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# Carcinomas of the minor salivary glands of the oral cavity. A population-based study from the Swedish Head and Neck Cancer Register for 2008–2018

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## ABSTRACT

**Background and objectives:** Carcinomas of the minor salivary glands are rare with a heterogeneous pathology. This study explored the demographics, histology, treatment and survival in the Swedish population over 11 years.

**Material and methods:** Cases of salivary gland carcinomas in the oral cavity were extracted from the 'Swedish Head and Neck Cancer Register' (2008–2018). Statistical analyses with cross tabulation, age grouping, chi-square, the Kaplan–Meier method and log-rank tests were performed.

**Results:** Three hundred thirty cases were included (62% female; mean age 60 years; 83% were WHO Performance Status 0). The carcinomas were mostly stage I (57%), and the most common site was the palate with 165 tumours (50%). The most common histology was mucoepidermoid carcinoma (30%), followed by polymorphous low-grade adenocarcinoma (25%) and adenoid cystic carcinoma (24%). The distribution of histology differed between age groups. The five-year predicted overall survival rate was 83%. Most patients (89%) were treated with primary surgery.

**Conclusion and significance:** The demographics, histology, and survival of minor salivary gland carcinomas in the oral cavity in the Swedish population correspond well with previously published material. The demographics and histology differ from carcinomas of the major salivary glands in the same population.

## ARTICLE HISTORY

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## KEYWORDS

Head and neck cancer; oral cavity cancer; minor salivary gland carcinoma; demographics; histology; treatment; survival

## Main text introduction

Carcinomas of the minor salivary gland are rare with an incidence of 0.4 per 100,000 population per year [1] and show a heterogeneous pathology [2]. The most common localisation is the oral cavity with a preference for the hard palate, and the most common pathologies are reported to be mucoepidermoid carcinoma (MEC) and adenoid cystic carcinoma (ACC) [3].

Since 2008, all types of head and neck carcinomas in Sweden are registered in the national population-based 'Swedish Head and Neck Cancer Register' (SweHNCR). SweHNCR has a coverage of 98% of patients with head and neck cancer in Sweden [4].

The aim of the present study was to explore the demographics, histology, treatment, and survival of patients with minor salivary gland carcinomas in the Swedish population over 11 consecutive years.

## Materials and methods

### Patient cohort

Data from the SweHNCR (collected 11 November /2021) included patients with carcinoma of the oral cavity and

parts of the oropharynx (uvula and the inferior surface of the soft palate) (ICD 10: C003–C009, C020–C023, C028–C031, C039–C041, C048–C052, C058–C062, C068–C069) with date of diagnosis during 2008–2018 (1 January 2008–31 December 2018). The data excluded squamous cell carcinomas and mucosal melanomas. From the data set ( $n = 375$ ), cases judged as non-salivary gland histological types ( $n = 35$ ) and cases sorted as 'Undifferentiated' ( $n = 10$ ) were excluded. This resulted in 330 cases being included. Cases were sorted according to histology into groups in accordance with the pre-defined groups in SweHNCR ('MEC', 'ACC', 'Adenocarcinoma NOS', 'Acinic cell carcinoma' and 'Others'). All cases that were indicated in free text as 'polymorphous low-grade adenocarcinoma' (PLGA) ( $n = 72$ ) or 'low-grade adenocarcinoma' ( $n = 9$ ) were defined as 'PLGA'. The description of morphology in free text was given preference to the pre-defined group if there was a contradiction.

The UICC 7th edition was used as tumour classification [5].

The study was approved by the Swedish Ethical Review Authority (registration number 299-14, 2020-01098 and 2021-05039).

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**Table 1.** Demographics – distribution of age and gender.

		Count (n)	%
Age group	0–20 years	9	3
	21–40 years	42	13
	41–60 years	97	29
	61–80 years	137	42
	81 year + ears	44	13
Gender	Female	205	62
	Male	125	38

**Table 2.** Tumour stage, site and histology.

		Count (n)	%
Stage	I	187	57%
	II	56	17%
	III	20	6%
	IV A	46	14%
	IV B	11	3%
	IV C	6	2%
Primary site	Palate including:	165	50%
	Hard palate	115	35%
	Soft palate	50	15%
	Bucca	61	18%
	Gingiva	34	10%
	Lip	28	8%
	Tongue and Floor of mouth	20	6%
Not known	22	7%	
Histology	MEC	100	30%
	PLGA	81	25%
	ACC	79	24%
	Adenocarcinoma NOS	29	9%
	Acinic cell carcinoma	13	4%
	Other	28	8%

MEC: mucoepidermoid carcinoma; PLGA: polymorphous low-grade carcinoma; ACC: adenoid cystic carcinoma.

