Impact of Comorbidities on Acute Toxicity in Patients Receiving Radiation Therapy for Locally Advanced Lung Cancer

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PURPOSE / OBJECTIVE(s)

Approximately three quarters of patients with lung cancer present with one or more comorbid medical conditions – most commonly COPD, diabetes, and CHF[1] – and the presence of comorbidities has been shown to be independently prognostic of survival in this patient population.[1-4] One way in which comorbidities impact survival is by limiting the diagnostic or therapeutic modalities for which a patient is eligible; however, it is not well known if comorbidity burden impacts tolerance of thoracic radiation treatment (TRT). We hypothesized that patients with more comorbidities are more likely to experience acute toxicity from TRT for locally advanced lung cancer.

MATERIAL & METHODS

We queried two patient databases: data from four prospective institutional investigator-initiated trials (IIT) as well as data from a state-wide quality consortium (SWQC). To assess comorbidities, we used the Charlson Comorbidity Index (CCI) for IIT cohort and created a Comorbidity Index (CI) using similar, available data for the SWQC cohort. Logistic regression was used to determine the relationship between comorbidity indices and radiation-induced toxicities, specifically grade ≥2 esophagitis and pneumonitis. Adjustments were made for PTV volume, concurrent chemotherapy, and radiation dose to organs at risk. Weighting variables were applied for SWQC patients for modeling pneumonitis outcome because of heterogeneity in follow-up time.

RESULTS

- A total of 1188 patients were analyzed in the IIT and SWQC cohorts (112 and 1076, respectively), with average age 65 and 67 years and PTV volume of 465 and 369 mL.
- Total incidence of grade ≥2 radiation pneumonitis was 13.5% and 6.8%, and grade ≥2 esophagitis was 41.4% and 54.3%, respectively, for the IIT and SWQC cohorts.
- Mean CCI for the IIT cohort was 3.7; mean CI for the SWQC cohort was 1.5.
- The data were concordant that there is **no evidence linking comorbidity indices to any toxicity outcome** (Table 1).
- However, **esophagitis was significantly associated with concurrent chemotherapy** (p<0.0001 in the SWQC cohort, NS in the IIT cohort) **and mean esophageal dose** (p<0.0001 in the SWQC cohort and p=0.04 in the IIT cohort).
- **Pneumonitis was also significantly related to mean lung dose** in the IIT cohort (p=0.04).

Table 1. **Effect of Clinical Variables on Radiation-Induced Toxicities**

	Esophagitis				Pneumonitis			
Odds Ratio (OR) & p-value (p)	SWQC		IIT		SWQC		IIT	
Variable	OR	p	OR	p	OR	p	OR	p
PTV vol.	1.0	0.92	0.9	0.28	1.1	0.17	1.1	0.43
Conc. Chemo	2.5	<0.0001	5.8	0.11	1.1	0.89	1.3	0.81
Mean Esoph. Dose	1.1	<0.0001	1.1	0.04				
Mean Lung Dose					1.1	0.11	1.2	0.04
Comorbidity Index	1.0	0.4	0.9	0.7	1.0	1.0	0.7	0.1

SUMMARY / CONCLUSION

- This is the largest study using prospectively-collected data of lung cancer patients treated with definitive TRT evaluating comorbidity burden and radiation-induced acute toxicity.
- As an independent variable, comorbidity indices are not associated with higher rates of esophagitis or pneumonitis in lung cancer patients undergoing TRT.
- Our data suggest that **treatment-related rather than patient-specific factors are most important in determining the toxicity profile for these patients.**
- These data inform clinical practice by suggesting that patients with multiple comorbidities should not be denied definitive cancer treatment because of a presumed increased incidence in treatment-associated morbidity.

REFERENCES / ACKNOWLEDGEMENTS

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