Egyptian Journal of Ear, Nose, Throat and Allied Sciences (2013) **14**, 175–183

Egyptian Society of Ear, Nose, Throat and Allied Sciences

Egyptian Journal of Ear, Nose, Throat and Allied Sciences

www.ejentas.com

ORIGINAL ARTICLE

Concurrent radiochemotherapy versus surgery followed by radiotherapy for hypopharyngeal carcinoma: A single-center study

Mohamed S. Taha [a,*], Tamer S. Sobhy [a], Ossama M. Hamid [a], Lobna M. Alfeky [a], Samer A. Ebrahim [a], Hany M.A. Alaziz [b], Sherif A.A. Alfatah [b], Aly M. Azmy [a,b]

[a] *Otorhinolaryngology Head and Neck Surgery, Ain Shams University Hospitals, Egypt*
[b] *Radiotherapy and Medical Oncology Department, Ain Shams University Hospitals, Egypt*

Received 16 May 2013; accepted 16 July 2013
Available online 6 August 2013

KEYWORDS

Hypopharyngael carcinoma;
Surgery;
Concurrent radiochemotherapy;
Treatment outcomes

Abstract *Background:* Hypopharyngeal cancer is a rare disease representing about 0.5% of all human malignancies and constituting only 3–5% of all head and neck cancer. Concurrent radiochemotherapy has been recommended as a standard of care in patients with locally advanced squamous cell head and neck carcinomas. There were very few reports about these tumors arising from North Africa.

Objecttive: This work was a retrospective study at the Ain Shams University hospitals comparing induction chemotherapy and concomitant radiochemotherapy to surgery followed by radiotherapy as regards over all survival.

Methods: This study included 49 patients with hypopharyngeal carcinoma, twenty-three (46.93%) were treated surgically. Surgical excision of the tumor was by pharyngo-laryngo-esophagectomy, except for 2 patients treated by conservative surgery. Postoperative radiotherapy was given to all patients. Twenty sex patients (53.07%) were treated by induction chemotherapy and concomitant radiochemotherapy.

Results: The mean age was 52.6 years (range 25–82). In the present study, females (55.1%) dominated males (44.9%).The most commonly involved subsite, in this study, was the postcricoid area (31 patients = 63.3%), followed by the pyriform sinus (16 patients = 32.6%), while the posterior pharyngael wall was the site of origin in only two patients (4.1%). According to the AJCC-

* Corresponding author. Address: 33B Ben Sender Street, Saray Alkobba, Cairo, Egypt. Tel.: +20 1154886.
E-mail addresses: mshehata90@yahoo.com, mshtaha@gmail.com (M.S. Taha).

Peer review under responsibility of Egyptian Society of Ear, Nose, Throat and Allied Sciences.

ELSEVIER Production and hosting by Elsevier

2090-0740 © 2013 Production and hosting by Elsevier B.V. on behalf of Egyptian Society of Ear, Nose, Throat and Allied Sciences.
http://dx.doi.org/10.1016/j.ejenta.2013.07.001

TNM staging system, 40 patients (81.6%) were advanced stages III and IV, while only 9 patients (18.4%) had an early presentation as stages I and II. Cox proportional-hazard regression was used to compare survival in the two study groups. There was no statistically significant difference in the failure function (death) between patients treated with concomitant radiochemotherapy or surgery followed by radiotherapy after adjusting for the age category, tumor grade, T stage and N stage (proportional hazard, 1.114; 95% CI, 0.574 to 2.163; *P*, 0.751).Of the variables included in the model, only N1 stage was an independent predictor for the hazard of death after adjusting for the treatment group, age category, tumor grade and T stage (proportional hazard, 2.321; 95% CI, 1.073–5.022; *P*, 0.033). The model had a −2 log likelihood (likelihood ratio statistic, LRS) of 277.316, which was not statistically significant (*P*, 0.0501) indicating adequate fit of the full model.

Conclusion: Postcricoid carcinoma comprises the majority of hypopharyngeal tumors in Egypt. Females are more commonly affected by these tumors, especially postcricoid carcinoma. There was no survival difference between the intended therapy for organ preservation and radical surgery groups. Patients who received concurrent radiochemotherapy had a better chance of survival with a preserved larynx compared with patients who underwent surgery.

1. Introduction

Hypopharyneal carcinoma is rare with an incidence of 1 in 100,000 in UK. Sweden has an excellent national cancer database and reported just over 2000 cases of this cancer over a period of 30 years with a tumor specific five year survival of 13%.[1] In the UK post cricoid carcinoma makes up around 40%, the pyriform fossa accounts for between half and two thirds with less than 10% originating on the posterior pharyngeal wall.[2,3] The hypopharyngeal carcinoma has the poorest prognosis of any head and neck carcinoma.[2] The etiology of hypopharyngeal tumors has not been extensively studied.[4,5] The most important risk factor is the excessive consumption of alcohol.[6] The risk of combined high alcohol intake and smoking was multiplicative.[7] Patients diagnosed with hypopharyngeal carcinoma are typically men aged 55–70 years. One exception is an increased incidence of postcricoid carcinoma (PCC) in women aged 30–50 years with Plummer Vinson or Paterson–Kelly syndrome.[8,9] Currently in the United States, because of the reduced incidence of the Plummer–Vinson syndrome, postcricoid carcinoma is more common in men.

