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Prognostic role of pneumonia in supracricoid and supraglottic laryngectomies

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Summary The goal of this study was to identify host and tumour factors associated with postoperative pneumonia (PP) in a selected population of laryngeal cancer patients, treated by partial laryngectomy in 20 years at our Institution and to assess its potential prognostic impact.
Clinical records of 416 consecutive patients were retrospectively reviewed. Tobacco consumption, body mass index (BMI), previous pulmonary disease, age, sex, preoperative blood gas analysis values, tumour stage and type of surgery were tested as potential risk factors for PP. Finally, the prognostic impact of these variables, including PP, in terms of disease-free and actuarial survival by Kaplan–Meier and Cox analyses were evaluated.
PP developed in 73 patients (16.8%). We identified two groups of patients: 26 patients experienced an early PP within the first 7–9 days after surgery, whilst 44 experienced an *ab ingestis* PP following attempts of oral food intake restoration, three patients died for PP related sepsis.
At multivariate Cox analysis, age older than 60 years and BMI greater than 30 were statistically associated with early PP; whereas male gender and laryngectomy with neck dissection were statistically related to a higher risk of *ab ingestis* PP.
Interestingly, the occurrence of early PP was a negative independent prognostic factor for 5-years disease-free and actuarial survival ($p = 0.049$ and $p = 0.001$, respectively).
The occurrence of early-onset pneumonia in laryngeal cancer patients selected for conservative laryngectomies is predictable and associated with poor clinical outcome.

Introduction

Partial laryngeal surgery in patients with squamous cell carcinoma aims to preserve the natural protective, respiratory and phonatory functions of the larynx in contrast to total

Abbreviation: PP, postoperative pneumonia.

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laryngectomy where all these functions are lost.[1] Partial excision of the larynx with alteration of its physiological mechanisms affects not only the phonatory but also the swallowing function with possible aspiration that can lead to life-threatening complications, mainly pneumonia.[2,3] Despite any attempt to preserve and reconstruct a normal physiology of the larynx, conservative approaches, such as supraglottic and supracricoid partial laryngectomies cause a consistent alteration of the laryngeal anatomy and physiology affecting laryngeal elevation, laryngeal closure and bolus progression. These impaired function need to be managed by postoperative swallowing rehabilitation.

The occurrence of PP represents a primary source of increased cost and morbidity not only after partial laryngectomy, but also after other major head and neck surgery, particularly with a tracheotomy, occurring in 20% or more of cases.[4]

The aetiology of PP following partial laryngeal surgery, however, is most likely multifactorial considering that several host and tumour factors such as age, obesity, poor preoperative pulmonary function tests, smoking history, type of surgery, extension of disease and blood gas analysis values might play a crucial role in predisposing for PP.[5,6]

In the attempt to minimise PP onset patients eligible for partial laryngeal surgery are carefully pre-selected upon pulmonary and performance status, nevertheless PP remains the most important and feared complication even in this selected population, despite antibiotic prophylaxis.[7]

The aim of this study is to review our experience with supracricoid and supraglottic laryngectomies at our Institution over a 20 years period in a series of 416 consecutive patients, to investigate possible PP risk factors. Since several reports from other districts[8,9] suggest a possible PP prognostic significance, we also investigated the prognostic role of PP in our series.

Methods

The charts of 416 consecutive laryngeal cancer patients that underwent a partial laryngectomy at the Otolaryngology Head and Neck Surgery Department of the University of Florence from 1980 to 2000 were retrospectively reviewed. We considered eligible for partial surgery laryngeal cancer patients with: Karnofsky physical index superior to 80%, no dispnea whilst climbing two flights of stairs, satisfactory pulmonary functional tests according to Morris and Koski,[10] and basal pO_2 values above 85 mm Hg. Furthermore, patients with severe cardio-vascular diseases, diabetes mellitus, gastro-oesophageal reflux, chronic obstructive pulmonary disease and rheumatoid arthritis were considered not eligible for partial laryngectomy.

