

## The retrospective analysis of recurrent salivary gland cancer after surgery and adjuvant radio- or chemoradiotherapy

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**Introduction.** The aim of the study was to analyse the survival and progression rates in patients with recurrent salivary gland cancer after surgery and adjuvant radio- or chemoradiotherapy.

**Material and methods.** The study included 43 patients treated in 2006–2016 and evaluated in terms of PFS and OS.

**Results.** The 6-, 12- and 24-month OS rates were: 51%, 41%, and 14%, respectively, while the 6-, 12- and 24-month PFS rates were: 44%, 27%, and 14%, respectively. Any treatment improves OS and PFS, with surgery having the greatest effect on improving PFS, followed by chemotherapy and radiotherapy. A multivariate analysis has shown that predictors of PFS are: irradiated volume and radiation technique, while irradiated volume is the predictor of OS.

**Conclusions.** Prognosis in patients with recurrent gland cancer is poor and does not depend on the type of relapse, but rather on further management.

NOWOTWORY J Oncol 2018; 68, 5–6: 245–252

**Key words:** salivary gland cancer, toxicity, recurrences, radiotherapy, chemoradiotherapy.

### Introduction

Salivary gland neoplasms constitute from 3% to 11% of all cancers in the head and neck region and 0.2% of all cancers [1]. These neoplasms represent a diverse spectrum of tumours with the course of the disease based on such factors as: histopathology, tumour location and stage [2]. The relative rarity and significant diversity of these cancers prevent the widespread use of standardised therapy that is based on studies with the highest degrees of reliability. For this reason, treatment requires an individualised multidisciplinary approach and therapeutic decision-making based on a number of risk factors for relapse. These factors, according to different authors, include age, general condition, primary location, stage, surgical margin and histopathological type [3–4]. In the group of patients with locally advanced disease and with the risk factors described above, radical surgery followed by a radio- or chemoradiotherapy is the standard of care [5].

Despite such aggressive treatment, local recurrences are relatively frequent, and prognosis in patients with relapse is

poor. The possibilities of surgical treatment are limited due to the location and infiltrative tumour growth. Moreover, the proximity of critical organs and the use of a tolerance dose in previously irradiated patients prevent conventional radiotherapy due to a high risk of complications. In numerous cases, the only remaining treatment is conventional palliative chemotherapy or biological treatment, which is still being investigated. This study presents an analysis of a group of patients with recurrences after radical surgical treatment and adjuvant radio- or chemoradiotherapy in terms of overall survival and progression rate. An attempt was also made at the identification of risk factors that may affect the type of relapse, further treatment and prognosis.

### Material and methods

The primary analysis involved 126 patients treated for cancer of the large salivary glands in the Centre of Oncology of the Lubelskie Region, Poland, in the years 2006–2016. These patients underwent radical surgery, followed by radical radio- or chemoradiotherapy. A retrospective analysis of the disease

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history allowed the identification of 43 patients with a recurrent disease. Subsequently, a retrospective analysis involved both pre-defined clinical and epidemiological factors (type of involved salivary gland, sex, TNM stage, histopathological type, angio- or neuroinvasion at the diagnosis), as well as previous management (the extent of surgery, technique, dose and area of radiotherapy, and type of chemotherapy, if used). Moreover, epidemiological factors present at the time of relapse were also analysed, including the general condition (according to the WHO classification) and age at relapse as well as a patient's further management (treatment or the lack of treatment and type of treatment). The patient characteristics are presented in Table I. The present study was approved by the Ethics Committee of the Lublin Medical University (Lublin, Poland) (approval no. 0254/340/2018). Written informed consent was obtained from all participants.

In the studied group, the following curves were analysed: progression-free survival (PFS) and overall survival (OS). The Kaplan-Meier test was used for a statistical analysis. The study has investigated the impact of the above-described clinical and epidemiological factors as well as the type of management on OS and PFS. The log-rank test was employed to determine differences in OS and PFS between individual groups of patients. The Cox proportional hazard

model was applied to analyse the influence of continuous independent variables on survival rates. When investigating the relationship between variables, the non-parametric Mann-Whitney U test (for independent variables) was used in order to compare the differences between two groups of patients, or the Kruskal-Wallis test was used to compare the differences between numerous groups of patients. To compare the frequency of the analysed categories depending on the studied parameters, the nonparametric chi-square test (for qualitative variables) was applied. The significance level in all tests was  $p = 0.05$ . The statistical calculations were performed in Statistica ver. 13.1. (StatSoft Poland).

