European Archives of Oto-Rhino-Laryngology (2019) 276:3113–3122
https://doi.org/10.1007/s00405-019-05601-7

RHINOLOGY

Comparative outcome of surgical and nonsurgical therapy for T4bN0M0 sinonasal squamous cell carcinomas

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Received: 23 June 2019 / Accepted: 10 August 2019 / Published online: 26 August 2019

Abstract

Purpose Definitive radiotherapy (RT) is recommended by NCCN guidelines for T4b tumors of sinonasal squamous cell carcinomas (SNSCC). However, no multi-institutional clinical studies have proved its advantage over surgery-based modalities. The aim of this study was to assess the survival of T4bN0M0 SNSCC patients who received surgery plus postoperative radiation (S + PORT) compared with those who received RT.

Methods This study extracted 220 patients from the SEER database from 2004 to 2015. Propensity score matching (PSM) was used to eliminate the baseline variations.

Results In SEER database, 43.6% of patients received S + PORT, and subsequently followed by RT (36.4%). Five-year overall survival (OS) and cancer-specific survival rates (CSS) in S + PORT were 42.5% and 46.9%, respectively, significantly better than for RT (21.7% and 26.7%). Multivariate analysis showed that therapy of RT had higher cancer-specific mortality risk than S + PORT [hazard ratio (HR) 1.578, $p = 0.032$]. After PSM, 57 pairs of patients were selected. There was still a significant difference noted with regard to 5-year OS or 5-year CSS between patients receiving S + PORT and RT (43% vs 22.5%, $p = 0.012$; 45.8% vs 27.7%, $p = 0.025$). The univariate and multivariate analyses of factors predictive of CSS showed that therapy of RT (HR 1.877, $p = 0.018$) and primary subsite of maxillary sinus (HR 2.629, $p = 0.001$) were significantly correlated with adverse outcomes.

Conclusion Combination of surgery and postoperative radiotherapy may contribute to prolonged survival in T4bN0M0 SNSCC. Invasion of the sites of T4b tumors is not an absolute contraindication for surgery.

Keywords Sinonasal squamous cell carcinomas · Surgery · Radiotherapy · Survival · SEER

Introduction

Sinonasal squamous cell carcinomas (SNSCC) are uncommon and usually diagnosed at a locally advanced stage [1, 2]. They commonly invade critical structures and are at close proximity to base of skull, orbit, and brain, which result in poor survival. The 5-year survival was 80% in patients with T1 stage, which fell to 30% in patients with T4 stage [3–5]. As a consequence, it has been confirmed that complete surgical resection with postoperative radiotherapy is the mainstay of therapy for SNSCC [2, 6, 7]. However, the complex anatomical location, as well as visual and facial structures, is "challenging" in terms of performing radical treatment while preserving critical organs and improving local control rates at the same time [8–10]. The sixth edition of AJCC classification divides T4 tumors into T4a (resectable) and T4b (unresectable) [11], which means tumor involvement of sites of T4b is associated with poor prognosis. The definition of

Ruichen Li, Shu Tian and Lan Lin have contributed equally to this work.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00405-019-05601-7) contains supplementary material, which is available to authorized users.

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unresectable tumor is based on technical inability to obtain clear margins [11–13], so definitive radiation or systemic therapy/radiation is recommended by NCCN guidelines for T4b [12–14].

With the development of surgical and reconstructive techniques, the indication of surgery in locally advanced cancers has been broadened over years [11, 15, 16]. The experience of surgeon often strongly influences the decision, and there is no universally accepted definition of unresectable. Overwhelming evidence indicated that en bloc resection is not always necessary and tumors can be fragmented if radical removal of tumors is guaranteed at the end of treatment [6, 16–18]. More importantly, no multi-institutional clinical trials have proved that definitive radiotherapy has an advantage over surgery-based modalities.

The aim of the present study was to assess the survival of T4bN0M0 SNSCC patients who received surgery plus postoperative radiation (S + PORT) compared with those who received definitive radiotherapy (RT) with data from the SEER database. A second objective was to explore comprehensive factors affecting the prognosis of T4bN0M0 patients.

