2012. Patients were prescribed to 60-87.5 Gy (relative biological effectiveness, RBE) in 30-37 fractions. Radiation-induced esophagitis (RE) was graded by physicians according to the CTCAE v3.0. The primary endpoint of this study was grade 2 or higher RE within 6 months from the start of treatment. Biological uncertainty due to RBE variation was quantified as the product of physical dose and dose-averaged linear energy transfer (DL). DL was obtained by recalculating the plans using a Monte Carlo-like fast dose calculator (FDC). In addition, FDC was used to calculate the dose distributions using 3 variable RBE models-Wedenberg (RW), McNamara (RM), and repair-misrepair-fixation (RF). Dose-response curves based on the dose delivered to 1cc (D1cc) of esophagus were derived for constant and variable RBE models.

Results: Of the 119 patients, 52 (43.7%) patients had grade 2-3 RE, and no grade 4-5 RE was reported. In univariable logistic regression analysis, maximum and mean DLs were significantly associated with the risk of RE (DL_{max}, odds ratio (OR): 1.33, 95% confident interval (CI): 1.15-1.54, $p < 0.001$; DL_{mean}, OR: 2.08, 95% CI: 1.50-2.90, $p < 0.001$). However, the indices of DL were no longer significant in the multivariable logistic regression analysis incorporating with constant RBE dose and DL, whereas the volume receiving 75 Gy (RBE) (V75) was still a significant risk factor (OR: 1.35, 95% CI: 1.02-1.77, $p = 0.03$). The dose-response curves using constant RBE and RF models were found to be almost identical, while the curves of RW and RM models were slightly shifted toward higher dose. The resulting tolerance doses at the 50% complication risk were 64.54 (constant), 63.04 (RF), 67.49 (RW), and 67.47 (RM) Gy (RBE), respectively. The differences between the predicted NTCPs yielding from constant and variable RBE models were statistically non-significant ($p = 0.37$-0.71).

Conclusion: Biological uncertainty was a minor risk factor of RE compared with constant RBE dose, and predicted risk using constant RBE dose only agree well with the observed outcome. Constant and variable RBE models predict statistically the same NTCP. External validation and in vivo experiments are warranted.

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Predictors of Early Death or Hospice in Curative Inoperable Lung Cancer Patients

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Purpose/Objective(s): The current treatment approach for inoperable stage II-III non-small cell lung cancer (NSCLC) involves aggressive chemo/radiotherapy (CRT). While outcomes have improved with immunotherapy, some patients transition to hospice or die early into their treatment. To help identify these patients and tailor treatment interventions, we developed a predictive model for early poor outcomes in this population.

Materials/Methods: We included patients who received definitive CRT for stage II-III lung cancer from April 2012 - November 2019. Patient information was collected prospectively as part of a statewide consortium involving 27 sites. We defined an early poor outcome as termination of treatment due to hospice enrollment or death within 5 months of initiating radiation therapy. Potential predictors included patient and disease characteristics, patient reported outcomes (PROs), and treatment variables. Generalized linear models were used to describe the relationships between single predictors and outcomes of interest. Due to missing data, we imputed 25 datasets to fit multivariable models. We used Lasso regression on all 25 datasets to select variables of interest. Using these selected variables, we fit generalized linear models on all 25 imputed data sets and present pooled results.

Results: A total of 2127 patients met criteria, of which 96 patients discontinued treatment early due to hospice enrollment or death. Of the 96 patients, 59% received concurrent chemotherapy and the mean age was 71 years old. When modeled individually, age, ECOG performance status, PTV volume, distance to critical structures, mean heart dose, insurance status, functional and physical well-being scale, and lung cancer symptom scale were all significant predictors of early hospice or death. Additionally, specific PRO questions, including "I have a lack of energy", "I have been coughing", and "I have been short of breath" were significant univariable predictors. Gender, marital status, baseline FEV1, treatment center, lung radiation dose (V5, V20, mean), and esophageal dose (D2cc) were not significant univariable predictors. Our Lasso procedure selected the following predictors for multivariable analysis: age, ECOG performance status, PTV volume, patient reported lack of energy, patient reported cough, mean heart dose, and patient insurance status. The pooled estimate of AUC for this multivariable model was 0.71.

Conclusion: Our models identified a combination of initial patient, disease and treatment characteristics, and PROs that may help identify individuals undergoing curative CRT who are at high risk of early hospice enrollment or death. Further research to determine if interventions for this group (e.g. treatment modifications, supportive care) may help improve patients' outcomes.

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Abscopal Response Rates after Salvage Radiation in Patients with Progressive Disease on Immunotherapy

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