## Results

Of all 43 relapses, 28 (65%) were locoregional. There were 22 relapses in the surgical bed (these were recurrences in the primary tumour area, in the area of removed salivary glands and in the area of primarily involved lymph nodes). In 6 patients, recurrences were observed in the regional lymph nodes beyond the surgical bed. Only one of these recurrences was found beyond the irradiated area. Of 11 systemic relapses, 7 occurred in the lungs, 3 in the liver, 2 in the bones, 2 in the brain and 1 in the mediastinal lymph nodes (Tab. I).

**Table I.** Characteristics of patients

Number of patients with relapses	All	Local relapses	Generalised relapse
	43 (100%)	28 (65%)	15 (35%)
<b>Type of relapse*</b>			
Local	28 (65%)	28 (100%)	0
in bed	22 (51%)	22 (79%)	0
in regional lymph nodes	6 (14%)	6 (21%)	0
Generalised	15 (35%)	0	15 (100%)
in lung	7 (16%)	0	7 (47%)
in liver	3 (7%)	0	3 (20%)
in bones	2 (5%)	0	2 (13%)
in brain	2 (5%)	0	2 (13%)
in non-regional lymph nodes	1 (2%)	0	1 (7%)
<b>Age**</b>	62,5 (20–88)	65,2 (44–88)	54 (20–75)
<b>Sex*</b>			
female	24 (56%)	15 (54%)	9 (60%)
male	19 (44%)	13 (46%)	6 (40%)
<b>General condition*</b>			
WHO 1	25 (58%)	15 (54%)	10 (67%)
WHO 2	15 (40%)	11 (39%)	4 (27%)
WHO 3	3 (7%)	2 (7%)	1 (7%)
<b>Type of salivary gland*</b>			
parotid	25 (58%)	16 (57%)	9 (60%)
submandibular	18 (42%)	12 (43%)	6 (40%)
<b>Primary radicality*</b>			
R0	23 (54%)	15 (54%)	8 (53%)
R1	17 (40%)	10 (36%)	7 (47%)
R2	3 (7%)	3 (11%)	0
<b>Histopathologic type*</b>			
squamous	12 (28%)	10 (37%)	2 (13%)
adenocarcinoma	9 (21%)	5 (19%)	4 (27%)

