## Original Research Article

# Treatment times in locally advanced oropharyngeal cancer: evolution from 2011 to 2016 in a Portuguese Head and Neck Oncology Centre

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**ABSTRACT**

**Background:** Delays in cancer diagnosis and treatment are usually associated with patient anxiety, tumour progression and lower survival. This study aims to analyse the potential impact of rescheduling adjuvant treatments on survival outcome of patients with locally advanced oropharyngeal squamous cell cancer (OPSCC).
**Methods:** A retrospective review of medical records comprising all patients with advanced oropharyngeal cancer who underwent primary surgery and postoperative radiotherapy (PORT) in a Tertiary Oncologic Centre from 2011 to 2016 was performed.
**Results:** 63 patients with a male/female ratio of 8:1 and mean age of $57.5 \pm 9.6$ years were enrolled. Patients waited a mean of $47.2 \pm 18.2$ days from diagnosis to surgery and a median of 61 days from surgery to radiotherapy. Median radiotherapy duration was 43 days and the mean package time was $104.5 \pm 21.0$ days. Analysis of these parameters has shown decreasing intervals from 2011 to 2016, although this was only significant for duration of PORT (p=0.022). Longer time span from surgery to PORT and PORT duration were predictive of superior package times (p<0.001). Five-year overall survival and disease-free survival was 63.8% and 64.8% respectively with no statistically significant impact of waiting times on clinical outcome.
**Conclusions:** Despite presenting favourable long-term outcomes, patients with locally advanced OPSCC have experienced longer waiting times than recommended. Waiting times were not prognostic factors in this condition, although efforts to reduce it might provide superior quality of care. Future studies assessing the factors involved in treatment delays might provide means to offer timely treatments.

**Keywords:** Oropharynx, Radiotherapy, Surgery, Treatment time, Survival, Quality of care

## INTRODUCTION

According to the Medicine Committee on Quality of Healthcare in America timeliness of treatments is an important indicator of care quality.[1] Several organizations have been addressing the quality of cancer care and it is well documented that delays in diagnosis and treatment result in patient anxiety and decreased quality of life.[2-3] The fact that advanced head and neck cancers usually require multimodality treatments may, by itself, cause delays in adjuvant therapies, raising the concern about

waiting times.[4] Deferred treatments have also been associated with stage progression and poorer loco-regional control and overall survival.[5-8] Nevertheless, the impact of timeliness of treatments is not fully understood and there is no consistent correlation between waiting times and clinical outcome.[9,10] Several studies have shown that increasing duration of radiotherapy was associated with lower loco-regional control and survival but the impact of other treatment times remains controversial.[9,11-14] In fact, the only available recommendation of National Comprehensive Cancer

Network (NCCN) guidelines regarding this subject is that adjuvant therapies should be initiated within 6 weeks within surgery, since it has been proven that superior time spans were related with disease recurrence.[13-18] Meanwhile, optimal treatment timings have been under profound debate and there is growing evidence that package time (period of time from surgery to the end of adjuvant therapy) is an independent prognostic factor of outcome in head and neck squamous cell carcinoma (HNSCC); conversely, it is globally accepted that it should not be superior to 100 days.[4,19-22] More recently, Tribius et al and Chen et al have documented superior loco-regional control and survival with package times inferior to 87 and 77 days, respectively.[4,23]

Despite all the concern, waiting times have been rising worldwide.[7,9,24-28] A review of the American National Cancer Database (ANCD) has shown that the median time from diagnosis to treatment have increased from 1998 to 2011, with negative impact on overall survival, especially when superior to 60 days.[26,27] Additionally, Graboyes et al studied the compliance of the NCCN guideline and concluded that only 44.3% of patients initiated PORT within 6 weeks within surgery.[28]

The aim of the present study is to perform a critical analysis of treatment times of locally advanced oropharyngeal tumours over the last six years in a Tertiary Oncologic Centre and to assess if delays in initiation/duration of treatments have significant impact on survival and loco-regional control.

## METHODS

### Patients

In this retrospective study, medical files of all patients with locally advanced OPSCC who underwent primary surgery resection and postoperative adjuvant radiotherapy from January 2011 to December 2016 at Instituto Portugues de Oncologia Francisco Gentil-Porto were reviewed. Collected data were registered in a database program, including: age, gender, cigarettes and alcohol consumption, tumour location, clinical and pathologic T and N stage, type of surgery, margin status, limpho vascular and perineural infiltration, extranodal extension, depth of tumour invasion, radiotherapy characteristics and treatment times-diagnosis to surgery, surgery to post-operative radiotherapy (PORT) initiation, PORT duration and overall treatment time (Figure 1). Patients who have not completed adjuvant treatments owing to death or recurrence of disease were excluded from the present study.