Nearly all tumors of the hypopharynx are malignant and most are squamous cell carcinoma, with 70% moderately or well differentiated tumors.[10] The cardinal symptoms and signs are dysphagia, hoarseness of voice, sore throat, otalgia and weight loss with or without a lump in the neck. Hypopharyngeal carcinoma often presents at an advanced stage, as the hypopharynx is a silent area allowing tumors to attain advanced stages before symptoms occur. Other causes contributing to its poor prognosis are: tendency for submucosal spread, early metastasis to the regional lymph nodes and tendency to direct extension to adjacent structures in the neck.[8,11,12]

Hypopharyngeal carcinoma may be treated by surgery or an organ preservation protocol. Choice of resection and reconstruction technique will depend on patient and surgeon's preference and expertise, tumor size and location within the hypopharynx. External beam radiotherapy with concurrent chemotherapy, rather than radiotherapy alone improves the laryngeal preservation rate in patients with resectable disease and results in a survival benefit for those with resectable and non-resectable disease.[13,14] Survival is comparable to laryngopharyngectomy and postoperative radiotherapy.[15]

The aim of this study was to compare the results of definitive concurrent radiochemotherapy (CRCT) and surgery followed by radiotherapy regarding overall survival of patients with hyopharyngeal carcinoma.

2. Patients and methods

This is a retrospective study of all patients with hypopharyngeal carcinoma, who presented to the Ain Shams University hospitals, Cairo, Egypt, in the period between October 2005 to April 2012. The records of these patients were reviewed to collect the demographic data, special habits, presenting symptoms and signs. Endoscopic data, biopsy results and available imaging were also collected. The study was approved by the Institutional Research Ethics Board of the Ain Shams University.

The patients were then divided into two groups: group I or surgical group with post operative radiotherapy and group II or organ preservation protocol group receiving (CRCT). The surgical details and complications were reviewed as well as the post-operative radiotherapy sessions received in group I. In group II, the details of chemotherapy regimen and radiotherapy sessions were collected. The follow-up record regarding survival was compared.

3. Statistical methods

Statistical analysis was done on a personal computer using MedCalc® version 12.2.1.0 statistical package (MedCalc® Software, Mariakerke, Belgium).

Normality of quantitative data distribution was tested using the Shapiro–Wilk goodness-of-fit test. Normally distributed quantitative data were presented as mean (standard deviation) and between-group differences were compared parametrically using the independent samples Student's t test. Qualitative data were presented as ratio or number (percentage) and differences between the two groups were compared using the Pearson's chi square test with the application of Fisher's exact test when appropriate.

Cox proportional-hazard regression was used to compare survival in the two study groups. Besides the treatment group, other variables expected to influence survival were included in the model to adjust for their effect on the failure function of interest (i.e., death). These covariates included age, tumor grade (differentiation), T stage, and N stage. Since our study included 49 failure events (i.e., deaths), we included only five predictors in the regression model in line with the rule that to avoid over fitting of the model, only one predictor should be included in a survival model for at least 10 failure events.[16] All reported P values are two tailed. $P < 0.05$ is considered statistically significant.

4. Results

A total of 69 patients' records with hypopharyngeal carcinoma were found. Only 49 patients were included in this study, as the remaining 20 patients did not complete their treatment in our center or were lost for follow up. Females were more common than males with a male to female ratio of 3:4. Twenty-four patients were smokers, all were males except for two females. No single patient was an alcohol consumer (Table 1).

All patients were pathologically diagnosed as squamous cell carcinoma, 57.1% had moderately differentiated, and 32.7% had well differentiated, while only 10.2% had poorly differentiated carcinoma.

The most commonly involved subsite, in this study, was the postcricoid area (31 patients = 63.3%), followed by the pyriform sinus (16 patients = 32.6%), while the posterior pharyngeal wall was the site of origin in only two patients (4.1%) (Table 2). Females comprised 21 (67.7%) patients with postcricoid carcinoma, while males were only 10 (32.3%), Pyriform fossa tumor was found in 10 (62.5%) males and in 6 (37.5%) females (Table 2). The age ranged from 25 to 82 years (mean = 52.6 years). The incidence of this tumor was found

Table 1 Demographic data.

Variable	Surgery group (n = 23)	Radiochemotherapy group (n = 26)	P value
Age (yr)	48.5 (10.4)	56.5 (16.7)	0.047
Male/Female	10/13	12/14	0.851
Smoker/Non-Smoker	11/12	13/13	0.879

Data are presented as mean (SD) or ratio.

Table 2 Tumor pathology data.

