

A Retrospective Analysis of Hypopharyngeal carcinoma Cases Treated in Menia Cancer Center and Gharbia Cancer Society Egypt in the Period from 2007-2014.

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Abstract: Purpose: The aim was to define all clinico-pathological data, different treatment modalities and to define the different prognostic factors which affect the locoregional control, distal metastatic disease, overall survival (OAS) and disease free survival (DFS). **Patients and Methods:** This is a retrospective study on 126 patients with hypopharyngeal cancer who were treated at the Gharbia Cancer Society and Menia Oncology Center from the year 2007 to 2014. All patients with hypopharyngeal cancer with complete file data were eligible for this study. All the patients who were treated by either radical or post operative radiotherapy were treated in supine position and were planned through 2-D simulator, patients were treated by a dose of 50-70 Gy according to the patient tolerance together with concurrent cisplatin. **Results:** This research also observed that considerable statistical connection among surgical therapy, locoregional control, and survival averages. Patients who were treated by radical surgery had an excellent locoregional control than to other patients who were treated by radical radiotherapy, and they also had the best survival averages between all the other therapy groups. The intermediate 6 months DFS and OAS averages for all studied patients were 40.1% and 47.5% respectively, while 12 months survival rates were 20.9% and 15.2% respectively. The median DFS was 5 months and median OAS was 7 months. **Conclusion:** This study supports that radical surgical treatment and post operative radiotherapy is recommended as the treatment of choice for operable hypopharyngeal cancer.

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1. Introduction:

Hypopharyngeal cancer is relatively uncommon. It has strong association with tobacco use ⁽¹⁾. In the past, observed that over 90% of patients were cigarette utilize. Patients with vocational exposure to coal and steel dust, and also, iron compounds, and fumes may be caused a great danger ⁽²⁾. Generally, the happening of hypopharyngeal cancer illustrated and some slowly was happened decline. From 1975 to 2001 the happening reduced by about 35%, maybe caused as an outcome of smoking cessation efforts.

Occurring ceremonially indicates and symptoms contain dysphagia, hoarseness, weight loss >10 pounds, and neck mass. Few patients suffering from these signs maybe first come to medical attention with a grievance of unilateral ear pain perhaps to tumor participation of the nerve of Arnold, a part of the superior laryngeal nerve.

The majority of patients present with advanced local and/or regional disease (stage III and IV disease) due to the nonspecific nature of early symptoms and the rich lymphatic drainage of the hypopharynx, at lower 50% of patients at the time of diagnosis. Considerably the patients are usually administered for presumed infectious or gastrointestinal etiology.

Various prognostic agents have been specified for patients with hypopharyngeal cancer. Age, especially >70 years, has been specified as a disadvantageous predictor of the result may be caused to the lessened probability of elderly patients to successfully afford the aggressive treatment approximation ⁽³⁾. As well as, tumor location has an influence on the result with cancers of the pyriform sinus mostly faring best compared with those appearing in the post cricoid ⁽⁴⁾. Generally, hypopharyngeal cancer patients fare unwell than patients hiding tumors from other sites.

Concerning all tumors of the head and neck area, multidisciplinary estimation and administration is definitive and may could include a head and neck surgeon, radiation oncologist, medical oncologist, nurse, nutritionist, swallow therapist, and social worker.

Radical surgery like laryngopharyngectomy is usually needed for patients who afford an essential worker process for hypopharyngeal cancer. This available procedure can stimulate considerable cosmetic and role alterations. Greatly, the choose therapy option is concerted chemoradiation that has explained equivalence to occurring surgery in cancer

survival, meanwhile, with becoming better organ keeping and effective results.

Estimation of measurable has containing effective case, organ keeping, therapy cost, and patient-estimate of fineness of life plays a greatly a significant role in the assessment of overall therapy performance. Regardless of the particular therapy approach, all patients demanded active rehabilitation treatment in the potential to great their ultimate speech and swallow role.

Regardless an aggressive approach in the overall management of hypopharyngeal cancer patients, ultimate cure rates remain quite poor and it is difficult to obtain long-range control. Even for those patients with outstanding reaction to treatment, there occurs a persistent danger for the advantage of second malignancies.

