

Prognostication Based on Texture Analysis of Baseline ¹⁸F Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Nonsmall-Cell Lung Carcinoma Patients Who Underwent Platinum-Based Chemotherapy as First-Line Treatment

Abstract

Objective: Our study aims to establish the potential for tumor heterogeneity evaluated using ¹⁸F fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT) texture analysis in nonsmall-cell lung carcinoma (NSCLC) patients who underwent platinum-based chemotherapy to provide an independent marker for overall survival (OS) of more than 1-year. **Materials and Methods:** A total of 42 patients (34 male and 8 female) with biopsy-proven NSCLC and mean age 55.33 ± 10.71 years who underwent a baseline F-18 FDG PET/CT and received platinum-based chemotherapy as first-line treatment were retrospectively included in the study. Ten first order, 21 s order texture parameters and 7 SUV and metabolic tumor volume (MTV) based metabolic parameters were calculated. All these parameters were compared between the two survival groups based on OS ≥1 year and OS <1 year. Cut-offs of significant parameters were determined using receiver operating characteristic curve analysis. Survival patterns were compared by log-rank test and presented using Kaplan-Meier curves. Cox proportion hazard model was used to determine the independent prognostic marker for 1 year OS. **Results:** In univariate survival analysis, 3 first order texture parameters (i.e. mean, median, root mean square with hazard ratios [HRs] 2.509 [P = 0.034], 2.590 [P = 0.05], 2.509 [P = 0.034], respectively) and 6 s order texture parameters (i.e. mean, auto correlation, cluster prominence, cluster shade, sum average and sum variance with HRs 2.509 [P = 0.034], 2.509 [P = 0.034], 3.929 [0.007], 2.903 [0.018], 2.954 [0.016] and 2.906 [0.014], respectively) were significantly associated with 1 year OS in these patients. Among the metabolic parameters, only metabolic tumor volume whole-body was significantly associated with 1 year OS. In multivariate survival analysis, cluster prominence came out as the independent predictor of 1 year OS. **Conclusion:** Texture analysis based on F-18 FDG PET/CT is potentially beneficial in the prediction of OS ≥1 year in NSCLC patients undergoing platinum-based chemotherapy as first-line treatment. Thus, can be used to stratify the patients which will not be benefitted with platinum-based chemotherapy and essentially needs to undergo some other therapy option.

Keywords: ¹⁸F Fluorodeoxyglucose positron emission tomography/computed tomography, overall survival in nonsmall-cell lung carcinoma, texture analysis

Introduction

Lung cancer is the leading cause of cancer incidence and mortality in both sexes worldwide with 2.1 million estimated new cases and 1.8 million estimated deaths for 2018.^[1] The WHO has classified lung cancer into two broad categories: small-cell lung carcinoma (SCLC) and nonsmall cell lung carcinoma (NSCLC). NSCLC accounts for more than 83% of all lung cancer cases which includes two major types: nonsquamous carcinoma and squamous cell carcinoma.^[2]

Early-stage NSCLC can be treated with curative intent, largely surgery. However, the majority of NSCLC patients present with incurable advanced stage IIIB or IV, which reflects the aggressive nature of the disease and poor prognosis. At present, various new therapies are available for advanced-stage NSCLC like targeted therapies and immunotherapies which have shown to improve survival in these patients.^[3] However, only a small proportion of the total population of patients with advanced NSCLC remains the candidates

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for these therapies as they require genetic drivers and usually have high costs. For patients with NSCLC who do not have drug-targetable driver mutations (approximately 85%–90%) or cannot opt for costly treatments, platinum-based chemotherapy remains the unchallenged standard of care.^[3,4]

Prediction of prognosis before the start of treatment and during the treatment would be helpful as this might allow the change in the treatment planning for the betterment of the patient.^[5] The most important prognostic factors which can predict survival in NSCLC are the stage of disease at diagnosis, performance status, weight loss, and gender.^[6] However, these prognostic factors may be the surrogate of the underlying tumor burden which may be a more direct predictor of disease progression and survival of the patients.^[7] The quantification of tumor burden was initially performed by using computed tomography (CT).^[8] CT has limitations in measuring tumor burden as the whole assessment of tumor and its spread in the body is based on the size of the lesion. Moreover, it does not provide any information about the metabolic activity of tumor. F-18 Fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) is a functional imaging technique which has its advantages over the CT and is now routinely used for prognosis, staging, and response evaluation in NSCLC patients. The most important metabolic parameter evaluated from F-18FDG PET/CT is the maximum standardized uptake value (SUVmax). In the past, some studies have shown the role of SUVmax in the prediction of survival in NSCLC^[9-11] whereas other studies are also present in the literature which shows that SUVmax is not associated with survival in NSCLC.^[12,13] Additionally, metabolic parameter evaluation of F-18 FDG PET/CT provides false-negative results in some instances in NSCLC. The most important example of this is mucinous type NSCLC in which FDG uptake remains very less.^[14] Other than SUVmax, there are other metabolic parameters which are metabolic tumor volume (MTV) based parameters. Recent studies have suggested that as compared to SUVmax, MTV-based parameters might have a better role in the prediction of prognosis in NSCLC.^[15,16]

