

# Radiotherapy-Related Quality of Life in Nasopharyngeal Carcinoma Patients: A Systematic Review and Meta-Analysis

Kai Chen Yuan Cai Luyun Jiang Li Tian

Department of Otorhinolaryngology, Hospital of Chengdu University of Traditional Chinese Medicine, Chengdu, China

## Keywords

Nasopharyngeal carcinoma · Quality of life · Meta-analysis · Radiotherapy

## Abstract

**Introduction:** This systematic review and meta-analysis evaluated the quality of life (QoL) for nasopharyngeal carcinoma (NPC) patients with radiotherapy. **Methods:** A systematic literature search was performed to identify relevant studies published until March 2022. Quality evaluation and data extraction were performed for the included studies, and meta-analysis was performed using Stata. **Results:** Nine studies, including 1,659 patients, were eligible. Most QoL scales developed at the end of the treatment course and then followed by a gradual recovery to 1 year and more than 1 year after treatment. However, some items have not changed significantly and have a deteriorating trend. Items of cognitive functioning and constipation in EORTC QLQ-C30, and sexuality, felt ill, and weight gain in EORTC QLQ-H&N35 showed that scales with follow-up of more than 1 year were worse than those within 1 year but still better than those after treatment. In the intensity-modulated radiotherapy (IMRT) subgroup in EORTC QLQ-C30, cognitive functioning was similar to those before, and there was no significant change in insomnia. There was no significant change in the teeth item in EORTC QLQ-H&N35. In the IMRT

subgroup, scales of swallowing, felt ill, and weight gain with follow-up of more than 1 year were worse than those within 1 year. **Conclusion:** The QoL of patients with NPC is significantly impaired after radiotherapy-treated compared to baseline, and most of these items will gradually improve.

© 2024 S. Karger AG, Basel

## Introduction

Nasopharyngeal carcinoma (NPC) is one of the most prevalent diagnosed malignant tumors of the head and neck [1]. Most NPCs are diagnosed in Eastern Asia, Southeast, and Northern Africa [2]. Given its anatomical location and proximity to critical organs, radiation therapy (RT) is the primary local modality [2]. The 5-year overall survival rate of patients with NPC is up to 80% [3, 4]. However, the complications and treatment-related adverse effects should also be paid attention to.

Health-related quality of life has become increasingly important in health care, especially in chronic and terminal diseases [5]. Evaluation of the treatment effect of chronic diseases has changed, which depends not only on the survival duration but also on the quality of

Kai Chen and Yuan Cai have contributed equally to this work and share first authorship.

life (QoL) of patients [6]. The majority of studies using the European Organization for Research and Treatment of Cancer quality of life core questionnaire (EORTC QLQ-C30) and the accompanying head and neck module (EORTC QLQ-H&N35) to assess the QoL of NPC patients and some of them chose Short Form 36 Health Survey Questionnaire (SF-36) and functional assessment of cancer therapy-head and neck (FACT-H&N) scale [7–9]. Results indicated that a maximal deterioration of most QoL scales developed during treatment or at the end of the treatment course and then followed by a gradual recovery to 1 year and 1–2 years after treatment [10].

In this article, we systematically review the current literature on patient-reported QoL after radiotherapy for NPC and perform a meta-analysis to determine which QoL domains are most clinically significantly affected by treatment. The results of QoL at three time points were included in the meta-analysis, including after treatment, within 1 year of follow-up, and within 1–2 years of follow-up, respectively.

## Methods

This article was conducted as specified in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram [11].

### Search Strategy

A systematic literature search in PubMed, Ovid, and EMBASE was performed to identify relevant studies published in English until March 2022. The following terms were used in the search procedure: (“nasopharyngeal carcinoma” OR “NPC” OR “nasopharyngeal neoplasm” OR “nasopharyngeal cancer”) AND (“quality of life” OR “EORTC QLQ-C30” OR “EORTC QLQ-H&N35”).

### Selection Criteria and Data Extraction

Two independent authors conducted the studies’ search, selection, and analysis with standardized data extraction tables, and any discrepancies were resolved through discussion or consultation with a third researcher. Studies that investigated the quality of life (the EORTC QLQ-C30 and QLQ-H&N35 questionnaires) of NPC patients treated with radiotherapy were considered for inclusion. We excluded (a) reviews, meta-analyses, and case reports; (b) studies with insufficient information to be included in the meta-analysis; and (c) studies published in non-English. The collected data included

authors, publication year, study type, recruitment time, age, surgical mode, sample size, follow-up time, TNM stage, and outcome.

### Quality Assessment and Statistical Analysis

The Cochrane Collaboration’s tool was used to assess the risk of bias to determine the quality of the randomized controlled trials and the Newcastle-Ottawa Scale to determine the quality of case-control studies and cohort studies. Data analysis was done using Stata version 15.0 (StataCorp, College Station, TX, USA). A random-effect model was used in this study. We analyzed the data as continuous variables (mean  $\pm$  standard deviation) and estimated with standard mean differences (SMDs). We used the Cochran’s Q test for assessing heterogeneity and quantified it using  $I^2$  statistics.  $p$  values of  $<0.1$  denoted heterogeneity.  $I^2$  values of  $>50\%$  were considered substantial heterogeneity. A subgroup meta-analysis of intensity-modulated radiotherapy (IMRT) was used to analyze sources of statistical heterogeneity. The publication bias was quantified using Egger’s regression test. For all tests,  $p$  values of  $<0.05$  were considered statistically significant.

