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Maxillary Sinus and Hard Palate Squamous Cell Carcinoma: Multi-institutional Delta Region Experience

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RESEARCH ARTICLE

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ABSTRACT

Background: Although maxillary cancers are rare, squamous cell carcinoma (SCC) is the most common pathologic type. As such, c, omplications of the tumor and its treatment can affect the quality of life. Accordingly, multidisciplinary treatment is a must. **Aim of the Work:** To review the clinico-epidemiologic features of maxillary sinus squamous cell carcinoma (MxSSCC) in 2 cancer institutions in the Delta region with an analysis of prognostic factors. **Patient and Methods:** Sixty-four MxSSCC cases were included from January 2000 to June 2018 inclusive. Descriptive and survival analyses were carried out. Cox regression analysis was done to define prognostic factors. **Results:** The majority of patients were male, smokers, of the age range (40-69 years) showing high T staging and high node positivity. The treatment of the primary tumor ranged from surgery +/- adjuvant treatment in 34 patients (53%), definitive radiotherapy (DRT) +/- chemotherapy; whether induction, concomitant, or both in 25(39%) patients. Neck treatment varied between node dissection +/- radiotherapy (RT) in 25 cases (39.1%), DRT [28 cases (43.7%)], and 6 patients (9.4%) were under the wait and watch strategy. The median overall survival (OAS) was 61 months (range: 2-121) and the 5-years OAS was 51.6%. The median progression-free survival (PFS) was 44 months (range: 1-117) and the 5-years PFS was 40.6%. Multivariate analysis of prognostic factors affecting OAS and PFS revealed that low stage and free safety margin were independent positive prognostic factors. **Conclusion:** MxSSCC is rare. Most of the cases were presented at a late stage. Surgery +/- adjuvant treatment was the commonest modality for treating the primary tumor, while DRT+/- was used for treating the primary and nodes in nearly 40% of the cases. Low stage and free safety margins were the positive independent prognostic factors. There is a need to investigate stronger treatments for this cancer.

Keywords: MMaxillary sinus neoplasms, MMandibular neoplasms, SSkull base neoplasms, SSinonasal tumors

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INTRODUCTION

Maxillary carcinoma is the most common sinonasal and paranasal cancer representing (60-70 %) (Dhanani et al., 2021). Maxillary sinus squamous cell carcinoma (MxSSCC) represents the most common pathological type (60 to 75 %) with a poor prognosis (Mirghani et al., 2013, Takes et al., 2014). This is attributed to the late presentation as the maxillary sinus is a pyramidal structure with air-filled space, so the tumor grows silently with few or no signs until it reaches a significant size. Moreover, symptoms are mostly nonspecific and resemble common complaints that can be presented to dentists, otorhinolaryngologists, ophthalmologists, neurologists, and oncologists, so all specialties need to be aware of these tumors (Takes et al., 2014, Santos et al., 2014). The most common etiological factors of maxillary sinus SCC are alcohol and smoking; they have synergistic effects like other head and neck sites. Other risk factors include wood dust and nickel exposure. Another challenge is the presence of nonspecific and vague symptoms, which can be mistaken for allergic, inflammatory, and infective causes. This is the reason for delayed diagnosis and hence an advanced stage in maxillary sinus malignancies (Mirghani et al., 2013). Multidisciplinary treatment is needed

(Dhanani et al., 2021). This study aimed at a clinico-epidemiological study of MxSSCC cases at 2 cancer institutions in our locality.

PATIENTS AND METHODS

Data of sixty–four MxSSCC cases from 2 cancer institutions in the Delta region (Mansoura& Tanta) were included in this study from January 2000 to June 2018 inclusive . Inclusion criteria were pathologically proven MxSSCC of adult age range 18-80 years. Exclusion criteria were distant metastasis at presentation and the existence of other malignancies.

Our institutional review board (IRB) approved the study (approval number is MS. 20.03.179 in June 2020).

The data reviewed included: age, gender, residence, occupation, habits, comorbidities, presenting symptoms, pathological data, laboratory profile, treatment plan, and follow-up. Disease extent was determined through physical examination and radiology [magnetic resonant imaging (MRI) or/and computerized tomography (CT)]. The general treatment policy applied for the primary tumor was surgery +/- adjuvant radiotherapy (RT) with or without ChT in resectable cases and definitive radiotherapy (DRT) with or without ChT in irresectable cases. The general plan of treatment for the neck nodes was that the N0 neck was not treated electively in early-stage cases.

Surgery: The decision depended on the disease site, the ability to achieve a free resection margin, and the expected complications and deformities. The approaches applied were mainly lateral rhinotomy, transfascial and endoscopic.

Radiotherapy: A linear accelerator of 6MV photon was used. CT planning was applied while the patient was immobilized with a tongue bite. Two-dimensional radiotherapy (2D-RT) was applied till 2013. Conformal radiotherapy (CRT) was applied thereafter. In the 2D-RT era, patients planning usually included an anterior and two lateral fields. The DRT dose was 65 -70 gray (Gy) within 6.5 -7 weeks (2 Gy/fraction), while the adjuvant dose was50- 60Gy within 5-6 weeks. In the CRT era, multiple beams were added aiming at more sparing organs at risk (OAR) and increasing the tumor dose homogeneity. The DRT dose distribution to the planning target volume (PTV) was risk-based and ranged from 44-50 Gy to low-risk sites up to 66Gy-70Gy to high-risk sites. While the adjuvant doses ranged from 44-50Gy to low-risk sites up to 60-66Gy to high-risk sites. Intensity-modulated radiotherapy (IMRT) was not available.

