Section: Otorhinolaryngology

Original Research Article

STAGING OF LARYNGEAL CANCER - ENDOSCOPY & RADIOLOGY VERSUS HISTOPATHOLOGY

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ABSTRACT

Background: Accurate staging of advanced laryngeal carcinoma is essential for selecting appropriate treatment modalities and improving oncological outcomes. Clinical endoscopy and radiological imaging are routinely used for staging; however, discrepancies with histopathological findings may influence treatment planning. The aim is to evaluate the accuracy of staging of advanced laryngeal cancer by comparing clinical endoscopic staging and radiological staging with histopathological staging in patients undergoing total laryngectomy. **Materials and Methods:** This prospective and retrospective study included 31 patients with advanced laryngeal carcinoma who underwent total laryngectomy between August 2011 and October 2013 at a tertiary care centre in Chennai. Clinical staging was performed using endoscopy, while radiological staging was done using computed tomography (CT). Histopathological staging of whole-organ serial sections served as the reference standard. Statistical analysis was performed using SPSS version 16.0 with significance set at $p<0.05$. **Results:** The mean age of patients was 56 years, and 96.8% were males. Transglottic tumours were the most common (45.2%), followed by supraglottic (32.3%) and glottic tumours (25.8%). Histopathology identified T4a disease in 74.2% cases, whereas clinical evaluation detected T4a disease in only 3.2% cases. Clinical staging underestimated tumour extent in 68% cases, while CT staging accurately assessed 67% cases, with underestimation and overestimation rates of 19% and 13%, respectively. CT demonstrated high sensitivity for anterior commissure involvement (100%) and paraglottic space involvement (88.8%). **Conclusion:** Clinical staging frequently underestimated advanced laryngeal tumours, particularly transglottic lesions. CT imaging showed superior staging accuracy and improved detection of tumour spread, thereby aiding appropriate surgical planning.

INTRODUCTION

Studies in surgical pathology with complete organ sectioning if the laryngectomy samples have significantly enhanced the understanding of the biological behaviour and patterns of the spread of laryngeal cancer.[1] Over the years, there have been evolution of a wide range of partial laryngectomy procedures that included the lesions occurring at different sites and of varied extent that were within the scope of the conservation laryngeal surgery.

Only about two decades ago, partial laryngectomy was considered only in the management of early laryngeal cancer. In the modern era, these procedures are also used in the management of advanced laryngeal cancers. Significant advancements in the imaging technologies, such as the computed tomography (CT) scan and the magnetic resonance imaging (MRI) have further contributed in the success of these procedures by accurately determining the extent of the laryngeal lesions. These advanced technologies provide detailed and accurate information about the tumour by evaluating the tumour depth and volume that are critical in selecting the treatment modality.[2]

Because of the technological immolations, it has now been possible to achieve the uniform dosing of the radiations that have made the radiation therapy a safe option for managing early lesions of the anterior commissure. In cases where radiation therapy has limited success, such as in the advanced lesions and large volume lesions, trials with hyper-

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fractionated treatment to achieve better control rates are progressing.[3]

The comparison of the final results of various treatment modalities has been possible because of the availability of internationally standardised TNM (Tumour, Nodes, Metastasis) staging accepted by both the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC). However, these standardised systems are evolving and have their own advantages and disadvantages.[4]

Despite the advancements in the surgical interventions and radiation therapy, a total laryngectomy generally followed by post-surgical radiation therapy is the only alternatives providing reasonable chance of cure in patients with advanced laryngeal lesions.

Treating the advanced lesions with radical radiation and reserving the salvage surgery in cases of treatment failure are reported to be effective in some of the cases; however, the cost generally compromised the cure rates, especially in cases of poor follow-up.[5]

In India, the population-based registry estimated the annual incidence of nearly 25,000 new cases of the laryngeal cancer. Supraglottic cancer is more than two times as common as glottic cancer. Marginal zone cancers (aryepiglottic fold and free border of the epiglottis) are more common than cancers of the false cord and the infrahyoid epiglottis.[6]

Analysis of the trends in the laryngeal cancer treatment in India reported two diverse trends. First, there is a heavy leaning and preference for the radiation therapy for all laryngeal cancers, whether early or advanced, as treatment with radiation therapy provides laryngeal preservation. Second, there is the practice of performing total laryngectomy for lesions that would have easily lent themselves to a voice-conserving surgical procedure.[7]

It is important to have a balance between the staging of the disease and the use of treatment modalities as the outcomes should be more focused on conserving the voice of the patient without compromising on the overall cure rate.

