

ONCOLOGY

Pharyngocutaneous fistula following total laryngectomy

Le fistole faringocutanee negli esiti di laringectomia totale

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SUMMARY

Pharyngocutaneous fistula is the most common complication after total laryngectomy. The aim of the study was to establish the incidence of this complication in our series and analyse the predisposing factors. This is a retrospective study comprising 55 patients who underwent total laryngectomy. The following aspects were considered: sex, age, tumour site, pathologic staging according to TNM, performance and type of neck dissection, previous radiation therapy, previous tracheotomy, Cumulative Illness Rating Scale for comorbidity analysis, the use of stapler for pharyngeal closure, and peri-operative blood transfusion. In the cases of pharyngocutaneous fistula, we considered the post-operative period in which it was diagnosed, duration, period of hospitalization, as well as therapeutic approach and the eventual result of this treatment. Pharyngocutaneous fistula was diagnosed in 7 patients (12.7%). There were no statistically significant associations between fistula development and sex ($p = 1.000$), previous radiation therapy ($p = 0.354$), stapler closure ($p = 0.577$), comorbidity ($p = 1.000$) or tumour site ($p = 0.926$). Patients previously submitted to tracheotomy presented higher fistula incidence (60%), compared to those that had not undergone this procedure (8%) ($p = 0.012$). Elderly patients (> 60 years) were also more predisposed to fistula development ($p = 0.051$). Although without statistical significance, fistula development was also associated with peri-operative blood transfusion, T stage, and type of neck dissection.

KEY WORDS: Laryngeal cancer • Total laryngectomy • Complications • Pharyngocutaneous fistula

RIASSUNTO

Le fistole faringocutanee rappresentano la più comune complicanza delle laringectomie totali. Lo scopo di questo studio è stato di stabilire l'incidenza di questa complicanza nella nostra casistica e di analizzarne i fattori predisponenti. In questo studio retrospettivo abbiamo valutato 55 pazienti che erano stati sottoposti a laringectomia totale. Sono stati presi in considerazione i seguenti dati: sesso, età, sede del tumore, stadio della neoplasia in accordo con il TNM, tipo di svuotamento laterocervicale eseguito, eventuale esecuzione di radioterapia pre-operatoria, esecuzione di tracheotomia precedentemente all'intervento, comorbidità mediante utilizzazione della Cumulative Illness Rating Scale, uso di suturatrice per la chiusura faringea, trasfusione ematica perioperatoria. Nei casi in cui era presente la fistola faringocutanea, abbiamo valutato la giornata post-operatoria in cui è stata diagnosticata, la durata dell'ospedalizzazione, l'approccio terapeutico e i risultati della terapia effettuata. In totale è stata diagnosticata una fistola faringocutanea in 7 pazienti (12,7%). Non è stata osservata un'associazione statisticamente significativa tra lo sviluppo della fistola e il sesso ($p = 1,000$), la radioterapia pre-operatoria ($p = 0,354$), la chiusura con suturatrice ($p = 0,577$), la comorbidità ($p = 1,000$) e la sede del tumore ($p = 0,926$). I pazienti sottoposti a tracheotomia precedentemente alla laringectomia totale hanno presentato una più alta incidenza di fistole (60%), in rapporto agli altri pazienti (8%) ($p = 0,012$). I pazienti più anziani (> 60 anni) hanno presentato anch'essi una incidenza più elevata di fistole ($p = 0,051$). Sebbene con valori non statisticamente significativi, sono risultati correlati all'incidenza di fistole anche le trasfusioni perioperatorie, lo stadio del tumore, e il tipo di svuotamento laterocervicale eseguito.

PAROLE CHIAVE: Carcinoma della laringe • Laringectomia totale • Complicazioni • Fistole faringocutanee

Acta Otorhinolaryngol Ital 2007;27:2-5

Introduction

Pharyngocutaneous fistula (PCF) is the most common complication after total laryngectomy. It considerably increases morbidity, hospitalization time and expense, and delays starting adjuvant radiation therapy¹. Besides prolonging hospital stay, the salivary fistula predisposes to major injury of neck vessels and causes discomfort because of feeding through a nasogastric tube². The reported incidence of PCF ranges from 3% to 65%^{3,5}. Aim of the investigation was to

establish the incidence of this complication in our series and analyse the predisposing factors.

Patients and methods

From January, 1996 to December, 2004, 55 patients underwent total laryngectomy in the Service of Head and Neck Surgery of Ana Costa Hospital, and Division of Head and Neck Surgery of Irmandade da Santa Casa da Misericórdia de Santos, Brazil.

The patients were retrospectively studied regarding PCF. Squamous cell carcinoma was the histopathologic diagnosis in all cases. The following aspects were considered: sex, age, tumour site, the pathological primary tumour staging according to TNM, the performance and type of neck dissection, previous radiation therapy, previous tracheotomy, the Cumulative Illness Rating Scale (CIRS) ⁶ for comorbidity analysis, the use of stapler for pharyngeal closure, and peri-operative blood transfusion.

