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Quality of life and its influencing factors in elderly patients with lung cancer during carbon-ion radiotherapy Running title: Quality of life during carbon-ion radiotherapy in elderly patients with lung cancer

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Research Article

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Abstract

Purpose To examine the longitudinal changes in quality of life (QoL) and its influencing factors in elderly patients with lung cancer during carbon-ion radiotherapy (CIRT), and to provide evidence for comprehensive supportive care.

Methods Eighty elderly patients (≥ 65 years) with lung cancer who received CIRT at the Heavy-Ion Therapy Center of Gansu Wuwei Tumor Hospital between January 2023 and July 2025 were prospectively enrolled in this longitudinal observational study. QoL (EORTC QLQ-C30), nutritional status (PG-SGA), anxiety (SAS) and depression (SDS) were assessed before, during, and at 1 and 6 months after radiotherapy. Linear mixed-effects models with Bonferroni correction, Spearman correlation and Kaplan–Meier methods were used.

Results QLQ-C30 global health status/QoL (GHS) scores increased continuously from 22.2 ± 13.0 before radiotherapy to 37.5 ± 12.4 at 6 months after radiotherapy ($F = 588.31$, $P < 0.001$); all 76 patients who completed follow-up improved, with a median increase of 15 points, exceeding the minimal clinically important difference. Nutritional risk (PG-SGA ≥ 2) increased from 23.8% to a peak of 63.8% and partly recovered to 53.8% ($F = 4.87$, $P = 0.003$); anxiety and depression decreased from 43.8% and 41.2% to 8.8% and 20.0%, respectively (both $P < 0.001$). Time was the strongest correlate of QoL improvement (6-month estimate $\beta = 15.26$, $P < 0.001$), and smoking was independently associated with higher QoL ($\beta = 8.08$, $P = 0.029$). The 12-month overall and progression-free survival rates were 92.5% and 89.8%, respectively.

Conclusion QoL improved continuously during CIRT in elderly patients with lung cancer, accompanied by marked relief of anxiety and depression but a persistently elevated nutritional risk. CIRT showed favorable patient-reported outcomes and short-term survival, and comprehensive management should include regular PG-SGA nutritional screening and continued psychological support for at least 6 months after radiotherapy.

Introduction

Lung cancer is one of the most common malignancies threatening the health of older adults in China, with incidence and mortality rates ranking among the highest of all cancers. Elderly patients frequently present with chronic cardiopulmonary disease, sarcopenia and functional decline, and their tolerance of treatment varies widely; treatment decisions should therefore incorporate functional status, nutrition and psychological wellbeing in addition to tumour stage [1–9]. Radiotherapy is a mainstay of multimodality treatment for lung cancer, and preserving quality of life (QoL) while controlling the tumour is a core goal of comprehensive geriatric oncology.

Carbon-ion (heavy-ion) radiotherapy exploits the dosimetric advantages of the Bragg peak to deliver a high dose to the target while markedly reducing the dose to surrounding normal tissue, and its biological effectiveness exceeds that of conventional photons. In recent years it has shown favourable local control and acceptable toxicity in non-small cell lung cancer (NSCLC) [10–22], and preliminary reports from domestically developed carbon-ion systems in China have also indicated good safety and efficacy [23]. Nevertheless, most existing studies have focused on local control and survival; patient-reported outcomes have been evaluated less systematically, and evidence specific to older patients is particularly scarce.

QoL is the treatment benefit that patients can perceive directly. The European Organisation for Research and Treatment of Cancer QLQ-C30 has been extensively validated and applied in lung cancer populations [24,25], and older patients face additional dimensions such as physical function, cognition and family support that require specific attention [28]. Several prospective studies have examined longitudinal QoL changes before and after radiotherapy for lung cancer, but their findings are not entirely consistent [29–31]. Nutritional status during treatment directly affects radiation tolerance and recovery, and radiotherapy-related dysphagia and taste changes can markedly increase nutritional risk [32–40]; nutritional status is also an important predictor of QoL [41]. Anxiety and depression are highly prevalent in patients with cancer, the psychological burden of Chinese patients being particularly prominent, and anxiety and depression frequently co-occur and jointly impair QoL [42–47].

However, the longitudinal trajectories of nutritional status, psychological status and QoL, and their determinants, during carbon-ion radiotherapy in elderly patients with lung cancer have not been systematically reported, and QoL during radiotherapy is influenced by multiple factors [48]. In this study, we prospectively collected clinical and questionnaire data from 80 elderly patients with lung

cancer who underwent CIRT and analysed QoL changes before, during and after treatment and their influencing factors, aiming to provide evidence for comprehensive management in general practice.

Materials and methods

Study design and ethics

This single-center prospective longitudinal observational study was conducted between January 2023 and July 2025. The study protocol was approved by the Ethics Committee of Gansu Wuwei Tumor Hospital (initial approval No. 2023-LLSC-10) before the first patient was enrolled, and is reviewed and renewed annually; the current approval number covering the data reported here is 2026-LLSC-23. Written informed consent was obtained from all patients before enrolment. The reporting of this study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline.

