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Salivary gland tumours in a northern Chinese population: a 50-year retrospective study of 7190 cases

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Abstract. The aims of this study were to investigate the epidemiological and clinical characteristics of epithelial salivary gland tumours in a northern Chinese population and to evaluate the current TNM classification system. A demographic and descriptive analysis of 7190 epithelial salivary gland tumours was performed. There were 4654 benign tumours and 2536 malignant tumours. The percentage of tumours located in the parotid, submandibular, sublingual, and minor salivary glands was 62.66%, 9.92%, 2.57%, and 24.85%, respectively; 22.26%, 35.76%, 92.97%, and 61.89% of the tumours, respectively, were malignant. Over 90% in the tongue and maxillary sinus were malignant. Warthin tumour, salivary duct carcinoma, and squamous cell carcinoma were predominant in males, while basal cell adenoma, myoepithelioma, and pleomorphic adenoma were predominant in females. Further, 2.55% of the tumours were in children and adolescents: 44.81% of the tumours were malignant, as opposed to 35.02% in adults. According to the 7th TNM classification, the percentages of T3 and stage III tumours were approximately 10%. Salivary gland tumours show distribution patterns according to histological type, location, and patient age and sex. The limitations of the current TNM classification of salivary gland carcinoma should be considered and revisions made.

Key words: salivary gland; tumour; histological type; TNM classification; epidemiology.

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Salivary glands are widely distributed in the oral and maxillofacial region and include the three paired major salivary glands and 600–1000 minor salivary glands located in the lip, buccal region, palate, tongue, retromolar area, paranasal sinus, etc.[1,2] They are associated with a highly heterogeneous group of tumours that show great diversity in the morphological features of their cells and tissues[1].

The global annual incidence of salivary gland tumours is 0.4–13.5 cases per 100,000 individuals.[1] Further, the frequency of malignant salivary gland neoplasms ranges from 0.9 to 2.6 cases per 100,000 individuals.[3–6] According to data from the seven main dental schools in China, salivary gland tumours account

for one-third of all oral and maxillofacial tumours.[7] It has been reported that of the 69,902 cases of oral and maxillofacial tumours registered at these seven schools, 23,010 were cases of epithelial salivary gland tumour, accounting for 32.92% of all oral and maxillofacial tumours.[7]

The World Health Organization (WHO) histological typing of salivary gland tumours of 2005 identifies 10 subtypes of benign epithelial salivary gland tumour and 24 subtypes of malignant tumour.[8] The usual tumour of the salivary gland is a tumour in which the benign variant is less benign than a usual benign tumour, and the malignant variant is less malignant than a usual malignant tumour.[9] Benign salivary gland tumours, in particular pleomorphic adenomas, are prone to recurrence and malignant transformation. In patients with malignant salivary gland tumours such as adenoid cystic carcinoma, despite recurrence and distant metastasis, the survival rate is quite good.[10] Nonetheless, more data are needed to clarify the clinicopathological features of this specific group of tumours.

The histopathological findings are sufficient for the diagnosis and treatment of benign epithelial salivary gland tumours. However, for malignant tumours, apart from histopathological examination, the extent of tumour spread is an important index. The TNM classification of malignant tumours is based on the primary tumour size, local tumour invasion, lymph node metastasis, and distant metastasis. It is the most widely used system for describing and classifying the anatomical extent of cancer spread. However, there are some limitations to the current T classification of primary salivary gland tumours. For example, the number and proportion of tumours classified in the T3 subgroup are low, often accounting for less than one-tenth of the whole group of T classes (T1, T2, T3, and T4).[11,12] It is therefore possible that this group of tumours is underestimated with the current T classification system.

The authors' institution is one of the largest research centres on salivary gland diseases in China and has gathered data on 7190 cases of salivary gland tumours over the last 50 years, from 1963 to 2012. The aims of this study were to investigate the epidemiological and clinical characteristics of epithelial salivary gland tumours in a northern Chinese population and to evaluate the validity of the current TNM classification of salivary gland carcinoma. This is the first such study in this population, which makes the findings highly valuable in this field of study.

Materials and methods

Research participants

This study included patients admitted and treated at a stomatology institute between January 1963 and December 2012, who were diagnosed with an epithelial salivary gland tumour.

