



Quality of Life during Head and Neck External Beam Radiotherapy

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Worldwide, head and neck carcinoma is sixth common cancer 2.8% of all malignancies. Radiotherapy play an integral role in management and used in approximately 60-70%. The study aimed to evaluate the radiation induced early side effects in patients receiving external beam radiotherapy. This is an observational cross-sectional survey, within 180 days from starting treatment. Forty patients were included, those attended at Oncology Teaching Center / Radiation Therapy Department, Medical City Complex. The data were collected from 1st of January 2016 to 1st of August 2016. All patients were evaluated for the early side effects, including fatigue, skin dermatitis, voice changes, xerostomia, altered taste, oral mucositis, and dysphagia. As well as the incidence of patients who required a tracheostomy and/or a gastrostomy after initiation of radiotherapy, and that of those who developed a significant weight loss (>10% of their initial weight). Dysphagia occurred in 88%, only 1 (3%) developed a grade 4 dysphagia and required a gastrostomy. Of the 40 patients, 14 (35%) had a significant weight loss ≥10% of their initial weight. Xerostomia occurred in 85%, while fatigue recorded in 83%. Dysphagia and xerostomia were the two most common early side effects. More than half of patients with dysphagia had a grade 2, and about three-quarters of those with xerostomia had a grade 2. We conclude to spare the salivary glands and pharynx during radiotherapy plan preparations as much as possible.

INTRODUCTION

Head and neck carcinoma is the sixth most common cancer worldwide, accounting for 2.8% of all malignancies (1). The incidence of head and neck cancer is increasing, predominantly due to increase in oropharyngeal cancers, this is in contrast to the decreasing incidence of head and neck cancer arising in other sub-sites (1, 25). In Iraq is estimated to be <2% of all cancers (1-3). Head and neck cancers are more common in males than females with a 2:1 male to female ratio (1). Current epidemiological data identify at least three important etiologic factors: genetic, environmental, and viral (1). Those with a first degree relative have a 2-3 fold increased risk, the most important genetic abnormality detected is tumor suppressor gene - P53 inactivation (4). However, tobacco smoking (2-6 folds increased risk) and alcohol consumption (5-25 folds increased risk), and when combined together the risk increases by up to 40 folds (5, 26). Epstein Barr virus (EBV) is associated with the pathogenesis of nasopharyngeal carcinoma, and Human Papilloma virus (HPV) infections are common associated with oro-pharyngeal carcinoma (tonsils and tongue base) (6, 7). Squamous cell carcinoma is common about 90%, and other less common tumors include adenocarcinomas, mucosal melanoma, lymphomas, sarcomas,

