Section: Radiation Oncology

Original Research Article

CLINICAL PROFILE AND TREATMENT OUTCOME OF SQUAMOUS CELL CARCINOMA HYPOPHARYNX: A RETROSPECTIVE ANALYSIS

Resmi Radha[1], K Rejnish Kumar[2], Cessal Thommachan Kainickal[3], Biju Azariah[4]

[1]Assistant Professor, Department of Radiation Oncology, Government Kilpauk Medical College, Tamilnadu, India
[2]Additional Professor, Department of Radiation Oncology, Regional Cancer Centre, Trivandrum, India
[3]Associate Professor, Department of Radiation Oncology, Regional Cancer Centre, Trivandrum, India
[4]Resident, Department of Medical Oncology, Tirunelveli Medical College, Tamilnadu, India

Received : 26/08/2023
Received in revised form : 30/09/2023
Accepted : 11/10/2023

Keywords:
Hypopharyngeal cancer, Survival outcomes, Radiotherapy, Pyriform sinus, Post-cricoid, Posterior pharyngeal wall.

Corresponding Author:
Dr. Resmi Radha,
Email: drresmi277@gmail.com

DOI: 10.47009/jamp.2023.5.5.280

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (5); 1414-1421

Abstract

Background: Hypopharyngeal cancers constitute about 11% of all Head and Neck cancers among Indian males, in contrast to just 1% worldwide. Further, these malignancies are associated with the worst prognosis. Significant changes in the treatment approaches have come about in managing these cancers due to definitive evidence supporting the role of organ preservation. These changes have been incorporated in our setting, but their clinical outcome has not been quantified adequately. This study aimed to analyse hypopharyngeal cancer patients' clinical profiles and treatment outcomes and evaluate the impact of various patient, tumour and treatment-related factors on outcomes. **Materials and Methods:** This retrospective analysis was conducted on 356 patients with biopsy-proven carcinoma hypopharynx registered at a tertiary cancer centre between January 2010 and December 2014. The patient, tumour and treatment-related factors were documented and were correlated with disease-free survival and overall survival. The median duration to relapse and the failure patterns were also studied for the patients who had relapsed. **Result:** Patients stratified into ages <70 and ≥70 showed significant differences in survival outcomes. No significant differences were found among gender, literate and illiterate, socioeconomic status, tobacco or alcohol addiction, or comorbid illness. Overall survival was higher in pyriform sinus tumours, followed by post-cricoid and posterior pharyngeal wall tumours. Stage II had the highest overall survival probability at 90%, while stage IV b had a 27.6% probability. No statistical difference was found between radiotherapy techniques and patients who completed treatment without interruptions had higher survival rates. Patients with a complete response at first follow-up had significantly improved overall and disease-free survival compared to patients with partial or no response. In patients treated with radical intent,3-year disease-free survival was 47.4%, and overall survival was 47.9%. **Conclusion:** Despite the extreme disease burden in our country and considering the limited resources, the results of this study are on par with the internationally published results, highlighting the existence of quality cancer care in our setup. Focusing further on improving the nutritional status of the patients, routine implementation of conformal radiation and ensuring strict follow up post treatment completion might help improve the outcomes of these patients significantly.

INTRODUCTION

Head and neck cancer describes a range of tumours that arise in the head and neck region, which includes the oral cavity, pharynx, larynx, nasopharynx, nasal cavity, paranasal sinuses, thyroid and salivary glands.[1] The worldwide incidence of head and neck cancer exceeds half a million cases annually, ranking it the fifth most common cancer worldwide. The vast majority of head and neck cancers arise in the mucosa of the upper aerodigestive tract, and 80-90% are squamous cell carcinoma (SCC). 57.7% of global head and neck cancer occurs in Asia, especially India, accounting for 30% of all cancers in India. Among

ISSN (O): 2687-5365; ISSN (P): 2753-6556

head and neck cancers, hypopharyngeal cancers constitute about 7% of head and neck malignancies.[2-4]

