in T1N0 and T2N0 sinonasal SCCs of nasal cavity and paranasal sinus and which additional radiological studies would be applied to decide on the necessity of END. Among 38 consulted centers, 20 (52.6%) have completed the online survey, but one questionnaire was incomplete and therefore removed from further analysis. In total, data of 19 centers (50.0%) was eligible for subsequent analyses.

Analysis of Clinical Data

A retrospective, multicenter chart review of patients with T1N0 and T2N0 sinonasal SCCs was performed. Patients were treated at the Department of Otorhinolaryngology, Head and Neck Surgery, Medical University of Vienna, Austria (Center 1), the Institute of Head and Neck Diseases, Evangelical Hospital Vienna, Austria (Center 2) and the Center Mangfall-Inn in Rosenheim, Germany (Center 3). Data of patients were provided by attending centers and evaluated individually regarding appropriateness by two authors (C.L., S.J.). Finally, 58 patients were eligible for inclusion and analysis.

Compliance with ethical standards: All procedures performed were in accordance with the ethical standards of the National Research Committee (Local Ethical committee). The local ethical committee numbers were: center 1 2329/2016, center 2 04/2018, center 3 515/2016. An informed consent was waived by the local ethic committee of the Evangelical Hospital of Vienna.

Clinical Data

In total, 58 patients (34 males; 24 females) with a median age of 63.2 years (range: 35.1 – 89.2) were included. We had 37 (63.8%) T1 and 21 (36.2%) T2 tumors and the majority of them showed moderate-differentiation (G2; 60.3%). Tumors most commonly originated from nasal septum followed by nasal vestibule, lateral nasal wall and ethmoidal sinus in 22 (37.9%), 20 (34.5%), 13 (22.4%) and 3 (5.2%) cases, respectively. All septal SCCs were located in the cartilaginous anterior part of the septum. We had no appropriate cases of T1-T2N0 tumors originating from maxillary sinus. Data is shown in Table 1.

Therapy

Surgical tumor resection was applied in 57 patients (98.3%) and free resection margins (R0) were achieved in 52 (89.7%) of those. Surgery alone was done in 46 patients (79.3%), surgery and postoperative RT was applied in 10 patients (17.2%) and one patient (1.7%) underwent surgery and postoperative chemoradiotherapy (CRT). Only one patient (1.7%) was treated with primary CRT. Only tumor sites were irradiated either in an adjuvant or curative setting, but elective neck irradiation was not performed. END was performed in only 9 patients (15.5%), whose characteristics are indicated in Table 2.

Statistical Methods

Statistical analysis was performed using the SPSS software (version 27; IBM SPSS Inc., Chicago, IL, USA). Data are indicated as absolute numbers with corresponding percentages in brackets. The Chi-square test was used to assess associations between nominal variables. An unpaired student's T-Test was used to compare means of normally distributed variables. Univariate cox-regression analysis was performed to evaluate the impact of different clinical variables on freedom from regional and distant recurrence (FFR) and cancer specific survival (CSS). Kaplan-Meier analysis and Log-rank test were assessed for survival analysis. All tests were two-sided, and p-values below 0.05 were considered statistically significant. A nomogram was created for the two predictors T-Classification and Anatomic Origin which was visualized using the R package "rms" (Figure 3).

Results

Questionnaire

Elective Neck Dissection in T1N0 sinonasal SCCs

In total, 17 (89.5%) and 18 (94.7%) European head and neck cancer centers would not perform END in T1N0 SCCs of the paranasal sinuses or nasal cavity, respectively. Answers and recommendations did not significantly differ among centers from different countries ($p=0.964$). Only two German centers (10.5%) would perform END, comprising stage I-IV in one center and only level II in another (Figure 1A).

Elective Neck Dissection in T2N0 sinonasal SCCs

Similarly, END would not be performed by 13 (68.4%) and 14 (73.7%) respondents for T2N0 SCCs of the paranasal sinuses or nasal cavity, respectively. Again, approaches did not significantly differ among countries ($p=0.792$). However, END would be performed in 2 Austrian and 4 German centres (31.6%). Those centers would do particularly level I (5/19; 26.3%) and level II (5/19; 26.3%) ND followed by level III (3/19; 15.8%) and IV (1/19; 5.3%), respectively (Figure 1B).

