

RESEARCH COMMUNICATION

Quality of Life and Radiotherapy Complications of Chinese Nasopharyngeal Carcinoma Patients at Different 3DCRT Stages

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Abstract

Purpose: the study aimed to compare the quality of life (QOL) and radiotherapy complications among Chinese nasopharyngeal carcinoma (NPC) patients at different 3-dimensional conformal radiotherapy (3DCRT) stages adjusting for other variables. **Methods:** 511 NPC patients at different 3DCRT stages were enrolled. They were interviewed regarding SF-36, complications and socio-demographic variables and cancer- or treatment- related variables. Analysis of covariance (ANCOVA) based on SF-36, complications scores as dependent variables, 3DCRT stages as independent variables, and other variables as covariate were established. **Results:** The influencing factors of PCS included 3DCRT stages and age group. The influencing factors of MCS included 3DCRT stages and income. Most QOL scores of NPC patients were significantly associated with 3DCRT stage, after accounting for other variables. QOL scores of the patients receiving 3DCRT were the lowest, QOL scores of people after 3DCRT gradually increased. PCS scores of people greater than 5 years after 3DCRT was improved to or even better than the level before 3DCRT. The complications with significantly different scores of patients at different 3DCRT status included xerostomia, throat ache, hypogeusia, caries, hearing loss, snuffles. **Conclusions:** Clinicians should pay more attention to older NPC patients and patients with lower income. When patients receive 3DCRT, measures should be taken to reduce radiation injury to improve the patients' QOL.

Keywords: Nasopharyngeal carcinoma - SF-36 - 3-dimensional conformal radiotherapy - complications

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Introduction

Health-related quality of life (HRQOL) is playing important roles in measuring the therapeutic effects of nasopharyngeal carcinoma (NPC) patients. HRQOL is a multidimensional construct which can assess aspects of physical health such as physical functioning, bodily pain, and general health and aspects of mental health such as vitality, social functioning and role emotional for NPC patients.

Radiotherapy (RT) is one of the most important methods to treat NPC patients. Over the past decade, RT techniques had developed from two-dimensional RT (2DRT) to the 3-dimensional conformal RT (3DCRT). The use of 3DCRT provided a potentially therapeutic benefit of dose escalation to tumour tissue with reduced toxicity to normal tissues (Teo et al., 2004).

Previous researchers reported that 3DCRT had detrimental effects on NPC patient's health status and quality of life. After NPC patients received 3DCRT, they were also faced with lots of side effects or the

complications such as xerostomia (dryness of mouth), hearing impairment, and hypomnesia (Chen et al., 2000; McMillan et al., 2004; Yeh et al., 2005; Pow et al., 2006; Sumitsawan et al., 2009). The complications resulted in chronic health problems such as discomfort and pains and resulted in chronic mental stress such as sleep disturbances, and increasing rates of anxiety, which seriously had a bad effect on QOL (McMillan et al., 2004). Some papers reported that socio-demographic variables and cancer- or treatment- related variables played a significant role in the QOL of NPC patients, such as the dose of 3DCRT, gender, age, dialect, economic status, occupational status, educational level, monthly income, economic status, numbers of comorbidities, treatment method, and RT dose (Fang et al., 2002; Y. Wu et al., 2007; Demiral et al., 2008).

To provide a better understanding of the relationships between 3DCRT and QOL, this paper will compare a large group of NPC patients at different RT stages. Because patients' QOL would be expected to be affected by other variables, we sought to examine the adjusted

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analysis of RT stages (adjusting for other variables) and QOL. Another goal is to investigate the relationships between 3DCRT stages (adjusting for other variables) and complications.

Materials and Methods

Study sample

A sampling frame was developed to assure enrolment of adequate numbers of NPC patients at different 3DCRT stages. All NPC patients in Cancer Centre of Sun Yat-sen University from January 1st to February 15th in 2007 were enrolled in this study. Inclusion criteria were as follows: patients pathologically confirmed with NPC, receiving 3DCRT treatment, greater than 18 years old. NPC patients of inclusion criteria included three kinds: those newly pathologically confirmed with NPC without any treatment, those receiving 3DCRT now, and cancer free survivals who ever received 3DCRT treatment. Patients who had other types of malignant disease, or those who received 3DCRT due to other chronic disease, or those once received other RT such as 2DCRT or intensity-modulated radiotherapy (IMRT) were excluded.

