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Estimation of life expectancy and quality-adjusted life expectancy in non-metastatic nasopharyngeal cancer patients treated by intensity-modulated radiotherapy with or without chemotherapy

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SUMMARY

Purpose: This study was designed to estimate the life expectancy (LE) and quality-adjusted life expectancy (QALE) in non-metastatic nasopharyngeal cancer (NPC) patients.
Methods and materials: Patients were eligible for the present study if they were diagnosed with NPC and had been treated with intensity-modulated radiotherapy (IMRT) between January 1, 2003 and December 31, 2010. The quality of life (QOL) data were collected using the questionnaires of the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and QLQ-H&N35. The LE of NPC patients was obtained using linear extrapolation of a logit-transformed curve and was adjusted by the corresponding QOL function to calculate the QALE.
Results: During the study period, 110 patients met the inclusion criteria, and 53 of these completed questionnaires. The median follow-up was 65.2 months (range 4.0–117.3 months). The average LE and QALE were estimated to be 20.6 years and 11.6 quality-adjusted life years (QALYs) for NPC patients and 24.4 years and 24.4 QALYs for the reference population, respectively. Compared to the reference population, the loss of LE and QALE for NPC patients were 3.8 years and 12.8 QALYs, respectively.
Conclusions: This study offers a quick overview of the LE and the QALE of NPC patients treated with IMRT. Moreover, the results appear more understandable than the 5 year survival outcomes when communicating with patients or the general population regarding cancer risk. In the future, evaluating the robustness of comparative assessments for the outcome of NPC patients undergoing different treatment protocols will be possible.

Introduction

Several studies have shown excellent tumor control and patient survival rates in treating nasopharyngeal cancer (NPC) patients by intensity-modulated radiotherapy (IMRT) [1–4]. Compared to two-dimensional radiotherapy (2D-RT), IMRT also improves patient quality of life (QOL) by reducing normal tissue toxicity, such as preserving parotid function [5]. Though long-term survival can be achieved in more than half of patients and the survival rate during the observed study period can be estimated by survival analysis, a reliable method for lifetime extrapolation is lacking [6]. Moreover, outcome measures over the full cycle of care for NPC patients should account for both survival and QOL in estimating quality-adjusted life expectancy (QALE). This goal can be achieved by adjusting the survival function with mean QOL at each time point t, and then summing the result across the entire lifetime of the patient as expressed in the following equation [7–10]:

$$\mathrm{QALE} = \int E[Qol(t/x)]S(t/x)dt$$

where $S(t/x)$ denotes the survival function for condition x at time t and $Qol(t/x)$ denotes the QOL function for condition x at time t.

The present study was conducted to estimate life expectancy (LE) and QALE in non-metastatic NPC patients treated by IMRT with or without chemotherapy.

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Materials and methods

Patients

Between January 1, 2003 and December 31, 2010, there were 161 newly diagnosed NPC patients in our institution. Patients were eligible for this study if they were treated by IMRT. Other inclusion criteria were ages between 18 and 75 years, Zubrod performance status 0–2, no evidence of distant metastasis at diagnosis, and no previous or synchronous malignancies. During the study period, 110 patients met the inclusion criteria. All patients who completed questionnaires provided written informed consent. The study protocol was approved by the institutional review board. Pretreatment evaluation included a complete history and physical examination, direct flexible fiber-optic nasopharyngoscopic examination, chest X-ray, bone scan, abdominal sonogram, computed tomography or magnetic resonance imaging (MRI) scans of head and neck. The disease was staged according to the 2002 American Joint Committee on Cancer (AJCC) staging classifications [11].

Treatment methods

IMRT

The Eclipse Treatment Planning System (Varian Oncology System, Palo Alto, CA, USA) was used for IMRT planning. IMRT was delivered by the computer-controlled autosequencing segmented or dynamic multileaf collimator of a Varian linear accelerator (Linac 21 EX). The high-risk clinical target volume (CTV) was defined as CTV1, including gross tumor and gross nodes and received 68.4–75.2 Gy. The CTV2 included the entire nasopharynx, the posterior third of the nasal cavity and maxillary sinus, pterygoid fossae, parapharyngeal space, retropharyngeal lymph nodes, clivus, skull base, inferior sphenoid sinus and bilateral level Ib–III nodes and received 58.8–61.2 Gy. The CTV3 included the low neck or supraclavicular field and received 46.8 Gy unless there were gross nodes in which all gross nodes received the same dose as the CTV1. Planning target volume (PTV) included CTV with a 3–5 mm margin. Radiotherapy was delivered once daily, five fractions per week, with a daily fraction size of 1.8–2.1 Gy.