Applied imaging tools to decide on the necessity of Elective Neck Dissection

Ultrasound, CT-scan, MRI or PET-CT/MRI are performed by 10 (52.6%), 10 (52.6%), 8 (42.1%), and 6 (31.6%) centers to obtain additional information regarding lymph node status. Six centers (31.6%) applied one imaging technique (ultrasound: $n=1$; CT-scan: $n=3$; PET-CT/MRI: $n=2$), while the majority of centers combined two ($n=10$; 52.6%) or three different techniques ($n=3$; 15.8%). The number of applied radiological studies did not significantly differ between institutes who perform END (2.0 ± 0.0) compared to those who did not (1.79 ± 0.8 ; $p=0.336$).

Correlation and Analysis of Clinical Data

Recurrence and Risk Score

Local, regional and distant recurrences were noticed in 7 (12.1%), 10 (17.2%) and 1 (1.7%) patient, respectively. The mean and median time between diagnosis and recurrence was 50.9 and 43.0 months. Regional recurrence was significantly more often observed in tumors originating from nasal vestibule (20.0%) and nasal septum (22.7%; $p=0.013$). In addition, we noticed a trend towards local failure in T1 tumors and towards regional failure in T2 tumors ($p=0.116$; Table 1). Although difference failed to reach statistical significance, none of the 9 electively neck-dissected patients (15.5%) experienced recurrence ($p=0.188$). Adjuvant radiotherapy was applied in 11 patients and significantly more often in patients with incomplete tumor resection (80% vs. 13.5%; $p=0.004$) and more likely in T2 than T1 tumors (28.6% vs 13.5%; $p=0.181$).

Based on our data, we supposed that T-classification ($T2 > T1$) and tumor site (septum and vestibule > other origin) seem to represent risk factors for occurrence of regional and/or distant recurrence.

Therefore, we created a risk score based on T-classification (T1 tumor = 0 points (=pts.); T2 tumor = 1 pts.) and tumor site (nasal septum or vestibule = 1 pts.; other origin = 0 pts.) to better estimate on whether or not patients may benefit from END. After risk stratification of all patients according to our proposed risk score, we had 9 patients with low risk (0 pts.), 35 patients with moderate risk (1 pt.) and 14 patients with high risk (2 pts.) for regional recurrence (Figure 2).

Nomogram

Based on our data, we further calculated a nomogram to predict the risk of regional recurrence in all patients based on T-Classification and anatomic subsite (Figure 3). Anatomic origin (0=other subsite; 1= nasal septum or vestibule) was quantified with a higher impact on regional recurrence than T-classification (1=T1; 2=T2). As exemplified, a T1 SCCs originating from the nasal septum or vestibule had a 13-14% risk for regional recurrence (Figure 3).

Outcome Analyses

Subsequently, we performed log-rank test and univariate cox-regression analyses to assess the effect of different clinical variables and our risk-scoring system on freedom from regional and distant recurrence (FFR) and cancer specific survival (CSS).

The 5-year FFR was 49.9% in T2 tumors compared to 88.1% in T1 tumors, which was significantly different ($p=0.016$). Moreover, elder patients and those who have not undergone END showed a worse but not significantly different FFR ($p=0.052$; $p=0.086$). Applying our risk score, patients with high-risk score, indicating T2 tumors originating from nasal septum or vestibule, showed significantly worse FFR ($p<0.001$). Indeed, even at univariate cox-regression analysis, high-risk scores showed a 9.52-fold higher risk for regional and or distant recurrence (HR 9.52; $p=0.002$; Table 3).

Similarly, the 5-year CSS was 96.4% in T1 tumors compared to 58.3% in T2 sinonasal tumors ($p=0.009$). Noteworthy, 5-year CSS was almost halved in patients with high-risk scores (44.4% vs. 92.8%) compared to patients with moderate or low risk ($p=0.017$). Occurrence of regional recurrence was also associated with significantly worse CSS (40.0% vs. 95.7%; $p=0.005$). High-risk scores (HR 6.62; $p=0.039$) and regional recurrences (HR 8.13; $p=0.016$) represented significantly worse prognostic factors for CSS (Table 4).