Variable	Surgery group (n = 23)	Radiochemotherapy group (n = 26)	P value
Site of tumor			0.064
Postcricoid	11 (47.8%)	20 (76.9%)	
Piriform fossa	11 (47.8%)	5 (19.2%)	
Posterior pharyngeal wall	1 (4.3%)	1 (3.8%)	
T stage			0.062
T1	1 (4.3%)	3 (11.5%)	
T2	7 (30.4%)	5 (19.2%)	
T3	12 (52.2%)	7 (26.9%)	
T4	3 (13%)	11 (42.3%)	
N stage			0.743
N0	10 (43.5%)	14 (53.8%)	
N1	9 (39.1%)	8 (30.8%)	
N2	4 (17.4%)	4 (15.4%)	
AJCC staging			0.419
Stage I	1 (4.3%)	2 (7.7%)	
Stage II	3 (13%)	3 (11.5%)	
Stage III	13 (56.5%)	9 (34.6%)	
Stage IV	6 (26.1%)	12 (46.2%)	
Tumor grade			0.153
Grade 1 (well differentiated)	5 (21.7%)	11 (42.3%)	
Grade 2 (moderately differentiated)	14 (60.9%)	14 (53.8%)	
Grade 3 (poorly differentiated)	4 (17.4%)	1 (3.8%)	

Data are presented as number (%).

to be 28.6% in those below 40 years and 71.4% in those above 40 years.

According to AJCC-TNM staging system,[17] 33 (67.4%) patients were staged T3 and T4, while 16 (32.6%) patients presented as stages T1 and T2. Twenty-five patients (51%) had clinically palpable lymph nodes (17 N1 & 8 N2), while 24 patients (49%) had no clinically palpable lymph nodes at the time of diagnosis.

Forty patients (81.6%) had advanced stages III and IV, while only 9 patients (18.4%) had an early presentation as stages I and II.

The two patients with posterior pharyngeal wall tumor, presented as T4 N0 and T3N2 with a final stage IV. No patient of the 49 included in this series had distant metastasis at the time of diagnosis.

Group I included 23 (46.9%) patients .Ten patients (43.4%) were males and 13 (56.6%) were females (Mean age = 48.5 ± 10.4). Post-cricoid carcinoma (PCC) was diagnosed in 11 (47.8%) patients, while 11 (47.8%) had pyriform fossa tumor, and one (4.3%) patient had posterior pharyngeal wall tumor.

Five (21.7%) patients had well differentiated tumor, 14 (60.9%) had moderately differentiated tumor and 4 (17.4%) had poorly differentiated tumor (Table 2). 8 (34.7%) patients had early T1 and T2 tumor, while 15 (65.3%) had late T3 and T4 stages. 10 (43.5%) patients were N0, 9 (39.1%) were N1 and 4 (17.4%) were N2. The final staging in this group was one patient (4.3%) with stage I, 3 patients (13%) with stage II, 13 patients (56.5%) with stage III, and 6 patients (26.1%) with stage IV.

Total pharyngo-laryngo-esophagectomy was done in 21 cases with subsequent reconstruction by mobilization of the stomach through the posterior mediastinum to allow stomach pull-up for pharyngo-gastric anastomosis (Fig. 1). Two patients with early stage had total laryngectomy and partial pharyngectomy with primary pharyngeal repair. Neck dissection was done in 13 patients with clinically positive nodes.

Figure 1 Layered anastomosis between the stomach and upper pharyngeal mucosa.

Figure 2 Post-operative dye study with passage of contrast without leak.

All patients were admitted to the ICU postoperatively for three days. Patients were allowed to swallow after a gastrographin swallow- done to them 10 days to 2 weeks postoperatively showing no anastomotic leak (Fig. 2). Operative mortality occurred only in one patient (4.3%) who died on the table due to an unrepairable posterior tracheal tear during mediastinal dissection.

Post-operative unilateral pleural effusion occurred in 5 (21.6%) patients but only two of them required the insertion of chest drains. Anastomotic leak high in the neck, occurred in two cases (8.7%), and settled spontaneously by conservative treatment and compression without further complications. Two patients developed neck hematoma and one of them necessitated surgical evacuation. Two patients developed dysphagia after 3 months of starting oral feeding and required the dilatation of a stricture at the pharyngo-gastric anastomosis. Discomfort due to reflux of gastric content was noted in 12 (52%) patients during follow-up .Chest infection occurred in 8 (34.8%) patients and resolved after proper antibiotic treatment. Electrolytes disturbance in the form of resistant hypokalaemia for 3 days, was noted in 6 (26%) patients and was corrected before the patients were discharged from the hospital. Two patients developed severe depression that required psychotherapy sessions and anti-depressive medications.

Postoperative (2–4 weeks) radiotherapy was given to all 23 patients in a dose of 60–66 Gy fractionated as 200 cGy/day for 5 days/week along 6–7 weeks. Spinal cord shield was used after 50 Gy.

Group II included 26 patients who received CRCT. Twelve patients (46.1%) were males and 14 (53.9%) were females (mean age = 56.5 ± 16.7). Twenty (76.9%) of them were diagnosed as PCC, 5 (19.2%) had pyriform fossa tumor and 1 patient (3.8%) had posterior pharyngeal wall tumor. Eleven (42.3%) patients had well differentiated tumor, 14 (53.8%) had moderately differentiated tumor and 1 (3.8%) had poorly differentiated tumor (Table 2). 8 (30.7%) patients had early T1 &

Table 3 Cox proportional hazard model.