Participants

Consecutive elderly patients with lung cancer who received carbon-ion (heavy-ion) radiotherapy at the Heavy-Ion Therapy Center of Gansu Wuwei Tumor Hospital between January 2023 and July 2025 were enrolled. Inclusion criteria were: (1) pathologically confirmed stage I–III NSCLC; (2) age ≥ 65 years; (3) receipt of radical or palliative carbon-ion radiotherapy; (4) normal cognition and communication ability allowing independent completion of the questionnaires; and (5) availability of complete baseline clinical data and willingness to complete the scheduled follow-up assessments. Exclusion criteria were: (1) previous thoracic radiotherapy; (2) a concurrent second malignancy; and (3) interruption of radiotherapy because of severe complications with failure to complete follow-up assessments.

Sample size was estimated on the basis of previous longitudinal QLQ-C30 studies in lung cancer radiotherapy, assuming a moderate effect size (Cohen f2 = 0.15), a power of 0.80, a two-sided alpha of 0.05 and a repeated-measure correlation of r = 0.5, yielding a required sample of 68 patients; after allowing for a 20% loss to follow-up, the target enrolment was 85 patients, and 80 patients were ultimately enrolled.

Instruments and outcome measures

All questionnaires and patient-reported assessment instruments used in this study were previously published; no questionnaire, survey, or interview instrument was developed specifically for this study. The Chinese-language versions were administered according to their published instructions and standard scoring procedures, and no items were added, removed, or modified. QoL was assessed with the Chinese version of the EORTC QLQ-C30 (version 3.0) using the standardised scoring procedure. The global health status/QoL (GHS) scale was prespecified as the primary outcome; GHS scores range from 0 to 100, with higher scores indicating better QoL [24,25]. The minimal clinically important difference (MCID) of the QLQ-C30 GHS was defined as 5–10 points on the basis of previous literature [26,27]. Nutritional status was evaluated with the Patient-Generated Subjective Global Assessment (PG-SGA), and a score of ≥ 2 was considered to indicate nutritional risk [33,34]; geriatric nutritional risk screening also followed the conceptual framework of the Mini Nutritional Assessment Short Form (MNA-SF) [35]. Psychological status was assessed with the Zung Self-Rating Anxiety Scale (SAS) and Self-Rating Depression Scale (SDS), using standard scores of ≥ 50 and ≥ 53 to define anxiety and depression, respectively [49,50]. ECOG performance status, haemoglobin and serum albumin were also collected. Demographic and clinical data were recorded before radiotherapy.

Smoking status was defined as follows: a cumulative lifetime history of ≥ 100 cigarettes together with current smoking or cessation for < 1 year was classified as “smoking”; a cumulative lifetime history of ≥ 100 cigarettes with cessation for ≥ 1 year, or a cumulative lifetime history of < 100 cigarettes, was classified as “non-smoking”. No patient used e-cigarettes or other nicotine-replacement products.

Carbon-ion radiotherapy protocol

All patients underwent pre-treatment chest non-contrast and contrast-enhanced CT and PET/CT, and an individualised carbon-ion treatment plan was formulated after multidisciplinary consultation. CT simulation was performed on a Philips Brilliance CT Big Bore scanner (Philips, the Netherlands). The Wuwei carbon-ion medical accelerator (HIMM) was developed by the Institute of Modern Physics, Chinese Academy of Sciences, and the ciPlan treatment planning system (TPS, version V1.0) was used for treatment planning.

Immobilisation and simulation: patients were positioned supine with both arms raised and crossed above the head on a dedicated armrest to expose the chest. A thermoplastic mask combined with a vacuum cushion or body frame was used, and the three-dimensional reference centre was marked with the laser positioning system together with metallic fiducial markers for subsequent image registration. Respiratory training was provided to ensure stable and regular breathing; respiratory gating or deep-inspiration breath-hold techniques were applied when indicated, and a high-frequency oscillatory respiratory control technique was used to further reduce target displacement related to respiratory motion.

CT simulation included: (1) non-contrast CT, the basis for the tissue density-to-stopping-power conversion used in range calculation, with a slice thickness of 1.0–2.5 mm; (2) contrast-enhanced CT for clear delineation of tumour boundaries, mediastinal lymph nodes and vascular relationships; and (3) four-dimensional CT (4D-CT) for lesions in the middle or lower lobes significantly affected by respiratory motion, acquiring 10 phases covering a complete respiratory cycle and reconstructing maximum-intensity and average-intensity projections to evaluate tumour motion and define the internal target volume (ITV) or the gating window. Images were reviewed immediately after acquisition to confirm the absence of motion artefacts and complete visualisation of the target and organs at risk, and were transferred in DICOM format to the TPS. Positioning was verified with cone-beam CT using a six-dimensional robotic couch, with residual setup errors calibrated to within 0.5 mm.

