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MAIN ARTICLE

Surgical treatment of glottic cancer: retrospective analysis of 192 cases in a multidisciplinary tertiary care centre in Pune, India

D S KELKAR[1], S S GANDHI[1], G A OKA[2]

[1]*Division of Surgical Oncology, and* [2]*Department of Research, Deenanath Mangeshkar Hospital and Research Centre, Pune, India*

Abstract

Objectives: A multidisciplinary team approach is required for the preservation of voice and appropriate management of glottic cancer. This study aimed to investigate the outcomes of surgically treated glottic cancers of all stages. All aspects of surgical management, such as laser cordectomy, partial laryngectomy, total laryngectomy with voice prosthesis, and salvage laryngectomy, conducted at a single tertiary care institute in India, were reviewed.

Method: A retrospective analysis of hospital records was performed for 192 glottic cancer patients who were surgically treated between 2003 and 2007.

Results: Patients with tumour stages 1 or 2 glottic cancer treated with laser cordectomy had a local control rate of 85 per cent and five-year survival rate of 98.6 per cent. The findings suggest that the number of partial laryngectomies performed for stage 3 tumours is declining. Patients with a tumour stage 3 lesion with a fixed hemilarynx or a tumour stage 4 lesion, treated with total laryngectomy, were found to have a five-year survival rate of 61.6 per cent. Nodal status was significantly associated with five-year survival rate.

Conclusion: Surgery offers a viable five-year survival rate in glottic cancer patients.

Key words: Laryngectomy; Laser; Adjuvant Radiotherapy; Voice Prosthesis

Introduction

India has a population of 1.2 billion (according to the 2011 census[1]). Approximately 68.7 per cent of the population are from rural areas. It is very difficult for such patients to access tertiary healthcare for cancer treatment because of factors such as poor infrastructure and socio-economic conditions.

Indian cancer registries are of 2 types; namely, hospital-based registries covering 6 metropolitan cities and 22 population-based registries covering 7.45 per cent of the population. Although there are some shortcomings of the approach, the same registries are used for projections of cancer incidence and treatment (National Cancer Registry Programme, Indian Council of Medical Research[2]). In the year 2010, the total number of cancer cases in India was estimated to be 979 786, out of which 28 200 (2.8 per cent) were cases of glottic cancer. To cater to this huge burden of glottic cancer, India needs many more multidisciplinary treatment centres. In India, there are 33 carbon dioxide (CO_2) laser centres (as of 2013) (5 in Delhi, 8 in Mumbai, 3 in Pune, 2 in Kolkata, 2 in Bangalore, 2 in Lucknow, 2 in Chandigarh and 9 in other cities; Lumenis Laser Company, unpublished data), 301 linear accelerator radiation centres providing chemoradiation (75 in North India, 116 in South India, 80 in West India and 30 in East India[3]) and about 1500 surgical centres where laryngeal cancer surgical procedures are performed.

Hence, there are 33 centres in India that offer comprehensive and multidisciplinary care for the management of glottic cancer. The Deenanath Mangeshkar Hospital and Research Centre is a 1000-bedded, non-profit, non-government hospital, which provides multidisciplinary services such as: videostroboscopy, a high-speed camera, a Lumenis CO_2 laser with UltraPulse® technology, a surgical oncology unit, a linear accelerator radiation unit with intensity-modulated radiation therapy (RT), image-guided RT, speech therapy, and voice rehabilitation.

The present retrospective study focuses on the outcomes of 192 patients with glottic cancers who were surgically treated in the Deenanath Mangeshkar Hospital and Research Centre between 2003 and 2007.

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Materials and methods

The Division of Oncology at the Deenanath Mangeshkar Hospital and Research Centre in India treated 253 glottic cancer patients between 2003 and 2007 using surgery and chemoradiation. Our study presents a retrospective analysis of the hospital records for the 192 patients who underwent surgical treatment, focusing on their post-operative outcomes and 5-year survival rates.

Ethical consideration

This study was approved by the institutional ethics committee.

Statistical methods

Data were analysed using SPSS® software version 20. Kaplan–Meier analysis was used to calculate cumulative probability of survival. The chi-square test was used to investigate associations between variables.

