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Original Article

Real-world outcomes of consolidative radiotherapy following first-line chemo-immunotherapy in metastatic non-small cell lung cancer: a retrospective cohort study

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Abstract: The role and efficacy of consolidative radiotherapy (CRT) in patients with metastatic non-small cell lung cancer (mNSCLC) treated with first-line chemo-immunotherapy remain to be clarified. In this retrospective cohort study, we divided mNSCLC patients who achieved disease control with initial chemo-immunotherapy into CRT and non-CRT groups. Propensity score matching was employed to balance baseline characteristics. Results showed that the median overall survival (OS) was significantly longer in the CRT group (38.5 months) compared to the non-CRT group (25.1 months) (HR=0.48, P=0.004). Similarly, median progression-free survival (PFS) was 16.2 months in the CRT group versus 9.8 months in the non-CRT group (HR=0.52, P=0.005). CRT was identified as an independent favorable prognostic factor, with OS benefits consistent across all subgroups. Safety analysis revealed no significant difference in the incidence of grade ≥3 adverse events between the groups. These findings indicate that consolidative radiotherapy following first-line chemo-immunotherapy is associated with significantly improved survival outcomes in mNSCLC patients, demonstrating a favorable risk-benefit profile in real-world practice.

Keywords: Non-small cell lung cancer, consolidative radiotherapy, immunotherapy, real-world evidence, survival outcomes

Introduction

Lung cancer is the leading cause of cancer-related mortality worldwide, with non-small cell lung cancer (NSCLC) accounting for approximately 85% of cases [1]. For a substantial proportion of patients with mNSCLC lacking actionable driver mutations, first-line treatment has evolved to include a combination of platinum-based chemotherapy and immune checkpoint inhibitors (ICIs), which has demonstrated superior overall survival compared to chemotherapy alone [2, 3]. Despite this advance, most patients eventually succumb to the disease due to primary or acquired resistance, highlighting an urgent need to improve and extend the efficacy of first-line therapy [4].

Radiotherapy (RT) has long been central to the locoregional management of lung cancer. In both limited-stage small cell lung cancer (SCLC) and locally advanced NSCLC, consolidative thoracic radiotherapy improves local control and confers a survival benefit [5]. Inspired by this success and the 'oligometastasis' hypothesis, there is growing interest in applying local consolidative therapy (LCT) to patients with limited metastatic burden or residual disease after initial systemic therapy. Modern precision techniques like stereotactic body radiotherapy (SBRT) enable effective local tumor ablation. Importantly, RT also possesses significant immunomodulatory potential. By inducing immunogenic cell death, releasing tumor antigens, and remodeling the tumor microenvironment, RT can function as an in situ vaccine [6]. This may synergize with ICIs by priming a systemic anti-tumor immune response against non-irradiated sites - a phenomenon known as the 'abscopal effect' [7].

Several phase II trials have explored this strategy in mNSCLC [8, 9]. However, these studies primarily involved small, highly selected patient populations, often using restrictive oligometastatic definitions (typically ≤3-5 metastases),

with LCT administered after first-line systemic therapy. In the current era of frontline immunotherapy, key questions persist. Is consolidative radiotherapy effective and safe in a broader, real-world population beyond narrowly defined oligometastatic disease? How should this integrative approach be combined with modern immunotherapy in terms of optimal radiation dose, fractionation (BED10), and target volume (primary tumor and/or metastases) [10]? It remains unclear whether benefits observed in selective trial settings translate to routine clinical practice.

To address this evidence gap, we conducted this retrospective cohort study to evaluate the real-world impact of consolidative radiotherapy on survival outcomes in mNSCLC patients who achieved disease control after first-line chemo-immunotherapy. Our study aims to investigate this question in a less selective cohort encompassing a range of metastatic burdens and to characterize real-world radiotherapy practices (dose and targets). This research seeks to provide pragmatic evidence on the risk-benefit profile of this combined modality approach, informing its potential role in the current treatment landscape.

Methods

Study design and patient selection

This study is a single-center, retrospective cohort analysis conducted at Xingtai People's Hospital. The study protocol was approved by the institutional ethics committee of Xingtai People's Hospital (Approval No.: 2025-059). The ethics approval document is provided as a supplementary file. Since this clinical research was conducted in a retrospective manner, there was no need to request patients' consent, and all patients' information was anonymized.