Target delineation followed the principles of ICRU reports 50, 62 and 83. Gross tumour volume (GTV) was defined as the total volume of the primary tumour, metastatic lymph nodes and other malignant lesions detectable on imaging and clinical examination. The internal target volume (ITV) was generated by Boolean union of the GTV delineated on each of the 10 respiratory phases of the 4D-CT (integrated GTV, IGTV). The clinical target volume (CTV) was created by expanding the ITV, and the planning target volume (PTV) by a further expansion, with adjustments made individually when the tumour was adjacent to organs at risk such as the spinal cord, heart or oesophagus. Organ-at-risk constraints were: bilateral lung V20 ≤ 25%, oesophageal maximum point dose ≤ 50 Gy (RBE) and heart V30 ≤ 30%.

(1) Inoperable stage I NSCLC (radical hypofractionated radiotherapy): prescribed dose 60–66 Gy (RBE) in 6–9 Gy (RBE) per fraction, 3–5 fractions per week over 1–4 weeks, with the actual number of fractions individualised according to target volume, organ-at-risk constraints and patient tolerance; CTV = ITV + 5–8 mm, PTV = CTV + 3–5 mm.

(2) Inoperable stage II–III NSCLC (radical radiotherapy): prescribed dose 66–72 Gy (RBE) in 5.5–6 Gy (RBE) per fraction, 3 fractions per week for a total of 12–19 fractions over 4–5 weeks; CTV = IGTV + 8–10 mm, also covering subclinical disease in involved regional lymph nodes; PTV = CTV + 3–5 mm.

Quality assurance: the target coverage was re-verified on each 4D-CT phase to confirm that the tumour lay completely within the ITV throughout the respiratory cycle, and the ITV was matched with the beam-on window of respiratory gating to avoid cold spots. The final ITV, CTV and PTV contours were reviewed by senior physicians before dose optimisation with the ciPlan TPS.

Data collection

Questionnaires and laboratory tests were completed at four time points: within 1 week before radiotherapy (T0), at the midpoint of the radiotherapy course (T1), at 1 month (T2) and at 6 months (T3) after completion of radiotherapy. After treatment, patients were followed up by outpatient visits and telephone contacts. When telephone contact was used, the same previously published instruments were administered according to their published instructions; no separate study-specific interview schedule was used. Clinical outcomes, including disease progression and death, were recorded.

Statistical analysis

Statistical analyses were performed with IBM SPSS Statistics 27.0 (IBM Corp., Armonk, NY, USA) and R 4.6.1 (R Foundation for Statistical Computing, Vienna, Austria), and key results were cross-validated between the two packages. Continuous variables are presented as mean ± standard deviation and categorical variables as frequencies (percentages). Missing data at individual time points were handled by available-case analysis without imputation; linear mixed-effects models provide valid estimates under a missing-at-random assumption, and the proportion of missing values was low (≤ 5% at 6 months).

Longitudinal changes in QoL and the other indicators were analysed with linear mixed-effects models (LMM) with time as a fixed effect and patient as a random intercept, using an unstructured covariance matrix; pairwise comparisons were adjusted with the Bonferroni correction, and model fit was evaluated with the Akaike information criterion (AIC) and Bayesian information criterion (BIC). For the multivariable analysis, a prespecified model was fitted with time, age, sex, smoking, BMI, clinical stage, KPS and nutritional/psychological indicators as fixed effects; because of the limited sample size (n = 80), an AIC-based selection procedure (variables retained when the AIC decreased by ≥ 2) was additionally applied as a sensitivity analysis to check the robustness of the prespecified model. Continuous variables (age, BMI) were standardised (per 1 SD) before inclusion, and conditional and marginal R2 values were reported. Associations between nutritional, psychological and QoL indicators were examined with Spearman correlation.

Overall survival (OS) and progression-free survival (PFS) were estimated with the Kaplan–Meier method, using death and disease progression as the events of interest, respectively; patients without an observed event were censored at the last follow-up. Survival rates are presented as percentages and median survival times are reported; because the Kaplan–Meier curves did not reach zero, mean survival time was not estimable, and the restricted mean survival time (RMST) over a prespecified 24-month horizon is therefore reported instead, together with numbers at risk at each landmark. Follow-up time is described as the median (interquartile range). Because this was a single-cohort descriptive survival analysis, no between-group log-rank tests were performed. On the basis of the prespecified sample size (n = 80), the study had 82% power to detect a moderate effect (f2 = 0.15) at alpha = 0.05 with a repeated-measure correlation of r = 0.5; this was derived a priori for study planning. Effect sizes are reported as standardised beta coefficients. Two-sided $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics

A total of 80 elderly patients with lung cancer were enrolled, aged 65–85 years (mean 72.3 ± 5.0 years); 56 patients (70.0%) were men and 24 (30.0%) women; 41 (51.2%) had a smoking history; 42 (52.5%) had squamous cell carcinoma and 38 (47.5%) adenocarcinoma; 58 patients (72.5%) had stage III disease; KPS was 80 in 51 patients (63.7%) and 90 in 29 (36.3%); ECOG performance status was 0, 1 and 2 in 33 (41.3%), 33 (41.3%) and 14 (17.5%) patients, respectively; mean BMI was 23.9 ± 2.6 kg/m2; and the mean total dose was 70.3 ± 6.9 Gy (RBE) in a mean of 15.4 fractions. Sixty-one patients (76.2%) received CIRT as initial treatment, 42 (52.5%) had received chemotherapy before radiotherapy, 52 (65.0%) received concurrent therapy and 24 (30.0%) received maintenance therapy after radiotherapy. With a median follow-up of 17.5 months, 9 patients (11.2%) developed disease progression and 11 (13.8%) died. All 80 patients completed the assessments before (T0) and during (T1) radiotherapy; 78 (97.5%) completed the 1-month (T2) and 76 (95.0%) the 6-month (T3) assessment, and the four patients without a T3 assessment did not complete it because of disease progression or death (these events were captured in the survival analysis). Baseline characteristics are summarised in Table 1.