Materials and methods

Data collection

Data were collected from SEER and included patients with a diagnosis of SNSCC between the years 1973 and 2015 (year of diagnosis) (https://seer.cancer.gov). The SEER is an authoritative source of data on cancer incidence and survival in US, and covers approximately 28% of the US population. All records were found at the following sites, using the site codes of the International Classification of Disease for Oncology, 3rd Edition (ICD-O-3): C30.0 (nasal cavity), C31.0 (maxillary sinus), C31.1 (ethmoid sinus), C31.2 (frontal sinus), C31.3 (Sphenoid sinus), C31.8 (Overlapping lesion of accessory sinuses), C31.9 (Accessory sinus, NOS). Exclusion criteria were as follows: not squamous cell carcinomas; without positive histology confirmation; without complete survival information; not T4bN0M0 (tumor stage); not the first tumor; total number of tumors was not 1; radiation prior to surgery (treatment modalities). The selection process is provided in Fig. 1. Tumor stage was decided at the first diagnosis and based on the AJCC staging manual (8th edition).

Clinical and sociodemographic characteristics including age, race, gender, year of diagnosis, primary subsite, differentiated grade, surgery, radiotherapy, chemotherapy, insurance, and marital status at the time of diagnosis were included in the analysis. The SNSCC cancer-specific survival and non-cancer-specific survival were extracted from the SEER variables of cause-specific death classification and other cause of death classification. The correlation between surgery and radiation was extracted from the variables of radiation sequence with surgery, reason no cancer-directed surgery, and radiation recode. The type of surgery of the primary site was extracted from the variable of RX Summ–Surg Prim Site (1998 +). According to SEER Program Coding and Staging Manual 2018, the code 26 (Polypectomy—Local tumor excision), code 27 (Excisional biopsy—Local tumor excision), code 30 (Simple/partial surgical removal of primary site), and code 50 (Surgery stated to be "debulking") were defined as partial resection. While code 40 (Total surgical removal of primary site; enucleation) and code 60 (Radical surgery) were defined as total resection.

Statistical analysis

All statistical analyses were performed using SPSS, version 22 (IBM, Chicago, IL). The baseline characteristics between different groups were compared using the chi-squared test or Fisher's exact test, as appropriate. Overall survival (OS) and cancer-specific survival (CSS) were analyzed with the Kaplan–Meier method, and log-rank test was used for comparing survival curves. The Cox proportional hazards model was used for univariate and multivariate analyses. Variables with $p < 0.05$ in the univariate analyses were included in the multivariate analyses. Propensity score matching (1:1 matching ratio) was adopted to adjust for clinical factors. The significant difference was defined as a two-tailed p value < 0.05.

Results

Patient characteristics

As shown in Fig. 1, SNSCC accounted for 55% (6868 out of 12,487) of sinonasal cancer cases in the SEER database. Patients who were diagnosed in the period from 1973 to 2003 were excluded from the selection process, as their AJCC TNM stage status was unavailable. As a consequence, 220 cases with T4bN0M0 were included in our study. Patient demographic and clinical information are presented in Table 1. The majority of patients were white (73.6%), male (67.7%), arising from the maxillary sinus (50.5%), poorly or undifferentiated tumors (45.9%), and had insurance (78.2%). Most of patients received chemotherapy (61.4%). Approximately 43.6% of patients received S + PORT, and subsequently followed by RT (36.4%). The remaining patients received surgery without radiation (14.5%) or other unknown treatment (5.5%). Treatment patterns changed over the study period. Receipt of RT increased from 34.1% (31 out of 91) in 2004–2009 to 38% (49 out of 129) in 2010–2015, whereas