We systematically included all consecutive patients with metastatic NSCLC who initiated first-line treatment at our institution between January 2018 and December 2021, a period during which chemo-immunotherapy became the standard of care in our practice.

Inclusion criteria were: (1) pathologically confirmed stage IV NSCLC according to the American Joint Committee on Cancer (AJCC) 8th edition; (2) first-line treatment with a platinum doublet plus an immune checkpoint inhibitor; (3) receipt of at least two cycles of systemic therapy (e.g., carboplatin/pembrolizumab or pemetrexed/pembrolizumab) to ensure adequate exposure for disease assessment, consistent with pivotal trial schedules [3]; and (4) achievement of disease control (complete response, partial response, or stable disease) after first-line systemic therapy, as determined by radiographic assessment.

Exclusion criteria included: (1) diagnosis of another active malignancy within the previous five years; (2) receipt of any local therapy prior to completion of initial systemic treatment; and (3) incomplete clinical information or loss to follow-up.

PD-L1 expression status was evaluated for all enrolled patients as part of routine clinical practice using immunohistochemistry (IHC) with the PD-L1 IHC 22C3 pharmDx assay.

Eligible patients were stratified into two groups based on treatment received within 90 days after completing first-line therapy. The consolidative radiotherapy (CRT) group comprised patients who received radical radiotherapy targeting residual lesions (primary and/or metastatic). Treatment decisions for this group were approved by a multidisciplinary team (MDT). The non-CRT group included patients who proceeded to active surveillance or maintenance immunotherapy without any local consolidative therapy.

The patient selection process is illustrated in **Figure 1**.

Treatment and grouping

All patients received first-line, platinum-based doublet chemotherapy. Patients with non-squamous histology typically received pemetrexed plus carboplatin or cisplatin, while those with squamous histology received gemcitabine or a taxane plus carboplatin/cisplatin. Chemotherapy was administered concurrently with an immune checkpoint inhibitor (ICI), such as pembrolizumab or sintilimab. The chemotherapy component was generally administered for 4-6 cycles, followed by maintenance immunotherapy when appropriate.

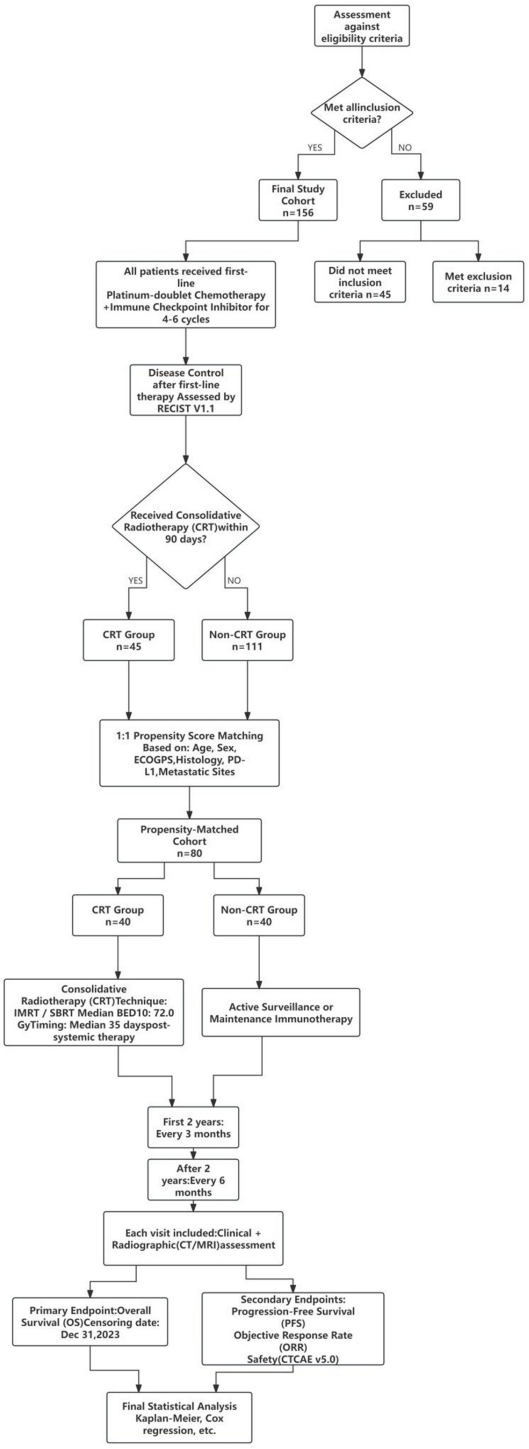

Figure 1. The figure illustrates the patient selection process.

