



The impact of treatment on quality of life of patients with head and neck cancer and its association with prognosis[☆]

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Abstract

Background: Information is scarce regarding the impact of treatment on Health-Related Quality of Life (HRQL) of patients with Head and Neck (H&N) cancers. We assessed the effect of treatment on HRQL and its association with prognosis in H&N cancer.

Patients and methods: Patients with H&N cancer in whom HRQL was assessed before and after treatment. The European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and QLQ-H&N35 instruments were used. Association of changes in patients' HRQL after treatment with Loco-Regional Recurrence (LRR) and Overall Survival (OS) was investigated.

Results: One hundred sixty patients were included; scales of the baseline assessment of HRQL were moderately associated with LRR and OS, but the impact of treatment on most HRQL scales was strongly associated with OS. By multivariate analysis, baseline assessment of Global Health, Physical, HN Teeth, HN Dry mouth, and HN Cough scales, and impact of treatment on the Physical and Pain scales comprised independent variables associated with LRR. Male gender, positive lymph nodes, baseline assessment of Role, HN Pain, HN Cough, and impact of treatment on Emotion, Pain, Financial, HN Swallowing, HN Social contact, and the interaction of HN Pain-change in Pain scales were associated with OS. Both multivariate models were adjusted by the neoplasm's site of origin.

Conclusion: Aside from well-known clinical-pathologic prognostic factors in H&N cancers, HRQL assessment, both prior to and after treatment, provides significant prognostic information and should be measured. Design of therapeutic clinical trials in patients with H&N cancers should consider these novel prognostic factors.

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Keywords: Head and neck neoplasms; Quality of life; Prognosis; Locoregional neoplasm recurrence; Survival analysis

Introduction

Health-Related Quality of Life (HRQL) has been recognized as a major outcome measurement in different areas of Medicine.¹ HRQL is particularly relevant in Oncology because disease and treatments produce a significant impact on the patients' feeling of well-being² and because

physicians and family members are poor judges of these experiences.¹ Therefore, constant improvements of instruments designed for this estimation have been reported.^{1–3} At present, there is a growing interest for the inclusion of HRQL assessment in clinical trials in Oncology, allowing for comparison, contrast, or combining as appropriate, in order to ensure the production of high-quality evidence.³

Recent reports have evaluated the association of HRQL and prognosis in cancer,^{4,5} and specifically in Head and Neck (H&N) squamous cell carcinoma.^{6,7} However, there is scarce information that explores improvement in HRQL as a result of adequate treatments in the prognosis of H&N cancers, although this interesting association has been reported in other neoplasms.^{8,9}

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In addition to analyses of factors such as Tumor Node Metastasis (TNM) staging, comorbidities, physical performance, location of malignancies, histopathology, or treatments, HRQL assessment has not been considered consistently in recent trials.^{10–12} Available studies that have evaluated HRQL to date have short follow-up times or transversal measurements and a lack of precise timing for these estimates or evaluation of treatment impact.^{13,14} Inadequate description of survival assessments and lack of adjustment for confounders, such as the site in the H&N area, are major concerns as well.¹⁵ Hence, the impact of treatment on HRQL is unknown. Despite the scarcity of studies designed to analyze the effect of HRQL on survival, some review studies were unable to define specific symptom domains that could exert a real influence on the prognosis of H&N cancers.^{15,16}

Integrated and consistent reports of the impact of improvement in HRQL on classic oncologic outcomes in patients with H&N cancer are scarce,^{17,18} although some insight has been afforded regarding global HRQL change.¹⁵ Consequently, the aim of this study was to assess the impact of the treatments of patients with H&N cancer on HRQL, as well as its association with Loco-Regional Recurrence (LRR) and Overall Survival (OS).

Patients and methods

Patients

This is a cohort study of patients who were treated in the H&N Department of the Instituto Nacional de Cancerología (INCan) in Mexico City, with a diagnosis of H&N cancer, regardless of subsites or histopathological diagnoses. Inclusion criteria were: females or males whose ages were 18 years or over, recruited from January 2007 to December 2012, who completed treatment with curative attempt. Confirmation of malignancy by biopsy and adequate surgical pathology study was accomplished, and clinical history, physical examination, and panendoscopy were performed in all cases where invasion to upper aerodigestive structures was suspected or occurred. Imaging studies included chest X-ray, as well as Computed Tomography (CT) scan and Magnetic Resonance Imaging (MRI) in T2 stages cases and higher. Patients with thyroid cancer had major invasion to aerodigestive structures and were classified as T4 in all cases. The 2010 Tumor Node Metastases (TNM) Classification of Malignant Tumors by the American Joint Committee on Cancer (AJCC) was employed.¹⁹ All patients had Karnofsky Performance Status (KPS) scores ≥ 80 , as well as normal renal, hematological, and hepatic function.

Instruments

Patients had baseline evaluations of HRQL employing the Mexican-Spanish versions of the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30

and QLQ-H&N35 instruments^{20,21}; all cases had a new HRQL assessment at 6 months or more after treatment completion. Paper copies of the instruments were responded to in the outpatient clinic, and a research associate was present to supervise the process. The QLQ-C30 comprises a global health status and five functional and nine symptom subscales. The QLQ-H&N35 includes seven symptom subscales that measure pain, swallowing, sense, speech, social eating, social contact, and sexuality, and also has 11 subscales related with teeth, mouth opening, dry mouth, sticky saliva, coughing, ill feeling, weight loss, weight gain, use of painkillers, nutritional supplements, and feeding tubes. Both questionnaires were utilized with the permission of EORTC Quality of Life Study Group. The Institutional Review Board and Bioethics Committee approved this study (registry numbers 009/049/CCI and CB/551/09), and all patients signed an informed consent form.

Analyses

Scores for scales were calculated by linear transformation of raw scores into a 0–100-point score, with 100 representing best global health, functional status, or worst symptoms, depending on the measuring property of each scale, and missing data were treated as recommended by EORTC.²² Primary endpoints were LRR and OS; LRR was defined as any evidence of disease at the original primary site, or regional lymph nodes at >3 months after treatment completion; OS was calculated from date of diagnosis to last appointment at the H&N Department's Outpatient Clinic. Association of factors with LRR or OS was assessed employing logistic regression analysis or the Cox model, respectively. Sample size was calculated assuming five events for each covariate introduced in multivariate analysis; that represents 10 covariates for 50 recurrence events for LRR or 10 covariates for 50 death events for OS (1). Bivariate analysis was performed initially, and all factors associated with the outcome with a probability value of 0.2 or less were used in the multivariate analysis. Interaction analyses were performed in the final models, and proportionality assumptions were tested in the final Cox model.

Survival curves were generated utilizing the Kaplan–Meier method, and significance of differences between groups was analyzed using the Log-rank test. Any probability value of 0.05 or less was considered significant; two-tailed statistics were taken into account in all cases, and SPSS for Mac version 20 statistical software was employed to perform all computations (IBM Corp., Armonk, NY, USA).

Results

Patients

In this study 179 patients were invited initially to participate, but only 160 completed the second survey. Therefore,

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