Aim

To evaluate the accuracy of staging of advanced laryngeal cancer performed in patients who underwent total laryngectomy by comparing staging by endoscopy and radiology with histopathology.

MATERIALS AND METHODS

This prospective and retrospective study was conducted in the tertiary care Rajiv Gandhi Government general hospital and Madras Medical College in the department of upgraded institute of otorhinolaryngology, Chennai, between August 2011 and October 2013. Ethical clearance was obtained from the Thesis and Ethical Committee of Madras Medical College prior to commencement of the study.

Study Population: Patients with advanced stages of laryngeal cancer presented to upgraded institute of otorhinolaryngology were evaluated.

Sample Size: The study included 31 cases of total laryngectomy.

Inclusion and Exclusion Criteria

The study included all cases of laryngeal cancer who underwent total laryngectomy with or without neck dissection/total or hemithyroidectomy, which includes radio recurrent cases and primary cases. Patients who underwent total laryngopharyngo-oesophagectomy and total laryngopharyngectomy were excluded.

Methods

Patients with advanced stages of laryngeal cancer who came to upgraded institute of otorhinolaryngology were evaluated. Supraglottic, transglottic, glottic and subglottic tumours, and recurrent tumours were staged clinically with help of endoscopy. Patients who are staged T3/T4a clinically were sent for radiological examination. CT is performed in all the cases. MRI was not done. Chest X-ray and ultrasound of the neck and abdomen were performed to evaluate the neck nodes.

Radiological staging of laryngeal cancer was also done. Patients with or without tracheostomy if fit for surgery underwent total laryngectomy with or without neck dissection. Site of tracheostomy (high, mid, low) if done were not taken in to study as variables. Most of the (clinical and radiologically) T3 cases with laryngectomy had opposite side of laryngeal involvement. Laryngectomy specimen for histopathology sent in every case after assessing tumour extension macroscopically.

Whole organ serial sections were studied in axial plane and final histopathological staging was assessed which was compared with radiological and clinical staging (AJCC, TNM).

Statistical Analysis

Distribution of the variables was assessed by Kolmogorov-Smirnov tests. Pearson's chi square was applied to all categorical variables. Fischer's Exact was applied wherever required. Chi square for trends was applied for ordinal data. A $p < 0.05$ was taken as significant. SPSS version16.0 was used for analysis.

RESULTS

The total number of total laryngectomy cases included in the study were 31. The mean age of the study population was 56 years. 96.8% of the study population were males and the remaining were females. The study reported one case of supraglottic tumour without neck dissection and recurrence in a female. There were a total of seven selective neck dissections. Of the total 31 cases analysed, 30 had total thyroidectomy. Of these 30 cases, one case of

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transglottic tumour was reported to have papillary cancer of thyroid infiltrating the larynx. The remaining one case was of hemithyroidectomy done without any tumour involvement. The total nodal recurrences with minimum 6 months follow-up were 7/31, of which 3/7 were supraglottic and the remaining were transglottic. Of the three nodal recurrences of the supraglottic tumour, one recurred even after the selective neck dissection on the same side and one recurred from an N1 neck that was not surgically managed.

Tumour Location Distribution

The study analysed the distribution of the tumour location among patients. The highest frequency was of the transglottic tumours that were reported in 45.2% (n=14) patients. The frequency of supraglottic tumours was 32.3% (n=10), followed by glottic tumours (25.8%; n=7). [Table 1]

Table 1: Tumour Location Distribution

Tumour Location	Number of Cases	Percentage
Supraglottic tumours	10	32.3%
Transglottic tumours	14	45.2%
Glottic tumours	7	25.8%

Clinical, Radiological, and Histopathological Evaluation

Clinical evaluation showed ventricular involvement in 24 cases (77.4%), anterior commissure involvement in 17 cases (54.8%), marginal zone involvement in 10 cases (32.3%), arytenoid involvement in 7 cases (22%), subglottic spread in 4 cases (12.9%), and extra-laryngeal spread in 1 case (3%). CT evaluation demonstrated paraglottic space involvement in 25 cases (80.6%), anterior commissure involvement in 19 cases (61.2%), thyroid cartilage invasion in 18 cases (58.1%), arytenoid involvement in 13 cases (41.9%), subglottic extension in 10 cases (32.3%), cricoid cartilage involvement in 4 cases, and extra-laryngeal spread in 2 cases (6.5%). Histopathology confirmed paraglottic space involvement in 27 cases (87.1%), thyroid cartilage invasion in 22 cases (71%), anterior commissure involvement in 19 cases (61.3%), subglottic extension in 17 cases (54.8%), arytenoid involvement in 8 cases (25.8%), cricoid cartilage involvement in 7 cases (22.6%), and extra-laryngeal spread in 1 case (3.2%), with no pre-epiglottic space involvement. Clinically, 96.8% cases were staged as T3, whereas CT and histopathology identified T4a disease in 71% and 74.2% cases, respectively. [Table 2]