Research methods

All of the medical information relating to the patients, including sex, age, location of the tumour, pathological findings, and extent of the tumour, was collected and analyzed using SPSS version 13.0 software (SPSS Inc., Chicago, IL, USA).

With regard to malignant tumours, the clinical staging was carried out according to the 2010 criteria of the International Union Against Cancer (UICC).[13] The criteria for staging of squamous cell carcinoma (SCC) were used for the clinical staging of the minor salivary gland tumours.[13]

Results

Distribution of tumours according to histological type

A total of 7190 patients underwent surgical treatment over the 50-year period at the stomatology institute. Among these patients, 4654 (64.73%) had benign epithelial salivary gland tumours and 2536 (35.27%) had malignant tumours.

This case series encompassed almost all of the WHO histological types of epithelial salivary gland tumour, except for sebaceous lymphadenocarcinoma and metastasizing pleomorphic adenoma. In this study, pleomorphic adenoma was the most common salivary gland tumour. There were 3062 cases of pleomorphic adenoma, accounting for 42.59% (3062/7190) of all epithelial salivary gland tumours and 65.79% (3062/4654) of benign salivary gland tumours. There were 751 cases of mucoepidermoid carcinoma, accounting for 10.45% (751/7190) of epithelial salivary gland tumours and 29.61% (751/2536) of malignant salivary gland tumours. This was the most common malignant epithelial salivary gland tumour. The most common epithelial salivary gland tumours were pleomorphic adenoma, Warthin tumour, mucoepidermoid carcinoma, adenoid cystic carcinoma, and basal cell adenoma, in descending order of their incidence. The data are presented in detail in Tables 1 and 2.

Table 1. Location and histopathological type of benign epithelial salivary gland tumours.

	Major salivary gland			Minor salivary gland							Total (%)
	Parotid	Submandibular	Sublingual	Palate	Buccal	Tongue	Lip	Retromolar	Maxillary sinus	Nose	
Pleomorphic adenoma	2044	438	8	431	49	6	30	51	2	3	3062 (65.79)
Warthin tumour	930	4	0	1	1	0	0	1	0	0	937 (20.13)
Basal cell adenoma	326	5	2	3	4	0	0	1	0	0	341 (7.33)
Myoepithelioma	118	9	1	47	2	0	3	1	3	0	184 (3.95)
Cystadenoma	46	1	1	22	4	1	6	3	0	0	84 (1.80)
Oncocytoma	32	1	1	1	0	0	0	1	0	0	36 (0.77)
Canalicular adenoma	3	0	0	0	1	0	2	0	0	0	6 (0.13)
Ductal papilloma	1	0	0	1	0	0	0	0	0	0	2 (0.04)
Sebaceous adenoma	1	0	0	0	0	0	0	0	0	0	1 (0.02)
Lymphadenoma	1	0	0	0	0	0	0	0	0	0	1 (0.02)
Total (*n*), (%)	3502 (75.25)	458 (9.84)	13 (0.28)	506 (10.87)	61 (1.31)	7 (0.15)	41 (0.88)	58 (1.25)	5 (0.11)	3 (0.06)	4654 (100)

Table 2. Location and histopathological type of malignant epithelial salivary gland tumours.

