

Multivariable logistic regression modeling

Data exploration

Both clinical and dosimetric factors were tested. The clinical factors were age, sex, stage, and the use of concomitant chemotherapy. The dosimetric factors were the equivalent uniform dose, mean dose, maximum dose, V_x values, and the relative volume (%) of esophagus receiving dose higher than x Gy (RBE) (x ranges from 10 to 75 in increments of 5). The correlation between variables was quantified using Spearman's correlation coefficient, and the results for clinical factors and dosimetric factors are shown in Figure S2.

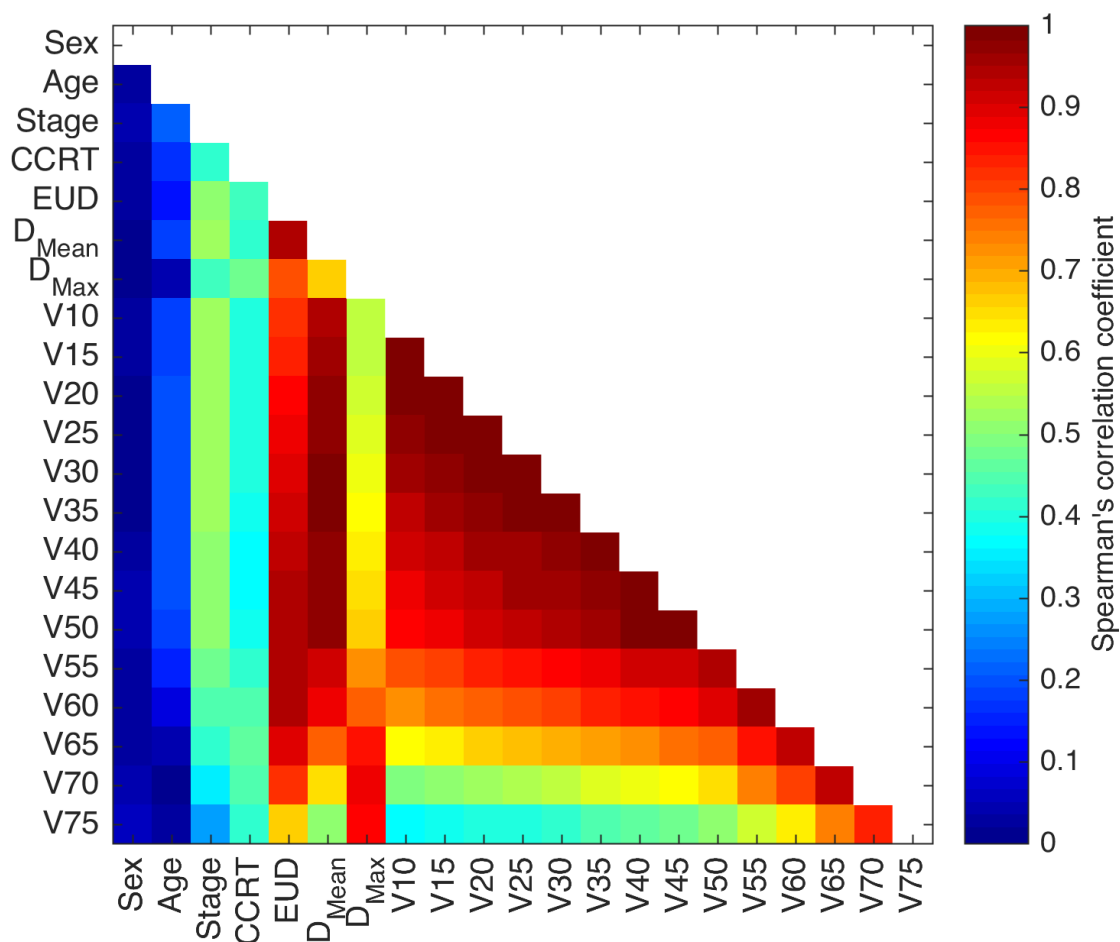


Figure S2 Spearman's correlation coefficient for clinical and dosimetric factors.

Variable selection

Variables were selected using stepwise forward selection with the significance criteria given by log-likelihood ratio test. The significant level was set as $p < 0.05$. All candidate variables were included. The variable selection process was repeated in 1000 bootstrap resamples, and model metric of the highest selection frequency was chosen [1].

Modeling results and performance evaluation

Table S3 shows the coefficients of the final model. Internal validation was performed using the bootstrap approach, and the optimism results are shown in Table S4.

Table S3 Results of the multivariable logistic regression model and the variations of the coefficients in bootstrap validation.

Predictor	Estimate	Standard deviation	Bootstrap median	Bootstrap 2.5 th percentile	Bootstrap 97.5 th percentile
CCRT	0.851	0.291	0.857	0.297	1.470
EUD	0.066	0.010	0.067	0.049	0.092
Constant	-3.585	0.462	-3.620	-4.678	-2.795

CCRT = concomitant chemotherapy; EUD = equivalent uniform dose.

Table S4 Bootstrap validation for multivariable logistic regression model performance.

Performance measure	Apparent	Bootstrap mean (95% CI)	Validated mean (95% CI)	Optimism mean (95% CI)	Optimism-corrected mean (95% CI)
Overall					
Negelkerke's R ²	0.344	0.349 (0.246-0.452)	0.334 (0.315-0.352)	0.015 (-0.093-0.123)	0.329 (0.244-0.366)
Scaled Brier score	0.263	0.268 (0.183-0.353)	0.256 (0.243-0.270)	0.012 (-0.075-0.099)	0.251 (0.183-0.282)
Discrimination					
AUC	0.800	0.802 (0.753-0.850)	0.799 (0.795-0.803)	0.003 (-0.046-0.051)	0.798 (0.768-0.819)
Discrimination slope	0.262	0.267 (0.182-0.352)	0.262 (0.222-0.303)	0.005 (-0.043-0.053)	0.258 (0.224-0.277)
Calibration					
Hosmer-Lemeshow test	$\chi^2 = 5.18$ ($p = 0.79$)				

AUC = area under the receiver operating curve; CI = confidence interval.

Reference

[1] El Naqa I, Bradley J, Blanco AI, Lindsay PE, Vicic M, Hope A, et al. Multivariable modeling of radiotherapy outcomes, including dose-volume and clinical factors. *Int J Radiat Oncol Biol Phys.* 2006;64:1275-86.