Surgery included 309 supraglottic horizontal laryngectomies (SHL), 85 supracricoid laryngectomies with crico-hyoidopexy (CHP) and 22 with crico-hyoid-epiglottopexy (CHEP).

Clinical characteristics of the series with several clinical conditions potentially involved in the onset of PP are summarised in Table 1. All tumours were squamous cell carcinomas (SCC) classified using UICC TNM staging system.[11] Of the 416 cases, 392 (94.2%) were previously untreated whilst 13 patients were treated as salvage procedure following a radiotherapy failure and 11 a laser CO_2 failure. The mean follow-up time was 67.9 months (range 60–300 months).

Table 1 Series overview

Series overview	
No. of patients	416
Sex (M/F)	382/31
Age at intervention	
Range	20–79
Mean	57
Median	
Body mass index (BMI)	
<18.5	10 (2.40%)
18.5–25	190 (45.67%)
25–30	167 (40.14%)
30–40	49 (11.77%)
>40	0
Smoking history	
No smokers	10 (2.40%)
Light smokers (<20 p-y)	25 (6.00%)
Moderate smokers (20–40 p-y)	158 (37.98%)
Heavy smokers (>40 p-y)	223 (53.60%)
History of previous pneumonia	
No	287 (69%)
Yes	129 (31%)
Preoperative haemoglobin values	
⩽14 g/dL	35 (8.5%)
>14 g/dL	381 (91.5%)
Preoperative pO_2 values	
⩽90 mm Hg	273 (65.62%)
>90 mm Hg	143 (34.37%)
Stage of disease	
I	132 (31.7%)
II	154 (37%)
III	66 (15.86%)
IV	64 (15.38%)
Type of surgery	
Supraglottic horizontal laryngectomies	309 (74.27%)
Supracricoid laryngectomies with crico-hyoidopexy	85 (20.43%)
Supracricoid laryngectomies with crico-hyoid-epiglottopexy	22 (5.28%)
Neck dissection	
No	163 (31.18%)
Elective	162 (38.94%) (114 MRND+48 SND)
Therapeutic	91 (21.87%) (all MRND)
Postoperative pneumonia	73
Deaths	3 (4.10%)
Early pneumonia	26 (35.61%)
Ab ingestis pneumonia	44 (60.27%)

We defined a patient affected by PP if at least three of the following conditions were found: temperature above 37.5 °C, purulent sputum with an increase in volume (>20%), positive blood and/or sputum culture, white cell blood count more than 10,000/mm^3 or less than 3000/mm^3, positive findings at chest X-rays, persistent localised signs on chest examination (crackles, bronchial breathing and wheeze).

For what concerns PP in our series we defined three groups of patients: Group 0 (G0), patients without PP; Group I (GI), patients developing PP within the first postoperative 7—9 days, before any attempt to achieve oral food intake; Group II (GII), those who developed PP because of aspiration at the time of achievement of oral intake. The postoperative period was considered as the period of time from the end of the surgical procedure until hospital discharge. To understand our grouping it is relevant to mention that our Institutional policy previews that all patients after surgery must be admitted to a swallowing rehabilitation program by a speech therapist, starting with tongue exercises from the third postoperative day; oral intake, always under assistance of the speech therapist, usually starts around the ninth postoperative day, in general never before postoperative day seven.

In our series antibiotic prophylaxis with 1 g cefazolin intravenously was standard administrated. According to international guidelines this prophylaxis is reported as able to control infective complications like pulmonary infections, wound infections, urinary tract infections and septic phlebitis.[7]

Statistical analysis

The statistical analysis was performed with an IBM computer using STATA (Stata Corporation, College Station, TX). We used the chi-square test for categorical variables and the student *t*-test for continuous variables to test the relationship between each potential risk factor and pneumonia. All potential risk factors (sex, age, BMI, pack-years score, history of previous pneumonia, haemoglobin and pO_2 preoperative values at blood gas analysis, type of surgery and stage of disease) were entered into a logistic regression model with pneumonia as the dependent variable and the potential risk factors as the independent variables. Significance was defined at $p < 0.05$ level. To determine if these variables predicted pneumonia independent of one another, we also added them to a multivariable logistic regression model in a stepwise manner. The entry criterion for multivariate analysis was set at $p < 0.20$ and an exit criterion was set at $p < 0.05$.