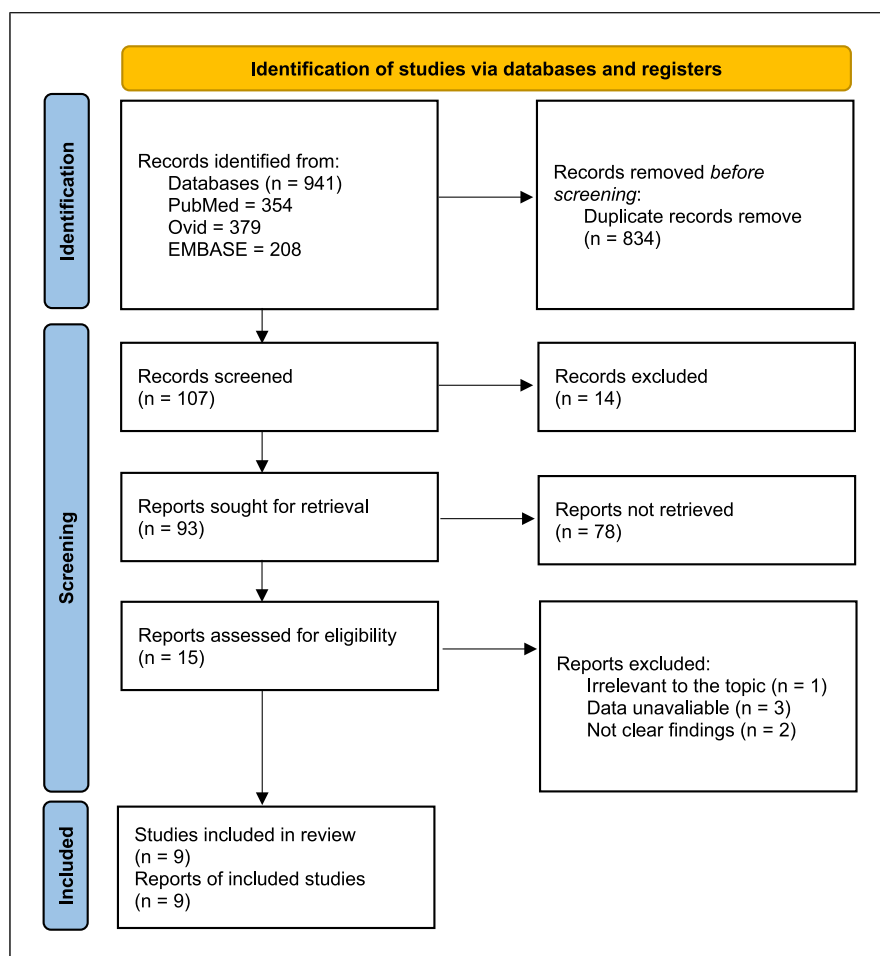
## Results

Nine studies that met the inclusion criteria for the meta-analysis involving 1,659 patients were published between 2006 and 2021 (Fig. 1) [12–20]. All the articles passed the quality assessment (Fig. 1; Table 1). There were 8 prospective trials and 1 randomized study. All the studies were performed in China. Of the selected studies, 8 involved EORTC QLQ-C30 [12–15, 17–20], and 9 involved EORTC QLQ-H&N35 [12–20]. Table 1 shows the general characteristics of the included studies.

### EORTC QLQ-C30

EORTC QLQ-C30 comprises a scale for global health status, five scales for multidimensional functioning (physical, cognitive, role, emotional, and social functioning), and nine scales/items for disease symptoms (fatigue, nausea, vomiting, pain, dyspnea, insomnia, diarrhea, constipation, appetite loss, and financial difficulties) [21]. The higher scores of global health status and five functional scales represent better QoL, while the lower scores of symptom items represent better QoL.

The meta-analyses of global health status are shown in Tables 2, 3. According to meta-analysis, NPC patients who were treated with radiotherapy showed a statistically significant increase in the scores of the global health status



**Fig. 1.** Flowchart for record selection process of the meta-analysis.

compared to pre-treatment. The pooled SMDs of global health status were 0.87 (95% CI: 0.62–1.11),  $-0.02$  (95% CI:  $-0.32$  to  $0.3$ ), and  $-0.4$  (95% CI:  $-0.6$  to  $-0.2$ ) at after therapy, followed-up within 1 year, and more than 1 year, respectively. There was no obvious evidence of heterogeneity in the trials after therapy and followed-up within 1 year, while medium heterogeneous in trials of followed-up more than 1 year. The meta-analyses of the subgroup of IMRT showed that the scores of the global health status significantly increased compared to pre-treatment. The pooled SMDs of the trials of followed-up within 1 year and more than 1 year were  $0.03$  (95% CI:  $-0.62$  to  $-0.69$ ) and  $-0.48$  (95% CI:  $-0.69$  to  $-0.27$ ), respectively. There was no obvious evidence of heterogeneity in the two trials.