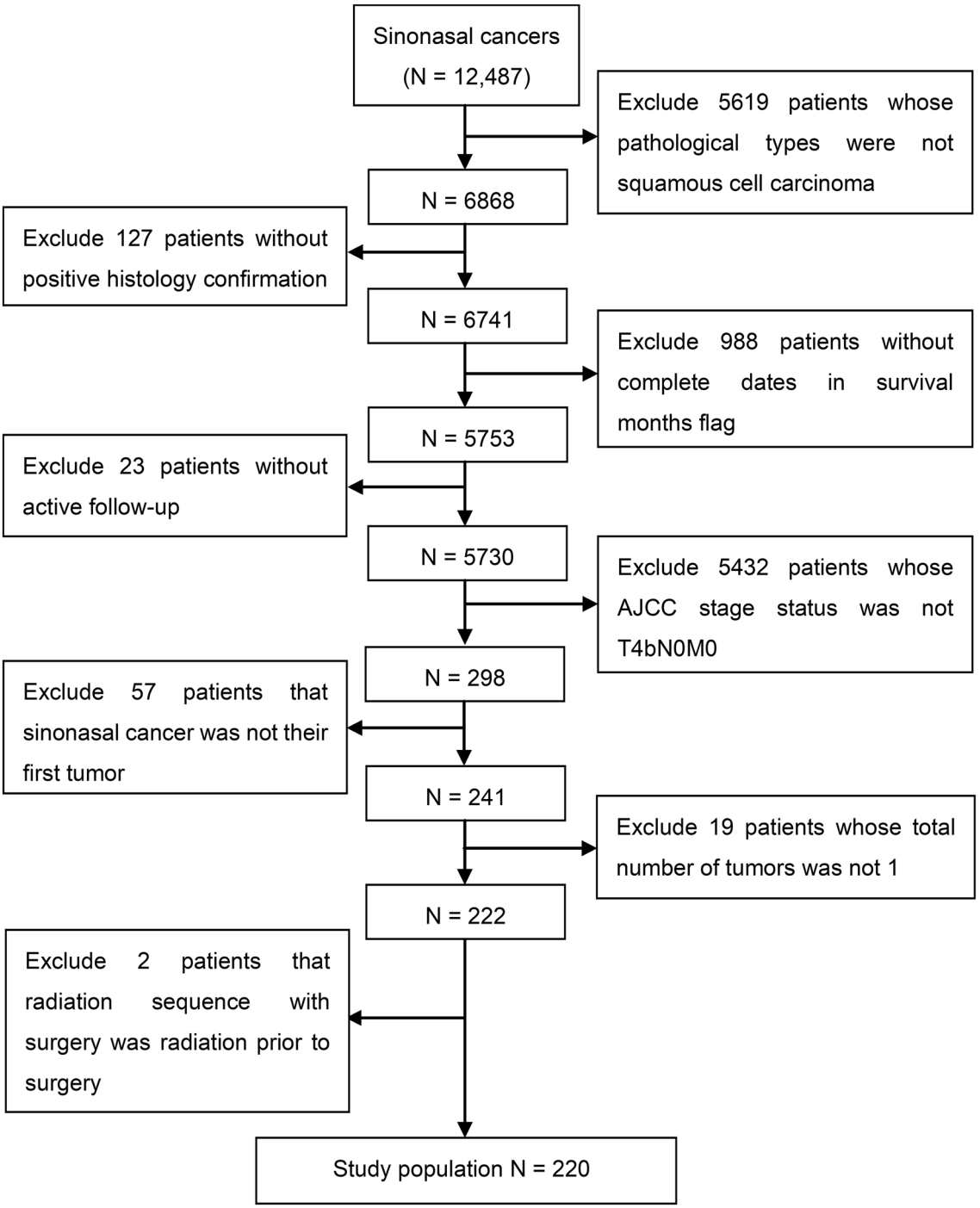

Fig. 1 Data selection process

S + PORT slightly decreased from 46.2% (42 out of 91) in 2004–2009 to 41.9% (54 out of 129) in 2010–2015. Among patients receiving S + PORT, 40.6% of tumors were arising from the maxillary sinus, compared to 61.3% among group of RT ($p = 0.006$). Patients in group of S + PORT had higher proportions of poorly or undifferentiated tumors than group of RT (55.2% vs 37.5%, $p = 0.001$). Patients who received surgery without radiation or other unknown treatment were less likely to receive chemotherapy ($p < 0.0001$).

Survival outcomes obtained from the SEER database

The survival outcomes for different medical modalities are shown in Fig. 2. There was a significant difference noted with

