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Does the Brown classification of maxillectomy defects have prognostic prediction for patients with oral cavity squamous cell carcinoma involving the maxilla?

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Q. Sun, W.-B. Zhang, M. Gao, S. Yu, C. Mao, C.-B. Guo, G.-Y. Yu, X. Peng: Does the Brown classification of maxillectomy defects have prognostic prediction for patients with oral cavity squamous cell carcinoma involving the maxilla?. Int. J. Oral Maxillofac. Surg. 2020; 49: 1135–1142.

Abstract. The aim of this study was to investigate the correlation between the maxillectomy defect, T stage, and prognosis of patients with maxillary squamous cell carcinoma (SCC). The Brown classification system was used to appraise the maxillectomy defects due to maxillary SCC. The clinical data of 137 patients with maxillary SCC during the period 2000–2010 were reviewed; 105 patients were followed up. Preoperative T stage and postoperative maxillectomy class were recorded. The relationship between the maxillectomy defect class and T stage of maxillary SCC was analysed. Correlations between the maxillectomy defect class, local recurrence rate, and survival rate were assessed using IBM SPSS Statistics v19.0. The most common maxillectomy defect class was IIb (54.7%, 75/137). The maxillectomy defect class was significantly associated with the T stage ($P < 0.001$). Both T stage and the maxillectomy defect class were significantly associated with the survival rate of patients with maxillary SCC (both $P < 0.001$). In conclusion, the class of the maxillectomy defect was found to be associated with the T stage. Both of these were prognostic factors for patients with maxillary SCC. The class of the maxillectomy defect is suitable for clinical application in predicting the prognosis compared with T stage.

Key words: maxillary SCC; maxillectomy defects; Brown classification system; prognosis.

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The main therapy for patients with maxillary squamous cell carcinoma (SCC) is surgical resection. The scope of surgical resection depends on the size of the primary tumour, with size evaluated using the T stage of the TNM system[1–5].

The TNM classification is the most common system for malignant tumours. It was developed by Pierre Denoix between 1943 and 1952. Since then, it has been adopted by the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC) and is now widely applied to various cancers[4,5]. For prognostic evaluation, the TNM system tends only to regard the very important factors associated with disease. Moreover, the T stage is known to influence the prognosis, treatment planning, and postoperative adjuvant therapy. However, the anatomical structure of the maxilla is more complex than that of other parts of the oral cavity. For example, when compared to SCC of the tongue, buccal mucosa, or floor of the mouth, the size and scope of the neoplasm in maxillary SCC are more difficult to accurately quantify, and this can affect the clinical utility of the T stage[4,6].

Currently, the widely accepted classification used by surgeons and prosthodontists for maxillectomy defects is the Brown classification system[7,8], as it is clear and the classes can be distinguished easily. The aim of this retrospective study was to appraise the classification of maxillectomy defects using the Brown classification system and to investigate the correlation between the maxillectomy defect, T stage, and prognosis of maxillary SCC.

Patients and methods

Patients with SCC originating from the hard palate and maxillary alveolus or gingiva, who were treated in the Department of Oral and Maxillofacial Surgery of the Peking University School and Hospital of Stomatology, Beijing, China between 2000 and 2010, were reviewed. All patients were pathologically diagnosed according to the fourth edition of the World Health Organization classification of tumours[9]. The following inclusion criteria, based on clinical, radiographic, and histopathological examinations, were applied: pathologically confirmed primary SCC of the hard palate and maxillary alveolus or gingiva; primary treatment comprising surgery only. In all cases, the primary tumour sites were treated with radical resection aimed at 1.0–1.5 cm margins with negative margins. The margins were confirmed intraoperatively by frozen section and verified postoperatively by paraffin section. Exclusion criteria were the following: SCC with an intraosseous origin, or arising in the nasal cavity or paranasal sinus; primary tumour invading the soft palate, oropharynx, or retromolar area; preoperative radiotherapy. Sex, age, pregnancy, breastfeeding, and race were not considered as standard inclusion or exclusion criteria. Patients were followed up every 3 months in the first 2 years and then every 6 months until the fifth year. Thereafter, patients were followed up annually. Local recurrence and regional failure were determined by clinical and radiographic examinations, while histopathology was only performed if necessary.