Table 1
Baseline characteristics of elderly patients with lung cancer treated with carbon-ion radiotherapy (n = 80)

Variable	Value	Percentage (%)
Age (years, mean ± SD)	72.3 ± 5.0	—
Sex	Male 56 / Female 24	70.0 / 30.0
Smoking history	Yes 41 / No 39	51.2 / 48.8
Histology	Squamous cell carcinoma 42 / Adenocarcinoma 38	52.5 / 47.5
Clinical stage	I 11 / II 11 / III 58	13.8 / 13.8 / 72.5
KPS score	80 51 / 90 29	63.7 / 36.3
ECOG score	0 33 / 1 33 / 2 14	41.3 / 41.3 / 17.5
BMI (kg/m2, mean ± SD)	23.9 ± 2.6	—
Treatment setting	Initial treatment 61 / Post-progression treatment 19	76.2 / 23.8
Total dose (Gy, RBE, mean ± SD)	70.3 ± 6.9	—
Number of fractions (mean ± SD)	15.4 ± 4.9	—
Chemotherapy before radiotherapy	Yes 42 / No 38	52.5 / 47.5
Concurrent therapy	Yes 52 / No 28	65.0 / 35.0
Maintenance therapy after radiotherapy	Yes 24 / No 56	30.0 / 70.0
Disease progression	Yes 9 / No 71	11.2 / 88.8
Death	Yes 11 / No 69	13.8 / 86.2
Follow-up (months, median)	17.5	—

KPS Karnofsky performance status; ECOG Eastern Cooperative Oncology Group; BMI body mass index; RBE relative biological effectiveness.

Longitudinal changes in quality of life

Repeated-measures linear mixed-effects models showed a continuous increase in QLQ-C30 global health status/QoL scores over time: 22.2 ± 13.0 before radiotherapy, 25.5 ± 12.4 during radiotherapy, 30.1 ± 12.7 at 1 month and 37.5 ± 12.4 at 6 months after radiotherapy ($F = 588.31$, $P < 0.001$), with statistically significant differences between all time points (all $P < 0.001$). All 76 patients who completed the 6-month follow-up improved relative to baseline, with a median increase of 15 points (IQR 11–20), exceeding the MCID of 5–10 points for the QLQ-C30 (Fig. 1).

Longitudinal changes in nutritional and psychological status

The prevalence of nutritional risk (PG-SGA ≥ 2) increased from 23.8% before radiotherapy to 61.2% during radiotherapy and 63.8% at 1 month, then partly recovered to 53.8% at 6 months ($F = 4.87$, $P = 0.003$). The prevalence of anxiety decreased from 43.8% to 8.8% and that of depression from 41.2% to 20.0% at 6 months after radiotherapy (both $P < 0.001$) (Figs. 2 and 3). SAS and SDS scores were strongly positively correlated at all time points ($r = 0.67–0.94$, all $P < 0.001$), while SAS and SDS were weakly negatively correlated with QLQ-C30 scores ($r = -0.07$ to -0.19); PG-SGA scores showed a weak correlation with QLQ-C30 scores ($r = 0.02–0.21$) (Supplementary Figs. S3 and S4). Changes in QoL, nutritional, psychological and laboratory indicators across time points are shown in Table 2.

Table 2
Changes in quality of life, nutritional, psychological and laboratory indicators across time points (mean ± SD)

Indicator	Before RT	During RT	1 month after RT	6 months after RT	F	P
QLQ-C30 (score)	22.2 ± 13.0	25.5 ± 12.4	30.1 ± 12.7	37.5 ± 12.4	588.31	< 0.001
PG-SGA (score)	1.4 ± 2.1	2.2 ± 2.0	2.4 ± 1.8	2.1 ± 2.0	4.87	0.003
SAS (score)	48.5 ± 15.4	49.2 ± 16.1	43.5 ± 11.6	40.2 ± 8.8	36.14	< 0.001
SDS (score)	47.6 ± 14.7	48.4 ± 15.8	44.8 ± 14.6	40.1 ± 12.9	79.13	< 0.001
ECOG (score)	0.8 ± 0.7	0.9 ± 0.8	0.5 ± 0.5	0.4 ± 0.5	8.14	< 0.001
Haemoglobin (g/L)	122.6 ± 16.7	123.2 ± 19.8	122.6 ± 22.1	122.9 ± 24.1	0.10	0.961
Serum albumin (g/L)	42.0 ± 5.6	44.2 ± 5.8	44.3 ± 6.3	46.6 ± 6.4	99.46	< 0.001

RT radiotherapy; GHS global health status/QoL. All 80 patients completed the assessments at T0 (before radiotherapy) and T1 (during radiotherapy); 78 (97.5%) completed T2 and 76 (95.0%) completed T3. A small number of individual indicator values were missing at T2 and T3 (≤ 4 patients per indicator), and analyses used all available data without imputation. F and P values were derived from linear mixed-effects models with patient as a random effect (results cross-validated with SPSS MIXED).