Number of patients with relapses	All	Local relapses	Generalised relapse
	43 (100%)	28 (65%)	15 (35%)
<b>Histopathologic type*</b>			
undifferentiated	7 (16%)	1 (4%)	6 (40%)
adenoid-cystic	5 (12%)	5 (19%)	0
acinic	4 (9%)	3 (11%)	1 (7%)
others	6 (14%)	4 (15%)	2 (13%)
<b>Neuroinvasion*</b>			
yes	19 (44%)	11 (39%)	8 (53%)
no	24 (56%)	17 (61%)	7 (47%)
<b>Angioinvasion*</b>			
yes	7 (16%)	5 (18%)	2 (13%)
no	36 (84%)	23 (82%)	13 (87%)
<b>Primary stage*</b>			
I	1 (2%)	0	1 (7%)
II	7 (16%)	5 (18%)	2 (13%)
III	10 (23%)	8 (29%)	2 (13%)
IV	25 (58%)	15 (54%)	10 (67%)
<b>Tumour*</b>			
1	2 (5%)	0	1 (7%)
2	10 (23%)	6 (22%)	4 (27%)
3	13 (30%)	11 (41%)	2 (13%)
4	18 (42%)	10 (37%)	8 (53%)
<b>Nodes*</b>			
positive	22 (51%)	16 (57%)	6 (40%)
negative	21 (49%)	12 (43%)	9 (60%)
<b>Time to wait for adjuvant treatment*</b>			
≤ 9 weeks	21 (49%)	13 (46%)	8 (53%)
> 9 weeks	22 (51%)	15 (54%)	7 (47%)
<b>Type of surgery*</b>			
tumour excision	9 (21%)	7 (25%)	2 (13%)
salivary excision	5 (12%)	3 (11%)	2 (13%)
tumour/salivary excision with selective lymphadenectomy	11 (26%)	8 (29%)	3 (20%)
tumour/salivary excision with unilateral lymphadenectomy	16 (37%)	9 (32%)	7 (47%)
tumour/salivary excision with bilateral lymphadenectomy	2 (5%)	1 (4%)	1 (7%)
<b>Radiation therapy planning technique*</b>			
2D	11 (26%)	9 (32%)	2 (13%)
3D	11 (26%)	6 (21%)	5 (33%)
IMRT	21 (48%)	13 (46%)	8 (53%)
<b>Dose*</b>			
< 60 Gy	15 (35%)	10 (36%)	5 (33%)
≥ 60 Gy	28 (65%)	18 (64%)	10 (67%)
<b>Radiation area*</b>			
only surgical bed with margin	7%	5 (18%)	2 (13%)
surgical bed + LND group I-II	8%	5 (18%)	3 (20%)
surgical bed + unilateral LND	12%	10 (36%)	2 (13%)
surgical bed + bilateral LND	16%	8 (29%)	8 (53%)
<b>Chemotherapy + radiotherapy*</b>			
yes	8 (18%)	6 (21%)	2 (13%)
no	35 (82%)	22 (78%)	13 (87%)
<b>Treatment after relapse*</b>			
Yes	37 (86%)	23 (82%)	14 (93%)
surgery	11 (26%)	11 (39%)	0
radiotherapy	7 (16%)	4 (15%)	3 (20%)
chemotherapy	19 (44%)	8 (29%)	11 (73%)
No	6 (14%)	5 (18%)	1 (7%)
<b>Progression after relapse*</b>			
yes	37 (86%)	23 (82%)	14 (93%)
no	6 (14%)	5 (18%)	1 (7%)

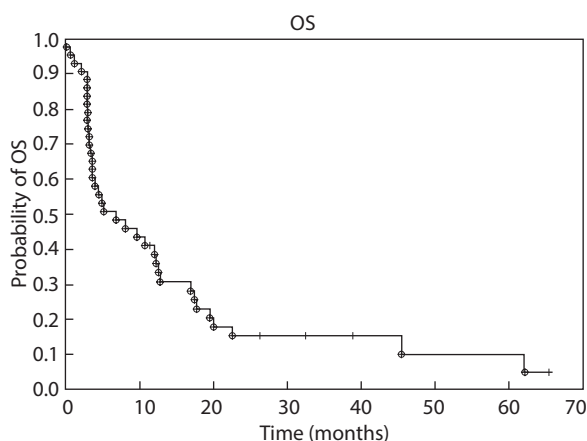
\* number of patients (percent),\*\* median (range), R0 — radical resection, T — tumour stage in TNM classification, N — nodal status in TNM classification, R1 — microscopically non-radical resection, R2 — macroscopically non-radical resection, 2D — two-dimensional planning, 3D — three-dimensional planning, IMRT — Intensity-modulated radiation therapy, Gy — gray

The median follow-up of relapsed patients was 5.16 months (0.1–65 months). Six of 86 patients (14%) died during this period. The probability of overall survival at 6 months, 12 months and 24 months was 51%, 41%, and 14%, respectively. The median survival over the entire period was 4.96 months (0.1–62.07 months) (Fig. 1). Of 43 relapses, further disease progression occurred in 37 (86%) patients (including 6 patients who did not receive any treatment due to relapse). The 6-, 12-, and 24-month probability of progression-free survival was 44%, 27% and 14%, respectively (Fig. 2).