According to the 2 institutes' delineation protocols, the target volume delineation was as follows:

- Postoperative radiotherapy (PORT) involves the whole tumor bed using preoperative initial radiological and clinical examination data as a guide and any residual disease with adding 5-8mm as a margin for covering areas with risk of microscopic disease.
- PORT of neck was not routinely given for N0 disease, but it may be received in cases having other risk factors (neck levels (Ib – V) were covered), while in pN+ cases levels II-IV were covered.
- Ipsilateral lymph nodes irradiation was usually received but bilateral neck irradiation was given only if the tumor was near or cross the midline.
- DRT covered the gross tumor volume (GTV) as presented clinically, radiologically, and by the endoscope beside involved lymph nodes with adding a 10mm margin to create the clinical target volume (CTV). CTV was modified to exclude air and/or bone without evidence of invasion.
- PTV was generated by an auto-expansion of 5-10 mm to the CTV.
- Organs at risk were the optic nerves, chiasma, eyes, brainstem, and spinal cord.

Chemotherapy: The use of adjuvant ChT, induction chemotherapy (IChT) or concomitant chemo-radiotherapy (CCRT) was decided by the treating team according to the radiologic and pathologic risk factors. ChT was 5FU and cisplatin-based, while the concomitant chemotherapy was weekly cisplatin. Follow-up after therapy was by physical examination and radiologically by CT scan or MRI every 3 months in the first year, every 6 months in the second year, and at longer intervals thereafter.

TNM staging was done according to the 7th edition of the American Joint Committee on

Cancer (AJCC) (Deschle et al., 2014). Overall survival (OAS) and progression-free survival (PFS) were our endpoints.

STATISTICAL ANALYSIS

Quantitative data were summarized as mean and standard deviation or median and range while qualitative data were presented as percentages. Comparison of group medians was done by using the Mann-Whitney test and Kruskal-Wallis test, while comparisons of percentages were made by the Chi-square test. Cox regression analysis was made to determine prognostic factors. OAS was calculated from diagnosis till death or last follow-up. PFS was calculated from the start of treatment till the date of progression, death or last follow-up. The survival was displayed by the Kaplan-Meier survival curve. The results were significant if the p-value was <0.05. All statistics were performed using the software tool Statistical Package for Social Sciences (SPSS) version 26.

RESULTS

This is a retrospective study of 64 patients with MxSSCC from 2 cancer institutions in our locality who were registered during the period from January 2000 to June 2018 inclusive. The patients and tumor characteristics are presented in Table 1.

The commonest age range (40-69 years) existed in 45 cases (70.3%). Males slightly exceeded females [34 (53.1%), 30(46.9%)] respectively. Smokers were nearly double the non-smokers [40(62.5%) versus 24 (37.5%)]. T4 exceeded T2 and T3 together [36(56.3%) versus [28(43.7%)]. Node-positive were nearly equal to node-negative cases [33(51.6%) versus 31(48.4%)]. For the primary tumor, surgery +/- adjuvant treatment (whether ChT or RT or both) was applied in 34 cases (53.1%), DRT was applied in 25 cases (39.1%), and five patients (7.8%) received ChT only and did not complete their treatment plan. Regarding neck node management, lymph node dissection (LND) +/- PORT was applied for 25 patients (39.1%), while DRT alone was applied for 28 patients (43.7%). Six patients (9.4%) were under wait and watch strategy (all were T2N0).

Table 1. Patient and tumor characteristics

	Total	
	N	%
Age		
18-39	8	12.5
40-69	45	70.3
70-75	11	17.2
Gender		
Female	30	46.9
Male	34	53.1
Residence		
Urban	41	64.1
Rural	23	35.9
Smoking		
Non-smoker	24	37.5
Smoker	40	62.5
Co-morbidities		
No	33	51.6
Yes	31	48.4
Symptoms		
Oral mass/ulcer	28	43.8
Headache	14	21.9
Cheek mass/ulcer	5	7.8
Proptosis	8	12.5
Nasal obstruction	7	10.9
Bleeding/epistaxis	2	3.1
Primary site		
Maxilla	54	84.4
Hard palate	10	15.6
T stage		
T2	15	23.4
T3	13	20.3
T4	36	56.3
N stage		
N0	31	48.4
N positive (N1-2)	33	51.6
Grade of differentiation		
GI	18	28.1
GII	19	29.7
GIII	27	42.2
LVI		
No	22	34.4
Yes	13	20.3
Unknown	29	45.3
Safety margin status		
Surgically treated	34	53.1%
Free	19	29.6
Close	6	9.4
Positive	9	14.1
Non surgically treated	30	46.9
Primary site treatment modality		
Surgically treated	34	53.1
DRT	25	39.1
ChT	5	7.8
Cervical LN treatment modality		
Wait and watch	6	9.4
LND	8	12.5
LND + PORT	17	26.6
DRT	28	43.7
ChT	5	7.8

LVI lymphovascular invasion, DRT definitive radiotherapy, ChT chemotherapy, RT radiotherapy, PORT postoperative radiotherapy, CCRT concomitant chemoradiotherapy, LND lymph node dissection

Lastly, 5 patients (7.8%) received only ChT and didn't complete the treatment plan.

