International Journal of Advances in Medicine
*Florindo A et al. Int J Adv Med. 2021 Mar;8(3):341-347*
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20210535

**Original Research Article**

# Adjuvant radiotherapy in the management of major salivary gland tumors: retrospective analysis

**Andre Florindo[1]*, Saulo Saraiva[1], Tiago Cruz Tomas[2], Andre Abrunhosa-Branquinho[1], Jorge Santos[1], Vera Mendonça[1], Maria Filomena de Pina[1]**

[1]Department of Radiotherapy, Centro Hospitalar Universitário Lisboa Norte, E.P.E., Lisbon, Portugal
[2]Department of Medical Oncology, Hospital Professor Doutor Fernando Fonseca, Lisboa, Portugal

**Received:** 03 February 2021
**Revised:** 12 February 2021
**Accepted:** 15 February 2021

***Correspondence:**
Dr. Andre Florindo,
E-mail: andre.daniel.florindo@gmail.com



## ABSTRACT

**Background:** This study evaluates long-term survival outcomes of patients submitted to surgery (with or without neck dissection) and adjuvant radiotherapy for major salivary gland tumors, as well as prognostic factors affecting clinical outcomes.
**Methods:** Retrospective analysis was performed on patients treated for major salivary gland tumors between 2006 and 2018. Kaplan-Meier curves for disease-free survival (DFS) and overall survival (OS) were calculated, Cox regression was used for uni- and multivariate analysis to assess prognostic factors. Log-rank tests were used to compare survival outcomes according to neck dissection status, stratified by stage and by histopathological risk.
**Results:** 38 of 77 pts were eligible for analysis. Median follow-up was 63.1 months and median dose delivered was 66 Gy. The 2- and 5-years DFS rates were 79.2% and 72%, and the 2- and 5-years OS rates were 81.5% and 66.6%, respectively. Lymphovascular invasion and neck dissection were identified as possible prognostic factors for DFS and lymphovascular invasion, positive nodes, high histopathological risk and positive margins, for OS. There were no differences observed in DFS and OS curves for high histopathological risk patients according to neck dissection. A difference was found comparing DFS on stage III-IV patients (p=0.02), OS was not different.
**Conclusions:** DFS and OS improvements were not observed in high-risk histology and III-IV stage disease due to study limitations, regardless of neck dissection status. Some of the results shown, although with no statistically significant differences, could reveal the potential of adjuvant radiotherapy in pts unable to perform neck dissection.

**Keywords:** Major salivary glands, Radiotherapy, Prognosis, Risk factors, Neck dissection

## INTRODUCTION

Salivary gland tumors represent 5 to 10% of head and neck cancer.[1,2] Salivary gland malignancies represent a heterogeneous group of neoplasms, with 24 different types recognized by the World Health Organization.[3] Eighty percent are localized in the parotid glands, 10% in the submandibular glands and 8% in the accessory glands. Surgery is the mainstay treatment for resectable tumors in operable patients and adjuvant treatment is based on presence of adverse features. Radiotherapy is mainly used in post-operative setting to treat possible microscopic residual disease and improve locoregional control. The use of primary radiotherapy is reserved for unresectable disease, some minor salivary gland cancers (for which resection would result in unacceptable functional or cosmetic morbidity) and palliation. As there are no concluded prospective trials randomizing to postoperative radiation, available evidence is limited to tumor and treatment heterogeneity and retrospective analyses. Nonetheless, single-institution series have demonstrated

improved survival with adjuvant radiation.[4-7] Indications for postoperative radiation on primary site include: gross disease, positive/close margins (≤1 mm), T3/T4 tumor, high-grade, bone involvement, lymphovascular or perineural invasion.[8] Adjuvant neck radiotherapy should be considered if: gross nodal disease, pathologic node-negative with risk factors (T3/T4 tumor, high-grade, facial nerve deficit, recurrent disease), pathologically involved lymph nodes and extracapsular extension.[7] Ipsilateral neck dissection (levels I-III) is recommended in presence of high-grade disease, cN+ and/or T3-4 tumor.[9,10] The management of node-negative neck remains controversial. The incidence of occult neck disease is affected by histopathology, T-stage, and grade of differentiation.[11] Contralateral neck dissection is advised if multilevel nodes and if there are more than half of the evaluated nodes clinically positive. This study aims to evaluate the long-term survival outcomes of patients who underwent surgery (with or without neck dissection) and adjuvant radiotherapy for major salivary gland tumors, as well as prognostic factors that affect clinical outcomes.

