CLINICOPATHOLOGICAL EVALUATION AND SURVIVAL RATE OF ADVANCED LARYNGEAL MALIGNANCY (T3, T4) MANAGED WITH WIDEFIELD TOTAL/NEAR TOTAL LARYNGECTOMY WITH NECK DISSECTION


ABSTRACT:

Objective: This is a study of clincopathological features and outcome of surgical management with 3 years survival pattern following total/near total laryngectomy in advanced III, IV squamous cell carcinoma larynx.

Methods: Retrospective observational study conducted between January 2000 to December 2013. with 87 patients of biopsy proved squamous cell carcinoma of larynx in advanced stage T3 & T4. Radio residual cases were also included in the study. 79 patients were treated surgically with Wide field total laryngectomy and 8 with near total laryngectomy along with bilateral neck dissection. Average follow up period was 15 months postoperative. All cases received post op radiotherapy except the radio-residual cases which were managed with salvage surgery alone. Chemotherapy was added in 7 cases due to extra-capsular metastasis. Data was analyzed using Kaplan Meier method of estimation to estimate the median survival time wherever applicable. Statistical analysis was carried out using STATA 13.

Results: The age range was 40 years to 85 years. The maximum incidence was found in 6th and 7th decade. 84% of the total patients were male. About 69/87 (79.31%) were smokers. 51/87 (58.6%) were T3, 36/87 (41.4%) were T4 lesions. 42/87 (48.27%) were N0, 30/87 (34.48%) were N1 and 15/87 (17.2%) were N2 lesions. Overall incidence of nodal metastasis was 51.7%. 71% of the supraglottic carcinomas had nodal metastasis at time of presentation and 44% of glottis tumors had nodal metastasis. There were no cases of distant metastasis. Topographical Distribution showed 46% were glottic lesions, 35.6% were supraglottic lesions and 18.4% were transglottic lesions. 22/87 (25.28%) were cases of post RT recurrence and the mean duration of recurrence was 21 months. 65/87 cases who underwent the surgical intervention received radiotherapy 3 to 4 weeks following surgery. 22/87 radio residual cases underwent salvage surgery. This study showed overall survival rate of 87.3% and disease specific survival rate at 3 years to be 86.7% for all stage III, IV laryngeal carcinoma who underwent wide field total laryngectomy/near total laryngectomy.

Conclusions: This study demonstrates the overall survival and 3 year specific disease free survival rates with Wide field total laryngectomy in patients with stage III, IV laryngeal carcinoma.

Keywords: Supraglottis, glottis, Wide field laryngectomy, Near total laryngectomy, laryngeal spread, bilateral arytenoid joint involvement, posterior commissure tumors, circumferential sub-glottic involvement.

INTRODUCTION

Laryngeal cancer is one of the most commonly encountered head & neck malignancy under a broader terminology that comprises of carcinoma of the supraglottis, glottis, and subglottis. Indian patients comprise 18% of the global laryngeal cancer burden. Most of the cases with advanced disease require Total/Neartotal laryngectomy as a surgical treatment option depending on the extent. Patients with advanced T3, T4 laryngeal cancer includes tumors with extra-
mucosal disease and subglottic extension with extensive
invasion of the cricoid cartilage.

Various surgical treatment options have been
available depending on the stage and site of laryngeal
cancer. These include vertical or horizontal partial
laryngectomy, near total laryngectomy, widefield total
laryngectomy and also the laser assisted organ
preserving surgeries. Owing to the propensity of
lymphatic metastasis seen in advanced laryngeal cancers
especially supraglottic ones, it is mandatory to perform
bilateral neck dissections in even N0 cases. Post-op
radiotherapy is advocated in all T3, T4 cases with
chemotherapy being added in cases with extra-capsular
spread, vascular spread, and positive margins. Surgical
salvage can be considered for patients who fail to
respond to radiation therapy or partial laryngectomy
procedures. Speech rehabilitation plays an important
role in the overall quality of life of patients. With the
upcoming better voice prosthesis and artificial larynx,
patients have been provided a better social life.

This study evaluates the clinicopathological features
and outcome of surgical management with survival
patterns following definitive treatment of laryngeal
cancers. Various factors were considered in this study
like age, sex distribution, predisposing factors,
locoregional and systemic extent of disease. The efficacy
of total/near total laryngectomy in advanced T3, T4
squamous cell carcinoma was assessed with the overall
and 3 year disease specific survival rate in these set of
patients. The aim of this study was to retrospectively
assess the clinical outcomes of total/near total
laryngectomy and its potential postoperative
complications. This knowledge would help in better
counseling of patients and improving quality of life.