Table 1 Patient characteristics by treatment modalities

Categories	Total *N* = 220 No. (%)	S + PORT *N* = 96 (43.6) No. (%)	RT *N* = 80 (36.4) No. (%)	S *N* = 32 (14.5) No. (%)	Other *N* = 12 (5.5) No. (%)	*p* value
Median age, year (range)	63 (12–95)	59 (27–91)	63 (12–95)	68.5 (22–91)	70.5 (47–94)	
Race						0.77
White	162 (73.6)	70 (72.9)	59 (73.8)	26 (81.3)	7 (58.3)	
Black	31 (14.1)	13 (13.5)	11 (13.8)	4 (12.5)	3 (25.0)	
Others	27 (12.3)	13 (13.5)	10 (12.5)	2 (6.3)	2 (16.7)	
Gender						0.652
Male	149 (67.7)	63 (65.6)	53 (66.3)	23 (71.9)	10 (83.3)	
Female	71 (32.3)	33 (34.4)	27 (33.8)	9 (28.1)	2 (16.7)	
Year of diagnosis						0.47
2004–2009	91 (41.4)	42 (43.8)	31 (38.8)	11 (34.4)	7 (58.3)	
2010–2015	129 (58.6)	54 (56.3)	49 (61.3)	21 (65.5)	5 (41.7)	
Primary subsite						0.162
Maxillary sinus	111 (50.5)	39 (40.6)	49 (61.3)	15 (46.9)	8 (66.7)	
Ethmoid sinus	35 (15.9)	20 (20.8)	9 (11.3)	5 (15.6)	1 (8.3)	
Nasal cavity	74 (33.6)	37 (38.5)	22 (27.5)	12 (37.5)	3 (25.0)	
Grade						0.014
Well differentiated	12 (5.5)	5 (5.2)	4 (5.0)	3 (9.4)	0 (0.0)	
Moderately differentiated	74 (33.6)	32 (33.3)	24 (30.0)	14 (43.8)	4 (33.3)	
Poorly or undifferentiated	101 (45.9)	53 (55.2)	30 (37.5)	12 (37.5)	6 (50.0)	
Unknown	33 (15.0)	6 (6.3)	22 (27.5)	3 (9.4)	2 (16.7)	
Chemotherapy						< 0.0001
Yes	135 (61.4)	64 (66.7)	58 (72.5)	11 (34.4)	2 (16.7)	
No/unknown	85 (38.6)	32 (33.3)	22 (27.5)	21 (65.5)	10 (83.3)	
Insurance status at diagnosis						0.495
Any	172 (78.2)	72 (75.0)	63 (78.8)	28 (87.5)	9 (75.0)	
None or unknown	48 (21.8)	24 (25.0)	17 (21.3)	4 (12.5)	3 (25.0)	
Marital status at diagnosis						0.151
Any	110 (50.0)	55 (57.3)	34 (42.5)	17 (53.1)	4 (33.3)	
None or unknown	110 (50.0)	41 (42.7)	46 (57.5)	15 (46.9)	8 (66.7)	

S + PORT surgery plus postoperative radiotherapy, *RT* radiotherapy without surgery, *S* surgery without radiotherapy

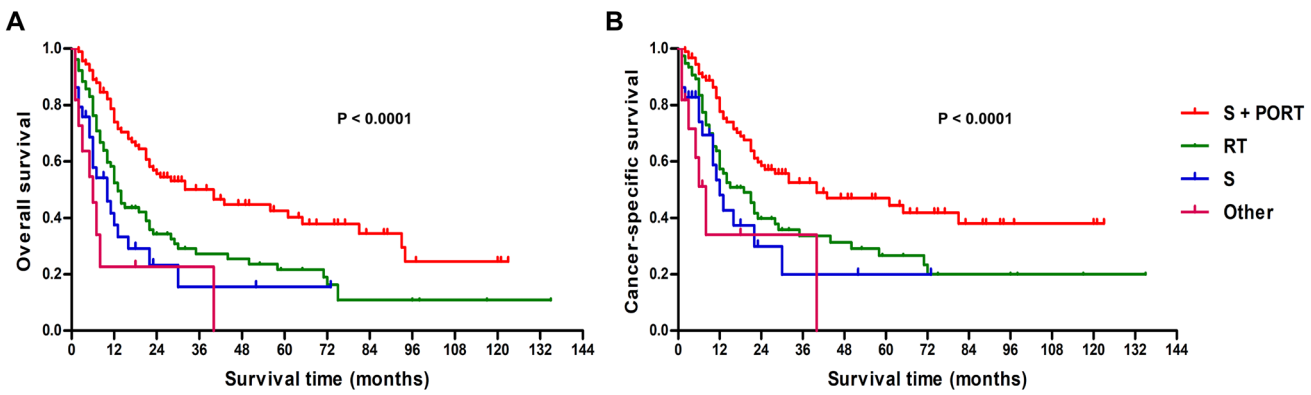

Fig. 2 Kaplan–Meier representation of survival outcome according to the treatment modalities before propensity score matching. **a** Overall survival; **b** cancer-specific survival. *S + PORT* surgery plus postoperative radiotherapy, *RT* definitive radiotherapy, *S* surgery without radiotherapy

regard to OS or CSS between patients receiving S + PORT and other methods [5-year OS rates of 42.5% in S + PORT vs 21.7% in RT ($p = 0.001$ using the log-rank test) and 5-year CSS rates of 46.9% vs 26.7% ($p = 0.005$ using the log-rank test), respectively].