## METHODS

A retrospective study was conducted by researching clinical records of patients with diagnosis and treatment of major salivary gland carcinoma in Centro Hospitalar Universitário Lisboa Norte. Seventy-seven patients who received radiotherapy for major salivary gland tumors between January 2006 and December 2018 at the Radiotherapy Department were identified and reviewed. Of these, 39 patients were excluded due to not being treated in the adjuvant setting, insufficient medical records or squamous cell carcinoma (SCC) histology. The study was pursued analyzing the remaining 38 patients who were eligible. Clinical and pathological data such as age, gender, location, T and N staging, histopathological classification, lymphovascular invasion, perineural invasion, surgical margins and type of surgery. The 8th edition of American Joint Committee on Cancer (AJCC) staging system was used to retrospectively stage all patients, as there were instances of incomplete and outdated reports. The last available histopathological diagnosis was used, histology was recorded and later stratified by risk according to WHO proposal (low risk and high risk).[3]

Postoperative radiotherapy (PORT) was administered as either 3D conformal radiotherapy or intensity-modulated radiotherapy (IMRT) with photons, electrons or both using a linear accelerator. The definition of volumes, prescription point and dose homogeneity were in accordance with ICRU Reports #50, #62 and #83.[12-14] Gross tumor volume included all gross disease on physical examination and imaging, residual tumor and positive nodes. Primary clinical target volume (CTV-P) resulted from an isometric expansion of 5 mm from previously contoured GTV. CTV-P encompassed the entire GTV or the surgical bed according to primary. Elective CTV covered the rest of the ipsilateral neck (levels Ib–V) in clinically node-positive tumors and at least levels Ib–III on clinically node-negative tumors with presence of the previously mentioned high risk features.

Follow-up visits were performed 4-8 weeks after completion of therapy, and then every 3-6 months for 2 years. Thereafter, appointments were scheduled every 12 months. A physical exam was performed at each follow-up visit and image studies were requested as needed. Follow-up records were searched for evidence of recurrence, time to recurrence, treatment at recurrence and cause of death.

**Table 1: Patient clinical features and treatment modalities.**

| Patient characteristics | N (%) |
|---|---|
| **Gender** | |
| Male | 17 (45) |
| Female | 21 (55) |
| **Location** | |
| Parotid gland | 26 (68) |
| Submandibular gland | 11 (29) |
| Sublingual gland | 1 (3) |
| **AJCC 8th edition staging** | |
| I and II | 15 (39) |
| III and IVA | 20 (53) |
| N/A | 3 (8) |
| **Histopathological stratification WHO** | |
| Low risk | 20 (53) |
| High risk | 18 (47) |
| **Lymphovascular invasion** | |
| No | 32 (84) |
| Yes | 6 (16) |
| **Perineural invasion** | |
| No | 20 (53) |
| Yes | 18 (47) |
| **Surgical margins** | |
| Negative / Unknown | 14 (37) |
| Positive or close | 24 (63) |
| **Cervical lymph node resection status** | |
| No neck dissection | 20 (53) |
| Neck dissection | 18 (47)[a] |
| **Type of surgery** | |
| Total tonsillectomy | 29 (76) |
| Partial excision | 9 (24) |
| **Surgery outcome** | |
| R0 | 32 (84) |
| R1 | 1 (3) |
| N/A | 5 (13) |

[a]6 patients had positive lymph nodes in neck dissection

The baseline follow-up date was the day of biopsy report or the date of surgery; the last follow-up date was the last hospital visit or last clinical registry found on the Portugal's National Health Data Platform. Overall survival (OS) was calculated since baseline date until date of

patient's death. Disease-free survival (DFS) was calculated since baseline date until first recurrence date, locoregional or metastatic. Kaplan-Meier method was used to produce DFS and OS curves. Cox regression was used for uni- and multivariate analysis to assess prognostic factors and Log-rank tests were used to compare survival outcomes according to neck dissection status, overall and then stratified by stage (I and II versus III and IV) and by histopathological risk (low versus high) according to WHO risk stratification. Multivariate analysis was conducted using statistically significant variants from the previously performed univariate analysis. All statistical analyses were carried out using IBM SPSS Statistics (Windows Version 24.0. Armonk, NY: IBM Corp.).