### Treatment

All patients enrolled in the study had surgery with curative intent followed by adjuvant radiotherapy or chemoradiotherapy decided in a Multidisciplinary Head and Neck Decision Board (Figure 1). PORT option was based on histological results of the surgical specimen and included pathological T stage ≥T3, or any pathological T-stage with surgical margins <5 mm, perineural or vascular infiltration; regarding neck disease, all pN ≥2 or presenting extranodal extension were also selected for adjuvant therapy. Accordingly, all tumours resected with positive margins that were not candidates for revision surgery, were considered locally advanced tumours, with the rational that patients with these tumours have worse prognosis and, therefore should benefit of adjuvant treatments, according to the NCCN guidelines.[15,29] Intensity-modulated radiotherapy was given at 2 Gy per fraction, with a total radiation dose ranging from 60-70 Gy. Patients were treated five days per week, once time per day, except on public holidays. In patients with good performance status, unless contraindicated, radiotherapy was complemented with cisplatin or carboplatin-based chemotherapy. Overall treatment time was defined as the period from diagnosis to the completion of radiotherapy and package time was defined as the period of time from surgery to the completion of radiotherapy (Figure 1).
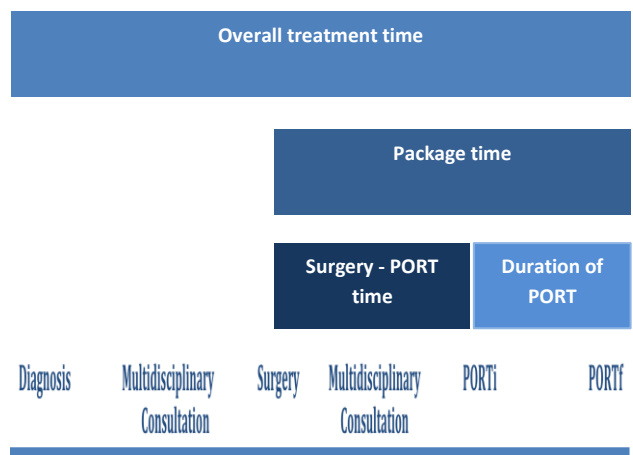


**Figure 1: Schematic diagram of workup of oropharyngeal cancer patients with the studied treatment times.**

### Assessments

The routine follow-up consisted of visits every 1-2 months in the first year, 2-3 months in the second year, 4-6 months from the third to fifth year and annually beyond. Imaging tests were not routinely requested, unless there was a clinical suspicion of tumour recurrence. For study purposes, local and regional recurrences–were grouped as loco-regional recurrences. Survival was defined as the period of time from the end of adjuvant treatments to the event or last follow-up.

### Statistical analysis

Data analyses were performed with SPSS software version 23.0 (SPSS INC. 2011, Chicago, Illinois, USA).

Differences in proportions between groups were tested with Fisher exact test and Chi-square test. Time spans were compared using ANOVA and Mann-Whitney test. A multiple linear regression was performed to assess the factors that made a significant contribution to delays in package time and overall treatment duration.

Cox hazard regression models were used to evaluate the influence of patient, tumour and treatment factors on overall survival (OS) and recurrence free survival. Actuarial curves for loco regional control and survival were estimated using Kaplan-Meier method. All statistical tests were 2-sided and significance was defined as p value<0.05.

## RESULTS

### Population characteristics

Of the 94 patients with locally advanced OPSCC treated with primary surgery between 2011 and 2016, 31 patients were excluded, due to missing data (n=7) or not having completed adjuvant radiotherapy (n=24).