Patients were stratified based on whether they received radical radiotherapy targeting residual disease within 90 days of completing first-line chemo-immunotherapy (calculated from the last dose of chemotherapy/immunotherapy). The CRT group received MDT-approved radiotherapy targeting the primary tumor and/or metastases, delivered via intensity-modulated radiotherapy (IMRT) or stereotactic body radiotherapy (SBRT). Following completion of first-line chemo-immunotherapy, patients in the CRT group continued to receive maintenance immunotherapy with PD-1/PD-L1 inhibitors. Radiotherapy was administered during this maintenance phase sequentially, not concurrently. Specifically, radiotherapy was initiated at a median of 35 days after the last chemotherapy dose. During radiotherapy and for management of potential acute toxicity, maintenance immunotherapy was typically temporarily withheld and resumed after resolution of radiotherapy-related adverse events. To facilitate comparison, the biologically effective dose (BED) was calculated using an α/β ratio of 10 (BED10). Representative regimens included SBRT with 50 Gy in 4 fractions (BED10=112.5 Gy) or 48 Gy in 4 fractions (BED10=105.6 Gy), reflecting an aggressive, curative-intent strategy. Overall, prescribed doses ranged from 60 to 100 Gy (BED10), delivered in 5 to 20 Gy per fraction, consistent with SBRT or hypofractionated IMRT protocols. Radiation targets included: (1) the thoracic primary site only; (2) the thoracic primary plus selected metastases; or (3) metastatic sites only, with a controlled or unirradiated primary.

The non-CRT group did not receive any local consolidative therapy and proceeded directly to active surveillance or maintenance immunotherapy if residual disease was present.

To mitigate potential selection bias in this retrospective analysis, propensity score matching (PSM) was performed using nearest-neighbor matching with a 1:1 ratio and a caliper width of 0.02. Matching variables included age, gender, ECOG performance status, histology, PD-L1 expression level, and sites of metastasis.

Data collection

Data were extracted through a comprehensive review of electronic medical records, radiology archives, laboratory databases, and radiotherapy charts. To ensure quality, data extraction was performed independently by two reviewers, with discrepancies resolved through joint review of source documents or consultation with a principal investigator. Patients were fol-

lowed every 3 months for the first 2 years and every 6 months thereafter. Tumor response was assessed by CT or MRI at baseline, after every 2-3 cycles of systemic therapy, and at suspected progression.

The collected dataset included: (1) Clinical baseline characteristics: age, sex, smoking history, ECOG performance status, histology, metastatic pattern, and PD-L1 expression level; (2) Treatment information: details of each chemo-immunotherapy and radiotherapy session, including timing, modality, targets, and for CRT, the biological equivalent dose (BED); (3) Efficacy endpoints: Best Overall Response (independently and blindly reviewed by two radiologists using RECIST v1.1), progression-free survival (PFS), and overall survival (OS); (4) Safety data: all treatment-related grade ≥3 adverse events, graded according to CTCAE v5.0.

Patient survival status was followed until December 31, 2023, primarily through outpatient registers, supplemented by telephone calls when necessary. Cross-validation using multiple sources (e.g., family contact, local hospital records, death registries) was employed to improve the accuracy of outcome ascertainment.

Statistical analysis

Statistical analyses were performed using R software (version 4.2.0) with the 'survival' and 'MatchIt' packages. Continuous variables are expressed as median with interquartile range (IQR), and categorical variables as number (percentage). Patient survival status was monitored until December 31, 2023, with follow-up conducted via outpatient registers and telephone recall. Cross-validation from multiple sources enhanced outcome measure accuracy.