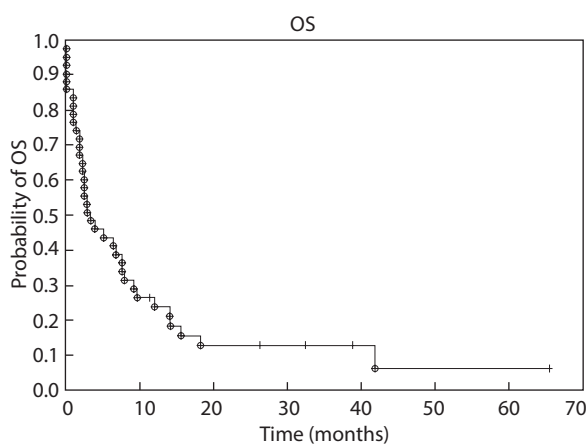
The frequency of various types of relapse was also analysed depending on risk factors. There were statistically significant differences in the frequency of relapses depending on age. In younger patients, systemic relapses were more frequent, while local recurrences predominated in older patients. The results were statistically significant (Mann Whitney U Test  $Z = 2.459$ ,  $p = 0.014$ ). Moreover, there were statistically significant differences in the frequency of various relapses depending on the result of a histopathological examination ( $\chi^2$  test = 12.935,  $p = 0.024$ ). It was demonstrated that

local recurrences predominate in squamous cell carcinoma, adenocarcinoma, adenoid cystic carcinoma, acinic cell carcinoma and other types of carcinoma (83%, 56%, 100%, 75% and 66%, respectively), while systemic relapses were more common in undifferentiated cancer (100%). Differences in the occurrence of the remaining analysed factors were not statistically significant ( $p > 0.05$ ).

The influence of epidemiological factors on overall and progression-free survival in patients with recurrences after surgery and adjuvant chemoradiotherapy was also analysed. There were no statistically significant differences in overall survival and progression-free survival depending on age, sex and type of involved salivary gland (submandibular or parotid). However, a statistically significant difference in OS was found depending on the general condition. The likelihood of 6-, 12-, and 24-month survival in patients with WHO performance status 0–1 was 64%, 51%, and 23%, respectively, in patients with WHO 2: 40%, 33%, and 6%, respectively, and in patients with WHO 3: 0%. A statistically significant difference depending on the general condition was also found for PFS. The likelihood of 6-, 12-, and 24-month survival in patients with WHO performance status 0–1 was: 56%, 30%, and 20%, respectively, in patients with WHO 2: 34%, 27% and 7%, respectively, and in patients with WHO 3: 0%. There was also a statistically significant difference in the probability of overall survival depending on the histopathological type of tumour. Six-month survival was observed in 33% of patients with squamous cell carcinoma, 50% of patients with undifferentiated cancer, 57% of patients with acinic cell carcinoma, 77% of patients with adenocarcinoma and 100% of patients with adenoid cystic cancer. Differences in the probability of progression-free survival depending on the histopathological type were of borderline statistical significance. Local control at 6 months was observed in 33% of patients with squamous cell carcinoma, 43% of patients with undifferentiated cancer, 50% of patients with acinic cell carcinoma, 66% of patients with adenocarcinoma, and 80% of patients with adenoid cystic cancer. The likelihood of 12- and 24-month OS and PFS was not assessed due to a low number of observations. A difference in PFS of borderline statistical significance was demonstrated for the primary lymph node status. Primarily N+ patients had shorter survival rates (6-, 12- and 24-month OS rates in the N+ group were 41%, 31%, and 7%, respectively, while in the N- group, the rates were: 59%, 50%, and 23%, respectively). Furthermore, the study revealed a statistically significant difference in PFS depending on the primary technique of radical RT. Patients receiving postoperative IMRT or 3D RT had longer PFS rates than those undergoing 2D RT (6, 12 and 24-month PFS for IMRT was: 54%, 27%, and 18%, respectively; for 3D RT; 57%, 30%, and 18%, respectively; for 2D RT: 18%, 5%, and 0%, respectively). Similarly, longer PFS was observed in patients irradiated postoperatively



**Figure 1.** Overall survival in all patients with relapses



**Figure 2.** Progression free survival in all patients with relapses

only to the area of the surgical bed or regional lymph nodes (group I-II) (6-, 12- and 24-month PFS was: 53%, 47%, and 27%, respectively) compared to patients with radiation administered to all cervical lymph nodes, either uni- or bilaterally (6, 12 and 24-month PFS was 39%, 16%, and 5%, respectively). There were no statistically significant differences regarding the dose of radical radiotherapy and the use of previous chemotherapy. Moreover, the influence of the type of chemotherapy for cancer recurrence on OS and PFS was also analysed. Platinum-based chemotherapy was used as second-line treatment in 13/18 patients (72%). The remaining patients received a monotherapy with paclitaxel. There were no statistically significant differences in OS ( $\chi^2 = 0.412$ ,  $p = 0.680$ ) or PFS ( $\chi^2 = 0.049$ ,  $p = 0.960$ ) between these groups of patients (Tab. II).