**Table 1: Baseline characteristics of the population (n=63).**

| Patients characteristics | N |
|---|---|
| **Gender** | |
| Male | 56 |
| Female | 7 |
| Mean age (years) | 57.5±9.6 |
| **Smoking habits** | |
| Never smoker | 10 |
| Current smoker | 48 |
| Past smoker | 5 |
| **Tumour characteristics** | |
| **Primary site** | |
| Tonsil | 36 |
| Base of the tongue | 17 |
| Soft palate | 6 |
| Other | 4 |
| **Clinical T stage[1]** | |
| T1 | 11 |
| T2 | 31 |
| T3 | 14 |
| T4 | 7 |
| **Clinical N stage[1]** | |
| N0 | 29 |
| N1 | 19 |
| N2 | 13 |
| N3 | 2 |
| **Clinical stage (AJCC)[1]** | |
| Stage I | 2 |
| Stage II | 20 |
| Stage III | 22 |
| Stage IV | 19 |
| **Pathologic T stage** | |
| T1 | 6 |
| T2 | 26 |
| T3 | 26 |
| T4 | 5 |
| **Pathologic N stage** | |
| N0 | 14 |
| N1 | 16 |
| N2 | 30 |
| N3 | 3 |

Continued.

| Patients characteristics | N |
|---|---|
| **Pathologic stage (AJCC)** | |
| Stage I | 2 |
| Stage II | 2 |
| Stage III | 24 |
| Stage IV | 35 |
| **Margin status** | |
| Negative/close | 32 |
| Positive | 31 |
| Perineural infiltration | 35 |
| Lymphovascular infiltration | 23 |
| **Depth of invasion** | |
| <5 mm | 13 |
| >5 mm | 49 |
| Unknown | 1 |
| **Treatment characteristics** | |
| **Type of resection** | |
| Partial pharyngectomy (transoral approach) | 27 |
| Basiglossectomy | 3 |
| Basiglossectomy with supraglotic laringectomy | 3 |
| Glossopelvectomy | 20 |
| Glossopelvectomy with mandibulectomy | 6 |
| COMMANDO[2] | 4 |
| Flap reconstruction | 14 |
| **Type of neck dissection** | |
| None | 5 |
| Unilateral | 27 |
| Bilateral | 31 |
| **Treatment times, days** | |
| Diagnosis to surgery (mean) | 47.2±18.2 |
| From surgery to radiation stars (median) | 61.0 |
| Radiation treatment (median) | 43.0 |
| Package time (mean) | 104.5±21.0 |
| Time from diagnosis to the end of radiation (mean) | 150.2±30.1 |

[1]Clinical stage defined at time of diagnosis; [2]COMMANDO-Combined Mandibulectomy and Neck Dissection Operation.

Reasons for not completing adjuvant therapies included death in the postoperative period (n=5), patient refusal (n=1) and clinical contra-indications (n=18). The total number of patients enrolled in the present study was 63, distributed in the following six cohorts according to the year that they had begun treatment: 2011 (n=6), 2012 (n=13), 2013 (n=14), 2014 (n=12), 2015 (n=8) and 2016 (n=10). The average number of patients who completed treatments was 10.5±3.1 per year. There were not significant differences in patient, tumour or treatment characteristics between these groups. Study population's characteristics are summarized in Table 1. Ages ranged from 39 to 78 years (mean 57.5±9.6) and a male preponderance with a male/female ratio of 8:1 was observed.

### Time factors

Waiting time from diagnosis to surgery ranged from 5 to 112 days, with a mean 47.2±18.2 days. Postsurgical average length of hospital stay was 15.3±11.2 days and causes of prolonged stay included pneumonia (38.1%), dehiscence (4.8%), fistula (4.8%) and local infection (28.6%). Median time from surgery to PORT initiation was 61.0 days (25-75% IQR 4-69) and the median duration of PORT was 43.0 days (25-75% IQR 41-45). Package time has varied from 72 to 182, presenting an average of 104.5±21.0 days. Regarding the overall period of treatment since the diagnosis (day 0), it has ranged from 96 to 218 days, with a mean of 150.2±30.1 days. Analysis of evolution of treatment parameters (Figure 2) has shown that although the intervals have globally shortened from 2011 to 2016, this reduction was only statistically significant for duration of PORT (p=0.22).

### *Influence of patient, tumour or treatment characteristics on treatment times*

#### *Time from diagnosis to surgery*

Patients' characteristics, namely gender (p=0.42), age (p=0.32) and smoking habits (p=0.76) were not

