

Predictors of salivary fistula after total laryngectomy

Fatores preditores de fístula salivar pós-laringectomia total

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A B S T R A C T

Objective: To evaluate the incidence of pharyngocutaneous fistula after total laryngectomy and try to identify its predictors. **Methods:** From May 2005 to April 2010, 93 patients underwent total laryngectomy. We evaluated complications during and after surgery and compared them with the following variables: gender, nutritional status, previous tracheotomy, tumor location, type of surgery, TNM staging, prior treatment with chemotherapy and/or radiotherapy, use of flaps for reconstruction and surgical margin. All patients presented with advanced neoplastic disease according to TNM. **Results:** 14 (15.1%) patients developed postoperative salivary fistula. The mean time to onset of salivary fistula was 3.5 days, with a standard deviation of 13.7 days. Comparing salivary fistula with TNM variables, type of operation and neck dissection, prior tracheotomy, use of flap, preoperative radio and chemotherapy and surgical margin, there was no statistically significant difference ($p > 0,05$). **Conclusion:** The incidence of salivary fistula was 15.1% and no predictive factor for its formation was found.

Key words: Digestive system fistula. Salivary gland fistula. Postoperative complications. Laryngectomy. Laryngeal neoplasms.

INTRODUCTION

Surgery for head and neck cancer routinely addresses elderly, smoker patients, with vascular diseases, diabetes and other diseases that predispose to various postoperative complications that are directly associated with increased morbidity, hospitalization time and cost of treatment¹⁻⁵.

Complications may be general or specific. Among the former, there are hematomas, wound infection and systemic complications such as pulmonary embolism and acute myocardial infarction. As for the specific complications, they are related to the surgical procedure performed.

Amongst the complications related to laryngectomy, pharyngocutaneous fistula is most common after total laryngectomy, with an incidence of 3% to 65%. The risk factors identified as predictors of fistula are: malnutrition, compromised surgical margins, radiotherapy, neck dissection, previous tracheotomy, advanced tumor stage and poor surgical technique¹⁻⁶.

The aim of this study was to evaluate the profile of patients with laryngeal cancer, to determine the incidence of complications after total laryngectomy and try to identify the predictive factors for postoperative complications.

METHODS

We conducted a retrospective study with review of medical records of patients who underwent total laryngectomy in the period from May 2005 to April 2010 by the Head and Neck team of the Alfa Institute of Gastroenterology, Hospital das Clínicas. Patients were operated on at the Hospital of the Whale, on the Hospital das Clínicas in Belo Horizonte and on São João de Deus Hospital in Divinópolis, all in the State of Minas Gerais. The study was approved by the Research Ethics Committee of UFMG - number 0584.1.203.000-09.

All patients had squamous cell carcinoma, with primary site in the larynx, the vallecula or piriform sinus. We revised pre, peri and post-operative routines to check whether there were differences in the treatment of patients. We evaluated the complications during and after surgery and compared with the following variables: gender, nutritional status, previous tracheotomy, tumor location, type of surgery (primary site and cervical dissection), staging according to the TNM⁷, prior chemotherapy and / or radiation therapy, use of flaps for reconstruction and surgical margin.

Statistical analysis was performed using a significance level of 5% for all tests.

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RESULTS

From May 2005 to April 2010, 93 patients were operated, 33 in the Hospital of the Whale, 32 in the Hospital das Clínicas and 28 at Sao Joao de Deus Hospital.

Surgical treatment was standard with regard to the surgical technique and care before, during and after surgery. Patients received clindamycin at a dose of 600mg of 6/6 hours in the immediate preoperative period, intraoperatively, and in the first 24 hours after the procedure.

After laryngectomy pharyngeal closure was performed primarily with 3-0 Vycril®, with a continuous suture in "T".

For patients in whom the pharyngeal remnant was considered inadequate for primary closure and in cases in which chemoradiotherapy was used as the primary treatment, we applied a flap of pectoralis major muscle in the reconstruction of the pharynx. In such cases the edges of the pharyngeal remains were sutured to the skin of the flap with 3-0 Vycril®.

All patients received enteral feeding from the first postoperative day (POD) via a nasogastric catheter. In patients without salivary fistula, oral diet was started in the seventh POD, and its consistency changed gradually in the following days, starting with a liquid diet, then pasty and finally solid.