Thus the aim of this work is to analyze the results of different treatment modalities for loco-regional and disseminated disease and their effect on overall survival (OAS) and disease free survival (DFS).

2. Patients and methods

This is a retrospective study on 126 patients with hypopharyngeal cancer who were treated at the Gharbia Cancer Society and Menia Oncology Center from the year 2007 to 2014.

All patients with hypopharyngeal cancer with complete file data were eligible for this study.

As regarding chemotherapy Cisplatin + 5-FU was the regimen used with patients who received chemotherapy only (80-100mg/m² of cisplatin at day1 + 1000mg/m² continuous infusion of 5-FU at day1-5). The chemotherapy dose and number of cycles was adjusted according to patient's general condition and tolerance, labs results and toxicity to previous cycle. For the patients who received concurrent chemoradiotherapy, they received 40mg/m² of cisplatin as a weekly single agent with radical radiotherapy.

Regarding radiotherapy all the patients who were treated by either radical or post operative radiotherapy were treated in supine position and were planned through 2-D simulator planning using isocentric technique and all of them had proper fixation by a head and neck mask.

The treated volume was irradiated by two opposing fields in which its lower border was matched with the upper border of a separate anterior direct field to cover the neck nodes. Some patients with short neck were treated by 2 big lateral opposed fields which included the neck nodes. For palliation 2 lateral opposed fields were used to cover the target volume with adequate safety margin.

Radical radiotherapy dose to the target volume ranged from 50 to 70 Gy according to patient tolerance

and response with a spinal cord shield after 40Gy and for post operative radiotherapy the dose ranged from 60 to 66 Gy according to the surgical margin while palliative dose was limited to 30Gy to the target volume. For radical and post operative treatment 1.8 or 2 Gy/fraction were used and for palliative treatment the dose per fraction was 3Gy.

Follow up

All of the surviving patients had regular post-treatment follow up. The median follow up was for 3 years. In each visit complete physical examination was performed and investigations (in the form of CBC, liver functions, kidney functions, local CT and pan endoscopy) were done every 6 months, some other investigations (chest X ray, abdominal ultrasound and bone scan) were selectively ordered on suspicion.

Any abnormal finding was well documented and relapse was confirmed radiologically (e.g. lung, liver, bone, brain secondaries), and /or histopathologically (e.g. locoregional relapse or soft tissue secondaries).

Statistical analysis

The data were summarized by descriptive statistics [i.e., mean, standard deviation (SD), frequencies]. Mean values and standard deviation were compared using simple t test (2 variables). Percentages were compared using Chi-square test or Fisher's exact test. Logistic regression was used whenever the dependant factor was binary in nature (e.g. yes or no) during multivariate analysis. Kaplan-Meier test was used for predictive survival rates. *P value* less than 0.05 was considered to be statistically significant.

3. Results:

The age of the patients ranged between 17 and 91 years, the mean age was 50 years with the peak incidence in the fifth decade then the fourth decade of life, regarding patients' sex, males had higher incidence of hypopharyngeal cancer than females with a ratio of 57.1% to 42.9% respectively. More than two thirds of the tumors were located in the postcricoid region, the pyriform fossa and post pharyngeal wall had almost the same incidence with 14.3% and 15.9% respectively.

Regarding local control, table (1) showed better local control for patients with lower stages and those who were treated by surgery followed by postoperative radiotherapy with significant p values.

Regarding disease free survival, Table (2) showed also better disease free survival for with lower stages and those who were treated by surgery followed by postoperative radiotherapy with significant p values.

Tumors of the pyriform fossa showed significantly higher overall survival with average survival of 12 months compared to post cricoids and

posterior pharyngeal wall cancers which had an average survival of 6 and 3 months respectively.

Survival rate was significantly higher among with N0&1 than N2&3, the probability of death was 1.8 times more among N2&3 than N0&1. They were also higher among T1&T2 cases, with a probability of

death approximately 3 times more among T4a&T4b cases.

Finally those who underwent surgery had a better survival rate than those who didn't. The probability of death was 2.2 more among those who didn't have surgery.