For functional scales, the heterogeneity of functional scales among the trials is presented in Tables 2, 3. The SMDs of physical functioning and role functioning decreased gradually, and all of them were greater than 0, indicating that the scores of them were lower than pre-treatment. For emotional functioning and social func-

tioning, NPC patients treated with radiotherapy showed a significant increase in the scores compared to pre-treatment. The pooled SMDs of emotional functioning and social functioning were greater than 0 after therapy, while less than 0 in 2 trials with a follow-up within 1 year and more than 1 year, and the latter scored lower than the former. For cognitive functioning, the SMD with more than 1 year of follow-up was less than those within 1 year but still greater than those after treatment. The meta-analyses of the subgroup of IMRT of functional scales are shown in Table 3. For follow-up within 1 year, the SMD of physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning were  $0.4$  (95% CI:  $0.3$ – $0.5$ ),  $0.15$  (95% CI:  $-0.09$  to  $-0.4$ ),  $-0.42$  (95% CI:  $-0.74$  to  $-0.1$ ),  $0.12$  (95% CI:  $0.02$  to  $0.22$ ), and  $-0.09$  (95% CI:  $-0.36$  to  $-0.18$ ), respectively. For follow-up more than 1 year, the SMDs were  $0.18$  (95% CI:  $0.07$  to  $0.28$ ),  $-0.03$  (95% CI:  $-0.19$  to  $0.12$ ),  $-0.62$  (95% CI:  $-0.89$  to  $-0.34$ ),  $0.14$  (95% CI:  $0.04$  to  $0.25$ ), and  $-0.28$  (95% CI:  $-0.62$  to  $-0.06$ ), respectively.

**Table 1.** Characteristics of included studies

Study	Study design	Recruitment time	Follow-up, months	Patients	Gender of patients (male/female)	Age, years	TNM stage	Treatment	Outcome
Pow et al. [12] (2012)	Prospective study	2000 and 2007	24	57	/	46.9±9.5	I/II	IMRT	EORTC QLQ-C30, EORTC QLQ-H&N35
Poon et al. [13] (2021)	Randomized study	December 2017 and August 2018	15.5 (15.2–15.8)	10	4/6	47.6 (10.1)	I/II	IMRT	EORTC QLQ-C30, EORTC QLQ-H&N35
				11	5/6	43.9 (8.9)	I/II	2DRT	
Liao et al. [14] (2021)	Prospective study	April 2003 and December 2017	90.8 (50.8)	682	519/163	49.4 (11.5)	I/II/III/IV	IMRT	EORTC QLQ-C30, EORTC QLQ-H&N35
Deng et al. [15] (2019)	Prospective study	July 2011 to December 2014	3	359	275/84	44.2 (16–72)	I/II/III/IV	CCRT (IMRT) or IC + IMRT	EORTC QLQ-C30, EORTC QLQ-H&N35
He et al. [16] (2017)	Prospective study	November 2013 and February 2015	6	92	71/21	43.26±10.37	I/II/III/IV	CCRT (IMRT) or IC + IMRT or IC + CCRT (IMRT)	EORTC QLQ-H&N35
Tsai et al. [17] (2013)	Prospective study	March 2003 to December 2007	45 (range, 3–83)	273	212/61	51 (22–81)	I/II/III/IV	IMRT/3DCRT	EORTC QLQ-C30, EORTC QLQ-H&N35
Yang et al. [18] (2013)	Prospective study	June 2007 and August 2011	29 (range, 4–54)	86	55/31	52 (28–73)	I/II/III/IV	IMRT with replanning after computed tomography images	EORTC QLQ-C30
				43	23/20	57 (26–77)	I/II/III/IV	IMRT	EORTC QLQ-H&N35
Oates et al. [19] (2007)	Prospective study	January 21, 2002, to December 31, 2003	24	14	/	/	I/II/III/IV	CCRT (IMRT)	EORTC QLQ-C30, EORTC QLQ-H&N35
McMillan et al. [20] (2006)	Prospective study	June 2000 to December 2003	12	32	19/13	45.9±9.0	I/II	IMRT	EORTC QLQ-C30, EORTC QLQ-H&N35

CRT, chemoradiotherapy; IMRT, intensity-modulated radiotherapy; CCRT, concurrent chemoradiotherapy; 2DRT, two-dimensional radiotherapy; EORTC QLQ-C30, the European Organization for Research and Treatment of Cancer QOL core questionnaire; EORTC QLQ-H&N35, the European Organization for Research and Treatment of Cancer Head and Neck Module.

The heterogeneity and *p* value of symptom items are presented in Tables 2, 3. The pooled SMDs of symptom items in 3-time nodes are shown in Table 2. The pooled SMDs were on the rise as a whole, except item of constipation. NPC patients treated with radiotherapy showed a significant increase in the scores of fatigue and constipation compared to pre-treatment. The SMDs of fatigue and constipation were less than 0 in 3-time nodes. The SMD of the items of nausea and vomiting, pain, insomnia, diarrhea, and financial difficulties were less than 0 after therapy, while greater than 0 in two trials with a follow-up within 1 year and more than 1 year. In dyspnea and appetite loss, the SMDs were less than 0 after therapy and in follow-up within 1 year, and more than 0 in trial of more than 1 year. The meta-analyses of the subgroup of IMRT of symptom items are shown in Table 3. The SMDs of symptom items of IMRT in 2-time nodes were on the rise as a whole, except for dyspnea and insomnia items. In the trial after therapy, the SMDs were less than 0 in items of pain, dyspnea, appetite loss, and constipation, and others were greater than 0. In the follow-up trial of more than 1 year, the SMDs were less than 0 in items of fatigue, dyspnea, and constipation, and others were greater than 0.