## RESULTS

### *Patient clinical features and treatment characteristics*

A total of 38 patients were reviewed, with a median age of 64 years. Primary location of disease was the parotid gland in 26 patients (68%), while 11 patients (29%) had disease in the submandibular gland and one in the sublingual gland. Fifteen patients (39%) had stage I or II disease, 20 patients had stage III or IV disease (53%) and stage could not be assessed in 3 patients (8%). Most common presenting symptom was a swollen parotid or submandibular gland; it was present in 36 (95%) patients. Pain was reported in 7 patients (18%) and facial nerve dysfunction was found in 2 patients (5%), both T3 tumors. None of the patients had ulceration or dysphagia at presentation. Median time between onset of symptoms and histopathological diagnosis was 8,3 months.

Poor prognostic pathologic features were prevalent in both groups. Overall, lymphovascular invasion was present in 6 patients (16%), perineural invasion was present in 18 patients (47%), 24 patients (63%) had close or positive surgical margins. The histopathologic risk stratification according to WHO revealed a low-risk group with 20 patients (53%) and a high-risk group with 18 patients (47%).

All the patients underwent surgical excision of the malignant lesion. Type of surgery was total tonsillectomy in 29 patients (76%) and partial excision in 9 (24%). Additionally, 18 patients (47%) underwent neck dissection, of which 6 had pathologically positive lymph nodes, and neck lymph node dissection was not performed in 20 patients (53%).

**Table 2: Univariate and multivariate analysis.**

| Variables | Univariate analysis | | | | Multivariate analysis | | | |
|---|---|---|---|---|---|---|---|---|
| | Progression-free survival | | Overall survival | | Progression-free survival | | Overall survival | |
| | $\chi 2$ | P value | $\chi 2$ | P value | HR (95% CI) | P value | HR (95% CI) | P value |
| **Age (<64 versus ≥64)** | 0.5 | 0.46 | 1.1 | 0.31 | 0.26 (0.03-2) | 0.2 | 0.62 (0.1-3.1) | 0.56 |
| **Stage (I-II versus III-IV)** | 1.4 | 0.23 | 1.14 | 0.29 | 1.88 (0.3-11.8) | 0.5 | 1.33 (0.3-6.7) | 0.72 |
| **Histopahological risk (low versus high)** | 2.8 | 0.1 | 3.8 | 0.05 | 6.12 (0.7-55.2) | 0.11 | 10.03 (1.4-73.1) | 0.02 |
| **Positive or close margin** | 0.3 | 0.6 | 5.2 | 0.02 | 4.74 (0.5-42.1) | 0.16 | 0.22 (0.04-1.3) | 0.09 |
| **Neck dissection** | 5.8 | 0.02 | 0.3 | 0.56 | 4.75 (0.4-56) | 0.22 | 1.08 (0.1-7.2) | 0.94 |
| **pN+** | 2.1 | 0.15 | 7.6 | 0.01 | 2.23 (0.2-24.8) | 0.51 | 0.98 (0.1-7.4) | 0.99 |
| **Perineural invasion** | 2.8 | 0.1 | 0.3 | 0.56 | 0.28 (0.01-5.6) | 0.41 | 0.38 (0.1-2.8) | 0.38 |
| **Lymphovascular invasion** | 6 | 0.01 | 7.6 | 0.01 | 21.81 (2.4-197.3) | 0.01 | 7.07 (1.5-34.1) | 0.02 |
| **Neck irradiation** | 0.2 | 0.65 | 01 | 0.75 | 0.78 (0.1-4.4) | 0.77 | 5.24 (0.7-41.2) | 0.12 |

Residual disease was found in one patient, was unknown in 5 patients and absent in 32 (84%). Median count of excised nodes per patients submitted to neck dissection was 16 (range: 2-73). In six patients where formal neck dissection was not performed, nodes were excised along primary tumor surgery, and all of them were pathologically negative.

Adjuvant radiotherapy was performed in all patients. Median dose was 66 Gy and median number of fractions

for treatment delivery was 33. Twenty-five patients (66%) received neck irradiation with median dose of 50 Gy, and median number of fractions was 25. Precise information on which node levels were covered could not be accessed through our medical records. Two patients (5%) received adjuvant chemotherapy. There were no interruptions of radiotherapy due to toxic effects. Most common iatrogenic effect was skin-related toxicity, reported in 30 patients (79%), followed by mucositis in twenty-nine patients (76%) and dysphagia in 19 (50%). One case of grade 3 mucositis was reported.