The mean follow-up time was 67.9 months, ranging from 60 to 300 months. Follow-up end points included evidence of local recurrence, death from disease and death from other causes. The actuarial survival time was defined as the interval between the date of surgery and either the date of the last consultation for censored observations or the date of death for uncensored observations. The disease-free interval was measured on the basis of the dates of surgery and diagnosis of first recurrence.

Prognostic factors were then investigated for their unadjusted association with recurrence and survival in univariate analysis using chi-square test. The covariate were also included in a multivariate analysis using the Cox regression model to estimate the hazard ratios of recurrence and death due to the combined effects of 2 or more prognostic factors. Statistical significance was set at $p < 0.05$ level. The entry criterion for multivariate Cox analysis was set at $p < 0.20$ and an exit criterion was set at $p < 0.05$.

The impact of PP in disease-free and actuarial survival was analysed using the Kaplan—Meier curves considering the day of partial laryngectomy as the starting day of observation; the difference between groups was compared using the log-rank test.

Results

We documented a PP in 73 cases (17.54%): early PP arose in 26 patients (GI: 6.25%), whereas *ab ingestis* PP developed in 44 cases (GII: 10.65%); three PP patients died in the postoperative period because of sepsis with respiratory failure (0.07%) and were excluded from our analysis. The remaining 343 patients (G0: 83.2%) were free from PP, amongst them 48 patients (13.99%) did experience postoperative major swallowing problems without PP. Overall the incidence of major postoperative swallowing problems is 95 out of 416 (22.83%).

In 42 of the 70 PP patients (60%) microbiological data of the sputum culture are available. The most common microorganism detected was *Staphylococcus aureus*. Amongst them, multiple bacteria were isolated in 22 patients. According cultural analysis no differences between GI and GII were recorded for what concerns the type of microorganism responsible for PP.

Overall, the postoperative complication rate, including pulmonary and non pulmonary complications (urinary tract infections, septic phlebitis, wound infections and postoperative bleeding), was 25.90% (107 out of 413). A higher incidence of non pulmonary complication was documented in PP patients (13 out of 70 *vs.* 37 out of 343) (Fisher's exact test $p = 0.057$).

Definitive functional unsuccessful results were recorded in only 13 cases out of 413 (3.14%). Amongst them, 10 were PP patients: seven underwent a total laryngectomy, three patients a permanent gastrostomy because of untreatable swallowing problems; the remaining three were free from PP but experienced laryngeal stenosis that prevented decannulation (Fisher's exact test $p < 0.001$).

The mean time of nasogastric tube placement was 15.3 days (range 36, median 14) for G0, 21.2 days (range 40, median 15) for GI, and 29.3 days for GII (range 52, median 20) (Fisher's exact, $p = 0.11$). The mean length of time before tracheotomy tube removal was 28.1 (range 485, median 22) for G0, 17.6 (range 205, median 31) for GI and 21.40 (range 84, median 33) for GII (Fisher's exact; $p = 0.10$). The mean discharge time of G0 (29.3 days; range 85, median 32) was significantly lower from those documented in GI and GII patients (38.39 days, range 61, median 37; 46.17 days, range 101, median 34, respectively) (Fisher's exact; $p = 0.005$).

Univariate and multivariate logistic regression analyses

In Tables 2 and 3 logistic regression analysis according to the main prognostic factors for each type of PP are summarised.