#### *EORTC QLQ-H&N35*

EORTC QLQ-H&N35 includes seven symptom scales (problems of pain, swallowing, speech, senses, social contact, social eating, and sexuality), six symptom items (trouble with opening the mouth, teeth, sticky saliva, dry mouth, coughing, and feeling ill), and five dichotomous items (use of painkillers, nutritional supplements, feeding tube, and weight loss or weight gain) [10]. The lower the scores of EORTC QLQ-H&N35 represent better QoL.

The meta-analyses of EORTC QLQ-H&N35 are shown in Table 4. Because few studies comply with feeding tube in 3-time nodes, and painkillers, nutritional supplements, weight loss, and weight gain after therapy, they were not included in the analysis. In this analysis of sexuality with more than 1 year of follow-up, publication bias was assessed using Egger's test ( $p = 0.037$ ). However, the trim-and-fill analysis revealed that the publication bias did not affect the estimated results. The pooled SMDs were on the rise as a whole, except for items of sexuality, teeth, and felt ill. In the trial after therapy, the SMDs of all the items were less than 0. In follow-up trial within 1 year, the SMDs were more significant than 0 in items of coughing, felt ill, painkillers, and weight loss, and others were less than 0. In the follow-up trial of more than 1 year, the SMDs were more significant than 0 in items of pain,

coughing, felt ill, painkillers, and weight loss, and others were less than 0.

The meta-analyses of the subgroup of IMRT of EORTC QLQ-H&N35 were shown in Table 5. Because few studies comply with feeding tube, they were not included in the analysis. The SMDs of IMRT in 2-time nodes were on the rise as a whole, except for items of swallowing and weight gain. In the follow-up trial within 1 year, the SMDs were more significant than 0 in items of swallowing, coughing, felt ill, painkillers, and weight loss, while others were less than 0. In the follow-up trial of more than 1 year, the SMDs were more significant than 0 in items of pain, coughing, felt ill, painkillers, nutritional supplements, and weight loss, while others were less than 0.

## Discussion

This meta-analysis described the QoL of patients with NPC. The present meta-analysis showed that among the reported study population, most QoL scales developed at the end of the treatment course and then followed by a gradual recovery to 1 year and more than 1 year after treatment, as evaluated by most of the validated measures. However, there are still some items that have not changed significantly and even have a deteriorating trend. For EORTC QLQ-C30, analysis of cognitive functioning and constipation items showed that scales with follow-up of more than 1 year were worse than those within 1 year but still better than those after treatment. In the subgroup of the IMRT, the analysis of cognitive functioning was similar to those before. However, the subgroup of constipation showed a recovery trend. In addition, there was no significant change between the two follow-up stages of insomnia. For EORTC QLQ-H&N35, analysis of items of sexuality, felt ill, and weight gain showed that scales with follow-up of more than 1 year were worse than those within 1 year but still better than those after treatment. In addition, there was no significant change between the two follow-up stages of the item of teeth. In the subgroup of the IMRT, analysis of swallowing, felt ill, and weight gain showed that scales with follow-ups of more than 1 year were worse than those within 1 year.

This study found that although most of the QoL indicators began to gradually recover after the treatment ended and continued to improve over a year and beyond, some symptoms remained unchanged or even showed a tendency to worsen during the recovery process, which significantly affected the patients' QoL. Especially in terms of cognitive functioning, constipation, sexuality, felt ill, weight gain, and swallowing, patients generally

**Table 2.** Outcome of meta-analyses for EORTC QLQ-C30

Dimension	After therapy [15, 18]					Follow-up within 1 year [12–15, 18–20]					Follow-up more than 1 year [12–14, 17–20]							
	patients, n	SMD	95% CI	p value	heterogeneity test	patients, n	SMD	95% CI	p value	heterogeneity test	patients, n	SMD	95% CI	p value	heterogeneity test			
																$I^2$	p value	$I^2$
Global health status	454	0.87	0.62 to 1.11	0	43.9	0.168	1,260	-0.02	-0.32 to 0.3	0.917	88	0.16	1,174	-0.4	-0.6 to -0.2	0	66	0.003
Physical functioning	454	1.14	0.94 to 1.34	0	26.6	0.256	1,260	0.35	0.24 to 0.46	0	17.9	0.283	1,174	0.18	0.05 to 0.3	0.005	24	0.233
Role functioning	454	1.08	0.94 to 1.22	0	0	0.392	1,260	0.18	-0.02 to 0.39	0.073	69.3	0.001	1,174	0.03	-0.15 to 0.2	0.771	55	0.022
Emotional functioning	454	0.38	0.25 to 0.51	0	0	0.938	1,260	-0.36	-0.51 to -0.21	0	43.8	0.076	1,131	-0.54	-0.74 to -0.34	0	61	0.013
Cognitive functioning	454	0.53	0.4 to 0.66	0	0	0.707	1,260	0.09	0.01 to 0.17	0.027	0	0.756	1,174	0.13	0.44 to 0.22	0.003	0	0.564
Social functioning	454	0.71	0.26 to 1.17	0.002	82.7	0.003	1,260	-0.19	-0.37 to 0	0.051	63.8	0.005	1,174	-0.28	-0.5 to -0.07	0.01	71	0.001
Fatigue	454	-1.3	-1.54 to -0.95	0	57.7	0.094	1,260	-0.18	-0.35 to 0	0.044	57.8	0.015	1,174	-0.06	-0.15 to 0.02	0.149	0	0.662
Nausea and vomiting	454	-0.9	-1.43 to -0.27	0.004	89.7	0	1,165	0.07	-0.14 to 0.27	0.515	63.7	0.011	1,065	0.28	0.19 to 0.37	0	0	0.922
Pain	454	-1.2	-1.62 to -0.7	0	81.6	0.004	1,260	0.05	-0.03 to 0.12	0.257	0	0.636	1,174	0.2	0.02 to 0.37	0.025	54	0.026
Dyspnea	402	-0.5	-0.98 to 0.07	0.092	82.1	0.018	1,208	-0.08	-0.16 to 0	0.06	0	0.668	1,079	0.05	-0.08 to 0.18	0.45	24	0.246
Insomnia	454	-0.4	-0.76 to -0.13	0.006	67.5	-0.046	1,260	0.11	-0.01 to 0.24	0.081	30.3	0.176	1,174	0.22	0.13 to 0.3	0	0	0.958
Appetite loss	454	-1.1	-1.96 to -0.2	0.016	95.4	0	1,260	-0.12	-0.35 to 0.12	0.328	78.1	0	1,079	0.26	0.09 to 0.42	0.003	43	0.106
Constipation	454	-0.5	-1.1 to 0.07	0.086	90.3	0	1,217	-0.12	-0.3 to 0.07	0.211	60.9	0.013	1,131	-0.13	-0.22 to -0.05	0.003	0	0.461
Diarrhea	411	-0.1	-0.22 to 0.05	0.229	0	0.402	1,217	0.08	-0.04 to 0.2	0.216	25.2	0.228	1,065	0.11	0.02 to 0.2	0.013	0	0.463
Financial difficulties	454	-0.1	-0.21 to 0.09	0.401	8.2	0.336	1,260	0.29	0.1 to 0.49	0.003	66.1	0.003	1,131	0.38	0.18 to 0.58	0	62	0.011