Factors associated with quality of life

In the univariable analysis, smoking was associated with higher QoL (F = 5.31, P = 0.024) and KPS 90 showed a near-significant association (F = 3.47, P = 0.066); age, sex, histology, clinical stage, BMI and nutritional, anxiety and depression status were not significantly associated with QoL (all P > 0.05).

In the multivariable linear mixed-effects model (Table 3, Fig. 4), time was the strongest correlate of QoL improvement: QLQ-C30 global health status/QoL scores increased by 3.19, 7.72 and 15.26 points during radiotherapy and at 1 and 6 months after radiotherapy, respectively, compared with baseline (all P < 0.001). Smoking was independently associated with higher QoL (β = 8.08, P = 0.029), and KPS 90 showed a negative trend (β=−5.37, P = 0.070). After adjustment for time, age, sex, BMI, clinical stage and PG-SGA, SAS and SDS scores were not significantly associated with QoL (all P > 0.05). The marginal and conditional R2 values of the model were 0.27 and 0.97, respectively.

Table 3
Multivariable linear mixed-effects model of factors associated with QLQ-C30 scores

Variable	β	SE	t	P
Intercept	22.66	3.86	5.87	< 0.001
During radiotherapy (vs. before)	3.19	0.41	7.79	< 0.001
1 month after radiotherapy (vs. before)	7.72	0.42	18.34	< 0.001
6 months after radiotherapy (vs. before)	15.26	0.45	34.28	< 0.001
Age (per 1 SD increase)	0.99	1.35	0.73	0.467
Male (vs. female)	−3.04	4.05	−0.75	0.454
Smoking (vs. non-smoking)	8.08	3.62	2.23	0.029
Stage III (vs. I–II)	−0.12	3.25	−0.04	0.971
KPS 90 (vs. 80)	−5.37	2.92	−1.84	0.070
BMI (per 1 SD increase)	−2.36	1.45	−1.63	0.108
Nutritional risk (vs. none)	−0.28	0.37	−0.77	0.445
Anxiety (vs. none)	−0.15	0.55	−0.27	0.789
Depression (vs. none)	−0.24	0.65	−0.37	0.715

Dependent variable: QLQ-C30 global health status/QoL score. Continuous variables were standardised (per 1 SD). The model was a linear mixed-effects model with patient as a random intercept (outputs cross-validated with SPSS MIXED). Marginal R2 = 0.27, conditional R2 = 0.97.

Stratified trajectories showed similar upward trends in QoL across sex, clinical stage, pre-treatment anxiety status and nutritional status; after stratification by smoking, scores in the smoking group were higher at every time point than in the non-smoking group, with parallel trajectories in the two groups (Supplementary Figs. S5 and S6).

Clinical outcomes

The Kaplan–Meier estimates of survival after CIRT are shown in Fig. 5. With a median follow-up of 17.5 months (IQR 14.0–21.4), 9 patients (11.2%) developed disease progression and 11 (13.8%) died. The 6-, 12-, 18- and 24-month overall survival rates were 96.3%, 92.5%, 85.4% and 82.3%, respectively; the median overall survival was not reached, and the restricted mean survival time (RMST) at 24 months was 21.99 months (95% CI 20.86–23.12; numbers at risk 77, 71, 33 and 12 at 6, 12, 18 and 24 months). The 6-, 12-, 18- and 24-month progression-free survival rates were 91.1%, 89.8%, 89.8% and 85.1%, respectively (numbers at risk 70, 62, 27 and 8); the median progression-free survival was not reached, and the RMST at 24 months was 21.75 months (95% CI 20.37–23.14). Overall, the short-term prognosis after CIRT in this cohort was favourable, with the majority of patients remaining free of progression at 12 months. Because the 24-month estimates rest on a small number of patients at risk (12 for overall survival and 8 for progression-free survival), they should be regarded as exploratory, and the corresponding 18-month estimates are more stable. The standardised mean values of the nutritional, psychological, QoL and laboratory indicators across time points are presented in Supplementary Fig. S7.