The classification of maxillectomy defects using the Brown classification system was initially described in October 2010[7] (Fig. 1). The defect is classified according to the vertical and horizontal dimensions or palatal aspect of the maxillectomy.

All patients were staged according to the eighth edition of the AJCC TNM classification[1–3], and the postoperative defects were classified using the Brown classification system (October 2010). To investigate the correlation between the maxillectomy defect and T stage, we assessed the difference in recurrence and prognosis comparing the defect classes.

The data collection and statistical analysis were performed using IBM SPSS Statistics version 19.0 (IBM Corp., Armonk, NY, USA). The χ^2 test or Fisher's exact test was used to determine the correlation between maxillectomy defect and T stage, as well as the difference in recurrence between the defect classes. A Kaplan–Meier plot was used to determine the overall survival rate and a *P*-value less than 0.05 was considered statistically significant.

Results

A total of 137 patients fulfilled the inclusion criteria; 59 were male and 78 were female. The median age of the patients at the time of diagnosis was 72 years (range 44–99 years). Detailed clinical information was available for only 105 of these 137 patients. The follow-up rate was 76.6%. The follow-up period ranged from 3 to 140 months and the median period of follow-up was 36 months.

Patients were classified using the Brown classification system (October 2010) and the most common class was IIb ($n = 75$, 54.7%), followed by IId ($n = 28$, 20.4%) (Table 1). The locations of the tumours (palate or gingiva) are reported in Table 1; there was a significant difference in Brown defect class between the primary sites ($P < 0.001$). However this was only the case for the horizontal classification of the primary site: 'a', palatal primary only and 'c', gingiva primary only. Therefore, when classes Ia, Ic, IIa, and IIc were

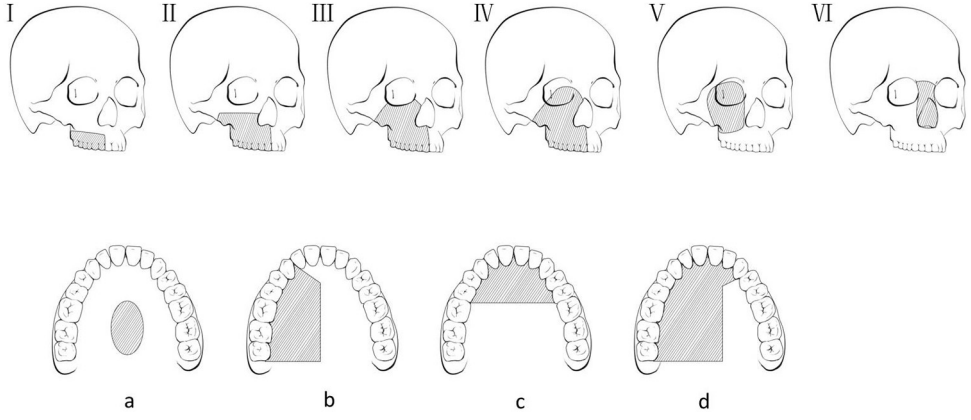

Fig. 1. The Brown classification. The vertical classification is as follows: I, maxillectomy without oronasal fistula; II, not involving the orbit; III, involving the peri-orbital area or with orbital floor; IV, with orbital enucleation or exenteration; V, orbitomaxillary defect; VI, nasomaxillary defect. The horizontal classification is as follows: 'a', palatal defect only; 'b', ≤1/2 unilateral; 'c', ≤1/2 bilateral or transverse anterior; 'd', >1/2 maxillectomy[7].

Table 1. Classification of maxillectomy defects in patients with maxillary squamous cell carcinoma[a].