Hypopharyngeal cancers are distinct among cancers of the head and neck region because of their poor clinical outcome due to various associated factors such as advanced stage at diagnosis, abundant lymphatic drainage of the region and a greater propensity for distant metastatic spread. The use of tobacco and alcohol, compromised nutritional status, and low socioeconomic status add to the poor outcome. Five-year survival rates following definitive therapy for hypopharyngeal cancer range from 60-70% for stage I to <20% for stage IV disease.[5,6]

On the treatment front, the primary treatment modalities, namely, surgery and radiation therapy, have been refined over the last few years to reduce morbidity and improve efficacy. In the early 90s, platinum-based chemotherapy was shown to improve the efficacy of radiation therapy.[7,8] Significant changes in the treatment approach have come about in managing these cancers due to definitive evidence supporting the role of organ preservation. These changes have been incorporated in our setting, but their clinical outcome has not been quantified adequately.

The study aimed to analyse the clinical profiles and treatment outcomes of hypopharyngeal cancer patients treated at a tertiary care centre and to evaluate the impact of various patient, tumour and treatment-related factors on outcomes.

MATERIALS AND METHODS

This retrospective analysis was conducted in a tertiary care centre on 356 patients with biopsy-proven squamous cell carcinoma hypopharynx registered at a tertiary cancer centre between January 2010 and December 2014. After approval from the Institutional Scientific Review Board, the case files of these patients were retrieved from the hospital database and evaluated for analysis.

Inclusion Criteria

Biopsy-proven squamous cell carcinoma hypopharynx patients who received radical/palliative treatment from the centre during the specified period were included.

Exclusion Criteria

Histologies other than squamous cell carcinoma, patients who did not turn up for treatment after registration, and patients who presented after primary treatment elsewhere for salvage procedures were excluded.

Out of the 824 patients registered, only 356 patients who satisfied the above criteria were included. Each patient's details were retrieved from the case files and recorded into a structured proforma. All the patient, tumour and treatment-related factors were documented and were correlated with disease-free survival and overall survival. The median duration to relapse and the pattern of failure were also studied for the patients who had relapsed.

Disease-free survival (DFS) was defined as the period between the date of treatment completion to the date of first documentation of any disease, in the form of residual disease at first visit or recurrence. Overall survival (OS) was defined as the period from the date of diagnosis until death due to any cause.

Statistical analysis: Survival estimates were generated using the Kaplan–Meier method. Univariate analysis was done using Chi-square and Fisher's exact tests. Multivariate analysis using the Cox-regression model was performed to determine the impact of various patient, tumour and treatment-related factors on outcome. For those factors with significant p-values, the Log-rank test was used to determine the survival probability and significance.

RESULTS

Most patients were males (80.3%), and the mean age of the target population was 58.9 years. (min-22, max -86). Most of the patients (50.8%) were between 40 and 60.

Most of the patients registered were literate (87.4%), which goes along with the good literacy rate of the state. Study populations were evenly distributed among low and high socioeconomic groups. Most patients had an addiction to either smoking/tobacco or betel chewing.

About 31.5% of the patients had comorbid illnesses like diabetes, hypertension, coronary artery disease, thyroid dysfunction or a history of pulmonary TB.

The most common subsite in this series was the pyriform sinus (71.9%), followed by the post-cricoid and posterior pharyngeal wall. The incidence of post-cricoid malignancies was significantly higher in females when compared to males [Table 1].

Of the 79 post-cricoid tumours reported, 43 (61.4%) were in females. Most patients had advanced disease at presentation, stage IV A being most common, followed by stage IV B. Second primaries were reported in 4 % of the patient population, the most common being lung primary, probably due to field cancerisation.

Among the 356 patients, 272 were treated with radical intent and 78 with palliative intent. Six patients initially taken up for radical treatment were changed to palliative intent because of poor response.

Of the 272 patients planned for radical intent treatment, 251 (92.3%) patients could complete the treatment. Twenty-one patients either refused further treatment or died during therapy. About 10.7% of patients had to undergo tracheostomy before, during, or after treatment; the former scenario was the most common.