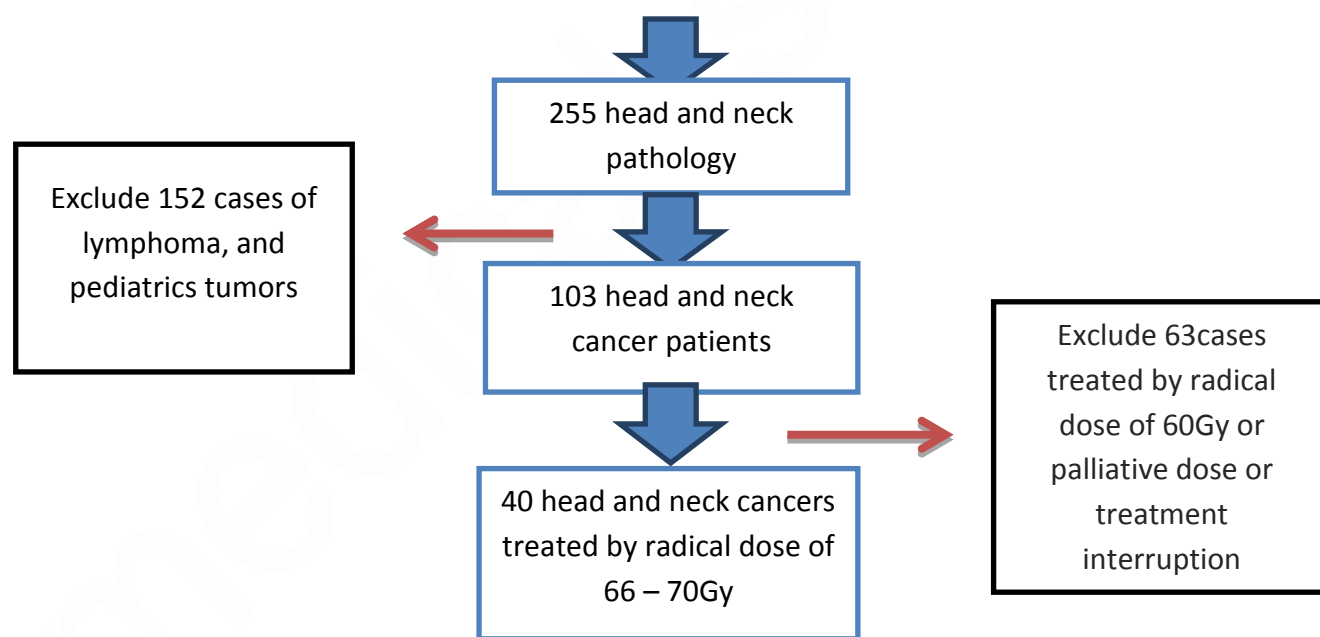
and neuroendocrine tumors (8, 24). Head and neck cancers tend to spread locally to involve adjacent sub-sites involving soft tissues, muscles, nerves, and bones leading to destruction and loss of function (7, 8). Tumors can also spread through lymphatics to regional lymph nodes either on one or both sides of the neck (8). The clinical presentation depends on the anatomical site of primary disease and tumor stage including a persistent mucosal ulcer, dysphonia, dyspnea, stridor, dysphagia, odynophagia, otalgia, epistaxis, nasal obstruction, nasal discharge, cranial nerve palsies, and cervical nodes enlargement (9). The choice of treatment depends on a number of patient, tumor, and treatment factors. In general, the early stages disease are managed with a single modality treatment, either surgery or radiotherapy and those with locally advanced stages are managed with multi-modality treatment with the aim of organ and function preservation. Patients with metastatic disease are considered for palliative treatments and/or best supportive care (9-11). Radiation treatment is given to cure or control diseases and/or symptoms, it used with or without concurrent chemotherapy in approximately 60 – 70% of cases either as a definitive treatment, as an adjuvant treatment following surgery, and/or as a palliative treatment (10). The delivery of radiation therapy has improved significantly in the past decade due to advances in the technology, leading to improved control and reduced morbidity (11). 70 Gy is the common dose used for definitive radiotherapy, 60 – 66Gy for adjuvant radiotherapy, and 20 – 30Gy for palliative radiotherapy (11, 27). Even with recent advancements radiation therapy is associated with certain treatment-induced reactions that may affect the quality of life during and after treatment (12). Early side effects are defined as events that happen

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Table 1 Early side effects of EBRT to the H&N region and grades (10-12)

Side effect	Grade 1	Grade 2	Grade 3	Grade 4
Fatigue	Mild fatigue over baseline	Moderate causing difficulty in performing some daily activities	Severe fatigue interfering with daily activities	Disabling
Skin Dermatitis	Faint erythema or dry desquamation	Moderate to brisk erythema, moist desquamation	Moist desquamation with bleeding induced by minor trauma	Skin necrosis with spontaneous bleeding from involved site
Voice Change	Mild or intermittent hoarseness or voice change, fully understandable	Moderate or persistent voice changes, may require repetition, understandable on telephone	Severe voice changes, whispered speech, require frequent repetition or face to face contact for understandability	Disabling, non-understandable voice or aphonic, requires voice aid or written communication
Xerostomia	Symptomatic (dry or thick saliva) without significant dietary alteration	Significant oral intake alteration (copious water, other lubricants)	Sever, leading to inability to adequately aliment orally	
Altered Taste	Unpleasant taste (metallic)	Loss of taste		
Oral Mucositis	Erythema of the mucosa	Patchy ulcerations	Confluent ulcerations, bleeding with minor trauma	Tissue necrosis, spontaneous bleeding
Dysphagia	Symptomatic, able to eat regular diet	Altered eating & swallowing, able to eat pureed diets and thick fluids	Severely altered eating & swallowing, only thin liquids with inadequate oral caloric or fluid intake	Life-threatening consequences (e.g., obstruction, perforation)

**Figure 1** Study and data collection design of this study (inclusion and exclusion criteria)

during radiotherapy or within 180 days after starting treatment (12). While late side effects are defined as those occurring many months to years after completion of treatment (12), (Table 1).