Brown class	Primary site*		T stage*				Total (%)
	Palate	Gingiva	T1	T2	T3	T4	
Ia	6	0	0	6	0	0	6 (4.4)
Ib	2	6	4	3	0	1	8 (5.8)
Ic	0	4	2	2	0	0	4 (2.9)
Id	1	0	0	1	0	0	1 (0.7)
IIa	6	0	1	5	0	0	6 (4.4)
IIb	19	56	12	29	16	18	75 (54.7)
IIc	0	4	1	3	0	0	4 (2.9)
IId	8	20	0	4	7	17	28 (20.4)
IIIb	1	2	0	0	0	3	3 (2.2)
IIId	0	2	0	1	0	1	2 (1.5)
Total (%)	43 (31.3)	94 (68.6)	20 (14.6)	54 (39.4)	23 (16.8)	40 (29.2)	137 (100.0)

[a] Results are presented as the number. *$P < 0.05$.

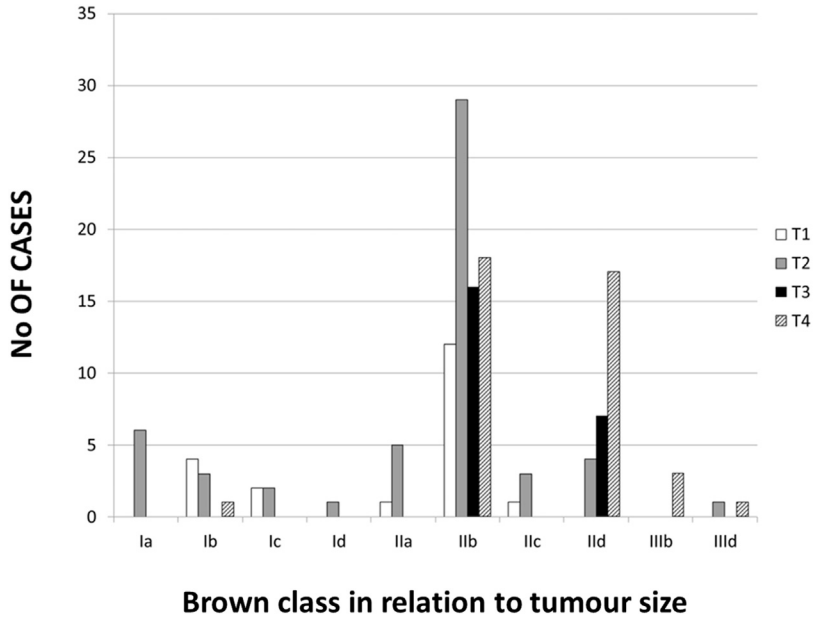

Fig. 2. Brown classification of the maxillary defects according to the T stage. The most frequent Brown class was IIb. There was a significant correlation between maxillectomy defect class and T stage ($P < 0.001$).

excluded, there was no significant difference in Brown defect class between the primary sites ($P = 0.595$).

Examining the Brown class according to the different T stages, the results showed that the most frequent class was always IIb. However, as the T stage increased, the Brown class was significantly higher ($P < 0.001$) (Table 1, Fig. 2). Thirty-two patients (23.4%) were reconstructed with free flaps (Fig. 3), and there was a significant association with the Brown class ($P = 0.016$).

Of the 105 patients with detailed clinical information, 15 (14.3%) presented with local recurrence and 26 (24.8%) presented with regional recurrence. However there was no significant association between the Brown class and local recurrence ($P = 0.494$) or regional recurrence ($P = 0.290$) (Table 2). Twenty-four patients (22.9%) were reconstructed with free flaps and 12 cases (11.4%) followed adjuvant radiation; however there was no significant association for the reconstruction ($P = 0.075$) or adjuvant radiation ($P = 0.066$) with the overall survival rate by Kaplan–Meier survival analysis.

The 105 patients with detailed clinical information were staged according to the AJCC TNM criteria. The mean survival time and the 5-year survival rate tended to decrease as the T stage increased; this difference among the groups was statistically significant ($P < 0.001$) upon Kaplan–Meier survival analysis (Table 3, Fig. 4).