94.8% of patients underwent an organ preservation approach, and only 5.2% underwent primary surgery. Out of 13 patients who underwent radical surgery [total laryngopharyngectomy + bilateral modified radical neck dissection], 12 patients received

ISSN (O): 2687-5365; ISSN (P): 2753-6556

adjuvant radiotherapy (+ chemotherapy) for the mentioned risk factors [Table 2].

Two hundred fifty patients received radiotherapy as part of radical treatment in the definitive or adjuvant setting. Per the institution protocol, the most commonly used dose fractionation for radical treatment was 60 Gy in 26 fractions over 5.1 weeks. The BED for the above fractionation is 73.8 Gy. The most often used fractionation for adjuvant radiotherapy was 60 Gy in 30 fractions.

Most patients (94.4%) were treated by a 2-dimensional technique using an X-ray simulator and customised MLC shielding of the fields. 181 (72.1%) patients received some form of chemotherapy [Induction/ concurrent/ adjuvant concurrent] during their radical treatment programme. Chemotherapy, in a majority of patients, was given concurrently with RT. The most common regime used for induction was Cisplatin and 5 Fluorouracil. TPF chemotherapy (Cisplatin+ 5 flurouracil+ Taxanes) was given only in about five patients.

Cisplatin was the most common concurrent chemotherapy regimen used (46.2%). Carboplatin, Cetuximab and gefitinib were used in decreased frequency as concurrent agents for patients unfit for cisplatin. Eleven patients had treatment interruption exceeding seven days [reason being Machine failure/ Toxicity/Poor compliance], while the rest completed the planned treatment without interruptions [Table 3].

At a median follow-up of 31 months, 76 patients (30.2%) relapsed. Patterns of recurrence (locoregional or distant) and the treatment at relapse were analysed and documented.

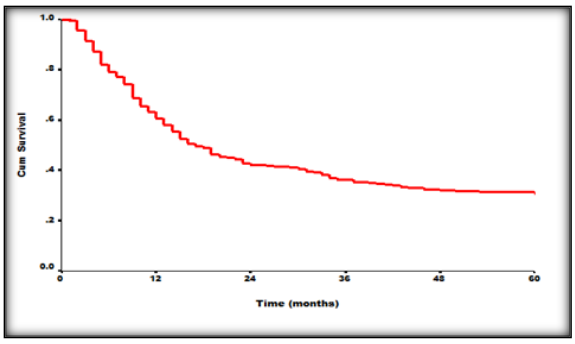

Figure 1: Kaplan Meier graph showing the overall survival

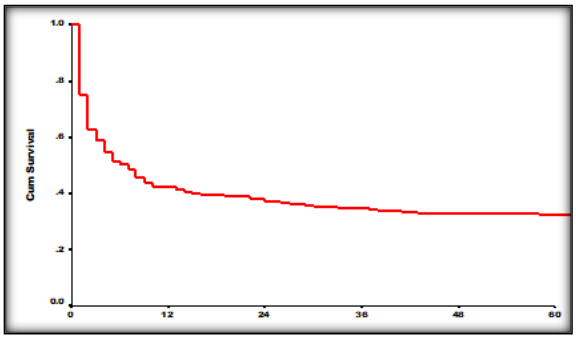

Figure 2: Kaplan Meier graph showing the disease-free survival

The most common site of recurrence was local (17.1 %), followed by nodal recurrence and then locoregional recurrence. The mean time to recurrence was nine months [Table 3].

The three-year overall survival for the entire group was 36.2%, and the disease-free survival probability at three years was estimated to be 34.8% [Table 4, Figures 1 and 2].

The three-year actuarial survival was 47.9%, and the three-year disease-free survival was 47.4% [Table 5, Figures 3 and 4].