Results

A total of 253 glottic cancer patients were treated at the institute between 2003 and 2007. There were 233 males and 20 females, with ages ranging from 36 to 76 years. Of the 192 who were surgically treated, 120 (62.5 per cent) were smokers, 172 (89.5 per cent) were tobacco chewers and 65 (33.8 per cent) were drinkers; tobacco and alcohol consumption are known causative agents for glottic cancer.[4]

The distribution of the 253 glottic cancer patients according to disease stage (determined according to the International Union Against Cancer tumour–node–metastasis classification[5]) and treatment received is shown in Table I. All patients underwent stroboscopy, direct laryngoscopy, biopsy, computed tomography (CT) and a pre-surgical fitness evaluation.

Tumour stage 1 or 2

Seventy-four patients (64 males and 10 females) had early glottic cancer (tumour (T) stages 1 or 2 vocal fold lesions). Of these, 63 (85 per cent) had unilateral vocal fold involvement and 11 (15 per cent) had bilateral vocal fold involvement.

Once the diagnosis had been confirmed (on the basis of clinical, stroboscopic and CT scan staging and biopsy findings), all patients were counselled about the pros and cons of laser surgery and RT. There was a clear preference for undergoing laser surgery, which offered equitable results and involved a shorter hospital stay. This can be explained by the fact that 80 per cent of the patients were from outside of Pune city and the cost for both treatments (laser surgery and RT) was comparable.

Surgery was performed by a single surgeon using a Lumenis CO_2 UltraPulse laser with a Zeiss microscope. The types of cordectomies performed, categorised based on the European Laryngological Society guidelines (2000),[6] are detailed in Table II. Partial excision of the false cord was performed for better exposure in type III and IV cordectomies. The specimens were fixed on a paraffin block and sent for histopathological examination, with margins and bases labelled as per hospital protocol.

On histopathological examination, 60 (81 per cent) of the 74 T_1 and T_2 stage patients were found to have tumour-free margins; margins were positive in 14 patients (19 per cent). Of these 14 patients, 8 underwent

TABLE I
TREATMENT TYPE ACCORDING TO DISEASE STAGE*

Disease stage	Surgical procedures†		Post-surgery RT‡ (*n*)	RT alone** (*n*)	CRT§ (*n*)
	Type	Frequency (*n* (%))			
T_1 or T_2	Laser cordectomy	74 (38.5)	8	30 (55 Gy)	–
T_3 lesion with mobile arytenoid	Partial laryngectomy	3 (1.5)	1	–	11
T_3 lesion with fixed hemilarynx, or T_4 lesion	Total laryngectomy	107 (55.7)	35	–	20 (70 Gy)
Post-RT salvage	Total laryngectomy	8 (4.1)	–	–	–

*Total *n* = 253; †*n* = 192; ‡*n* = 44; **n* = 30; §*n* = 31. RT = radiation therapy; CRT = chemoradiation therapy; T = tumour stage

TABLE II
CORDECTOMY TYPE ACCORDING TO DISEASE STAGE*

Stage	Type of cordectomy (*n*)								Total (*n*)
	I	II	III	IV	Va	Vb	Vc	Vd	
CIS	6	–	–	–	–	–	–	–	6
T_{1a}	–	20	19	9	5	–	–	–	53
T_{1b}	–	1	–	–	9	–	–	–	10
T_2	–	–	–	–	–	1	1	3	5

*Total *n* = 74. CIS = carcinoma in situ; T = tumour stage

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TABLE III
RECURRENCES ACCORDING TO MARGIN INVOLVEMENT, LESION SITE AND TUMOUR GRADE*

Parameter	Total (*n*)	Recurrences† (*n* (%))
Margins‡		
– Negative	60	12 (20)
– Initially positive but resected	8	1 (12.5)
– Positive but monitored	6	0 (0)
Site**		
– Anterior third	25	11 (44)
– Middle third	47	2 (4.26)
– Posterior third	2	0 (0)
Tumour grade§		
– Well differentiated	35	3 (8.57)
– Moderately differentiated	34	8 (23.5)
– Poorly differentiated	5	2 (40)

*Total $n = 74$; †$n = 13$. ‡Chi-square = 1.39; $p = 0.23$. **Chi-square = 28.22; $p < 0.000$. §Chi-square = 3.28; $p = 0.19$

further surgery to attain tumour-free margins and 6 were closely monitored having refused re-operation.