The detailed treatments of the different T-stages are presented in Table 2. Table 3 presents the different neck treatment modalities of N0 cases. The wait-and-watch policy was applied only in T2 N0 cases [6(9.37%)]. LND was done in 3 (4.62%) T2 N0 cases versus 8 (12.5%) T3N0 and T4N0 cases. Six of those 8 T3,4N0 cases received PORT.

The median OAS was 61 months (range: 2-121 months) and the 5-years OAS was 51.6% as illustrated in Figure 1. Median PFS was 59 months (range: 1-117 months). The 5-years PFS was 40.6% as demonstrated in Figure 2. Univariate analysis of prognostic factors affecting 5-years OAS and PFS are presented in Table 4.

Table 5 presents multi-variate analysis of prognostic factors affecting OAS and PFS. As regards OAS, low T staging, node negativity, and free safety margin were all positive independent prognostic factors (*P = 0.032, 0.033, and 0.008* respectively). As regards PFS, node negativity and free safety margin were the only independent positive factors (*P = 0.033, 0.007* respectively).

The Median follow-up time was 63 months (range: 6 to 120 months). At the end of the study, 22 patients (34.4%) died, 5 cases (7.8%) lost follow-up without completing the treatment plan due to treatment toxicity, 8 cases (12.5%) were still alive till the end of the study, and 29 cases (45.3%) lost follow up after completing their treatment plan after variable periods of follow up.

Treatment failure was reported in 19 cases (29.7%). Locoregional recurrence was the main mode of failure in 16 cases (25%), while distant metastasis occurred in 3 cases (4.7%). Recurrence at the primary site, nodal recurrence, or both were reported in 8 cases (12.5%), 3 cases (4.7%), and 5 cases (7.8%) respectively. Salvage surgery was the main palliative modality used in 10 cases (15.6%) with or without adjuvant treatment (PORT+/- ChT). Palliative chemotherapy was received by 7 cases (10.9%) while palliative RT was applied to 2 cases (3.2%).

DISCUSSION

Maxillary tumors are rare. Otorhinolarygologists, oncologists, dentists, and general physicians should all be aware of such tumors.

Our commonest age range was (40-69 years) which is younger than Western and Asian reported ages (Santos et al., 2014, Dubal et al., 2016). This is due to the relatively lower age range in our region.

Our male and female incidence was nearly equal which is like the report of Suh et al. (2016) who reported a male: female ratio of 2.3:1. However, our results were unlike the reports of Shen et al. (2017) and Wang et al. (2020) who reported a higher male incidence and explained that by the higher incidence of smoking among males. Our equal incidence in both sexes may be due to the effect of passive smoking on females. Our higher reported incidence among smokers is in line with different reports like those of Wang et al. (2020) and Duru Birgi et al. (2015) and is so encouraging to all efforts to fight smoking. The higher incidence of cases among those from urban areas in our locality could be due to higher occupational exposure and that parallels the reports of Santos et al. (2014) and Lai et al. (2013) who related MxSSCC to industrial pollution.

Grade III tumors existed in more than one-third of our cases (42.2%), while T4 was documented in more than half of them (56.3%). These results were to some extent homogenous with results reported by Sangal et al. (2018) and Wang et al. (2020) who reported Grade III rates of 33% and 33% and T4 rates of 50.4% and 44.9% respectively. However, Parikh et al (Parikh et al., 2021) reported higher percentages of grade III (50%) and T4 (63%), while Moratin et al. (2018) and Ranasinghe et al. (2020) reported lower rates of grade III (19% and 26%) and T4 (26.5% and 31%) respectively.

Our node positivity rate was (51.6%), which was much higher than the reported rates in 2 recent meta-analyses (Ferrari et al., 2021, Galloni et al., 2021) who reported incidences of 21% and 28% respectively.

Table 2. The treatment modalities applied for each T staging.

	T2		T3		T4		Total	
	15	**(23.4%)**	**13**	**(20.3%)**	**36**	**(56.3%)**	**64**	**(100%)**
Primary site treatment								
DRT	3	(4.67%)	5	(7.81%)	17	(26.5%)	25	(39%)
RT alone	2	(3.12%)	4	(6.25%)	4	(6.25%)	10	(15.6%)
CCRT	0	(0%)	0	(0%)	6	(9.37%)	6	(9.37%)
IChT + CCRT	0	(0%)	1	(1.5%)	4	(6.25%)	5	(7.81%)
IChT + RT	1	(1.5%)	0	(0%)	3	(4.67%)	4	(6.25%)
Surgery	12	(18.75%)	8	(12.5%)	14	(21.8%)	34	(53.1%)
Surgery	5	(7.81%)	6	(9.37%)	1	(1.5%)	12	(18.75%)
Surgery + ChT	2	(3.12%)	0	(0%)	1	(1.5%)	3	(4.67%)
Surgery + PORT	5	(7.81%)	1	(1.5%)	4	(6.25%)	10	(15.6%)
Surgery + PORT + ChT	0	(0%)	1	(1.5%)	3	(4.67%)	4	(6.25%)
Surgery + CCRT	0	(0%)	0	(0%)	5	(7.81%)	5	(7.81%)
Chemotherapy	0	(0%)	0	(0%)	5	(7.81%)	5	(7.81%)
Cervical lymph node treatment								
Wait and watch	6	(9.37%)	0	(0%)	0	(0%)	6	(9.37%)
DRT	6	(9.37%)	5	(7.81%)	17	(26.5%)	28	(43.75%)
LND	2	(3.12%)	4	(6.25%)	2	(3.12%)	8	(12.5%)
LND + PORT	1	(1.5%)	4	(6.25%)	12	(18.75%)	17	(26.5%)
Chemotherapy	0	(0%)	0	(0%)	5	(7.81%)	5	(7.81%)