Interviewers who were medicine graduate students received specific training for this study including NPC treatment and management. They explained the study and obtained informed consent according to a protocol approved by the Sun Yat-sen University. Participants were interviewed face to face, by the study interviewer, lasting approximately 0.5 hour.

Treatment methods

The immobilization, targets, and dose/fractionation prescription of 3DCRT to treat NPC followed the guidelines of Cadplan (Varian, Milpitas, CA) or Pinnacle 3D treatment planning system (Pinnacle3, Philips, Fitchburg, WI) (Hsiung et al., 2002). Nasopharyngeal dose of all patients ranged 60-80 Gy/day, and Neck dose of all patients ranged 46~76 Gy/day. Every patient received RT treatment for 6~7 weeks. The total dose was about 6000~8000 GY.

Study instruments

The questionnaires consisted of three parts: SF-36 scale, the complications checklist and the variables sheet. SF-36 was composed of 8 domains: physical functioning (PF), role limitations due to physical problems (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), mental health (MH) (Ware et al., 1992; Özaras et al., 2010). PF, RP, BP, GH domains generated a physical component score summary (PCS), with other domains generating mental component score summary (MCS).

The complication checklist was composed of 11 items: xerostomia (dry mouth), throat ache, skin injury, radiation-induced temporomandibular joint lesion (RTJL), hypogeusia (taste loss), dysphonia, caries, hearing loss, snuffles, dysopia (vision loss), hypomnesia. The score of these items ranged from 0 to 10. The lower score meant that more severe of complications to health. The patients without 3DCRT treatment had not fill in the complications checklist.

The variables sheet was used to collect information about the variables of age, gender (male vs. female), marital status (married vs. unmarried), educational level (≤ 9 years vs. >9 years), monthly income, dialect, other chronic disease (yes vs. no), clinical stage (I+II, III+IV), treatment method (3DCRT vs. 3DCRT and chemotherapy), nasopharyngeal dose (≤ 70 GY/day vs. >70 GY/day), neck dose (≤ 60 GY/day vs. >60 GY/day), RT course (1 course vs. ≥ 1 course), 3DCRT stages. According to the first time of 3DCRT, 3DCRT stages was divided into 6 groups: before 3DCRT, under 3DCRT, ~1 year after 3DCRT, ~3 years after 3DCRT, ~5 years after 3DCRT, and > 5 years after 3DCRT. Patient's age in years was measured and analyzed on a continuous scale. Monthly income which was defined as per-capita monthly income was dichotomized at above or below RMB1300 per month. Dialect was divided into Cantonese dialect (Cantonese people) and other dialects, which included Hakka people, Chaoshan people and people from other provinces.

Data analysis

SPSS17.0 was used for data analysis. Chi-square and Variance of analysis (ANOVA) were used to compare socio-demographic and treatment variables of different RT status. Analysis of covariance (ANCOVA) based on SF-36 or complication scores as dependent variables, RT stage as independent variables, and other variables such as age, gender, marital status, educational level, monthly income, dialect, other chronic disease, treatment method, nasopharyngeal dose, neck dose, 3DCRT course as covariate were established. After adjusting for other variables, the SF-36 scores of different RT stage can be compared. The multivariate ANOVA was used to select the influencing factors of PCS and MCS. P-value less than 0.05 were considered statistically significant.

Results

Demographics

The data presented in table 1 provided the descriptions of the samples in terms of socio-demographic and

Table 1. The QOL Scores of NPC Patients at Different 3DCRT Stages Using ANCOVA

	Before 3DCRT	Under 3DCRT	≤ 1 year after	~ 3 years after	~ 5 years after	> 5 years after	P value
GH	52.1	49.1	53.7	48.9	50.2	51.6	0.293
PF	89.5	78.8	82.7	83.8*	86.9*	86.1*	0.012
RP	54.3	27.1	34.7	36.8	37.3	41.1	0.148
BP	73.2	63.8	69.2	73	71.4	69.6	0.121
VT	65.9	57.7	62.6	63.7	63.7	62.6	0.128
SF	72.3	55.6	69.0*	67.9*	66.7*	79.7*	0
RE	55.6	35	46.8*	49.2*	45.8	53.2*	0.044
MH	66.5	64.4	70.1*	70.5*	68.5	73.7*	0.015
PCS	70.7	57	63.8*	64.3*	65.3*	67.9*	0
MCS	68.6	61.1	67.7*	68.8*	69.0*	70.3*	0