PATIENTS AND METHODS

Study design and setting

An observational descriptive cross-sectional survey conducted for those have external beam radiotherapy for a head and neck tumor, within 180 days from starting treatment. All patients treated at the Oncology

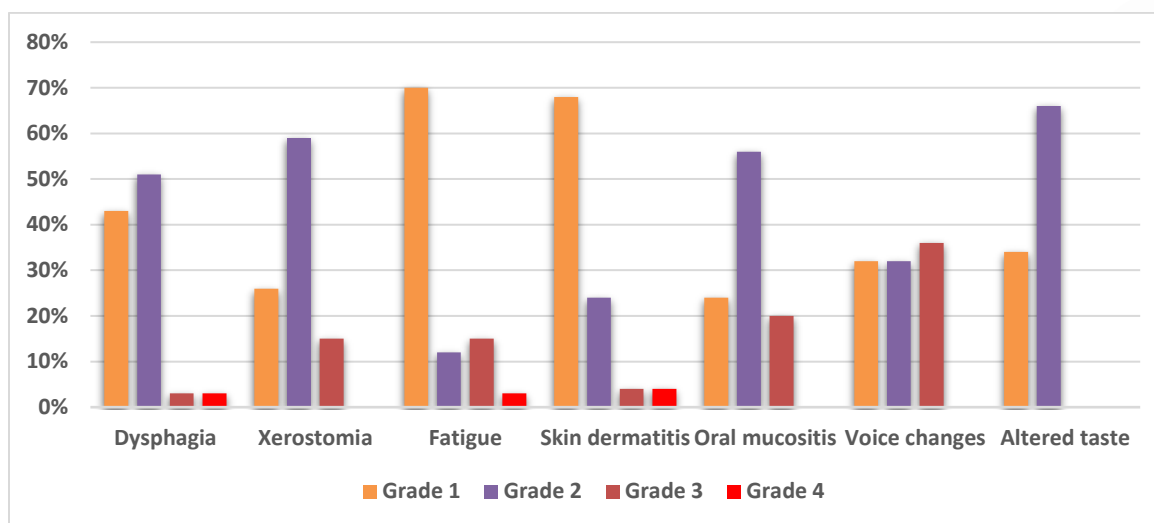
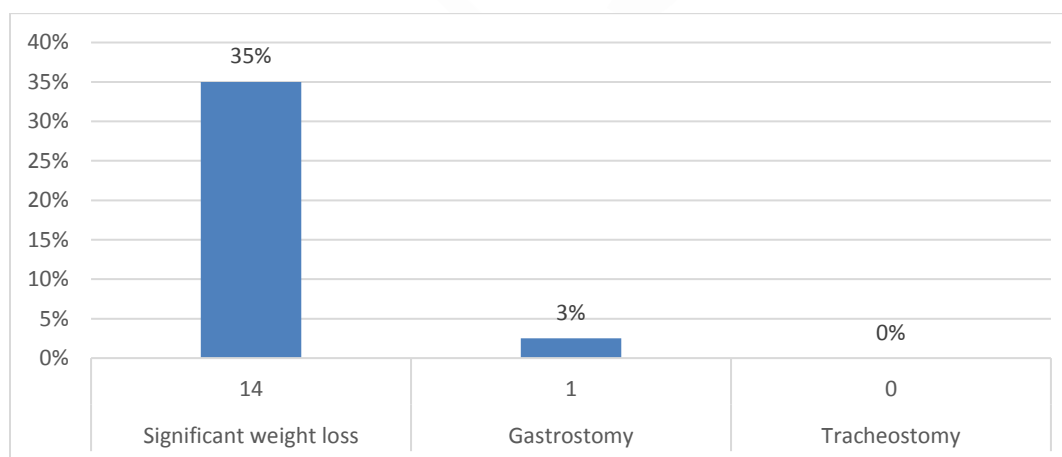
Teaching Center / Radiation Therapy Department at the Medical City Complex, Baghdad, Iraq.