As illustrated in Table 1, patients in group of S + PORT had higher proportions of poorly or undifferentiated tumors than group of RT. Among the patients with poorly or undifferentiated tumors, also S + PORT had higher 5-year CSS rate than RT (49.9% vs 27.8%, $p = 0.22$), although the difference was not statistically significant. Among the 96 patients who received S + PORT, surgery with partial resection was performed in 42 patients, while 54 patients were performed with total resection. To our surprise, our analysis showed that partial resection plus PORT seems to have better 5-year OS and 5-year CSS than total resection plus PORT, although the difference was not statistically significant (53.6% vs 33%, $p = 0.085$; 55.1% vs 39.6%, $p = 0.145$).

We further examined the correlation between survival and other parameters. Univariate analyses revealed that therapy ($p < 0.0001$), gender ($p = 0.049$), and primary subsite ($p < 0.0001$) were significant predictors of CSS, as shown in Table 2. No significant difference was demonstrated for age, race, year of diagnosis, grade, chemotherapy, insurance status, and marital status. Based on multivariate analysis, therapy of RT had higher cancer-specific mortality risk than S + PORT [hazard ratio (HR) 1.578, $p = 0.032$]. Male (HR 1.54, $p = 0.042$) and primary subsite of maxillary sinus (HR 1.919, $p = 0.001$) were also independent predictors for CSS.

To better characterize the impact of therapeutic approaches on survival of SNSCC patients and to adjust for possible selection bias, we conducted analyses using a propensity score-matched subcohort to compare the survival outcomes between S + PORT and RT (Table 3). After matching, 57 pairs of patients were selected; one-half were treated with S + PORT and another half underwent RT. The p value for age, race, gender, year of diagnosis, primary subsite, grade, chemotherapy, insurance status, or marital status was greater than 0.05. As a consequence, the results were similar to the primary findings (Fig. 3): there was still a significant difference noted with regard to 5-year OS or 5-year CSS between patients receiving S + PORT and RT (43% vs 22.5%, $p = 0.012$; 45.8% vs 27.7%, $p = 0.025$). The univariate and multivariate analyses of factors predictive of CSS showed that therapy of RT (HR 1.877, $p = 0.018$) and primary subsite of maxillary sinus (HR 2.629, $p = 0.001$) were significantly correlated with adverse outcomes (Table 4).

Discussion

Using a population-based cancer database, we observed that 43.6% of patients with T4bN0M0 SNSCC received S + PORT, and subsequently followed by RT (36.4%). Based on univariate and multivariate analyses, patients treated with RT all had higher cancer-specific mortality risk than with S + PORT before and after adjusting for available confounders. To our knowledge, this is the largest study of T4bN0M0 SNSCC reported to date.

Postoperative radiation after complete surgical resection remains a cornerstone of treatment for locally advanced SNSCC [2, 6, 7]. However, the sixth edition of AJCC classification divides T4 tumors into T4a and T4b, which was defined as unresectable disease with involvement of orbital apex, dura, brain, middle cranial fossa, nasopharynx, clivus, or the cranial nerve other than V2 [11–13]. As a consequence, definitive RT or systemic therapy/RT is recommended by NCCN guidelines for T4b, although this is a category 2B recommendation for patients with T3-4a, N0 disease [19]. However, due to the low incidence of sinonasal cancers [1, 2], there were few related reports with adequate sample specially investigating the treatment and survival of very locally advanced SNSCC. Furthermore, the head and neck oncologists have opposed the formal definition of unresectable for decades [11]. For instance, cavernous sinus involvement [20] and orbital apex extension [21] were not regarded as contradictions for curative treatment in some hospitals. It should be emphasized that indication for resectability continue to develop and that a patient considered resectable by one surgeon may not be operable by another. Just as in SEER database, among the 96 patients who received S + PORT, 54 patients were still performed with radical surgery with total removal of the primary site.

Before the specific sites from T4 tumors were generally regarded as unresectable by NCCN guidelines, the extent of surgery was the focus of discussion. As early as 2000, Jansen et al. [22] had reported the survival outcome of debulking surgery in 73 patients with paranasal sinus tumors, and 59% of patients were diagnosed with T4. Combination of debulking surgery with high-dose radiotherapy gave significantly better 5-year OS (60% vs 9%, $p = 0.001$) and 5-year disease-free survival (DFS) (53% vs 6%, $p < 0.0001$) than radiotherapy alone. They held that surgery gave quick palliation of complaints and thereafter to adjust radiation fields to the involved sites. The result could be achieved without a high orbital exenteration rate. One hundred two patients with sinonasal cancers with skull base involvement were retrospectively reviewed by Resto et al. [23]. Complete resection was predictive of improved DFS and DMFS even though excellent

Table 2 Results of univariate and multivariate analyses of cancer-specific survival among all the patients with stage of T4bN0M0