### *Follow-up*

Median follow-up was 63.1 months (range 3.5-167.3). Progressive disease occurred in 10 patients. Both types of recurrent disease were observed, locoregional and metastatic disease. Locoregional recurrence occurred in 3 patients, metastatic disease in 3 patients and 4 patients with unkown site of progression. Neck irradiation was delivered to 6 patients whom later had progressive disease. We performed analyses on time to both locoregional and distant progression, which did not considered death as an event of interest.

Median DFS of all 38 patients was 56.2 months, corresponding to 2- and 5-year recurrence-free survival rates of 79.2% and 72%, respectively. Median OS was 67.4 months, corresponding to 2- and 5-year OS rates of 81.5% and 66.6%, respectively.

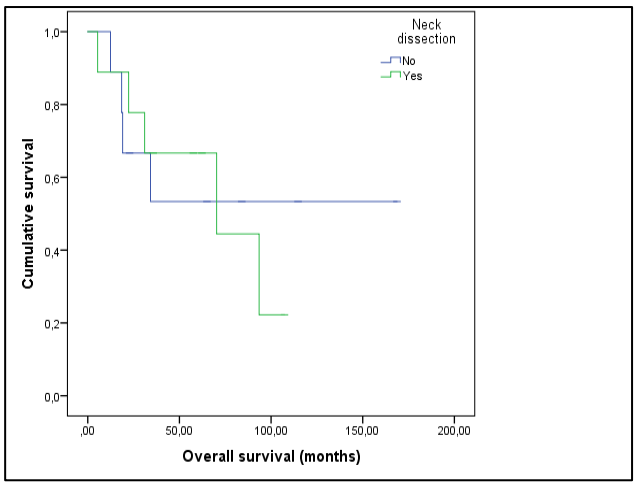


**Figure 1: Overall survival in high histopathological risk patients with no neck dissection versus neck dissection prior to adjuvant radiotherapy.**

### *Risk factor analysis*

Regarding univariate analysis, decreased DFS was associated with lympho-vascular invasion (p=0.01), and neck dissection (p=0.02). Decreased OS was also associated with lympho-vascular invasion (p<0.01), positive lymph nodes (p=0.01), high histopathological risk (p=0.05) and positive surgical margins (p=0.02).

Table 2 shows the multivariate cox regression on DFS and OS. It revealed that lympho-vascular invasion predicted poorer DFS (HR 21.8; IC 95% 2.41 – 197.28; p<0.01). That factor was also predictor of poorer OS (HR 7.07; 1.47 – 34.1; p=0.02). OS was influenced by higher histopathological risk (HR 10; 1.38 – 73.1; p=0.02).

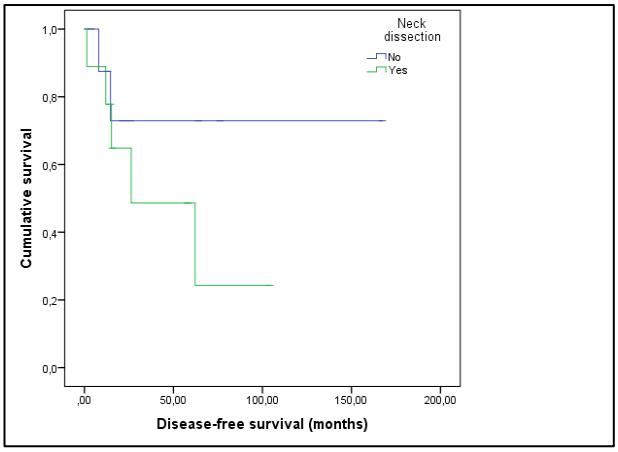


**Figure 2: Disease-free survival in high histopathological risk patients with no neck dissection versus neck dissection prior to adjuvant radiotherapy.**