Table 2 Univariate and stepwise multivariate analysis for two groups: no pneumonia and yes early pneumonia GI

Early pneumonia 26 cases						
Variable	Univariate analysis			Multivariate stepwise analysis		
	Odd ratio	*Z*	*p* Value	Odd ratio	*Z*	*p* Value
Tobacco exposure						
No						
Yes	0.97 (0.55; 1.70)	−0.10	0.91			
BMI						
<30						
⩾30	2.80 (1.22; 6.44)	2.44	**0.02**	3.14 (1.29; 7.59)	2.54	**0.01**
Previous pneumonia						
No						
Yes	1.20 (0.46; 3.13)	0.39	0.69			
Age (years)						
<60						
⩾61	2.18 (0.97; 4.87)	1.90	**0.05**	2.49 (1.07; 5.67)	2.13	**0.03**
Sex						
Female						
Male	1.04 (0.23; 4.62)	0.05	0.95			
Hb						
⩽14 g/dL						
>14 g/dL	2.01 (0.46; 8.75)	0.93	0.35			
pO_2						
⩽90 mm Hg						
>90 mm Hg	1.09 (0.49; 2.42)	0.23	0.82			
Type of surgery						
Supracricoid surgery						
Supraglottic surgery	1.30 (0.55; 3.09)	0.61	0.55			
Stage						
I—II						
III—IV						
	1.22 (0.84; 1.79)	1.08	0.28			
Neck dissection						
No						
Yes	0.87 (0.38; 1.94)	−0.34	0.73			

In GI, BMI > 30 and age > 60 were significant prognostic factors in both univariate and multivariate analyses ($p = 0.02$ and 0.05, $p = 0.01$ and 0.03, respectively). In GII, patients receiving a neck dissection were at higher risk of *ab ingestis* PP in both analyses ($p = 0.01$ and $p = 0.02$, respectively). Smoke habits, history of previous pneumonia, haemoglobin values and pO_2 blood levels, TNM Stage and type of reconstructive surgery were not significantly associated with the onset of GI or GII pneumonia.

Prognostic impact of PP on disease-free and actuarial survival

We evaluated the prognostic impact of PP (GI and GII) in terms of disease-free and actuarial survival. These results are summarised in Tables 4 and 5. According to disease-free survival, tumour stage at diagnosis, haemoglobin blood level under 14 g/dL and early pneumonia were statistically significant, whilst type of surgery, history of previous pneumonia and pO_2 blood gas level under 90 mm Hg lost their statistical significance in multivariate model. According to 5 years actuarial survival, univariate analysis indicated analysis tumour stage ($p < 0.001$), history of previous pneumonia ($p = 0.010$) and early-PP ($p = 0.001$) as prognostic factors; however, only advanced tumour stage and early-PP maintain their prognostic value in multivariate analysis.

The Kaplan—Meier estimated disease-free and actuarial survival is shown in Figure 1A and C. Accordingly, early-PP was an adverse prognostic factor in terms of both disease-free and actuarial survival (Fig. 1B and D) (log-rank test $p = 0.030$ and $p < 0.001$, respectively).

Table 3 Univariate analysis and stepwise multivariate analysis for two groups: no pneumonia and yes *ab ingestis* GII pneumonia