Characteristics	Univariate analysis			Multivariate analysis		
	HR	95% CI	*p* value	HR	95% CI	*p* value
Therapy						
S + PORT	Reference	Reference		Reference	Reference	
RT	1.746	1.156–2.638	0.008	1.578	1.039–2.397	0.032
S	2.511	1.425–4.426	0.001	2.374	1.344–4.195	0.003
Other	4.47	2.081–9.603	< 0.0001	3.355	1.545–7.282	0.002
Age						
< 60	Reference	Reference				
≥ 60			0.214			
Race						
White	Reference	Reference				
Black			0.127			
Others			0.067			
Gender						
Female	Reference	Reference		Reference	Reference	
Male	1.513	1.003–2.283	0.049	1.54	1.016–2.335	0.042
Year of diagnosis						
2004–2009	Reference	Reference				
2010–2015			0.357			
Primary subsite						
Ethmoid sinus/nasal cavity	Reference	Reference		Reference	Reference	
Maxillary sinus	2.087	1.427–3.052	< 0.0001	1.919	1.302–2.828	0.001
Grade						
Well differentiated	Reference	Reference				
Moderately differentiated			0.365			
Poorly or undifferentiated			0.358			
Unknown			0.618			
Chemotherapy						
Yes	Reference	Reference				
No/unknown			0.457			
Insurance status at diagnosis						
Any	Reference	Reference				
None or unknown			0.429			
Marital status at diagnosis						
Any	Reference	Reference				
None or unknown			0.778			

S + PORT surgery plus postoperative radiotherapy, *RT* radiotherapy without surgery, *S* surgery without radiotherapy, *HR* hazard ratio

local control outcomes have been obtained irrespective of margin status after high-dose radiotherapy. Interestingly, the extent of surgery correlated with decreased distant metastasis. These findings indicated that management of local lesions may be beneficial in addressing the distant metastasis. The study which was conducted by Kawashima [24] illustrated that debulking followed by ≥ 60 Gy of RT can provide satisfactory local control though macroscopic tumor remains unresected. While a series by Chen et al. [11] showed that 5-year local control among 82 patients treated postoperatively after gross total resection was 65%, compared with 44% for the 45 patients in the presence of macroscopic lesions.

After definitive RT or systemic therapy/RT was recommended by NCCN guidelines, only a few studies have dealt with nonsurgical treatment of T4b tumors. Chopra et al. [12] analyzed 23 nonsurgically and definitively treated patients with locally advanced sinonasal carcinomas. Five-year PFS and OS were 30% and 60%, respectively, and 59% of patients had relapsed or progressed. Higher-dose radiation was associated with shorter OS. The survival of 39 patients with unresectable stage IVB sinonasal carcinomas was analyzed

Table 3 Clinical characteristics before and after propensity score matching for patients who were treated with surgery plus postoperative radiotherapy or radiotherapy without surgery

Characteristics	Before propensity score matching			After propensity score matching		
	S + PORT	RT	*p* value	S + PORT	RT	*p* value
	N = 96	*N* = 80		*N* = 57	*N* = 57	
Age			0.053			0.85
< 60	50	30		25	24	
≥ 60	46	50		32	33	
Race			0.979			0.704
White	70	59		41	39	
Black	13	11		6	9	
Others	13	10		10	9	
Gender			0.931			0.413
Male	63	53		42	38	
Female	33	27		15	19	
Year of diagnosis			0.503			0.85
2004–2009	42	31		24	25	
2010–2015	54	49		33	32	
Primary subsite			0.006			0.706
Ethmoid sinus/nasal cavity	57	31		24	26	
Maxillary sinus	39	49		33	31	
Grade			0.001			0.051
Well differentiated	5	4		2	4	
Moderately differentiated	32	24		17	18	
Poorly or undifferentiated	53	30		33	21	
Unknown	6	22		5	14	
Chemotherapy			0.403			0.687
Yes	64	58		40	38	
No/unknown	32	22		17	19	
Insurance status at diagnosis			0.558			0.519
Any	72	63		44	41	
None or unknown	24	17		13	16	
Marital status at diagnosis			0.051			0.453
Any	55	34		29	25	
None or unknown	41	46		28	32	

S + PORT surgery plus postoperative radiotherapy, *RT* radiotherapy without surgery