associated with superior time intervals from diagnosis to surgery. A significant effect of tumour location on this treatment time was determined by one-way ANOVA (F (3.59)=4.01, p=0.01) and Tukey and Bonferroni post hoc tests have indicated that SCC of soft palate and uvula presented with significantly shorter mean time from diagnosis to surgery (25.3±17.1 days, p=0.03) than tumours of the tonsil (50.9±16.8 days) or base of the tongue (48.3±17.0 days). A significant association between clinical T stage and the time elapsed from diagnosis to surgery was found by one-way ANOVA (F (3.59)=3.43, p=0.02), but no significant difference was attributable to any stage on post hoc tests. Clinical n stage (p=0.129) and AJCC stage (p=0.167) have not been related with delays between diagnosis and surgery.
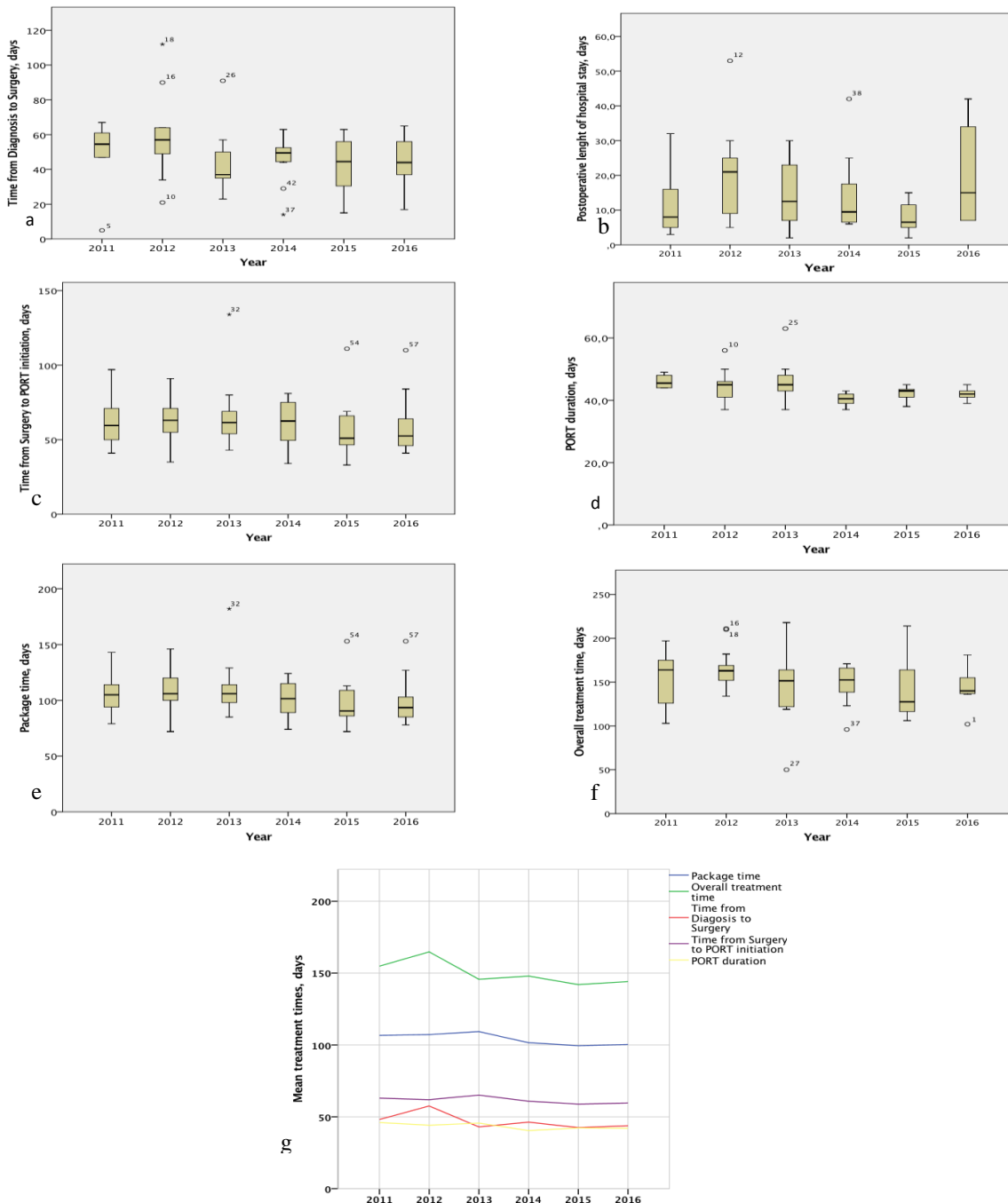


**Figure 2: Evolution of median work-up time of patients from 2011 to 2016: a) time from diagnosis to surgery; b) postoperative length of hospital stay; c) time from surgery to PORT initiation; d) PORT duration; e) package time; f) overall treatment time; g) global evolution of the measured treatment times.**

A multiple linear regression was performed and neither clinical T-stage (p=0.20) nor tumour location (p=0.77) were significant predictors of longer time span between diagnosis and surgery, after adjustment for confounding variables.

