The Journal of Laryngology & Otology

cambridge.org/jlo

Survival and function following pharyngo-laryngo-oesophagectomy in Wales: a twelve-year case series

D R Edwards[1], L Pope[2] and S Berry[3]

[1]Department of ENT/Head and Neck Surgery, Royal Gwent Hospital, Wales, UK, [2]Department of ENT/Head and Neck Surgery, Morriston Hospital, Wales, UK and [3]Department of ENT/Head and Neck Surgery, University Hospital of Wales, Cardiff, Wales, UK

Main Article

Mr D Edwards takes responsibility for the integrity of the content of the paper

Presented at ENT Wales Annual Meeting, 4th October 2019, Saundersfoot, UK.

Cite this article: Edwards DR, Pope L, Berry S. Survival and function following pharyngo-laryngo-oesophagectomy in Wales: a twelve-year case series. *J Laryngol Otol* 2021; **135**:259–263. https://doi.org/10.1017/S0022215121000207

Accepted: 30 August 2020
First published online: 29 January 2021

Key words:
Hypopharyngeal Neoplasms; Laryngectomy; Pharyngectomy; Morbidity; Deglutition; Voice

Author for correspondence:
Mr Daniel Rhys Edwards, Department of ENT/Head and Neck Surgery, Royal Gwent Hospital, Cardiff Road, Newport NP20 2UB, Wales, UK
E-mail: daniel.edwards@wales.nhs.uk

Abstract

Objective. Treatment of locally advanced hypopharyngeal cancer can cause significant morbidity and late toxicity. Pharyngo-laryngo-oesophagectomy can achieve adequate surgical margins, but data on survival and functional outcome are limited, especially in Wales. This study aimed to describe mortality, morbidity and functional outcome following pharyngo-laryngo-oesophagectomy in a Welsh population.
Method. This study was a retrospective case note review of pharyngo-laryngo-oesophagectomy cases in Wales over 12 years.
Results. Fifteen patients underwent pharyngo-laryngo-oesophagectomy; all but one underwent gastric pull-up. Median survival and disease-free survival were 17 months (range, 2–53 months) and 14 months. Censored 3-month, 1-year and 3-year survival was 93, 71 and 50 per cent, respectively. Common Terminology Criteria for Adverse Events grading of long-term dysphagia was 1 in 58 per cent, 2 in 33 per cent and 3 in 8 per cent, and 87.5 per cent achieved a 'moderate' or 'good' voice rehabilitation.
Conclusion. These results demonstrate favourable survival and reasonable functional outcome following pharyngo-laryngo-oesophagectomy, suggesting pharyngo-laryngo-oesophagectomy should be considered in all appropriate surgical candidates.

Introduction

Options for the radical treatment of locally advanced tumours of the hypopharynx and cervical oesophagus are often limited. The high frequency of submucosal tumour extension in the hypopharynx[1] necessitates an extensive resection for oncological clearance if surgical treatment is favoured; this is reflected in national guidelines where a wide surgical margin is recommended.[2] Resection of disease involving the distal aspect of the cricopharyngeus or cervical oesophagus through the neck alone is difficult and likely to produce an involved surgical margin. Pharyngo-laryngo-oesophagectomy can be used to achieve a more adequate surgical margin and subsequent reconstruction.

For some patients, pharyngo-laryngo-oesophagectomy may represent the only radical treatment option, with alternative regimes taking a palliative approach. However, pharyngo-laryngo-oesophagectomy has been associated with significant morbidity and mortality, as well as a long in-patient stay and significant functional change. Estimates of early and late mortality, morbidity and complications of pharyngo-laryngo-oesophagectomy vary significantly.[3] In addition, there is little published data regarding voice and swallow rehabilitation in the small population of patients who have undergone pharyngo-laryngo-oesophagectomy.