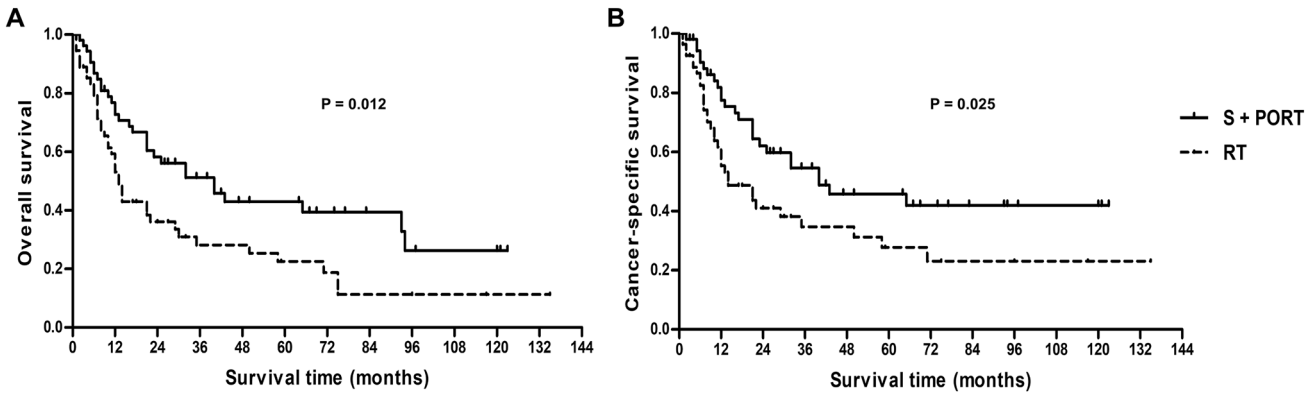

Fig. 3 Kaplan–Meier representation of survival outcome according to the treatment modalities after propensity score matching. **a** Overall survival; **b** cancer-specific survival. *S + PORT* surgery plus postoperative radiotherapy, *RT* definitive radiotherapy

Table 4 Results of univariate and multivariate analyses of cancer specific survival among a propensity score matched subcohort

Characteristics	Univariate analysis		*p* value	Multivariate analysis		*p* value
	HR	95% CI		HR	95% CI	
Therapy						
S + PORT	Reference	Reference		Reference	Reference	
RT	1.79	1.062–3.019	0.029	1.877	1.113–3.167	0.018
Age						
< 60	Reference	Reference				
≥ 60			0.888			
Race						
White	Reference	Reference				
Black			0.332			
Others			0.234			
Gender						
Female	Reference	Reference				
Male			0.903			
Year of diagnosis						
2004–2009	Reference	Reference				
2010–2015			0.469			
Primary subsite						
Ethmoid sinus/nasal cavity	Reference	Reference		Reference	Reference	
Maxillary sinus	2.544	1.427–4.538	0.002	2.629	1.473–4.692	0.001
Grade						
Well differentiated	Reference	Reference				
Moderately differentiated			0.442			
Poorly or undifferentiated			0.346			
Unknown			0.799			
Chemotherapy						
Yes	Reference	Reference				
No/unknown			0.057			
Insurance status at diagnosis						
Any	Reference	Reference				
None or unknown			0.4			
Marital status at diagnosis						
Any	Reference	Reference				
None or unknown			0.889			

S + PORT surgery plus postoperative radiotherapy, *RT* radiotherapy without surgery, *HR* hazard ratio

by Hoppe et al. [14] Patients primarily experienced a local recurrence (64%), and the only predictor for improved local PFS and OS was a dose of radiation of ≥ 65 Gy, even though the 5-year local PFS and OS were relatively low (21% and 15%). On the contrary, 28 patients with T4b SNSCC who were treated with induction chemotherapy followed by concurrent chemoradiotherapy and/or epidermal growth factor receptor inhibitor [25] achieved better 3-year OS and local control rate (59.2%, 80.2%). Combination of intra-arterial chemotherapy and concomitant radiotherapy [26] has also been reported for treating of advanced sinonasal carcinomas with favorable outcomes (a 5-year OS of 69.3%). On the basis of these studies, definitive RT or systemic therapy/RT may become standard treatment method in the future. However, on the basis of our limited experience, its long-term survival and control rates are not satisfactory. The histology of sinonasal carcinomas was extremely heterogeneous in previous studies, thus resulting absolutely different conclusions. More importantly, no multi-institutional clinical trials have proved its advantage over surgery-based modalities. Robin et al. [2] reviewed the National Cancer Data Base and reported 11,160 patients with sinonasal malignancies. Patients who received radiotherapy alone (HR 1.294, $p = 0.001$) or chemotherapy alone (HR 1.834, $p < 0.001$) had worse outcomes. The findings concluded that surgery was the mainstay of therapy for sinonasal malignancies. In our study, the histology was limited to SNSCC. Because of a combination of surgery and radiotherapy, there

was a significant difference noted with regard to OS or CSS between patients receiving S + PORT and RT. Patients treated with RT all had higher cancer-specific mortality risk than with S + PORT before and after propensity score matching.