DRT definitive radiotherapy, RT radiotherapy, CCRT concomitant chemo-radiotherapy, IChT induction chemotherapy, ChT chemotherapy, PORT postoperative radiotherapy, LND lymph node dissection

Table 3. The different neck treatment modalities of N0 cases

	T2N0		T3N0		T4N0		Total	
	13	(18.75%)	6	(9.37%)	12	(18.75%)	31	(48.4%)
Wait and watch	6	(9.37%)	0	(0 %)	0	(0%)	6	(9.37%)
DRT	4	(6.25%)	3	(4.67%)	7	(10.9%)	14	(21.8%)
LND	2	(3.12%)	2	(3.12%)	0	(0%)	4	(6.25%)
LND + PORT	1	(1.5%)	1	(1.5%)	5	(7.81%)	7	(10.9%)
Chemotherapy	0	(0%)	0	(0%)	0	(0%)	0	(0%)

DRT definitive radiotherapy, LND lymph node dissection, PORT postoperative radiotherapy

Our general policy was to treat N0 electively in T3 and T4 cases (18 cases) but not in early-stage (T2) cases that had no other risk factors (6/13). The issue of non-generalization of elective node treatment (ENT) was investigated in the literature. Park et al. (2017) studied retrospectively 67 patients (34% of them were T1&T2). The 5-year OAS was 51.9% for the ENT group and 74.0% for the non-ENT group. The difference was statistically non-significant. Moreover, Lee et al. (2018) in their retrospective study of 124 cases, 32% (40/124) patients received ENT and 68% (84/124) did not. T1 &T2 cases were 12%. There was no statistical difference between ENT and the non-ENT groups as regards OAS and PFS (*P=0.67 and 0.50* respectively). Ferrari et al. (2021) explained these insignificant differences by the existence of multiple poor prognostic factors in MxSSCC that may outweigh any benefit from ENT. However, Galloni et al. (2021) revealed statistically higher nodal recurrence in cases who did not have an upfront ENT (15.0%) versus (5.9%) for patients who were treated with surgical dissection or irradiation. However, it was stated that it remains unclear whether the added morbidity of ENT does outweigh the risk of having a regional failure (Mirghani et al., 2013, Dooley et al., 2015).

Although surgery is considered the main treatment of MxSSCC (Duru Birgi et al., 2015), DRT for treating the primary site and neck was applied in 39.1% and 43.7% of our cases respectively. This could be explained by the high percentage of both T4 and node positivity (56.3% and 51.6%) respectively which minimizes the chances of safe complete respectability.