Patients with locoregional and distant recurrences had similar prognoses. There were no statistically significant differences in OS or PFS. However, there were statistically significant differences in patient management. Patients who received any treatment had better prognosis than those without treatment. Patients undergoing surgery due to recurrence had the best prognosis (6-, 12- and 24-month OS was: 81%, 61%, and 40%, respectively; 6-, 12- and 24-month PFS was: 82%, 51%, and 31%, respectively), followed by patients receiving chemotherapy (6-, 12- and 24-month OS: 58%, 53%, and 12%, respectively, 6-, 12- and 24-month PFS: 47%, 25%, and 14%, respectively). The shortest PFS was noted in patients undergoing palliative radiotherapy (6-, 12- and 24- month OS: 28%, 15%, and 15%, respec-

tively, and 6-, 12- and 24-month PFS: 14%, 14%, and 14%, respectively). Patients receiving no treatment had very poor prognosis (6-month OS = 0%, 6-month PFS = 0%) (Tab. II). Moreover, Cox's multivariate analysis showed that the only independent predictor of overall survival was the irradiated area ( $\chi^2 = 4.395$ , HR 1.439 (1.023–2.013)  $p = 0.036$ ) in postoperative treatment. Patients with a smaller area irradiated had a more favourable prognosis.

Also, independent predictors of progression-free survival in patients with relapse after radical treatment included: irradiated area ( $\chi^2 = 9.727$ , HR 1.863 (1.260–2.755)  $p = 0.002$ ) and radiation technique ( $\chi^2 = 5.281$ , HR 0.542 (0.321–0.913)  $p = 0.022$ ). Patients in whom a smaller area was irradiated with a more modern planning technique were characterised by better prognosis.

Of all relapses, locoregional relapses accounted for 63% (28/43). Of these, 22 relapses (51%) occurred within the surgical bed, while the remaining 6 (14%) developed in the cervical lymph nodes. As for the factors that may have had an influence on the type of relapse, statistically significant differences were noted for the type of surgical treatment. It was demonstrated that locoregional recurrences beyond the surgical bed were significantly more frequent after selective lymphadenectomy (50%, 4/8 relapses) than after other types of surgical treatment ( $\chi^2 = 10.842$ ,  $p = 0.028$ ). The use of simultaneous chemoradiotherapy was characterised by borderline significance ( $\chi^2 = 3.702$ ,  $p = 0.054$ ). Patients who received chemotherapy tended to develop recurrences beyond the surgical bed (3/6, 50%), while all those who did

**Table II.** The impact of various factors on the PFS OS

Factor	OS		PFS	
	Chi-square	p	Chi-square	p
Age	0.540	0.910	0.833	0.842
Sex	0.307	0.759	0.206	0.837
WHO	10.036	0.006	8.698	0.013
Type of salivary gland	0.058	0.954	0.640	0.949
Histopathologic type	12.034	0.034	10.594	0.050
Neuroinvasion	0.448	0.654	0.509	0.611
Angioinvasion	0.931	0.352	0.976	0.329
Tumour	4.070	0.264	4.924	0.177
Nodes	1.883	0.049	1.810	0.070
Type of surgery	1.674	0.093	1.103	0.270
Dose	1.136	0.255	0.764	0.445
Radiation therapy planning technique	1.794	0.073	6.069	0.048
Radiation therapy area	2.005	0.045	2.055	0.039
Chemotherapy	0.839	0.402	0.176	0.860
Type of relapse	0.438	0.661	0.721	0.471
Treatment yes/no	2.385	0.017	2.500	0.012
Type of treatment	4.815	0.090	7.409	0.024

OS — overall survival, PFS — progression free survival, p — level of significance

not receive chemotherapy mostly had relapses within the surgical bed (19/23, 83%). As for other factors, differences were not statistically significant ( $p > 0.05$ ). In patients with local recurrence, 23 patients (81%) were treated: all patients with relapses beyond the surgical bed and 17 patients (77%) with a relapse within the surgical bed. Differences were not statistically significant in these patients ( $\chi^2 = 1.660$ ,  $p = 0.197$ ). In the treated patients, all with a relapse within the surgical bed were re-operated (11/11, 100%), 2/2 (50%) underwent re-radiation, and 4/8 (50%) underwent chemotherapy. These differences were statistically significant ( $\chi^2 = 4.212$ ,  $p = 0.024$ ).