For survival analysis, Kaplan-Meier curves were generated, and intergroup differences were compared using the log-rank test. To create a robust analytical framework, univariate Cox regression was first performed on all potential confounding factors to identify variables associated with survival outcomes (P<0.1). These variables were then included in a multivariate Cox proportional hazards model to identify independent prognostic factors. To reduce selection bias and approximate a randomized study design, propensity score matching (PSM) was applied using the key confounding variables. PSM was performed using a 1:1 nearest-neighbor matching algorithm with a caliper width of 0.02, based on age, gender, ECOG performance status, histology, PD-L1 level, and sites of metastasis.

Variables with P<0.1 in univariate analysis were included in the multivariate Cox models to identify independent prognostic factors for OS and PFS. Subgroup analyses with interaction tests were conducted to assess the consistency of the treatment effect across different patient groups.

Safety analysis primarily involved comparing the incidence of grade ≥3 treatment-related adverse events between groups. All statistical tests were two-sided, with a *P*-value <0.05 considered statistically significant.

Results

Patient baseline characteristics

The initial cohort comprised 156 mNSCLC patients who achieved disease control after first-line chemo-immunotherapy. Of these, 45 patients (28.8%) received consolidative radiotherapy (CRT group), and 111 patients (71.2%) did not (non-CRT group).

Before matching, several baseline parameters differed significantly between the groups (**Table 1**). Patients in the CRT group tended to be younger and have a higher frequency of oligometastatic disease (≤2 metastatic sites) compared to the non-CRT group. A higher proportion of CRT patients also had PD-L1 expression ≥50%, although this difference was not statistically significant. To mitigate these potential confounders, 1:1 propensity score matching was performed, resulting in a well-balanced cohort of 80 patients (40 in each group). After matching, all parameters - including age, gender, ECOG performance status, smoking history, histology, PD-L1 expression level, and number of metastatic sites - were comparable between the two groups (all P>0.05, standardized mean differences <0.1). Notably, the distribution of specific metastatic sites, including brain and liver metastases (known poor prognostic factors), was also well-balanced after matching (see Supplementary Table 1).

Table 1. Patient baseline characteristics (before and after propensity score matching)

Characteristic	Before PSM				After PSM			
	Consolidative RT Group (n=45)	Non-Consolidative RT Group (n=111)	*P* Value	Standardized Mean Difference	Consolidative RT Group (n=40)	Non-Consolidative RT Group (n=40)	*P* Value	Standardized Mean Difference
Age (years), Median [IQR]	62 [55-68]	66 [60-72]	0.018*	0.451	63 [56-69]	64 [58-70]	0.501*	0.125
Sex, n (%)			0.521#	0.112			0.820#	0.052
Male	28 (62.2)	75 (67.6)			25 (62.5)	26 (65.0)		
Female	17 (37.8)	36 (32.4)			15 (37.5)	14 (35.0)		
ECOG PS, n (%)			0.344#	0.174			0.500#	0.109
0-1	42 (93.3)	98 (88.3)			38 (95.0)	37 (92.5)		
≥2	3 (6.7)	13 (11.7)			2 (5.0)	3 (7.5)		
Smoking History, n (%)			0.327#	0.169			0.817#	0.052
Smoker	30 (66.7)	65 (58.6)			26 (65.0)	25 (62.5)		
Non-smoker	15 (33.3)	46 (41.4)			14 (35.0)	15 (37.5)		
Histology, n (%)			0.743#	0.057			0.812#	0.053
Adenocarcinoma	30 (66.7)	71 (64.0)			27 (67.5)	26 (65.0)		
Squamous	15 (33.3)	40 (36.0)			13 (32.5)	14 (35.0)		
PD-L1 Expression, n (%)			0.210#	0.224			0.932#	0.029
<1%	12 (26.7)	35 (31.5)			10 (25.0)	11 (27.5)		
1-49%	15 (33.3)	48 (43.2)			14 (35.0)	15 (37.5)		
≥50%	18 (40.0)	28 (25.2)			16 (40.0)	14 (35.0)		
Number of Metastases, n (%)			0.024#	0.395			0.814#	0.053
≤2 (Oligometastatic)	32 (71.1)	58 (52.3)			28 (70.0)	27 (67.5)		
>2	13 (28.9)	53 (47.7)			12 (30.0)	13 (32.5)		

Abbreviations: PSM, propensity score matching; IQR, interquartile range; ECOG PS, Eastern Cooperative Oncology Group performance status; RT, radiotherapy. *Student's t-test or Mann-Whitney U test for continuous variables. #Chi-square test or Fisher's exact test for categorical variables.