Table 2: Clinical, Radiological, and Histopathological Evaluation

Clinical Evaluation	Radiological Evaluation (CT)	Histopathology (Comparing Variables with CT)
Arytenoids – 7 (22%)	Arytenoids – 13 (41.9%)	8 (25.8%)
Marginal zone – 10 (32.3%)	Anterior commissure – 19 (61.2%)	19 (61.3%)
Anterior commissure – 17 (54.8%)	Paraglottic space – 25 (80.6%)	27 (87.1%)
Ventricle – 24 (77.4%)	Preepiglottic space – 0	0
Subglottis – 4 (12.9%)	Subglottis – 10 (32.3%)	17 (54.8%)
Extra laryngeal spread – 1 (3%)	Extra laryngeal spread – 2 (6.5%)	1 (3.2%)
	Thyroid cartilage – 18 (58.1%)	22 (71%)
	Cricoid cartilage – 4 (41.9%)	7 (22.6%)
T3 – 30 (96.8%)	T3 – 9 (29%)	8 (25.8%)
T4a – 1 (3.2%)	T4a – 22 (71%)	23 (74.2%)
N0 – 30 (96.8%)	N0 – 30 (96.8%)	6/7 (85.7%)
N1 – 1 (3.2%)	N1 – 1 (3.2%)	1/7 (14.3%)
N2 – 0	N2 – 0	0

Comparative results of CT with histopathological findings

The CT sensitivity was highest for anterior commissure followed by paraglottic space, arytenoids, thyroid cartilage, subglottis, and cricoids. 30% of supraglottic tumours and 28.5% transglottic tumours with most of them with clinically N0 neck had nodal recurrences. [Table 3]

Table 3: CT Results

CT Findings	Sensitivity (%)	Specificity (%)	PPV (%)
Anterior commissure	100	66	82.6
Arytenoids	75	69.5	46
Thyroid cartilage	72.7	77.7	88.8
Cricoids	28	91	50
Subglottis	58.8	100	100
Paraglottic space	88.8	75	96
Preepiglottic space	No involvement in any case	100	50
Extra-laryngeal tissue spread	100	100	100

Underestimation of the clinical staging was reported in 21 of 31 cases (about 68%), while the accurate estimation was demonstrated in 10 cases (about 32%). None of the cases demonstrated overestimation. The most common location for underestimation were the transglottic tumours

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(n=11) followed by supraglottic and glottic tumours (n=5 each). [Table 4]

Table 4: Comparison of the Clinical Staging and Histopathological Staging

Tumour Location	Underestimation	Accurate Assessment	Overestimation
Supraglottic	5	5	Nil
Transglottic	11	3	Nil
Glottic	5	2	Nil
Total	21/31	10/31	Nil
Percentage	68%	32%	0%

Comparison of the Radiological Staging and Histopathological Staging

Radiological evaluation accurately staged about 68% (21/31) cases. Overestimation was reported in about 13% of the cases (4/31), while about 19% (6/31) cases demonstrated underestimation.

In the tumour types, highest rate of accurate radiological diagnosis was demonstrated in transglottic tumours (n=10), followed by supraglottic (n=8) and glottic tumours (n=3). Glottic tumours reported highest underestimation (n=3), followed by transglottic (n=2) and supraglottic tumours (n=1). The highest overestimation was reported in transglottic tumours (n=2) followed by supraglottic and glottic tumours (n=1 each). [Table 5]

Table 5: Comparison of the Radiological Staging and Histopathological Staging

Tumour Location	Underestimation	Accurate Assessment	Overestimation
Supraglottic	1	8	1
Transglottic	2	10	2
Glottic	3	3	1
Total	6	21	4
Percentage	19%	67%	13%

DISCUSSION

In our study, most patients were young, in their early in the present study accurate clinical staging performed in 10 out of 31 cases (33%). Accuracy of CT scan imaging overall in tumour staging in the study was 83%. These findings were quite similar to those reported by Pillsbury and Kirchner8, Katsantonis et al,[9] Vogl et al,[10] Sulfaro et al,[11] Thabet et al,[12] Becker et al,[13] Zbaren et al,[14] and Ferri et al.[15]

Pillsbury and Kirchner,[8] reported clinical and CT accuracy of 43% and 76%, respectively, Katsantonis et al,[9] 62% and 82% respectively, Vogl et al,[10] reported 54% and 84%, respectively, Sulfaro et al,[11] demonstrated 49% and 71%, respectively. Thabet et al,[12] reported 52% and 68% respectively, and Ferri et al,[15] reported 51% and 70%, respectively. Becker et al,[13] found 58% clinical accuracy, while Zbaren et al,[14] reported 57% clinical accuracy. Slight differences between the results of the prior studies and the current study might be because of the presence of large number of superficial and small mucosal tumours.