Discussion

Since surgical management of node negative neck patients presenting with small sinonasal carcinoma is still challenging, new treatment algorithms are needed to provide best patient care. Therefore, we performed a questionnaire survey among different European head and neck cancer centers to evaluate the value of END in the management of T1 and T2 sinonasal SCCs. In addition, we analyzed oncological outcome in 58 patients to set up a new risk score to predict the need for END.

The majority of respondents (70-90%) do not routinely perform END in stage I and II sinonasal SCCs, because of the relatively low rate of occult metastasis suspected in early stage carcinomas. No literature

is published in these early stages, but overall, for all tumor stages, the rate of occult metastasis ranges from 13.5 – 22.2% [13]. Though occult metastasis seems to be rare in T1 and T2 sinonasal SCCs, the regional control was significantly better in patients who had received elective neck treatment [12,14,16]. Several studies could underline the fact that END is linked to decreasing regional recurrent disease, but is rather recommended in higher stages [13,17,19]. Castelnau-Marchand et al [17] investigated 87 patients with neck negative SNSCC including 15% (n=17) early stages carcinomas. Treatment of neck was performed in 87 N0 (T1- T4) patients with no difference in overall survival but a significant difference in locoregional control [17]. Even more, our data are strongly supporting the effectiveness of END since we could not observe any regional or distant failure in patients who underwent END.

Based on the study of Ahn [2] and colleagues reporting on a higher risk for lymph node involvement in T2 (9.8%) and T3 (10.3%) SCCs of the nasal cavity compared to T1 (4%) tumors, we hypothesize that T-classification may represent an additional risk factor for regional failure. This data highlights that oncological behavior of T2 tumors, indicated by lymph node involvement, is more likely that of T3 than of T1 tumors, respectively.

In accordance to that, we found that risk of regional recurrence is significantly correlated with locality of tumor origin. Lymph node metastasis particularly occurred in tumors originating from nasal vestibule and nasal septum and more likely in T2 tumors. Subsequently, we created a risk score stratifying patients according to T-classification and anatomic subsite into low, moderate or high risk categories for regional failure. In our analysis, high-risk scores were associated with 9.5-times higher risk for regional or distant recurrence, which represented a significantly worse prognostic factor for cancer specific survival (CSS). Based on our data, we created a nomogram illustrating that anatomic origin has a greater impact on regional recurrence than T-Classification. A T1 SCCs of the nasal septum would carry a risk of 13-14% for regional recurrence, while T2 tumors of the nasal septum would carry an almost doubled risk. However, these results need to be interpreted with caution since the nomogram is based on our patient cohort without controls. Therefore, further studies are warranted to evaluate both our nomogram as well as our risk score combining T-classification and anatomic subsite.

Based on our data and analyzing the pros and cons of an elective neck dissection, END should be favoured over the wait and watch approach or even elective neck irradiation due to following reasons: (i) low complication rate and morbidity [24,25]; (ii) END provides additional beneficial histopathological information resulting in accurate staging and also guides the future possibility of adjuvant chemotherapy; (iii) radiation induced side-effects, such as xerostomia or mucositis [26]; (iv) and irradiation should be preserved as curative treatment option in the case of neck failure, which might be severely limited by possible long term complications such as spinal cord toxicity if irradiation was applied electively before.

Clinical outcome data, online survey data reflecting the current European neck management in stage I and II sinonasal SCCs and the set-up of a risk score for regional failure represents the strength of the current study. However, there are three limiting factors. Firstly, it is a huge challenge to clearly define

tumors' arising within the nasal cavity and therefore comparison of tumour subsites may be hampered. Secondly, the decreased quantity of performed ENDs and thirdly the retrospective study-design including a low number of patients represent a drawback of this study. In contrast, considering the current literature regarding T1 and T2 sinonasal SCCs, published cases are ranging from 10 to 35 cases that proofs that our cohort is representative [6,9,11,17, 19, 30, 32]. Additionally, sinonasal tumors are known to be very rare tumors with an incidence of 5.6 cases per million [30].