Data collection

The data collected from January 2016 to August 2016 using simple random sampling technique. Forty patients included (excluded palliative neck radiotherapy, neck lymphoma, pediatrics group, and on-off patients who make interpretation to radiotherapy schedules), figure (1) and selected regardless of their age, sex and the specific sub-site of the

Table 2 Incidences of early side effects of EBRT for H&N tumors in the studied patients

Side effect	N (%)
Dysphagia	35 (88)
Xerostomia	34 (85)
Fatigue	33 (83)
Skin dermatitis	25 (63)
Oral mucositis	25 (63)
Voice changes	22 (55)
Altered taste	21 (53)

**Figure 2** Distribution of the grades of the side effects in the studied patients**Figure 3** Incidences of significant weight loss, gastrostomy, and tracheostomy in the studied patients

disease. All patients included had no distant metastasis and treated with either a radical or adjuvant intent with a dose of 66 – 70Gy standard fractionation (2Gy per fraction, 5 fractions per week); those who treated with a palliative intent were not included. All patients received EBRT alone with no concurrent chemotherapy. Radiation delivered with 3D conformal forward planned IMRT technique. All patients' demographic details missed and destroyed by ISIS war in Iraq during 2015-2016.

Variables

This study concentrated to evaluate the early side effects of external beam radiotherapy for head and neck tumors including fatigue, skin dermatitis, voice changes, xerostomia, altered taste, oral mucositis, and dysphagia. As well as the incidence of patients who required a tracheostomy and/or a gastrostomy after initiation of radiotherapy, and

that of those who developed a significant weight loss (>10% of their initial weight). All kind of side-effects level (whether increases or decreases) addressed by grading as grad 1, 2, 3, and 4.

Statistical methods

Percentages obtained, categorized and organized into tables and figures using Microsoft Excel version 2015 for MAC under OS X EL CAPITAN version 10.11.

RESULTS

The incidence of the early side effects of EBRT for H&N tumors showed in Table 2. Patients with each of these side effects divided into four groups according to the severity (grade) of reaction. The distribution of the grades of these side effects in the studied patients are

shown in figure (2). 14 patients (35%) had a significant weight loss $\geq 10\%$, but only 1 (3%) required a gastrostomy after initiation of EBRT and no one ($n=0$) required a tracheostomy, of note, this does not include patients who had an initial gastrostomy and/or tracheostomy prior to initiation of treatment, figure (3).

DISCUSSION

Head and neck carcinoma is the sixth common cancer worldwide, accounting for 2.8% (1). Even with recent advancements in the radiation therapy, it is still associated with certain side effects that altered the quality of life of patients (12). We focused on evaluating the early side effects of EBRT to the H&N region in our own country at our own center, a follow up of our own work, to evaluate those side effects and to compare them with what other studies have found, also to emphasize on the significance of those side effects in our own patients so as to address those issues and hence, and to enhance the quality of life of our own patients during their journey of treatment.

In this study, dysphagia and xerostomia were common early side effects affecting 88% and 85% of the patients respectively. This is consistent with a study done by Nerina et al, (13), which stated that dysphagia occurred in 90% and a study done by Jensen et al, (14), which found that xerostomia occurred in 93% of patients. Furthermore, patients with grade 2 or higher dysphagia accounted over 50%, and those with grade 2 or higher xerostomia accounted 60% of all, these findings are consistent with the study mentioned earlier by Nernia et al, (13). Xerostomia is defined as the subjective feeling of thirst, and radiation induced xerostomia is attributed to the damage of the salivary glands, both major and minor. On the other hand, dysphagia is defined as the alteration in ability to swallow (14). A 3% of all patients ($n=1$) had a grade 4 dysphagia and required a gastrostomy tube placement. This finding is consistent with several studies, of those, a study done by Rafal et al, (15), reported that the tube feeding was rarely used and that only 3 patients out of 129 participants required a tube feeding. This low incidence of required gastrostomy after initiation of EBRT may be attributed to the fact that recent guidelines highly recommend for patients with locally advance disease to have a prophylactic gastrostomy tube placed prior to initiation of EBRT and thus those patients no longer contribute to the number of patients who required a gastrostomy after initiation of treatment. Regarding required tracheostomies after initiation of EBRT, William et al, (16), stated that in patients who recovered from the direct laryngoscopy and biopsy without obstruction, a tracheotomy has rarely required during a fractionated course of EBRT. This is consistent with the findings of this study where no patient ($n=0$) required a tracheostomy after initiation of EBRT.