The mean survival time of the T4 patients was similar to that of the T3 patients (Table 3); however, the 5-year survival rate of the T4 group was higher than that of the T3 group. Although the overall survival rate of the T3 group was higher than that of the T4 group as calculated by Kaplan–Meier survival analysis (Fig. 4), this was not significantly different ($P = 0.620$). Similarly, there was no significant difference in the overall survival rates between the T1 and T2 groups ($P = 0.187$), and the mean survival times of these groups were also similar (Table 3). The survival rate for those with early stage tumours (T1/T2) was higher than that for

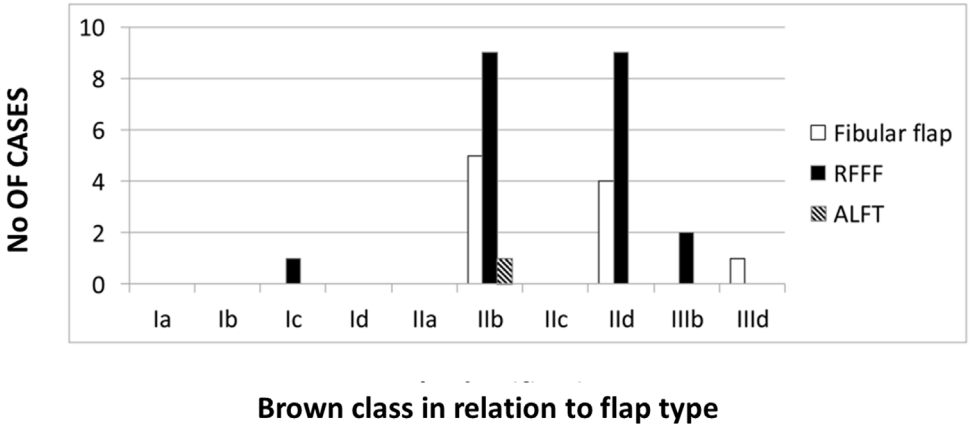

Fig. 3. Brown classification of the maxillary defects according to the free flap applied. RFFF, radial forearm free flap; ALTF, anterolateral thigh flap. There was a significant correlation between maxillectomy defect class and free flap type ($P = 0.016$).

Table 2. Correlation between local recurrence, regional recurrence, and the Brown class.

Brown class	Number of patients	Local recurrence[a] (%)	Regional recurrence[b] (%)
Ia	3	0 (0.0)	0 (0.0)
Ib	7	1 (14.3)	2 (28.6)
Ic	1	0 (0.0)	1 (100.0)
Id	1	1 (100.0)	0 (0.0)
IIa	3	1 (33.3)	0 (0.0)
IIb	61	7 (11.5)	13 (21.3)
IIc	3	1 (33.3)	1 (33.3)
IId	22	4 (18.2)	7 (31.8)
IIIb	3	0 (0.0)	1 (33.3)
IIId	1	0 (0.0)	1 (100.0)
Total	105	15 (14.3)	26 (24.8)

[a] $P = 0.494$.
[b] $P = 0.290$.

Table 3. Survival outcome according to T stage and Brown class[a].

Factors	Survival time (months)	3-year survival rate (%)	5-year survival rate (%)	*P*-value
T stage				<0.001*
T1	118.4 ± 6.4	93.3	93.3	
T2	100.4 ± 8.5	87.2	84.6	
T3	56.1 ± 14.7	35.3	35.3	
T4	56.0 ± 10.1	52.9	47.1	
Brown class				0.001*
I	96.6 ± 15.2	83.3	83.3	
IIa, IIb	98.4 ± 7.6	75.0	70.3	
IIc, IId	61.9 ± 12.4	52.0	52.0	
III	30.3 ± 15.6	25.0	25.0	

[a] Results are presented as the number (*n*), or as the mean ± standard deviation value. *$P < 0.05$.

those with advanced stage tumours (T3/T4), and the analysis by Kaplan–Meier plot indicated that this was statistically significant ($P < 0.001$) (Fig. 5).

The 105 patients were divided into four groups by defect class according to the Brown classification system: Brown class I, Brown classes IIa/IIb, Brown classes IIc/IId, and Brown class III. The mean survival time and the 5-year survival rate tended to decrease as the Brown class increased, and there was a significant difference ($P = 0.001$) between the groups using Kaplan–Meier survival analysis (Fig. 6).