Survival analysis

In the propensity score-matched cohort, the median follow-up time was 28.5 months (95% CI: 25.8 to 31.2 months). At the last follow-up, 21 patients (52.5%) in the CRT group and 29 patients (72.5%) in the non-CRT group had died.

Overall survival analysis demonstrated a significant benefit for patients treated with CRT (**Figure 2A**). The median OS was significantly longer in the CRT group compared to the non-CRT group (HR=0.48, 95% CI =0.29-0.79, P=0.004).

A significant benefit was also observed for progression-free survival (**Figure 2B**). The median PFS was significantly increased in the CRT group versus the non-CRT group (HR=0.52, 95% CI =0.33-0.82, P=0.005).

Multivariate cox regression analysis

Multivariate Cox proportional hazards analysis was performed to determine whether CRT was an independent predictor of OS and PFS after adjusting for potential confounders (treatment group, age [≥65 vs. <65 years], gender, ECOG PS [≥2 vs. 0-1], and PD-L1 expression [<1% as reference]).

As shown in **Table 2**, consolidative radiotherapy was an independent protective factor for OS (HR=0.52, 95% CI=0.32-0.85, P=0.008). Having more than two metastatic sites was an independent risk factor for OS (HR=1.79, 95% CI=1.11-2.88, P=0.017). Age, gender, ECOG PS, and PD-L1 expression level were not independently prognostic. Similar results were found for PFS, with CRT remaining an independent protective factor (HR=0.55, 95% CI =0.35-0.86, P=0.009) and >2 metastatic sites an independent risk factor (HR=1.68, 95% CI =1.08-2.61, P=0.021).

Subgroup analysis

Subgroup analysis for overall survival demonstrated a consistent benefit from consolidative radiotherapy across all predefined subgroups (**Figure 3**). Hazard ratios favored the CRT group in all subsets analyzed, including those defined by age, gender, ECOG PS, histology, PD-L1 expression level (<1%, 1-49%,

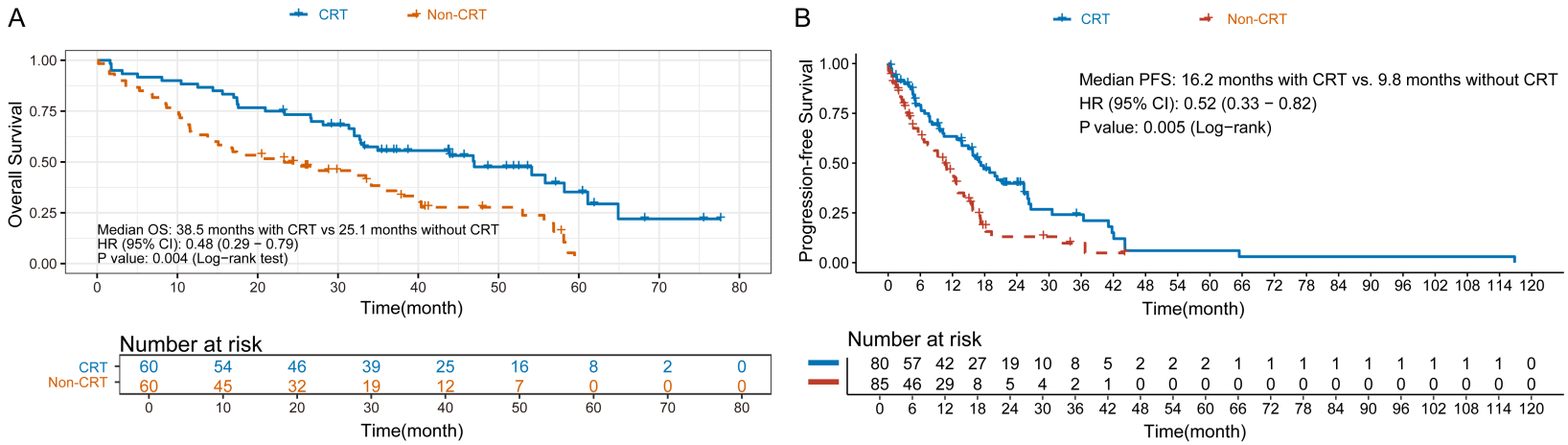

Figure 2. Kaplan-Meier survival analysis in the matched cohort.

