

Original Paper

Larynx Preservation Protocols: Long-Term Functional Outcomes in Good Responders to Induction Chemotherapy for Pyriform Sinus Carcinoma

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Key Words

Pyriform sinus · Carcinoma · Larynx preservation · Induction chemotherapy · Functional outcome

Abstract

Background/Aims: Larynx preservation for laryngopharyngeal carcinomas aims to avoid the mutilation of a total laryngectomy without compromising survival or functionality. The aim of the present study on pyriform sinus squamous cell carcinoma (SCC) is to evaluate the long-term functional outcomes of larynx preservation in good responders to induction chemotherapy (ICT). **Methods:** The study was carried out in a tertiary referral cancer center in France. The subjects were good responders to ICT for pyriform sinus SCC, subsequently treated with adjuvant radiation therapy (RT) – with or without concomitant chemotherapy – between 1999 and 2008. Only patients without recurrence at 3 years were included. The evaluated pharyngolaryngeal functions were airway patency, oral communication and oral feeding, based on a self-administered questionnaire and the patients' medical records. **Results:** Twenty-eight patients were retained. Two (7%) patients needed a tracheotomy during or after the treatment and 2 (7%) had total laryngectomy for a late local recurrence. At least 3 years after the end of treatment, all patients were exclusively fed by mouth. All the evaluated patients judged their voice performance as 'adequate for everyday oral communication'. **Conclusions:** In the long run, patients with pyriform sinus SCC who are candidates for larynx preservation and respond favorably to ICT present a satisfactory functional outcome when treated with adjuvant RT.

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Introduction

Hypopharyngeal cancers have a significant geographic variation; certain regions in France are among the most endemic presenting an age-standardized incidence rising up to 10.2 per 100,000 males [1]. The vast majority of hypopharyngeal cancers (>95%) are squamous cell carcinomas (SCC) [2]. In the USA, hypopharyngeal cancers represent approximately 1/15 of all upper aerodigestive tract malignancies [3], and 75% (65–85%) of them involve the pyriform sinuses [4].

For selected patients, organ preservation strategies may represent a therapeutic alternative to total laryngectomy as the majority of patients are diagnosed in advanced stages (90% in stages III and IV) [5]. Larynx preservation has been validated in terms of survival in randomized prospective trials [6, 7]. Nevertheless, preservation is meaningful when associated with function preservation and improved quality of life [8].

The present study focuses on preservation protocols with induction chemotherapy (ICT) for pyriform sinus SCC. The aim is to evaluate the long-term functional outcomes (≥ 3 years) in good responders treated with adjuvant radiation therapy (RT) with or without concomitant chemotherapy. Survival and preservation rates are not objects of the present study.

Subjects and Methods

The study was carried out in the tertiary referral cancer center Institut Gustave Roussy in Villejuif, France. Patients eligible for analysis had to fulfill the following inclusion criteria: (1) histologically confirmed SCC of the pyriform sinus; (2) inclusion in an ICT-based larynx preservation protocol; (3) good response to ICT defined as tumor regression $\geq 80\%$ and remobilization of a previous immobile arytenoid; (4) definite treatment with RT with or without concomitant chemotherapy, and (5) follow-up documented in the Institut Gustave Roussy. Exclusion criteria were: (1) death or recurrence within the first 3 years after the end of RT; (2) history of another cancer in the last 5 years; (3) previous treatment for the same cancer; (4) metastatic disease; (5) treatment with palliative intent, and (6) synchronous tumors.

Patients treated during a 10-year period (1999–2008) were identified from the database of the Head and Neck Tumor Board. Data were collected from the medical records of the patients who were reviewed in detail, and 3 parameters were used for the evaluation of the functional outcome: (1) history of tracheotomy; (2) swallowing performance and the need for enteral feeding, and (3) speech/voice performance. Data were completed with information provided by the patients who had to fill out a self-administered questionnaire developed for the needs of the present study. The questionnaire included 10 questions divided into 3 parts: 4 questions focusing on history, timing and duration of the tracheotomy, 4 concerning swallowing (feeding pattern, food texture, history of parenteral feeding and aspiration problems) and 2 concerning oral communication. Regarding this last aspect, we were not interested in a detailed evaluation of the voice performance but simply focused on whether the patients themselves perceived their voice as adequate for everyday life needs allowing them an exclusive oral communication.

Results

A total of 28 patients fulfilled the inclusion criteria and were considered for analysis. The patients' age varied from 42 to 68 years (mean = 57), with a 9:1 male-to-female sex ratio. Two patients presented with stage II disease, 13 with stage III and another 13 with stage IV. Concerning the ICT regimen, 13 patients received neoadjuvant chemotherapy with a platinum salt and 5-fluorouracil (PF), 13 patients received docetaxel in addition to PF (TPF), 1 patient had ICT with TP, and in 1 patient the ICT regimen was not clearly documented. After induction treatment, RT alone was offered to 15 and concomitant chemoradiation therapy (CRT) to 13 patients.

Table 1. Summary of the long-term functional outcomes (≥3 years)

Parameter	RT, n (%)	CRT, n (%)	All patients, n (%)
Airway			
History of tracheotomy	2/15 (13)	0/13 (0)	2/28 (7)
Swallowing			
Exclusive oral feeding	14/14 (100)	13/13 (100)	27/27 (100)
Feeding tube history	0/9 (0)	4/7 (57)	4/16 (25)
Normal texture	10/14 (71)	8/11 (73)	18/25 (72)
Aspiration	2/12 (17)	6/11 (55)	8/23 (35)
Voice			
Very satisfactory	5/9 (56)	4/7 (57)	9/16 (56)
Adequate	4/9 (44)	3/7 (43)	7/16 (44)

All patients were followed for at least 3 years and most of them for 5 years or more. In total, 5 patients presented late recurrences, which were diagnosed between 4 and 7 years after the treatment. Three recurrences were isolated in the hypopharynx and treated with salvage total pharyngolaryngectomy, 1 isolated nodal recurrence was treated with salvage neck dissection and reirradiation, and 1 patient with simultaneous locoregional recurrence was offered palliative treatment.

Questionnaires were sent to 22 patients (79%); 6 patients (21%) were already deceased when the present study was carried out. Out of the 22 patients, 18 returned the questionnaires (82%), although some of them were only filled out partially. Data collection for the 6 deceased patients was exclusively based on the follow-up records. Hence, some parameters of pharyngolaryngeal function could not be evaluated in all patients.

Functional Outcomes

Table 1 resumes the long-term functional outcomes (≥3 years).

Airway

Information concerning airway patency and breathing was available for all 28 patients selected for analysis (for 18 of them, the information was taken from the questionnaires). None of them had a tracheotomy at the beginning of the treatment and 2 patients (7%) presented a respiratory distress necessitating a tracheotomy later on (1 during treatment and 1 in the follow-up period; both belonging to the subgroup treated with RT alone). Only 1 patient (4%) needed to keep the cannula in the long run. However, 3 patients (11%) had salvage laryngectomy for local recurrence in the fourth year after the end of RT, among them the only patient necessitating a tracheotomy during treatment. An overall 86% of the good responders (24/28) and 96% of those who finally preserved their larynx (24/25) had a normal airway at the last follow-up visit.

Swallowing

Information could be obtained for 27/28 patients (96%); for 16 patients from the questionnaires and for the other 11 from their sufficiently detailed medical records. All 27 patients reported an exclusive oral feeding at the last follow-up. Among the 16 patients who answered to the relevant questions in the questionnaire, 4 (25%) reported a history of temporary enteral feeding (3–18 months), all of them being treated with CRT (table 1). Details about meal texture were available for 25 patients; the texture was described as ‘normal’ by 18 of

them (72%) and as ‘in small pieces, mashed or blended’ by 7 (28%). Persisting but minor aspiration problems were described by a third of 23 patients (8/23) for whom data was available; no ‘functional’ laryngectomies were reported in this series.

Voice

Data were available for 16 patients who had replied properly to the questions concerning the subjective perception of their voice performance. At least 3 years after the end of treatment, 9 patients (56%) described their voice as ‘normal’ (no significant voice difficulties) and 7 (44%) as ‘altered but still adequate’ for all needs in everyday life. Hence, all 16 patients perceived their voice as adequate for exclusive oral communication. Two thirds of them (11/16) described their voice as ‘unchanged from treatment’, 19% (3/16) considered it deteriorated and 13% (2/16) considered that it had improved compared to before the beginning of treatment.

Discussion

Various symptoms of pharyngolaryngeal dysfunction may already be eminent at the initial presentation of hypopharyngeal tumors [9]; swallowing difficulties and odynophagia are among the most prominent symptoms seen at the initial presentation in 53 and 34% of cases, respectively. Dysphonia is also frequent (39%) and may or may not be associated with laryngeal infiltration, while dyspnea is usually a manifestation of locally advanced disease. The first prospective trials on larynx preservation [6] had focused on survival and preservation rates in order to investigate the interest of nonsurgical protocols compared to the well-known upfront surgery approach. Once the interest of these protocols had been established [7], more attention was given to the functional outcome, as symptoms of pharyngolaryngeal dysfunction may persist and evolve for prolonged periods after the end of treatment. The present study was interested in good responders to ICT for pyriform sinus SCC and focused on the long-term functional outcomes as all patients were followed for at least 3 years after treatment.

The patency of the natural airway did not seem to be a problem for the majority of the treated patients; 96% of those who preserved their larynx in the long run (24/25) did not necessitate any surgical airway management during or after treatment. These data are consistent with similar data found in the literature. In the EORTC 24891 trial for pyriform sinus SCC, for instance, among 52 patients treated with ICT and adjuvant RT with no need for salvage surgery, only 7 patients (14%) needed a tracheotomy during the follow-up [10].

Swallowing performance was also satisfactory, despite the fact that hypopharyngeal tumors may represent a natural and functional obstacle for swallowing mechanisms. In the present study, 3 or more years after the end of RT, all patients were fed exclusively by mouth. Similarly, in the EORTC 24891 trial, 90% of the 52 patients treated with ICT and adjuvant RT without salvage surgery reported exclusive oral feeding (47/52) [10]. Moreover, in our series only 28% of the patients had to modify meal textures, while 72% had no texture restrictions. Interestingly, swallowing in patients with advanced laryngeal carcinomas treated with an ICT-based preservation protocol seems to be comparable to that in patients with pyriform sinus carcinomas, as testified by the results of the RTOG 91-11 trial [11, 12]; in the ICT arm almost all patients who preserved their larynx were fed exclusively by mouth and less than 15% of them were limited to eating soft food or worse.

For the speech assessment, we decided to focus on a simple and essential question, i.e. whether patients were capable to maintain exclusive oral communication with others in everyday life at least 3 years after the end of treatment. All patients who could be evaluated

in our series were capable to do so, although voice performance was considered normal (or almost normal) by slightly more than half of all patients. The interpretation of these results should be made with caution as we chose not to use a detailed questionnaire for the voice assessment and the collected answers reflect the opinion of merely 60% of the study population (16/28). For laryngeal tumor patients such as those included in the RTOG 91-11 laryngeal cancer trial [11], one might expect more voice difficulties compared to the hypopharyngeal tumor patients in our study. Interestingly, the results concerning voice performance in the RTOG 91-11 trial are similar to ours; 97% of the patients who could be analyzed 2 years after the end of ICT and adjuvant RT had a normal or slightly altered voice.

This paper focused on the pharyngolaryngeal function in patients responding to ICT before definite treatment with RT or CRT; patients treated with direct CRT were not included in the study. A proper comparison of the functional outcome between these two nonsurgical approaches should certainly take into consideration the T-stage and the pretreatment pharyngolaryngeal function in the two groups. The long-term results of the laryngeal cancer RTOG 91-11 trial [12] show a satisfactory functional outcome with preservation approaches both in terms of voice and swallowing despite a slightly more frequent swallowing dysfunction (soft foods or worse) in the CRT arm (17–24%) compared to the ICT arm (13–14%).

In our study, comparing the RT and the CRT arms after ICT would not allow any definite conclusions due to the small number of patients included in each of them (15 vs. 13, respectively). Nevertheless, some trends observed in table 1 should be highlighted; in this series, patients treated with CRT were more likely to have swallowing difficulties compared to patients treated with RT, reporting a more frequent history of enteral feeding (57 vs. 0%) and more frequent aspiration problems (55 vs. 17%). An association between more frequent aspiration problems and CRT (compared to RT alone) has already been speculated [13], and the trend was partially attributed to the advanced disease stage of patients treated with CRT compared to those treated with RT. Interestingly, in our study, disease stages in the 2 arms were comparable (70% T3/T4 tumors in the CRT vs. 60% in the RT arm).

One of the limitations of the present study was the relatively limited number of patients along with the fact that data for some parameters of the pharyngolaryngeal function were not available in all patients. Another limitation concerns oral communication; we decided to evaluate voice adequacy in everyday life needs with no further evaluation of voice characteristics. Voice performance under more demanding conditions such as those related to professional activity were not assessed. Finally, it is hard to estimate the degree to which the Tumor Board had already excluded patients presenting with signs of significant pharyngolaryngeal dysfunction (tracheotomy, enteral feeding) from larynx preservation protocols. Hence, we should be skeptical before generalizing expectations for similar functional results in all candidates for larynx preservation and especially for those with a significant pharyngolaryngeal dysfunction at initial presentation.

Conclusions

Larynx preservation for selected patients with pyriform sinus SCC provides an overall satisfactory functional outcome when good responders to ICT are subsequently treated with adjuvant RT or CRT. Tracheotomy is exceptional and voice performance is adequate for exclusive oral communication in everyday life needs. In the long run, all patients in this series were exclusively fed by mouth and the majority of them did not need to modify meal textures.

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