

Analysis of oncological and functional failures following near-total laryngectomy

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Abstract

Objective: To improve case selection for near-total laryngectomy by identifying the causes of poor oncological and functional outcomes.

Methods: Analysis of prospectively accrued data for 28 consecutive cases of near-total laryngectomy undertaken between 1996 and 2005 at a tertiary care centre. We analysed the impact of tumour extent and location, patient physiological status, and surgical technique on disease-free survival and on functional outcome.

Results: Patients' average four-year Kaplan–Meier disease-free survival was 74 per cent (95 per cent confidence intervals, 46–89 per cent). Eighty-two per cent of patients had good to excellent functional outcomes. Pre-operative tumour extension to the ipsilateral arytenoid significantly compromised disease-free survival (patients with this development had a two-year survival of 40 per cent; $p = 0.001$). Internal communicating fistula formation (i.e. a fistula between the neopharynx and myomucosal shunt lumens) occurred in five of 28 cases and was uniformly associated with a poor functional outcome (i.e. lack of phonation with or without aspiration). Fistula formation was significantly more likely in cases with tumour involving the ipsilateral arytenoid and the ipsilateral subglottis.

Conclusions: Significant disparity exists for the functional outcome of near-total laryngectomy in patients who develop post-surgical internal fistula, compared with those with uneventful healing. Tumour involvement of the ipsilateral arytenoid compromises the oncological and functional results. Tumour extension to the subglottis may compromise functional outcome. Near-total laryngectomy should be avoided in cases with ipsilateral arytenoid involvement, and undertaken with caution in cases with subglottic extension.

Key words: Larynx Neoplasms; Laryngectomy; Otorhinolaryngologic Surgical Procedure

Introduction

Near-total laryngectomy was initially described over two decades ago.¹ Despite excellent published results regarding its oncological adequacy and functional outcomes,^{2–5} this procedure has not been enthusiastically accepted by head and neck surgeons. Reasons for this include its technical complexity,⁶ and also concerns regarding surgical complications and long term aspiration. The development of alternate strategies for organ preservation (chemoradiation) and for speech restoration (tracheoesophageal prosthesis) has also provided alternate options to near-total laryngectomy.

The tracheoesophageal prosthesis technique has become the preferred method of speech restoration in many centres around the world. The technique is attractive as it does not in any way compromise surgical resection. However, the technique does

have limitations, as it leads to the patient's dependence on the treatment centre for regular prosthesis replacement and for treatment of ongoing minor morbidity.^{5,7–9} Even in societies in which the replacement costs of the tracheoesophageal prosthesis are not directly borne by the patient, a decline in usage over time has been reported.¹⁰ Near-total laryngectomy is free of such disadvantages. It incurs no replacement costs and is practical for patients who cannot regularly access head and neck treatment teams. Speech, once attained, is retained over time. Recent literature from Turkey,⁶ Spain,^{11,12} South America,⁴ India,^{3,5} Egypt¹³ and China¹⁴ has indicated that near-total laryngectomy remains a relevant procedure in many societies.

In centres in which near-total laryngectomy is routinely practiced, it is preferred to tracheoesophageal

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prosthesis usage.^{3,5,13} Our own policy is to prefer near-total laryngectomy to tracheoesophageal prosthesis usage whenever oncologically feasible. Oncological considerations limit the feasibility of near-total laryngectomy to about 20 per cent of cases with advanced laryngeal or hypopharyngeal cancer undergoing surgery.⁵ The literature indicates general unanimity with regard to the oncological adequacy and survival results of the procedure in the select group to which it is applicable.²⁻⁵ However, wide disparity exists in the reported surgical morbidity among different series, with the incidence of post-operative fistula varying from 8.7 to 48 per cent.^{5,3,11-13,15}

The present study comprised a critical review of experience with near-total laryngectomy at one treatment centre, with the specific intent of identifying the causes of complications and poor outcomes.

Patients and methods

Twenty-eight patients underwent near-total laryngectomy at our institution between 1996 and 2005. All procedures were performed by one of two surgeons (AT and SB). Data regarding physiological status, involvement of each subsite, extent of resection, method of closure, post-operative course, functional status and disease-free follow up were prospectively accrued for each patient, using a uniform, pre-defined pro forma.