Table 2. Multivariate cox regression analysis for overall survival and progression-free survival

Variable	Overall Survival (OS)			Progression-Free Survival (PFS)		
	Hazard Ratio (HR)	95% CI	*P* Value	Hazard Ratio (HR)	95% CI	*P* Value
Treatment Group (Consolidative RT vs. Non-Consolidative)	**0.52**	**0.32-0.85**	**0.008**	**0.55**	**0.35-0.86**	**0.009**
Age (≥65 vs. <65 years)	1.21	0.76-1.92	0.423	1.15	0.75-1.77	0.519
Sex (Male vs. Female)	1.15	0.71-1.86	0.571	1.08	0.69-1.69	0.739
ECOG PS (≥2 vs. 0-1)	1.52	0.78-2.94	0.218	1.41	0.76-2.63	0.278
PD-L1 Expression			0.334			0.401
1-49% vs. <1%	0.80	0.48-1.33	0.388	0.83	0.52-1.32	0.428
≥50% vs. <1%	0.72	0.42-1.23	0.227	0.76	0.47-1.24	0.271
Number of Metastases (>2 vs. ≤2)	**1.79**	**1.11-2.88**	**0.017**	**1.68**	**1.08-2.61**	**0.021**

Abbreviations: CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; RT, radiotherapy. PD-L1 expression used "<1%" as the reference group. Significant *P* values are shown in bold.

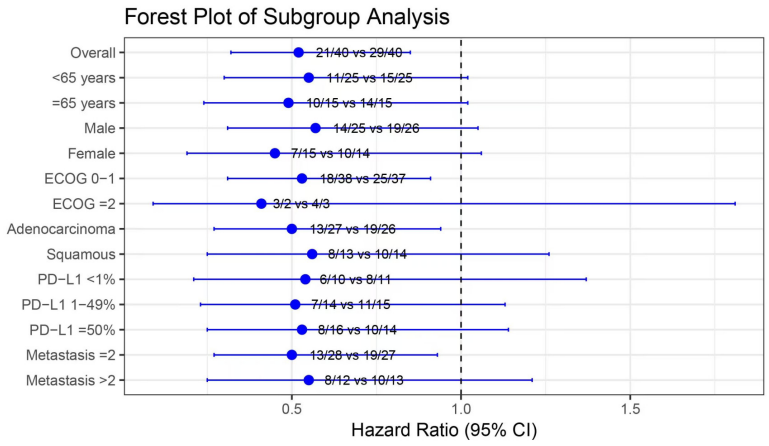

Figure 3. Forest plot of subgroup analysis for overall survival.

≥50%), and metastatic burden (≤2 vs. >2 sites). Interaction tests revealed no significant difference in treatment effect across any subgroup (all P-interaction >0.05), indicating that the survival benefit of CRT was independent of these patient characteristics.

This finding has significant clinical relevance, suggesting that the survival advantage from consolidative radiotherapy may extend broadly across advanced NSCLC patients in the immunotherapy era. Notably, even patients traditionally considered less likely to benefit from local therapy, such as those with negative PD-L1 expression or multiple metastases, derived similar benefit in our analysis.

Treatment response and radiotherapy details

We analyzed the best objective response to first-line chemo-immunotherapy, assessed prior to initiating consolidative radiotherapy. As shown in **Table 3**, the objective response rate (ORR) was numerically higher in the CRT group (77.5%, 31/40) compared to the non-CRT group (65.0%, 26/40), although this difference was not statistically significant (P=0.205). Disease control rates (DCR) were high and comparable between both groups (95.0% vs. 92.5%, P=0.500).

Radiotherapy details for the CRT group are also presented in **Table 3**. All patients received high-precision radiotherapy (IMRT/SBRT). The median biologically effective dose (BED10) was 72.0 Gy (IQR: 68.4-78.8 Gy; range: 60.0-100.0 Gy), indicative of an aggressive, curative-intent strategy. Regarding targets, 45.0% of patients received irradiation to the thoracic primary only, 37.5% to both the primary and selected metastases, and 17.5% to metastatic sites only (with controlled or unirradiated primary disease). The median time from completing systemic therapy to starting radiotherapy was 35 days (range: 21-78 days).