The analysis of survival in the group of patients with local recurrences showed that 6-, 12- and 24-month OS was 53%, 38%, and 17%, respectively, while the 6-, 12- and 24-month PFS was 50%, 27%, and 13%, respectively. There were no statistically significant differences in OS between patients with a relapse within the surgical bed and in the regional lymph nodes ( $\chi^2 = 0.442$ ,  $p = 0.658$ ). The probability of 6-, 12- and 24-month OS in patients with surgical bed relapses was 46%, 36%, and 18%, respectively, and in patients with nodal recurrences: 83%, 42%, and 0%, respectively. Similarly, there were no statistically significant differences in PFS between patients with a relapse in the surgical bed and regional lymph nodes ( $\chi^2 = 0.689$ ,  $p = 0.490$ ). The probability of 6-, 12- and 24-month PFS in patients with surgical bed relapses was 46%, 23%, and 14%, respectively, and with nodal recurrences: 67%, 45%, and 0%, respectively.

Of 15 systemic relapses, 7 (47%) developed in the lungs, 3 (20%) in the liver, 2 (13%) in the bones, 2 (13%) in the brain, and 1 (7%) in the extra-regional lymph nodes (mediastinal nodes). No statistically significant factors were found that could affect the frequency of a given type of relapse. The survival analysis in the group of patients with local recurrences showed that 6-, 12- and 24-month OS was 46%, 40%, and 13%, respectively, while 6-, 12- and 24-month PFS was 33%, 27%, and 14%, respectively. There were no statistically significant differences in OS ( $\chi^2 = 0.432$ ,  $p = 0.979$ ) or PFS between patients with relapse in different sites ( $\chi^2 = 3.216$ ,  $p = 0.522$ ).

Of 43 relapses, further progression was found in 37 patients. In patients with local recurrences, 7 (16%) had local progression, 5 (12%) distant metastases, and 5 (12%) had both local progression and distant metastases. As for the remaining patients, there were no data on the type of progression. Among patients with systemic relapse, 5 patients suffered further progression of the size and number of metastases. In the remaining patients, data on the type of progression remain unknown. Of 37 patients with progression, next-line treatment was administered to 4 patients — only those with local recurrences. The median PFS in these patients was 5 months (2–26 months). Three patients suffered from disease dissemination (to the lungs and to

the liver in one case), and one patient presented with local progression. All patients received palliative chemotherapy, and one was treated with palliative brachytherapy to 20 Gy in 5 fractions of 4 Gy. Various treatment regimens were used (paclitaxel with carboplatin and cisplatin, navelbine with fluorouracil, doxorubicin with cyclophosphamide). Another chemotherapy line was given to two patients. Ifosfamide monotherapy (IFO 7) and palliative brachytherapy (10 Gy in 1 fraction) were used. In the patient treated with ifosfamide, PFS was 3 months, and in the patient treated with brachytherapy, it was 1 month.

## Discussion

The above analysis shows that prognosis in patients with recurrent salivary gland cancer after surgery and adjuvant radio- or chemoradiotherapy is poor. Six-, 12-, and 24-month OS was only 51%, 41%, and 14%, respectively, and 6-, 12- and 24-month PFS was 44%, 27%, and 14%, respectively. The prognosis was not different between patients with local and systemic relapse. However, it was dependent on the type of employed treatment. Patients eligible for salvage surgery presented the best prognosis, but prognosis was worse in those treated with chemotherapy or radiotherapy (12-month PFS was 51%, 25% and 14%, respectively).