Conclusion

Performing END is associated with better regional control and better survival in sinonasal SCC patients. Since T2 tumors and tumors of the nasal septum or vestibule show significantly higher rates of regional failure we created a new risk score, that is helpful to identify patients who will benefit from END. We strongly recommend to reconsider END in early staged sinonasal SCCs to increase oncologic outcome in these small group of patients.

Declarations

Ethics approval and consent to participate: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Evangelical Hospital (protocol code 04/2018 , date of approval: September 19th 2018).

Consent for publication: not applicable

Availability of data and materials: The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Conflict of interest/Competing interests: The authors state no conflict of interest.

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Conflicts of Interest: The authors declare no conflict of interest

References

1. Dulguerov P, Jacobsen MS, Allal AS, Lehmann W, Calcaterra T. Nasal and paranasal sinus carcinoma: are we making progress? A series of 220 patients and a systemic review. *Cancer* 2001 Dec 15;92:3012-29
2. Ahn PH, Mitra N, Alonso-Basanta M, Palmer JN, et al. Risk of lymph node metastasis and recommendations for elective nodal treatment in squamous cell carcinoma of the nasal cavity and maxillary sinus: a SEER analysis. *Acta Oncol* 2016 Sep-Oct;55(9-10)
3. AJCC 8th Edition: <https://cancerstaging.org/About/news/Pages/AJCC-8th-Edition-Cancer-Staging-Form-and-Histology-and-Topography-Supplements-Available-Now.aspx>
4. Turner JH, Reh DD. Incidence and survival in patients with sinonasal cancer: a historical analysis of population-based data. *Head Neck* 34:877-885
5. Dutta R, Dubal PM, Svider PF, Liu JK, Baredes S, Eloy JA. Sinonasal malignancies: a population-based analysis of site-specific incidence and survival. *Laryngoscope* 125:2491-2497
6. Becker C, Kayser G, Pfeiffer J. Squamous cell cancer of the nasal cavity: new insights and implications for diagnosis and treatment. *Head Neck* 38:2112-2117
7. Lund VJ, Stammberger H, Nicolai P et al. European position paper on endoscopic management of tumors of the nose, paranasal sinuses and skull base. *Rhinol Suppl* 22:1-143
8. Scurry WC, Goldenberg D, Chee Y, Lengerich EJ, Liu Y, Fedok FG. Regional recurrence of squamous cell carcinoma of the nasal cavity. A systematic review and meta-analysis. *Arch Otolaryngol Head neck Surg* 133:796-800
9. Janik S, Gramberger M, Kadletz L, Pammer J, Grasl MC, Erovcic BM. Impact of anatomic origin of primary squamous cell carcinomas of the nasal cavity and ethmoidal sinus on clinical outcome. *Eur Arch Otorhinolaryngol* 2018;275:2363-2371
10. <https://www.cancer.org/content/dam/CRC/PDF/Public/8751.00.pdf>
11. Mirghani H, Hartl D, Moruaire G, Armas GL et al. Nodal recurrence of sinonasal cancer: Does the risk of cervical relapse justify a prophylactic neck treatment? *Oral oncology* 2013; 49:374-380
12. Crawford KL, Jafari A, Qualliotine JR, Sutart E et al. Elective neck dissection for T3/T4 cN0 sinonasal squamous cell carcinoma. *Head Neck* 2020;42:3655-3662
13. Sangal NR, Lee YJ, Brady JS, Patel TD, Eloy JA, Baredes S, Park RCW. The role of elective neck dissection in the treatment of maxillary sinus squamous cell carcinoma. *Laryngoscope*. 2018 Aug;128(8):1835-1841. doi: 10.1002/lary.27009. Epub 2017 Nov 29. PMID: 29193120.
14. Berger MH, Tajudeen BA, St John MA, Tjoa T, Kuan EC. Should an elective neck dissection be performed for maxillary sinus squamous cell carcinoma? *Laryngoscope*. 2019 Nov;129(11):2445-2446. doi: 10.1002/lary.28242. Epub 2019 Aug 16. PMID: 31418862.
15. Abu-Ghanem S, Horowitz G, Abergel A, Yehuda M, Gutfeld O, Carmel NN, Fliss DM. Elective neck irradiation versus observation in squamous cell carcinoma of the maxillary sinus with N0 neck: A meta-analysis and review of the literature. *Head Neck*. 2015 Dec;37(12):1823-8. doi: 10.1002/hed.23791. Epub 2014 Aug 1. PMID: 24913744.