**Table 3.** Outcome of meta-analyses for EORTC QLQ-C30 of IMRT

Dimension	Follow-up within 1 year (IMRT) [12–14, 18, 20]					Follow-up more than 1 year (IMRT) [12–14, 18, 20]						
	patients, n	SMD	95% CI	p value	heterogeneity test	patients, n	SMD	95% CI	p value	heterogeneity test		
					I <sup>2</sup>					I <sup>2</sup>		
Global health status	824	0.03	-0.62 to 0.69	0.924	93.4	0.5	824	-0.48	-0.69 to -0.27	0	40.4	0.152
Physical functioning	824	0.4	0.3 to 0.5	0	0	0.553	824	0.18	0.07 to 0.28	0.001	0	0.702
Role functioning	824	0.15	-0.09 to 0.4	0.225	54.8	0.065	824	-0.03	-0.19 to 0.12	0.674	17.4	0.304
Emotional functioning	824	-0.42	-0.74 to -0.1	0.01	71.5	0.007	781	-0.62	-0.89 to -0.34	0	50.8	0.107
Cognitive functioning	824	0.12	0.02 to 0.22	0.015	0	0.772	781	0.14	0.04 to 0.25	0.008	0	0.977
Social functioning	824	-0.09	-0.36 to 0.18	0.501	60.4	0.039	824	-0.28	-0.62 to 0.06	0.105	74.8	0.003
Fatigue	824	-0.16	-0.44 to 0.11	0.245	62.8	0.03	824	-0.06	-0.16 to 0.04	0.261	0	0.942
Nausea and vomiting	781	0.16	-0.25 to 0.57	0.449	78.4	0.003	781	0.29	0.18 to 0.4	0	0	0.763
Pain	824	-0.01	-0.1 to 0.09	0.887	0	0.974	824	0.19	0.08 to 0.29	0	0	0.543
Dyspnea	824	-0.02	-0.12 to 0.07	0.647	0	0.887	781	-0.04	-0.14 to 0.07	0.48	0	0.439
Insomnia	824	0.24	-0.01 to 0.49	0.065	55.3	0.062	824	0.24	0.13 to 0.34	0	0	0.862
Appetite loss	824	-0.05	-0.45 to 0.35	0.804	82.3	0	781	0.32	0.21 to 0.43	0	0	0.455
Constipation	781	-0.25	-0.35 to -0.15	0	0	0.811	781	-0.08	-0.19 to 0.02	0.129	0	0.904
Diarrhea	781	0.01	-0.09 to 0.11	0.885	0	0.637	781	0.12	-0.06 to 0.29	0.202	21.1	0.284
Financial difficulties	824	0.16	-0.01 to 0.34	0.067	25.7	0.25	781	0.38	0.2 to 0.56	0	21	0.284
IMRT, intensity-modulated radiotherapy.												