Ab ingestis pneumonia 44 cases						
Variable	Univariate analysis			Multivariate stepwise analysis		
	Odd ratio	*Z*	*p* Value	Odd ratio	*Z*	*p* Value
Tobacco exposure						
No						
Yes	0.80 (0.53; 1.21)	−1.02	0.32			
BMI						
<30						
⩾30	1.28 (0.68; 2.38)	0.72	0.44			
Previous pneumonia						
No						
Yes	0.54 (0.28; 1.04)	−1.83	0.07	0.56 (0.29; 1.09)	−1.70	0.09
Age (years)						
<60						
⩾60	1.51 (0.81; 2.84)	0.31	0.19	1.37 (0.72; 2.61)	0.98	0.32
Sex						
Female						
Male	3.20 (1.34; 7.65)	2.62	**0.01**	1.61 (0.92; 2.82)	1.68	0.09
Hb						
⩽14 g/dL						
>14 g/dL	0.69 (0.30; 1.58)	−0.85	0.39			
pO_2						
⩽90 mm Hg						
>90 mm Hg	0.73 (0.38; 1.37)	−0.97	0.32			
Type of surgery						
Supracricoid surgery						
Supraglottic surgery	0.83 (0.39; 1.75)	−0.48	0.962			
Stage						
I—II						
III—IV	1.11 (0.83; 1.49)	0.73	0.47			
Neck dissection						
No						
Yes	2.37 (1.13; 4.95)	2.31	**0.01**	2.52 (1.13; 5.63)	2.26	**0.02**

Discussion

During deglutition, the larynx elevates under the tongue base and moves forward placing the epiglottis to protect the laryngeal inlet, this movement stretches the crico-pharyngeal region contributing to upper oesophageal sphincter opening. Airway protection is guaranteed by vocal cords and arytenoids adduction. Any surgical procedure that significantly affects these mechanisms, like partial laryngectomy, usually results in some degree of aspiration during the swallow with patients always requiring postoperative rehabilitation.

In supraglottic laryngectomy, the removal of the larynx above the true vocal cords and the hyoidopexy reducing the distance between base of tongue and glottic region is responsible for early swallowing impairment despite the maintenance of laryngeal closure valve.

In supracricoid laryngectomy both vocal cords are removed with only preservation of one or both arytenoids, thus, directly affecting laryngeal closure. In partial laryngectomies, oedema of the arytenoids may also contribute to laryngeal closure failure. Furthermore, food might collect around the arytenoids thus, increasing the risk of aspiration.[12,13]

To minimise PP, elderly patients and those with poor pulmonary function tests are considered not eligible for conservative laryngeal surgery because of the high risk of aspiration, due to a decreased ability to cough and clear secretions. Despite this selection, PP still represents the most frequent potentially life-threatening complication in partial laryngectomized patients, requiring more intensive care, delay rehabilitation and discharge from the hospital and inevitably leading to greater health care costs.[3]

In our series, PP had an incidence of 16.8%. Being postoperative deaths confined amongst PP patients with peri-operative mortality in this group of 4.2%, thus highlight the clinical relevance of such a complication. Moreover, we

Table 4 Statistical analysis for disease-free survival

Disease-free survival							
Variables	Univariate analysis				Stepwise multivariate analysis		
	Score	HR (95% CI)	*Z*	*p*	HR	*Z*	*p*
Surgery							
SHL	0						
CHP	1	0.50 (0.30; 0.84)	−2.61	**0.009**	0.79 (0.47; 1.35)	−0.83	0.408
CHEP	2	0.75 (0.33; 1.72)	−0.67	0.504	0.98 (0.39; 2.44)	−0.04	0.970
Sex							
Male	0						
Female	1	0.91 (0.46; 1.79)	−0.27	0.788			
Age (yr)							
<60	0						
⩾60	1	1.03 (0.72; 1.47)	0.17	0.815			
Stage							
Stage I—II	0						
Stage III—IV	1	2.67 (1.88; 3.79)	5.53	**0.000**	4.41 (2.33; 8.35)	4.56	**0.000**
Previous pneumonia							
No	0						
Yes	1	0.62 (0.43; 0.88)	2.61	**0.010**	0.70 (0.48; 1.02)	1.85	0.065
Other complications							
No	0						
Yes	1	1.55 (0.85; 2.82)	1.46	0.120	1.17 (0.36; 3.72)	0.27	0.790
Pneumonia							
No	0						
Early-GI	1	2.02 (1.08; 3.78)	2.23	**0.026**	1.87 (1.00; 3.49)	1.97	**0.049**
Ab ingestis-GII	2	1.39 (0.83; 2.32)	1.26	0.207	1.40 (0.83; 2.35)	1.30	0.195
Smoke (py)							
No smokers	0						
<20	1	3.92 (0.84; 18.3)	1.74	0.076			
20 < py < 40	2	1.71 (0.39; 7.38)	0.72	0.469			
>40	3	1.84 (0.42; 7.92)	0.82	0.411			
Hb							
⩽14 g/dL	0						
>14 g/dL	1	3.29 (1.04; 10.3)	2.04	**0.012**	1.99 (1.01; 17.4)	1.99	**0.047**
pO_2							
⩽90 mm Hg	0						
>90 mm Hg	1	0.58 (0.39; 0.87)	−2.60	**0.006**	0.62 (0.41; 0.95)	−2.17	**0.030**
BMI							
<30	0						
⩾30	1	0.88 (0.56; 1.39)	−0.52	0.060			