In the defect class groups, the mean survival time of the Brown class I patients was similar to that of the Brown class IIa and IIb patients (Table 3), and the overall survival rate did not differ significantly between these groups ($P = 0.644$). Similarly, there was no significant difference in the overall survival rate between the Brown class IIc/IId and Brown class III groups ($P = 0.477$). The patients were further divided into Brown class I/IIa/IIb and Brown class IIc/IId/III groups; the survival rate of the Brown class I/IIa/IIb group was significantly higher ($P < 0.001$) (Fig. 7).

Discussion

The T stage is related to tumour size, depth of invasion (DOI), and close proximity of the tumour to the surrounding structures. It is an attempt to help guide treatment and estimate the prognosis[10]. However, some studies have reported that T staging is neither consistently nor independently prognostic[4]. Other studies have reported that the DOI negatively impacts upon the prognosis.

As one of the most important changes in the eighth edition of the AJCC staging system, the T categories have been revised taking into account the DOI[11]. Generally, DOI is distinct from tumour thickness and diagnosed by histopathological assessment[12]. However, there are also many institutions that have demonstrated the prognostic impact of tumour thickness in oral SCC and the distinction is not always clear in the literature[2].

Concerning the maxillary location, the local anatomical characteristics are intricate and the definition of the T stage is unclear. Regarding anatomical characteristics, the cortical nature of the maxillary bone is thinner and the bone lies directly below the mucosal tissue. Clinicians cannot use physical examination to assess the subtle differences in size and extension of the tumour. The DOI can be confirmed by histopathological assessment, although this has been shown to be subjective. Furthermore, the effect of interference from peripheral oedema, necrosis, or formalin shrinkage, as well as the effect of inter-observer error, is unknown[4]. Consequently, the assessment of tumour invasion has mainly relied upon radiographic examination rather than visual examination, palpation, or histopathological assessment[13].

Previous studies of bone tissue invasion in patients with oral SCC have mainly been confined to the area of the mandible, and the current imaging methods used to detect invasion by SCC have high diagnostic accuracy[14,15]. However, reports concerning the maxilla are limited. Araki et al.[16] reported that computed tomography (CT) was helpful for assessing the extent of the tumour in SCC of the upper gingiva and hard palate, while the destruction of the floor of the maxillary sinus is not always consistent with sinus invasion. Meanwhile, several studies have reported that destruction associated with carcinoma invasion is mediated by osteoclasts rather than directly by the carcinoma itself[17,18]. This phenomenon can also increase the difficulty of diagnosis. Although there is the additional explanation that superficial erosion alone of the bone/tooth socket by a gingival primary tumour is not sufficient in itself for the tumour to be classified as T4, the clinical practice of considering the T stage is also different. Tumours that exhibit radiographically low density images exist between the cortical and cancellous bone, while tumours not exceeding 4 cm at the greatest dimension both confuse the practitioner.

The surgical defect is determined by the size of the tumour. Surgery is based on intuitive visual examination and palpation, and combines the preoperative radiographic diagnosis and intraoperative or postoperative histopathological diagnosis. Consequently, the defect better reflects the tumour size. The present study considered the Brown classification system (October 2010). This classification evaluates the bilateral and three-dimensional maxillary defect through the horizontal and vertical dimensions. The initial classification included classes I–IV in the vertical dimension, with horizontal classifications of a–c[8]. The newer Brown classification system includes further classes in the vertical dimension with the addition of orbitomaxillary defects (class V) and nasomaxillary defects (class VI), while the horizontal dimension includes categories a–d[7].