	Major salivary gland			Minor salivary gland							Total (%)
	Parotid	Submandibular	Sublingual	Palate	Buccal	Tongue	Lip	Retromolar	Maxillary sinus	Nose	
Mucoepidermoid carcinoma	325	38	28	201	37	30	12	71	9	0	751 (29.61)
Adenoid cystic carcinoma	126	107	108	190	39	83	12	36	31	1	733 (28.90)
Adenocarcinoma, NOS	94	40	9	29	9	10	2	9	12	0	214 (8.44)
Carcinoma ex pleomorphic adenoma	107	22	8	54	10	5	1	3	0	0	210 (8.28)
Acinic cell carcinoma	112	4	2	22	9	3	5	0	1	0	158 (6.23)
Cystadenocarcinoma	65	9	1	10	5	0	3	7	4	0	104 (4.10)
Myoepithelial carcinoma	25	8	2	23	6	0	1	3	0	0	68 (2.68)
Polymorphous low-grade adenocarcinoma	3	1	3	28	6	2	1	2	0	0	46 (1.81)
Basal cell adenocarcinoma	19	5	4	8	4	0	3	0	0	0	43 (1.70)
Salivary duct carcinoma	23	10	1	6	1	0	0	1	1	0	43 (1.70)
Lymphoepithelial carcinoma	21	3	1	6	2	0	0	0	1	0	34 (1.34)
Squamous cell carcinoma	33	1	0	0	0	0	0	0	0	0	34 (1.34)
Epithelial–myoepithelial carcinoma	21	3	1	6	0	0	0	1	0	0	32 (1.26)
Oncocytic adenocarcinoma	17	2	0	2	0	0	0	2	0	0	23 (0.91)
Clear cell carcinoma	1	0	3	10	2	1	0	1	2	0	20 (0.79)
Sebaceous carcinoma	4	0	0	1	0	1	0	0	0	0	6 (0.24)
Mucinous adenocarcinoma	0	1	1	3	0	0	0	1	0	0	6 (0.24)
Carcinosarcoma	0	1	0	0	2	0	0	0	0	0	3 (0.12)
Sialoblastoma	3	0	0	0	0	0	0	0	0	0	3 (0.12)
Small cell carcinoma	2	0	0	0	0	0	0	0	0	0	2 (0.08)
Large cell carcinoma	1	0	0	0	0	0	0	1	0	0	2 (0.08)
Low-grade cribriform cystadenocarcinoma	1	0	0	0	0	0	0	0	0	0	1 (0.04)
Total (*n*), (%)	1003 (39.55)	255 (10.06)	172 (6.78)	599 (23.62)	132 (5.21)	135 (5.32)	40 (1.58)	138 (5.44)	61 (2.41)	1 (0.04)	2536 (100)

NOS, not otherwise specified.

Distribution of tumours according to location

With regard to tumour location, the tumours were located in the major salivary glands in 5403 patients, and therefore the major salivary glands accounted for 75.15% (5403/7190) of all epithelial salivary gland tumours. Among them, 3973 (73.53%) tumours were benign and 1430 (26.47%) were malignant. The total number of tumours located in the parotid, submandibular, and sublingual glands was 4505 (62.66%), 713 (9.92%), and 185 (2.57%), respectively. In 1787 patients, the tumour was located in a minor salivary gland, and these tumours accounted for 24.85% (1787/7190) of all epithelial salivary gland tumours. Among the minor salivary gland tumours, 681 (38.11%) were benign and 1106 (61.89%) were malignant. Most major salivary gland tumours were benign, that is, about three-fourths of them. However, most minor salivary gland tumours – more than three-fifths – were malignant. There was a significant difference in the proportion of malignant tumours between the major and minor salivary gland tumours ($P < 0.001$). The common locations of epithelial salivary gland tumours were the parotid gland, palate, and submandibular gland.

As shown in Table 3, the ratio of benign to malignant tumours varied across locations. Most of the epithelial salivary gland tumours in the parotid and submandibular glands were benign, while over 90% of the tumours located in the sublingual gland, tongue, and maxillary sinus were malignant.

Distribution of tumours according to sex

Among the 7190 patients, 3563 (49.55%) were male and 3627 (50.45%) were female, giving a male-to-female ratio for this population of 1:1.02.

There was an obvious sex-based trend in some histological types of salivary gland tumour. Warthin tumour, salivary duct carcinoma, SCC, cystadenocarcinoma, and adenocarcinoma not otherwise specified (NOS) were more frequent in male patients: the corresponding male-to-female ratios were 9.65:1, 6.17:1, 4.67:1, 2.00:1, and 1.78:1, respectively. However, basal cell adenoma, pleomorphic adenoma, myoepithelioma, acinic cell carcinoma, and mucoepidermoid carcinoma were more common in female patients, with the male-to-female ratios being 1:1.75, 1:1.55, 1:1.49, 1:1.38, and 1:1.37, respectively.

Table 3. Location-, sex-, and age-based distribution of benign and malignant epithelial salivary gland tumours. .