All patients were discharged after 48 hours and followed up for a minimum of 5 years. This consisted of visits at three-monthly intervals for the first year and at six-monthly intervals for the next four years. The patients were subjected to microlaryngoscopy and biopsy in the presence of suspicious granulation or suspicious appearance at the operated site during follow up. There were two patients who came from outside of India; these patients did not visit the hospital for follow up, but were alive and well on telephonic follow up.

Thirteen (17.5 per cent) of the patients had local recurrence during the follow-up period (Table III). The time of recurrence ranged from three months to two years. Of these 13 patients, 5 underwent a second laser excision, 1 of whom suffered a second recurrence and underwent total laryngectomy. The remaining eight patients received RT; one of these patients suffered a second inoperable recurrence and died after three years.

Table III also depicts the recurrences according to lesion site and tumour grade. Most recurrences occurred in those with lesions involving the anterior third of the vocal fold (44 per cent). It is clear from Table III that the tumour site was statistically significantly associated with local recurrence, while other factors, such as resection margins and tumour grade, were not statistically significant.

The overall five-year survival rate for early glottic cancer patients was 98.6 per cent. The local control rate for cases treated with laser excision alone, including the five laser surgical procedures conducted for recurrences, was 85 per cent. The laryngeal preservation rate was 98 per cent.

Tumour stage 3 with mobile arytenoid

All 14 patients with T_3 lesions, with no paraglottic space spread and no subglottic extension, who were found to be fit (as per their cardiorespiratory status), were offered a choice between vertical partial laryngectomy and chemoradiation. These patients had been counselled by surgeons and radiotherapists about the risks, pros and cons, and survival statistics of both modalities.

Three (21.4 per cent) of the patients underwent vertical partial laryngectomy and 11 (78.6 per cent) chose chemoradiation. Of the three partial laryngectomy patients, one had positive margins and was given post-operative RT. He subsequently developed regional recurrence and died of disease after two years. The remaining two patients were alive and well after five years.

Tumour stage 3 with fixed hemilarynx, or tumour stage 4

All 127 patients in this group were thoroughly counselled and offered an informed choice between total laryngectomy with voice prosthesis and chemoradiation.

A total of 118 patients (117 males and 1 female) underwent laryngectomy (Table I). Of these, 3 underwent partial laryngectomy and 115 underwent total laryngectomy. The total laryngectomy patients underwent 1 of 3 types of neck dissection, depending on node status: 69 clinically node-negative patients underwent selective lateral, compartmental nodal clearance on both sides (levels II, III and IV); 38 patients with clinically or radiologically involved nodes on 1 side underwent radical neck dissection and type 3 modified neck dissection on the other side; and 8 salvage laryngectomy patients underwent selective lateral, compartmental nodal clearance bilaterally.

All primary (non-irradiated) laryngectomy patients had a Provox2™ voice prosthesis fitted intra-operatively. Pharyngeal closure was performed in two layers, in a single vertical line. Operative time for primary laryngectomy ranged from 2 hours to 3 hours and 30 minutes, with an average operative time of 2 hours and 30 minutes. All primary laryngectomy patients were discharged on the 7th post-operative day with a nasogastric feeding tube. Oral feeding was started after two weeks.

Average blood loss in the primary laryngectomy patients was 150 cc. There were no peri-operative (30-day) mortalities. One patient had secondary haemorrhage on the second post-operative day and was managed by exploration and haemostasis. Pharyngocutaneous fistulae occurred in 6 out of 107 patients who underwent total laryngectomy (5.6 per cent). This healed spontaneously within three weeks and none of the affected patients required exploration, resuturing or flap repair. Table IV depicts the morbidities associated with primary laryngectomy and adjuvant RT.

Although adjuvant RT is necessary in advanced glottic cancer cases, the combination of radiation with total laryngectomy leads to considerable adverse events, as shown in Table IV.