Because of this, the pre-operative counselling of candidates for pharyngo-laryngo-oesophagectomy is problematic; it is difficult to give an evidence-based treatment recommendation to patients with advanced tumours of the hypopharynx or cervical oesophagus. We aimed to produce a Welsh dataset in order to examine in-patient and longer-term survival of patients having undergone pharyngo-laryngo-oesophagectomy, as well as their quality of speech and swallow rehabilitation.

Materials and methods

Ethical considerations

Approval was gained for retrospective data collection from each health board as a service evaluation. All data was anonymised from the source and stored securely.

Data collection

Cases of pharyngo-laryngo-oesophagectomy were identified using a national cancer database. A retrospective review of paper and electronic case notes was used to record

demographics, tumour staging, operative details and early and late morbidity and mortality. Identification and investigation of complications was aided by review of radiology. Data regarding functional outcome were collected using electronic records of post-operative clinic reviews and speech and language therapy notes. Functional outcome was recorded from the latest documented follow up.

Data analysis

Data were analysed using SPSS® statistical software. Survival was examined using Kaplan–Meier analysis and was censored for follow-up time. Information from speech and language therapy notes was used to generate data on functional outcome. The degree of reported dysphagia was categorised using the Common Terminology Criteria for Adverse Events grading.

Outcomes

The primary outcome was survival over time. Secondary outcomes were frequency of post-operative complications, quality of voice rehabilitation and degree of post-operative dysphagia.

Results

Demographics

Over a 12-year period, 15 patients underwent pharyngo-laryngo-oesophagectomy in 4 Welsh surgical centres: the University Hospital of Wales, Cardiff; Royal Gwent Hospital, Newport; Morriston Hospital, Swansea and Glan Clwyd Hospital, Rhyl.

Thirteen patients had hypopharyngeal tumours, with one primary tumour in the subglottis and one cervical oesophageal tumour. In 14 patients, the histological diagnosis was squamous cell carcinoma (SCC), with one subglottic adenoid cystic carcinoma. Disease in 2 out of 15 patients was considered to represent recurrent head and neck cancer, but a further 3 patients had been previously treated for another head and neck primary cancer. In all, 5 patients (33 per cent) had undergone previous head and neck radiotherapy. Recurrences were not staged; all but one remaining patient with SCC had locally advanced T4 disease. The cohort comprised 3 females and 12 males. Mean age at time of procedure was 61.5 years. Mean follow up was 23 months (Table 1).

Table 1. American Joint Committee on Cancer tumour–node–metastasis staging

Parameter	Staging	Frequency (*n*)
Tumour	3	1
	4a	10
Node	0	4
	1	1
	2a	0
	2b	2
	2c	3
	3	1
Metastasis	0	11
	1	0
Un-staged recurrence		3
Missing data		1

Surgical technique

All patients underwent pharyngo-laryngo-oesophagectomy with at least ipsilateral selective level II–IV neck dissection where neck staging was N0, with further surgical treatment of the neck depending on nodal staging. All patients with SCC underwent at least ipsilateral hemithyroidectomy. Reconstruction in all but one patient was by gastric pull-up and anastomosis of the gastric fundus to remaining pharyngeal tissue close to the tongue base following tumour excision with macroscopic margin. One patient underwent transverse colon interposition graft. Procedures were performed by head and neck surgeons from the relevant Department of Otorhinolaryngology with support from upper gastrointestinal surgeons. Gastric mobilisation was performed laparoscopically in the two most recent cases, with an open approach used in all others.

Surgical margins

Mucosal and deep surgical resection margin status was recorded. Seventy-seven per cent of procedures achieved clear mucosal margins, with 8 per cent close (less than 1 mm from tumour front to resection margin) and 15 per cent involved. The tumour extended to deep resection margins in 23 per cent of cases and was close in a further 23 per cent, with 54 per cent of deep margins being clear.