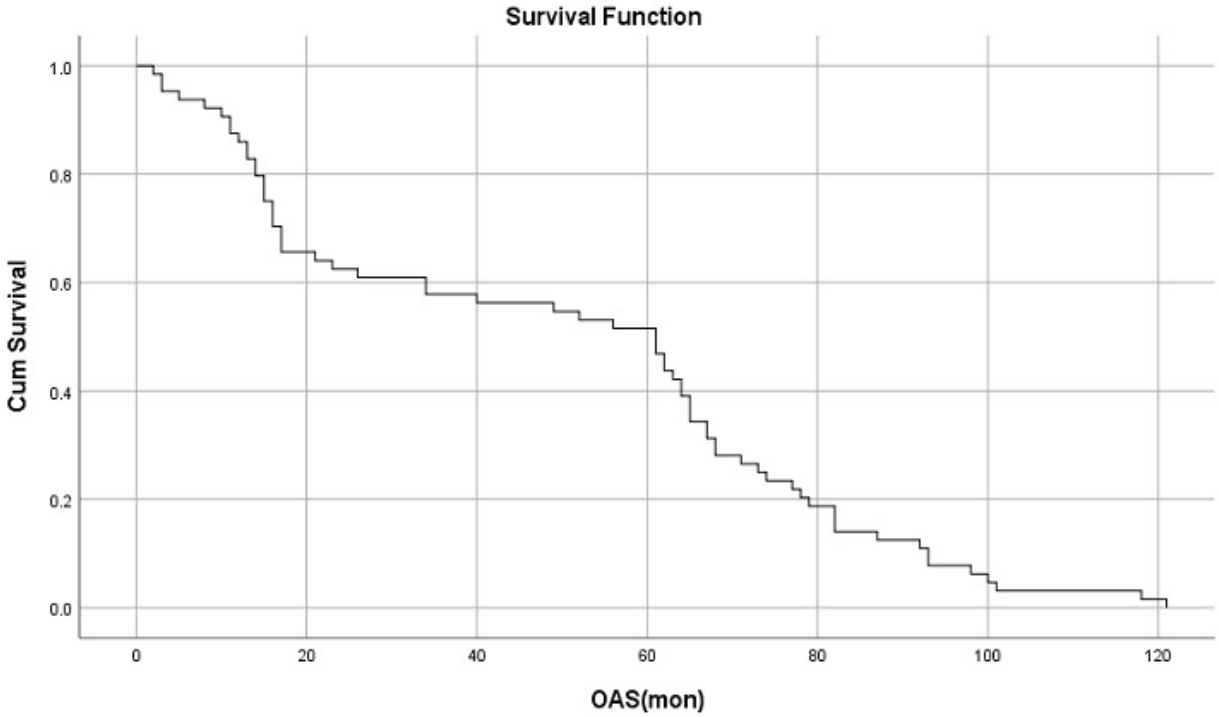

Figure 1. Kaplan-Meier curve of OAS

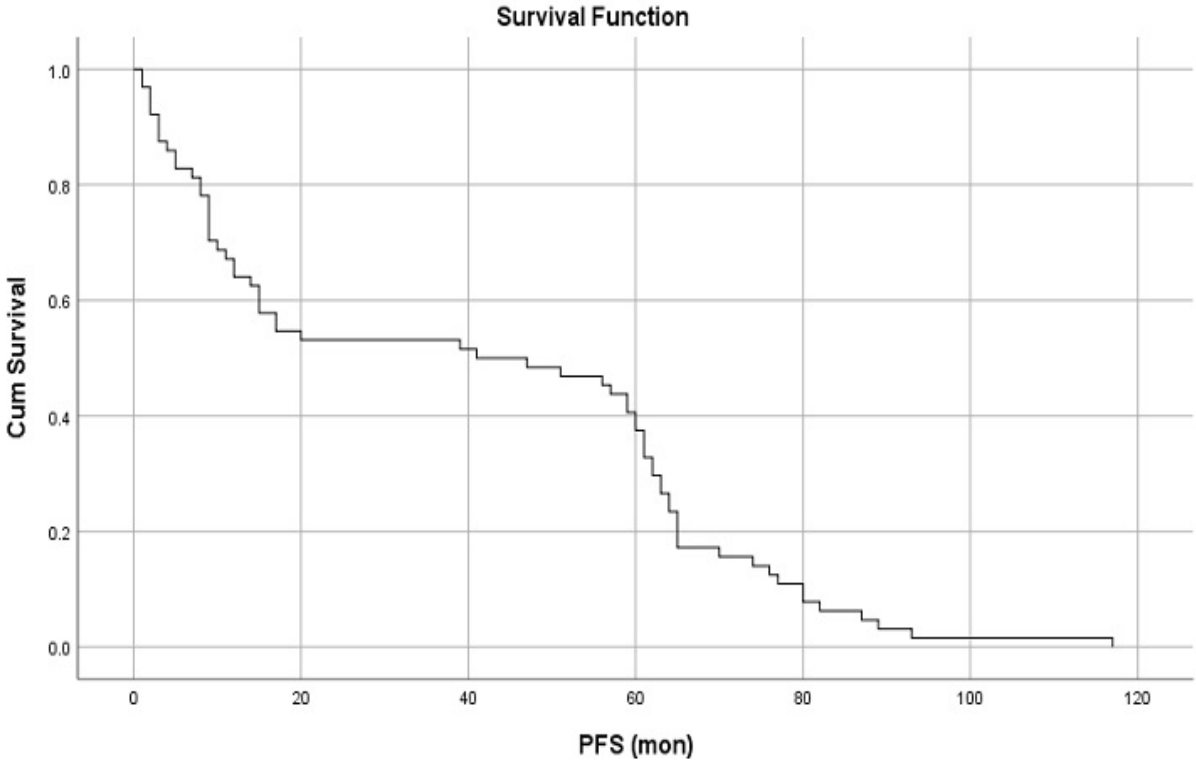

Figure 2. Kaplan-Meier curve of PFS

Table 4. Univariate analysis of 5-years OAS and PFS prognostic factors

	5-years OAS %	p-value	5-years PFS %	P-value
Age				
18-39	87.5%		50%	
40-69	48.9%	0.071	40%	0.826
70-75	36.4%		36.4%	
Gender				
Female	46.7%	0.462	36.7%	0.545
Male	55.9%		44.1%	
Residence				
Urban	46.3%	0.264	34.1%	0.159
Rural	60.9%		52.2%	
Smoking				
Non-smoker	79.2%	0.001**	70.8%	<0.001**
Smoker	35%		22.5%	
Co-morbidities				
No	69.7%	0.003**	60.6%	0.001**
Yes	32.3%		19.4%	
Symptoms				
Oral mass/ulcer	60.7%	0.499	39.3%	0.958
Headache	35.7%		35.7%	
Cheek mass/ulcer	40%		40%	
Proptosis	37.5%		37.5%	
Nasal obstruction	71.4%		57.1%	
Bleeding/epistaxis	50%		50%	
Primary site				
Maxilla	50%	0.561	37%	0.174
Hard palate	60%		60%	
T stage				
T2	93.3%	<0.001**	66.7%	0.012**
T3	61.5%		53.8%	
T4	30.6%		25%	
N stage				
N0	93.5%	<0.001**	74.2%	<0.001**
N positive (N1-2)	12.1%		9.1%	
Grade of differentiation				
GI	94.4%	<0.001**	72.2%	<0.001**
GII	73.7%		63.2%	
GIII	7.4%		3.7%	
LVI				
No	95.5%	<0.001**	72.7%	0.001**
Yes	23.1%		15.4%	
Unknown	31%		27.6%	
Safety margin status				
Surgically treated	67.6%		52.9%	
Free	94.7%	<0.001**	89.5%	<0.001**
Close	50%		16.7%	
Positive	22.2%		0%	
Non surgically treated	33.3%		26.7%	
Primary site treatment modality				
Surgically treated	67.6%	0.006**	52.9%	0.042**
DRT	40%		32%	
ChT	0%		0%	
Cervical LN treatment modality				
Wait and watch	100%	0.02**	50%	0.374
LND	62.5%		50%	
LND + PORT	52.9%		47.1%	
DRT	46.4%		39.3%	
ChT	0%		0%	