Table (1): Local control

Locoregional control							
Factors	Number cases	of	6 months locally free (%)	12 months locally free(%)	Locoregional control (months)	median	P-value*
All	126		40.9	15.2	5		
T stage							
T1&T2	26		66.7	42.8	10		
T3	17		62.6	35.3	8		
T4a&T4b	72		29.5	4.3	5		<0.001
N stage							
0&1	67		52	23.4	7		
2&3	48		23.2	3.6	4		<0.001
Stage grouping							
Stage I-II	13		71.6	49.3	12		
Stage III-IV	97		26.4	6.1	5		<0.001
Treatment							
Surgery ± PORT	50		56.0	24.6	6		
Radical radiotherapy	24		17.7	6.6	3		<0.001

* P-values ≤ 0.05 is considered significant

Table (2): Disease free survival

Disease free survival rate					
Factors	Number of cases	6 months(%)	12 months(%)	Median (months)	P-value*
All	126	40.1	15.2	5	
T stage					
T1&T2	26	66.7	42.8	10	
T3	17	62.6	35.3	8	
T4a&T4b	72	29.5	4.3	5	<0.001
N stage					
0&1	67	52	23.4	7	
2&3	48	23.2	3.6	4	<0.001
Stage grouping					
Stage I-II	13	71.6	49.3	12	
Stage III-IV	97	26.4	6.1	5	<0.001
Treatment					
Surgery ± PORT	50	56.0	24.6	6	
Radical radiotherapy	24	17.7	6.6	3	<0.001

