The impact of pharyngocutaneous fistula on the survival of patients submitted to total laringectomy

Original Article

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Abstract

Objectives: The pharingocutaneous fistula (FFC) is an important post-operatory complication after total laryngectomy (LT), often associated with an increase in peri-operatory morbidity. Studies about the impact of FFC on long-term survival on patients submitted to LT remain scarce. The objective of this work was to study the relation between the presence of FFC and the survival rate of patients submitted to total laryngectomy. Material and methods: A retrospective cohort study was performed on patients submitted to LT between January 2013 and December 2017. The evaluation of survival and associated risk was preformed through a Kaplan-Meier analysis and multivariate Cox regression. Results: 50 patients were included, with an average follow-up time of 67 months. The overall survival and disease-free survival were similar between the two groups, with no significant statistical difference. Conclusions: Our study didn't find any relation between the presence of FFC and the survival rates of patients submited to LT.

Keywords: Faringocutaneous Fistula, Total laryngectomy, Survival.

Introduction

Pharyngocutaneous fistula (PCF) is the most common postoperative complication in the initial period after total laryngectomy, with incidence rates varying between 8.7% and 58.0%.[1, 2] Its etiology is multifactorial and several studies have reported the risk factors associated with its occurrence, including previous radiotherapy (RT), presence of positive margins, tumor location, and preoperative tracheostomy.[1,3,4,5] Some retrospective studies have investigated the relationship between postoperative wound infection and long-term survival, namely in patients who underwent rescue laryngectomy[6, 7]; however, studies on the impact of PCF on the long-term survival

of patients undergoing total laryngectomy are still scarce. The objective of this study was to analyze the relationship between the presence of a PCF and survival among patients undergoing total laryngectomy.

Materials and Methods

Patients

This retrospective cohort study evaluated patients who underwent total laryngectomy (TL) or total pharyngolaryngectomy (TPL) for primary epidermoid carcinoma of the larynx or hypopharynx from January 1, 2013 to December 31, 2017 at a tertiary hospital. The follow-up period was until December 31, 2022.

All patients who had undergone previous partial laryngectomy or surgery for other head and neck primary tumors, and those with a second primary tumor or distant metastases at the time of diagnosis were excluded.

All the included patients underwent TL or TPL with bilateral neck dissection. Tracheostomy was performed during the same operation or before the surgery, depending on the need to secure the airway. Closure and construction of the neopharynx were performed with simple sutures using absorbable synthetic material (Vicryl®) 3/0 in planes. All patients had a nasogastric probe placed perioperatively and were fed exclusively through it until the 12th postoperative day, when an oral test was performed to investigate the presence of a fistula. All patients whose oral test showed the absence of a fistula started oral diet on the same day. A PCF was defined as any clinically identified communication between the pharynx and skin. It was treated conservatively with regular dressing care and neck compression in all patients.

The analyzed variables were collected from the patients' electronic clinical records and included demographic data, medical comorbidities, tumor stage, and presence of a PCF postoperatively. The outcomes were overall survival (OS) and disease-free survival (DFS). OS was defined as the interval from the date of the surgical procedure to the date of all-cause death. DFS time was defined as the interval from the date of the surgical procedure to the date of disease recurrence (local, regional, or distant) or death. The date of disease recurrence was determined by the results of biopsies or imaging exams.

The reported tumor stage was based on the 7th edition of the AJCC TMN staging manual[8].

Statistical analysis

Kaplan-Meier and multivariate regression analyses using the Cox proportional hazards model were used to analyze survival and factors associated with OS/DFS, respectively. Descriptive and inferential statistical analyses were performed using the Statistical Package for the Social Science (SPSS®) software, version 29, and the level of statistical significance was set at $p < 0.05$.

This study was conducted according to the STROBE guidelines for observational studies[9].