LVI lymphovascular invasion, DRT definitive radiotherapy, ChT chemotherapy, RT radiotherapy, PORT postoperative radiotherapy, CCRT concomitant chemoradiotherapy, LND lymph node dissection

Table 5. Multivariate analysis of OAS and PFS prognostic factors

	Multivariate analysis of OAS prognostic factors				Multivariate analysis of PFS prognostic factors			
	B	P-value	Odds ratio	95% CI of Odds ratio	B	P-value	Odds ratio	95% CI of Odds ratio
Smoking	0.185	0.838	1.203	0.204 – 7.075	-0.348	0.662	0.706	0.148 – 3.370
Co-morbidities	0.391	0.572	1.478	0.381 – 5.743	0.302	0.618	1.352	0.413 – 4.430
T stage	1.118	0.032*	3.060	1.103 – 8.493	-0.113	0.776	0.893	0.410 – 1.948
N stage	2.747	0.033*	15.589	1.251 – 194.311	2.058	0.033*	7.830	1.181 – 51.909
Grade of differentiation	0.902	0.256	2.464	0.519 – 11.698	0.452	0.498	1.571	0.426 – 5.799
LVI	-0.830	0.308	0.436	0.088 – 2.153	-1.030	0.162	0.357	0.084 – 1.515
Safety margin status	1.934	0.008*	6.919	1.657 – 28.896	1.303	0.007*	3.681	1.436 – 9.438
Primary site treatment modality	-0.168	0.837	0.845	0.170 – 4.192	-0.349	0.677	0.706	0.137 – 3.642
Cervical LN treatment modality	0.204	0.485	1.226	0.692 – 2.173				

LVI lymphovascular invasi

The relative success of DRT in treating advanced cases without suffering the morbidities of surgical maneuver was reported by Duru Birgi et al. (2015) who studied 43 patients with sinonasal squamous cell carcinoma. T3&T4 were 72% (31/43), while N+ were 12%. There was no significant difference in outcome comparing patients who underwent surgery+PORT with patients who received DRT (2- year disease-free survival was 75% and 70% respectively, *P= 0.98*). Similarly, Park et al. (2016) studied 73 patients, 52 patients (71.2%) were treated with DRT and 21 (28.8%) were treated with surgery+PORT. Fifty-eight (79.45%) were T3&T4 and 17.8% were LN+ve. The 5-year local PFS, regional PFS, and OAS in the DRT and PORT groups were 50.6%, 82.1%, and 84.4% versus 85.7%, 72.1%, and 83.5%, respectively with statistically insignificant differences.

Our cases receiving RT after surgery exceeded the number of cases who underwent surgery alone for the primary (19 versus 15 cases) or the neck nodes (17 versus 8). This copes with the recommendations of Su et al. (2008) who reported the superiority of multimodality therapy in general. He studied 92 patients with stage T3-T4 MxSSCC, 21/92 received RT alone, 8 received surgery alone, and 63 received multimodality therapy (51 received surgery combined with RT, and 12 received chemoradiotherapy). The 5-year survival rates were significantly lower in RT group and surgery group than in multimodality therapy group (9.5% and 12.5% vs. 33.3%, *P<0.05*). Ashraf et al. (2010) studied 379 patients with MxSSCC managed with curative intent. Twenty-eight patients had T2, 237 patients had T3, and 114 had T4 tumors. The N classification was N0 in 316 patients and N+ in 63 patients. Treatment to the primary comprised of surgery+ RT in 284 patients, RT alone in 57 patients, and ChT + RT in 38 patients. There was a difference in survival between patients who underwent surgery + RT compared with patients who received RT alone or ChT + RT. Local control at 3 and 5 years was 71% and 63.8% respectively in the surgery + RT group, 31.6%, and 28% in RT, and 28.9% and 26% in the ChT + RT group (*P= 0.0002*). So, Ashraf et al. (2010) reported the superiority of multimodality therapy when it includes surgery. A recent meta-analysis by Slieker et al. (2021) confirmed the superiority of surgery + adj/neoadjuvant treatment over surgery alone as regard outcomes in cases with risk factors.

Treatment modalities were not among our independent prognostic factors. This contradicts the reports of Li et al. (2019) and Nguyen et al. (2022) who reported a significant effect of PORT+/-chemotherapy in high stages. Our result might be due to the small number of patients.

Our 5-year OAS was 51.6% and the 5-year PFS was 40.6%. These results cope with those of Nguyen et al. (2022) but are much higher than those of Slevin et al. (2021) who reported a 5-year OAS and PFS of 30.2% and 24.2%, respectively, and lower than the results reported by Slieker et al. (2019) and Tiwari et al. (2000) who reported a 5- years OAS > 60%. The heterogeneity of results may be due to the different stages of patients and different treatment modalities included in the different series.

Multivariate analysis of OAS confirmed the positive prognostic impact of low T staging, node negativity, and free safety margin. This result is concordant with Nguyen et al. (2022) and Ackall et al. (2021). Age and gender were not of prognostic impact in our study as reported by Santos et al. (2014) but that is unlike the reports of Sundermann et al. (2018) who reported that younger age and female gender were poor prognostic factors and Jain et al. (2019) who reported that older ages were poor prognostic value.

Most treatment failures were in the form of local recurrence. This coincides with data published by Mirghani et al. (2013), Wang et al. (2020) and Slevin et al. (2021). This fact maximizes the importance of promoting local treatment techniques. Limitations of this study are the retrospective nature, the small patient number, and missing data regarding lymphovascular invasion and extracapsular extension.