MATERIALS AND METHODS:

This is a retrospective observation study carried
out from January 2000 to December 2013 in a tertiary
care centre. A total of 87 biopsy proven squamous cell
carcinoma of larynx of advanced T3 & T4 stage who
opted for total/ near total laryngectomy as primary
modality of treatment were taken up for study. Twenty
two cases of radio-residual/recurrent laryngeal cancer
treated with total laryngectomy with a curative intent
were also included in the study. Complete clinical
evaluation of patients was done with detailed history,
personal habits, direct Laryngoscopy with preoperative
assessment of extent of the growth and staging. Contrast
enhanced CT neck and thorax was done in all cases to
evaluate the extent of primary and for loco-regional
distant metastasis. Direct telescopy of larynx carried
out using 70degree endoscope in all patients to evaluate
the larynx. Microlaryngoscopy was preformed to
further access the extent of growth involving larynx
and to perform biopsy. 79 patients were managed
surgically with widefield total laryngectomy as there
was involvement of both arytenoid/ gross subglottic
extension/ involvement of interarytenod region while
8 suitable cases underwent near-total laryngectomy
along with bilateral modified neck dissection. In
addition to laryngectomy, ipsilateral thyroidectomy
was performed in 48 individuals. T3 cases involving
paraglotic spread with mobile vocal cords treated with
trans-oral microendoscopic KTP-532 laser surgery were
excluded from this study. Laryngeal cancer extending
to hypopharynx that required total laryngo-
pharyngectomy / laryngo-pharyngo-esophagectomy
were also excluded from the study. All the cases treated
with surgery as primary modality, received post
operative radiotherapy (65-70 gray in multiple
fractions). The radio-residual/ recurrence cases were
managed with salvage wide field total laryngectomy
alone. Locoregional radiotherapy usually commenced
within 4-6 weeks after definitive surgery except when
wound healing complications occurred. Chemotherapy
with Cisplatin on day 1, 22 and 43 was added in 7 cases
due to extra-capsular metastasis. Minimum follow-up
period of fifteen months was standardized. At each
post-op visit, endoscopy of larynx and other
radiological investigations were carried out to assess for
loco-regional recurrence and distant metastasis.

SURGICAL TECHNIQUE:

Patient is prepared under general anesthesia after
procuring written and informed consent. Arterial and
venous line secured and urinary catheter inserted. An
apron flap incision is planned extending from both
mastoid processes to approximately 2 fingerbreadths
above the level of the sternal notch. A planned U shaped
incision is given in all cases with lateral limit till the
posterior border of sternocleidomastoid muscle. A
superior subplatysmal flap is then elevated till the hyoid
bone. A subplatysmal flap is also raised inferiorly to
the level of the sternum and clavicles on both sides. The
skin flaps are secured using or sutures and rubber bands.
The superficial layer of the deep cervical fascia overlying
the sternocleidomastoid muscle is incised along its anterior margin. Dissection of the “outer and deep tunnels” is performed. The sternocleidomastoid muscle is laterally retracted to identify the contents of the carotid sheath. Dissection is carried out bluntly between the laryngotracheal complex and the great vessels on both sides. This frees the medial contents of the neck from the surrounding tissues. Meticulous neck dissection is carried out in all cases resecting the lymph nodes and fibro-fatty tissue from levels II, III, IV, and V on both sides depending on the case. Resection of sternocleidomastoid and internal jugular vein and preservation of spinal accessory was done in all the cases that undergone modified neck dissection. The strap muscles are then divided at the level of the sternal notch. Dissection proceeds superiorly until the thyroid gland is identified. The thyroid lobe ipsilateral to the tumor is resected along with the specimen while the contralateral lobes along with parathyroid glands are preserved with their blood supply in selected cases. Diathermy is used to skeletonize the hyoid bone. In total laryngectomy, the lateral aspects of the hyoid are then dissected and care is taken not to injure either the lingual artery or hypoglossal nerve. The opposite thyroid ala is identified and retracted medially. The inferior constrictor muscles are divided off of the thyroid ala, and the underlying pyriform mucosa is bluntly dissected off of the undersurface of the thyroid cartilage. A similar procedure is carried on the right side. The trachea is entered transversely between the second and third tracheal cartilages. An angled cut is then carried out superiorly and posteriorly using Mayo scissors beveling the tracheotomy incision. In case the patient had a prior tracheostomy, a new stoma is created by including the old stoma in the patient. The endotracheal tube is then slowly removed, and an armored flexo-metallic tube placed in the tracheal stump. An incision is made directly onto pharynx at the level of vallecula contralateral to the primary tumor. The epiglottis is then identified through the pharyngeal incision and grasped with an Allis forceps. Under direct visualization, mucosal cuts are given to resect the tumor with 1cm margin of normal appearing mucosa and also to preserve enough mucosa for later closure. In near total laryngectomy, the middle 1/3rd of contralateral thyroid cartilage is resected. The larynx is entered through vallecula on the healthier side and cuts are given in such a way that one functional cricoarytenoid unit is retained along with superior laryngeal nerve of contralateral side if not diseased. It is followed by creation of a cricotracheal shunt. The shunt was closed in a layer over a 14F red rubber catheter. Ryle’s tube passed under vision. The pharyngeal mucosa was closed in layers. The entire specimen is handed off for histopathological examination. Cricopharyngeal myotomy is carried out. Pharyngeal closure is done in ‘L’ fashion. Stomal suturing is done by creating a window on the anterior tracheal wall and the incision site is closed in layers. A secondary TEP was performed to facilitate speech, minimum three months after completion of RT. Primary TEP was performed in five cases only due to financial factors.