*Package time*

There was not significant effect of gender (p=0.89), age (p=0.44) or smoking habits (p=0.58) on the time interval from diagnosis to the end of adjuvant therapy. Tumour location (p=0.32), type of resection (p=0.65), flap reconstruction (p=0.65), neck dissection (p=0.32) and PORT interruptions (p=0.10) have also not caused significant variation on package time. Regarding histological results, depth of invasion (p=0.99), perineural invasion (p=0.77), lympho vascular infiltration (p= 0.50) and extranodal extension (p=0.76) have not been associated with longer package intervals. Clinical (p=0.71) and pathological T-stages (p=0.83), as well as clinical (p=0.41) and pathological AJCC (p=0.38) also had no clear effect on package time. Mean package time was significantly different among patients with different pathological nodal stage, as determined by one-way ANOVA (F (3.59)= 7.7, p<0.001). Tukey and Bonferroni post hoc tests revealed that this interval was significantly longer for N3 stage (164.0±25.5 days, p<0,001) compared to N2 (100.7±15.7 days), N1 (106.3±12.8 days) and N0 (100.7±21.6 days). Analysis of treatment metrics has revealed that time span from surgery to PORT [F (1.61)= 875.3, p<0.001, $R^2$= 0.94] and PORT duration [F (1.61)=12.8, p<0.001, $R^2$=0.17] were associated with longer package times, whereas length of postoperative hospital stay (p=0.07) was not.

**Table 2: Multiple linear regression model for package time and overall treatment time.**

| Variables | β (95% IC) | P value |
|---|---|---|
| **Package time** | | |
| Time from surgery to PORT | 1.001 | 0.000 |
| PORT duration | 0.970 | 0.000 |
| Pathological nodal stage | 0.187 | 0.707 |
| **Overall treatment time** | | |
| Tumour location | 1.425 | 0.425 |
| Package time | 0.939 | 0.002 |
| Time from surgery to PORT | 0.101 | 0.744 |
| Time from diagnosis to surgery | 1.036 | 0.000 |

A multiple linear regression was performed to identify predictors of longer package time. After correction for confounding factors, patients with superior interval time from surgery to PORT and longer PORT duration were more likely to have prolonged package times (p<0.001) (Table 2).

*Overall treatment time*

There was not any association between gender (p=0.65), age (p=0.69) or smoking habits (p=0.95) and overall treatment time. A significant effect of tumour location on this treatment time was determined by one-way ANOVA (F (3.59)=2.88, p=0.04) and Tukey and Bonferroni post hoc tests have shown that SCC of soft palate and uvula presented with significantly shorter length of treatment (122.0±26.2 days, p=0.04) than tumours of the tonsil (152.1±29.0 days) or base of the tongue (159.5±28.9 days). Regarding treatments, type of resection (p=0.20), performing flap reconstruction (p=0.70) or neck dissection (p=0.68) and the presence of PORT interruptions (p=0.37) have not caused significant variation on overall treatment time. Histological characteristics as depth of invasion (p=0.58), perineural invasion (p= 0.64), lymphovascular infiltration (p= 0.90) and extranodal extension (p=0.21) have also not been associated with longer treatments. Clinical T-stage (p=0.29), N-stage (p=0.13) and AJCC stage (p=0.36) as well as pathologic T-stage (p=0.88), N-stage (p=0.57) and AJCC stage (p=0.36) have not presented any clear effect on treatment duration. Package time [F (1.61)=54.89, p<0.001, $R^2$=0.474], time from diagnosis to surgery [F (1.61)= 31.76, p<0.001, $R^2$=0.342] and time from surgery to PORT [F (1.61)=51.31, p<0.001, $R^2$=0.457] initiation have all been associated with overall treatment time. No relation of length of postoperative hospital stay (p=0.191) or PORT duration (p=0.06) on the total duration of treatment in our department has been observed.

To assess factors associated with prolonged overall treatment time, a multiple linear regression was performed and after correcting for confounding variables, it was found that longer time intervals from diagnosis to surgery and from surgery to the end of adjuvant therapy (package time) were more likely to have prolonged overall treatment times (p<0.001) (Table 2).