CONCLUSION

MxSSCC is rare. A high percentage of T4 and N positivity existed. Surgery +/- radiotherapy was applied in more than half of the cases. Low staging and free safety margin were the most important positive independent prognostic factors. Stronger treatment modalities are needed.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interests

REFERENCE

Ackall FY, Issa K, Barak I, Teitelbaum J, Jang DW, Jung SH, et al. (2021). Survival outcomes in sinonasal poorly differentiated squamous cell carcinoma. The Laryngoscope; 131(4): E1040-e8. 2020/09/23. https://doi.org/10.1002/lary.29090.

Ashraf M, Biswas J, Dam A, Bhowmick A, Jha, Sing V, et al. (2010). Results of treatment of squamous cell carcinoma of maxillary Sinus: A 26-Year Experience. World Journal of Oncology; 1(1): 28-34. 2010/02/01. http://doi.org/10.4021/wjon2010.02.191w.

Deschler, Daniel G., Michael G. Moore, and Richard V. (2014). Smith. Quick reference guide to TNM staging of head and neck cancer and neck dissection classification. American Academy of Otolaryngology–Head and Neck Surgery Foundation.[Internet]: 1-34.http://www.entnet.org/wpcontent/uploads/files/NeckDissection_QuickRefGuide_highresFINAL.pdf.

Dhanani R, Faisal M, Shahid H, Malik KI, Jamshed A, Hussain R. (2021). Outcomes of Management of Sinonasal Malignancies at a Dedicated Cancer Institution: A Retrospective Study. Annals Maxillofacial Surgery.;11(1):115-120. doi: 10.4103/ams.ams_16_21. Epub 2021 Jul 24. PMID: 34522665; PMCID: PMC8407647.

Dooley L, Shah J. (2015). Management of the neck in maxillary sinus carcinomas. Current Opinion in Otolaryngology Head Neck Surgery; 23(2): 107-14. 2015/02/19. http://doi.org/10.1097/moo.0000000000000138.

Dubal PM, Bhojwani A, Patel TD, Zuckerman O, Baredes S, Liu JK, et al. (2016). Squamous cell carcinoma of the maxillary sinus: A population-based analysis.Sourh Asian Journal of Cancer; 126(2): 399-404. https://doi.org/10.1002/lary.25601.

Duru Birgi S, Teo M, Dyker KE, Sen M, Prestwich RJD. (2015). Definitive and adjuvant radiotherapy for sinonasal squamous cell carcinomas: a single institutional experience. Radiation Oncology; 10(1): 190. http://doi.org/10.1186/s13014-015-0496-3.

Ferrari M, Taboni S, Carobbio ALC, Emanuelli E, Maroldi R, Bossi P, et al. (2021). Sinonasal squamous cell carcinoma, a narrative reappraisal of the current evidence. Cancers; 13(11). 2021/07/03. https://doi.org/10.3390/cancers13112835.

Galloni C, Locatello LG, Bruno C, Cannavicci A, Maggiore G, Gallo O. (2021). The role of elective neck treatment in the management of sinonasal

carcinomas: A systematic review of the literature and a meta-Analysis. Cancers, 13(8). 2021/05/01. https://doi.org/10.3390/cancers13081842.

Jain S, Li Y, Kuan EC, Tajudeen BA, Batra PS. (2019). Prognostic factors in paranasal sinus squamous cell carcinoma and adenocarcinoma: A SEER Database Analysis. Journal of neurological surgery. Part B, Skull Base; 80(03): 258-63. 24.08.2018. http://doi.org/10.1055/s-0038-1669420.

Lai PS, Christiani DC.(2013). Long-term respiratory health effects in textile workers. Current Opinion in Pulmonary Medicine; 19(2): 152-7. https://doi.org/10.1097/MCP.0b013e32835cee9a.

Lee WH, Choi SH, Kim S-H, Choi EC, Lee CG, Keum KC. (2018). Elective neck treatment in clinically node-negative paranasal sinus carcinomas: impact on treatment outcome. Radiation Oncology Journal; 36(4): 304-16. 2018/12/31. http://doi.org/10.3857/roj.2018.00416.

Li R, Tian S, Lin L, Liu Q, Wang S. (2019). Comparative outcome of surgical and nonsurgical therapy for T4bN0M0 sinonasal squamous cell carcinomas. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS): affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery, 276(11): 3113-22. http://doi.org/10.1007/s00405-019-05601-7.

Mirghani H, Hartl D, Mortuaire G, Armas GL, Aupérin A, Chevalier D, et al. (2013). Nodal recurrence of sinonasal cancer: does the risk of cervical relapse justify a prophylactic neck treatment? Oral Oncology; 49(4): 374-80. 2012/11/03. https://doi.org/10.1016/j.oraloncology.2012.10.002.

Moratin J, Fuchs A, Zeidler C, Müller-Richter UD, Brands RC, Hartmann S, et al.(2018). Squamous cell carcinoma of the maxilla: Analysis of clinicopathological predictors for disease recurrence and metastatic behavior. Journal of Cranio-Maxillofacial Surgery; 46(4): 611-6. https://doi.org/10.1016/j.jcms.2018.01.002.

Nguyen ES, Risbud A, Birkenbeuel JL, Murphy LS, Goshtasbi K, Pang JC, et al. (2022). Prognostic factors and outcomes of de novo sinonasal squamous cell carcinoma: A systematic review and meta-analysis. Otolaryngolo--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery; 166(3): 434-43. 2021/07/14. https://doi.org/10.1177/01945998211021023.