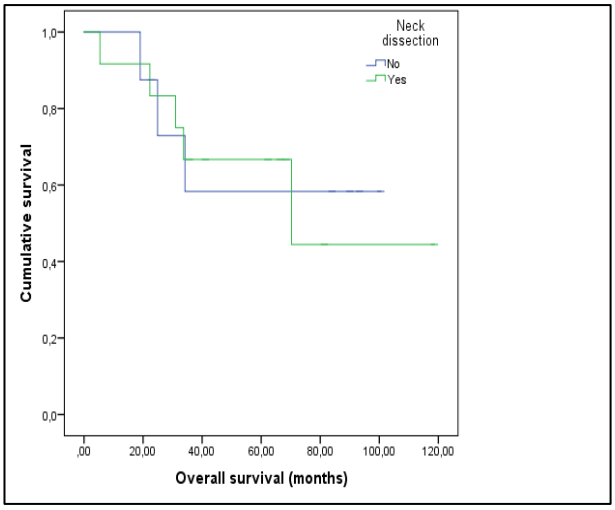


**Figure 3: Overall survival in stage III-IV patients with no neck dissection versus neck dissection prior to adjuvant radiotherapy.**

When analyzing the 18 patients with high histopathological risk disease, there was a 1:1 distribution regarding neck dissection. Comparing both groups there were no significant differences on DFS (p=0.27) and OS (p=0.84). Figures 1 and 2. Analyzing patients with low histopathological risk disease and comparing the neck dissection curves, a difference was observed (p=0.05) as there were no progression cases in the group not submitted to neck intervention.

Comparing both group of patients who had stage III and IV disease, there was a statistically significant difference

(p=0.02) between DFS observed as there was no disease progression under the circumstance of stage III or IV disease without neck dissection. The same difference wasn't detected in the OS analysis comparing both curves (p=0.87). Figure 3 and 4.

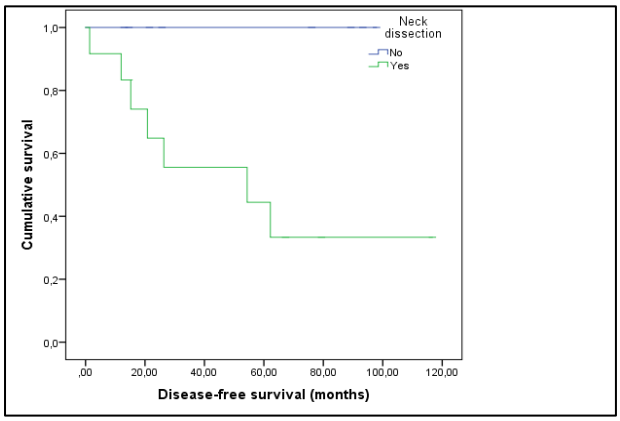


**Figure 4: Disease-free survival in stage III-IV with no neck dissection versus neck dissection prior to adjuvant radiotherapy.**

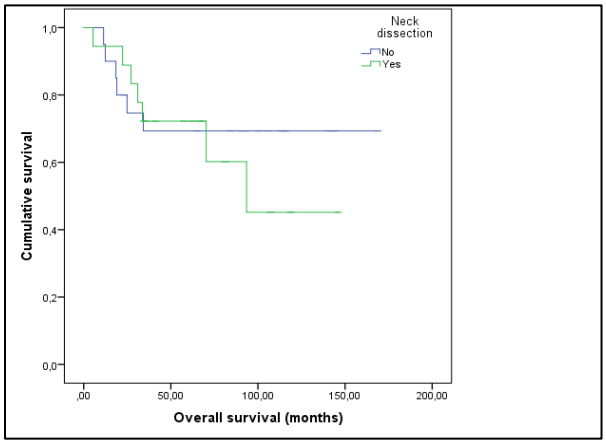


**Figure 5: Overall survival: no neck dissection versus neck dissection prior to adjuvant radiotherapy.**

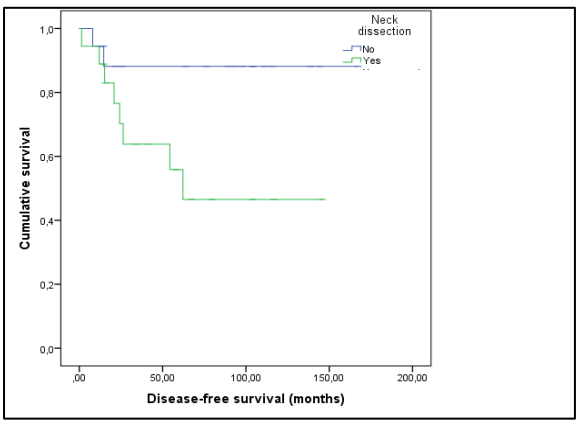


**Figure 6: Disease-free survival: no neck dissection versus neck dissection prior to adjuvant radiotherapy.**

On the overall comparison between groups with and without neck dissection shown in Figures 5 and 6, a statistically significant difference is shown regarding DFS (p=0.03) as there were 2 disease progressions in a group of 20 patients who didn't underwent neck surgery comparing with 8 out of 18 progressions in the neck surgery group.