No cases had been previously treated. The patients' mean age was 51 years (range, 29-73 years), and they comprised 27 men and one woman. Sixteen cases had laryngeal cancers (12 supraglottic and four glottic) and 12 had pyriform sinus cancers. Twenty-seven patients had squamous cell cancers and one a supraglottic leiomyosarcoma. Patients' pre-treatment tumour (T) and nodal (N) status is listed in Table I. After surgery, pathological examination of the surgical specimen upstaged two T₃ tumours to T₄ and five N₀ necks to N₊. On final pathological staging, 10 cases had T₄ disease and 15

had N₊ disease. The upstaging from T₃ to T₄ was consequent to histological evidence of invasion of the thyroid cartilage or of extralaryngeal spread.

In keeping with the standard surgical criteria for suitability for near-total laryngectomy, in all cases the posterior commissure, contralateral arytenoid, posterior vocal fold and underlying subglottis were clinically free of tumour, and the contralateral vocal fold and arytenoid were fully mobile. Surgery involved near-total laryngectomy in all patients, accompanied by an ipsilateral, comprehensive neck dissection in 11 patients and a selective (level II-IV) neck dissection in 15. The cricoid lamina was sectioned in the midline and the contralateral arytenoid was preserved, along with the cricoarytenoid joint, the posterior and lateral cricoarytenoid muscles, and the recurrent and superior laryngeal nerves. The anterior limit of the laryngeal remnant was dependent on the tumour extent, and in general more larynx could be preserved in pyriform sinus cancers than in laryngeal cancers. The laryngotracheal remnant was tubed to form a 'myomucosal shunt'. The lumen of the shunt was sized by wrapping it snugly over a 14 French gauge nasogastric tube. Redundant mucosa, if any, was excised; if the mucosa was short it was supplemented by an inferiorly based, random, full thickness mucosal flap from the adjacent hypopharynx (as per the standard described technique).¹⁶ Eighteen of the 28 cases required a hypopharyngeal flap for adequate sizing of the neo-laryngotracheal tube (i.e. myomucosal shunt).

Negative surgical margins were achieved in all cases. All cases were advised to undergo post-surgical radiation therapy; however, two cases did not comply, resulting in only 26 patients receiving post-operative radiation therapy. All patients attended for regular review following treatment.

Survival analysis was undertaken by the Kaplan-Meier method. The duration of observation was from the date of surgery. For determination of disease-free survival, all instances of local or regional failure, distant metastasis and second primary cancers were taken as events (i.e. censored observations). Cases undergoing continuing follow up with no recurrent disease, metastatic disease or second primary cancers were taken as uncensored observations. The mean duration of disease-free follow-up in the uncensored observations was 42 months.

Evaluation of speech and swallowing was undertaken in the immediate post-operative period and at six to nine months post-treatment. Speech status was assessed by subjective evaluation by a speech pathologist, and by objective measurements (i.e. fundamental frequency and maximum phonation time). Overall functional status was graded at six to nine months post-treatment, as per the scheme shown in Table II.

All data were recorded in a computerised data set designed using Epi-info version 6.04 software (CDC, Atlanta, Georgia, USA). Statistical analysis was undertaken using Epi-info version 6.04 and Stata version 5.0 (Stata, College Station, Texas, USA) software.

TABLE I

PRIMARY TUMOUR AND NECK NODE STATUS OF 27 SCCS AT PRESENTATION

T stage	N stage				Total
	N ₀	N ₁	N ₂	N ₃	
<i>Larynx</i>					
T ₂	0	0	0	0	0
T ₃	8	3	1	0	12
T ₄	2	0	1	0	3
Total	10	3	2	0	15
<i>Pyriform sinus</i>					
T ₂	0	1	1	1	3
T ₃	3	0	1	0	4
T ₄	4	0	1	0	5
Total	7	1	3	1	12

One case with a supraglottic leiomyosarcoma was not included as the tumour-node-metastasis (TNM) staging was not applicable. On pathological staging subsequent to surgery, two T₃ tumours were upstaged to T₄, and five N₀ necks were upstaged to N₊. SCC = squamous cell carcinoma

TABLE II

COMPOSITE GRADING OF FINAL FUNCTIONAL STATUS,
INCORPORATING SPEECH ACQUISITION AND EASE OF SWALLOWING

Grade	Function
I	Speech excellent or good Normal swallow
II	Speech fair or strained with limited phonation time (shunt stenosis) or Occasional cough on swallow, corrected by swallowing therapy or careful swallowing, with no episodes of chest infection
III	Significant immediate post-op morbidity (fistula formation) leading to delay in post-op radiation, or conversion to total laryngectomy or Significant long term swallowing morbidity, with ≥ 1 aspiration-related chest infection in last 6 months