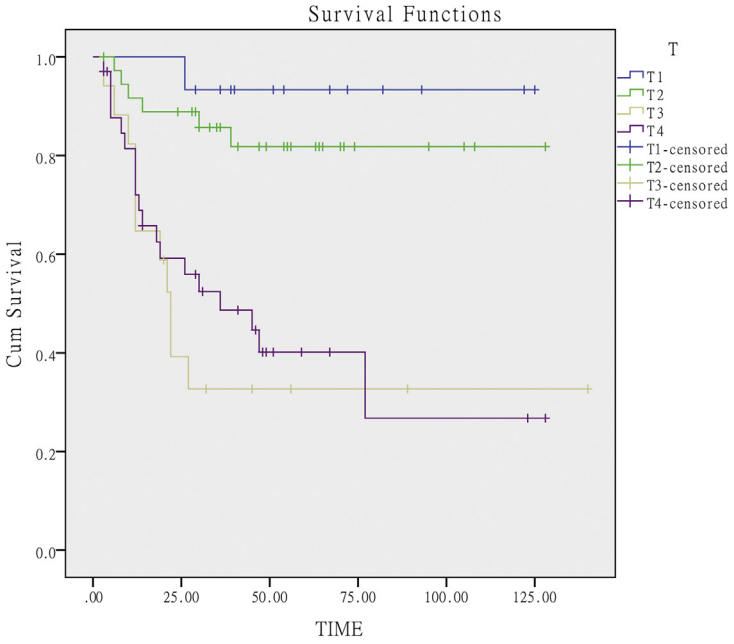

Fig. 4. Kaplan–Meier overall survival curves based on the T stage. The analysis indicated that the T stage affected the survival rate.

In the present study cohort, the most common class was IIb (54.7%). There were rare Brown class III and there were no Brown class IV. According to the definition of Brown III/IV, the defects all involve the orbital adnexa. While SCC can encompass a wide range of tumours, SCC tumours originating mainly from the maxillary sinus region do not belong strictly to the field of oral cancer[19], due to the differences in treatment plan, biological behaviour, and prognosis[20]. Such cases were therefore excluded from this study.

Regarding the relationship between T stage and the Brown class, it was noted that increasing T stage resulted in a significantly higher Brown class (Table 1, Fig. 2). Meanwhile, it was also noted that the Brown class of T1 tumours was similar to that of T2 tumours, and this was also the case for T3 and T4. This reflected the significant difference in the defect class between early T stage and advanced T stage.

In the group of 105 patients, there were some differences in the recurrence rates (local and regional) associated with different types of maxillary defect in maxillary SCC. However, these were not statistically significant. Previous authors have reported that positive margins worsen the prognosis and the best way to reduce the risk of tumour recurrence is to obtain free resection margins. With the improvements made in surgery and the application of free flap surgery or other methods of reconstruction, complete resection can be achieved for advanced tumours (T3 and T4) in the same way as for early tumours (T1 and T2)[21–23]. Hence, no significant correlation was found between the Brown class and tumour recurrence.

High risk factors for postoperative radiation therapy are the T stage and positive margins[24]. With the improvements in therapies and methods of reconstruction, the need for adjuvant radiation should be evaluated carefully. All of the maxillectomy patients in this study had negative margins. The margins were confirmed intraoperatively by frozen section and verified by postoperative paraffin section. Thus the number of patients undergoing adjuvant radiation was limited and there was no significant difference in survival rate between the patients with and without adjuvant radiation.

It has been reported that the T stage of oral cancer has a significant effect on the survival rate in oral cancer patients[22], while several studies have considered that the T stage may also influence the prognosis. Poeschl et al.[25] reported the cases of 93 patients with maxillary SCC, of whom nine were categorized as stage T1, 14 as T2, nine as T3, and 61 as T4. There were no significance differences in the 5-year survival rates or the cumulative survival rates between the T stages using Kaplan–Meier survival analysis. The T stage does not appear to have a significant impact on recurrence and patient long-term survival and is therefore an unreliable prognostic parameter in this cancer type. The most crucial factor appears to be the free resection margins. Yokoo et al.[26] and Sasaki et al.[27] also reported that the 5-year cumulative survival rates associated with high T stage (T4) according to the UICC criteria were not significantly different to those of patients assigned a T1–T3 stage. They defined T4 as primary tumour invasion that has extended to the bottom of the nasal cavity or the maxillary sinus and nasal floor. For early tumours (T1/T2), Hubert Low et al.[28] demonstrated that there was no significant difference in the survival rate between patients categorized as T1 and T2 stage according to the current TNM classification. They suggested that tumour thickness was important and should be incorporated into the TNM classification for this cancer type.