Inpatient morbidity and mortality

Three-month survival was 93 per cent; one patient died from hospital-acquired pneumonia. Median length-of-stay on the intensive care or high dependency unit was 6.5 days. There were no reported intra-operative complications. Non-fatal post-operative cardiorespiratory complications were reported in 5 patients (33 per cent) and hypocalcaemia was reported in 6 patients (40 per cent)

Anastomotic leak

Six patients (40 per cent) had a post-operative leak at the pharyngogastric anastomosis. This was reported as a pharyngocutaneous fistula in one patient. In all but one patient with an anastomotic leak, conservative management resulted in resolution and successful delayed enteral feeding. One patient required a revision procedure with resection of the proximal stomach, pharyngostomy and pectoralis major flap reconstruction.

Survival

Survival data were available for all 15 patients (Figure 1; Table 2). Median survival after pharyngo-laryngo-oesophagectomy was 17 months (range, 2–53 months) and median disease-free survival was 14 months. Disease recurrence was recorded in 7 patients (47 per cent) during the follow-up period, of which 4 cases were loco-regional and 3 cases were distant. Censoring for follow-up time, survival at 3 months, 1 year and 3 years was 93 per cent, 71 per cent and 50 per cent, respectively. Ten out of 15 patients died within observed follow-up; 3 of these deaths were not disease related.

https://doi.org/10.1017/S0022215121000207 Published online by Cambridge University Press

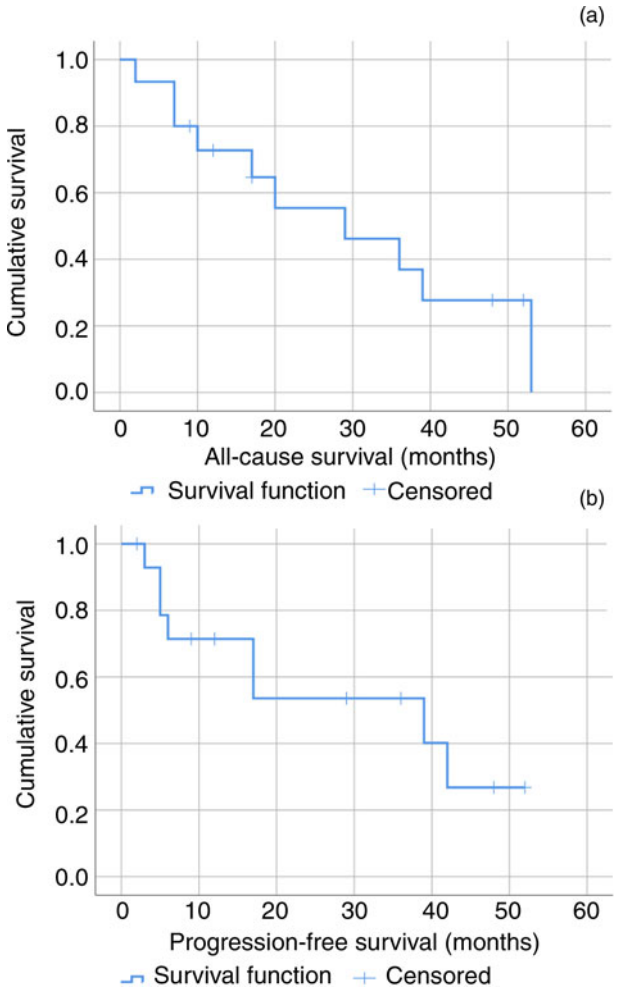

Fig. 1. Kaplan-Meier survival charts showing (a) all-cause and (b) progression-free survival.

Table 2. Survival

Survival	Patients (%)
Survival	
– Three months	93
– One year	71
– Two years	50
– Three years	50
Median overall survival (months)	17
Median disease-free survival (months)	14

Voice

Data regarding voice rehabilitation were available for 9 out of 15 patients. One patient did not voice, and used written communication. Four patients used an electrolarynx, three used gastric speech and one patient voiced using a tracheogastric valve. Speech and language therapy notes were used to subjectively categorise voice rehabilitation; one patient had a poor voice (electrolarynx), but all other patients had moderate or good voice rehabilitation.