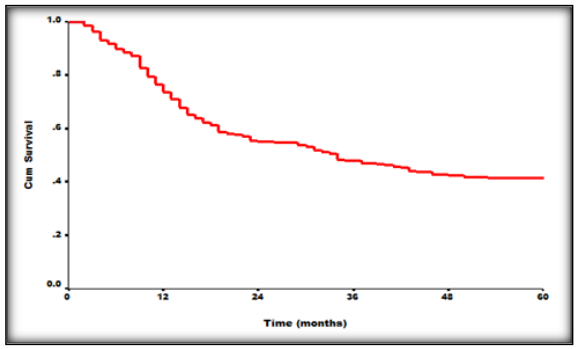

Figure 3. Kaplan Meier graph showing the overall survival

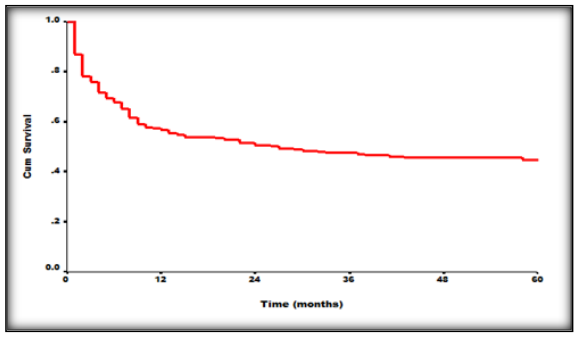

Figure 4. Kaplan Meier graph showing the disease-free survival

Of all these factors, age >70 years alone was significantly associated with outcome. When patients were initially stratified into three age groups <40, 40-60, >60 years and outcome studied,there was no statistically significant difference in survival probability between 3-year overall survival (p= 0.1825) or disease-free survival (p=0.1171). However, when patients were stratified into age<70 years and age ≥70, their survival outcome showed a significant difference.

There was no statistically significant difference in survival probability when male and female gender was compared.

There was no significant difference in disease-free survival (P= 0.2649) or overall survival (P= 0.1245) among the literate and illiterates.

There was no significant difference in disease-free or overall survival among low and high socioeconomic statuses.

There was no significant difference in disease-free survival or overall survival among patients with or

ISSN (O): 2687-5365; ISSN (P): 2753-6556

without addiction to tobacco products or alcohol consumption.

There was no significant difference in disease-free or overall survival among patients with or without comorbid illness [Table 6].

The overall survival was significantly higher in pyriform sinus tumours, followed by post-cricoid and posterior pharyngeal wall tumours.

There was a significant difference among various tumour stages for overall and disease-free survival, with OS probability for stage II being the highest at 90% and stage IV b being 27.6% [Table 7, Figures 5 and 6].

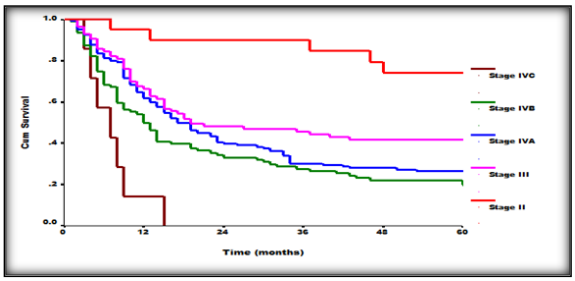

Figure 5. Kaplan Meier graph for overall survival

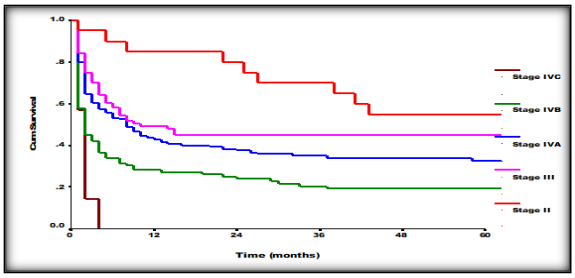

Figure 6. Kaplan Meier graph for disease-free survival

There was no statistical difference in survival observed between various radiotherapy techniques.

There was a statistically improved survival in terms of disease-free and overall survival in patients who completed the planned treatment without interruptions.

Though the survival rates were higher for patients who received both induction and concurrent chemotherapy than those who received concurrent or induction chemotherapy alone, the OS difference was not statistically significant.

There was a significant improvement in disease-free survival in patients who did not undergo tracheostomy compared to those who underwent tracheostomy, but the OS difference was not statistically significant.