In recent years, computerized analysis of F-18 FDG PET/CT imaging has received a great deal of attention as a means to improve the clinical management of oncology patients including NSCLC.^[17-19] It is believed that texture analysis has the potential to improve on traditional, manual interpretation by detecting features and patterns that otherwise would go unnoticed to the human eye.^[20] However, the ability for texture analysis to provide prognostic information for patients with advanced NSCLC is largely unexplored. Our study aims to retrospectively establish the potential for tumor heterogeneity evaluated using F-18 FDG PET/CT texture analysis in NSCLC patients who underwent platinum-based chemotherapy to

provide an independent marker for overall survival (OS) of more than 1-year.

Materials and Methods

Patient population

This study was approved by the institutional ethics committee (*Ref. No. IECPG-58/22.03.2017*). A total of 42 patients with biopsy-proven NSCLC who underwent a baseline F-18 FDG PET/CT between the period June 2015 and July 2017 and platinum-based chemotherapy as first-line therapy were retrospectively included in the study.

Whole body ¹⁸F fluorodeoxyglucose positron emission tomography/computed tomography acquisition protocol

The acquisition was performed on Siemens Biograph mCT PET/CT scanner (Siemens Healthcare, Erlangen, Germany) with 64-slice CT. The patients were kept fasting for a minimum of 6 h before F-18 FDG injection. Preinjection blood glucose was ensured to be <200 mg/dL. Whole-body F-18 FDG PET/CT was acquired 45–60 min after injecting 0.10–0.14 mCi/kg (3.7–5.1 MBq/kg) body weight FDG dose intravenously. In the PET/CT system, CT scan acquisition was performed first on a spiral dual slice CT system with slice thickness of 4 mm and a pitch of 1. After the CT scan, the table was moved towards the field of view of PET and PET acquisition of the same axial range started with the patient in the same position on the table. PET acquisition was done for 2–3 min per bed position for 8–9 beds depending on the height of the patient. PET data were acquired using the matrix of 128 × 128 pixels with a slice thickness of 1.5 mm. CT-based attenuation correction of the emission images was employed. PET images were reconstructed by the iterative method of ordered subset expectation maximization (OSEM; 2 iterations and 8 subsets).

Image analysis

Image analysis for evaluation of ¹⁸F fluorodeoxyglucose positron emission tomography/computed tomography metabolic parameters

Analysis and interpretation of the PET, CT, and fused F-18 FDG PET/CT images was done after displaying the images in transaxial, coronal, and sagittal planes on vendor-provided workstation “Multimodality Workplace” (Siemens Healthcare, Erlangen, Germany). PET images were looked for area of increased radiotracer uptake. The corresponding area in the CT images and fused F-18 FDG PET/CT images were corroborated for identification of disease and a 3-D ellipsoid isocontour region of interest (ROI) with threshold 2.5 SUV was marked around the primary tumor for measurement of SUVmax, SUVavg, and MTV of primary tumor.^[21] For the calculation of TBR, normal liver parenchyma was used

as the background. Five ROIs of the same diameter were drawn on the normal liver and TBR was calculated by dividing the SUVmax of tumor with the mean SUVavg of the liver.

Total Lesion Glycolysis (TLG) of primary tumor was calculated by multiplying SUVavg of primary tumor with MTV. metabolic tumor volume whole-body (MTVwb) was calculated by adding the MTV of all the metabolically active lesions in the whole-body F-18 FDG PET/CT scan and TLGwb was generated by calculating the TLG of every lesion separately and then adding the TLGs of all the lesions in the whole-body F-18 FDG PET/CT.