Discussion

QoL is an indispensable outcome in the evaluation of cancer treatment. Historically, efficacy has been judged primarily by local control and survival; for older patients, however, the ability to eat, remain active and feel at ease may matter more than a modest extension of survival. Previous longitudinal studies of QoL around radiotherapy for lung cancer have yielded inconsistent findings, some showing an early decline followed by gradual recovery and others showing sustained improvement after the end of treatment [29–31]. The present real-world data extend these observations to CIRT: QLQ-C30 scores increased steadily from 22.2 before radiotherapy to 37.5 at 6 months after radiotherapy, and every one of the 76 patients who completed follow-up improved, with a median increase of 15 points. This improvement exceeded the MCID and therefore represents a clinically meaningful change rather

than a minor fluctuation, indicating that CIRT did not compromise QoL in these elderly patients and that a clear recovery trend emerged after treatment. Importantly, the survival outcomes in this cohort support the same conclusion: the 12-month overall and progression-free survival rates were 92.5% and 89.8%, respectively, indicating that the improvement in QoL was not achieved at the expense of efficacy. Two features of these data nevertheless warrant caution. First, the baseline GHS score was unusually low (22.2 of 100); when a cohort is identified at a low baseline, part of any subsequent improvement is attributable to regression to the mean rather than to treatment, and the uncontrolled design cannot separate the two. Second, the finding that all 76 patients who completed follow-up improved should be read in that light, although the median gain of 15 points exceeds the MCID and is therefore unlikely to reflect measurement error alone.

Several mechanisms may explain this improvement. First, CIRT exploits the Bragg peak to concentrate the dose in the target while sparing normal tissues, and acute radiation oesophagitis and pneumonitis were generally mild and manageable [11–19,23], with the symptom burden decreasing after treatment; this is consistent with reports of preserved or improved patient-reported QoL after stereotactic ablative radiotherapy [51,52]. Second, the prevalence of anxiety decreased from 43.8% to 8.8% and that of depression from 41.2% to 20.0%, and the relief of psychological distress coincided closely in time with the recovery of QoL. It should be acknowledged, however, that the QoL data derive from a single-centre, uncontrolled longitudinal observation without parallel comparison with photon radiotherapy or untreated populations; the improvement therefore cannot be attributed solely to CIRT itself. Completion of treatment, disease stabilisation and gradual adaptation of the patients may all have contributed.

Regarding the determinants of QoL, the time effect dominated, with a mean increase of more than 15 points at 6 months relative to baseline, whereas traditional factors such as age, sex, BMI and stage were not statistically significant after adjustment. Smoking was the only factor independently associated with higher QoL ($\beta = 8.08$, $P = 0.029$). Although this counterintuitive finding may reflect confounding—smokers in this cohort were predominantly men with squamous cell carcinoma who received concurrent and maintenance therapy more frequently and may have had greater treatment engagement and follow-up adherence—it may also be attributable to the limited sample size. We therefore regard this association cautiously, as evidence for a protective effect of smoking would be unjustified, and confirmation in larger prospective studies is required. A further source of confounding is the heterogeneity of systemic treatment: 52.5% of patients had received chemotherapy before radiotherapy, 65.0% received concurrent therapy and 30.0% received maintenance therapy. Because these treatments can themselves affect QoL, nutritional status and mood, and because they were not retained as covariates in the multivariable model, residual confounding by treatment intensity cannot be excluded, and the analysis was underpowered to test it.

The nutritional and psychological dimensions merit particular attention. Nutritional risk rose above 60% during and shortly after radiotherapy and remained at approximately 54% at 6 months, indicating that, despite the low toxicity of CIRT, dietary intake and weight management during treatment cannot be relaxed [32–36]. Nutritional status was closely related to QoL, and nutritional intervention may confer additional benefit [37,41]. The improvement in anxiety and depression was substantial, yet 20% of patients still had depressive symptoms at 6 months, so psychological care should not end with the completion of radiotherapy; integrated collaborative care models can provide support [42–47,53]. The strong correlation between SAS and SDS at all time points suggests that anxiety and depression frequently co-occur and can be screened for together.

From the perspective of comprehensive geriatric and general-practice management, this study provides a fairly complete chain of evidence: nutritional, psychological and functional status should be assessed before radiotherapy; PG-SGA and body weight should be monitored during treatment; and patient-reported outcomes should continue to be followed after treatment, linking hospital, community and family care [1–9]. The limitations of this study include its single-centre design, the modest sample size of 80 patients and the relatively short follow-up; QoL was represented by the global score, without decomposition into physical, role, emotional and other functional dimensions; and the uncontrolled design may introduce selection bias. Progression-free survival was defined by disease progression alone, with deaths without documented progression treated as censoring; when death was additionally counted as an event, the 12-month progression-free survival estimate was 84.8% rather than 89.8%, so the definition used here may overestimate progression-free survival. The 24-month survival estimates were based on few patients at risk and should be regarded as exploratory. Finally, systemic treatment intensity varied between patients and was not adjusted for in the multivariable model. Future multicentre studies with larger samples and longer follow-up, incorporating lung-cancer-specific modules such as the QLQ-LC13, are warranted to capture symptom-level changes in greater detail.