16. Ahn PH, Mitra N, Alonso-Basanta M, et al. Nodal metastasis and elective nodal level treatment in sinonasal small-cell and sinonasal undifferentiated carcinoma: a surveillance, epidemiology and end results analysis. *Br J Radiol.* 2016; 89(1058): 20150488
17. Castelnau-Marchand P, Levy A, Moya-Plana A, Mirghani H, Nguyen F, Del Campo ER, et al. Sinonasal squamous cell carcinoma without clinical lymph node involvement: Which management is best? *Strahlenther Onkol* 2016;192:537-544
18. Brown JS, Bekiroglu F, Shaw RJ, Woolgar JA, Triantafyllou A, Rogers SN. First report of elective selective neck dissection in the management of squamous cell carcinoma of the maxillary sinus. *Br J Oral Maxillofac Surg*;51(2):103-107
19. Guan X, Wang X, Liu Y, Hu C, Zhu G. Lymph node metastasis in sinonasal squamous cell carcinoma treated with IMRT/3D-CRT. *Oral Oncol* 2013;49(1):60-65
20. Le QT, Fu KK, Kaplan MJ, Terris DJ, Fee WE, Goffinet DR. Lymph node metastasis in maxillary sinus carcinoma. *Int J Radiat Oncol Biol Phys* 2000;46:541-9
21. Jiang GI, Ang KK, Peters LJ, Wendt CD, Oswald MJ, Goepfert H. Maxillary sinus carcinomas: natural history and results of postoperative radiotherapy. *Radiother Oncol* 1991;2:193-200
22. Paulino AC, Fisher SG, Marks JE. Is prophylactic neck irradiation indicated in patients with squamous cell carcinoma of the maxillary sinus? *Int J Radiat Oncol Biol Phys* 1997;39(2):283-9
23. Cantù G, Bimbi G, Miceli R, Mariani L, Colombo S, Riccio S, et al. Lymph node metastases in malignant tumors of the paranasal sinuses: prognostic value and treatment. *Arch Otolaryngol Head Neck Surg* 2008;134:170-7
24. Dirix P, Nuyts S, Geussens X, Jorissen M, Vander Poorten V, Fossion E, et al. Malignancies of the nasal cavity and paranasal sinuses: long-term outcome with conventional or three-dimensional conformal radiotherapy. *Int J Radiat Oncol Biol Phys* 2007;69:1042-50
25. Amit M, Na`ara S, Sharma K, Ramer N, Ramer I, Agbetoba A, Glick J, Yang X, Lei D, et al. Elective Neck Dissection in Patients with head and neck adenoid cystic carcinoma: an international collaborative study. *Ann Surg Oncol* 2015;22:1353-1359
26. Lobo BC, D`Anza B, Farlow JL, Tang D, Woodard TD, Ting JY, Sindwani R. Outcomes of sinonasal squamous cell carcinoma with and without association of inverted papilloma: a multi-institutional analysis. *Am J Rhinol Allergy* 2017;31:305-309
27. Freiser ME, Ojo RB, Lo K, Saint-Victor S, Bollig C, Nayak CS, Sargi ZB. Complications and oncologic outcomes following elective neck dissection with salvage laryngectomy for the N0 neck. *Am J Otolaryngol* 2016 May-Jun;37(3):186-94
28. Prendes BL, Aubin-Pouliot A, Egbert N, Ryan WR. Elective lymphadenectomy during salvage for locally recurrent head and neck squamous cell carcinoma after radiation. *Otolaryngol Head Neck Surg* 2014 Sep;151(3):462-7
29. Le NS, Janik S, Simmel H, Erovic BM. Bilateral vs ipsilateral adjuvant radiotherapy in patients with cancer of unknown primary of the head and neck: An analysis of the clinical outcome and radiation-induced side effects. *Head Neck.* 2019 Jun;41(6):1785-1794.