Results

Patient characteristics

Fifty patients were included in the study, of which 48 (96%) were men and two (4%) were women. The mean age was 59.6 ± 10.1 years. The median patient follow-up time was 67 months (minimum of seven months and maximum of 118 months). With regard to the affected site, 19 (38%) patients had a supraglottic tumor, 10 (20%) patients had a glottic tumor, 10 (20%) patients had a hypopharyngeal tumor, and 11 (22%) patients had a transglottic tumor. Regarding the type of surgery, 38 (76%) patients underwent TL and 12 (24%) patients underwent TPL. With respect to the TNM staging, five (10%) patients had stage II cancer, 13 (26%) had stage III disease, and 32 (64%) had stage IVa disease. Negative margins were obtained in 42 (84%) patients. There were 22 deaths during the follow-up period. The causes of death were locoregional relapse (2, 4%), distant relapse (4, 8%), locoregional and distant relapse (4, 8%), second primary tumor (6, 12%), and non-cancerous causes (6, 12%).

Survival analysis

The Kaplan-Meier survival curves for OS and DFS are shown in Figures 1 and 2, respectively. The 5-year OS rates for patients without and with a PCF were 57% and 60%, respectively, while the 5-year DFS rates were 54% and 60% for patients without and with a PCF, respectively. Survival analysis did not show significant differences between the two groups regarding OS and DFS (p=0.642 and p=0.610 in the logrank test, respectively).

Multivariate analysis was performed to identify the potential confounders among the clinicopathologic factors that affect the

Figure 1
Overall survival among patients with and without a pharyngocutaneous fistula

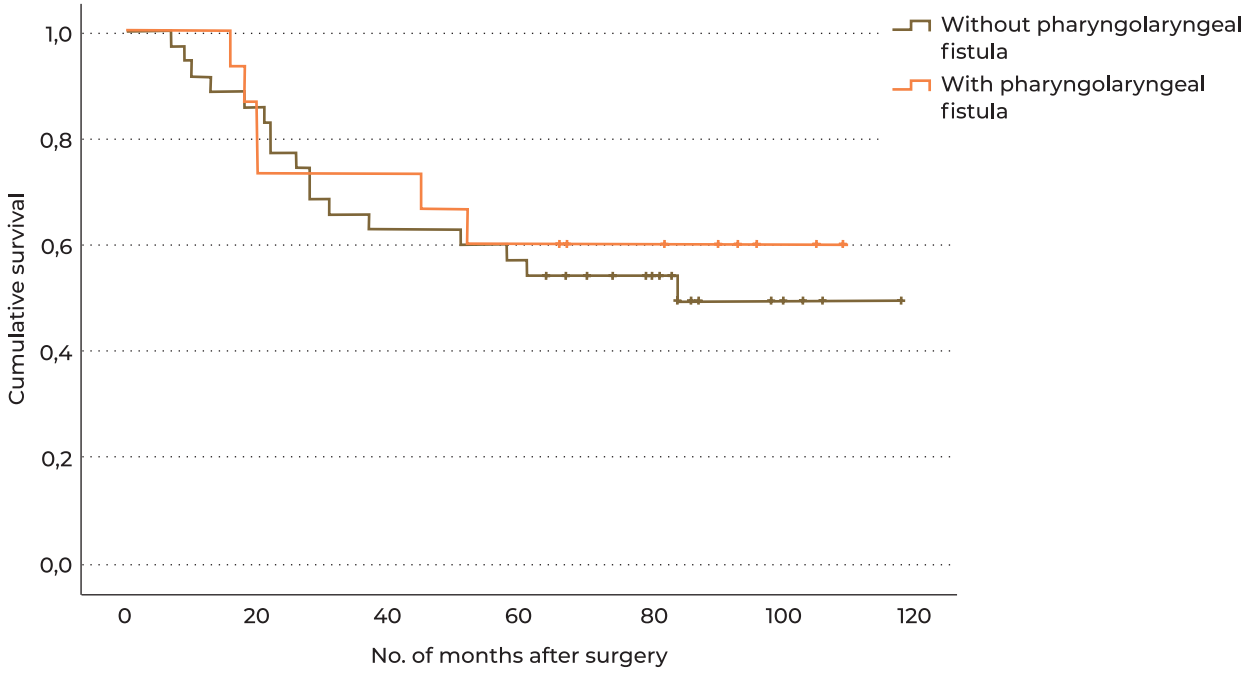

Figure 2
Disease-free survival among patients with and without a pharyngocutaneous fistula