Post-op = post-operative

Results

Oncological results

Of the 28 cases treated, two developed local recurrence, two developed regional recurrence and one developed a second primary cancer in the tonsil. Two of these five failed cases received salvage treatment with surgery and re-irradiation; one developed a further recurrence following the second treatment. The mean time to local recurrence was 12 months; the mean time to regional recurrence was 27 months. The two-year disease-free survival was 82 per cent (95 per cent confidence intervals (CI), 59–93 per cent), and the four-year disease-free survival was 74 per cent (95 per cent CI, 46–89 per cent). The two-year survival inclusive of salvage was 88 per cent (95 per cent CI, 66–96 per cent), and the four-year survival inclusive of salvage was 80 per cent (95 per cent CI, 52–92 per cent).

In the small data set evaluated, neither the tumour site, gross tumour characteristics nor histological grade demonstrated any significant effect on the final oncological outcome. Advancing T stage, N stage or subglottic spread did not adversely affect outcome. However, involvement of the ipsilateral arytenoid by squamous cell cancer was associated with a greater risk of locoregional failure (being associated with two cases of local recurrence and one of regional recurrence) and a significant reduction in disease-free survival (Figure 1 and Table III) ($p = 0.001$; log rank test for equality of survivor functions).

Surgical complications

Wound complications. Eight of the 28 patients developed wound complications: two suffered wound infections, one developed an external fistula from the neopharynx to the cervical skin, and five developed 'internal' fistulae from the neopharynx to the neo-laryngotracheal shunt (myomucosal shunt). The case of external fistula was iatrogenic – the patient accidentally removed his nasogastric tube on the fourth post-operative day, and the ward staff's enthusiastic attempts at reinsertion resulted

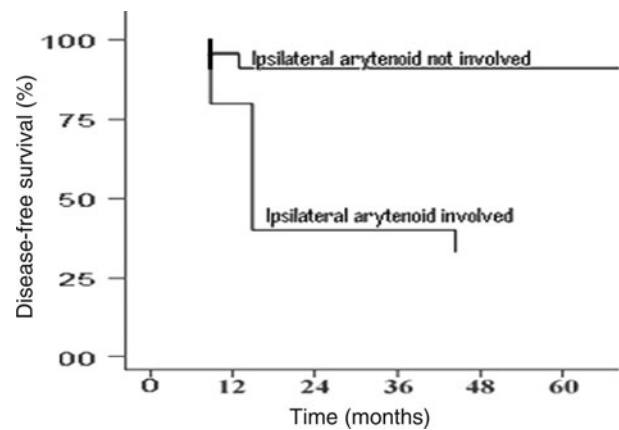


FIG. 1

Kaplan-Meier disease-free survival in patients with and without ipsilateral arytenoid involvement.

in a pharyngocutaneous fistula. This subsequently healed spontaneously.

All five cases of internal fistula occurred de novo, and presented between the seventh and tenth post-operative day with a salivary leak from the stoma. Two cases healed spontaneously over time, while the remaining three required completion laryngectomy (two with Pectoralis Major Myocutaneous Flap). At completion laryngectomy, the residual cricoid and thyroid cartilages were noted to be infected and avascular, and were deemed non-viable. All patients with internal fistulae were delayed in receiving their planned post-operative radiation therapy due to the complication. All five internal fistulae patients had poor final functional outcomes.

The rate of internal fistulisation was not related to tumour site, pre-operative tracheostomy, use of hypopharyngeal flap for neo-laryngotracheal shunt augmentation, or to other coexistent co-morbidities. However, a higher rate of fistula formation was noted in cases with tumour involvement of the ipsilateral arytenoid or the ipsilateral subglottis. All five internal fistula cases had involvement of either the ipsilateral arytenoid (three cases) or the ipsilateral subglottis (two cases) (Table III). No internal fistulae were encountered in cases without gross tumour involvement of the ipsilateral arytenoid or the ipsilateral subglottis.

Post-operative aspiration. All five patients who developed internal fistulae presented between the seventh and tenth post-operative days with salivary aspiration and leak from the tracheostoma. Three required a completion laryngectomy. The two remaining patients healed spontaneously but subsequently had occasional problems with chest infection.

