



Correlation of Tumor Volume, Symptom Relief, and Survival in Metastatic NSCLC Treated with Cyclical "Quad Shot" Radiotherapy



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INTRODUCTION

The optimal palliative radiation regimen for centrally located lung tumors remains unclear due to toxicity concerns. We conducted the first prospective Phase I trial of cyclical hypofractionated Quad Shot (QS) radiotherapy (14.8 Gy in 4 fractions over 2 days) for lung metastases from Non-Small Cell Lung Cancer (NSCLC). This study evaluated whether tumor volume change correlates with symptom relief and whether baseline tumor volume predicts overall survival.

METHODS

39 patients received at least 1 cycle of QS treatment (1 cycle, n=6; 2 cycles, n=16; 3 cycles, n=17) on a prospective phase I dose-escalation trial. The safety of QS treatment was assessed using the CTCAE v5.0, with dose-limiting toxicity (DLT) defined as any Grade 3 or higher treatment-related adverse event. Clopper-Pearson 95% confidence intervals (CI) were calculated for toxicity rates. Gross tumor volume (GTV) of each cycle of QS was measured on simulation CT images of each cycle. Local thoracic symptoms were assessed using the EORTC QLQ-LC13 at baseline (pre-RT), during each treatment cycle, and at 1-, 3-, and 6-month post-treatment, with symptom scores generated according to standard scoring protocols. Changes in scores from baseline were evaluated using one-sided Wilcoxon signed-rank tests. Additionally, Spearman's rank correlation coefficient (rho) was used to examine the relationship between changes in GTV and symptom score reductions. Cox proportional hazards regression was further performed to evaluate the association between baseline GTV and overall survival (OS).

KEY FINDINGS

- Cough and dyspnea improved during follow-up after cyclical Quad Shot treatment.
- Greater tumor volume reduction was associated with greater dyspnea improvement.
- Larger baseline GTV was associated with worse overall survival, with a 21% higher hazard of death per 100 cc increase in tumor volume.
- Treatment demonstrated an acceptable safety profile, with RT-related Grade ≥3 toxicity in 4/38 evaluable patients (10.5%).

CONCLUSION

The novel use of QS regimen for treatment of metastatic NSCLC provides effective symptom relief with an acceptable safety profile in patients with metastatic NSCLC. GTV reduction was significantly associated with improvement in dyspnea, with no significant correlations observed for other symptoms. Larger baseline GTV was significantly associated with worse OS.

ACKNOWLEDGEMENTS

This study included patients enrolled on the prospective Phase I clinical trial IRB 20-148: A Phase I Study of up to 3 cycles of Cyclical Hypofractionated Palliative Radiation (Quad Shot) for Lung Tumors in Patients with Stage IV NSCLC.

RESULTS

- Thirty-nine patients with lung metastases from NSCLC received cyclical Quad Shot radiotherapy (14.8 Gy in 4 fractions); 38 patients were evaluable for toxicity. Among 38 evaluable patients, RT-related Grade ≥3 toxicities occurred in 4 patients (10.5%; 95% CI, 2.94%–24.80%), including pneumonitis, esophagitis, tracheal fistula, and lung infection (n=1 each).
- Cough and dyspnea improved following Quad Shot treatment. Mean cough scores decreased from 53.9 at baseline to 38.9 at 1 month and 38.5 at 3 months. Mean dyspnea scores decreased from 39.8 at baseline to 29.6 at 1 month and 27.8 at 3 months, with the 3-month improvement reaching statistical significance (p=0.026).
- Greater GTV reduction during the third treatment cycle was significantly associated with greater improvement in dyspnea (p=0.52, p=0.040; n=16). A modest trend was observed between GTV change and cough improvement at 1 month (p=0.42, p=0.094; n=17).
- Larger baseline GTV was significantly associated with worse overall survival, with a 21% increase in the hazard of death per 100 cc increase in baseline GTV (HR 1.21; 95% CI, 1.04–1.40; p=0.013).

