The potential clinical impact of breathhold radiation therapy in radical radiation therapy for non-small cell lung cancer

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Introduction

Radical radiation therapy (RT) is one of the curative options for non-small cell lung cancer (NSCLC) but it is associated with significant risk of side effects. Breathing control technique can improve the RT dosimetry and may mitigate these complications.

Methods

Consecutive 125 NSCLC patients receiving radical RT (55Gy in 20 fractions in 4 weeks) in Northwest United Kingdom were reviewed. The volume of normal organs was contoured with Limbus AI® on planning CT images. Dosimetry data was retrieved through the Proknow® analytics and was annotated with clinical outcomes retrospectively. Radiation induced lung damage grading was defined by RTOG, CTCAE 5.0 and SWOG criteria.

Results

Median age of the cohort was 70 years old, ranged 53-93 years old. Median follow-up time of the cohort was 16.7 months. AJCC staging was stage 1 (8.4%); 2 (20%), 3 (60%), 4 (1.6%). Nearly half (48%) was squamous cell carcinoma. More than half received radical RT alone (52%), concurrent chemotherapy-RT was given in 39.8%. Adjuvant immunotherapy was applied in one-quarter (25.6%), subsequent palliative immunotherapy in 14.4%.

GTV volume is a strong predictor of both progression free survival and overall survival across different histology and AJCC stage (HR 1.004, P<0.001). Early mortality rate (within 6 months) post radical RT was significant (16%, 20/125), 13 of these had no evidence of disease progression or recurrence (10.4%)

RT induced lung damage was common (61.4%). The worst grading was grade 1 (asymptomatic) in 35.2%, grade 2 (require steroid) in 13.6%, grade 3 (needs oxygen) in 8%, grade 4 (life-threatening) in 0.8%, grade 5 (fatal) in 4%. Grade 3 or above lung damage was associated with worse overall survival (HR 3.1, p<0.01).

Larger normal lung volume (>4.5L, 1st quartile) (OR 0.42, p=0.03) was the only significant protective factor against RT induced lung damage (grade 1-5).

Radiation induced lymphopenia was significant (grade 3-4) in 58% of patients, which was associated with worse overall survival (HR 2.53, p=0.03). Normal organ dosimetry parameters are strong predictors of lymphocyte nadir – V5 (p=0.008), mean lung dose (p=0.009), mean heart dose (p=0.03), mean body dose (p=0.02). Effective radiation dose to immune cells (EDIC), a composite estimate of radiation dose to circulating lymphocytes, was also strongly correlated to post-RT lymphopenia (p=0.007).

Conclusion

Normal organ dosimetric parameters are strong predictors of complications after radical RT for NSCLC. Breath-hold technique, which improves normal lung dosimetry, may play an important role to mitigate RT induced lung damage and lymphopenia.