**Table 4.** Outcome of meta-analyses for EORTC QLQ-H&N35

Dimension	After therapy [15, 16, 18]					Follow-up within 1 year [12-16, 18-20]					Follow-up more than 1 year [12-14, 17-20]							
	patients, n	SMD	95% CI	p value	heterogeneity test	patients, n	SMD	95% CI	p value	heterogeneity test	patients, n	SMD	95% CI	p value	heterogeneity test			
																$I^2$	p value	$I^2$
Pain	546	-1.72	-2.08 to -1.36	0	77.9	0	1,352	-0.22	-0.47 to 0.03	0.091	84.4	0	1,174	0.02	-0.16 to 0.2	0.824	58.3	0.014
Swallowing	546	-1.78	-2.12 to -1.44	0	74	0.01	1,352	-0.7	-0.96 to -0.45	0	83.1	0	1,174	-0.63	-0.9 to -0.36	0	81.4	0
Senses Problems	546	-1.11	-2.07 to -0.16	0.023	97.4	0	1,352	-0.82	-1.09 to -0.55	0	73.3	0	1,174	-0.58	-0.74 to -0.42	0	45	0.069
Speech problems	546	-0.9	-1.24 to -0.56	0	79.8	0	1,352	-0.37	-0.54 to -0.19	0	64.9	0.002	1,174	-0.24	-0.39 to -0.08	0.003	45.5	0.065
Social eating	546	-1.27	-1.81 to -0.74	0	91.3	0	1,352	-0.53	-0.85 to -0.22	0.001	90	0	1,131	-0.46	-0.7 to -0.21	0	75.3	0
Social contact	546	-1.19	-1.32 to -1.06	0	0	0.5	1,352	-0.36	-0.52 to -0.19	0	60.4	0.007	1,174	-0.23	-0.39 to -0.06	0.006	47.5	0.055
Sexuality	546	-0.73	-1.12 to -0.33	0	85.6	0	1,342	-0.26	-0.46 to -0.06	0.012	74.1	0	1,121	-0.19	-0.37 to 0	0.05	55.7	0.027
Teeth	546	-0.33	-0.53 to -0.13	0.001	45.9	0.14	1,352	-0.14	-0.28 to 0	0.045	44.5	0.063	1,174	-0.14	-0.32 to 0.04	0.129	58.4	0.014
Opening mouth	546	-1.37	-1.87 to -0.88	0	89.3	0	1,320	-0.51	-0.76 to -0.26	0	82.8	0	1,174	-0.5	-0.74 to -0.26	0	73.6	0
Dry mouth	546	-1.73	-2.14 to -1.32	0	82.6	0	1,352	-1.4	-1.59 to -1.21	0	63	0.004	1,174	-1.07	-1.3 to -0.85	0	69.6	0.001
Sticky saliva	546	-1.64	-1.99 to -1.29	0	76.7	0.01	1,352	-1.07	-1.37 to -0.78	0	87.4	0	1,174	-0.85	-1.04 to -0.66	0	58.4	0.014
Coughing	546	-0.75	-1.21 to -0.3	0.001	87.9	0	1,352	0.06	-0.06 to 0.18	0.303	28.6	0.19	1,131	0.13	0.01-0.26	0.039	23.7	0.24
Felt ill	546	0.58	-0.84 to -0.32	0	66.8	0.03	1,352	0.3	0.03-0.57	0.03	86.6	0	1,174	0.2	0.01-0.39	0.044	62.4	0.006
Painkillers	/	/	/	/	/	/	1,151	0.37	0.29-0.45	0	0	0.432	792	0.43	0.32-0.54	0	0	0.686
Nutritional supplements	/	/	/	/	/	/	1,141	-0.39	-0.61 to -0.18	0	71.8	0.007	792	-0.01	-0.17 to 0.14	0.856	14.1	0.322
Weight loss	/	/	/	/	/	/	1,151	0.07	-0.27 to 0.4	0.696	88.2	0	792	0.43	0.23-0.64	0	28.3	0.233
Weight gain	/	/	/	/	/	/	1,151	-0.43	-0.61 to -0.24	0	56.8	0.041	792	-0.65	-1.03 to -0.28	0.001	71.6	0.007



**Table 5.** Outcome of meta-analyses for EORTC QLQ-H&N35 of IMRT

Dimension	Follow-up within 1 year (IMRT) [12–14, 18, 20]					Follow-up more than 1 year (IMRT) [12–14, 18, 20]					
	patients, n	SMD	95% CI	p value	heterogeneity	patients, n	SMD	95% CI	p value	heterogeneity	
					<i>I</i> <sup>2</sup>					test	<i>I</i> <sup>2</sup>
Pain	824	-0.41	-0.71 to -0.11	0.008	68.6	824	0.01	-0.2 to 0.23	0.899	41.6	0.144
Swallowing	824	0.99	-1.4 to -0.57	0	81.2	824	-0.81	-1.26 to -0.36	0	84.6	0
Senses problems	824	-0.9	-1.38 to -0.42	0	70.1	824	-0.5	-0.69 to -0.31	0	31.6	0.21
Speech problems	824	-0.53	-0.63 to -0.43	0	0	824	-0.2	-0.3 to -0.1	0	0	0.571
Social eating	824	-0.83	-1.31 to -0.34	0.001	86.9	824	-0.58	-0.89 to -0.28	0	59	0.062
Social contact	824	-0.5	-0.6 to -0.4	0	0	824	-0.26	-0.45 to -0.06	0.011	35	0.188
Sexuality	814	-0.33	-0.69 to 0.04	0.077	76.8	771	-0.26	-0.54 to 0.02	0.067	50.8	0.107
Teeth	824	-0.07	-0.32 to 0.18	0.573	55.4	824	-0.05	-0.29 to 0.19	0.682	51.1	0.085
Opening mouth	824	-0.96	-1.44 to -0.47	0	83.8	824	-0.59	-1.01 to -0.16	0.007	79.8	0.002
Dry mouth	824	-1.51	-1.92 to -1.11	0	77.5	824	-0.92	-1.16 to -0.69	0	46.3	0.114
Sticky saliva	824	-1.28	-1.56 to -0.99	0	59	824	0.97	-1.34 to -0.6	0	76.1	0.002
Coughing	824	0.08	-0.22 to 0.39	0.594	61.9	781	0.17	-0.15 to 0.49	0.29	63.3	0.043
Felt ill	824	0.18	-0.18 to 0.54	0.33	78.4	824	0.15	-0.08 to 0.38	0.211	48.9	0.098
Painkillers	781	0.32	1.15 to 0.49	0	17.7	781	0.42	0.31 to 0.53	0	0	0.76
Nutritional supplements	771	-0.36	-0.46 to -0.26	0	0	781	0.01	-0.19 to 0.2	0.929	31.5	0.232
Weight loss	781	0.1	-0.48 to 0.68	0.735	89.3	781	0.47	0.24 to 0.71	0	40.3	0.17
Weight gain	781	-0.37	-0.47 to -0.27	0	0	781	-0.58	-0.98 to -0.18	0.005	76.2	0.006
IMRT, intensity-modulated radiotherapy.											