documented a statistically significant higher rate of non pulmonary complications in the PP group (18.84%). Furthermore, most of all definitive functional unsuccessful results were PP patients.

Together with the impairment of laryngeal functions, other factors related to tumour stage, type of surgical resection and host clinical conditions have been reported as additional risk factors for PP, thus suggesting a multifactorial aetiology.[5,6]

It is well known that patients who require tracheotomy after major head and neck surgery (always performed during reconstructive laryngectomies) experience a higher incidence of pulmonary complications. Data from the literature indicate that almost 50% of these patients suffer of pulmonary complications including PP, early after surgery despite a course of antibiotic prophylaxis,[4] with elderly subjects and patients with co-morbid respiratory disease being at highest risk.

Interestingly, the analysis of our data evidences that PP not only develops as a result of food aspiration following the attempts to restore oral food intake, but can arise within the first 7—9 postoperative days, before any swallowing

Table 5 Statistical analysis for actuarial survival

Actuarial survival							
Variables		Univariate analysis			Stepwise multivariate analysis		
		HR	*Z*	*p*	HR	*Z*	*p*
Surgery							
SHL	0						
CHP	1	0.58 (0.30; 1.11)	−1.64	0.101	0.75 (0.20; 2.71)	−0.44	0.663
CHEP	2	1.34 (0.58; 3.10)	0.69	0.488	0.96 (0.19; 4.88)	−0.04	0.970
Sex							
Male	0						
Female	1	1.21 (0.55; 2.64)	0.49	0.621			
Age (yr)							
<60	0						
⩾60	1	1.05 (0.67; 1.66)	0.25	0.803			
Stage							
Stage I—II	0						
Stage III—IV	1	2.70 (1.93; 4.30)	5.24	**0.000**	3.57 (2.30; 5.55)	5.67	**0.000**
Previous pneumonia							
No	0						
Yes	1	0.53 (0.34; 0.83)	2.76	**0.006**	0.82 (0.51; 1.33)	0.78	0.437
Other complications							
No	0						
Yes	1	1.47 (0.68; 3.19)	0.99	0.321			
Pneumonia							
No	0						
Early-GI	1	3.29 (1.68; 6.44)	3.48	**0.001**	14.0 (2.49; 78.6)	3.00	**0.003**
Ab ingestis-GII	2	1.87 (1.02; 3.41)	2.04	**0.041**	1.53 (0.24; 9.65)	0.46	0.648
Smoke (py)							
No smokers	0						
<20	1	1.22 (0.29; 5.07)	0.28	0.776			
20 < py < 40	2	0.67 (0.19; 2.37)	0.61	0.544			
>40	3	0.74 (0.21; 2.58)	0.46	0.642			
Haemoglobin							
⩽14 g/dL	0						
>14 g/dL	1	1.30 (0.48; 3.49)	0.52	0.602			
pO_2							
⩽90 mm Hg	0						
>90 mm Hg	1	0.68 (0.36; 1.25)	−1.23	0.219			
BMI							
<**30**	0						
⩾**30**	1	1.02 (0.59; 1.57)	0.10	0.923			

rehabilitation. According to this finding we divided PP in two separate groups: GI enclosing early PP patients, GII those with *ab ingestis* PP.

Being patients undergoing partial laryngectomy pre-selected, we postulated that the occurrence of an early PP might have a different pathogenesis and prognostic impact when compared to the *ab ingestis* one. Theoretically, early PP could be linked to aspiration of blood, saliva and secretion during and immediately after surgery, events occurring in every patient. The low rate of early PP documented in our series, conversely, raises the question of its pathogenesis and potential prognostic significance. Accordingly, we evidence that early PP is sustained by different factors than *ab ingestis* PP. Age greater than 60 years and BMI greater than 30 were the prognostic factors linked to early PP ($p = 0.03$ and $p = 0.01$, respectively). On the other hand, partial laryngectomy with neck dissection statistically predicted *ab ingestis* PP ($p = 0.02$).

It is noteworthy that factors influencing the onset of early PP are strictly host related, whilst *ab ingestis* PP

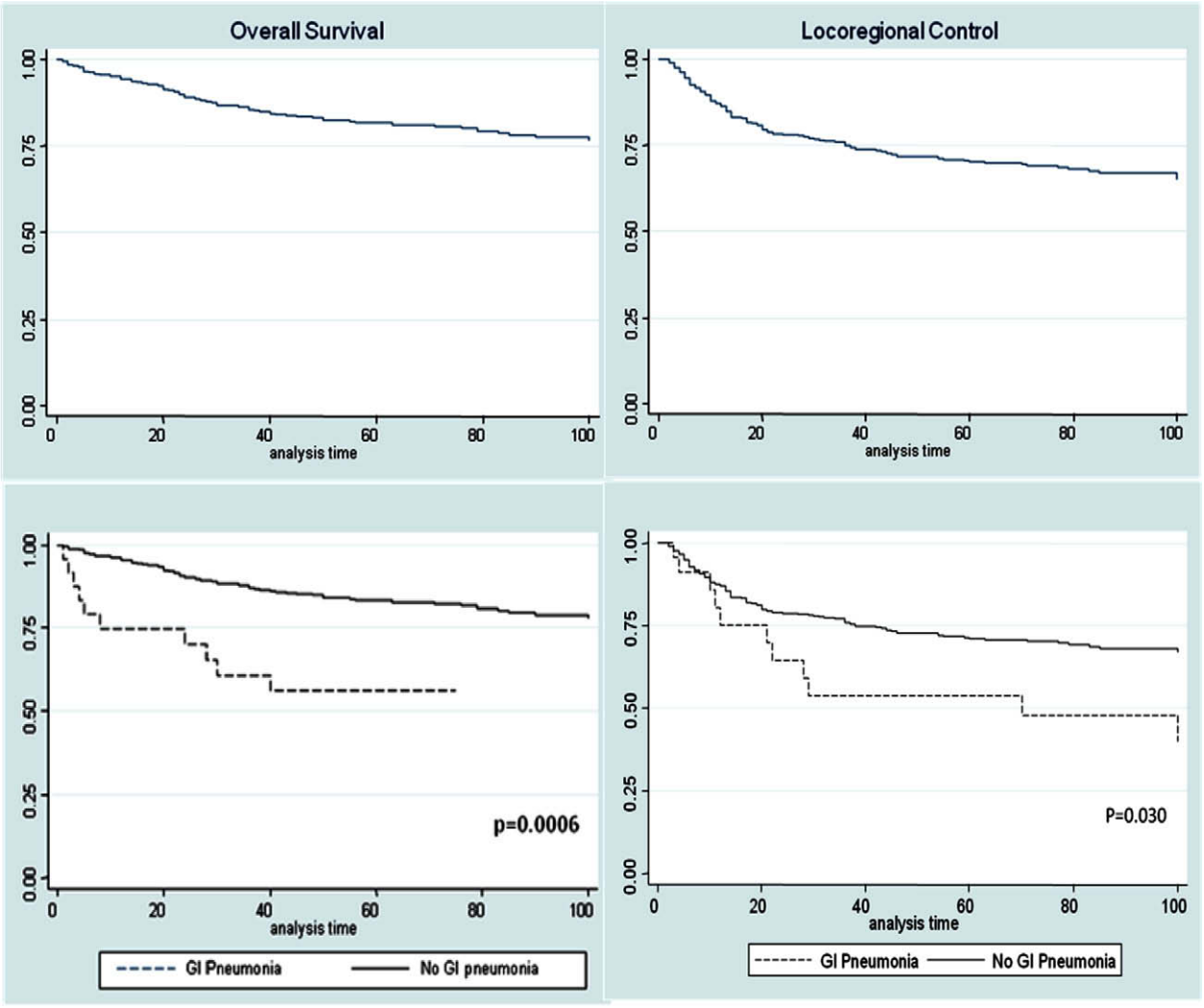

Figure 1 General and early-PP related Kaplan—Meier survival curves for disease-free survival (A and B) and actuarial survival (C and D).

seems to be related to type of surgical procedure, possibly affecting postoperative abilities that are crucial for swallowing rehabilitation.

Then, we analysed the prognostic impact of these complications by Cox univariate and multivariate tests. According to disease-free survival, univariate analysis indicates as significant the following factors: type of laryngectomy (supraglottic laryngectomy *vs.* supracricoid, $p = 0.010$), stage III—IV of disease ($p < 0.001$), history of previous pulmonary disease ($p = 0.010$), occurrence of early PP ($p = 0.026$), preoperative haemoglobin values less than 14 g/dL ($p = 0.042$), preoperative pO_2 values less than 90 mm Hg at blood gas analysis ($p = 0.006$). In the stepwise multivariate analysis, stage of disease ($p < 0.001$), occurrence of early-PP ($p = 0.049$), preoperative haemoglobin values less than 14 g/dL ($p = 0.047$) and preoperative pO_2 values less than 90 mm Hg at blood gas analysis ($p = 0.030$) maintained their prognostic relevance.