Salvage laryngectomies were performed on eight patients who were referred to our centre with

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TABLE IV
MORBIDITIES ASSOCIATED WITH PRIMARY LARYNGECTOMY, ADJUVANT RT AND SALVAGE LARYNGECTOMY

Morbidity	Frequency (*n* (%))
Primary laryngectomy*	
– Pharyngocutaneous fistula	6 (5.6)
– Haemorrhage	1 (0.93)
– Prosthesis problems (migration, blockage)	3 (2.8)
– Tracheostoma narrowing	5 (4.7)
Adjuvant RT†	
– Stricture requiring dilatation (dysphagia)	6 (17)
– Xerostomia	25 (71)
– Loss of taste	5 (14.2)
– Oedema	16 (45.7)
– Skin fibrosis	9 (25.7)
– Tracheostoma narrowing	8 (22.8)
– Prosthesis problems (migration, leak)	7 (20)
Salvage laryngectomy‡	
– Pharyngocutaneous fistula	2 (25)
– Haemorrhage	2 (25)
– Skin flap necrosis	1 (12.5)
– Tracheostoma narrowing	3 (37.5)
– Wound sepsis	2 (25)

*n = 107; †n = 35; ‡n = 8. RT = radiation therapy

post-radiation recurrence. Average operating time was 3 hours. Average blood loss was 150 cc. None of these patients underwent primary placement of the voice prosthesis. The prosthesis was fitted after three months as a second-stage procedure. Percutaneous endoscopic gastrostomy was used for feeding for all patients; oral feeding was commenced after three weeks. Two out of eight patients (25 per cent) suffered a pharyngocutaneous fistulae: one patient died on the 15th day as a result of sepsis and secondary haemorrhage, and the other experienced spontaneous healing within one month. Morbidities after salvage laryngectomies were as shown in Table IV.

Survival and prognosis

All patients were followed for a minimum of five years after surgery. Follow-up visits took place at three-monthly intervals for the first year, followed by six-monthly intervals for the next four years. Oesophagoscopy and neck ultrasonography were performed every year, and CT scans were conducted in cases of suspected recurrence. After 5 years, 66 primary laryngectomy patients and 4 salvage laryngectomy patients were alive and well. Two patients were lost to follow up.

The curve for cumulative probability of survival for 107 patients who underwent total laryngectomy shows a survival of 61.6 per cent, as seen in Figure 1.

Prognostic factors

An independent analysis of individual prognostic factors was carried out in relation to the survival of advanced glottic cancer patients. As seen in Table V, nodal status was found to be a highly statistically significant factor for survival at the end of five years.

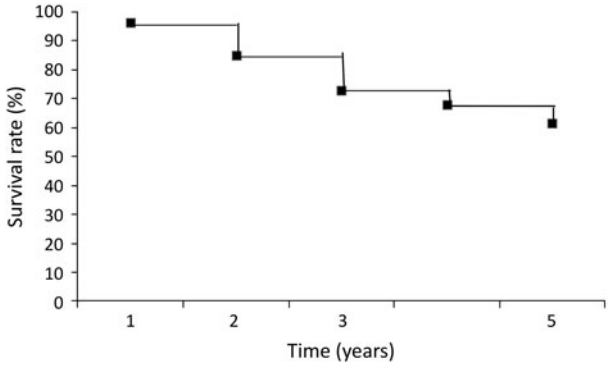

FIG. 1
Cumulative probability of survival (Kaplan–Meier curve) for patients who underwent total laryngectomy.

TABLE V
PROGNOSIS BY TNM STAGE, TUMOUR STAGE, NODAL STATUS AND TUMOUR GRADE*

Parameter	Total (*n*)	Survivors at 5 years† (*n* (%))
TNM stage – primary laryngectomy†		
– T_3 (fixed hemilarynx), N_0	20	16 (80)
– T_3 (fixed hemilarynx), N_1	9	4 (44.4)
– T_4 (cartilage, thyroid, soft tissue)	49	36 (73.4)
– T_4N_1	22	9 (40.9)
– T_4N_2	7	1 (14.2)
Tumour (T) stage – primary laryngectomy‡		
– T_3 (fixed hemilarynx)	20	14 (70)
– T_4	87	52 (59.7)
Nodal status**		
– N_0	69	52 (75.3)
– N_1	31	13 (41.9)
– N_2	7	1 (14.2)
Tumour grade§		
– Well differentiated	20	15 (75)
– Moderately differentiated	65	40 (61.5)
– Poorly differentiated	22	11 (50)

*Total n = 107. †Chi-square = 17.52; $p < 0.001$. ‡Chi-square = 0.72; $p = 0.39$. **Chi-square = 17.22; $p < 0.000$. §Chi-square = 2.77; $p = 0.25$. TNM = tumour–node–metastasis

No significant association was found between survival and tumour grade. There was a significant association between survival and tumour stage.