Evaluation of clinical tumour staging accuracy stratified by tumour location. In our study low accuracy in staging glottis tumours was 35%. Contrasting results were obtained by Thabet et al,[12] (85% accuracy), while Katsantonis et al,[9] reported 93% accuracy.

Lower accuracy (50%) in staging supraglottic tumours was reported in the current study. Thabet et al,[12] reported 45% accuracy, while Katsantonis et al,[9] reported 74% accuracy for supraglottic tumours.

In our series, the accuracy of clinical evaluation in staging transglottic tumours was 20%. Comparable results were obtained by Thabet et al,[12] (31%), while Katsantonis et al,[9] demonstrated contrasting results (45%).

In our series, high accuracy was reported in staging supraglottic, transglottic, and glottis tumours, i.e., 80%, 85%, and 85%, respectively in comparison to histopathological staging. Katsantonis et al,[9] reported high CT scan staging accuracy of 83% for supraglottic and 88% for transglottic tumours, while Thabet et al,[12] reported 68% for supraglottic and 88% for transglottic tumours. For staging glottic tumours, Katsantonis et al,[9] reported 74% accuracy, while Thabet et al,[12] reported 46% accuracy.

In the present series the clinical staging accuracy decreased from supraglottic to glottic to transglottic tumours, whereas CT scan staging became significantly more in transglottic and similar in glottis and supraglottic tumours. Similar results observed by Katsantonis et al,[9] Ferri et al,[15] and Thabet et al.[12]

In our study underestimation staging by clinical evaluation was 70%. Harrison,[16] reported clinical evaluation underestimation of the lesion extent in 40% of his patients. Pillsbury and Kirchner8 reported underestimation of 40% of all tumours in their series. Sulfaro et al,[11] reported underestimation for 51% of laryngeal tumours, while Thabet et al,[12] found 58% underestimation.

In our study radiological underestimation was 19% and overestimation was 13%. This is comparable to results obtained by Katsantonis et al,[9] and less than reported by Thabet et al.[12]

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In our study anterior commissure involvement was missed by endoscopy in 2 cases and all the 2 missed cases were diagnosed by CT. Sensitivity was 100% and specificity was 66% by CT imaging. The results were similar with Zbaren et al,[14] and Becker et al.[13]

CT sensitivity of paraglottic space in the current study was 88%. Results were similar and comparable with Kirchner et al.[17]

Pre-epiglottic space was not involved in any of the cases and CT was with 100% specificity. The results of this study were slightly better for these spaces than given in literature.

According to literature, CT accurately demonstrates gross cartilage invasion, but fails to detect minor invasion in many cases, as suggested by Becker et al,[13] and Zbaren et al.[14] The ability of CT to detect tumour invasion in cartilage varies with reported sensitivities of 46 to 66% and specificities of 84 to 94% in Becker et al,[13] and Zbaren et al.[14]

In our study, the sensitivity of thyroid cartilage was 72.7%, cricoid cartilage was 28%, and arytenoid cartilage was 75%. The irregular pattern of thyroid cartilage calcification does not match with tumour invasion or normal and pathology cartilage differentiated on basis of density values. Arytenoid and cricoid cartilage, however, can show a symmetric irregular sclerosis that suggest cartilage invasion. MRI shows non-ossified and ossified cartilage better than CT.

In the literature overall sensitivity of MRI in detection of neoplastic cartilage invasion was 89% and specificity between 82%-88%. Although MRI has better sensitivity it has low specificity due to severe inflammatory changes, fibrosis and extra medullary hematopoiesis within the cartilage that result in high false positive rate.

Limitations

Tracheostomy whether done or not was not taken into consideration. Tumour volume / thickness or depth was not assessed. There was a delay of 1- 2 weeks between surgery and CT evaluation.

CONCLUSION

The accuracy of clinical staging in our study of advanced stage laryngeal tumours decreased from supraglottic to glottic to transglottic tumours. The staging accuracy of sectional imaging is best in transglottic tumours and similar supraglottic tumours and glottic tumours. CT and MRI may improve and aid in reducing underestimation of cases.

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