Swallow

Information regarding quality of swallow was available for 12 out of 15 patients. Only one patient was reliant on enteral feeding at follow up (jejunostomy) with all other patients feeding orally. Seven patients (58 per cent) had a Common Terminology Criteria for Adverse Events swallow grade 1 (symptomatic but able to eat full oral diet). Four patients (33 per cent) were grade 2 (symptomatic with altered eating or swallowing), and one patient was grade 3 (enteral feeding). One patient required dilatation of the neopharynx because of late stricture formation.

Discussion

Survival

Three-month survival in our series (93 per cent) compared favourably to other recent European papers, with Meulemans *et al.* reporting 91.7 per cent[4] and Marion *et al.* reporting 83.4 per cent[5] in Belgian and French centres, respectively. This is significant given the high prevalence of T4-staged disease in our cohort compared with others.

The 2016 review by Butskiy *et al.* reported a decrease in the odds of mortality following gastric pull-up over each consecutive decade.[3] This may be in part due to a general improvement in peri-operative care but also because of the role of the multidisciplinary team in selecting suitable surgical candidates. Two- and 3-year survival in our series was 50 per cent. This compares favourably with the above two series as well as older British data[6] and a more recent Chinese series.[7]

Disease recurrence was recorded in 47 per cent of patients in our series. This is broadly in line with published data. In patients with documented recurrence, median disease-free survival was 10 months. Most of these cases recurred within the first two post-operative years, but two patients had recurrent disease diagnosed in the fourth post-operative year. This highlights the need for maintaining regular follow up and a specialist support network for such patients. There was no correlation between prior head and neck irradiation or positive surgical excision margin and the incidence of disease recurrence.

- Surgical and oncological treatments of locally advanced hypopharyngeal carcinoma are associated with significant morbidity, mortality and late toxicity
- Pharyngo-laryngo-oesophagectomy can allow excision with adequate surgical margins
- Data regarding survival and function following pharyngo-laryngo-oesophagectomy are limited
- Our series demonstrated favourable survival and functional outcomes when compared with existing literature
- Pharyngo-laryngo-oesophagectomy should be considered as a viable surgical treatment option in all suitable patients with locally advanced hypopharyngeal carcinoma

Anastomotic leak

We report a post-operative anastomotic leak rate of 40 per cent. A greater proportion of patients with a history of previous head and neck irradiation (60 per cent) leaked, compared with those without (33 per cent); however, this association was not significant using Fisher's exact test. With the exception of the study by Marion *et al.*, our rate of reported leak is greater than that described in the wider literature. This may be mitigated by the lack of consensus on definition and reporting of leak in other studies, as well as a discrepancy between description of leak versus pharyngocutaneous fistula. In addition, our review of radiological imaging may have increased the sensitivity of reporting a leak. We are reassured that all

https://doi.org/10.1017/S0022215121000207 Published online by Cambridge University Press

but one reported anastomotic leak in our series resolved with conservative management. The size of our cohort prevented analysis by method of surgical reconstruction.

Functional outcome

Successful voice rehabilitation has been shown to be a marker of quality of life following head and neck cancer treatment[8] and is an important factor in ensuring safety and a patient's ability to complete activities of daily living. In our series, 87.5 per cent of patients for whom voice rehabilitation data was available were able to achieve a moderate-to-good quality of voice. Although direct comparison of subjective measures is difficult, this compares well with published literature. Most of our patients used either gastric speech or an electrolarynx. Meulemans *et al.* reported 68 per cent of patients achieved functional voice following secondary tracheogastric puncture and insertion of a speech valve, when rehabilitation with an electrolarynx had failed. However, a relatively high proportion (24 per cent) required removal of the speech prosthesis because of complications. Our practice is to consider voice rehabilitation methods on a case-by-case basis.