Safety

The incidence of any grade ≥3 treatment-related adverse event was not significantly different between the CRT and non-CRT groups (32.5% vs. 25.0%; P=0.461) (**Table 4**).

Table 3. Best objective response to first-line chemo-immunotherapy and radiotherapy characteristics

Item	Consolidative RT Group (n=40)	Non-Consolidative RT Group (n=40)	*P*-value
Best Objective Response to First-Line Therapy, n (%)			0.205*
Objective Response Rate (ORR)	31 (77.5)	26 (65.0)	
Complete Response (CR)	2 (5.0)	1 (2.5)	
Partial Response (PR)	29 (72.5)	25 (62.5)	
Stable Disease (SD)	7 (17.5)	11 (27.5)	
Disease Control Rate (DCR)	38 (95.0)	37 (92.5)	0.500#
Radiotherapy Characteristics (Consolidative RT Group only)		Value	
Radiotherapy Technique, n (%)			
Intensity-Modulated RT/Stereotactic Body RT		40 (100.0)	
Biologically Effective Dose (BED_{10})			
Median (IQR), Gy		72.0 (68.4-78.8)	
Range, Gy		60.0-100.0	
Radiation Targets, n (%)			
Thoracic Primary Only		18 (45.0)	
Thoracic Primary + Metastases		15 (37.5)	
Metastases Only		7 (17.5)	
Timing of Radiotherapy			
Median (IQR), days&		35 (28-49)	
Range, days&		21-78	

Abbreviations: RT, radiotherapy; ORR, objective response rate; CR, complete response; PR, partial response; SD, stable disease; DCR, disease control rate; BED_{10}, biologically effective dose with α/β=10; IQR, interquartile range. *Comparison for ORR (CR+PR) was performed using the Chi-square test. #Comparison for DCR (CR+PR+SD) was performed using Fisher's exact test. &Timing from the end of first-line systemic therapy to the start of radiotherapy.

Table 4. Comparison of grade ≥3 treatment-related adverse events (matched cohort)

Adverse Event	Consolidative RT Group (n=40)	Non-Consolidative RT Group (n=40)	*P*-value
Any Grade ≥3 Event, n (%)	13 (32.5)	10 (25.0)	0.461#
Pneumonitis, n (%)	5 (12.5)	1 (2.5)	0.197*
Esophagitis, n (%)	2 (5.0)	0 (0.0)	0.494*
Dermatitis, n (%)	1 (2.5)	0 (0.0)	1.000*
Hematologic Toxicity, n (%)	8 (20.0)	9 (22.5)	0.787#
Neutropenia	5 (12.5)	6 (15.0)	
Anemia	2 (5.0)	2 (5.0)	
Thrombocytopenia	1 (2.5)	1 (2.5)	
Hepatitis, n (%)	1 (2.5)	2 (5.0)	1.000*
Colitis, n (%)	0 (0.0)	1 (2.5)	1.000*

Abbreviation: RT, radiotherapy. Adverse events were graded according to CTCAE v5.0. *Fisher's exact test; #Chi-square test.

Analysis by adverse event type revealed that grade ≥3 pneumonitis was numerically more frequent in the CRT arm (12.5% [5/40] vs. 2.5% [1/40]), although this difference did not reach statistical significance (P=0.197), which may be influenced by the limited sample size. All five pneumonitis events in the CRT group were assessed by the MDT as immune-related, with two cases having a potential overlapping component of radiation pneumonitis. These events were effectively managed by temporarily withholding immunotherapy and administering corticosteroids, with no treatment-related deaths due to pneumonitis. Grade ≥3 radiation esophagitis occurred in two patients (5.0%) in the CRT group and was not observed in the non-CRT group. The incidence of other adverse events (hematologic, gastrointestinal, hepati-

Table 5. Reasons for discontinuation of protocol therapy (matched cohort, n=80)

Reason	Number of Patients (%)
Disease Progression	8 (10.0)
Patient Preference/Withdrawal	4 (5.0)
Treatment-Related Adverse Events	3 (3.8)
Death	2 (2.5)
Lost to Follow-up	2 (2.5)
Other	1 (1.3)
Completed Planned Therapy/Ongoing	60 (75.0)

tis, dermatitis) was similar between the two groups.