**Observation and Results:**

The age range was 40 to 85 years. The maximum incidence was found in 6th and 7th decade. There was predominant male preponderance with 84% of the total patients being male. About 69/87 (79.31%) were smokers and more than 60% were beedi smokers consistent with other studies.

51/87 (58.6%) were T3, 36/87(41.4%) were T4 lesions. 42/87(48.27%) were N0, 30/87(34.48%) were N1 and 15/87(17.2%) were N2 lesions. Topographical distribution showed 46% were glottic lesions, 35.6% were supraglottic lesions and 18.4% transglottic lesions. Overall incidence of nodal metastasis was 51.7. 71% of the supraglottic carcinomas and 44% of glottis tumors had nodal metastasis at time of presentation. Of the T4 cases, 16 had tumor with thyroid cartilage invasion while 12 had extension to base of tongue and vallecula. Eight cases had extra laryngeal soft tissue involvement.

Histopathological grading showed that 64/87 (73.56%) of cases were moderately differentiated, 18/87 (20.68%) well differentiated and 5/87 (5.68%) poorly differentiated. 5 radio-residual cases were initially well differentiated while post surgery histopathology was suggestive of moderately differentiated squamous cell carcinoma.

22/87 (25.28%) had received primary radiotherapy and the mean duration of recurrence was 21 months. 23/87 (26.43%) of cases underwent preoperative tracheostomy of which 16/23 (69.5%) of these were transglottic tumors, 3/23 (13.04%) were glottic tumors and 4/23 (17.3%) was supraglottic tumors.

79/87 cases underwent widefield total laryngectomy while 8/87 cases were managed with near total laryngectomy along with bilateral modified neck
dissection. Post operative adjuvant radiotherapy was provided 2 to 3 weeks following surgery to all patients except the (22/87) radio-residual cases that underwent salvage surgery alone. Chemotherapy was added in 7 cases due to extra-capsular spread of cancer.

We had an overall 11 cases with locoregional recurrence during the study period with an average duration of recurrence being 34 months. 4/11 were the radio residual cases which were treated with salvage surgery. 53 patients were followed for a period of 3 years or more out of which 7 patients had locoregional recurrence. 4 cases presented with recurrence after 3 years of surgery. All cases (8/87) of near total laryngectomy were disease free at their last follow up.

Pattern of Complication-25/87(28.7%) of cases developed post surgical complications. Most common early complication noted was wound infection (29%) and pharyngo-cutaneous fistula 13%, chyle leak (7%) and pleural effusion (4%). The late complication were 4% persistent dysphagia, 13% had stomal narrowing and 12 patients developed hypothyroidism requiring oral thyroxin supplementation. Hypocalcaemia was noted in 15 cases treated with calcium tablets. Three patients died during follow up 1 due to carotid blow out and 2 of MI.

All these case of advanced T3, T4 laryngeal cancer were motivated for speech rehabilitation. 52/87 cases underwent secondary tracheo-esophageal puncture and insertion of Blom Singer prosthesis which was done 8 months to 1 year post surgery. 6 patients could afford an artificial larynx. Rest of cases were trained for esophageal speech.

This study showed overall survival rate of 87.3% and that at 3 years to be 86.7% for all T3,T4 laryngeal carcinoma who underwent widefield total/ Near total laryngectomy. 53 patients were followed up for a period of 3 years or more with 46 of them surviving without disease. The overall median survival time was 58 months and the 95% Confidence Interval (CI) ranged between 52 to 64 months. Similarly, for the specific 53 patients the mean survival time was 55 months with 95% CI (51.61, 57.67). These estimates were calculated based on the Kaplan Meier method. Figure 3a displays the Kaplan Meier (KM) curve for all patients who underwent widefield total/ near total laryngectomy and Figure 3b displays the KM curve for those patients who were followed up for 3 years or more. Stage specific survival showed 3year survival rate 27/31(87%) for T3 and (17/ 22)77.22% for T4 lesions.