Patients who had a complete response at first follow-up had significantly improved overall and disease-free survival compared to patients who had partial or no response [Table 8].

There was no statistically significant difference in OS between the various larynx preservation strategies employed in our setting. However, the DFS probability was higher in the induction chemo followed by the chemoRT group, with a significant p-value [Table 9].

On multivariate analysis, age > 70 years, subsite involvement, composite staging and treatment interruptions were found to impact disease-free survival significantly [Table 10].

Table 1: Demographic data

		n=356	%
Gender	Male	286	80.3
	Female	70	19.7
Age	20-40	23	6.5
	40-60	181	50.8
	>60	152	42.7
Literacy	Illiterate	48	13.5
	Literate	311	87.4
	Unknown	11	3.1
SES	Low	185	51.9
	High	171	48.1
Habits	No	47	13.2
	Yes	247	69.4
	Unknown	62	17.4
Comorbidities	Yes	228	64
	No	112	31.5
	Unknown	16	4.5
Subsite	Pyriform sinus	256	71.9
	Postcricoid	79	22.1
	Posterior pharyngeal wall	21	5.8

Table 2: Stage, treatment, and risk factors

		Frequency	%
Composite Stage	Stage II	20	5.6
	Stage III	84	23.6
	Stage IV A	145	40.7
	Stage IV B	95	26.7
	Stage IV C	7	2
	Unknown	5	1.4
Second malignancies	No	342	96

ISSN (O): 2687-5365; ISSN (P): 2753-6556

	Yes	14	4
Intent of Treatment	Radical	272	76.4
	Palliative	84	23.5
Completed Treatment	Yes	251	92.3
	No	21	7.7
Tracheostomy	No	267	75
	Yes	38	10.7
	Unknown	51	14.3
Treatment Modality	Organ preservation approach	238	94.8
	Radical surgery	13	5.2
Risk factors	Metastatic neck nodes	10	76.9
	Margin +ve or close	7	53.8
	Extracapsular spread	4	30.7
	Perineural invasion	4	30.7
	Lymphovascular emboli	2	15.3
	Soft tissue infiltration	3	23

Table 3: Dose, technique, chemotherapy, and follow-up

		Frequency	%
Dose of RT	60 Gy/26 #	177	70.8
	66 Gy/33 #	33	17.2
	60 Gy/30 #	14	5.2
	55 Gy/20 #	16	6.4
	Others	10	0.4
Technique	2D	236	94.4
	3D CRT	8	3.2
	IMRT	3	1.2
	Unknown	3	1.2
Sequencing of chemotherapy	Concurrent	69	27.4
	Induction +concurrent	65	25.8
	Induction	47	18.7
	Unknown	14	5.6
	No chemotherapy	56	22.3
Induction chemo agent	Nil	119	47.4
	CDDP + 5FU	80	31.8
	TPF	5	1.9
	MTX	1	0.3
	CDDP + Docetaxel	13	5.2
	CDDP + paclitaxel	3	1.1
	Carboplatin + 5FU	10	3.9
	Unknown	20	7.9
Larynx preservation strategy	Concurrent chemoRT	68	27
	Induction chemo-chemoRT	63	25
	Induction chemo-RT	45	17.9
	RT only	53	21.1
	RT + Chemo status unknown	9	3.5
Treatment Interruption	No	240	95.6
	Yes	11	4.3
Status at 1st follow-up (2 months after Rx completion)	Complete response	195	77.6
	Partial response	35	13.9
	No response	9	3.5
	Response not known [died within 2 months]	12	4.7
Patterns of recurrence	Local	43	17.1
	Regional	16	6.3
	Locoregional	10	3.9
	Distant	10	3.9
	Regional + distant	3	1.1

Table 4: Survival probability for all patients

	One year	Two years	Three years [SE]
Overall survival	60.70%	42.10%	36.2% [2.6%]
Disease free survival	42.10%	37.40%	34.8% (2.6%)

Table 5: Survival probability for radically treated patients

	Survival	SE
Overall survival at three years	47.9%	3.2 %
Disease-free survival at three years	47.4%	3.2 %