Our series showed only one patient (8 per cent) to be reliant on enteral feeding at latest follow up. All other patients reported some degree of dysphagia, but the majority reported a normal diet (Common Terminology Criteria for Adverse Events dysphagia grade 1); the remainder described altered diet. Pharyngo-laryngo-oesophagectomy, like any radical treatment of advanced hypopharyngeal cancer, necessitates significant functional changes. With this in mind, our results are not surprising and indeed are in line with published literature, although direct comparison is difficult because of differences in measuring such a subjective outcome. Meulemans *et al.*[4] reported 17.3 per cent remained reliant on enteral feeding; Marion *et al.*[5] reported 29 per cent were unable to recover oral feeding. Oncological treatment of locally advanced hypopharyngeal cancer is associated with a profound effect on long-term swallow function. A secondary analysis of the Radiation Therapy Oncology Group study reported the development of severe late toxicity in 40–50 per cent of patients,[9] of which dysphagia was the most frequent. In addition, radiation dose to the inferior hypopharynx showed a correlation with development of severe late toxicity.[10] Our data demonstrate that a reasonable swallowing outcome is achievable following pharyngo-laryngo-oesophagectomy when compared with alternative treatment modalities.

Other factors

In our cohort, the mucosal excision margins were clear of tumour in 77 per cent of cases, and the deep margins were clear in 54 per cent of cases. Although there was no correlation between involved surgical excision margin and disease recurrence, this highlights the need to plan a wide excision and subsequent reconstruction in the surgical treatment of hypopharyngeal cancer. No published series of pharyngo-laryngo-oesophagectomy patients has recorded the relationship between excision margin and disease course, but it is accepted that there is a high incidence of submucosal tumour extension in SCC of the hypopharynx and that close or involved surgical margins have been recognised as a predictor of disease recurrence.[11]

The management of locally advanced hypopharyngeal cancer remains controversial, and there are no studies directly comparing survival or functional outcome in patients undergoing pharyngo-laryngo-oesophagectomy with oncological treatment. For hypopharyngeal cancer, organ-preserving treatment is generally preferred in the presence of a functioning larynx and has been shown to confer no disadvantage to overall survival in this scenario.[12,13] However, all patients in our series presented with symptoms of either significant dysphagia or aspiration, in addition to some cases of airway compromise. In this situation, and in the presence of advanced volume disease, it is more accepted that radical surgery represents the best treatment option.[14]

Strengths and limitations

This case series provides an up-to-date description of survival and functional outcome in patients undergoing pharyngo-laryngo-oesophagectomy in Wales over the past twelve years. It may act as a guide for the often-difficult joint decision-making process when considering treatment options with a patient and the multidisciplinary team.

Limitations of this series include its reliance on subjective outcome measures. The small size of the series prevented detailed analysis of predictors of poor outcome.

Conclusion

Pharyngo-laryngo-oesophagectomy is a life-changing operation requiring significant functional change. However, this case series has shown that it can be performed in Wales with low in-patient mortality and a 50 per cent 3-year survival rate. In addition, functional outcomes of swallow and speech rehabilitation have been shown to be favourable compared with the published literature. In the situation of a compromised larynx, extensive locally advanced hypopharyngeal cancer or oncological treatment failure, we would advocate offering pharyngo-laryngo-oesophagectomy as a treatment option to any suitable patient.

Acknowledgements. The authors acknowledge the hard work of the Welsh Head and Neck Cancer Multidisciplinary teams and thank them for allowing access to patient records. The authors also thank the Head and Neck surgeons under whose care the patients in this series were treated, including but not limited to: Mr Carl Passant, Mr Duncan Ingrams, Mr Alun Tomkinson, Mr Stuart Quine, Mr David Owens, Mr David Smith, Mr Sotiris Exarchos, Mr Connor Marnane, Mr Hisham Zeitoun and Professor Arvind Arya.