In cases of wound infection or salivary fistula, antibiotic therapy with ceftriaxone and clindamycin was indicated and maintained for ten to 14 days. During this period, patients were kept in exclusive enteral nutrition.

The average age of patients was 58.9 (32-86) years, 87 (93.5%) were male and six (6.5%) female.

Regarding nutritional status, 35 (64.7%) patients were nourished in the immediate preoperative period. The malnourished, classified as mild, moderate and severe, were, respectively, five (9.3%), nine (16.7%) and five (9.3%). In 39 patients there was no information in the medical records. Seven (20.0%) nourished and seven (36.8%) malnourished patients progressed to salivary fistula postoperatively, no statistically significant difference being found between the two groups ($p = .15$).

A tracheostomy prior to definitive surgical treatment was performed in 43 (46.2%) patients.

The staging of patients according to the TNM is shown in Table 1. For this staging, we considered the data from the histopathological examination.

Regarding the location of the tumor, 25.7% were supraglottic, 22.5% transglottic, 22.5% in the hypopharynx, 20.3% in the glottis, 6.5% in the vallecula and 2.5% were subglottic.

Resection was the first therapeutic option in 78 (83.9%) patients and 15 (16.1%) were submitted to prior radiotherapy and / or chemotherapy, and of these, two patients underwent total laryngectomy associated with neck dissection (bilateral jugular in one patient and jugular + radical in another). The other 13 (14.0%) patients underwent only rescue total laryngectomy (Table 2). After excision of the tumor we found that ten patients had infiltrated surgical margins, they being resected (Table 3).

Twenty-two (23.6%) patients required reconstruction of the pharynx with pectoralis major flap. In the other 71 cases, the closure was primary.

The mean operative time was 308.9 minutes, with a minimum of 120 and maximum of 550 minutes.

The nasogastric catheter was kept for seven to 150 days for enteral nutrition, with an average of 26.08 days. Oral intake was started on average at 17.7 + 14.7 PODs, ranging from seven to 90 days.

Among the surgical complications, 14 (15.1%) patients had postoperative salivary fistula, and the mean time to onset was 3.5 days, with a standard deviation of 13.7 days. Thirteen (14.0%) patients had wound infection, three (3.2%) developed cervical hematoma requiring

Table 1 - Staging of patients according to TNM (n = 93).

Stage		N	%
Stage T	T3	23	24.7
	T4	70	75.3
Stage N	N0	42	45.2
	N1	20	21.5
	N2	27	29.0
	N3	4	4.3

Table 2 - Surgical Treatment employed, including procedures performed on the neck (n = 93).

Surgical procedure		N	%
Primary Tumor	Total laryngectomy	48	51.6
	Total Pharyngolaryngectomy	37	39.8
	Base Glossectomy + total laryngectomy	8	8.6
Neck	Without cervical emptying	13	14.0
	Bilateral Cervical radical emptying	15	16.1
	Cervical radical emptying + jugular emptying	46	49.5
	Bilateral jugular emptying	19	20.4

surgical intervention and two (2.2%) developed pneumonia.

Considering only the salivary fistula and comparing it with the variables studied, there was no statistically significant difference ($p = 0.19$) between the presence of metastasis and tumor stage and the presence of salivary fistula (Tables 4 and 5). Table 6 shows the comparison between these variables and the incidence of salivary fistula.

DISCUSSION

Surgical complications are directly associated with increased length of hospital stay, treatment costs and delay in the start of radiotherapy, and consequent worse outcomes in oncological control^{1,3}.

Several factors may contribute to increase in the incidence of complications, including radiation therapy with or without preoperative chemotherapy, malnutrition, operative time and tumor stage^{2-6,8,9}.

In this study, like most in the literature, the most frequent complication after total laryngectomy was pharyngocutaneous fistula. The incidence was 15.1%,

which is consistent with that found in the literature^{1-4,8,10}. The average time from onset of salivary fistula was 3.5 days, which was also observed in other studies^{5,11}. Wound infection is directly related to the presence of salivary fistula.

Clinical signs of onset of salivary fistula include edema and hyperemia of the neck skin, increase in drainage of wound drains and sometimes fever^{4,12}. The identification of those signs enables early diagnosis and treatment of salivary fistulae, reducing the risk for more serious infections¹³.