experienced worsening symptoms, which not only affected their daily living abilities but also increased their psychological burden.

While some symptoms remained relatively unchanged during the follow-up period, they still significantly impacted the patients' QoL, include insomnia and teeth. Especially, insomnia, as one of the most common side effects of radiation therapy, greatly affected the patients' activity and social function, further degrading their QoL [22].

In previous QoL-related meta-analyses, NPC was always analyzed as a kind of head and neck malignancy but not as a separate disease [23, 24]. Clinically, there are various ways to treat NPC, and radiotherapy is one of the most common and essential methods. As far as we know, this study was the first meta-analysis conducted on the QoL of patients following treatment of NPC with radiotherapy. Data from our meta-analyses of observational studies provide evidence that QoL is, on the whole, developed at the end of the radiotherapy-treatment course and then followed by a gradual recovery. Based on our study, it appears that there remains a need to pay more attention to the QoL of patients with NPC and reduce exposure to health risk factors, especially after treatment.

The strongest strength of our study was that it was the first meta-analysis about related factors of the QoL of patients following treatment of NPC with radiotherapy. We calculated the EORTC QLQ-C30 and QLQ-H&N35 questionnaires, and we classified these factors into 3 groups with follow-up time to make it much clearer to understand. Our study conducted a meta-analysis based on the data of 9 studies. Similar to previous studies' results, patients' overall QoL gradually improved over time. Some variables had high heterogeneity, which may be because of the bias due to the lack of blinding of participants, personnel, or outcome assessment.

This study has several limitations. First, we only investigated the effects of QoL from pre-treatment to within 2 years after treatment. We could not further analyze the changes in QoL in NPC patients over time. Second, our

meta-analysis included 2 design studies. Therefore, confounding bias for inclusion in the study could not be excluded. Finally, most of the included studies were from China, where the cause of NPC and the factors associated with QoL might differ from Europe, North America, or African countries. The QoL of patients with NPC is significantly impaired after radiotherapy-treated compared to baseline, and most of these items will gradually improve.

### Statement of Ethics

The included studies were conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Funding Sources

The authors received no financial support for the research, authorship, and/or publication of this article.

### Author Contributions

Kai Chen collected and analyzed data, contributed to drafting, and revised the article. Yuan Cai collected and analyzed data and contributed to drafting; Luyun Jiang revised the article and contributed to final approval; Li Tian contributed to the design of the study and final approval and is accountable for all aspects.

### Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

## References

- 1 Su L, She L, Shen L. The current role of adjuvant chemotherapy in locally advanced nasopharyngeal carcinoma. *Front Oncol.* 2020;10:585046. <https://doi.org/10.3389/fonc.2020.585046>
- 2 Gabani P, Barnes J, Lin AJ, Rudra S, Oppelt P, Adkins D, et al. Induction chemotherapy in the treatment of nasopharyngeal carcinoma: clinical outcomes and patterns of care. *Cancer Med.* 2018;7(8):3592–603. <https://doi.org/10.1002/cam4.1626>
- 3 Zhang MX, Li J, Shen GP, Zou X, Xu JJ, Jiang R, et al. Intensity-modulated radiotherapy prolongs the survival of patients with nasopharyngeal carcinoma compared with conventional two-dimensional radiotherapy: a 10-year experience with a large cohort and long follow-up. *Eur J Cancer.* 2015;51(17):2587–95. <https://doi.org/10.1016/j.ejca.2015.08.006>
- 4 Lin S, Lu JJ, Han L, Chen Q, Pan J. Sequential chemotherapy and intensity-modulated radiation therapy in the management of locoregionally advanced nasopharyngeal carcinoma: experience of 370 consecutive cases. *BMC cancer.* 2010;10:39. <https://doi.org/10.1186/1471-2407-10-39>