30. Gangl K, Nemec S, Altorjai G, Pammer J, Grasl MC, Erovic BM. Prognostic survival value of retropharyngeal lymph node involvement in sinonasal tumors: a retrospective, descriptive, and exploratory study. *Head Neck* 2017;39:1421-1427

31. Faisal M, Seemann R, Lill C, Hamzavi S, Wutzl A, Erovic BM, Janik S. Elective neck treatment in sinonasal undifferentiated carcinoma: Systemic review and meta-analysis. *Head Neck* 2020;42:1057-1066

32. Ledderose GJ, Reu S, Englhard AS, Krause E. Endonasal resection of early stage squamous cell carcinoma of the nasal vestibule. *Eur Arch Otorhinolaryngol* 2014;271:1051-1055

Tables

Table 1. Data of patients regarding T classification, tumor side, grading and therapy.

	TOTAL	Type of Recurrence				
		Local	Regional	Distant	No	
VARIABLES	n (%)	n (%)	n (%)	n (%)	n (%)	p-value
Sex						
Male	34 (58.6)	7 (20.6)	5 (14.7)	1 (2.9)	21 (61.8)	
Female	24 (41.4)	0 (0)	5 (20.8)	0 (0)	19 (79.2)	0.087
Tumor Site						
Septum	22 (37.9)	3 (13.6)	4 (18.2)	0 (0)	15 (68.2)	
Lateral Wall	13 (22.4)	2 (15.4)	1 (7.7)	0 (0)	10 (76.9)	
Vestibule	20 (34.5)	3 (15.0)	4 (20.0)	0 (0)	13 (65.0)	
Ethmoid	3 (5.2)	0 (0)	0 (0)	1 (33.3)	2 (66.6)	0.013
T-Classification						
T1	37 (63.8)	6 (16.2)	4 (10.8)	0 (0)	27 (73.0)	
T2	21 (36.2)	1 (4.8)	6 (28.6)	1 (4.8)	13 (61.9)	0.116
Grading						
G1	6 (10.3)	1 (16.7)	0 (0)	0 (0)	5 (83.3)	
G2	35 (60.3)	4 (11.4)	7 (20.0)	3 (8.6)	24 (68.6)	
G3	17 (29.3)	2 (11.8)	0 (0)	1 (5.9)	11 (64.7)	0.684
END						
Yes	9 (15.6)	0 (0)	0 (0)	0 (0)	9 (100.0)	
No	49 (84.4)	7 (14.3)	10 (20.4)	1 (2.0)	31 (63.3)	0.188
Adjuvant Therapy						
Yes	11 (19.0)	1 (9.1)	1 (9.1)	0 (0)	9 (81.2)	
No	47 (81.0)	6 (12.8)	9 (17.1)	1 (2.1)	31 (66.0)	0.757

Table 2
Elective Neck-Dissection and Recurrence.

Case	Sex	Age	Tumor	Tumor Site	TNM	Grading	Therapy	Recurrence
1	M	69,14	Primary	Septum	T1 N0	G3	Surgery	No
2	F	43,97	Primary	Vestibule	T1 N0	G2	Surgery	No
3	M	58,64	Primary	Lateral Wall	T1 N0	G3	Surgery	No
4	M	62,07	Primary	Vestibule	T1 N0	G2	Surgery	No
5	M	49,22	Recurrence	Lateral Wall	T2 N0	G2	Surgery + RT	No
6	M	73,36	Primary	Vestibule	T2 N0	G2	Surgery	No
7	M	36,36	Primary	Septum	T1 N0	G2	Surgery	No
8	F	58,47	Primary	Lateral Wall	T2 N0	G2	Surgery	No
9	M	59,17	Primary	Lateral Wall	T1 N0	G2	Surgery	No