Parikh AS, Fuller JC, Lehmann AE, Goyal N, Gray ST, Lin DT. (2021). Prognostic Impact of Adverse Pathologic Features in Sinonasal Squamous Cell Carcinoma. Journal of neurological Surgery. Part B, Skull Base; 82(Suppl 3): e114-e9. 2021/07/27. https://doi.org/10.1055/s-0040-1710516.

Park SH, Lee JE, Ahn D.(2016). Outcome of definitive and postoperative radiotherapy in patients with sinonasal squamous cell carcinomas. Tumori; 102(4): 426-32. 2015/10/03. http://doi.org/10.5301/tj.5000431.

Park J-H, Nam W, Kim HJ, Cha I-H. (2017). Is elective neck dissection needed in squamous cell carcinoma of maxilla? Journal of the Korean Association of Oral and Maxillofacial Surgeons; 43(3): 166-70. 2017/06/28. http://doi.org/10.5125/jkaoms.2017.43.3.166.

Ranasinghe VJ, Stubbs VC, Reny DC, Fathy R, Brant JA, Newman JG (2020). Predictors of nodal metastasis in sinonasal squamous cell carcinoma: A national cancer database analysis. World J of Otorhinolaryngol - Head and Neck Surg; 6(2): 137-41. 2020/07/01. https://doi.org/10.1016/j.wjorl.2020.01.006.

Sangal NR, Lee Y-J, Brady JS, Patel TD, Eloy JA, Baredes S, et al. (2018). The role of elective neck dissection in the treatment of maxillary sinus squamous cell carcinoma. The Laryngoscope; 128(8): 1835-41. https://doi.org/10.1002/lary.27009.

Santos MRM, Servato JPS, Cardoso SV, de Faria PR, Eisenberg ALA, Dias FL, et al. (2014). Squamous cell carcinoma at maxillary sinus: clinicopathologic data in a single Brazilian institution with review of literature. International journal of clinical and experimental pathology; 7(12): 8823-32. https://pubmed.ncbi.nlm.nih.gov/25674251. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4313952/.

Shen W, Sakamoto N, Yang L. (2017). Prognostic models and nomograms for predicting survival of patients with maxillary sinus carcinomas. International forum of allergy & rhinologyn; 7(7): 741-8. https://doi.org/10.1002/alr.21950.

Slevin F, Pan S, Mistry H, Denholm M, Shor D, Oong Z, et al. (2021). A multicentre UK study of outcomes for locally advanced sinonasal squamous cell carcinoma treated with adjuvant or definitive intensity-modulated radiotherapy. Clinical Oncology (Royal College of Radiologists (Great Britain)); 33(10): e450-e61. https://doi.org/10.1016/j.clon.2021.05.012.

Slieker FJB, de Bree R, Van Cann EM. (2019). Predicting individualized mortality probabilities for patients with squamous cell carcinoma of the maxilla: Novel models with clinical and histopathological predictors. Head & Neck; 41(10): 3584-93. https://doi.org/10.1002/hed.25879.

Slieker FJB, Rombout DAA, de Bree R, Van Cann EM. (2021). Local recurrence and survival after treatment of oral squamous cell carcinoma of the maxilla: A systematic review and meta-analysis. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. https://doi.org/10.1016/j.oooo.2021.10.003.

Su YR, Wu GH, Zeng ZY, Guo ZM, Chen WK, Wei MW, et al. (2008). Treatment of advanced maxillary sinus squamous carcinoma: an analysis of 92 cases. Ai zheng Chinese Journal of Cancer; 27(5): 535-8. 2008/05/16. http://www.cancercommun.com/fulltextnew.asp?y=2008&m=5&ym=535

Suh Y-G, Lee CG, Kim H, Choi EC, Kim SH, Kim C-H, et al. (2016). Treatment outcomes of intensity-modulated radiotherapy versus 3D conformal radiotherapy for patients with maxillary sinus cancer in the postoperative setting. International Journal of Radiation Oncology and Biological Physics; 38(S1): E207-E13. doi: https://doi.org/10.1002/hed.23971.

Sundermann BV, Uhlmann L, Hoffmann J, Freier K, Thiele OC. (2018). The localization and risk factors of squamous cell carcinoma in the oral cavity: A retrospective study of 1501 cases. Journal of Cranio-Maxillofacial Surgery; 46(2): 177-82. https://doi.org/10.1016/j.jcms.2017.10.019.

Takes RP, Ferlito A, Silver CE, Rinaldo A, Medina JE, Robbins KT, et al. (2014). The controversy in the management of the N0 neck for squamous cell carcinoma of the maxillary sinus. European archives of oto-rhino-laryngology :official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery Eur Arch Otorhinolaryngol; 271(5): 899-904. https://10.1007/s00405-013-2591-0.

Tiwari R, Hardillo JA, Mehta D, Slotman B, Tobi H, Croonenburg E, et al. (2000). Squamous cell carcinoma of maxillary sinus. Head& Neck; 22(2): 164-9. https://doi.org/10.1002/(SICI)1097-0347(200003)22:2.

Wang Y, Yang R, Zhao M, Guo W, Zhang L, Zhang W, et al. (2020). Retrospective analysis of 98 cases of maxillary sinus squamous cell carcinoma and therapeutic exploration. World Journal of Surgical Oncology; 18(1): 90. 2020/05/08. https://doi.org/10.1186/s12957-020-01862-3.