*Loco regional control and survival*

Patients with locally advanced OPSCC treated with surgery and PORT presented, after a mean follow up of 35.4±38.0 months, 18 loco regional failures. Disease free survival at and 1, 3 and 5 years was 88.3% (95% CI, 87.2% - 89.3%), 74.7 % (95% CI, 73.3% - 76.2%) and 64.8% (95% CI, 63.0% - 66.6%) (Figure 3a). Sixteen patients (25.4%) have died at last follow-up and, among these, previous local (n=14), distant (n=8) or combined (n=11) failure had been documented. 1, 3 and 5-year overall survival were 88.6% (95% CI, 87.6% - 89.6%), 76.2 % (95% CI, 74.8% - 77.7%) and 63.8 % (95% CI, 61.7% - 65.9%) (Figure 3b). No significant differences at mortality (p=0.638) or recurrence (p=0.488) rates from 2011 to 2016 were observed.
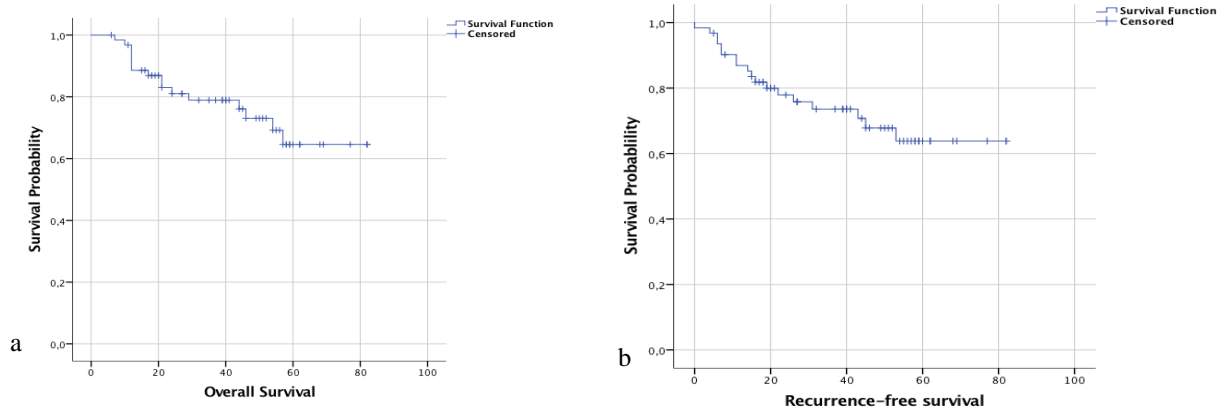
**Figure 3: Kaplan-Meyer survival analysis demonstrating (a) overall survival and (b) recurrence free-survival.**

Univariate analysis to access the impact of timeliness of treatments on patient's outcome has revealed that delays for diagnosis-surgery, surgery-PORT, RT duration and package time and over all treatment duration were not associated with increased recurrence or decreased overall survival (Table 3).

**Table 3: Cox regression for hazard ratios of mortality and recurrence.**

| Variables | N | HR (95% IC) | Overall survival HR (95% IC) |
|---|---|---|---|
| Time from diagnosis to surgery | 63 | 1.00 (0.99-1.02) | 1.01 (0.99-1.03) |
| Package time (days) | 63 | 0.98 (0.95-1.01) | 0.98 (0.95-1.01) |
| Time between surgery and PORT | 63 | 0.98 (0.95-1.01) | 0.98 (0.95-1.01) |
| Overall treatment time (days) | 63 | 0.99 (0.98-1.01) | 1.00 (0.98-1.02) |
| RT duration (days) | 63 | 0.97 (0.88-1.08) | 0.98 (0.88-1.09) |

**DISCUSSION**

*Treatment times*

Several studies have been made addressing waiting times and its impact on survival. In the present series, patients with oropharyngeal cancer have waited a mean of 47 days for surgery, thus comparing unfavourably with the literature review, in which the mean time to treatment initiation ranges from 26 to 37 days.[9-10,23,27] A major importance has always been given to the period of time from surgery to radiotherapy initiation, which should be inferior to 6 weeks according to NCCN guidelines.[15] This study has shown a median of 61 days, which is significantly superior to the 47 days reported by