Table 3
Freedom from Regional and Distant Recurrence

VARIABLES	Log-Rank Test				Cox-Regression Analysis		
	1y	3y	5y	<i>p</i>	HR	<i>p</i>	95% CI
Sex							
Male	82.5	76.2	76.2		1		
Female	88.8	74.5	74.5	0.769	1.41	0.591	0.40–4.96
Age							
< 63.2 y	96.3	86.4	86.4		0.34	0.117	0.09–1.31
≥ 63.2 y	76.7	62.0	62.0	0.052	1		
T-Classification							
T1	92.3	88.1	88.1		0.29	0.058	0.08–1.04
T2	75.3	49.9	49.9	0.016	1		
Tumor Site							
Septum + Vestibule	84.8	73.4	73.4		3.70	0.215	0.47–29.4
Lateral Wall + Ethmoid	90.9	79.5	79.5	0.426	1		
Grading							
G1	100.0	100.0	100.0		0.04	0.452	0.0–195.9
G2 + G3	85.2	73.0	73.0	0.217	1		
END							
Yes	100.0	100.0	100.0		1		
No	83.4	68.7	68.7	0.086	30.1	0.326	0.04–26776.1
Adjuvant Therapy							
Yes	100.0	87.5	87.5		1		
No	83.4	72.8	72.8	0.255	2.72	0.344	0.34–21.7
Risk Score *							
High	63.6	35.4	35.4		9.52	0.002	2.35–38.5
Low	93.5	86.2	86.2	< 0.001	1		

Table 4. Cancer Specific Survival

CANCER SPECIFIC SURVIVAL

	Log-Rank Test				Cox-Regression Analysis		
VARIABLES	1y	3y	5y	<i>p</i>	HR	p	95% CI
Sex							
Male	100.0	91.2	79.8		1		
Female	100.0	100.0	87.5	0.219	0.28	0.250	0.03 - 2.43
Age							
< 63.2 y	100.0	94.1	94.1		0.19	0.124	0.02 - 1.59
≥ 63.2 y	100.0	95.5	73.6	0.084	1		
T-Classification							
T1	100.0	96.4	96.4		0.10	0.035	0.01 - 0.85
T2	100.0	90.0	58.3	0.009	1		
Tumor Site							
Septum + Vestibule	100.0	95.8	85.6		0.36	0.220	0.07 – 1.83
Lateral Wall + Ethmoid	100.0	91.7	78.6	0.202	1		
Grading							
G1	100.0	100.0	100.0		0.04	0.558	0.0 - 1834.2
G2 + G3	100.0	94.0	81.4	0.361	1		
END							
Yes	100.0	100.0	100.0		1		
No	100.0	93.1	78.6	0.187	30.3	0.418	0.01 - 11669.5
Adjuvant Therapy							
Yes	100.0	100.0	83.3		1		
No	100.0	93.3	83.1	0.714	1.49	0.715	0.17 - 12.8
Risk Score *							
High	100.0	83.3	44.4		6.62	0.039	1.10 - 40.0
Low	100.0	97.0	92.8	0.017	1		
Regional Recurrence							
Yes	100.0	75.0	40.0		8.13	0.016	1.47 - 45.5
No	100.0	100.0	95.7	0.005	1		

Figures

A

B

Figure 1

Elective Neck Dissection in T1 and T2 sinonasal carcinomas. Figure 1 shows the answers of 19 evaluable centers regarding the performance of neck dissection in T1 and T2 sinonasal SCCs

A

		T-Classification	
		T1	T2
Anatomic Origin	Nasal Septum or Vestibule	1	2
	Other Subsite	0	1

Risk Score

0 points – low risk

1 point – moderate risk

2 points – high risk

B

Risk for Regional Recurrence

Low risk: 1/9 (11.1%)

Moderate risk: 3/35 (8.6%)

High risk: 6 /14 (42.9%)

Figure 2

Risk Score. Algorithm and Cross table of the risk score including tumor site and T-classification.

A **B**

Case: T1 SCCs originating from nasal septum

Figure 3

Nomogram. Nomogram to predict the risk for regional recurrence based on T-Classification (1=T1; 2=T2) and Anatomic Origin. In accordance to our risk score, we differentiated whether tumors originated from high-risk areas (nasal septum or vestibule – 1) or from other subsites (0). As exemplified, a T1 SCCs originating from nasal septum has a 13-14% risk for regional recurrence.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryQuestionnaire.docx](#)