Treatment compliance and discontinuation

Treatment completion rates were high in both groups. All patients in the CRT group (40/40) completed the planned radiotherapy course. In the non-CRT group, 85% (34/40) of patients received maintenance immunotherapy for a median duration of 8.5 months (IQR: 4.2-14.0 months). Reasons for discontinuing protocol therapy in the overall matched cohort (n=80) are summarized in **Table 5**. The most common reason was disease progression (10.0%), followed by patient preference/withdrawal (5.0%) and treatment-related adverse events (3.8%). The majority of patients (75.0%) completed the planned therapy or were still on treatment at the time of analysis.

Discussion

Our study provides important insights into the management of advanced NSCLC, suggesting that consolidative radiotherapy following effective first-line chemo-immunotherapy is associated with significant survival benefits and generally acceptable toxicity. This highlights the potential value of combined local and systemic strategies in metastatic disease.

These findings extend to the immunotherapy era the promising results from prior studies on local consolidative therapy [7, 8]. A key strength of our study is its reflection of a more realistic, less selective patient population, including individuals who might not meet strict oligometastatic criteria. This suggests the potential beneficiary population for consolidative radiotherapy may be broader than previously thought, raising important questions about optimal patient selection.

The observed improvements in PFS and OS support the hypothesized synergistic effect between radiotherapy and immunotherapy [11-14]. High-precision radiotherapy achieves potent local tumor control and can modulate the immune tumor microenvironment. The immunogenic cell death and tumor antigen release triggered by radiotherapy may potentiate a systemic anti-tumor immune response. This in situ vaccination effect, when combined with immune checkpoint blockade, may underlie the sustained clinical benefits observed in our cohort [15, 16].

Regarding safety, the numerically higher incidence of grade ≥3 pneumonitis in the CRT group (12.5% vs. 2.5%) warrants careful attention, as raised by the reviewers. Although not statistically significant in our cohort, this observation underscores the importance of vigilance for pulmonary toxicity when combining thoracic radiotherapy with immunotherapy. In our series, all such events were managed through a standardized protocol involving temporary immunotherapy hold and corticosteroid administration under MDT guidance, with no fatal outcomes. This practical experience confirms that with proactive monitoring and multidisciplinary management, the toxicity profile of this combined regimen remains manageable. The overall comparable rate of severe adverse events between groups supports the acceptable safety profile and favorable risk-benefit ratio of adding consolidative radiotherapy in this setting, consistent with other reports of combined modality therapy [17-21].

As a single-center retrospective analysis, there are some limitations with this study. Firstly, although we did propensity score matching, there may still be residual confounders. Secondly, there may be differences in radiotherapy regimens, thus creating heterogeneity in outcome. Regardless, they make this analysis more practical and closer to what is really done.

On the basis of these findings there is a need for randomized clinical trials defining and establishing the place of consolidative radiation therapy within Chemo-immunotherapy. Future investigations should focus on searching for biomarkers, standardizing radiation

treatment scheduling and dosing, as well as defining uniform toxicity management approaches in the context of maximizing the therapeutic ratio in advanced NSCLC.

Conclusion

This study provides real-world evidence that consolidative radiotherapy following effective first-line chemo-immunotherapy is associated with significantly improved survival outcomes in patients with mNSCLC, with a manageable toxicity profile. These findings support consideration of this combined modality approach in the management of advanced lung cancer. Future clinical studies are needed to optimize patient selection criteria and treatment strategies to maximize survival benefit while minimizing toxicity.

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Disclosure of conflict of interest

None.

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Supplementary Table 1. Distribution of metastatic sites in the propensity score-matched cohort (n=80)

Metastatic Site	Consolidative RT Group (n=40)	Non-Consolidative RT Group (n=40)	*P* Value
Brain, n (%)	7 (17.5%)	6 (15.0%)	1.000
Liver, n (%)	4 (10.0%)	5 (12.5%)	1.000
Bone, n (%)	18 (45.0%)	16 (40.0%)	0.820
Adrenal, n (%)	8 (20.0%)	6 (15.0%)	0.770
Contralateral Lung, n (%)	12 (30.0%)	14 (35.0%)	0.814
Distant Lymph Nodes, n (%)	21 (52.5%)	19 (47.5%)	0.820
Other Sites, n (%)	3 (7.5%)	4 (10.0%)	1.000