Rosenthal et al and the 30 days found by Bastit et al.[22,30] More recently, Chen et al have described median waiting times of 34.5 days to PORT initiation. Regarding PORT, the median duration was 43 days, which is shorter than the previously described in similar studies with the exception of a report of 38 days.[4,9,22,23] Nonetheless, there is growing evidence in the literature that package time might be more important than other timing metrics.[13,23] Rosenthal et al have shown that a period from surgery to the end of adjuvant radiotherapy superior to 100 days was associated with increased loco-regional recurrence and decreased OS.[22] Other studies have, more recently, proposed that package time should be inferior to 87 days and 77 days, in contrast to the value traditionally recommended by Rosenthal.[4,22] In the present study, the mean package time was 104 days, which is significantly higher than the values reported in the literature, in which it ranges from 72 to 101 days.[9,22,23] The median timespan from diagnosis to the end of adjuvant therapies was 150 days, which is longer than the 136 days previously described by Fujiwara et al.[9]

*Predictors of delays*

Although a significant association between pathological N3 stage and package time was found on multivariate analysis, only time interval from surgery to PORT and PORT duration were predictors of delay in package time. A possible explanation for this might be the reduced sample of patients with N3 stage. An association between tumour location and overall treatment time was also observed, but after correction for confounding variables, the number of days from diagnosis to surgery and the package time were the only significant predictors of overall treatment time. In the literature, pT4 and adjuvant chemotherapy have been associated with prolonged package time and overall treatment time.[9] Regarding delays from surgery to PORT initiation, the only variable that have been related, in our patients, was the postoperative length of hospital stay (p=0.03), in contrast to the previous study of Fujiwara and colleagues that had identified age and comorbidities as predictors of prolonged diagnosis-to-surgery intervals.[9] It is noteworthy to mention that clinical staging was

performed at the moment of diagnosis and during the waiting period, an upstaging might have occurred with more extensive surgery, longer hospital stay and deferment of adjuvant treatments.

### Impact of waiting times on patients' outcome

Despite the fact that waiting times, with the exception of duration of PORT, have been longer than the previously described in the literature, outcome measures, namely overall survival and recurrence free survival, were not generally worse in the present series. Conversely, regarding long-term results, patients have presented a 5-year OS of 63.8%, similar to the literature, in which it ranges from 33 to 77% and a 5-year DFS of 64.9% comparable to previous reports.[9,10,30]

Waiting times were not predictors of overall survival or local control in this study. Impact of waiting times on patient outcome is highly controversial in the literature. Bastit el al have studied the influence of time from surgery to that PORT and have not found a significant influence on survival or loco-regional recurrence in concordance with previous authors.[12,30-32] Nonetheless, several authors have argued that delays in starting radiation therapy was associated with decreased OS and DFS.[10,22,33] The rational for this was that the repopulation of cancer cell that might occur in the period between surgery and radiotherapy, that was detrimental for tumour control. Duration of PORT superior to 45 days has been associated with poorer recurrence free survival and OS.[9,11,22,33,34] Accordingly, these results suggest that offering PORT with the recommended duration might be an important factor on patients' outcome. Recently, Chen et al have found that delays from diagnosis to surgery had not impact on patient outcome, that the period from surgery to PORT was associated with loco-regional control, but not with survival and, finally, that package time was associated with decreased survival and increased recurrence.[23] These findings have raised doubts whether the package time might be a potential quality metric, which have already been suggested by a previous study of Tribius et al that had found superior OS and DFS with package times inferior to 87 days.[4,23]

### Assessment of timeliness of treatments

Given the proven impact of the waiting times on patient outcome, several studies have been enrolled in order to evaluate the timeliness of treatment in HNSCC. van Harten et al designed a study to assess if the Dutch Head and Neck Society Guideline that recommends treatment initiation within 30 days of diagnosis was being achieved and found that the median period from diagnosis to treatment was 37 days and that only 36% of patients were treated within the recommended period.[10] Nevertheless, they could not find survival differences with the 30 days cut-off. Fujiwara et al reviewed the American National Cancer Data (ANCD) from 1998 to 2001 to understand the national trends in waiting times and have observed that only 31.5% of patients had received adjuvant radiotherapy in less than 6 weeks after surgery, having, however, noticed that there was not any significant decrease in OS comparing to patients who had received PORT earlier. Similarly, Graboyes et al reviewed the ANCD from 2006 to 2014 with the purpose of evaluating the adherence to NCCN guideline, having observed that only 45.3% patients had received adjuvant therapy within 6 weeks of surgery and that a progressive increase in the interval between surgery and PORT had occurred over the studied period.[28] Variables correlated with increasing waiting times included low socioeconomic status, poor performance status, increased postoperative length of stay, unplanned hospital readmissions and receiving IMRT as radiation modality. Failure to achieve NCCN guideline had previously been described.[34,35] Murphy et al have also reported an upward trend in the time to treatment initiation for all HNSSC in USA.[26] They argued that this evolution might be due to the growing number of pre-treatment investigations, complexity of treatments and transitions in care. Recently, it has been advocated that the period from diagnosis to treatment is an independent predictor of mortality and that delays beyond the recommended 46 to 52 days represent a public health issue.[27]