All patients staged as T4 underwent partial pharyngectomy in addition to total laryngectomy. The patients received prophylactic intravenous amikacin and clindamicyn association during the immediate post-operative day starting at the anaesthetic induction. All pharyngeal closures were primary without flap rotation. Two types of closure were performed: a "T-shaped" closure by means of 3-0 polygalactin suture material or using the TCL75 Ethicon® (Johnson & Johnson) linear stapler. Primary tracheo-oesophageal puncture was routinely carried out.

In the cases of PCF, we took into consideration the post-operative day on which it was diagnosed, its duration, the period of hospitalization, therapeutic approach and outcome. All patients received oral intake after the tenth post-operative day, if the fistula survey resulted negative. Fistulas were not observed thereafter in those patients in whom the examination was initially negative.

Statistical analysis included assessment of central trend and dispersion, absolute and relative frequencies and Fisher's Exact Test to verify association between all categorical variables and development of fistula. For all the statistical tests, alpha error was equal to 5%.

Results

The cohort comprised 55 patients: 50 male (90.9%) and only 5 female (9.1%). Mean age was 59.7 ± 9.4 years (range 35-80). Most patients had glottic tumours (54.5%), and mainly pT3 (69.1%). Comorbidity level, according to CIRS, varied from 0 to 8 (median = 1). Overall, 47 patients (85.5%) underwent neck dissection and 14 (25.5%) received pre-operative radiation therapy. Pre-operative tracheotomy was performed only in 5 cases (9.1%), whereas closure using the stapler and peri-operative blood transfusion were performed in 6 and 9 patients, respectively (Table I).

PCF was diagnosed in 7 patients, achieving an incidence rate equal to 12.7%. There were no statistically significant associations between fistula development and sex ($p = 1.000$), previous radiation therapy ($p = 0.354$), stapler closure ($p = 0.577$), co-morbidity ($p = 1.000$) or tumour site ($p = 0.926$). Patients previously submitted to tracheotomy presented a higher fistula incidence (60%), compared to those not undergoing this procedure (8%) ($p = 0.012$). Elderly patients (> 60 years) were also more predisposed to fistula development ($p = 0.051$). Although not statistically significant, fistula development was also associated with peri-operative blood transfusion, T stage, and type of neck dissection (Table II).

The fistulas were diagnosed from the 3rd to the 8th post-operative day. According to the classification system of Horgan and Dedo ⁷, there were 5 minor fistulas (that persisted less than 8 weeks) and 2 major fistulas (that persisted more than 8 weeks). The hospitalization time varied from 2 to 30 days

Table I. Patient distribution according to demographic, clinical, and treatment characteristics (n = 55).

Variables	N.	%
Sex		
Male	50	90.9
Female	5	9.1
Age, y		
≤ 60	28	50.9
> 60	27	49.1
Tumour site		
Glottis	30	54.5
Supraglottis	15	27.3
Subglottis	3	5.5
Piriform sinus	7	12.7
pT stage		
pT2	1	1.8
pT3	38	69.1
pT4	16	29.1
Neck dissection		
No	8	14.5
Bilateral jugular	10	18.2
Radical + jugular	8	14.5
Bilateral radical	28	51.0
Unilateral jugular	1	1.8
Previous radiation therapy		
Yes	14	25.4
No	41	74.6
Previous tracheotomy		
Yes	5	9.1
No	50	90.9
Comorbidity (CIRS)		
0	8	14.5
≥ 1	47	85.5
Closure with stapler		
Yes	6	10.9
No	49	89.1
Blood transfusion		
Yes	9	16.4
No	46	83.6

(mean, 12.8) in contrast to those without this complication, whose mean hospitalization time was 3 days.

Some patients were discharged with their fistula still open if their conditions were good enough for treatment at home. The PCF did not delay the onset of radiation therapy in the patients referred for adjuvant treatment. In 5 patients, the fistula resolved after clinical care, whereas in the other 2, surgical intervention was required with successful deltopectoral flap rotation. Two patients submitted to clinical care, died from the cancer without resolution of

Table II. Patient distribution according to demographic, clinical, and treatment characteristics and occurrence of pharyngocutaneous fistula (n = 55).

Variables	Category	Pharyngocutaneous fistula (%)		p
		No	Yes	
Sex	Male	43 (86.0)	7 (14.0)	1.000
	Female	5 (100.0)	0 (0.0)	
Age (years)	> 60	27 (96.4)	1 (3.6)	0.051
	≤ 60	21 (77.8)	6 (22.2)	
Tumour site	Glottis	26 (86.7)	4 (13.3)	0.926
	Subglottis	3 (100.0)	0 (0.0)	
	Supraglottis	13 (86.7)	2 (13.3)	
	Piriform sinus	6 (85.7)	1 (14.3)	
pT stage	T2-3	36 (92.3)	3 (7.7)	0.175
	T4	12 (75.0)	4 (25.0)	
Neck dissection	No/Other types	26 (96.3)	1 (3.7)	0.101
	Bilateral radical	22 (78.6)	6 (21.4)	
Previous radiation therapy	No	37 (90.2)	4 (9.8)	0.354
	Yes	11 (78.6)	3 (21.4)	
Previous tracheotomy	No	46 (92.0)	4 (8.0)	0.012
	Yes	2 (40.0)	3 (60.0)	
Comorbidity (CIRS)	0	7 (87.5)	1 (12.5)	1.000
	≥ 1	41 (87.2)	6 (12.8)	
Peri-operative blood transfusion	No	42 (91.3)	4 (8.7)	0.078
	Yes	6 (66.7)	3 (33.3)	
Closure with stapler	No	43 (87.8)	6 (12.2)	0.577
	Yes	5 (83.3)	1 (16.7)	