Chemotherapy

Patients with stage $\geqslant$T2b and/or node-positive patients received concurrent chemotherapy. Whether adjuvant chemotherapy was administered or not was determined according to the judgment of each oncologist. Concurrent chemotherapy with weekly cisplatin 30–40 mg/m^2 was administered in seven courses. Adjuvant chemotherapy with cisplatin 80 mg/m^2 on day 1 and fluorouracil 1000 mg/m^2/d on days 1–4 was administered every 4 weeks in two courses.

QOL instruments and QOL weights (utility scores)

The Taiwan Chinese versions of the questionnaires of the EORTC QLQ-C30 and QLQ-H&N35 were obtained from the Quality of Life Unit, EORTC Data Center in Brussels, Belgium [12–14]. All scales pertaining to the EORTC QLQ-C30 and QLQ-H&N35 ranged from 0 to 100. A high score for a functional or global QOL scale represented a relatively high/healthy level of functioning or global QOL, whereas a high score for a symptom scale represented the presence of a symptom or problems.

QOL weights (or utility scores) reflected the preference for a certain health state and were measured on a 0–1 scale. A value of 1 reflected perfect health and 0 represented death. Although utility scores were not elicited directly in this study, the QLQ-C30 global QOL item was used to derive utility scores by the following equation: $Y = 0.0086x + 0.1616$, where x is the QLQ-C30 score on the global QOL item and Y is the estimated utility score. The mean scores of the QOL scales were calculated according to the EORTC QLQ scoring manual [15]. The reasons and methods to convert QLQ-C30 scores into utility scores were described in a previously published study [16]. The EORTC QLQ-C30 and QLQ-H&N35 questionnaires completed between December 1, 2011 and October 31, 2012 were collected.

Follow-up

Patients were regularly followed up after radiotherapy (RT) until death or their last follow-up appointment. They were scheduled to visit the clinics at 3–6 month intervals in the first 3 years and every 6–12 months thereafter. Physical and fiber-optic nasopharyngoscopic examinations were performed routinely at each visit. MRI scans of the head and neck were performed 2 months after RT, then every 3–6 months in the first 3 years after RT, and every 6–12 months thereafter or when there were clinical indications. Locoregional failure was determined based on pathological diagnosis or progressive deterioration shown on consecutive image studies. To identify distant metastases, patients were examined by chest X-ray annually and by abdominal sonogram or bone scan whenever indicated.

Statistical analysis

The duration of survival was calculated from the date of diagnosis. Patients alive on the last day of follow-up were censored. Survival curves were estimated by the Kaplan–Meier method. The SPSS 17.0 software was used for data analysis.

The survival function for an age- and gender-matched reference population was generated using the Monte Carlo method from the life table of the general population in the Taiwan area from 1970 to 2010. Lifetime survival of NPC patients (up to 50 years) was obtained using linear extrapolation of a logit-transformed curve of the survival ratio between NPC patients and reference population. The details were described in previous studies [7–9].

The average QOL function was estimated by kernel-smoothing the data of a random sample from a cross-sectional QOL survey of the living individuals [9]. For each duration to date (the time elapsed since the diagnosis of NPC), the utility score of each surviving patient was multiplied by the survival rate of the cohort, whereas utilities for the reference population were assumed to be 1 throughout the survival period. A random sample size of 50 has been suggested as the minimal requirement to establish the mean QOL function curve over time [9].

The lifetime survival function of NPC patients was obtained and adjusted by the corresponding QOL function consistent with the duration beginning with the diagnosis of NPC to calculate the QALE based on a 9 year follow-up period with 50 years of extrapolation. To facilitate this computation, we used a software program (iSQoL) built on R language (freely available at http://www.stat.sinica.edu.tw/jshwang/web/isqol/). Our method of extrapolation of long-term survival using this statistical method has been validated in previous studies [17–20].

Results

Patients' characteristics

During the study period, 110 patients met the inclusion criteria (17 females, 93 males; mean age = 52 years). Table 1 shows the patients' characteristics. The distributions of clinical stages according to the AJCC staging system published in 2002 were as follows: stage I ($n = 9$; 8.2%), stage II ($n = 25$; 22.7%), stage III ($n = 42$;