		Benign		Malignant		*P*-value
		No.	%	No.	%	
Location	Parotid	3502	77.74	1003	22.26	<0.001
	Submandibular	458	64.24	255	35.76	
	Sublingual	13	7.03	172	92.97	
	Palate	506	45.79	599	54.21	
	Buccal	61	31.61	132	68.39	
	Tongue	7	4.93	135	95.07	
	Retromolar	58	29.59	138	70.41	
	Sinus	5	7.58	61	92.42	
	Lip	41	50.62	40	49.38	
	Nose	3	75	1	25	
Sex	Male	2316	65.00	1247	35.00	0.632
	Female	2338	64.46	1289	35.54	
Age (years)	≤16	101	55.19	82	44.81	0.006
	>16	4553	64.98	2454	35.02	

Distribution of tumours according to age

The age of patients ranged from 8 months to 89 years, with the median age being 47 years. The median age of patients with benign tumours was 46 years and with malignant tumours was 48 years. No difference was found between the two large groups of benign and malignant tumours ($P > 0.05$). The median age of patients with Warthin tumour was 59 years and with oncocytoma was 62 years. The median age was over 50 years for patients with malignant salivary duct carcinoma, SCC, adenocarcinoma NOS, mucinous adenocarcinoma, and oncocytic carcinoma. The peak age of patients with epithelial salivary gland tumours was 30–69 years – this age group comprised 75.94% of the total population (5460/7190).

Among the 7190 patients, 183 (2.55% of the total population) were children and adolescents under 16 years of age. Among these young patients, 101 (55.19%) had benign tumours (86 had pleomorphic adenoma), while 82 (44.81%) had malignant tumours (43 had mucoepidermoid carcinoma and 10 had acinic cell carcinoma). With regard to the adult patients, 35.02% had malignant tumours. Compared with the adult patients, the children and adolescents had a greater percentage of malignant tumours ($P = 0.006$). The distribution of benign and malignant epithelial salivary gland tumours based on location, sex, and age are summarized in Table 3.

Distribution of salivary gland carcinomas according to the TNM classification

Among the 2536 patients with malignant tumours, 662 had loco-regional recurrent malignant epithelial salivary gland tumours. Therefore, the remaining 1874 patients had primary malignant tumours that were classified according to the TNM system. The T classification and clinical stage of the salivary gland tumours are shown in Table 4. Regardless of whether the tumour was present in the major or minor salivary gland, the proportion of T3 tumours was 9.55% and of stage III tumours was 10.25%.

Table 4. Distribution and comparison of different T classes and clinical stages of salivary gland carcinoma by different TNM classifications.

		7th TNM classification		New TNM classification	
		No.	%	No.	%
T class	T1	536	28.60	513	27.37
	T2	691	36.87	645	34.42
	T3	179	9.55	248	13.23
	T4	468	24.97	468	24.97
	T4a	363	19.37	363	19.37
	T4b	105	5.60	105	5.60
Clinical stage	I	523	27.91	500	26.68
	II	665	35.49	621	33.14
	III	192	10.25	259	13.82
	IV	494	26.36	494	26.36
	IVA	360	19.21	360	19.21
	IVB	99	5.28	99	5.28
	IVC	35	1.87	35	1.87

Discussion

This study presents the epidemiological and clinical features of salivary gland tumours in a northern Chinese population. The validity of the TNM classification system for salivary gland tumours was examined.

Through classification with the new WHO histological classification system published in 2005,[8] this case series encompassed all of the types of benign tumour and a vast majority of the malignant ones, with the exception of metastasizing pleomorphic adenoma and sebaceous lymphadenocarcinoma. According to the literature, the ratio of benign to malignant tumours is 1.17–3.76:1 for salivary gland tumours.[5,8,14–17] The common benign tumours are pleomorphic adenoma and Warthin tumour, while the common malignant tumours are mucoepidermoid carcinoma and adenoid cystic carcinoma.[5,8,14–17] The findings of the present study are consistent with those of previous studies: the malignant tumours accounted for 35.27% of all salivary gland tumours, with the ratio of benign to malignant tumours being 1.84:1. Further, the common benign tumours were pleomorphic adenoma, Warthin tumour, and basal cell adenoma, and the common malignant tumours were mucoepidermoid carcinoma, adenoid cystic carcinoma, and adenocarcinoma NOS.

Table 5. New T classification for high-grade salivary gland carcinomas.

T3	Tumour of any size
T4a	Tumour invades skin, mandible, ear canal, or facial nerve
T4b	Tumour invades base of skull, pterygoid plates, or encases carotid artery

High-grade salivary gland carcinomas comprise salivary duct carcinoma, high-grade mucoepidermoid carcinoma, squamous cell carcinoma, oncocytic carcinoma, small cell carcinoma, large cell carcinoma, and carcinosarcoma. For other salivary gland carcinomas, the primary tumour classification is in accordance with the 7th TNM classification.