The results of the present study showed a significant difference in the survival rate among the different T stage groups. The mean survival time and the 5-year survival rate tended to decrease as the T stage increased. It was also found that the mean survival time of the T4 patients was similar to that of the T3 patients, and the 5-year survival rate did not differ significantly between them. Similarly, there was no significant difference between the T1 and T2 stage patients. However, there was a statistically significant difference between early stage tumours (T1/T2) and advanced stage tumours (T3/T4).

In the same patients, the mean survival time and the 5-year survival rate tended to decrease as the Brown class increased, and this was statistically significant as evi-

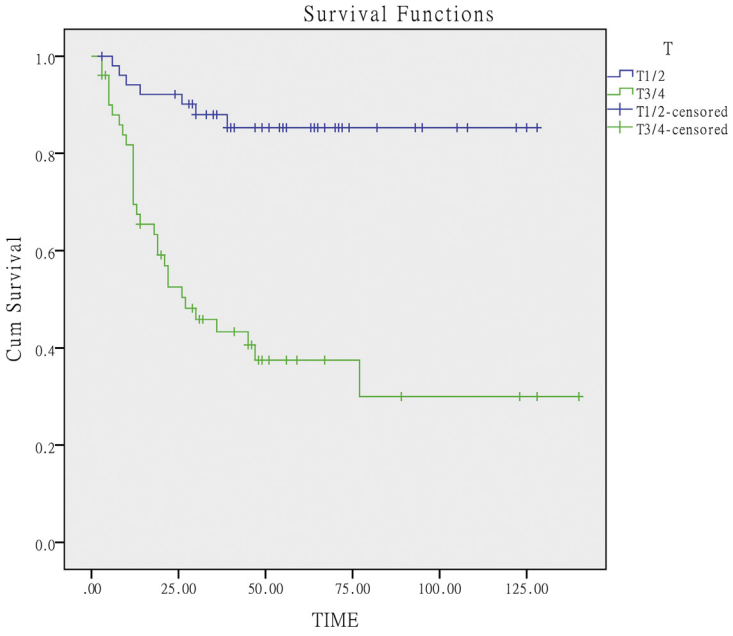

Fig. 5. Kaplan–Meier overall survival curves based on early (T1 and T2) and advanced (T3 and T4) T stages. The analysis indicated that early T stages had a better survival rate compared with advanced T stages.

denced by the Kaplan–Meier survival analysis. Further, the difference in prognosis suggested that there was a correlation between maxillectomy defect and T stage, and a correlation between the T stage and the prognosis of the maxillary SCC. Given the difficulty in the clinical application of the T stage, it would appear that the classification of the maxillectomy defect is a more convenient measure for clinical application in predicting the prognosis compared with the T stage.

The limitations of this study are those inherent to retrospective reports. Twelve patients (11.4%) in this study were followed up for less than 12 months. However, these 12 patients were cancer death cases. The duration of follow-up for the patients who survived was more than 12 months in all cases.

The majority of patients did not receive adjuvant radiotherapy because the majority of the cases were T1/T2 and all of the patients had negative margins. The reported 5-year survival rates of patients with maxillary SCC range from 32% to 71%[10,25,29,30]. The overall 5-year survival

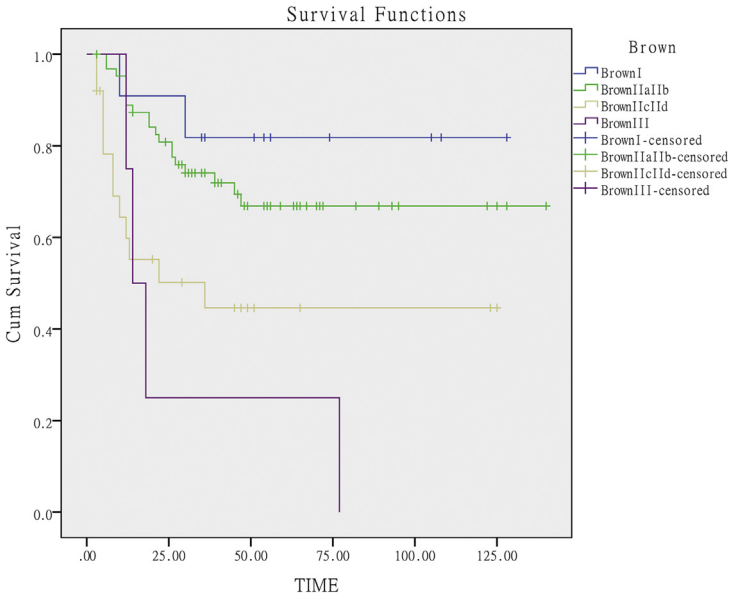

Fig. 6. Kaplan–Meier overall survival curves according to the Brown defect class. The analysis indicated that the defect class affected the survival rate.

