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Global quality of life during the acute toxicity phase of multimodality treatment for patients with head and neck cancer: Can we identify patients most at risk of profound quality of life decline?

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SUMMARY

Purpose: Treatment intensification has improved outcomes for patients with head and neck cancer (HNC), but little has been reported on health-related quality of life (QoL) consequences. We investigated changes in QoL after (chemo)radiotherapy to identify patient characteristics that predict those whose QoL deteriorates most profoundly in the acute post-treatment period.

Materials and methods: Patients with locally advanced HNC treated with curative intent received intensity-modulated radiotherapy (60–70 Gy) in this prospective study. (Chemo)radiotherapy was either definitive or adjuvant. Induction chemotherapy consisted of three cycles of docetaxel, cisplatin, and 5-fluorouracil; responders received (chemo)radiotherapy; nonresponders underwent salvage surgery followed by (chemo)radiotherapy if appropriate. Patients completed the EORTC QLQ-C30 and HNC-specific HN35 module before and at the end of (chemo)radiotherapy and 6–8 weeks after therapy completion.

Results: Ninety-five patients participated. At baseline, patients reported significantly lower Global health status, functioning, and symptom scale scores than a reference German population (all $p < 0.001$). At the end of (chemo)radiotherapy, patients had significantly lower QoL scores vs. baseline on all functioning scales ($p < 0.05$). Most symptom and HN35 scores worsened during (chemo)radiotherapy but many recovered 6–8 weeks post-treatment. QoL deteriorated more in patients with high vs. low baseline QoL; no clinical or sociodemographic characteristics of patients most likely to experience a significant deterioration in QoL during treatment were identified.

Conclusion: These standard QoL instruments did not predict patients at risk of profound global QoL impairments during acute treatment. Other than baseline QoL, no patient characteristics associated with significant QoL deterioration were identified.

Introduction

The concept of health-related quality of life (QoL) refers to aspects of life that are important to an individual and that may be affected – positively or negatively – by health and illness. The development of intensive cancer treatment regimens has improved response rates, but toxicities have become more burdensome and difficult to quantify.[1] However, little information is available on the QoL consequences of these more aggressive approaches.

Randomized studies defining new oncology therapies are often not applicable in practice because the general health status of many patients is too poor. For example, the recommended (chemo)radiotherapy regimen for head and neck cancer (HNC) is cisplatin 100 mg/m^2 every 3 weeks, combined with 70 Gy radiation delivered in 1.8–2.0 Gy daily fractions. This regimen causes severe toxicities, e.g. nephro-, oto-, and neuro-toxicities, nausea and vomiting, and severe mucositis, which in daily practice means the regimen is suitable only for patients with normal creatinine clearance and good performance status. To limit toxic effects, and so get patients through therapy, reduced administration schedules are used, but without equivalent efficacy being established.

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Patients undergoing multimodal regimens experience functional and psychosocial consequences of treatment.[2] QoL measurement should be integrated into all clinical studies in patients with HNC to provide data for treatment planning and to try to identify patients at most risk of profound QoL deterioration. Methods for measuring QoL in patients with cancer include generic instruments that apply to all cancer populations, those that are specific to the disease in question, and treatment-, symptom-, and site-specific instruments.[3]

The present study was designed to examine the evolution of QoL in patients with advanced HNC, initially during and just after (chemo)radiotherapy, and then over 5 years. The initial goal was to identify patient characteristics that may predefine those in need of support before treatment and immediately after treatment. In future studies, the effect of such support could then be assessed for any meaningful impact on QoL.

Patients and methods

Patients

Enrollment into this prospective study was offered to patients with locally advanced HNC who were treated with curative intent at a single institution. Approval was obtained from the local ethics committee and all patients provided written informed consent.

All patients received intensity-modulated radiotherapy (total dose 60–70 Gy at 2 Gy/fraction with conventional fractionation). (Chemo)radiotherapy was definitive or adjuvant. Induction chemotherapy consisted of three cycles of TPF (docetaxel 75 mg/m^2 1-h infusion day 1, cisplatin 75 mg/m^2 1-h infusion day 1, and 5-fluorouracil 750 mg/m^2 continuous infusion days 1–5). Subsequently, responders received chemoradiotherapy and nonresponders underwent salvage surgery [followed by (chemo)radiotherapy depending on risk factors]. Adjuvant (chemo)radiotherapy consisted of radiotherapy (60–66 Gy at 2 Gy/fraction) with or without platinum-based chemo-therapy.