Covariate	*b*	SE	Wald	*P* value	Exp(b)	95% CI of Exp(b)	
						lower bound	Upper bound
Treatment with radiochemotherapy	0.108	0.340	0.101	0.751	1.114	0.574	2.163
Age > 40 years	0.159	0.410	0.150	0.698	1.173	0.527	2.610
Differentiation							
Grade 2 tumor	-0.031	0.337	0.008	0.927	0.970	0.502	1.872
Grade 3 tumor	-0.029	0.607	0.002	0.962	0.972	0.298	3.171
T stage							
T2 stage	-0.827	0.660	1.568	0.211	0.438	0.121	1.585
T3 stage	-0.649	0.610	1.132	0.287	0.523	0.159	1.717
T4 stage	0.552	0.641	0.742	0.389	1.736	0.498	6.055
N stage							
N1 stage	0.842	0.396	4.525	0.033	2.321	1.073	5.022
N2 stage	0.835	0.504	2.740	0.098	2.304	0.862	6.157
Overall model fit							
Null model -2 Log Likelihood	294.231						
Full model -2 Log Likelihood	277.316						
Chi-square	16.915						
DF	9						
P value	0.0501						

95% CI, 95% confidence interval; b, regression coefficient; DF, degrees of freedom; Exp(b), proportional hazard; SE, standard error; Wald, Wald Chi-square statistic.

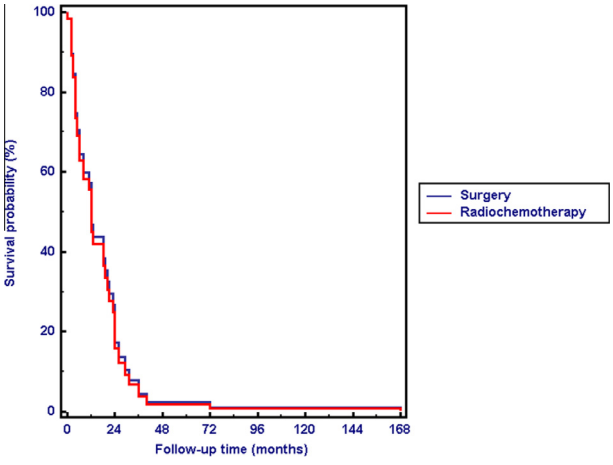

Figure 3 Survival curves produced by Cox proportional hazard regression. Distinct curves are plotted for the two treatment groups.

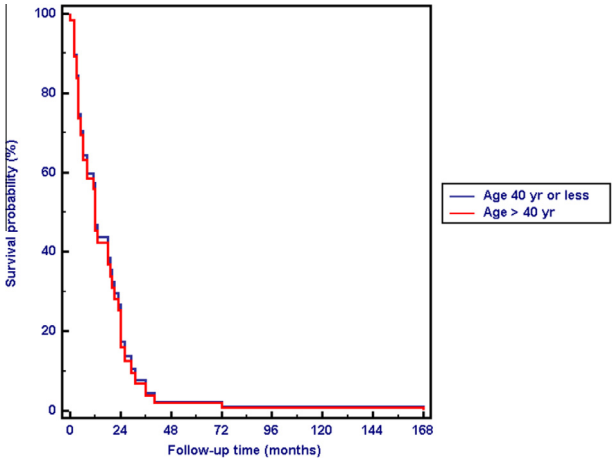

Figure 4 Survival curves produced by Cox proportional hazard regression. Distinct curves are plotted for the age categories. No statistically significant difference in overall survival between patients aged more than 40 years and those aged 40 years or less after adjusting for the treatment group, tumor grade, T stage and N stage (proportional hazard, 1.173; 95% CI, 0.527 to 2.61; P, 0.698).

T2 tumor while 18 (69.3%) had late T3& T4 tumor. 14 (53.8%) patients were N0, 8 (30.8%) were N1 and 4 (15.4%) were N2. This group included 2 patients (7.7%) with stage I, 3 patients (11.5%) with stage II, 9 patients (34.6%) with stage III and 12 patients (46.2%) with stage IV.

Prior to definitive chemoradiotherapy (CRT) comprehensive evaluation was done for all patients. This included speech and swallowing evaluation, comprehensive dental evaluation and cleaning, blood laboratory investigations, as well as evaluation of the nutritional status and its stabilization. Chemotherapy was given in the form of cisplatin 80 mg/m^2 in day 1 as a short infusion and 5- fluorouracil 1000 mg/m^2 daily from day 1 to 4 as a continuous infusion after appropriate hydration and preparation. This course was repeated after 4 weeks and radiotherapy initiated after 2 weeks of the 2nd cycle. Concurrent weekly cisplatin 25 mg/m^2 was administered during the course of irradiation.

All patients were treated by conventional fractionated course of radiotherapy (2D) over 6–7 weeks, with treatment delivered once per day, 5 days per week, with 2 Gy daily fractions. Treatment was given using 6 MV linear accelerator photon beam while 9 MeV electron beam was used only to boost the

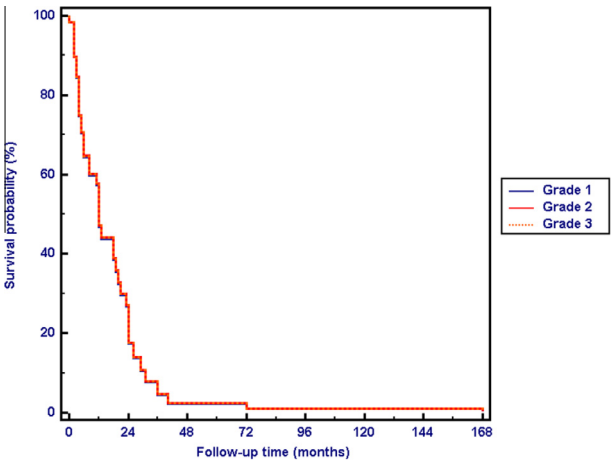

Figure 5 Survival curves produced by Cox proportional hazard regression. Distinct curves are plotted for the different tumor grades. No statistically significant difference in overall survival among patients with different tumor grades after adjusting for the treatment group, age category, T stage and N stage.