the fistula. There were no cases of neoplastic fistula. Three out of five patients who had undergone previous tracheotomy presented PCF.

Discussion

The management of PCF can considerably increase hospitalization time and expense, delay the initiation of adjuvant radiation therapy, when indicated, and has an impact on the well-being not only of the patient but also the family. PCF is a complication that appears in the early post-operative period after total laryngectomy – in our patients from the 3rd to the 8th post-operative day. Mean hospitalization time was 12.8 days whereas in the group of patients without fistula it was only 3 days. We discharge patients with PCF as soon as possible. Those who would have adequate home care were discharged even without resolution of their fistula.

As supraglottic tumours require resection of large amounts of pharyngeal mucosa leading to closure under tension, these were considered as a risk factor for fistula formation⁵. In another series, only partial pharyngectomy associated with total laryngectomy was statistically significant as a risk factor for PCF².

Patients undergoing concurrent neck dissection had a higher incidence of PCF compared with those undergoing standard laryngectomy^{5,8}.

Within the total laryngectomy group, there was no significant difference between complication rates when either pre-operative or post-operative radiation was employed^{2,4,5}, in disagreement with other Authors^{8,9}. While there is a 2% to 3% risk of fistula development when primary laryngectomy is performed, the incidence increased to about 10% to 12% following radiation therapy, with an additional increase whenever previous operations on the neck had been performed and/or if the disease demanded more extensive surgery⁹. It is also reported that PCF appears earlier in patients with pre-operative radiation therapy⁵. Prior radiation therapy at a dose higher than 5,000 cGy was considered as the most significant risk factor in other reports¹⁰. A fistula rate of 80% was found in patients undergoing salvage total laryngectomy following 6,800 to 7,200 cGy¹¹.

Organ preservation treatment is considered an option for advanced laryngeal cancer. Whether the addition of chemotherapy to radiotherapy increases the risk of post-operative complications, in the setting of salvage total laryngectomy, is uncertain. In a randomized prospective trial, 517 patients were divided into 3 arms: 1) chemotherapy followed by radiation therapy; 2) concomitant chemotherapy and radiation therapy; and 3) exclusive radiation therapy. PCF was lowest in arm 3 (15%) and highest in arm 2 (30%)¹².

We found a higher rate of PCF in the patients who had previously undergone tracheotomy than in those who had not (60% vs. 8% – p = 0.012). This was probably due to higher

T stage, fibrosis, and contamination. Our study indicates that peri-operative blood transfusion, T stage, and neck dissection are marginally significant. Controversial reports have appeared in the literature. One series reports a 28% PCF rate in patients who received blood transfusion, compared with a rate of 7% in those who did not¹³. On the other hand, other Authors did not find any correlation¹⁴.

The weakest point as far as concerns the pharyngeal closure is the three-point junction when "T-shaped" closure is performed¹⁵. This point is avoided if the closure is performed using a stapler. Stapler closure does not increase PCF incidence¹⁶.

The histological infiltration of the surgical margins of the tumour (11% negative vs. 38% with positive margins) was correlated with early PCF¹⁷. In spite of this finding, these Authors did not consider PCF an adverse prognostic factor as far as concerns patient survival. We did not consider the surgical margins as a variable since we perform the frozen section examination of the margins removed from the patients' surgical field instead of the pathological specimen which represents a safety measure.

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We routinely remove the nasogastric tube after the tenth post-operative day. In one series, 48 patients were orally fed on the first post-operative day and the PCF rate was 12.5%. Resection of pharyngeal mucosa as an extension of total laryngectomy was the only statistically significant factor that increases this rate². Also in a case-controlled study, early initiation of oral feeding was not considered as a contributing factor in PCF¹⁸. In another study, PCF was lower in the group of patients fed before the seventh post-operative day (5.9%), whereas it was higher in those fed after this day (29.6%)¹⁹.

Conclusions

We conclude that PCF, after total laryngectomy, significantly increases patient hospitalization. Patients previously submitted to tracheotomy and elderly patients (> 60 years) presented a higher incidence of fistula. Although not statistically significant, fistula development was also associated with peri-operative blood transfusion, T stage, and type of neck dissection.

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Received: March 30, 2006 - Accepted: July 24, 2006