The 23 other patients with uneventful healing were tested with oral feeds around the 14th post-operative day. Transient aspiration on commencement of oral feeding was frequent (13/23). Five patients had minimal aspiration (i.e. they were asymptomatic, and aspiration was noted by the physician only on evaluation of the trachea during swallowing). Six patients had moderate aspiration (i.e. a cough

TABLE III
IMPACT OF ARYTENOID AND SUBGLOTTIS INVOLVEMENT ON OUTCOMES*

Site	ONCOLOGIC OUTCOME	FUNCTIONAL OUTCOME
<i>I/L ARYTENOID</i>	2 year Kaplan-Meier Disease-free survival	Internal Fistula/Grade III Functional outcome**
-involved (n = 6)	40%	3/6
-not involved (n = 21)	89%	2/21
	<i>p = 0.001 logrank test</i>	<i>p = 0.06 (two-tailed Fisher's Exact test)</i>
<i>I/L SUBGLOTTIS</i>		
-involved (n = 4)	100%	2/4
-not involved (n = 23)	79%	3/23
	<i>p-NS*** logrank test</i>	<i>p = 0.14 (two-tailed Fisher's Exact test)</i>

*N = 27. Analysis restricted to 27 cases with squamous cell carcinoma. 1 case with a leiomyosarcoma was excluded from analysis

**All cases with internal fistula had grade III functional outcome-see TABLE 4

***NS = Not significant

induced on swallowing) and two had severe aspiration (precluding normal swallowing). However, all cases of aspiration proved transient, and oral feeding was resumed by the 30th post-operative day in all patients.

Functional outcome

The final outcome at six to nine months following surgery, with regard to speech acquisition, aspiration-free swallow and overall functional grade (see Table II), is shown in Table IV. Poor overall functional outcome (i.e. grade III) was significantly more likely in cases that developed communicating internal fistulae than in cases that did not ($p < 0.01$; Fisher's exact two-tailed test).

Impact of arytenoid and subglottic involvement

Table III illustrates the impact of tumour involvement of the ipsilateral arytenoid and subglottis on the final oncological and functional outcomes.

TABLE IV

FINAL FUNCTIONAL OUTCOMES FOR SPEECH AND SWALLOWING

Parameter	Internal fistula	
	Yes (5)	No (23)
<i>Speech</i>		
Excellent	0	14
Good	0	5
Fair	0	1
Stenosis (strained, with limited phonation time)	0	3
Nil	2	0
TL convert	3	0
<i>Swallow</i>		
Normal (effortless, automatic swallow)	0	21
Voluntary (manoeuvre-assisted, no cough or aspiration)	0	2
Cough or occasional aspiration	2	0
TL convert	3	0
<i>Overall functional grade*</i>		
I	0	19
II	0	4
III	5	0

*See Table II. TL = total laryngectomy

Discussion

The exact role of near-total laryngectomy in the contemporary treatment of advanced laryngeal cancer remains controversial. The lack of universal acceptability of the operation is probably related to its technical complexity, and also to concerns about surgical complications and long term aspiration. As yet, no clear risk factors have been identified with which to predict cases at high risk of such complications. This study sought to identify factors contributing to poor functional and oncological results following near-total laryngectomy, in order to enable modification of case selection and surgical practice if required.

In this study, the overall oncological and functional results of near-total laryngectomy were satisfactory. Kaplan-Meier disease-free survival at four years was 74 per cent, and 82 per cent of cases had good to excellent speech and swallowing outcomes. Speech, once acquired, was always retained, and swallowing was usually completely normal, with no aspiration.

However, a subset of cases with tumour extension to the arytenoid and the subglottis did not do as well. Cases with involvement of the arytenoid had poor oncological and functional outcomes. Cases with subglottic extension had uncompromised oncological cure but poor functional outcomes. The poor functional outcome related to tumour extension to both these subsites was due to the high incidence of internal fistulae.

Internal fistulae, leading to salivary leakage from the pharyngeal tube to the laryngotracheal 'myomucosal shunt', proved devastating. All five cases with this complication had problems with aspiration and none developed satisfactory speech. Soiling of the sectioned cricoid and thyroid cartilages led to chondritis and sequestra formation, which hampered spontaneous healing. Three of these five cases required conversion to total laryngectomy. All were delayed in their scheduled post-operative radiation due to prolonged post-surgical healing. There was a clear distinction between the functional outcomes of patients developing fistulae and patients with uneventful healing. In retrospect, the outcomes of the fistulae patients may have been better had they

initially undergone a total laryngectomy, rather than a near-total laryngectomy.