### Trends in waiting times

Generally, waiting times in this Centre have been decreasing from 2011 to 2016, in contrast to what have been documented worldwide.[7,9,24-26,28] Longer waiting times appear to be the reflexion of growing referral to Cancer Centres and increasing complexity of diagnostic and treatment modalities.[27,35-37] Diagnostic imaging, adjuvant chemotherapy and extensive cancer resections with complex reconstructions have already been identified as predictors of longer treatment times.[26] The pursuit for a better quality of care might, indeed, be the underlying cause of longer times for treatment initiation, which is controversial, given the fact that failing the timeliness of cancer care is considered a manifestation of low quality of health care.[1,27] It is noteworthy to mention that referral to specialized centres might not be detrimental as the inherent longer waiting times are overcome by the improved survival rates, as it has been documented in the present study.[10,27]

Faced with the increasing waiting times on cancer care, several countries in Europe have introduced fast tracking programs in order to reduce treatment delays. Lyhne et al studied the impact of the introduction of the Danish fast track strategy and observed a reduction in the median time for treatment from 47 days to 25 days.[38] Conversely, Storm et al found a significant increase in 1-year survival since this measure was taken.[39] A similar program was adopted in Netherlands with a documented 20% reduction in waiting time for treatment.[40] It is noteworthy to mention that several variables may affect survival and, to date, it is not fully understood how much improvement

in outcome is attributable to the decrease in waiting times achieved with these programs.[38]

### Future perspectives

To the authors' knowledge, this was the first national study of waiting times for oropharyngeal cancer. Despite presenting comparable survival and loco-regional control rates to the literature, waiting times, with the exception of radiation duration, have been significantly longer. Authors believe that the main reason for delays from diagnosis to surgery is the lack of human and physical resources. Other potential factors involved in deferment of treatments might be medical and surgical wound complications, need for extensive dental work before radiation and hesitation in accepting adjuvant therapies.

Faced with these results, new strategies and resources are required to provide timely treatment to these patients. A fast tracking system, in which diagnostic and preparatory procedures were made simultaneously to reduce waiting times, might be a solution, although the substantial financial resources required for its implementation and maintenance makes this idea somehow obsolete. It seems reasonable, however, that efforts to reduce prolonged postoperative length of stay and to help patients understand the importance of timely initiation of adjuvant therapies, avoiding hesitations that might postpone treatments shall be made.

### Limitations

Despite the judicious selection of patients with oropharyngeal carcinoma treated with surgery and adjuvant radiotherapy to provide a homogeneous population, this was a single-institution retrospective study with an inherent selection bias given the size of sample. Possible confounding factors were the baseline characteristics of the patients (comorbidities and performance status) and tumours (e.g., more advanced tumours requiring more complex surgery) that may have been associated with wound or medical complications, which may by themselves have predisposed to longer waiting times. Additionally, psychological and socioeconomic status may have also been associated with treatment delays and these were not addressed in this review. At last, it is noteworthy to mention that given the fact that the majority of patients were admitted in this Centre after referral from other institutions, diagnosis date might lack some accuracy with an impact on outcome that has not been measured.

### CONCLUSION

The present study has shown that, in contrast to the international trends, waiting times for surgery and adjuvant therapies have been slowly decreasing in this Tertiary Oncologic Centre, although remaining longer than recommended. Delays in treatment initiation were not negative prognostic factors for patients with locally

advanced OPSCC and this study has demonstrated favourable long-term outcomes, supporting the theory that specialized Head and Neck Oncology Centres provide better survival for patients, despite the longer waiting times. Nevertheless, timeliness of treatments is a well-established indicator of quality of care and the present study suggests that new measures shall be taken in order to provide timely diagnosis and treatments to the patients. Future prospective studies might provide more information about the factors involved in treatment delays allowing the implementation of accurate measures targeted to risk groups.

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