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 6: Patient factors with potential prognostic value for overall and disease-free survival

	Survival probability (%)	Standard Error (SE) (%)	Survival probability (%)	Standard Error (SE) (%)	P-value
Age (in years)	<70		>=70		
Overall survival	38.7	2.9	23.6	5.6	0.004
Disease free survival	37.1	2.9	23.9	5.6	0.003
Gender	Male		Female		
Overall survival	35.8	2.9	37.7	5.8	0.79
Disease free survival	34.9	2.9	34.2	5.7	0.68
Socioeconomic status	Low		High		
Overall survival	33.4	3.5	39.2	3.8	0.11
Disease free survival	31.8	3.6	37.7	3.7	0.38
Habits	No		Yes		
Overall survival	46.6	7.3	39.6	3.2	0.34
Disease free survival	42.1	7.3	38.5	3.2	0.71
Comorbidities	No		Yes		
Overall survival	37.8	3.3	34.8	4.6	0.75
Disease free survival	34	3.2	38.1	4.7	0.66

Table 7: Tumour-related factors with potential prognostic value for overall and disease-free survival

3 Year	Survival (%)	SE (%)	Survival (%)	SE (%)	Survival (%)	SE (%)	P-value			P-value
Primary site	Pyriform Fossa		Post Cricoid		Posterior pharyngeal wall					
Overall survival	38.8	3.1	32.4	5.4	19.1	8.6	0.009			
Disease free survival	37.6	3.1	29	5.2	22.9	9.4	0.072			
Stage at presentation	Stage II		Stage III		Stage IVA		Stage IVB		Stage IVC	
Overall survival	90	6.7	45.7	5.5	30.2	3.9	27.6	4.7	0	<0.001
Disease free survival	70	10.3	45.2	5.5	35.1	4.1	20.6	4.2	0	<0.001

Table 8: Treatment-related factors with potential prognostic value for overall and disease-free survival

3 Year	Survival (%)	SE (%)	Survival (%)	SE (%)	Survival (%)	SE (%)	P-value
Radiotherapy technique	2D		3D		IMRT		
Overall survival	46.4	3.3	75	15.3	100		0.09
Disease free survival	46	3.3	62.5	17.1	100		0.14
Treatment interruption	No		Yes				
Overall survival	49.4	3.3	11.4	10.5			<0.001
Disease free survival	49.2	3.3	9	8.7			<0.001
Chemotherapy	Induction		Concurrent		Induction + concurrent		
Overall survival	35.8	7	46.8	6.1	52	6.3	0.33
Disease free survival	34.9	7.1	51.1	6.2	59.8	6.3	0.015
Tracheostomy	No		Yes				
Overall survival	55.1	3.5	31.9	9.9			0.09
Disease free survival	55.3	3.6	24.3	9.4			0.013
Status at 1st follow-up	No Response		Complete Response		Partial response		
Overall survival	11.1	10.5	59.7	3.6	8.6	4.7	<0.001
Disease free survival	11.1	10.5	60.6	3.6	0		<0.001

Table 9: Larynx preservation strategy

3 Year	Chemo RT	induction chemo ® chemo RT	Induction chemo ® RT	RT only	Rt taken+ chemo unknown	P-value
Overall survival	46 (6.1)	53.8 (6.4)	35.2 (7.2)	55.3 (7.3)	57.1 (13.2)	0.48
Disease free survival	50.3 (6.2)	60.2 (6.4)	34.2 (7.2)	44.1 (7.4)	35.7 (12.8)	0.04