Conclusion

Based on longitudinal observational data, this study systematically evaluated the dynamic changes in QoL in 80 elderly patients with lung cancer during CIRT. The main findings were: (1) QLQ-C30 scores increased continuously within 6 months after radiotherapy, with a median increase of 15 points exceeding the MCID, indicating favourable patient-reported outcomes of CIRT in elderly patients with lung cancer; (2) the prevalence of anxiety and depression decreased from 43.8% and 41.2% before radiotherapy to 8.8% and 20.0% at 6 months, respectively, with sustained relief of psychological burden after treatment; (3) nutritional risk followed a rise-then-partial-recovery trajectory, peaking at 63.8% and remaining at 53.8% at 6 months, indicating that nutritional problems require sustained attention throughout the continuum of care; and (4) the multivariable analysis identified time as the principal correlate of QoL improvement, whereas the independent association between smoking and higher QoL should be interpreted cautiously as it may be affected by unmeasured confounding.

On the basis of these findings, we suggest the following strategies for the comprehensive management of elderly patients with lung cancer during CIRT: PG-SGA nutritional screening every 2–4 weeks during radiotherapy, with prompt individualised nutritional intervention for screen-positive patients; psychological assessment (SAS/SDS) continued for at least 6 months after the completion of radiotherapy rather than being terminated with treatment; and the use of patient-reported outcomes as an important reference for dynamically adjusting supportive treatment. Given the single-centre, exploratory nature of this study, the conclusions require validation in multicentre studies with larger samples, and future work should incorporate lung-cancer-specific modules such as the QLQ-LC13 to capture symptom-level changes more precisely.

Declarations

Competing interests

The authors declare that they have no competing interests.

Ethics approval

This study was performed in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments. The study protocol was approved by the Ethics Committee of Gansu Wuwei Tumor Hospital (initial approval No. 2023-LLSC-10) and is reviewed and renewed annually; the current approval number covering the data reported here is 2026-LLSC-23. The reporting of this study follows the STROBE guideline.

Consent to participate

Written informed consent was obtained from all individual participants included in the study.

Consent for publication

Consent for publication of anonymised data was included in the informed consent obtained from all participants.

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Author Contribution

H.C. performed the statistical analysis, drafted the main manuscript text and prepared Figs. 1–5 and Tables 1–3. D.C. and B.X. conceived and designed the study, delivered the carbon-ion radiotherapy, acquired the funding and supervised the work. X.M. participated in patient recruitment, clinical data collection and follow-up assessment. All authors critically revised the manuscript, read and approved the final manuscript, and agree to be accountable for all aspects of the work.

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Availability of data and materials

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

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Figures

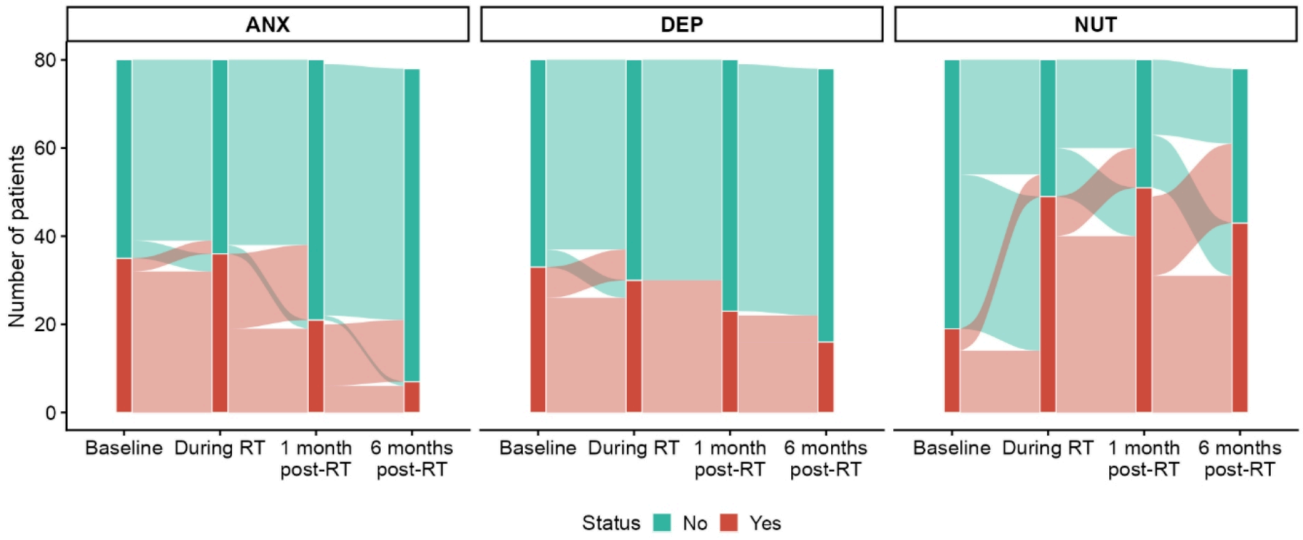


Figure 2

Alluvial diagram showing transitions of nutritional risk (PG-SGA≥2), anxiety (SAS≥50) and depression (SDS≥53) status during radiotherapy.