Competing interests. None declared

References

1 Ho CM, Ng WF, Lam KH, Wei WJ, Yuen AP. Submucosal tumor extension in hypopharyngeal cancer. *Arch Otolaryngol Head Neck Surg* 1997;**123**:959–65
2 Pracy P, Loughran S, Good J, Parmar S, Goranova R. Hypopharyngeal cancer: United Kingdom National Multidisciplinary guidelines. *J Larngol Otol* 2016;**130**(suppl S2):104–10
3 Butskiy O, Rahmanian R, White RA, Durham S, Anderson DW, Prisman E. Revisiting the gastric pull–up for pharyngoesophageal reconstruction: a systematic review and meta-analysis of mortality and morbidity. *J Surg Onc* 2016;**114**:907–14
4 Meulemans J, Couvreur F, Beckers E, Nafteux P, Van Veer H, Vander Poorten V *et al.* Oncologic and functional outcomes after primary and salvage laryngopharyngoesophagectomy with gastric pull-up reconstruction for locally advanced hypopharyngeal squamous cell carcinoma. *Front Oncol* 2019;**9**:735
5 Marion Y, Lebreton G, Brevart C, Sarcher T, Alves A, Babin E. Gastric pull-up reconstruction after treatment for advanced hypopharyngeal and

https://doi.org/10.1017/S0022215121000207 Published online by Cambridge University Press

cervical esophageal cancer. *Eur Ann Otorhinolaryngol Head Neck Dis* 2016;**133**:397–400
6 Ullah R, Bailie N, Kinsella J, Anikin V, Primrose WJ, Brooker DS. Pharyngo-laryngo-oesophagectromy and gastric pull-up for post-cricoid and cervical oesophageal squamous cell carcinoma. *J Laryngol Otol* 2002;**116**:826–30
7 Liu J, Zhang Y, Li Z, Liu S, Li H, Xu Z. Benefit of salvage total pharyngo-laryngoesophagectomy for recurrent locally advanced head and neck cancer after radiotherapy. *Radiat Oncol* 2017;**12**:164
8 Rinkel RN, Verdonck-de Leeuw IM, van den Brakel N, de Bree R, Eerenstein SE, Aaronson N *et al*. Patient-reported symptom questionnaires in laryngeal cancer: voice, speech and swallowing. *Oral Oncol* 2014;**50**:759–64
9 Machtay M, Moughan J, Trotti A, Garden AS, Weber RS, Cooper JS *et al*. Factors associated with severe late toxicity after concurrent chemoradiation for locally advanced head and neck cancer: an RTOG analysis. *J Clin Onc* 2008;**26**:3582–9
10 Machtay M, Moughan J, Farach A, Martin-O'Meara E, Galvin J, Garden AS *et al*. Hypopharyngeal dose is associated with severe late toxicity in locally advanced head-and-neck cancer: an RTOG analysis. *Int J Radiat Oncol Biol Phys* 2012;**84**:983–9
11 Li M, Xie M, Zhou L, Wang S. The impact of surgical margin status on the outcomes of locally advanced hypopharyngeal squamous cell carcinoma treated by primary surgery. *Acta Otolaryngol* 2018;**138**:1136–45
12 Iwae S, Fujii M, Hayashi R, Hasegawa Y, Fujii T, Okami K *et al*. Matched-pair analysis of patients with advanved hypopharyngeal cancer: surgery versus concomitant chemoradiotherapy. *Int J Clin Oncol* 2017;**22**:1001–8
13 Habib A. Management of advanced hypopharyngeal carcinoma: systematic review of survival following surgical and non-surgical treatments. *J Laryngol Otol* 2018;**132**:385–400
14 Siddiq S, Paleri V. Outcomes of tumour control from primary treatment of hypopharyngeal cancer. *Adv Otorhinolaryngol* 2019;**83**:90–108

https://doi.org/10.1017/S0022215121000207 Published online by Cambridge University Press