The incidence of tumours is greater in the major salivary glands than in the minor salivary glands.[18] However, it is important to note that the proportion of major and minor salivary gland tumours varies across different types of hospital. Among the 2579 cases of salivary gland tumour reported by Seifert and Sobin, which were mainly from general hospitals, tumours in the parotid, submandibular, sublingual, and minor salivary glands accounted for 80%, 20%, 1%, and 9% of the total salivary gland tumours, respectively.[16] The findings from the present study are similar to those reported from two other main stomatology hospitals in China.[17,20] The proportion of parotid, submandibular, sublingual, and minor salivary gland tumours was 62.66%, 9.92%, 2.57%, and 24.85%, respectively, in the present series of 7190 cases. Therefore, in contrast to the study by Seifert and Sobin, the proportion of parotid gland tumours was lower, while that of minor salivary gland tumours was higher. One possible reason for the relatively high number of tumours in the minor salivary glands in these studies (including the present one) is that they are located in the oral cavity and the patients first seek treatment at a stomatology hospital. The most common site of minor salivary gland tumours is the palate, with an incidence of 8–22% among all epithelial salivary gland tumours.[14,15,17,19] The proportion of minor salivary gland tumours in the palate was 15.37% in the present series of 7190 cases.

The proportion of benign and malignant tumours in the salivary glands varies according to location. Most tumours in the parotid gland are benign, while an equal proportion of benign and malignant tumours is found in the submandibular gland.[8,19] Further, it is well known that the majority of sublingual gland tumours are malignant in nature.[5,8] In this study, 22.26%, 35.76%, and 92.97% of tumours located in the parotid, submandibular, and sublingual glands, respectively, were malignant. These findings indicate that the smaller the size of the gland, the higher is the possibility of malignancy. Furthermore, more malignancies (61.89%) than benign tumours were found in the minor salivary glands in this series. Malignant tumours accounted for 54.21%, 68.39%, 70.41%, and 49.38% of the tumours in the palate, buccal region, retromolar area, and lip, respectively. These results are consistent with those of previous reports.[5,8,14,15,17–20] An important finding was that the percentage of malignancy in the maxillofacial sinus and tongue base in the present series was as high as 92.42% and 95.07%, respectively, which is similar to the percentage of malignant sublingual gland tumours.[18,20]

Certain types of tumour are prone to occur in specific salivary glands. For example, in this study, almost all Warthin tumours, basal cell adenomas, and oncocytomas, and most acinic cell carcinomas, cystadenocarcinomas, oncocytic carcinomas, and epithelial–myoepithelial carcinomas occurred in the parotid gland. The most common salivary gland tumour in the sublingual gland, base of the tongue, and maxillary sinus was adenoid cystic carcinoma, which accounted for 58.38% (108/185), 58.45% (83/142), and 46.97% (31/66) of the tumours in these regions, respectively. The percentages were adenoid cystic carcinoma in the salivary gland tumour of specific sites. Polymorphous low-grade adenocarcinoma was mainly located in the palate. More than 50% of salivary gland carcinomas in the retromolar region were mucoepidermoid carcinomas. These results are consistent with those of other studies.[5,6,8,10,14,15,17,19,20]

No significant differences have been reported before in the incidence of epithelial salivary gland tumours and the ratio of benign to malignant tumours between male and female patients.[5,8,19] Of the 7190 cases in this study, 3563 were male and 3627 were female, giving a male-to-female ratio of 1:1.02. For the male patients, the ratio of benign to malignant tumours was 1.85:1, and for the female patients, the ratio was 1.81:1. However, significant sex-based differences were found in the incidence of certain tumour types in this study. Warthin tumour, salivary duct carcinoma, SCC, and cystadenocarcinoma were more common in male patients, especially Warthin tumour, which had a male-to-female ratio of 9.65:1. However, basal cell adenoma, pleomorphic adenoma, myoepithelioma, acinic cell carcinoma, and mucoepidermoid carcinoma were more common in female patients.