Regarding the treatment of salivary fistula, there is a consensus that, initially, it should be conservative (antibiotics and dressing), as fistulas close spontaneously in most cases^{4,14,15}. Surgical treatment is reserved for cases of failure of the clinical treatment¹⁴. In this series, no patient required surgical closure of salivary fistula.

Patients with tumors in the head and neck are, in most cases, malnourished. Two factors are associated with, and contribute to, malnutrition: one is the cancer, which leads to inefficient metabolism of carbohydrates, accelerated catabolism of proteins and progressive depletion of lipids. The other is mechanical, due to the presence of the tumor, which leads, in some cases, to dysphagia, odynophagia and reduction of food intake⁸. The diagnosis of malnutrition is actually a combination of clinical and laboratory variables. From a clinical standpoint, weight loss greater than 10% of the usual weight in the preoperative period classifies the patient as with severe malnutrition. This weight loss is considered as a predictor for major postoperative complications⁴. In this study, although approximately 60% of patients were malnourished, this factor did not increase the incidence of salivary fistula ($p = .45$).

As for routine exams, we can make use of Plasma protein (albumin and transferrin), and lymphocyte

Table 3 - Condition of surgical margins in the 93 patients.

Surgical margin	N	%
Free margins	76	81.7
Invasive Carcinoma	7	7.5
Carcinoma in situ	2	2.1
Strenuous	1	1.2
No information	7	7.5

Table 4 - Incidence of salivary fistula according to the stage of metastases in 82 patients.

Stage N	Salivary fistula		Value of p
	Group with fistula n (%)	Group without fistula n (%)	
N0	10 (25.6%)	29 (74.4%)	0.09
Positive N	4 (9.3%)	39 (90.7%)	

* In 11 patients there was information in the medical records

Table 5 - Incidence of salivary fistula according to tumor stage in 79 patients.

Stage T	Salivary fistula		Value of p
	Group with fistula n (%)	Group without fistula n (%)	
T3	5 (23.8%)	16 (76.2%)	0.40
T4	9 (15.5%)	49 (84.5%)	

* In 14 patients there was information in the medical records

Table 6 - Incidence of salivary fistula according to their possible causes.

Variable	Salivary fistula		Value of p
	Yes n (%)	No n (%)	
Total laryngectomy	6 (12.5%)	42 (87.5%)	0.26
Total Pharyngolaryngectomy	8 (21.6%)	29 (78.4%)	
Total Glossectomy + total laryngectomy	0 (0.0%)	8 (100.0%)	
Without cervical emptying	4 (30.8%)	9 (69.2%)	0.25
Bilateral Cervical radical emptying	1 (6.7%)	14 (93.3%)	
Cervical radical emptying + jugular emptying	6 (13.0%)	40 (87.0%)	
Bilateral jugular emptying	3 (15.8%)	16 (84.2%)	0.46
Preoperative Chem/Rad	Yes	13 (20.0%)	
(n = 85)	No	11 (15.7%)	
Myocutaneous flap	Yes	4 (20.0%)	
(n = 84)	No	10 (15.6%)	
Prior tracheostomy	Yes	6 (14.6%)	
(n = 84)	No	8 (18.6%)	0.63
Surgical margin	Free	12 (16.0%)	
(n = 85)	Committed	2 (20.0%)	0.51

* N is less than 93 for some variables studied due to the absence of information in the medical records.
Chem/Rad: Chemotherapy and Radiotherapy.

count. Boscolo-Rizzo *et al.*³ showed in a multivariate analysis that low pre-operative albumin is associated with higher incidence of surgical complications, including salivary fistula. In this study, we did not find albumin values in the records studied. Lymphocytopenia, which could also be assessed, was not found in the preoperative blood counts either.

The tumor stage is one of the predictors of salivary fistula^{1,5-7,10,11,16} most discussed in the literature. Nevertheless, in our study, there was no increased incidence of salivary fistula in patients with advanced tumors.

According to Virtaniemi *et al.*¹¹, supraglottic tumors require more extensive resections, including the pharyngeal wall, which may result in more tension on the pharyngeal suture line and thus increased risk of salivary fistula. This finding was not observed in the current study. There was also no statistically significant difference between the sites of the operated tumors, perhaps by use of flap, used routinely in these cases, as well as in cases of prior treatment with chemoradiotherapy and in those with tension on the suture line.