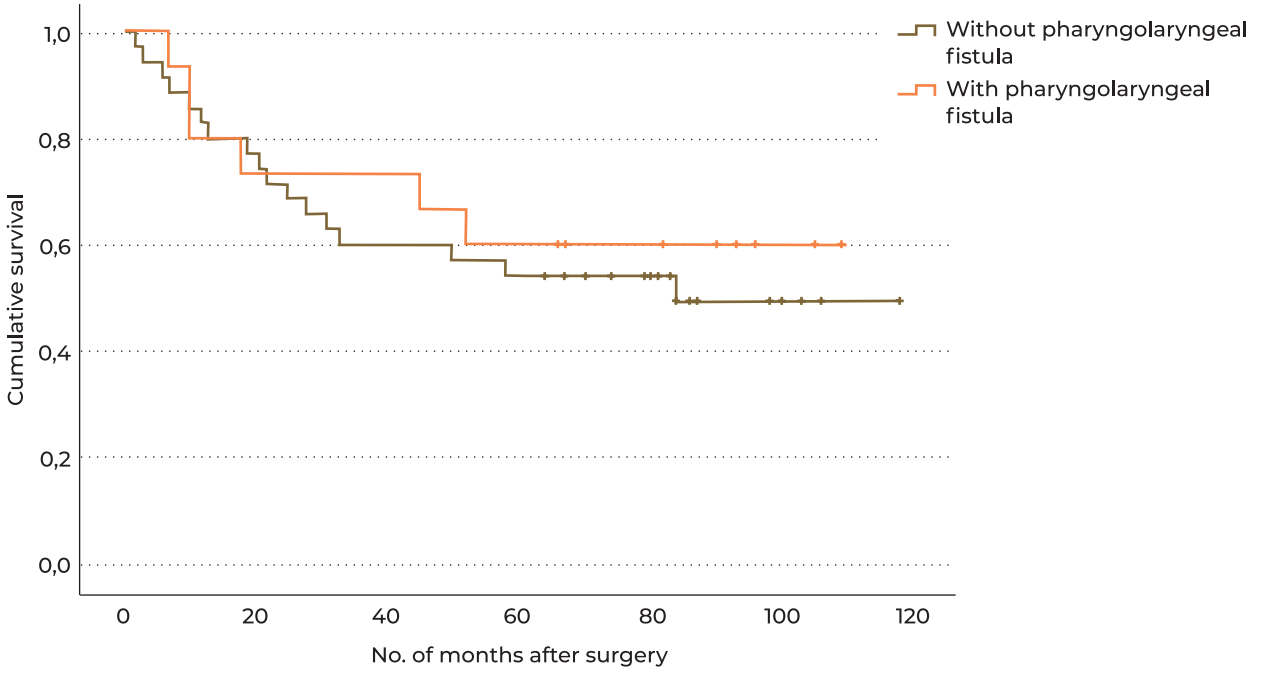

Table 1
Multivariate analysis for the clinical and pathological variables affecting overall survival and disease-free survival

	SG		SLD	
Variable	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**
Type of surgery				
Laryngectomy	Reference	0.698	Reference	0.839
Pharyngolaryngectomy	1.66 (0.13-21.17)		0.75 (0.05-12.24)	
Staging				
II	Reference		Reference	
III	1.16 (0.13-10.54)	0.898	1.29 (0.13-12.30)	0.828
IVa	1.54 (0.20-11.71)	0.677	1.79 (0.21-14.86)	0.591
Presence of fistula	0.31 (0.07-1.40)	0.128	0.34 (0.08-1.56)	0.165
Positive margins	2.77 (0.48-16.03)	0.257	1.54 (0.27-8.81)	0.625
Preoperative radiotherapy	9.25 (0.57-151.48)	0.119	13.77 (0.85-223.86)	0.065
Tracheostomy during the same surgery	0.39 (0.11-1.40)	0.147	0.59 (0.16-2.09)	0.410
Local				
Supraglottic	Reference		Reference	
Glottic	0.51 (0.10-2.49)	0.404	0.50 (0.10-2.41)	0.388
Hypopharynx	1.62 (0.07-36.27)	0.762	4.48 (0.13-146.02)	0.399
Transglottic	0.42 (0.79-2.21)	0.305	0.52 (0.10-2.56)	0.417
Arterial hypertension	5.12 (1.23-21.37)	0.025*	3.55 (0.84-14.95)	0.085
Diabetes Mellitus	0.15 (0.02-1.37)	0.092	0.24 (0.03-1.91)	0.177
Dyslipidemia	0.30 (0.06-1.40)	0.125	0.35 (0.07-1.73)	0.198
Heart failure	9.55 (1.07-85.14)	0.043*	3.76 (0.54-26.16)	0.181