Image analysis for evaluation of texture parameters

For each NSCLC patient, the PET/CT image with the largest cross-sectional area of the tumor was selected for texture analysis by a single operator. The image was exported in JPEG format. Further processing of the image related to extraction of texture features was performed in R programming language (R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>) installed on personal computer. A rectangular ROI was carefully drawn that included “tumor region” only and cropped (Simon Barthelme (2018). imager: Image Processing Library Based on “CImg.” R package version 0.41.1). The cropped PET/CT image was converted into gray scale image and the image grey level was discretized into 32 levels. The discretized image was used to extract 10 intensity histogram (IH) based on first-order statistics.

A Gray level co-occurrence matrix (GLCM) was formed from discretized image matrix. During the formation of the GLCM matrix, the pixel was at an angle of zero degree, at a distance of 1-pixel to which reference pixel was compared. Twenty-one second-order statistics (texture features) were calculated from GLCM matrix. To extract first and second-order statistics, “radiomics” was used.^[22] The list of first- and second-order statistics calculated is given in Table 1. Flow chart showing the workflow for extraction of texture features is given in Figure 1.

Treatment and follow up

After baseline F-18 FDG PET/CT, patients received chemotherapy. Chemotherapy regimens used in our study sample were carboplatin + paclitaxel in 40 patients and carboplatin + pemetrexed in two patients. Carboplatin of area under the curve 6 mg/mL per minute, paclitaxel 200 mg/m² body surface area and pemetrexed at a dose of 500 mg/m² were administered every 3 weeks.^[6]

Information regarding the prognosis of patients was taken from the medical records in the lung cancer clinic, Department of Pulmonary Medicine and Sleep Disorders of our institute. Also, information was collected telephonically regarding the patients who were unable to come to the

Table 1: List of intensity histogram-based first order and gray level co-occurrence matrix-based second-order texture parameters

IH-based first-order parameters	GLCM based second order parameters	
Energy	Mean	Entropy
Entropy	Variance	Homogeneity 1
Kurtosis	Auto correlation	Homogeneity 2
Mean deviation	Cluster prominence	IDMN
Skewness	Cluster shade	IDN
Uniformity	Cluster tendency	Inverse variance
Mean	Contrast	Maximum probability
Median	Correlation	Sum average
Variance/relative smoothness	Difference entropy	Sum entropy
RMS	Dissimilarity	Sum variance
	Energy	

GLCM: Gray level co-occurrence matrix, RMS: Root mean square, IDMN: Inverse difference moment normalized, IDN: Inverse difference normalized, IH: Intensity histogram

clinic. OS was calculated from the date of baseline F-18 FDG PET/CT performed to the date of death due to any cause or the last clinical follow-up.

Statistical analysis

SPSS version 22.0 (IBM Corporation in Armonk, New York) was used for the statistical analysis of data. The patients were categorized into two survival groups based on OS <1 year and ≥1 year. The association of different study variables with 1-year survival of patients was evaluated using Mann–Whitney *U*-test. The cut-off values for significant variables ($P < 0.05$) were evaluated using receiver operating characteristic (ROC) curve analysis. Univariate survival analysis of prognostic markers for OS was performed in which survival patterns were compared by log-rank test and presented using Kaplan-Meier curves. Cox proportion hazard model was used to determine the independent prognostic marker for OS in multivariate analysis.

Results

Patient characteristics

Of 42 patients, 34 were male and 8 were female with mean age of 55.33 ± 10.71 years (range: 32–80 years). Sixteen patients had squamous cell carcinoma, 20 had adenocarcinoma and 6 had NSCLC (NOS). The EGFR mutations were negative in all patients. The staging was done on the basis of the 8th edition of the AJCC TNM staging system. A detailed description of patient characteristics is given in Table 2.

Patient follow up and association of parameters with 1 year overall survival

The median follow-up period for 42 patients was 10.10 months (range, 1–61 months), of which 38 patients