* P-values ≤ 0.05 is considered significant

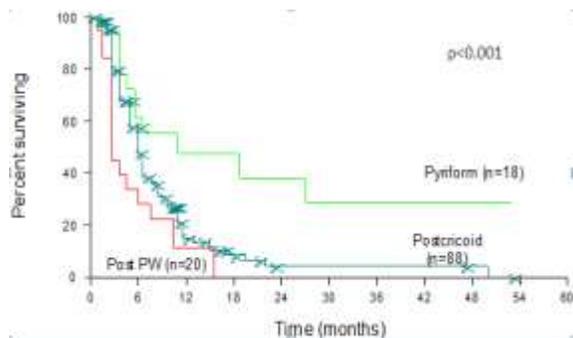


Figure 1: Overall survival in relation to tumor site curve

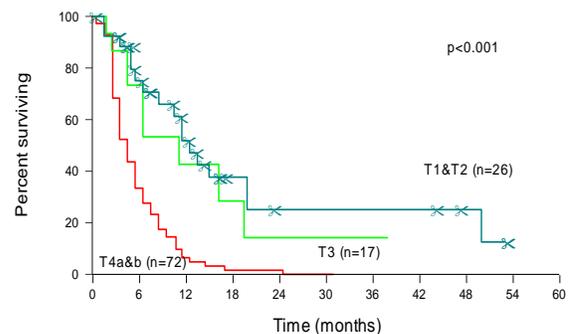


Figure 2: Overall survival in relation to T-stage curve

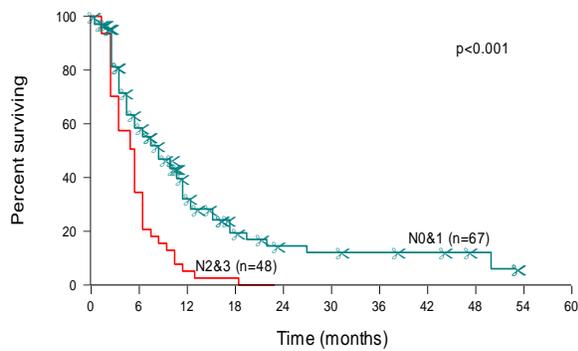


Figure 3: Overall survival in relation to N-stage curve

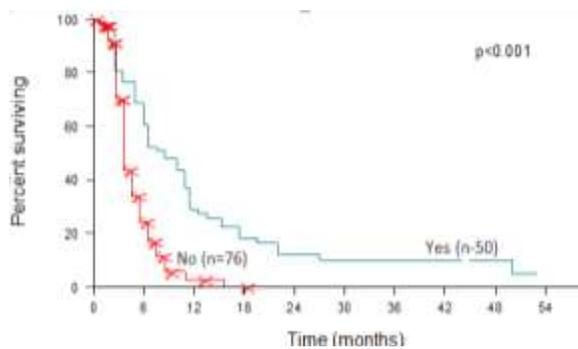


Figure 4: Overall survival in relation to Surgery curve

4. Discussion:

As regarding the age, the patients' age ranged between 17 and 91 years with a peak incidence in the fifth decade then the fourth decade of life (26.2%, 23.8% of cases respectively). The mean age was 50 years. **Nadia Mokhtar et al**⁽⁵⁾ also reported that the average age at submitting of hypopharyngeal tumors is about 55 years.⁽¹⁾

Concerning the tumor site, more than two thirds of the tumors were located in the post cricoids region, the pyriform fossa and post pharyngeal wall had almost the same incidence with 14.3% and 15.9% respectively. **Nadia Mokhtar et al**⁽⁵⁾ also found that postcricoid region is the predominant site in Egypt with a 59% of patients. All the other studies in Europe showed that pyriform fossa is the predominant site for hypopharyngeal cancer. The difference could be explained by different habits as smoking (type and quality of tobacco) and alcohol intake and racial predisposition could play a role and need further investigations.

Treatment outcomes

The present study showed a significant better locoregional control with surgical treatment compared to radical radiotherapy. Confirmatory results were reported by **Van den Brouck et al**⁽⁶⁾ who studied two

groups for a handle with essential surgery or radiotherapy, locoregional recurrence was much higher in the radiotherapy group (44% with Radiotherapy group compared to 17.5 with surgery group), this paper suggests that locoregional recurrence is much greater with radiation alone they found that the strategy of essential surgery and also postoperative radiation showed to be the best course. These results were also supported by **Talton et al**⁽⁷⁾ results which reported recurrence in 79% of cases of posterior hypopharyngeal wall carcinomas treated by radical radiotherapy. **El Badawi et al**⁽⁸⁾ found that locoregional recurrence rates were halved by primary surgery and radiotherapy as compared to radiotherapy alone for T3/4 pyriform lesions. And finally **Pene et al**⁽⁹⁾ had similar results after studying a group of oro- and hypopharyngeal malignancies, for the most part, handle with radiotherapy, 75% percent of patients died of local disease.

The study showed significant correlation between T-stage and both DSF and OAS rates. Confirmatory results were reported by **Farrington et al**⁽¹⁰⁾ who reported that T2,2,3,4 cause-specific 1-year survival was 80%, 55%, 30%, 25% respectively in a large series studying Post cricoids carcinomas treated with radiotherapy and salvage surgery.

This study also showed significant correlation between N-stage and both DSF and OAS rates. This result is similar to **Batani et al**⁽¹¹⁾ result who found that survival was significantly affected by nodal status and reported that N0,1,2,3 two years survival was 60%, 62%, 30%, 40% respectively.

The study showed significant correlation between tumor stage and both DSF and OAS rates. Confirmatory results were reported by **Jones and Stell**⁽¹²⁾ in the Liverpool series with a 5-year stage, I survival of 45–50% and there were no survivors for other stages disease. The study also showed significant correlation between tumor site and both DSF and OAS rates the pyriform fossa tumors showed better survival rates than other hypopharyngeal tumors. **El Badawi et al**⁽⁸⁾ at MD Anderson found that for the most part, T3/4 pyriform lesions have an actuarial survival at 2 and 5 years of 55% and 40%.

The study showed significant correlation between surgical treatment and both DSF and OAS. This is similar to **Van den Brouck et al**⁽⁶⁾ results after studying two groups treated with primary surgery or radiotherapy. Generally, survival was greater with surgery than radiation even although the lesions therapy with radiation were mostly previously, this study observed that survival is greater with surgery alone compared to irradiation for progressive diseases. Confirmatory results were also reported by **Axon et al**⁽¹³⁾ after comparing the influence of surgery and radiotherapy in therapy postcricoid carcinoma and

recommended that surgery was an excellent method of becoming better survival predominately in patients with no nodal disease. But the result is not similar to **Jones and Stell** ⁽¹²⁾ result who having been no variation in survival among essential surgery and essential irradiation.

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