Legend: OS, overall survival; DFS, disease-free survival; HR, hazard ratio; CI, confidence interval; SG p-values <0.05 are highlighted.

OS and DFS (Table 1). In the multivariate analysis of OS, arterial hypertension and heart failure demonstrated statistically significant differences (hazard ratio [HR] of 5.12 [p=0.025] and 9.55 [p=0.043], respectively). In the multivariate analysis of DFS, none of the variables showed statistically significant differences.

Discussion

PCF is an important postoperative complication of TL/TPL that often increases the length of hospital stay[7] and medical costs, and leads to increased perioperative morbidity and mortality. In addition, it contributes to delayed patient rehabilitation and need for other postoperative adjuvant treatments.

The rate of PCF obtained in the present study (30%) is in line with that reported in the literature, although it varies greatly among studies[1, 2, 3, 4, 5, 6, 10]. The relationship between local inflammation and tumor recurrence/progression has been studied in multiple cancers; however, data on how regional inflammation and infection affect the outcomes of patients with cancer remain scarce. Patients with PCF may develop intense local inflammation due to saliva coming into with neck tissues, which frequently leads to superjacent bacterial infection. It can also cause complications such as nutritional imbalance, aspiration pneumonia, carotid blow-out, and prolonged hospital stay[11, 12].

Recent studies have shown that PCF occurrence after salvage TL is associated with an increased risk of developing distant metastases, but has no apparent impact on OS or DFS[6]. Additionally, salvage TL is more

frequently associated with earlier formation of PCF than primary TL[3]. Several studies have analyzed the effect of surgical wound infection on epidermoid carcinoma of the head and neck; some found that it affected DFS[13], whereas others reported no impact on OS [14, 15]. Several factors have been proposed as the risk factors for the development of PCF, namely postoperative anemia and hypoalbuminemia, previous RT, previous tracheostomy, positive surgical margins, and tumor stage and location[2, 3, 4, 6, 10]. The identification of positive surgical margins as a risk factor for PCF may explain the association between PCF and increased risk of locoregional recurrence.

The present study showed that the presence of a postoperative PCF in patients who underwent TL or TPL did not have an impact on the long-term cancer outcomes, with similar rates of OS and DFS. Among the analyzed variables, only arterial hypertension and heart failure were found to influence OS, which can be explained by the cardiovascular risks associated with these diseases, which in turn have a substantial impact on OS. Tumor stage was not correlated with OS and DFS, which may be attributable to the small sample size. This study has the following limitations: the fact that it was a retrospective study did not allow controlling for confounding variables that were not available in the clinical records; the sample size was small, with few deaths caused by locoregional and distant recurrence, and larger samples are necessary to determine the differences in the cancer outcomes. Despite these limitations, this study is one of the few studies to directly assess the impact of PCF on the prognosis of patients undergoing TL/TPL. The literature on PCF and its relationship with cancer outcomes is, in general, very scarce. A multicenter prospective study is warranted to provide data with a higher statistical power and better external validation.

Conclusion

In this retrospective cohort study, the presence of a PCF was found not to influence the OS and DFS in patients who underwent TL/TPL for treatment of laryngeal/hypopharyngeal epidermoid carcinoma. However, further prospective studies are recommended for a better understanding of this relationship and the underlying mechanisms.

Conflict of interest

The authors declare no conflict of interest regarding this article.

Data confidentiality

The authors declare that they followed the protocols in use at their working center regarding the publication of patients' data.

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Availability of scientific data

There are no publicly available datasets related to this study.

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