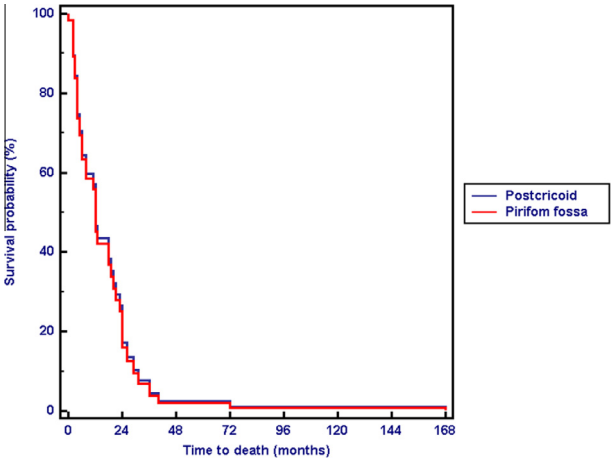

Figure 6 Survival curves produced by Cox proportional hazard regression. Distinct curves are plotted for the different tumor sites. No statistically significant difference was seen in overall survival among patients with different sites after adjusting for the treatment group, age category, tumor grade and N stage.

clinically gross lymph nodes. Due to the high likelihood of subclinical nodal metastases, even in the clinically N0 neck, all patients received comprehensive radiation to encompass nodal regions from the skull base to clavicle. Two laterally opposed portals encompassing the primary tumor and upper neck lymphatics as well as one anterior lower neck field were used for most of the patients while two lateral portals down to the clavicle were used only in patients in whom the shoulder permits these fields. Treatment involves a shrinking field technique at 46 Gy to exclude the cervical part of the spinal cord, as well as final mucosal field reduction after 54–60 Gy and posterior neck boosting with electrons to complete the nodal dosing without excessive dose to the spinal cord. The superior border of the lateral fields usually included base of skull, while the lower border was at the lower aspect of the cricoid cartilage unless extensive caudal tumor extension. The posterior border is placed behind vertebral spinous processes (or further if required to cover metastatic cervical lymph nodes) while the anterior border flashes the skin at the level of the thyroid cartilage .Gross nodal disease received 66–70 Gy while prophylactic lymphatic irradiation was limited to 50 Gy. All the patients who completed their course of treatment were followed clinically every two weeks and re-evaluated after 6–8 weeks by CT scan as well as endoscopic assessment and biopsy. All patients (100%) developed mucositis, 65% of them were WHO grade 1–2, while 35% were WHO grade 3–4. Management strategy included oral hygiene and optimal pain control. Seventeen (65.7%) patients developed transient dysphagia mostly due to post–radiotherapy edema. Four (15.3%) patients required multiple dilatations due to stenosis of the post cricoid region and cervical esophagus.

The endpoint of our study was the overall survival rate .The duration of survival was defined as the time from the first date of treatment to the date of the event, which was death for the overall survival rate. The follow up of both groups ranged from 2 to 84 months.

In group I, 9 (39.2%) patients survived for less than 6 months, 4 (17.4%) patients survived for less than 12 months, 5 (21.7%) patients survived for less than 24 months and 5 (21.7%) survived for more than 24 months (details of over all survival of group 1).

Meanwhile, in group II, 11(42.3%) patients survived for less than 6 months, 5 (19.2%) patients survived for less than 12 months, 6 (23%) patients survived for less than 24 months and 4 (15.5%) patients survived for more than 24 months (details of over all survival of group 2).

Cox proportional-hazard regression was used to compare survival in the study groups (Table 3). There was no statistically significant difference in overall survival between patients treated with concurrent radiochemotherapy or surgery after adjusting for the age category, tumor grade, T stage and N stage (proportional hazard, 1.114; 95% CI, 0.574–2.163; $p = 0.751$) (Fig. 3).

At the same time there was no statistically significant difference in overall survival in both groups between patients aged more than 40 years and those aged 40 years or less after adjusting for the treatment group, tumor grade, T stage and N stage (proportional hazard, 1.173; 95% CI, 0.527–2.61; *P*, 0.698) (Fig. 4).

Regarding tumor differentiation, there is no statistically significant difference in survival among patients with different tumor grades, and tumor site in both groups after adjusting other factors in both study groups (Figs. 5 and 6).

There was no statistically significant difference in overall survival among patients in both groups with different T stages after adjusting for the treatment group, age category, tumor grade and N stage (Fig. 7).

The Cox model yields that the N1 stage was the only independent predictor for the hazard of death after adjusting for the treatment group, age category, tumor grade and T stage (proportional hazard, 2.321; 95% CI, 1.073–5.022; *P*, 0.033) (Fig. 8).