*meant a significant difference compared with scores of patients under 3DCRT; PF, physical functioning; RP, role limitations; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health; PCS, physical component score summary; MCS, mental component score summary

Table 2. The Mean of Complications Scores of NPC Patients in Different 3DCRT Stage Using ANCOVA

	Under 3DCRT	≤1year after 3DCRT	~3years after 3DCRT	~5years after 3DCRT	>5years after 3DCRT	P value
xerostomia	4.11	3.41*	3.01*	3.51	3.15*	0.025
throat ache	4.97	5.42	6.26*	6.33*	6.18*	0.018
skin injury	5.99	5.92	5.72	6.6	6.77	0.308
RTJL	7.01	6.76	6.57	5.79	6.46	0.167
hypogeusia	4.61	5.2	5.73*	5.21	6.57*	0.003
dysphonia	6.59	6.87	7.46	6.11	6.67	0.146
caries	7.6	6.99	6.62*	6.47*	6.02*	0.004
hearing loss	6.61	6.1	5.01*	5.91	5.05*	0.001
snuffles	6.96	6.6	5.42*	6.44	5.15*	0
dysopia	7.39	7.73	6.57	7.31	6.77	0.055
hypomnesia	7.44	7.28	6.82	6.46	6.87	0.173

treatment variables. 6 patients refused to fill in the banks because of the long content of the questionnaires. At last, data of 511 (98.8%) patients was valid. 69 patients were newly pathologically confirmed with NPC without any treatment. The remaining patients were all receive RT treatment. 376 were man and 135 were women. The patients aged from 18 to 87 years, with a mean age of 45.6 years and SD of 12.1 years. Most of patients (93.7%) were married, almost two-fifths (39.7%) of the patients had monthly income of less than RMB 1300, almost two-thirds (65.6%) of the patients spoke Cantonese dialect, and 106 patients had other chronic disease. 81.4% of the patients were diagnosed as = 1 * ROMAN I+ = 2 * ROMAN II stage. The proportion of the variables such as gender, marital status, educational level, monthly income, dialect, clinical stage, other chronic disease, treatment method, nasopharyngeal dose, neck dose, and RT course among NPC people at different RT stages were not statistically significant.

SF-36

Mean of QOL score for NPC patients in different 3DCRT stage using ANCOVA were presented. PF, SF, RE, MH, PCS and MCS scores of NPC patients were significantly associated with 3DCRT stage, after accounting for other variables. PCS scores of patients receiving 3DCRT treatment were the lowest (57.0). The PCS scores of people after receiving 3DCRT gradually increased. However, the scores (67.9) of people greater than 5 years after 3DCRT was lower than those (70.7) before 3DCRT. MCS scores of the patients receiving 3DCRT were the lowest (61.1). MCS scores of people after 3DCRT gradually increased. The scores (70.3) of patients greater than 5 years after 3DCRT were higher than those (68.6) before 3DCRT. Pairwise comparison showed that the patients in other 3DCRT stage had higher PCS and MCS score than those receiving 3DCRT treatment.

The influencing factors of PCS included 3DCRT stages and age group. Comparing with patients before 3DCRT, other patients had lower PCS QOL. Comparing with patients >45 year, those ≤45 year had higher PCS QOL. Influencing factors of MCS included 3DCRT stages and income. Patients with lower income had lower MCS QOL.

Complications

Table 2 listed the complications scores of NPC patients at different 3DCRT stages adjusting for other variables. The complications with significantly different scores of patients at different 3DCRT stages included xerostomia, throat ache, hypogeusia, caries, hearing loss, snuffles. The patients who were under 3DCRT reported higher scores than those after 3DCRT in xerostomia, caries, hearing loss and snuffles, and the patients who were under 3DCRT reported lower scores than those after 3DCRT in throat ache and hypogeusia.

Discussion

Quality of life is an increasingly important concept in the health and well-being of NPC patients specifically for those who have experienced 3DCRT treatment. Past studies didn't pay enough attention to QOL of NPC patients who had survival for a long times after 3DCRT treatment.