Other workers too have observed such communicating or internal fistulae complicating near-total laryngectomy, and also the associated problems with aspiration and poor functional outcomes.^{2,15} Suits *et al.* have previously opined that patients at high risk of fistula should not be subjected to near-total laryngectomy but should instead undergo total laryngectomy.¹⁵ Our experience, as detailed above, further supports this opinion. The incidence of fistula in the literature varies from 8.7 to 48 per cent.^{3,5,11–13,15} However, no clear risk factors have yet been identified with which to predict cases at high risk of fistula formation. This study suggests tumour involvement of the ipsilateral arytenoid and the ipsilateral subglottis to be predictive of a high risk of post-operative internal fistula formation. These parameters may henceforth be useful in determining cases in which near-total laryngectomy may be unsuitable.

- **Near-total laryngectomy, where applicable for selected, locally advanced (T₄ and T₃) laryngeal and hypopharyngeal cancers, provides comparable oncological results, with preservation of voice in a large majority of cases**
- **Formation of an ‘internal fistula’ (i.e. connecting the pharyngeal lumen and the myomucosal shunt lumen) in the post-operative period is associated with significantly poorer functional outcomes. Near-total laryngectomy should be avoided in cases with compromised wound healing**
- **Oncological and functional results are liable to be compromised in cases with tumour extending to the ipsilateral arytenoid, and such involvement may constitute a relative contraindication to near-total laryngectomy**
- **Tumour extension to the ipsilateral subglottis is associated with a poorer functional outcome. This may be minimised by attention to surgical technique when creating the hypopharyngeal flap used for closure**

Conventionally, the oncological contraindications of near-total laryngectomy have been restricted to tumour involvement of the subsites not resected by this procedure, i.e. the posterior commissure, contralateral arytenoid, and contralateral paraglottic space. Our experience indicates that involvement of the ipsilateral arytenoid too is associated with a poor oncological outcome. Ipsilateral arytenoid involvement has also been associated with a high risk of fistula formation and poor functional outcomes. The proximity of the involved arytenoid to the resection margin presumably contributes to these high rates of fistulisation and oncological failure. Recent literature has indicated that histological evaluation of margins may be inadequate when compared with

molecular techniques.¹⁷ Negative surgical margins, as ascertained by frozen section analysis and definitive histopathological evaluation, may well be fallible in such close proximity to the tumour. In our current practice, tumour involvement even of the ipsilateral arytenoids constitutes a relative contraindication to near-total laryngectomy.

The limits of subglottic tumour extension amenable to near-total laryngectomy are not clearly defined in the literature. The initial descriptions by Pearson and colleagues^{1,2} indicated that glottic tumours with subglottic and even upper tracheal extension (and also some primary subglottic tumours if unilateral) could safely be extirpated with near-total laryngectomy. However, recent literature indicates that this may not be oncologically safe.⁶ Most workers have restricted the procedure to cases with limited subglottic spread.^{4,13} Our subglottic spread limits have been set similarly, and we restrict near-total laryngectomy to those laryngeal tumours in which the gross tumour extends no further than the upper half of the ipsilateral subglottis. Within these indications, satisfactory results have been obtained with regard to the oncological safety of near-total laryngectomy; however, we have obvious concerns regarding the high incidence of fistula formation and the consequent poor functional outcome.

The high fistulisation rate in cases with subglottic extension probably relates to partial necrosis of the hypopharyngeal flap used for closure of the neolaryngotracheal tube (myomucosal shunt). The flap (a random flap fashioned from the hypopharyngeal mucosa)¹⁶ is routinely used for augmenting the mucosa of the myomucosal shunt, and has generally proved reliable. However, in cases with extensive excision of subglottic mucosa, greater demands are made on the size and length of flap required, and this perhaps has led to stretching the limits of this random flap. In this study, internal fistulae were encountered in the initial two such cases with subglottis involvement. Since this experience, we have been conservative with the design of the flap, and further augmentation of the subglottic area, if required, is undertaken by preserving and advancing redundant mucosa from the adjacent trachea. As a result of attention to these technical factors, no further fistulae occurred in subsequent cases, and it is hoped that future experience will further corroborate this hypothesis.

Conclusion

This study observed a marked divergence in the functional results of near-total laryngectomy among patients with uneventful post-surgical healing, compared with patients who developed a communicating salivary fistula. Prevention of surgical fistulae, by attention to patient selection and to surgical technique, could significantly improve functional outcome.

Tumour involvement of the ipsilateral arytenoid has been associated with locoregional failure, post-operative fistula formation and poor functional

results, and thus should constitute a relative contraindication to near-total laryngectomy. Subglottic extension too is associated with an increased surgical complication rate, and this may be minimised by attention to the design of the hypopharyngeal flap used for closure.

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