The model had $a-2$ log likelihood (likelihood ratio statistic, LRS) of 277.316, which was not statistically significant ($p = 0.0501$) indicating adequate fit of the full model.

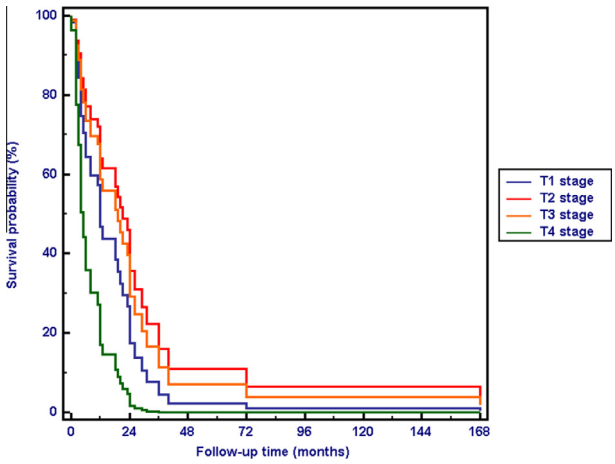

Figure 7 Survival curves produced by Cox proportional hazard regression. Distinct curves are plotted for the different T stages. No statistically significant difference was seen in overall survival among patients in both groups with different T stages after adjusting for the treatment group, age category, tumor grade and N stage.

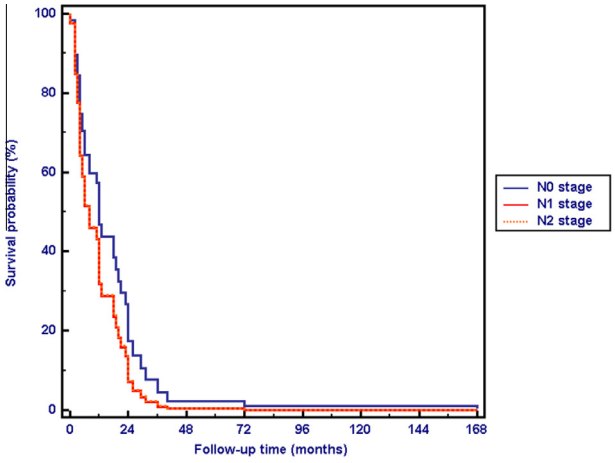

Figure 8 Survival curves produced by Cox proportional hazard regression. Distinct curves are plotted for the different N stages. N1 stage was the only independent predictor for the hazard of death after adjusting for the treatment group, age category, tumor grade and T stage (proportional hazard, 2.321; 95% CI, 1.073–5.022; *P*, 0.033).

5. Discussion

Hypopharyngeal carcinoma has the worst prognosis among all head and neck tumors. Patients tend to present with locoregionally advanced disease, with one-half of patients having nodal metastasis at diagnosis.[18]

Almost 81.6% of our patients presented with stage III and IV disease and 51% had lymph node metastases, which contributed largely to the advanced stage of the disease. The overall survival rates of these tumors vary from 10 to 60%.[19–21] The conventional treatment for locally advanced but resectable head and neck cancers has been surgery with post-operative adjuvant therapy. A huge progress in non-surgical organ preservation treatment for all head and neck cancer has been done in the last two decades, demonstrating that laryngeal preservation by different CRT protocols is a safe alternative for patients with T2–T4 tumors. Based on these encouraging results, CRCT as the definite treatment for advanced head and neck cancer has been studied in the past 15 years, including cancers arising from the hypopharynx.[22]

The ideal treatment strategy for the management of hypopharyngeal cancer is still unclear and the management of locally advanced disease, however, varies by institution.

In the literature only few studies are available to compare different treatment protocols in the treatment of specific subsites such as the hypopharynx. This study was intended to compare the overall survival in patients with hypopharyngeal cancer treated by CRCT versus surgery followed by radiotherapy.

The incidence of this tumor in the present study was found to be only 28.6% in those below 40 years in comparison to 71.4% in those above 40 years. This result agrees with most of the reports.[12] However there were reports that showed that the incidence of this tumor was found to be nearly the same in those below 40 years, and those above the same age.[23,24] Saleh et al.,[25] study of Upper Egypt showed two peaks of age among their patients: 13–35 years and 56–60 years.

Females were about 55.1% of the patients, while males were only 44.9%. Postcricoid carcinoma remains the only squamous head and neck cancer that is more common in women.[12,26] Most of patients in the present study were postcricoid carcinomas (63.4%), and so the female predominance can easily be understood.

Different studies, however, reported a male dominance in all cases of hypopharyngeal carcinoma.[27–29] This can be explained by the fact that, most of the studies reporting males to be more affected, have the pyriform sinus as the main subsite of affection with rare cases from the postcricoid area.

None of our patients was an alcohol consumer, a finding that can be explained by religious reasons. At the same time, smoking was found in only 48.9% of our patients, mostly men. As the postcricoid area was found to be the most common subsite in this study, and hence the large number of females, this caused a lower rate of smoking, which is still for social and cultural reasons less in females.