Regarding OS there was no difference between both groups (p=0.60).

## DISCUSSION

Defining optimal treatment strategy for salivary gland cancer remains a challenge for all involved medical specialties, particularly because of the rareness of this cancer and the diverse range of tumor entities. The low frequency of patients makes it especially difficult to acquire a sufficient number of relevant patients in an acceptable period of time for further analysis. Therefore, specific guidelines for treatment have, unsurprisingly, not been established. In particular, benefit of neck dissection to rule out occult lymph node metastasis in these patients remains controversial. Neck dissection usefulness resides in the attempt to remove occult lymph node metastasis in affected patients. The probability of success in that attempt lies in multiple factors including high-grade histology, primary tumor location and extent, as well as presence of lymphovascular space invasion, perineural involvement and/or skin involvement. In this study we try to define the impact of adjuvant radiotherapy, firstly by evaluating main factors that might affect survival outcomes and then by evaluating the role of neck dissection in patients with possible indication to perform it, combining one or both major risk features: high histopathological risk and/or stage III-IV disease. To do so we compared both groups with and without neck intervention stratified by histopathological risk, stage and then without any subgroup specification.

The role of adjuvant radiotherapy in patients with high-risk features or advanced stage is well documented. A matched pair analysis carried out on 46 patients submitted to surgery and post-operative radiotherapy for major salivary gland cancer at the Memorial Sloan Kettering Cancer Centre, revealed that for stages III and IV disease only, 5-year local control rate was improved by addition of radiotherapy (51 versus 17%). This translated into improved 5-year disease-specific survival (51 versus 10%), with a trend towards benefiting patients with high-grade disease (57 versus 28%).[4] In a large retrospective series from the Netherlands, patients were treated in a similar way as above mentioned.[7] Despite prognostic factors favoring patients submitted to surgery alone, actuarial local control rates after 5 and 10 years were 84 and 76%, respectively, for surgery alone and 94 and 91% with the addition of PORT. Multivariate analysis in the same study revealed that PORT significantly improved 10-year local control for T3–4 tumors, close (less than 5 mm) or involved margins, and perineural or bone invasion; furthermore, regional control was significantly improved

in the presence of one or more involved neck nodes. Our results were slightly lower than the Dutch study mainly because of a more favorable distribution regarding tumor stage (T1-2 73% versus 50%), but node distribution was equivalent (cN+ or pN+ 27% versus 26%).

Lymphovascular invasion was observed as a transversal prognostic factor on uni- and multivariate analysis and on both DFS and OS. Perineural and lymphatic invasion are common histological features in salivary gland tumors.[15,16] Previous studies have proposed that high incidence of these findings may reflect the tumor's high-grade biology. This assumption suggests that information about lymphovascular invasion is imperative to be included in the pathology report for clinicians.

The effect of neck dissection on DFS results from clinical indications for that procedure (stage and tumor grade) and their independent impact on prognosis. Positive lymph nodes and close or positive margins identified in our study as independent prognostic factors for OS are also identified as such in a large retrospective analysis using National Cancer Database (NCDB) data from 4068 patients.[17]