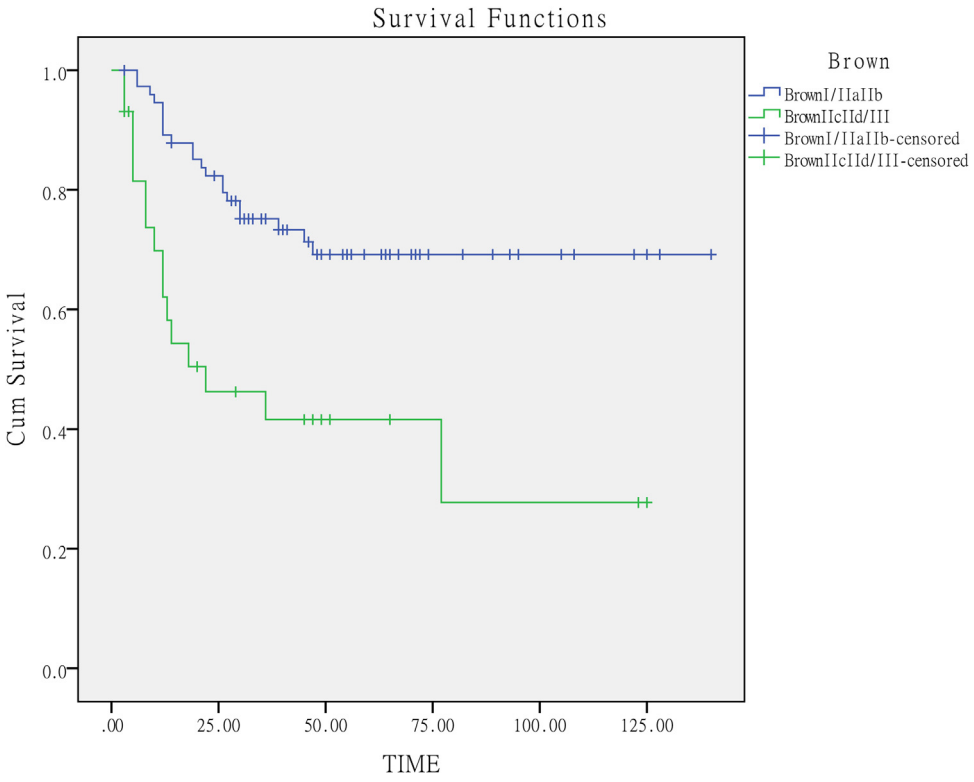

Fig. 7. Kaplan–Meier overall survival curves according to Brown class I/IIa/IIb and Brown class IIc/IId/III. The analysis indicated that Brown class I/IIa/IIb had a better survival rate compared with Brown class IIc/IId/III.

rate of the patients in the present study was 64.8%, which is similar to those reported in the previous literature. It was not possible to conclude whether adjunctive radiotherapy may affect the survival rates in this study, due to the limited sample size. We would certainly include more samples in any future studies.

In conclusion, the most common maxillectomy defect type according to the Brown classification system was Brown class IIb. The classification of the maxillectomy defect showed a correlation with the T stage. Both of these were prognostic factors for patients with maxillary SCC. The classification of the maxillectomy defect is a more convenient measure for clinical application in predicting the prognosis when compared with the T stage.

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Competing interests

All authors declare no conflict of interest.

Ethical approval

Ethical approval was obtained from the Peking University School and Hospital of Stomatology Biomedical Institutional Review Board PKUSSIRB-201631116.

Patient consent

Not required.

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