The relatively small percentage of smokers, and the absence of alcohol consumption among patients in this study, points that these two predisposing factors are not strongly involved in hypopharyngeal carcinoma in Egypt. This should raise our attention to shift to different predisposing factors such as dietary factors or malnutrition that can be particularly important in esophageal and postcricoid cases in malnourished areas of the world, and can be commonly found in our patient's population.[9]

The operative mortality (2%) of such a major surgery in these cases was acceptable and comparable to other series with even higher percentage.[23,24,30]

The different treatment regimens used in the two groups did not significantly differ with respect to overall survival. In the literature there are various comparisons between the surgical and organ preservation protocols, with none showing a significant improvement regarding the overall survival of one modality over the other.[20,28,31–34] Some studies even showed slightly improved outcome with a primary surgical procedure, but still not significant, as shown in our results.[19,35–37]

The shift to organ preservation protocols worldwide, are mainly due to improved laryngopharyngeal preservation in

such cases. However, one should not miss that these protocols have high toxicity rate and need intensive patient care and monitoring by experienced multi-disciplinary teamwork. Optimizing the compliance of CRCT while keeping adequate treatment dose remains challenging for advanced hypopharyngeal carcinoma. Moreover, the functional sparing of the laryngopharynx is not always granted with such protocols. Treatment-related toxicity, the need for permanent gastrostomy tube placement and overall preservation of laryngoesophageal function remains low.[38]

Successful CRCT laryngeal preservation for advanced hypopharyngeal carcinoma remains difficult to achieve and should be performed with caution. The importance of detailed pretreatment counseling cannot be overstated.

N1 stage was the only independent predictor for the hazard of death. This agrees with the study conducted by Jones,[12] who reported that patients with N0, N2a and N2b disease have a 38% 5-year survival, while N1 neck disease had a 20% 5-year survival rate. It is not clear why larger nodes can be better prognostically, however, the pathological node stage is still the most accurate method of assessing prognosis in head and neck carcinoma.

6. Conclusion

Postcricoid carcinoma comprises the majority of hypopharyngeal tumors in Egypt. The majority of these patients present at late stage with lymph node metastases. Patients who received CRCT had an equal chance of survival with a preserved larynx compared with patients who underwent surgery. We suggest that organ preservation intended therapy should be considered for patients with advanced hypopharyngeal carcinoma. The criteria for selecting patients who will respond to and complete the treatment remain key issues for future investigation .At the same time, functional and quality of life determination are essential to include in future evaluation of such protocols.

7. Conflict of interest

None declared.