Salivary gland pathology is considered one of the most challenging subspecialties because of its heterogeneous nature and overlap between benign and malignant disease. The WHO has identified 24 different histological subtypes, causing classification as well as prognostication extremely problematic.[3] To narrow that spectrum of entities we used the risk stratification provided by WHO to assess the histopathological risk. Indeed, we found that high histopathological risk was associated both in uni- and multivariate analysis with OS. Safdieh et al only demonstrated association regarding SCC, and prevalence of that histology was quite different compared to the Dutch retrospective study.[7,17] That difference, the fact that other studies have reexamined the cases of tumor registry patients diagnosed with primary parotid SCC and noted that only 20% were correctly diagnosed and our low sample size leads us to exclude that specific histology.[18] Another reason for excluding this histology in cohort was to avoid selection bias of parotid metastases from cutaneous SCC which is highly prevalent in our country and this entity is not properly documented in medical reports. Findings from Lau et al have demonstrated that histological subtype is the predominant factor predisposing to occult cervical lymph node involvement and may be useful in selecting patients for elective neck irradiation or dissection, with other studies showing similar results.[11,19,20] On the other hand, the difference between stage II and III is either due to tumor size or positive lymph nodes, two risk factors as mentioned above.[7,17] Based on those two premises we decide to analyze our data stratifying according to histopathological risk (low versus high) and stage (I-II versus III-IV) and then interpret through another stratification (neck dissection versus no neck dissection).

Our study found no cases of recurrences among low histopathological risk patients not submitted to neck dissection. Those results were in line with the literature as it shows that the highest crude rates of nodal relapse among those treated without elective neck irradiation were found in cN0 patients with undifferentiated carcinoma (50%), adenocarcinoma (34%), and mucoepidermoid carcinoma (29%), all of them considered high risk histologies.[21] This possibly reveals the futility of neck irradiation in low histopathological risk patients, even in those who did not underwent neck dissection. In high histopathological risk patients there were no differences, in DFS or OS, between groups according to neck dissection. Under that circumstance, adjuvant radiotherapy could possibly be useful in patients unable to perform neck dissection. Comparing stage III and IV patients according to neck dissection we found a difference in DFS, but not in OS. Similarly, we realized the adjuvant radiotherapy potential in patients with clinical indication to perform neck surgery but not submitted. The fact that a poorer local control was identified in neck-dissected patients could be due to other adverse prognostic factors simultaneously present in those patients beside their stage. In the case of parotid tumors, neck irradiation has been shown to have a benefit in regional control similar to selective neck dissection.[9] Comparable conclusions might be extrapolated regarding other primary tumor locations.

On the overall analysis according to neck dissection the results were as expected showing a difference in DFS. This possibly results from poorer prognosis clinical features which led to perform neck dissection in first place.

Present studies contain some caveats. A study that evaluates a treatment modality, such as radiotherapy, which by its nature selects patients with poor prognostic features incurs in a selection bias. This could influence the outcomes while we are evaluating prognostic factors. The study's retrospective design as well as its small sample size, limits results' interpretation. From a technical point of view, the range of used doses, the clinical target volumes, particularly the nodal areas treated, difficult the interpretation. Knowing that four patients with advanced stage disease were not submitted to neck irradiation, we excluded them from our survival analysis regarding stage III-IV disease. The inability to differentiate tumor progression in our study (local versus regional versus distant) is particularly important noting that local-regional control is historically a primary endpoint for radiotherapy treatments in head and neck cancer patients, however we assume that disease-free survival could be used as an important surrogate endpoint.

## CONCLUSION

Our findings regarding risk factors and their relation with survival measures are in line with previously reported literature. The possible use of adjuvant radiotherapy in patients with clinical indication to perform neck dissection but who weren't submitted to it could be an option in cases

of poor performance status, clinical contraindications or patient refusal. Further research of treatment strategies (example: selection for neck dissection with or without irradiation) should be investigated in multicentric trials if possible due to the scarcity and heterogeneity of salivary gland tumors.