The incidence of significant weight loss was 35%, which consistent with a study done by Mary et al, (17), which found that weight loss was 33%. This weight loss may attributed to the dysphagia, xerostomia, and oral mucositis that induced by radiation affecting patients' ability to masticate, swallow and thus affecting their daily caloric required intake resulting in such weight losses.

Fatigue ranked third in after dysphagia and xerostomia, 83% of the patients complained of fatigue, however, 70% of them complained only of a mild fatigue over baseline (grade 1). The incidence of fatigue varies significantly among different other studies, for example, a study done by Barbara et al, (18), reported that fatigue affected all patients undergoing radiotherapy for head and neck cancer, an incidence of 100%. While the study done by Biswa et al, (19), stated that radiation induced fatigue occurred only in 34% of the patients. These significant differences may be attributed to the fact that fatigue is a subjective feeling and that some

patients with only mild fatigue over baseline may not complain of such low levels of fatigue and hence, will not contribute to the total incidence of observed fatigue in the studied patients.

The skin dermatitis and oral mucositis had similar incidences, each occurring in 63%. Of those with skin dermatitis 68% had only mild erythema or dry desquamation (grade 1). While oral mucositis 80% had only mild oral mucositis (grade 1 & 2). These results are consistent with the results of the studies done by Calais et al, (22), which estimated skin dermatitis in 58%, Bourhis et al, (21), reported skin dermatitis in 73%, Kumar et al, (23), recorded oral mucositis in up to 66% of all patients, and Vera et al, (23), which stated that mild oral mucositis accounted for 71%. Radiation induced skin dermatitis is attributed to the damage caused by the rapidly shedding cells of the skin, erythema and dry desquamation. On the other hand, radiation induced oral mucositis is attributed to the damage caused by radiation to the normal mucosal lining of the oral cavity increasing the risk of opportunistic infections.

Radiation may induce damage to the taste buds and the vocal cords, the incidence of voice changes and altered taste were 55% and 53% respectively. In general, studies on those two side effects are scarce. The scarcity of studies on these two side effects may be attributed to the fact that these two side effects may not have a significant impact on the quality of life of patients compared to the disturbing difficulty in swallowing, stressful constant feeling of thirst, painful oral mucositis, and the discomfort of skin desquamation. For instance, all patients in this study never complained of these two side effects upon initial approach and that those who complained only did so after further investigation unlike the other side effects mentioned earlier.

CONCLUSIONS

Dysphagia and xerostomia were the two common early side effects of radiotherapy. More than half of the patients with dysphagia had a grade 2 or higher reaction, and about three-quarters of those with xerostomia had a grade 2 or higher reaction. Tracheostomy and gastrostomy were rarely required after initiation of EBRT. Weight loss is not uncommon during the course of EBRT to the H&N region. Although fatigue ranked third with an incidence. Skin dermatitis and oral mucositis had a similar incidence, about two-thirds of patients who developed skin dermatitis had only a mild erythema or a dry desquamation, a grade 1 reaction. Similarly, over three-quarters developed oral mucositis had only mild mucositis, a grade 2 or less reaction. Voice changes and altered taste were least common side effects of EBRT.

Recommendations

Avoiding any unnecessary irradiation to the major salivary glands as well as the pharynx, whenever possible, during plan preparations when treating a head and neck cancer, so as to reduce the risk of dysphagia and xerostomia. Providing the medications (Duke's solution, artificial saliva preparations, topical steroid creams) that are necessary to address the early side effects that may develop during the course of EBRT to the H&N region, so as to ease the journey of treatment. Patient education to avoid shaving, perfumed soaps, smoking, alcohol, hot and spicy foods/drinks consumption during the course of treatment, so as to avoid and/or reduce the intensity of skin dermatitis and oral mucositis. Encourage increasing daily caloric intake of patients to meet at least the minimum required calorie consumption per day during the course of treatment, so as to avoid weight loss. All above recommendations are required in the follow-ups required to prevent or manage the side-effects.

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Competing interests

We (authors) declare that we have no conflict of interest.

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Ethical approval

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee from College of Medicine / Baghdad University (Code number: 33 in 10/08/2016) and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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