References

1. Wahlberg PC, Andersson KE, BiorKlund AT, Moller TR. Carcinoma of the hypopharynx:Analysis of incidence and survival in Sweden over a 30 year period. *Head Neck*. 1998;20:714–719.
2. Bradley PJ. Survey of current management of laryngeal and hypopharyngeal cancer. *J R Coll Surg Edinb*. 1989;34:197–200.
3. Berrino F, Gatta T. variation in survival of patients with head and neck cancer in Europe by the site of origin of the tumours .EUROCARE working group. *Eur J Cancer*. 1998;34:2154–2161.
4. Cachin Y. Cancers du pharynx et du larynx Facteurs dietiques. *Gazette Medicale Francaise*. 1980;87(2845–2856):2849–2850, 2852–2855.
5. Lowenfels AB. Alcoholism and the risk of cancer. *Ann NY Acad Sci*. 1975;252:366–373.
6. Hall SF, Groome PA, Irish J, O'Sullivan B. The natural history of patients with squamous cell carcinoma of the hypopharynx. *Laryngoscope*. 2008;118:1362–1371.
7. Takezaki T, Shinoda M, Hatooka S, et al. Subsite specific risk factor for hypopharyngeal and esophageal cancer (Japan). *Cancer Causes Control*. 2000;11:597–608.
8. Kleinsasser O. Tumour of the larynx and hypopharynx. *Stuttgart: Georg Thieme*. 1988;110–114.
9. Chisholm M. The association between webs, iron and postcricoid carcinoma. *Postgrad Med*. 1974;50:215–219.
10. Jones AS. Cancer of the hypopharynx. In: Jones AS, Phillips OE, Thilgers FJM, eds. *Diseases of the Head, Neck, Nose and Throat*. London: Arnold; 1998.
11. Aguado DL. Wachstum und ausdehnung der geschwulste des sinus piriformis. *Arch Otorhinolaryngol*. 1979;225:87–95.
12. Olofsson J, Van Nostrand AW. Growth and spread of laryngeal and hypoharyngeal carcinoma with reflections on the effect of preoperative irradiation 139 cases studied by whole organ serial sectioning. *Acta Otolaryngologica*. 1973(Suppl. 308);1–84.
13. Forastiere AA, Goepfert H, Maor M, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *N Engl J Med*. 2003;349:2091–2098.
14. Soo KC, Tan EH, Wee J, et al. Surgery and adjuvant radiotherapy vs concurrent chemo radiotherapy in stage III/IV nonmetastatic squamous cell head and neck cancer: a randomized comparison. *Br J Cancer*. 2005;93:279–286.
15. L efebvre JL, Chevalier D, Luboinski B, Kirkpatrick A, Collette T, Sahmoud T. Larynx preservation in pyriform sinus cancer: preliminary results of a European Organization for Research and Treatment of Cancer phase III trial. EORTC Head and Neck Cancer Cooperative Group. *J Natl Cancer Inst*. 1996;88(13):890–899.
16. Vittinghoff E, Shiboski SC, Glidden DV, McCulloch CE. *Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models*. New York: Springer; 2004, 133–15.
17. Greene FL, Page DL, Fleming ID, et al. *AJCC Cancer Staging Manual*. New York: Springer-verlag; 2002, Vol. 6, 31–46.
18. Paximadis P, Yoo G, Lin HS, et al. Concurrent chemoradiotherapy improves survivalin patients with hypopharyngeal cancer. *Int J Radiat Oncol Biol Phys*. 2012;82(4):1515–1521.
19. Arriagada R, Eschwege F, Cachin Y, Richard JM. The value of combining radiotherapy with surgery in the treatment of hypopharyngeal and laryngeal cancers. *Cancer*. 1983;51:1819–1825.
20. Elias MM, Hilgers FJM, Keus RB, Gregor RT, Hart AAM, Balm AJM. Carcinoma of the pyriform sinus: a retrospective analysis of treatment results over a 20-year period. *Clin Otolaryngol*. 1995;20:249–253.
21. Kim KH, Sung MW, Rhee CS, et al. Neoadjuvant chemotherapy and radiotherapy for the treatment of advanced hypopharyngeal carcinoma. *Am J Otolayngol*. 1998;19(1):40–44.
22. Tai SK, Yang MH, Wang LW, et al. Chemoradiotherapy laryngeal preservation for advanced hypopharyngeal cancer. *Jpn J Clin Oncol*. 2008;38(8):521–527.
23. Jones AS, Husband D, Rowley H. Radical radiotherapy for squamous cell carcinoma of the larynx, oropharynx and hypopharynx: patterns of recurrence, treatment and survival. *Clin Otolaryngol*. 1998;23:496–511.
24. Stell PM, Missotten F, Singh SD, Ramadan MF, Morton RP. Mortality after surgery for hypopharyngeal cancer. *Br J Surg*. 1983;70:713–718.
25. Saleh EM, Abdullwahab AA, Kammal MM. Age and sex incidence of hypopharyngeal tumors in Upper Egypt: Assuit University experience. *J larygol Otol*. 1995;109:737–740.
26. Slotman BJ, Kralendonk JH, Snow GB, et al. Surgery and postoperative radiotherapy and radiotherapy alone in T3–T4 cancers of the pyriform sinus: treatment results and patterns of failure. *Acta Oncol*. 1994;33(1):55–60.
27. Watkinson JC, Gaze MN, Wilson JA. Tumors of the hypopharynx*Stell & Maran Head and Neck surgery*. fourth ed. Butterworth Heinemann; 2000:335–356.
28. Cox DR. Regression model and life tables (with discussion). *J Roy Stat Soc*. 1972;34:187–220.
29. Hung S-K, Chen H-L, Hsieh C-H, et al. Treatment of advanced hypopharyngeal cancer-comparison of two modalities. *Tzu Chi Med J*. 2006;18:15–21.

30. Hoffman HT, Porter K, Karnell LH, et al. Laryngeal cancer in the United States: changes in demographics, patterns of care, and survival. *Laryngoscope*. 2006;116(9 Pt 2 Suppl. 111):1–13.
31. Zelefsky MJ, Kraus DH, Pfister DG, et al. Combined chemotherapy and radiotherapy versus surgery and postoperative radiotherapy for advanced hypopharyngeal cancer. *Head Neck*. 1996;18:405–411.
32. Kojima K, Suzuki K, Ito Y, et al. Tracking of hypopharyngeal carcinoma over 10 years. *Acta Otolaryngol (Stockh)*. 1996;Suppl. 525:146–150.
33. Rades D, Schroeder V, bajrovic A, schild S. *Radiochemotherapy versus surgery plus radio (chemo)therapy for stage T3/T4 larynx and hypopharynx cancer – Results of a matched-pair analysis European journal of cancer*. 2011;2729–2734.
34. Tsou YA, Hua JH, Lin MH, et al. Analysis of prognostic factors of chemoradiation therapy for advanced hypopharyngeal cancer– does tumor volume correlate with central necrosis and tumor pathology? *ORL J Otorhinolaryngol Relat Spec*. 2006;68(4):206–212.
35. Nassar M, Ibrahim SA. *A 5 years experience with hypopharyngeal carcinoma in Ain Shams University Hospitals inter cong ser*. 2003;1240:1007–1014.
36. Lee NY, O'Meara W, Chan K, et al. Concurrent chemotherapy and intensity-modulated radiotherapy for locoregionally advanced laryngeal and hypopharyngeal cancers. *Int J Radiat Oncol BiolPhys*. 2007;69:459–468.
37. Llatas MC, Mollá CL, García RB, et al. Hypopharyngeal cancer analysis of the evolution and treatment results. *Acta Otorrinolaringol Esp*. 2009;60(1):3–8.
38. Tai SK, Yang MH, Wang LW, et al. Chemoradiotherapy laryngeal preservation for advanced hypopharyngeal cancer. *Jpn J ClinOncol*. 2008;38(8):521–527.