**DISCUSSION :**

Laryngeal cancer is a common treatable cancer among all head and neck malignancies presenting with early symptoms especially glottic cancers. The peak incidence is noted in the 5th and 6th decade. There is predominant male preponderance as noticed in the study. Our study also throws light on the affinity between smoking and laryngeal cancers with 45% of cases consuming alcohol which is also an additive risk factor. The presenting symptoms included hoarseness (55%), neck swelling (30%), foreign body sensation in throat (25%), referred otalgia (23%) and dysphagia (20%) with overlapping features. 10 patients presented with stridor and underwent emergency tracheostomy in our study.

The two most important adverse prognostic factors for laryngeal cancers include increasing tumor (T) stage and nodal (N) stage and comorbidities of the patient. Cases having more than 4 (with 2 being cardiovascular) comorbidities have a poorer prognosis. Other prognostic factors usually include age, performance status, male sex and features like tumor grade, extra laryngeal spread and depth of invasion. Cases with positive neck nodes have poor survival rated as compared to their counterparts as seen in our study. Prognosis for small laryngeal cancers that have not spread to lymph nodes is very good, with cure rates of 75% to 95% depending on the site, tumor bulk, and degree of infiltration.

We have obtained a 3-year specific survival rate of 86.7% which is noticeable and comparable if not better to other studies of recent times. A similar study by Young et al showed a survival rate of 85% at 25 months follow-up in 20 salvage cases. Stoekli et al. reported that the 5-year Disease specific survival (DSS) for 39 cases after salvage total laryngectomy was 0.63, with mortality rate of 49%. In contrast, the overall mortality after salvage surgery in this study was 65%. The overall 5-year DSS was poorer in a cohort of 83 Stage IV laryngeal squamous cell carcinoma studied by Spector et al. with survival rate of about 45%. Leong et al noted an overall mean survival period following total laryngectomy to be 42.4 months. Lilly-Tariah et al. found a recurrence rate of 47.5% within 9 months of total laryngectomy without a follow-up radiotherapy, in middle belt of Nigeria; they found
this operation to be unsatisfactory due to lack of proper follow-up radiotherapy.

The patients who received primary surgery followed by radiotherapy had better survival and quality of life as compared to the radio-residual/recurrence cases that underwent salvage surgery which is consistent with observations by Yuen et al. Spector et al. described that the chance of distant metastases developing was higher in the patients presenting with advanced-stage (T4) primary disease as seen in our study. Owing to better local and regional control of the primary malignancy, it is more likely that morbidity in these patients arise from distant metastases and radiation related changes.

The incidence of pharyngocutaneous fistula has also been reported to be dependent on pharyngeal closure technique and post-op radiotherapy. Sarker et al. reported a fistula rate of 34.7% of which 65% had received previous radiotherapy. Johansen et al. reported an overall fistula rate of 32%. It was 13% in our study all of which were managed conservatively.

Early suspicion, adequate radiological evaluation, Microlaryngoscopy and early tissue biopsy with prompt treatment are footholds of laryngeal cancer management. Voice preservation by near total laryngectomy was carried out in 8 cases in our study with roaring success. The pre-requisites for selecting a patient for this surgical procedure are:
1. Inter-arytenoid area should be disease free
2. No extension to cricoid cartilage
3. One crico-arytenoid unit should be free and functional.

All patients in our study underwent bilateral modified neck dissection of various types according to the clinical case scenario. Management of neck for all patients improves the prognosis of laryngeal cancer patients. Patients who have cancer recurrence after total laryngectomy for laryngeal cancer have poor prognosis and absolute lack of treatment options, particularly when radiotherapy already has been applied. The most important aim of regular follow-up visits after treatment for laryngeal cancer is the early detection of asymptomatic local or regional failure. Endoscopy of larynx with metastatic work up along thyroid and calcium levels were the basic protocols followed during each follow up. Our study emphasizes the role of early detection of laryngeal cancers and the
need for stringent selection criteria while choosing the surgical technique for laryngeal cancer patients.

CONCLUSION:

The present series comprises of 87 cases of which supraglottic, glottis, transglottic constituted 46%, 35.6% and 18.4% respectively. It puts forward the better survival rates of patients who have undergone total/near total laryngectomy with neck dissection for laryngeal cancers at our institute. Adequate post op management with radiotherapy, speech rehabilitation and counselling and psychological support go a long way in reducing the morbidity of patients. Further follow-up of these patients is in progress and long-term efficacy and complications of this surgical technique needs to be evaluated.

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(a) Competing interests/Interests of Conflict-None
(b) Sponsorships - None
(c) Funding - None
(d) No financial disclosures

REFERENCES: