Oral Oncology 51 (2015) 787–794

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Evaluation of long term (10-years+) dysphagia and trismus in patients treated with concurrent chemo-radiotherapy for advanced head and neck cancer

S.A.C. Kraaijenga [a,1], I.M. Oskam [a,1], L. van der Molen [a], O. Hamming-Vrieze [b], F.J.M. Hilgers [a,c,*], M.W.M. van den Brekel [a,c,d]

[a] The Netherlands Cancer Institute, Department of Head and Neck Oncology and Surgery, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands
[b] The Netherlands Cancer Institute, Department of Radiation Oncology, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands
[c] Institute of Phonetic Sciences/ACLC, University of Amsterdam, Spuistraat 210, 1012 VT Amsterdam, The Netherlands
[d] Academic Medical Center, Department of Oral and Maxillofacial Surgery, Meibergdreef 9, 1105AZ Amsterdam, The Netherlands

ARTICLE INFO

Article history:
Received 13 April 2015
Received in revised form 7 May 2015
Accepted 11 May 2015
Available online 28 May 2015

Keywords:
Head and neck cancer
Deglutition disorders
Dysphagia
Trismus
Long-term effects
Intensity modulated radiotherapy

SUMMARY

Objectives: Assessment of long term (10-years+) swallowing function, mouth opening, and quality of life (QoL) in head and neck cancer (HNC) patients treated with chemo-radiotherapy (CRT) for advanced stage IV disease.

Materials and Methods: Twenty-two disease-free survivors, participating in a multicenter randomized clinical trial for inoperable HNC (1999–2004), were evaluated to assess long-term morbidity. The prospective assessment protocol consisted of videofluoroscopy (VFS) for obtaining Penetration Aspiration Scale (PAS) and presence of residue scores, Functional Oral Intake Scale (FOIS) scores, maximum mouth opening measurements, and (SWAL-QOL and study-specific) questionnaires.

Results: At a median follow-up of 11-years, 22 patients were evaluable for analysis. Ten patients (46%) were able to consume a normal oral diet without restrictions (FOIS score 7), whereas 12 patients (54%) had moderate to serious swallowing issues, of whom 3 (14%) were feeding tube dependent. VFS evaluation showed 15/22 patients (68%) with penetration and/or aspiration (PAS $\geqslant$ 3). Fifty-five percent of patients (12/22) had developed trismus (mouth opening $\leqslant$ 35 mm), which was significantly associated with aspiration (p = .011). Subjective swallowing function (SWAL-QOL score) was impaired across almost all QoL domains in the majority of patients. Patients treated with IMRT showed significantly less aspiration (p = .011), less trismus (p = .035), and less subjective swallowing problems than those treated with conventional radiotherapy.

Conclusion: Functional swallowing and mouth opening problems are substantial in this patient cohort more than 10-years after organ-preservation CRT. Patients treated with IMRT had less impairment than those treated with conventional radiotherapy.

Introduction

Head and neck cancer (HNC) patients are at risk to develop substantial functional impairments after organ-preserving treatment with chemoradiotherapy (CRT) [1]. Dysphagia is commonly the most severe functional impairment following this treatment. Given its serious impact on quality of life (QoL), assessment of deglutition disorders has become an important functional endpoint measure [2]. It is therefore not surprising that prevention of dysphagia has become a major focus point in HNC research. In the past decade, improved radiotherapy protocols with intensity modulated radiotherapy (IMRT) have been introduced to reduce radiation dosage to swallowing musculature and structures, with the intention to decrease post-treatment dysphagia [3,4]. More recently, the prevalence of dysphagia also has led to the development of preventive exercise programs. These exercise programs are associated with better post-treatment swallowing function, in particular on the short-term [5–10], and probably also longer-term [11]. However, since dysphagia can develop and/or progress years after CRT [12,13], long term (10-years+)

* Corresponding author at: Dept. Head and Neck Surgery and Oncology, Netherlands Cancer Institute – Antoni van Leeuwenhoek, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands. Tel.: +31 205122550.
E-mail address: f.hilgers@nki.nl (F.J.M. Hilgers).
[1] Both authors contributed equally to the manuscript.

http://dx.doi.org/10.1016/j.oraloncology.2015.05.003
1368-8375/

prospectively collected swallowing and mouth opening data are of great importance to assess deglutition in HNC survivors [14]. In this study the prospectively collected objective and subjective functional results at 10-years+ post-treatment will be reported in a patient cohort treated with CRT for advanced, anatomical and functional inoperable HNC.

Material and methods

This study concerns the long term follow-up of all disease-free and evaluable patients, who participated in a randomized clinical trial (M99RAD) on two different cisplatin-based chemoradiation treatment protocols for advanced HNC [15]. The original cohort consisted of 237 patients diagnosed with advanced (stage IV), anatomical or functional [16] inoperable squamous cell carcinoma of the oral cavity, oropharynx, or hypopharynx. Patients were included between December 1999 and November 2004. The chemotherapy protocol consisted either of 100 mg/m^2 cisplatin in a 40 min intravenous (IV) infusion on days 1, 22, and 43, or of a weekly high-dose intra-arterial (IA) injection of 150 mg/m^2 cisplatin in combination with intravenous sodium thiosulphate rescue in weeks 1, 2, 3, and 4. Radiotherapy (70 Gy in 35 fractions) was administered over seven weeks, starting concurrently with chemotherapy. Since IMRT had been gradually introduced in our Institute during the trial period, roughly one fourth of the original patient population was treated with IMRT [4,17], while the remaining patients were treated with conventional radiotherapy (RT). During treatment, patients were encouraged to maintain an oral diet for as long as possible and prophylactic tube feeding was not applied. A (nasogastric or gastric) feeding tube only was given when the carefully monitored intake became troublesome. In the period the trial was conducted (1999–2004), the concept of standard preventive swallowing rehabilitation was not yet developed, and swallowing exercises were given post-treatment 'on demand', when removal of a feeding tube appeared troublesome because of aspiration and/or when sufficient oral intake could not be regained.

The original (phase III) trial compared standard IV with IA cisplatin infusion on oncological outcomes in 237 patients [17] and QoL in 207 patients [18,19]. Regarding oncological outcomes and toxicities, results showed that CRT with IA infusion is not superior to CRT with IV infusion. Toxicity results were comparable in both arms, although site and degree of toxicity differed. In short, renal toxicity was significantly lower in the IA treatment arm, and neurological toxicity was significantly more prevalent in the IA arm [17]. Regarding QoL results, no statistically significant differences between the groups (IA, IV) were found, and no statistically significant changes over time (1-year versus 5-years post-treatment) were observed for the total patient group during follow-up assessments [19]. Therefore, in the present study, functional swallowing and mouth opening results are reported for the combined patient cohort still alive and evaluable at 10-years+ post-treatment. All patient data and reasons for exclusion after 5-years and 10-years+ follow-up are provided in a consort flow-chart (Fig. 1). As can be seen, at 10-years+ post-treatment, besides the 20 evaluable patients from the 5-year cohort, 4 additional survivors, who had been unresponsive or refused to participate at the 5-years evaluation point, were also willing to participate. Two patients had major salvage surgery for recurrent disease during follow-up, and were excluded from swallowing/mouth opening analysis, since the functional outcomes in these patients were no longer (only) attributable to the CRT. Furthermore, two patients had minor (laser) surgery for a second primary at the oropharynx (pharyngeal arch and alveolar process, respectively) at 10-years and 11-years post-treatment. Subsequently, due to a recurrence the alveolar process patient two years later additionally required local resection with bone grafting. These latter two patients were kept in the functional analysis of in total 22 patients.

Multidimensional assessment

Assessment of functional sequels was performed with standard, multidimensional objective and subjective outcome-measures [20,21]. First, the protocol included standard videofluoroscopy (VFS) to determine swallowing function. All VFS studies were carried out by an experienced speech language pathologist. Patients were seated upright and were asked to swallow different consistencies of varying amounts twice (1, 3, 5 and 10 cc thin liquid; 3 and 5 cc paste; as well as solid [Omnipaque coated cake]). Testing was discontinued if the clinicians judged the swallowing potentially harmful to the patient. All VFS studies were reviewed in real-time, slow motion, and frame-by-frame, and rated in consensus by two experienced researchers (authors SK and LM). Results were expressed in terms of the Penetration and Aspiration Scale (PAS), as well as an overall 'presence of residue' score. The PAS, a tool with an acceptable reliability, consists of a 8-points scale, ranging from 1 to 8 (score 1: material does not enter the airway; score 2: material enters the airway, remains above the vocal folds, and is ejected from the airway; score 3: material enters the airway, remains above the vocal folds, and is not ejected from the airway; score 4: material enters the airway, contacts the vocal folds, and is ejected from the airway; score 5: material enters the airway, contacts the vocal folds, and is not ejected from the airway; score 6: material enters the airway, passes below the vocal folds, and is ejected into the larynx or out of the airway; score 7: material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort; score 8: material enters the airway, passes below the vocal folds, and no effort is made to eject) [22]. The overall 'presence of residue' score ranges from 0–3 (score 0: no residue, to score 3: residue above and below the vallecula, with minimal residue judged as normal). To interpret and compare results, individual test results were clustered with the highest score representing the total PAS or residue score per patient. The PAS was also simplified by dividing it into three categories (1: normal; 2–5: penetration; 6–8: aspiration), which roughly corresponds to normal, mild-to-moderate, and severe performance [23].

Secondly, oral intake/nutritional status was assessed with the Functional Oral Intake Scale (FOIS; range from 1 to 7 with score 1: nothing by mouth, score 2: tube dependent with minimal/inconsistent oral intake, score 3: tube dependent with consistent oral intake, score 4: total oral diet of a single consistency, score 5: total oral intake of multiple consistencies requiring special preparation or compensations, score 6: total oral intake of multiple consistencies without special preparation but with specific food limitations, and score 7: total oral diet without restrictions), and with data on oral nutritional supplements, tube feeding dependency, weight changes, and Body Mass Index (BMI).

Furthermore, maximum interincisor (mouth) opening (MIO) was measured in mm to determine trismus. MIO was measured using disposable TheraBite range of motion scales (Atos Medical, Sweden), and trismus was defined as a MIO of $\leqslant$35 mm [24].

Patients' subjective swallowing and mouth opening impairment was assessed with quality of life (QoL) questionnaires. The first questionnaire was the Swallowing Quality of Life Questionnaire (SWAL-QOL), which was administered to assess patients' perceived swallowing disorder. The SWAL-QOL has been translated and validated for use with Dutch oral, oropharyngeal, and laryngeal cancer patients [25,26]. The SWAL-QOL consists of 44-items that assess the effects of swallowing difficulties on 10 QoL domains (30 items), including food selection, eating duration, eating desire, fear, burden, mental health, social functioning, communication, sleep, and