### Statistical analysis

Overall survival was analysed using the Kaplan–Meier method. Significance in comparison of survival was calculated with log-rank tests. Significance in cross tabulation was calculated with chi-square tests. All statistical analyses were conducted using IBM SPSS Statistics version 27.0. A  $p$ -value  $<.05$  was considered statistically significant.

## Results

### Demographics

The mean age was 60 years (58–62 95% CI) and 62% ( $n=205$ ) were females. No significant difference was found in age distribution according to gender. The majority of patients (83%,  $n=250$ ) were in good physical condition, stated according to the WHO Performance Status 0 (Table 1).

### Tumour stage, site and histology

The majority of tumours were localized and small with 57% ( $n=187$ ) Stage I. Yet, a considerable number of tumours (18%,  $n=59$ ) were found to infiltrate major adjacent structures, classified as T4a-b. Metastasis at diagnosis was rare with 6% ( $n=20$ ) regional metastases and only 2% ( $n=6$ ) distant metastases. Hence, the majority of tumours were Stage I or II and the higher stages were mostly a result of an advanced primary tumour (Table 2).

**Table 3.** Specification of the histological group ‘Others’.

Diagnosis based on free text	Count (n)
Carcinoma of unclear origin	5
Adenosquamous carcinoma	1
Basal cell adenocarcinoma	2
Carcinoma ex pleomorphic adenoma	1
Clear cell carcinoma	6
Epithelial myoepithelial carcinoma	3
Mammary analogue secretory carcinoma	4
Myoepithelial carcinoma	4
Salivary duct carcinoma	2
Total	28

The most common site was the palate with 50% ( $n=165$ ) of the cases and 35% ( $n=115$ ) of these were located in the hard palate (Table 2). The most common histological type was MEC with 30% ( $n=100$ ) followed by PLGA (25%,  $n=81$ ) and ACC (24%,  $n=79$ ) (Table 2). In the category ‘Others’ (8%,  $n=28$ ), a range of exceedingly rare histological types were included ( $n=23$ ) (Table 3) together with unclear cases where salivary gland histology could not be ruled out ( $n=5$ ) (Table 3).

There was a significant difference in the distribution of histological types by tumour site ( $p=.014$ ). MEC was the most or the second most common type for all sites. The most common type in the palate was PLGA. MEC, PLGA and ACC were mostly located in the palate, whereas the dominant site for acinic cell carcinoma was the bucca (Table 4).

There was no significant difference of site or histology between male and female cases. However, there was a trend towards MEC being more common among females, and ACC being more common among males (Figure 1). There was a significant difference in histology when comparing age groups ( $p<.001$ ) where MEC was dominant in the younger cases and PLGA dominant in the largest age group of 61–80 years (Figure 2).

MEC, PLGA and acinic cell carcinoma were mostly stage I (76%, 66% and 69%, respectively), whereas ACC was mostly stage IV (37%,  $n=29$ ). Five out of six cases with distant metastasis were ACC (Figure 3).

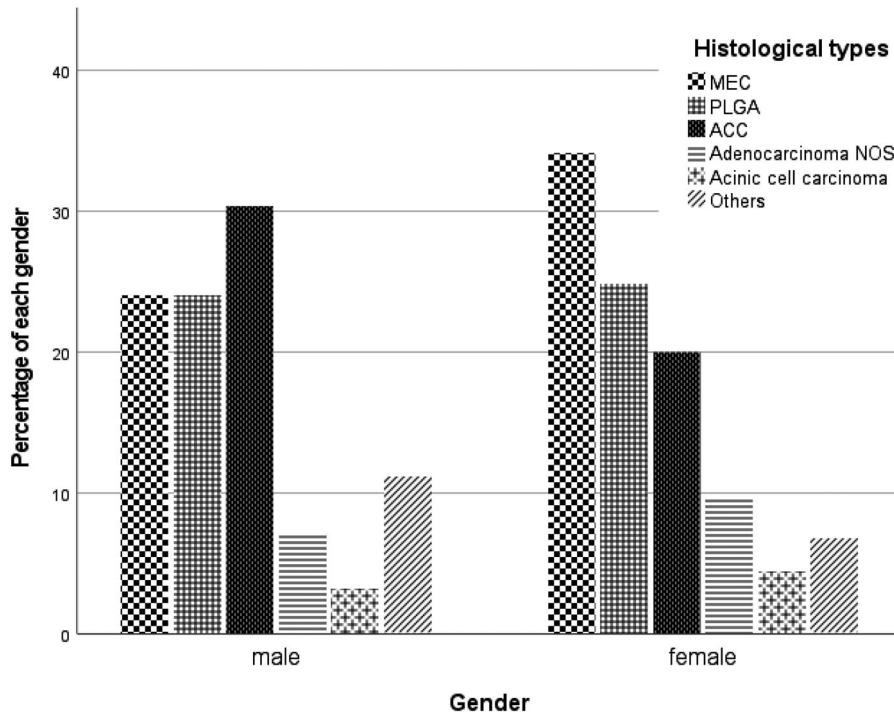
### Treatment

The majority of patients (94%,  $n=309$ ) were treated with a curative intent. Primary surgery was performed in 89% ( $n=293$ ) of the patients, and in 57% ( $n=189$ ), this was the only treatment. External radiotherapy was the most commonly added treatment with the combination of primary surgery and external radiotherapy given to 25% ( $n=82$ ) of the cases. Tumours in stage IV were treated with this combination in 54% ( $n=34$ ) of the cases, while 15% ( $n=28$ ) of stage I tumours received this combination. In 14% ( $n=47$ ), a neck dissection was performed. A small number (5%,  $n=18$ ) received external radiotherapy with no preceding primary surgery and more than half of them were treated with a non-curative intent. Only 3% ( $n=10$ ) received brachytherapy and 3% ( $n=11$ ) received medical oncological treatment.

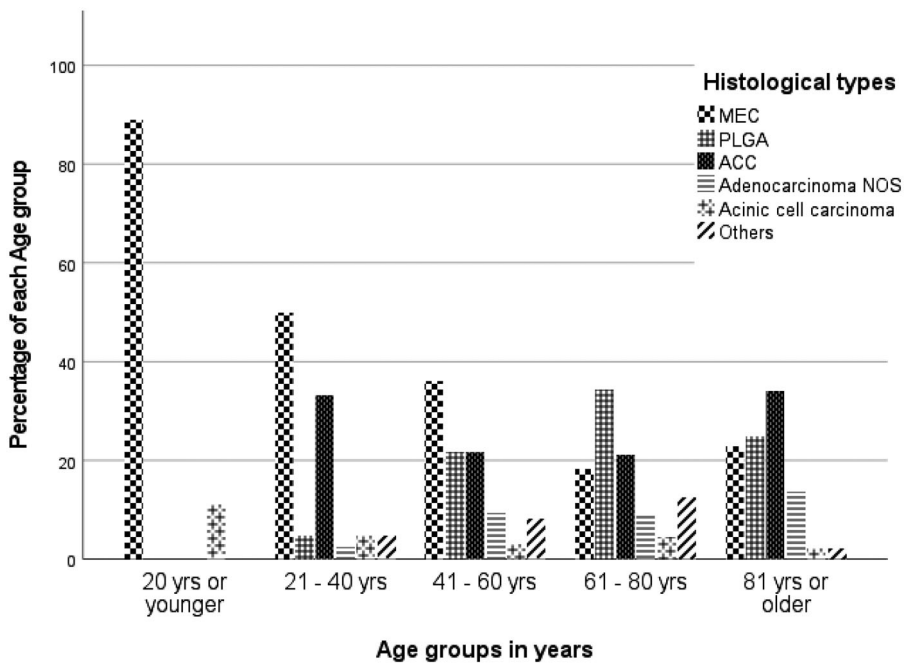
**Table 4.** Distribution of histology by site.

	MEC		PLGA		ACC		Adenocarcinoma NOS		Acinic cell carcinoma		Others	
	n	%	n	%	n	%	n	%	n	%	n	%
Palate	46	46	56	69	39	49	12	41	4	31	8	29
Bucca	20	20	6	7	14	18	9	31	7	54	5	18
Gingiva	14	14	6	7	7	9	2	7	1	8	4	14
Lip	7	7	8	10	6	8	2	7	0	0	5	18
Tongue/Floor of mouth	7	7	1	1	6	8	3	10	0	0	3	11
Unclear	6	6	4	5	7	9	1	3	1	8	3	11

Percentage shown is of the total count for each histological diagnosis.