At variance, actuarial survival analysis suggest that clinical evidence of nodal disease ($p < 0.001$), stage III—IV of disease ($p < 0.001$), previous pulmonary disease ($p = 0.006$), occurrence of early ($p = 0.001$) and *ab ingestis* PP ($p = 0.041$) were negative prognostic predictors in univariate analysis, whilst in multivariate tests only advanced stage ($p < 0.001$) and occurrence of early PP ($p = 0.003$) maintained its significance. The key prognostic role of early PP is confirmed by the Kaplan—Meier curves analysis (Fig. 1), overall suggesting that those patients who experienced early PP have a higher risk of cancer failure (log-rank test $p = 0.030$) with poor prognosis (log-rank test $p < 0.001$).

The fact that PP is predictive of poor outcome also in surgery of other districts,[14,15] supports the hypothesis that host immune system might be potentially involved in host cancer response. Data from the literature[16,17] indicate that head and neck cancer patients, also because of poor general condition due to tobacco/alcohol exposure, show host immune system impairment able to affect cancer prognosis. Accordingly, here, to the best of our knowledge, in patients who underwent partial reconstructive laryngectomies, we first describe early PP and report its negative impact in terms of disease-free and actuarial survival. Of course, only additional analyses evaluating host immune response in patient with this new clinical entity might address this issue and is currently under investigation at our Institution.

In conclusion, our study indicates a prognostic significance of early-onset pneumonia when compared with a classical late-onset pulmonary infection; if this evidence will be confirmed also by further investigations it should be wise to pay particular attention to the postoperative course of such patients at risk with a stricter follow-up schedule, and maybe these patients might be eligible for adjuvant treatment.

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