Salivary gland tumours are found across all age groups. In this study, the age of the patients ranged from 8 months to 89 years, with the median age being 47 years. No significant age-based difference was found between benign and malignant salivary gland tumours, which is in agreement with other studies.[14,15,17,21–24] However, it was found that patients with benign salivary gland tumours were relatively young; Warthin tumours and oncocytoma were the exceptions, which were more common in elderly patients. Further, malignant salivary gland tumours were common in the elderly, especially oncocytic adenocarcinoma, salivary duct carcinoma, and SCC, with the median age being 55 years.

According to the literature, teenagers account for only 1.7–5.0% of all patients with epithelial salivary gland tumours,[15,25–27] but the proportion of malignant tumours is higher among teenagers.[15,28,29] According to these studies, malignant tumours were found in more than half of the patients who were less than 16 years old and in more than 80% of patients who were less than 5 years old.[15,28,29] The common histopathological tumour types among adolescents are reported to be mucoepidermoid carcinoma and acinic cell carcinoma.[28–30] In the present series, 2.55% of all patients with epithelial salivary gland tumours were children and adolescents, and the ratio of benign tumours to malignant tumours in these patients was 1.23:1. Compared to adults, for whom the ratio of benign to malignant tumours was 1.85:1, children and adolescents were more prone to malignant salivary gland tumours. This is consistent with previous reports.[15,25–29]

In 2002, the UICC and American Joint Committee on Cancer (AJCC) released the 6th edition of the TNM classification. The clinical staging for salivary gland carcinoma, lip carcinoma, oral cavity carcinoma, and maxillary sinus carcinoma underwent major revision. In addition, anaplastic carcinoma of the thyroid gland was classified under a separate stage. Regardless of the size of the tumour, anaplastic carcinoma of the thyroid gland was defined as a locally advanced lesion.

After in-depth research on the biological behaviour of tumours, the UICC published the 7th edition of the TNM classification in 2010.[13] Malignant melanoma of the upper aerodigestive and respiratory tracts was classified and staged separately: T1 and T2 were abolished, tumours limited to the epithelium and/or

submucosa were classified under T3, and the criteria for T4a and T4b were not changed.

Numata et al. classified 1683 patients with major salivary gland carcinoma according to the 5th edition of the TNM classification and found that only nine patients belonged to stage III.[11] This finding indicated that the 5th edition of the TNM classification may have some limitations with regard to the classification of major salivary gland carcinomas. In addition, Schroeder et al. studied 202 patients with parotid carcinoma and classified them according to the 5th and 6th editions, and compared the classification results.[12] The results showed that the proportion of patients with stage III tumours was higher according to the 6th edition. This further indicates that the 5th edition may have limitations for classifying stage III tumours.

In the present study, TNM staging was performed for 1874 cases. According to the 7th UICC TNM classification, the percentage of T1, T2, T3, and T4 tumours was 28.60%, 36.87%, 9.55%, and 24.97%, respectively, and the percentage of tumours in clinical stage I, II, III, and IV was 27.91%, 35.49%, 10.25%, and 26.36%, respectively. As can be seen, the percentages of T3 and stage III tumours are low at approximately 10%.

Considering that T3 and stage III tumours are rare, the 7th and 6th UICC TNM classifications for malignant melanoma of the upper aerodigestive tract and anaplastic carcinoma of the thyroid were taken as references to reclassify high-grade salivary gland carcinomas, such as salivary duct carcinoma, high-grade mucoepidermoid carcinoma, SCC, oncocytic carcinoma, small cell carcinoma, large cell carcinoma, and carcinosarcoma.[8] For these high-grade salivary gland carcinomas, classifications T1 and T2 were abolished, and tumours of any size were classified as T3, T4a, or T4b, which was consistent with the criteria for T4a and T4b tumours of the major salivary gland and minor salivary gland located in the lip, oral cavity, and maxillary sinus. The T classification for high-grade salivary gland tumours according to this new proposal is listed in Table 5. For other salivary gland carcinomas, the primary tumour classification was in accordance with the 7th TNM classification. Based on the modified classification, the proportion of T3 tumours increased by 3.68%. Further, the proportion of stage III tumours increased from 10.25% to 13.82%. This proposed reclassification may partly solve the problem of the uneven distribution of T classifications and clinical stages of salivary gland tumours, and should be considered in future revisions of the TNM classification of salivary gland carcinoma.

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Competing interests

None declared.

Ethical approval

This study was a retrospective study of patient records. Ethical approval was not required.

Patient consent

Not required.

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