Patients undergoing neck dissection have higher incidence of salivary fistula than those treated with total laryngectomy^{8,13}. However, this finding was not observed in this study (p = 0.25), neither by other authors^{3-5,11,14,16}.

Previous tracheostomy was not a predictor of salivary fistula, which is in agreement with data found in the literature^{5,12,15,17}. In general, patients undergoing tracheostomy preoperatively had tumors in more advanced stage and therefore the predictor of salivary fistula was the tumor stage and not prior tracheostomy.

Surgical margin involvement by neoplasia occurred in 10.7% of cases, and this fact did not influence the onset of salivary fistula (p = 0.72), which is consistent with Dedivitis *et al.*'s findings⁶, although Markou *et al.*¹⁸ have observed a significant increase in incidence of salivary fistula in such cases.

Preoperative radiotherapy and chemotherapy did not predispose patients to salivary fistula, a finding also described by other authors^{1-5,10,11}. However, a higher incidence of salivary fistula in patients so treated, in addition to its earlier onset, have been reported^{6,12,14,17,19}. These authors showed that the incidence of salivary fistula was directly related to the radiation dose received by the patient, with doses above 5000 cGy displaying higher risk. Some studies show that the incidence of salivary fistula was not altered by previous radiotherapy treatment; nonetheless, those that occurred in these circumstances were more severe and long-lasting^{5,19}.

The use of myocutaneous flap for reconstruction of the pharynx was not a predictor for the onset of salivary fistula (p = .66). Perhaps the use of the flap has provided a lower rate of salivary fistula, whereas patients who needed them, at first, had a more advanced stage tumors or were subjected to rescue operations after radiotherapy and / or chemotherapy. Sarra *et al.*¹⁵ suggest the use of flaps in reoperations or in cases of pharyngeal stenosis observed still during the procedure. Smith *et al.*⁸ used the flap systematically in all cases of total laryngectomy and showed drastic reduction in the incidence of salivary fistula. Sousa *et al.*¹ and Tsou *et al.*¹⁴ also suggest the use of flap for closure of the pharyngeal wall in all cases after radio/

chemotherapy rescue surgery. This is the routine of our Service. The placement of a non-irradiated tissue in a bed that was already irradiated perhaps fosters a more appropriate healing and reduces the rates of fistula.

The wide variation in the incidence of salivary fistula found in the literature can be explained by the wide variation in patient selection and surgical techniques. In

this study, in order to evaluate the profile of patients and the incidence of complications, we included all patients who underwent total laryngectomy, even rescue ones, or requiring flap reconstruction, whether pharyngeal or of the tongue base. We conclude that there was no predictor of salivary fistula and that the incidence of salivary fistula was 15.1%, similar to that found in the literature.

R E S U M O

Objetivo: Avaliar a incidência de fistula faringocutânea após laringectomia total e tentar identificar os fatores preditores. **Métodos:** No período de maio de 2005 a abril de 2010, 93 pacientes foram submetidos à laringectomia total. Foram avaliadas as complicações per e pós-operatórias e comparadas com as seguintes variáveis: sexo, estado nutricional, traqueostomia prévia, localização do tumor primário, tipo de operação realizada, estadiamento de acordo com o TNM, tratamento prévio com quimioterapia e/ou radioterapia, utilização de retalhos para reconstrução e margem cirúrgica. Todos os pacientes apresentavam a neoplasia em estágio avançado segundo o TNM. **Resultados:** 14 (15,1%) pacientes evoluíram com fistula salivar no pós-operatório. O tempo médio de aparecimento da fistula salivar foi 3,5 dias, com desvio padrão de 13,7 dias. Comparando a fistula salivar com as variáveis TNM, tipo de operação e esvaziamento cervical, traqueostomia prévia, utilização de retalho miocutâneo, rádio e quimioterapia pré-operatória e margem cirúrgica, não foi observado diferença estatisticamente significativa ($p>0,05$). **Conclusão:** A incidência de fistula salivar foi 15,1% e não foi encontrado fator preditor para sua formação.

Descritores: *Fístula do sistema digestório. Fístula das glândulas salivares. Complicações pós-operatórias. Laringectomia. Neoplasias laríngeas.*

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