- 5 Hong JS, Tian J, Han QF, Ni QY. Quality of life of nasopharyngeal cancer survivors in China. *Curr Oncol*. 2015;22(3):e142-7. <https://doi.org/10.3747/co.22.2323>
- 6 Bottomley A. The cancer patient and quality of life. *Oncologist*. 2002;7(2):120-5. <https://doi.org/10.1634/theoncologist.7-2-120>
- 7 McDowell L, Corry J, Ringash J, Rischin D. Quality of life, toxicity and unmet needs in nasopharyngeal cancer survivors. *Front Oncol*. 2020;10:930. <https://doi.org/10.3389/fonc.2020.00930>
- 8 Chen J, Liu P, Wang Q, Wu L, Zhang X. Influence of intensity-modulated radiation therapy on the life quality of patients with nasopharyngeal carcinoma. *Cell Biochem Biophys*. 2015;73(3):731-6. <https://doi.org/10.1007/s12013-015-0638-0>
- 9 Gao M, Yuan T, Zhang F. Effect of nimotuzumab and PF induction chemotherapy combined with concurrent chemoradiotherapy in treating locally advanced nasopharyngeal carcinoma. *J BUON*. 2021;26(1):116-23.
- 10 Bian X, Song T, Wu S. Outcomes of xerostomia-related quality of life for nasopharyngeal carcinoma treated by IMRT: based on the EORTC QLQ-C30 and H&N35 questionnaires. *Expert Rev Anticancer Ther*. 2015;15(1):109-19. <https://doi.org/10.1586/14737140.2015.961427>
- 11 Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. <https://doi.org/10.1136/bmj.n71>
- 12 Pow EH, Kwong DL, Sham JS, Lee VH, Ng SC. Can intensity-modulated radiotherapy preserve oral health-related quality of life of nasopharyngeal carcinoma patients? *Int J Radiat Oncol Biol Phys*. 2012;83(2):e213-21. <https://doi.org/10.1016/j.ijrobp.2011.12.040>
- 13 Poon DMC, Kam MKM, Johnson D, Mo F, Tong M, Chan ATC. Durability of the parotid-sparing effect of intensity-modulated radiotherapy (IMRT) in early stage nasopharyngeal carcinoma: a 15-year follow-up of a randomized prospective study of IMRT versus two-dimensional radiotherapy. *Head Neck*. 2021;43(6):1711-20. <https://doi.org/10.1002/hed.26634>
- 14 Liao KC, Chuang HC, Chien CY, Lin YT, Tsai MH, Su YY, et al. Quality of life as a mediator between cancer stage and long-term mortality in nasopharyngeal cancer patients treated with intensity-modulated radiotherapy. *Cancers*. 2021;13(20):5063. <https://doi.org/10.3390/cancers13205063>
- 15 Deng J, He Y, Sun XS, Li JM, Xin MZ, Li WQ, et al. Construction of a comprehensive nutritional index and its correlation with quality of life and survival in patients with nasopharyngeal carcinoma undergoing IMRT: a prospective study. *Oral Oncol*. 2019;98:62-8. <https://doi.org/10.1016/j.oraloncology.2019.09.014>
- 16 He Y, Chen L, Chen L, Hu W, Wang C, Tang L, et al. Relationship between the comprehensive nutritional index and the EORTC QLQ-H&N35 in nasopharyngeal carcinoma patients treated with intensity-modulated radiation therapy. *Nutr Cancer*. 2017;69(3):436-43. <https://doi.org/10.1080/01635581.2017.1283422>
- 17 Tsai WL, Chien CY, Huang HY, Liao KC, Fang FM. Prognostic value of quality of life measured after treatment on subsequent survival in patients with nasopharyngeal carcinoma. *Qual Life Res*. 2013;22(4):715-23. <https://doi.org/10.1007/s11136-012-0213-8>
- 18 Yang H, Hu W, Wang W, Chen P, Ding W, Luo W. Replanning during intensity modulated radiation therapy improved quality of life in patients with nasopharyngeal carcinoma. *Int J Radiat Oncol Biol Phys*. 2013;85(1):e47-54. <https://doi.org/10.1016/j.ijrobp.2012.09.033>
- 19 Oates JE, Clark JR, Read J, Reeves N, Gao K, Jackson M, et al. Prospective evaluation of quality of life and nutrition before and after treatment for nasopharyngeal carcinoma. *Arch Otolaryngol Head Neck Surg*. 2007;133(6):533-40. <https://doi.org/10.1001/archotol.133.6.533>
- 20 McMillan AS, Pow EHN, Kwong DLW, Wong MCM, Sham JST, Leung LHT, et al. Preservation of quality of life after intensity-modulated radiotherapy for early-stage nasopharyngeal carcinoma: results of a prospective longitudinal study. *Head Neck*. 2006;28(8):712-22. <https://doi.org/10.1002/hed.20378>
- 21 Grønvold M, Grønvold M, Grønvold M. EORTC QLQ-C30 scoring manual; 2014.
- 22 Zhan ZJ, Huang HY, Xiao YH, Zhao YP, Cao X, Cai ZC, et al. Anxiety and depression in nasopharyngeal carcinoma patients and network analysis to identify central symptoms: a cross-sectional study from a high-incidence area. *Radiother Oncol*. 2024;197:110324. <https://doi.org/10.1016/j.radonc.2024.110324>
- 23 Gupta T, Kannan S, Ghosh-Laskar S, Agarwal JP. Systematic review and meta-analyses of intensity-modulated radiation therapy versus conventional two-dimensional and/or three-dimensional radiotherapy in curative-intent management of head and neck squamous cell carcinoma. *PLoS One*. 2018;13(7):e0200137. <https://doi.org/10.1371/journal.pone.0200137>
- 24 Ge X, Liao Z, Yuan J, Mao D, Li Y, Yu E, et al. Radiotherapy-related quality of life in patients with head and neck cancers: a meta-analysis. *Support Care Cancer*. 2020;28(6):2701-12. <https://doi.org/10.1007/s00520-019-05077-5>