The improvement in surgical and reconstructive techniques has broadened the indication of surgery in locally advanced cancers [11, 15, 16]. The extent of surgery and eligibility criteria for surgery remains an open question. A retrospective study which contained 47 patients with sinonasal adenoid cystic carcinoma was conducted by Lee et al. [20]. Cavernous sinus invasion was observed in eight patients, all of whom received surgery although the cavernous sinus lesions were treated solely by chemoradiotherapy. However, cavernous sinus invasion did not significantly impact survival. The author suggested that cavernous sinus invasion should not be regarded as a contraindication for surgery though it is not within the surgical field. Sakata et al. [15] reviewed 38 patients with sinonasal malignancies of T4 stage, 16 of whom presented with stage T4b. All the patients received craniofacial resection and postoperative radiotherapy. The 5-year OS and 5-year DFS were 55.5% and 59.4%, respectively. Surprisingly, the 5-year CSS was not statistically different between stage T4a and T4b tumors (58.9% vs 45.6%, $p = 0.5446$). Recently, orbital apex invasion was not regarded as contradictions for curative treatment in some hospitals [8, 21, 27]. Sugawara et al. [21] reported craniofacial resection with orbital exenteration for treatment of sinonasal malignancies with orbital apex extension. The 5-year recurrence-free survival was 86.7%, and 5-year OS was 86.2%. The author suggested that the technique provide sufficient margins, and the complication rate was acceptably low. With the implement of better imaging and technology, endoscopic resection of sinonasal malignancies has become increasingly popular [18]. Several studies [6, 16–18] have proved that piecemeal resection seems to have the same survival outcome as traditional open craniofacial resection. Thirty-four patients with SNSCC treated with endoscopic surgery were analyzed by Almeida et al. [16]. Six had either clivus or nasopharyngeal involvement, 6 had dura involvement (2 with concomitant orbital apex or optic nerve), and 2 had brain invasion, of which 10 had definitive resection and 4 had debulking surgery.

Traditionally, the goal of the surgery was no gross residual disease left. Then, high-dose postoperative radiation came into action. However, traditional surgical method of en bloc resection is not applicable to endoscopic surgery [6, 16–18], and how to decide clear margin status of endoscopic surgery remains an open question. Furthermore, tumors reach a very large size and invade the surrounding normal critical organs such as eyes, brain, or nerves. It is hard to perform complete resection while preserving the critical organs at the same time. Consequently, residual was unavoidable in some patients. Nonetheless, surgery followed by postoperative radiation still achieved higher OS and CSS than RT in our study. Surprisingly, the 5-year CSS was not statistically different between partial resection plus PORT and total resection plus PORT (55.1% vs 39.6%, $p = 0.145$). Due to the limitations of sample size and SEER database, we were unable to explore the reason. However, the result further indicated that adequate debulking with high-dose postoperative radiotherapy offers a good possibility of local cure and achieves comparable survival outcome to aggressive wide resection.

Our study had several limitations. It was purely a retrospective analysis based on database. The adverse feature like positive margins, perineural invasion or vascular invasion after primary surgery was not available in SEER database. The radiation dose of radiotherapy was also unclear. Some variable contained "unknown" category, which could introduce statistical bias. Furthermore, the sequence of chemotherapy was unknown in database. It is promising that neoadjuvant chemotherapy could be considered for downstaging patients with advanced T-stage disease (a reduction from T4b to T4a or T4a to a lower stage), which was preferable in converting patients with unresectable disease to resectable candidates [2, 13]. As a consequence, we strongly suggested that surgery for T4bN0M0 SNSCC should be performed by experienced surgeon. Immature surgical procedure may accelerate disease progression and cause great difficulty for postoperative radiotherapy.

Conclusion

In this study, we present what is to our knowledge the largest study to date of T4bN0M0 SNSCC. Combination of surgery and postoperative radiotherapy may contribute to prolonged survival. Invasion of the sites of T4b tumors is not an absolute contraindication for surgery.

Funding This work was supported by CSCO-Qilu Cancer Research Fund (Grant number: Y-Q2017-011) as well as grants from Shanghai Municipal Commission of Health and Family Planning Research Fund (Grant number 20164Y0201).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

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