**Figure 1.** Distribution of histology by gender.



**Figure 2.** Distribution of histology by age.

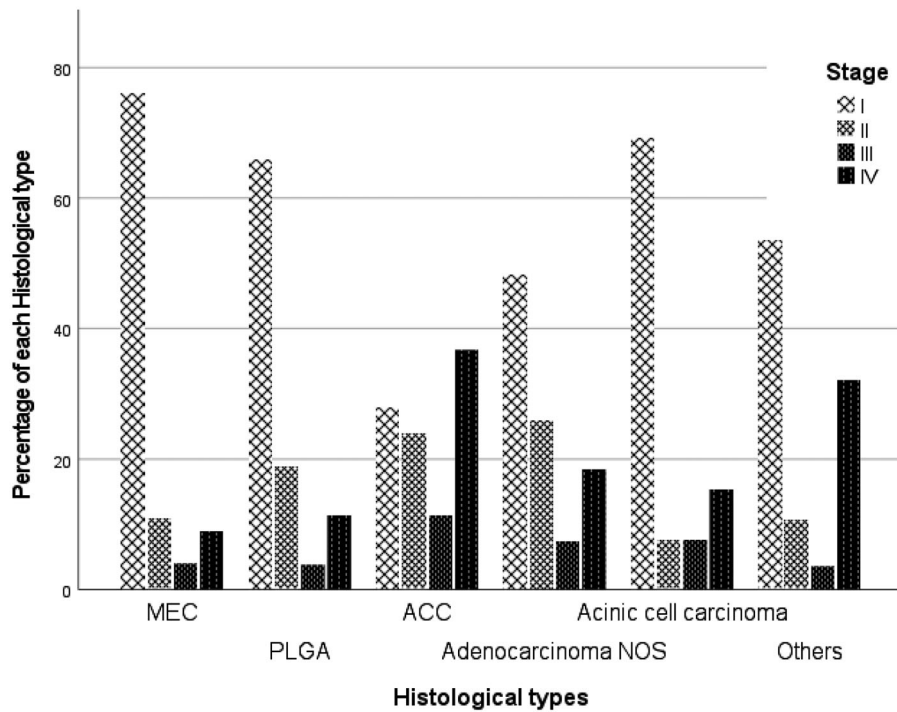


Figure 3. Distribution of stage by histology.

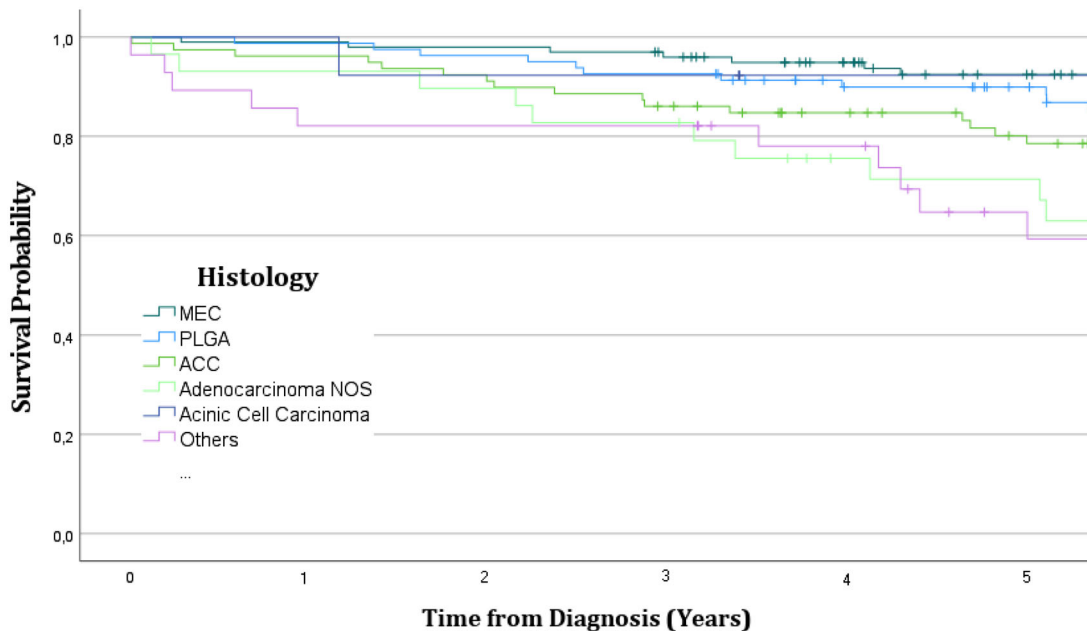


Figure 4. Five-year overall survival rate by histology.

**Overall survival**

The five-year predicted overall survival rate was high at 83% for all cases. The five-year predicted overall survival grouped by histological type showed a significant difference ( $p < .001$ ), and the Kaplan–Meier curve exhibited a lower survival rate for ‘Others’ and ‘Adenocarcinoma NOS’ (Figure 4).