## ACKNOWLEDGEMENTS

Authors would like to thank the support that was given by all of the staff from the Radiotherapy Department of the hospital centre.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Speight PM, Barrett AW. Salivary gland tumours. Oral Dis. 2002;8:229-40.
2. Spiro RH. Salivary neoplasms: Overview of a 35-year experience with 2,807 patients. Head & Neck Surgery. 1986;8:177-184.
3. Eveson JW, Auclair P, Gnepp DR, El-Naggar AK. Tumours of salivary glands. In: Barnes L, Reichart P, Evenson J, Reichart P, Sidransky D, World Health Organization Classification of Tumors: Pathology & Genetics. Lyon: IARC Press. 2005;210.
4. Armstrong JG, Harrison LB, Spiro RH, Fass DE, Strong EW. Malignant tumors of major salivary gland origin. A matched-pair analysis of the role of combined surgery and postoperative radiotherapy. Arch Otolaryngol Head Neck Surg. 1990;116:290-3.
5. Chen AM, Garcia J, Bucci MK, Quivey JM, and Eisele D W. The role of postoperative radiation therapy in carcinoma ex pleomorphic adenoma of the parotid gland. International Journal of Radiation Oncology, Biology, Physics. 2007;67:138-43.
6. North CA, Lee D-J, Piantadosi S, Zahurak M, Johns ME. Carcinoma of the major salivary glands treated by surgery or surgery plus postoperative radiotherapy. International Journal of Radiation Oncology, Biology, Physics. 1990;18:1319-326.
7. Terhaard C H J, Lubsen H, Rasch C R N, Levendag P C, Kaanders H H À M. The role of radiotherapy in the treatment of malignant salivary gland tumors. International Journal of Radiation Oncology, Biology, Physics. 2005;61:103-111.
8. Thomson D J, Slevin N J, and Mendenhall W M. Indications for Salivary Gland Radiotherapy. 2016;141-7.
9. Byrd S and Morris L G T. Neck dissection for salivary gland malignancies. Operative techniques in otolaryngology--head and neck surgery. 2018;29:157-161.
10. Kawata R, Koutetsu L, Yoshimura K, Nishikawa S, and Takenaka H. Indication for elective neck dissection for N0 carcinoma of the parotid gland: a single institution's 20-year experience. Acta Otolaryngol. 2010;130:286-92.
11. Kim Y H, Chung W K, Jeong J U, Cho I J, Yoon M S, et al. Evaluation of Prognostic Factors for the Parotid Cancer Treated With Surgery and Postoperative Radiotherapy. Clin Exp Otorhinolaryngol. 2020;13:69-76.
12. Hodapp N. [The ICRU Report 83: prescribing, recording and reporting photon-beam intensity-modulated radiation therapy (IMRT)]. Strahlenther Onkol. 2012;188:97-9.
13. Landberg T, Chavaudra J, Dobbs J, Gerard J-P, Hanks G. Report 62. Journal of the International Commission on Radiation Units and Measurements. 2016;os32:NP-NP.
14. Landberg T, Chavaudra J, Dobbs J, Hanks G, Johansson K-A. Report 50. Journal of the International Commission on Radiation Units and Measurements. 2016;os26:NP-NP.
15. Kim J Y, Lee S, Cho K J, Kim S Y, Nam S Y. Treatment results of post-operative radiotherapy in patients with salivary duct carcinoma of the major salivary glands. The British journal of radiology. 2012;85:e947-952.
16. Terhaard C H, Lubsen H, Van der Tweel I, Hilgers F J, Eijkenboom W M, et al. Salivary gland carcinoma: independent prognostic factors for locoregional control, distant metastases, and overall survival: results of the Dutch head and neck oncology cooperative group. Head Neck. 2004;26:681-92.
17. Safdieh J, Givi B, Osborn V, Lederman A, Schwartz D. Impact of Adjuvant Radiotherapy for Malignant Salivary Gland Tumors. Otolaryngol Head Neck Surg. 2017;157:988-94.
18. Flynn M B, Maguire S, Martinez S, Tesmer T. Primary squamous cell carcinoma of the parotid gland: the importance of correct histological diagnosis. Ann Surg Oncol. 1999;6:768-70.
19. Armstrong J G, Harrison L B, Thaler H T, Friedlander-Klar H, Fass D E. The indications for elective treatment of the neck in cancer of the major salivary glands. Cancer. 1992;69:615-9.
20. Régis De Brito Santos I, Kowalski L P, Cavalcante De Araujo V, Flávia Logullo A, and Magrin J. Multivariate analysis of risk factors for neck metastases in surgically treated parotid carcinomas. Arch Otolaryngol Head Neck Surg. 2001;127:56-60.
21. Chen A M, Garcia J, Lee N Y, Bucci M K, Eisele D W. Patterns of nodal relapse after surgery and postoperative radiation therapy for carcinomas of the major and minor salivary glands: what is the role of elective neck irradiation? Int J Radiat Oncol Biol Phys. 2007;67:988-94.

**Cite this article as:** Florindo A, Saraiva S, Tomás TC, Abrunhosa-Branquinho A, Santos J, Mendonça V et al. Adjuvant radiotherapy in the management of major salivary gland tumors: retrospective analysis. Int J Adv Med 2021;8:341-7.