QoL measurement

General cancer-related QoL was measured with the German-language version of the European Organisation for Research and Treatment of Cancer (EORTC) 30-item Quality of Life Questionnaire (QLQ-C30).[4] HNC-related QoL was measured using the EORTC 35-item Head and Neck Module (HN35).[4] The QLQ-C30 consists of a global health scale and five functioning scales (Emotional, Physical, Cognitive, Social, and Role). The QLQ-C30 also includes three multi-item and six single-item scales: Fatigue, Pain, Nausea and Vomiting, Dyspnea, Insomnia, Appetite loss, Constipation, Diarrhea, and Financial difficulties. The HN35 includes seven head and neck-specific multi-item scales (Pain in the mouth, Swallowing, Senses, Speech, Social eating, Social contact, and Sexuality) plus six single-item scales (Problems with teeth, Problems opening mouth, Dry mouth, Sticky saliva, Coughing, and Feeling ill). The HN35 includes five yes/no items relating to the use of painkillers, nutritional supplements, feeding tube, weight loss, and weight gain.

Questionnaires were self-completed in the physician's office before the start of (chemo)radiotherapy (t1), at the end of (chemo)radiotherapy (t2), and 6–8 weeks after completion of (chemo)radiotherapy (t3).

Mean scores (±standard deviation) for the QLQ-C30 and HN35 were calculated according to the EORTC scoring manual.[5] Scores for each scale range from 0 to 100. Higher scores on functioning scales indicate better health-related QoL; conversely, higher scores on symptom scales indicate more severe symptoms and worse QoL.

Data analysis

Data were analyzed using SPSS (Windows) Version 15.0. Missing data in QoL items were treated according to the EORTC scoring manual.[5]

Data for men and women were compared using analysis of variance (ANOVA). QoL was compared with published QLQ-C30 data for a reference German population. This reference group of 2081 randomly selected adults (mean age 49.4 years [standard deviation 17.2 years]) were interviewed in their own homes by skilled interviewers.[6] The present study used the cohort aged 60–69 years (n = 390) from this population, as 48% of our sample were in this age category. Comparisons were conducted using one-sample t-tests. QoL changes during (chemo)radiotherapy and follow-up were investigated by multivariate ANOVA with repeated measurements.

To determine potential predictors of QoL 6–8 weeks after (chemo)radiotherapy, two-step linear regression analyses were performed. First, univariate analyses were performed on the association between potential predictors and QoL at follow-up. The following independent predictors were investigated dichotomously: (A) disease- and treatment-related variables: (A1) tumor stage (T1/2 vs. T3/4/x), (A2) nodal stage (N0/1 vs. N2/3), (A3) grading (G1/2 vs. G3), (A4) previous surgery (yes/no), (A5) previous chemotherapy (yes/no), (A6) chemoradiotherapy (yes/no), (A7) body mass index (median split), (A8) Karnofsky index (median split) and (A9) hemoglobin (median split); (B) sociodemographic variables: (B1) age (median split), (B2) sex (male/female), (B3) marital status (married/not married), (B4) years of schooling ($\leqslant$9 years vs. >9 years), (B5) employment (employed vs. unemployed/retired) and (B6) household income ($\leqslant$€2000 vs. >€2000/month); (C) life-style factors: (C1): current smoking (yes/no) and (C2) current alcohol consumption (yes/no). For the analysis of QoL at follow-up, we also investigated (D) global health status at the beginning of radiation treatment: (D1) initial QoL (median split).

The second step was a multivariate stepwise regression. Age and sex were included as predictors because QoL changes with age and QoL-norm data are generally reported for each sex separately and according to age group. Additional variables were included that were associated with QoL at follow-up at a 10% significance level in the univariate analysis.

The dependent variable in the regression model was global health status. All predictors were included as either interval-scaled (age, initial QoL) or dichotomized (tumor stage, sex, current smoking status).

Results

This is an analysis of the first three timepoints (t1, t2, and t3) of the ongoing study, which commenced in April 2009. As of April 2011, 99 patients had enrolled. Table 1 summarizes clinical and demographic characteristics of 95 patients with data. One patient died shortly after completion of therapy and three were lost to follow-up.

There were no significant differences between men and women for any clinical, sociodemographic, or lifestyle variables.

Quality of life at baseline

The whole sample had statistically significantly lower QoL scores than the reference German population. QoL functioning scores in the study sample were between 10 (Physical function; $p < 0.001$) and 30 (Social function; $p < 0.001$) points lower than those of the reference group.[6] The study sample also had significantly lower global health status ($p < 0.001$) and symptom scale scores (Table 2). Domains particularly affected (difference of >20 points) included Role, Emotional, and Social function, as well as