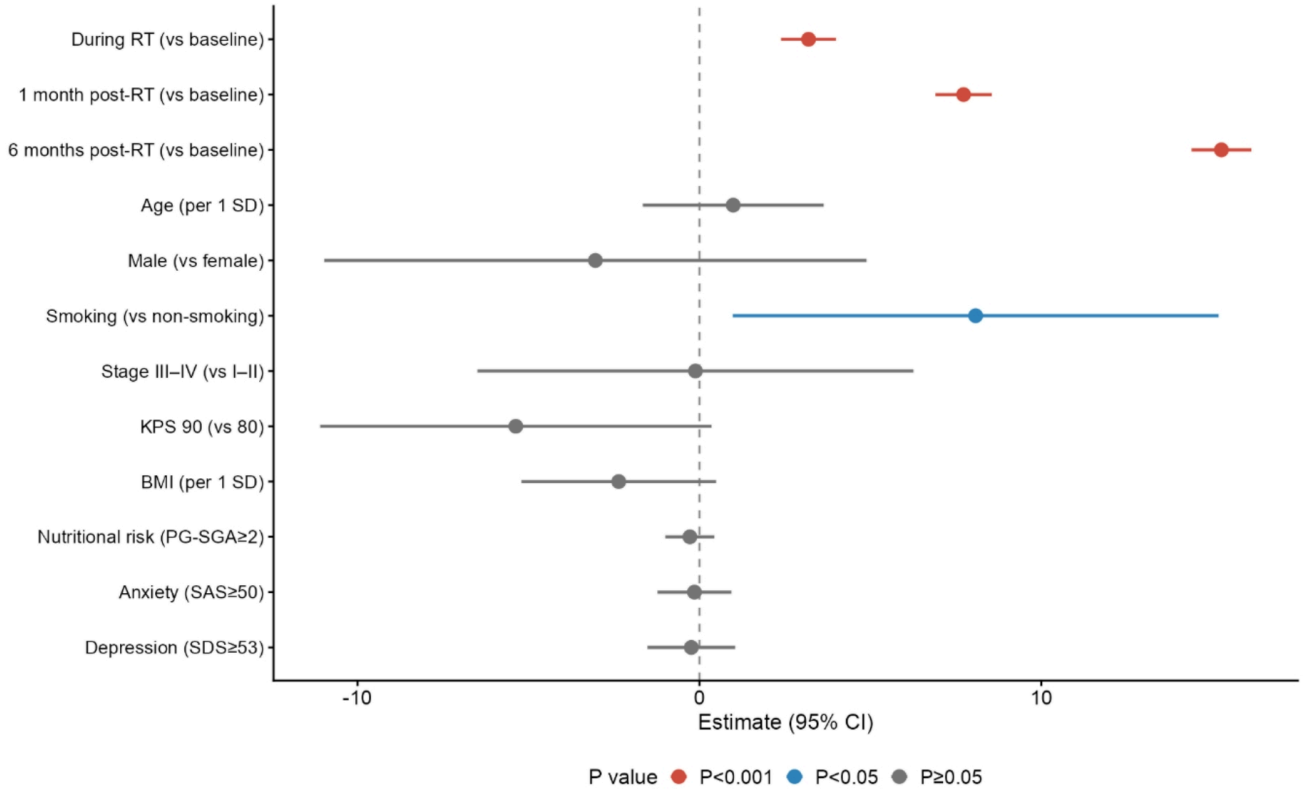


Figure 4

Forest plot of factors associated with quality of life from the linear mixed-effects model.

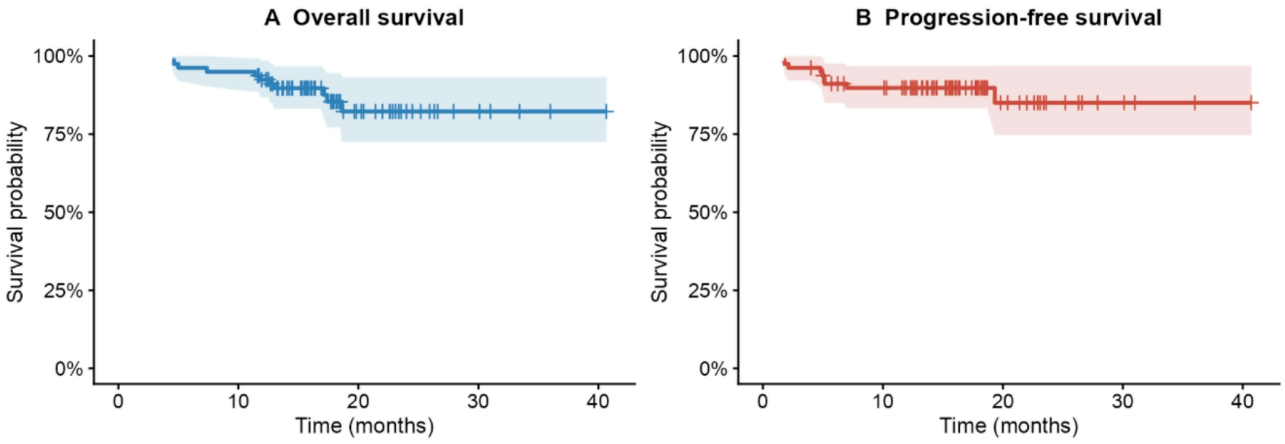


Figure 5

Kaplan–Meier curves for overall survival (A) and progression-free survival (B).

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