**Discussion**

This 11-year, population-based, consecutive study of minor salivary gland carcinomas in the oral cavity is

unique because of the high representation of the Swedish population during 11 consecutive years. Consistent with previous studies [3,6], the present study showed an increased incidence in females (62%) and the most common age between the sixth and seventh decades with occurrence at the extremes of age as well. Also in line with previous studies is the dominance of small tumours without regional or distant metastasis [6–8].

Our findings of the palate as the most common site (50%) and acinic cell cancer more often being found in bucca are supported by others [9,10].

The material of the present study includes the inferior part of the soft palate and the uvula because the splitting of the palate to oral cavity and oropharynx matches badly with the distribution of the minor salivary glands and the distinction can be clinically hard to make with a larger tumour. When analysing the material, no significant difference was found between the cases of hard and soft palate except for a larger rate of T4 tumours in the hard palate (20% in hard palate vs 4% in soft palate).

In accordance with most other studies, the three most common histological types were MEC, ACC and PLGA [3,7,9,11]. The cases of ACC stand out with a larger amount of stage IV disease (37%), both due to T4 tumours and distant metastasis, and this has been indicated in other studies [6,12]. The group of PLGA should be interpreted with some caution because of the diversity of labelling in SweHNCR. The extraction of PLGA from the group of 'Adenocarcinoma NOS' is still of importance considering its high survival rate compared to the rest of 'Adenocarcinoma NOS' [13]. It can be noted that the correct term since 2017 for PLGA is Polymorphus Adenocarcinoma, but this material is in better coherence with the older term.

The present study showed that the five-year overall survival rate was high at 83% and in accordance with Hay et al. [6] who presented a survival rate of 86%. The curves for 'Others' and 'Adenocarcinoma NOS' drop more rapidly (Figure 4), although this should be interpreted with caution due to the diversity of these small groups. Age is also a confounding factor to consider since the histological distribution differs due to age.

Data from SweHNCR concerning major salivary gland carcinoma were previously published in a report from 2017 [14] and that material is hence suitable for comparison with the data of our study. The major salivary gland carcinomas do not exhibit the same predominance of female cases as for the minor salivary glands (47% vs 62%). The average age of diagnosis of major salivary gland carcinomas (66–71 years) was slightly higher than in our study (60 years). A majority of the minor gland tumours were of stage I disease (57%); this is not in accordance with the major gland tumours where stage I accounts for 21–29%.

The distribution of histological types differs considerably between the minor and the major salivary glands, most notably being MEC (30% of minor salivary gland carcinomas) with only 8% of carcinomas in submandibular glands and 15% in parotid glands. Furthermore, acinic cell cancers had an occurrence as high as 18% in the parotid gland compared to only 4% in the minor salivary glands, which is in accordance with a study of the Danish population [10]. SweHNCR [14] does not make any distinction of PLGA from 'adenocarcinoma NOS', but other publications suggest that PLGA is a rare histology to find in the major salivary glands [10].

Only the relative survival of major salivary gland carcinomas (75%, 72–78 CI) was calculated in the report, but an extraction of data from SweHNCR (18/01/22) concerning the major salivary gland carcinomas gave an overall survival rate of 74% during 2008–2018. The present study hence

implies a higher overall survival rate of carcinomas in the minor salivary glands than in the major glands. A meta-analysis published in 2021 [15] that came to the opposite conclusion is mainly in regard to ACC (14 of 15 studies), and to draw conclusions for the whole group is precarious. Further studies are needed to evaluate if the difference in survival between major and minor glands is due to the distribution of carcinoma histology.

## Conclusion and significance

This population based consecutive study showed that minor salivary gland carcinomas have a higher incidence in females, occur at an average age of 60 years and are most commonly small, localized tumours found in the palate and classified as MEC. The distribution of histology differed between age groups. As a rule, these carcinomas are treated with primary surgery and have a high five-year survival rate as a group. Carcinomas of the minor salivary glands differ from those of the major salivary glands in histology and appear to differ as well in gender and age distribution.

## Methodological considerations/limitations

The high coverage rate of SweHNCR allows the possibility to study the heterogeneous and rare minor salivary gland carcinomas. However, there are limitations. The variety of carcinoma histology and difficulty to distinguish between these present a challenge and has necessitated a method where registries in free texts are given a higher significance than predefined choices. Validation of the group of adenocarcinoma NOS was requested before data retrieval to improve analysis. This does not, however, account for inter-personal differences in determining the histological diagnosis in this notably difficult field.

All cases defined as 'Undifferentiated' ( $n = 10$ ) were excluded due to squamous cell carcinoma being so dominating in the oral cavity such that this group was judged to be equally dominated by non-salivary gland carcinomas.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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