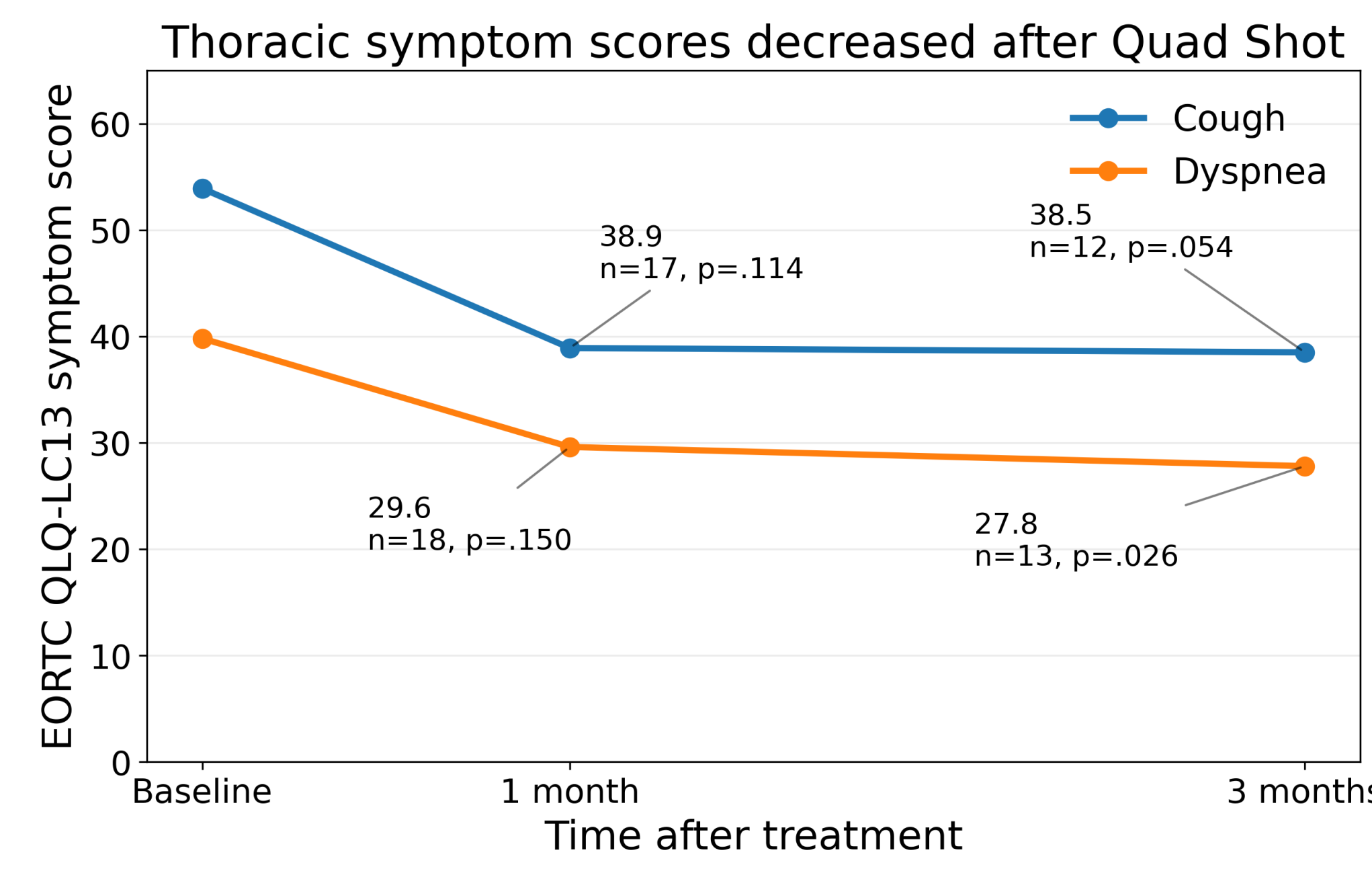


Figure 1: Mean EORTC QLQ-LC13 cough and dyspnea scores decreased following Quad Shot radiotherapy. Dyspnea improved from 39.8 at baseline to 27.8 at 3 months (n=13, p=0.026). Cough decreased from 53.9 to 38.5 at 3 months (n=12, p=0.054).