Table 10: Multivariate analysis of patient-related and tumor-related factors

	Variables compared	HR (95 % C.I)	P-value
Age	Age >70 years vs Age < 70 years	1.542 (1.132-2.099)	0.006
Primary site	Post cricoid vs pyriform sinus	1.510 (1.110-2.053)	0.009
	Posterior pharyngeal wall Vs. pyriform sinus	2.248 (1.359-3.718)	0.002
Composite stage	Stage III Vs II	3.021 (1.199 -7.614)	0.019
	Stage IV A Vs II	4.512 (1.833-11.105)	0.001
	Stage IV B Vs II	5.171 (2.071-12.910)	0.000
	Stage IV C Vs II	6.837 (2.081-22.47)	0.002
Response to treatment	No response Vs complete response	1.082 (0.399- 2.932)	0.877
	No response Vs partial response	0.845 (0.368 -1.942)	0.692
Treatment interruption	Yes, Vs No	3.096 (1.484- 6.460)	0.003
Tracheostomy	Yes, vs. no	1.109 (0.652- 1.885)	0.704

ISSN (O): 2687-5365; ISSN (P): 2753-6556

DISCUSSION

This study is probably the largest study from South India exclusively analysing outcome of hypopharyngeal cancers.In some series, age, particularly >70 years, has been identified as an unfavourable predictor of outcome. Over half of the patients with these cancers in the US are 65 years or older at presentation. However, the mean age at diagnosis appears to be lower in the Indian population, probably because of the increased addiction to tobacco products at a young age.

The present analyses stratified patients into three age groups: <40, 40-60 and > 60 years. The majority of patients presented between 40-60 years (50.8%), and a significant number of patients were also >60 years of age (42.7%). The mean age at diagnosis was 58.9 years, comparable with another important study from India by Gupta T et al, where the mean age was slightly less at 55.[9] The difference in the number of deaths in the three groups was not statistically significant to impact a difference in overall survival or disease-free survival. Hence, it is assumed that if the patient has a good performance status to complete a planned course of radical treatment, age alone may not act as an independent factor to affect outcome.

However, an analysis was also conducted to study the effect on survival by stratifying patients into two groups: <70 years and ≥70 years. A significant difference in survival was observed in favour of patients aged less than 70 years, probably because advanced-age people are treated radically less often.

The present study found that non-surgical treatment was the most common, with concurrent chemoradiation and induction chemotherapy being the most common organ preservation strategies. Surgery was used in only 5.2% of patients. The largest retrospective study from US way back in 1997, found surgery combined with irradiation as the most commonly used initial treatment for hypopharyngeal cancers,[10], indicating a significant evolution in treatment approaches.Also,no significant difference was observed in survival outcomes between non-surgical and surgical treatments.

However,this study did not address the best sequencing of chemotherapy and radiation for optimal results, as treatment comparisons based on non-randomised data are not recommended due to bias.

The present study found that radiotherapy was the most common treatment for radically treated patients, most receiving it as definitive therapy. The most common dose fractionation was 60 Gy/26#, with a 2D technique used most often.

In the US study, majority of patients in the non surgical arm underwent treatment with radiotherapy alone. In the present study, chemotherapy was an integral component of treatment in majority of the radically treated patients. This practice changing approach has come about in the light of numerous randomised trials and meta analysis, which revealed a significant survival benefit for the addition of chemotherapy to radiation in the treatment of locally advanced head and neck cancers.However, our study found no significant impact of chemotherapy addition or sequencing on survival outcomes probably due to limited data availability in a retrospective study.

Tracheostomy status did not have any impact on overall survival but positively impacted disease free survival in univariate analysis.The higher disease-free survival rate in patients undergoing tracheostomies is possibly due to more bulky disease. However, this factor loses significance in multivariate analysis due to the already accounting for the influence of advanced disease on survival in the composite stage.

The present study found that about a quarter of patients were candidates for palliative treatment, with 77.7% experiencing complete response in the first visit two months post-radiotherapy. However, response to treatment was not directly impacted on survival.

In the radically treated patients,about 17.5 % of patients were left with residual disease after treatment completion. Another 4.7 % of patients died within 2 months of treatment completion, either due to treatment related complications or progressive disease, before reporting for the first follow up. Hence, their response to treatment was taken as unknown. This emphasizes the need for proper counseling, reference and timely intervention in the immediate post treatment phase, when the treatment related complications are most likely to take a toll on the patient's life.30.2% experienced recurrence, with the most common being the primary site.