Studies on treatment of recurrent salivary gland cancer are limited to very small groups of patients and based on single-centre retrospective analyses. In the vast majority of these studies, survival outcomes are better, but the patient profile in all of these studies varies from the one in the present study. This analysis is predominated by squamous cell carcinoma, which has poor prognosis, and most patients were initially at an advanced stage (75% of patients in stages III and IV). For example, Spiro et al. [6] report 5-year OS at a level of 30% in patients treated surgically due to relapse, and Kobayashi et al. [7] observed 5-year OS of 67% in a group of only 12 patients after salvage surgery. However, it should be noted that these patients presented a favourable prognosis, because the remaining 8 patients from this group, with a disease assessed as inoperable, survived over 3 years on average. The outcomes after repeated radiotherapy also indicate positive treatment results. Pederson et al. [8] employed repeated radiation therapy to a dose of 32–66 Gy, which resulted in 1-month and 3-month OS at a level of 72% and 52%, respectively. In the patients described in the present study, the outcomes were also worse. However, only 4 patients underwent repeated radiation therapy, and all others received palliative radiotherapy. Moreover, data on the use of chemotherapy are also based on small groups and diverse treatment regimes, which makes it very difficult to draw unambiguous conclusions. Treatment responses vary from 0% to 100% with response period of 6–9 months [9]. As in the analysed group of patients, platinum-based regimens prevailed [10].



The present study analysed the influence of various factors on prognosis in patients with recurrent cancer. A multivariate analysis showed that patients irradiated to a smaller area presented better prognosis. This could be related to both lower initial cancer stage and better possibilities of salvage treatment (easier surgical treatment, greater possibilities of using repeated radiation therapy and lower risk of complications related to less aggressive treatment). Moreover, prior irradiation using modern planning techniques improved prognosis. The reasons for this may have been similar to those described above. Studies on primary tumour treatment indicate worse prognosis in patients with squamous cell carcinoma and undifferentiated cancer [11]. These histopathological types were also characterised by the worst prognosis in patients with the recurrent disease. Patients who were less advanced at the diagnosis and in better general condition presented a better prognosis, which seems to be obvious.

Based on the investigated patients, it was shown that systemic relapses are more common in younger patients, while local recurrences occur more often in older patients. These results are difficult to interpret in the light of research which indicates that younger patients tend to develop slow-growing local diseases (adenoid cystic and mucoepidermoid carcinoma), while more aggressive types occur in older individuals (NOS adenocarcinoma) [12, 13]. However, it should be noted that the patient profile was slightly different in the examined group of patients (all patients were initially at a higher risk of relapse and were therefore deemed eligible for adjuvant treatment). The analysis of the site of relapse depending on the histopathological type showed that patients with undifferentiated cancer were characterised by disease progression mainly in the form of distant metastases, whereas the remaining histopathological types were characterised by the predominance of local recurrences. This is probably related to the aggressiveness of this tumour compared with other histopathological types [14].

The role of chemotherapy combined with radiotherapy in the treatment of salivary gland tumours remains unclear. The study of relapsed patients does not indicate that the number of systemic relapses is lower in patients treated with a combination therapy compared to patients who received only postoperative radiotherapy. It was only shown that patients treated with radiotherapy combined with chemotherapy less often developed recurrences in the irradiated area, and the difference was on the verge of statistical significance. This may lead to a conclusion that chemotherapy probably increases local effectiveness of radiotherapy, which is supported by some studies [15–18]. Moreover, the study also indicates that a decision regarding the extent of surgery is crucial. In the analysed group of patients, nodal progression beyond the surgical bed was significantly more frequent in patients treated with selective

lymphadenectomy than in those receiving radical lymphadenectomy, which indicates the need for high caution when selecting patients for this method of surgical treatment.

## Conclusions

The prognosis in patients with recurrent salivary gland cancer after surgery and adjuvant radio- or chemoradiotherapy does not depend on the type of relapse, but rather on further management. Patients in whom any treatment is implemented present better prognosis. In this group, prognosis was the best in patients undergoing surgery, followed by those treated with chemotherapy, and the worst in those receiving radiation therapy. Moreover, general condition, cancer stage, histopathological type, radiotherapy technique, and irradiated volume, which can be directly related to the stage of the disease, also contribute to the success of treatment. Distant metastases are more common in younger patients with undifferentiated cancer. The prior use of chemotherapy and the extent of lymphadenectomy may also be of prognostic significance.

**Conflict of interest:** none declared

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*Received: 7 Jan 2019*

*Accepted: 15 Mar 2019*

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