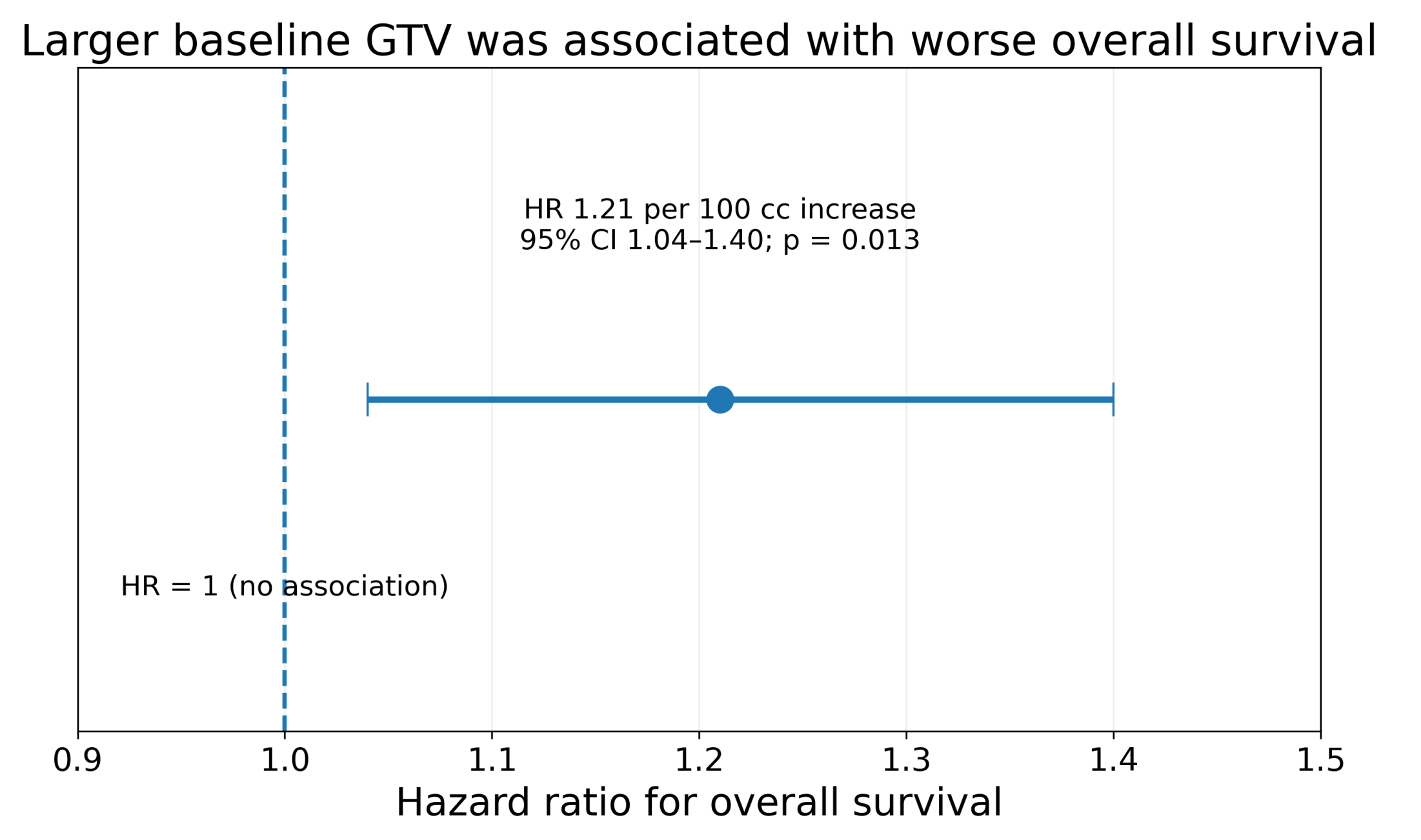


Figure 2: Association between baseline gross tumor volume (GTV) and overall survival. Cox proportional hazards regression showed that larger baseline GTV was significantly associated with worse overall survival.

Future Directions

- Validate these findings in a larger cohort with longitudinal symptom assessments.
 - Evaluate early GTV change as a potential imaging biomarker for subsequent symptom improvement and overall treatment response.
 - Determine whether serial tumor-volume changes can help guide additional QS cycles, including identifying patients most likely to benefit from continued treatment.
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