The present study found that only 14 patients could undergo salvage surgery for residual/recurrence, affecting overall and disease-free survival. The study did not analyse the toxicity of treatment due to its retrospective nature.4% of patients developed second malignancies, with lung cancer being the most common site.

Overall and disease-free 3 year survival rates were 36.2% and 34.8%, respectively. The study also found a decrease in survival probability from 90% in stage II to 27.6% in stage IV B. The radically treated group had higher overall survival rates(47.9%) and disease-free survival rates (47.4 %).

CONCLUSION

The outcome of hypopharyngeal cancer continues to be unsatisfactory because of the advanced stage at presentation and associated nutritional compromise of the patients. However, despite the extreme disease burden in our country and considering the limited resources, the results of this study are on par with the internationally published results, highlighting the existence of quality cancer care in our setup.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

However, the overall prognosis of hypopharyngeal cancers is dismal compared to other head and neck cancers. Focusing further on improving the nutritional status of the patients and routine implementation of conformal radiation and strict follow up might help improve the outcomes of these patients significantly. Also, further research into genetic assays to pick up these tumours early, evaluating the proper timing of chemotherapy to increase the effect of radiation and exploring the options of newer targeted therapies hold promise for these patients.

REFERENCES

1. Patel SG, Shah JP. TNM staging of cancers of the head and neck: Striving for uniformity among diversity. CA Cancer J Clin 2005;55:242–58. https://doi.org/10.3322/canjclin.55.4.242.
2. Veness MJ, Palme CE, Morgan GJ. High-risk cutaneous squamous cell carcinoma of the head and neck: Results from 266 treated patients with metastatic lymph node disease. Cancer 2006;106:2389–96. https://doi.org/10.1002/cncr.21898.
3. Divakar RR. Evaluation of glutathione s-transferase enzyme activity in correlation to the genotype of detoxification enzyme in oral cancer and premalignant lesions and conditions. ProQuest 2006.
4. Ridge JA, Glisson BS, Lango MN, Feigenberg S, Horwitz E. Head and neck tumors. Cancer management: a multidisciplinary approach. 2008;11:369.
5. Mao L, Hong WK, Papadimitrakopoulou VA. Focus on head and neck cancer. Cancer cell. 2004;5:311-6.
6. Mohanti BK, Nachiappan P, Pandey RM, Sharma A, Bahadur S, Thakar A. Analysis of 2167 head and neck cancer patients' management, treatment compliance and outcomes from a regional cancer centre, Delhi, India. J Laryngol Otol 2007;121:49–56. https://doi.org/10.1017/s0022215106002751.
7. Freeman KP, Hahn KA, Harris FD, King GK. Treatment of dogs with oral melanoma by hypofractionated radiation therapy and platinum-based chemotherapy (1987-1997). J Vet Intern Med 2003;17:96–101. https://doi.org/10.1111/j.1939-1676.2003.tb01329.x.
8. McCulloch M, See C, Shu X-J, Broffman M, Kramer A, Fan W-Y, et al. Astragalus-based Chinese herbs and platinum-based chemotherapy for advanced non–small-cell lung cancer: Meta-analysis of randomized trials. J Clin Oncol 2006;24:419–30. https://doi.org/10.1200/jco.2005.03.6392.
9. Gupta T, Chopra S, Agarwal JP, Laskar S-G, D'cruz AK, Shrivastava SK, et al. Squamous cell carcinoma of the hypopharynx: Single-institution outcome analysis of a large cohort of patients treated with primary non-surgical approaches. Acta Oncol 2009;48:541–8. https://doi.org/10.1080/02841860802488839.
10. Hypopharyngeal Cancer Patient Care Evaluation Henry T. Hoffman, MD; Lucy H. Karnell, MA, Jatin P. Shah, MD; Stephan Ariyan, MD; G. Stephen Brown, MD; Willard E. Fee, MD; Andrew G. Glass, MD; HelmuthGoepfert, MD; Robert H. Ossoff, MD; Amy M. Fremgen, PhD Laryngoscope,1997; 107:1006-17.

ISSN (O): 2687-5365; ISSN (P): 2753-6556