

# Prognostic significance of radiomic features from <sup>18</sup>F-FDG PET/CT in patients with stage III non-small cell lung cancer undergoing neoadjuvant chemoradiation therapy followed by surgery

Jang Yoo<sup>1</sup>, Jaeho Lee<sup>2</sup>, Miju Cheon<sup>1</sup>, Sang-Keun Woo<sup>3</sup>, Hojoong Kim<sup>4</sup>, Yong Soo Choi<sup>5</sup>, Hongryull Pyo<sup>6</sup>, Myung-Ju Ahn<sup>7</sup>, Joon Young Choi<sup>8</sup>

<sup>1</sup>Department of Nuclear Medicine, Veterans Health Service Medical Center, Seoul, Korea, <sup>2</sup>Department of Preventive Medicine, Seoul National University College of Medicine, Seoul, Korea, <sup>3</sup>Department of Nuclear Medicine, Korea Cancer Center Hospital, Korea Institute of Radiological and Medical Sciences (KIRAMS), Seoul, Korea, <sup>4</sup>Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, <sup>5</sup>Department of Thoracic and Cardiovascular Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, <sup>6</sup>Department of Radiation Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, <sup>7</sup>Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, <sup>8</sup>Department of Nuclear Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Variable	HR	95% CI	p value	Variable	HR	95% CI	p value		
<b>Age</b>	1.016	0.991-1.043	0.216	<b>PET1</b>	SUVmax	1.015	0.975-1.056	0.476	
<b>Sex</b>	Male vs. female	1.988	1.191-3.316	<b>0.009*</b>	SUVmean	1.023	0.928-1.128	0.653	
<b>Histology</b>	Non-adc vs. adc	1.595	1.023-2.487	<b>0.039*</b>	MTV	1.005	1.002-1.008	<b>&lt;0.001*</b>	
<b>T stage</b>	T3/4 vs. T1/2	1.966	1.256-3.079	<b>0.003*</b>	TLG	1.002	1.001-1.003	<b>0.005*</b>	
<b>N stage</b>	N2/3 vs. No/1	1.110	0.154-8.006	0.917	LASSO score	3.164	2.048-4.887	<b>&lt;0.001*</b>	
<b>Tumor stage</b>	IIIA vs. IIIB/IIIC	2.067	1.329-3.215	<b>0.001*</b>	<b>PET2</b>	SUVmax	1.008	0.941-1.080	0.823
<b>Pathologic response</b>	pCR vs. non-pCR	1.741	0.839-3.615	0.137	SUVmean	0.988	0.847-1.153	0.880	
	MPR vs. non-MPR	1.045	0.680-1.605	0.841	MTV	1.010	1.003-1.016	<b>0.003*</b>	
					TLG	1.003	1.001-1.005	<b>0.036*</b>	
					LASSO score	2.836	2.102-3.826	<b>&lt;0.001*</b>	

Table 1. Univariate cox regression analysis for OS

Variable	HR	95% CI	p value	Variable	HR	95% CI	p value		
<b>Sex</b>	Male vs. female	1.703	0.977-2.967	0.061	<b>Sex</b>	Male vs. female	1.674	0.960-2.919	0.067
<b>Histology</b>	Non-adc vs. adc	1.309	0.793-2.162	0.293	<b>Histology</b>	Non-adc vs. adc	1.352	0.812-2.249	0.246
<b>T stage</b>	T3/4 vs. T1/2	0.629	0.217-1.822	0.629	<b>T stage</b>	T3/4 vs. T1/2	0.639	0.222-1.844	0.408
<b>Tumor stage</b>	IIIA vs. IIIB/IIIC	1.848	0.686-4.980	0.225	<b>Tumor stage</b>	IIIA vs. IIIB/IIIC	1.863	0.694-5.005	0.217
<b>PET1 MTV</b>		1.001	0.995-1.008	0.712	<b>PET1 TLG</b>		0.999	0.999-1.001	0.883
<b>PET2 MTV</b>		0.994	0.981-1.008	0.393	<b>PET2 TLG</b>		0.999	0.994-1.004	0.670
<b>PET1 LASSO score</b>		1.707	0.907-3.212	0.097	<b>PET1 LASSO score</b>		1.787	0.950-3.362	0.072
<b>PET2 LASSO score</b>		2.297	1.437-3.669	<b>&lt;0.001*</b>	<b>PET2 LASSO score</b>		2.084	1.419-3.060	<b>&lt;0.001*</b>

Table 2. Multivariate cox regression analysis for OS in each MTV and TLG models

## Conclusion

The radiomic feature of stage III NSCLC using <sup>18</sup>F-FDG PET/CT was independent prognostic factor for the estimation of OS. Moreover, the newly developed LASSO score using radiomic features revealed the better performance for individualized OS estimation than conventional PET parameters.

## Aims

We evaluated prognostic significance of radiomic features extracted from <sup>18</sup>F-FDG PET/CT to predict overall survival (OS) in patients with stage III non-small cell lung cancer (NSCLC) undergoing neoadjuvant chemoradiation therapy followed by surgery, and compared the predictive performance of radiomics from conventional PET parameters.

## Methods

We retrospectively enrolled 300 patients with stage III NSCLC who underwent two <sup>18</sup>F-FDG PET/CT scans at initial work-up (PET1) and after neoadjuvant concurrent chemoradiotherapy (PET2). Radiomic features of primary tumor from both PET/CT images were subjected to the least absolute shrinkage and selection operator (LASSO) regression to select the most useful prognostic features. The prognostic significance of LASSO score and conventional PET parameters was assessed by cox proportional hazards regression analysis. To evaluate and compare the prognostic prediction between LASSO score and conventional PET parameters, time-dependent receiver operating characteristic (ROC) curve analysis was performed. Decision curve analysis (DCA) examined the potential net benefit of using LASSO score in the real clinical practice.

## Results

The mean follow-up duration was 43.2 months. Eighty four patients (28.0%) had died, and remaining 216 patients (72.0%) were alive. Their sex, histological cell type, T stage, and tumor stage were significant prognostic factors. In conventional PET parameters, metabolic tumor volume (MTV) and total lesion glycolysis (TLG) of each PET1 and PET2 were significantly associated with an increased risk of death. Also, both PET1-LASSO score and PET2-LASSO score were significantly associated with OS. In multivariate cox regression analysis, only PET2-LASSO score was independently significant factor for OS ( $p < 0.001$ ) after adjusting for clinical characteristics. In time-dependent ROC curve analysis, LASSO score could predict OS better than conventional PET parameters. In addition, the DCA using LASSO score showed a higher net benefit across the entire spectrum of probability thresholds than that of conventional PET parameters.