Discussion

While we believe that laser cordectomy offers better phonological correction (voice quality)[7,8] than radiotherapy, some studies have shown no advantage of laser over RT.[9,10] The local control rates and laryngeal preservation rates are comparable with those of European studies.[8,11,12] Higher recurrence rates were noted for lesions of the anterior third of the vocal fold and poorly differentiated tumours. Similar findings were observed by Peretti *et al*.[8]

It is currently unclear whether we can improve local control rates by conducting wider margin resection or if the addition of radiotherapy is necessary; these issues

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need to be investigated further. Many studies, including ours, have shown that margins of resection have no association with disease-free survival.[8,12,13] This is because of the occurrence of photocoagulation at the resection base, which may be responsible for the destruction of the tumour cells. Surgeons may carry out a narrower resection so as to avoid trauma to the anterior commissure, adopting an over-cautious approach.

For T_3 lesions with a mobile arytenoid, we have conducted fewer partial laryngectomies in recent years. With improvements in chemoradiation, patients are increasingly choosing this treatment over surgery.[14,15]

For T_3 lesions with a fixed hemilarynx and T_4 lesions, surgical results with total laryngectomy in terms of five-year survival rates (of 61.6 per cent) are comparable to those reported by other centres in the world.[16–18] Every patient in our study who underwent total laryngectomy had undergone neck dissection. Although some authors have recommended simply observing clinically negative neck nodes,[19–21] in the present study we found that 27 out of 69 node-negative patients (39 per cent) had occult neck node positivity. We therefore feel it is better to perform bilateral, selective lateral node dissection, which is not associated with significant morbidity.[22] In India, the patient compliance for follow up is highly irregular. Therefore, elective neck dissection is performed.

Post-operative radiation was administered to all patients who had cartilage invasion, soft tissue invasion or nodal positivity. Although it is known that surgery followed by radiotherapy improves survival,[23,24] there were considerable side effects in patients that underwent radiation. Repeat dilatation was required for 17 per cent of patients who had tight pharyngeal stricture following radiotherapy.

Salvage laryngectomies are associated with a higher incidence of mortality and morbidity. Morbidities can be minimised by delaying oral feeding, avoiding primary prosthesis placement and reducing the use of electrocautery during surgery.

- **Laser cordectomy has shifted choice of treatment in favour of surgery in tumour (T) stages 1 and 2 glottic cancer cases**
- **Lesions involving the anterior third of the vocal fold have a higher chance of local recurrence after laser cordectomy**
- **The number of partial laryngectomies performed is declining because of higher acceptance of chemoradiation, which preserves the larynx**
- **Salvage laryngectomy is associated with a higher incidence of morbidity**
- **In this study, five-year survival rates were 98.6 per cent for T_1 and T_2 lesions, and 61.6 per cent for T_3 and T_4 lesions treated with total laryngectomy**

With regard to recommendations for future studies, comparison of therapeutic outcomes would be useful; specifically, comparison of laser cordectomy versus RT outcomes in T_1 and T_2 glottic cancer cases,[25] and comparison of chemoradiation versus total laryngectomy outcomes in T_3 and T_4 glottic cancer cases.

Conclusion

For early glottic cancer, laser cordectomy, which is a safe, one-stage procedure, provides good local control and excellent five-year survival rates. There is increasing acceptance of chemoradiation used in cases of T_3 glottic cancer with a mobile arytenoid and, hence, the number of partial laryngectomies performed has declined. For T_4 or node-positive advanced glottic cancer, total laryngectomy (with or without radiation) has given a five-year survival rate of 61.6 per cent in our centre. Salvage laryngectomies were associated with a higher incidence of morbidity.

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Address for correspondence:
Dr D S Kelkar,
Division of Surgical Oncology,
Deenanath Mangeshkar Hospital,
Erandawane,
Pune – 411004,
MS, India

E-mail: dskelkar@gmail.com

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