Our results showed that 3DCRT stage was significantly associated with parts of SF-36 domain (PF, RP, SF, MH), PCS and MCS, after accounting for other variables. The results were similar to previously published research (Pow EH et al., 2006; McMillan et al., 2006; Fang et al., 2008). Fang et al. reported that NPC patients who received 3DCRT had a trend of maximal deterioration in most QOL scales (QLQ-C30 and QLQ-H&N35) during RT, followed by a gradual recovery at 24 months after RT (Fang et al., 2008). 3DCRT did harm to the surrounding tissue, and reduced the ability of patients' physical and psychological functioning. Pairwise comparison showed that the score (except GH) of NPC patient under 3DCRT were lower than those before 3DCRT. After 3DCRT, QOL of NPC patients gradually increased to or even exceeded the level before 3DCRT. Moreover, NPC patients surviving 5 years after 3DCRT in this study had worse PCS QOL than MCS QOL, although they had better PCS QOL before 3DCRT. NPC patients receiving 3DCRT treatment for a long time suffered more injuries in physical health than in mental health. This may be related with the complications after 3DCRT mainly reduced patients' physical functioning.

The patients who were older (>45 year) had lower PCS QOL. The older patient was suffered from more decrease of physical function, and their PCS QOL would be lower. The was consistent with others (Wu Y et al., 2005). Patients with lower income had lower MCS QOL. The people with highest income had the highest MCS QOL. The cost of NPC treatment was expensive. It was difficult for poor families to bear the cost of treatment, which resulted in a lower QOL. The result was consistent with others (Fang et al., 2002).

After accounting for other variables, 3DCRT had a significant impact on most of the complications such as xerostomia, throat ache, hypogeusia, caries, hearing loss, snuffles. The results were similar to previously published research (Huang et al., 2000; Pow EH et al., 2003; Palazzi et al., 2004; Pow EH et al., 2006; Oates et al., 2007). NPC patients with longer survival time reported lower scores of xerostomia, caries, hearing loss, snuffles than those under 3DCRT. NPC patients with longer survival

time reported higher scores of throat ache and hypogeusia than those under 3DCRT. It meant that RT had a long effect on xerostomia, caries, hearing loss and snuffles. When salivary gland (parotid gland, sublingual gland, submandibular gland, and so on) was damaged by rays, the post-RT parotid glands were significantly smaller than the pre-RT ones (Wu et al., 2011), which led to xerostomia and taste losing (hypogeusia).

Findings from this study indicate that NPC patients who receive 3DCRT had lower QOL scores and complications scores after accounting for other variables. 3DCRT was an effective method to treat NPC patients. However, some study reported that 3DCRT had more detrimental affects on QOL, and brought more complications to NPC patients than intensity-modulated radiotherapy (IMRT) (Pow et al., 2006; Jensen et al., 2010; Tribius et al., 2011). It suggested that doctors should try to utilize IMRT to treat NPC patients. NPC patients receiving 3DCRT for a long time suffered more injuries in mental health than in physical health, suggesting that clinicians and other medical personnel should provide more additional treatment such as reducing radiation dose, protecting surrounding tissue, and using traditional Chinese medicine to improve QOL.

The limitation of the current research included: (1) the design of the research was a cross-sectional study instead of longitudinal study. As there is individual differences response to treatment, and the sensitivity of each patient to 3DCRT was different, each patient may have different changes of QOL at different 3DCRT stages. The mean scores of patients at different RT status could not naturally reflect the change of QOL. Longitudinal study is needed to be carried out to document the ongoing changes of QOL at different time points. (2) SF-36 was available for evaluation of QOL for Chinese NPC patients due to its good reliability and validity. Yet, this scale is a generic QOL scale, which has no items to measure any cancer-specific symptoms of NPC. One strength of the study was that NPC patients were randomly sampled from Cancer Carter of Sun yat-sen University. The proportions of other variables among NPC people at different RT stages were not statistically significant.

In summary, 3DCRT not only decreased most domains of QOL; but also led to many complications such as xerostomia, throat ache, hypogeusia, caries, and throat ache. When the clinicians and other medical personnel treated NPC patients using 3DCRT, they should pay more attention to older NPC patients and patients with lower income. When patients received 3DCRT, measures should be taken to reduce radiation injury to improve the patients' QOL in the long term.

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