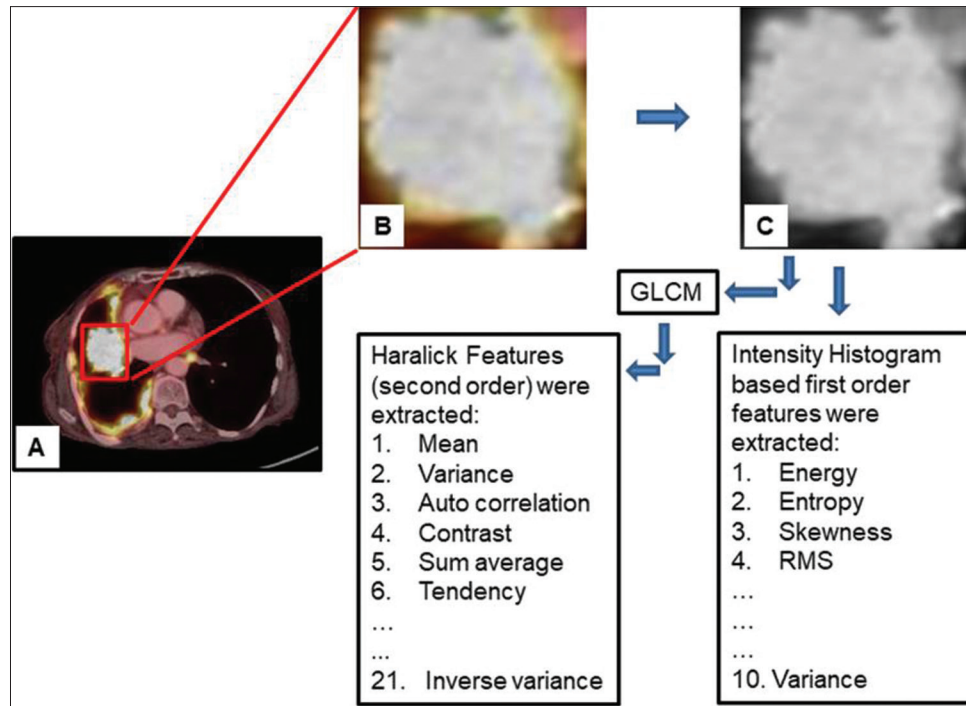


Figure 1: Flow chart showing the steps performed for extraction of texture features (A) JPEG image with the longest diameter of tumor, rectangular region of interest was drawn to segment the tumor; (B) Zoomed image of segmented tumor; (C) Image was converted to grayscale image which was then used to extract intensity histogram-based first-order features and gray level co-occurrence matrix based Haralick features

died during the follow-up. The median follow-up period was 8.65 months (range, 1–47 months) for patients who died during follow-up whereas, it was 54.3 months (range, 41–61 months) for survivors.

Among 42 patients, 24 had survival ≥ 1 year (median survival: 34.22 months, range: 12–61 months) and 18 patients had survival < 1 year (Median survival: 6.05, range: 1–11 months).

Among the metabolic F-18 FDG PET/CT parameters (SUVmax, SUVavg, TBR, MTV, TLG, MTVwb, and TLGwb), One metabolic parameter (MTVwb), 3 IH based first-order texture parameters (mean, median, and root mean square [RMS]) and 6 GLCM based second-order texture parameters (mean, auto-correlation, cluster prominence, cluster shade, sum average, and sum variance) were significantly different among the two survival groups ($P < 0.05$). These parameters were further considered for ROC curve analysis and their cut-off values were determined. The median values of parameters along with the results of ROC curve analysis of these variables in the two survival groups are given in Table 3.

Survival analysis

In univariate survival analysis, the survival fractions at the values higher and lower than cut-offs were significantly different (P value of log-rank test < 0.05) for MTVwb, three IH based first-order texture parameters (mean, median, RMS) and six GLCM based second-order texture parameters (mean, auto-correlation, cluster prominence,

cluster shade, sum average, sum variance) [Table 4]. None of the clinical parameters (age, sex, histopathology, stage of disease, ECOG, smoking history, and smoking index) were significantly associated with 1-year survival in the present study.

In univariate cox regression analysis, a significant association of 1 year survival was found with all 10 parameters, i.e. MTVwb (hazard ratios [HR] 2.542, $P = 0.039$), IH based 1st order mean (HR 2.509, $P = 0.034$), median (HR 2.259 $P = 0.034$), RMS (HR 2.509, $P = 0.035$) and GLCM based 2nd order mean (HR 2.509, $P = 0.035$), autocorrelation (HR 2.509, $P = 0.035$), cluster prominence (HR 3.929, $P = 0.007$), cluster shade (HR 2.903, $P = 0.018$), sum average (HR 2.954, $P = 0.016$), sum variance (HR 2.906, $P = 0.014$) [Table 4].

In multivariate cox regression analysis, GLCM based 2nd order cluster prominence came out as the independent predictor of 1-year survival with HR 3.929 (95% confidence interval: 1.455–10.611, $P = 0.007$). Kaplan-Meier curve of cluster prominence is shown in Figure 2 and Kaplan-Meier curves of all other parameters which were significantly associated with survival in univariate survival analysis are given in Supplementary Figures 1-3.

Representative F-18 FDG PET/CT images of patients with OS > 1 year and < 1 year are given in Figures 3 and 4, respectively.

Table 2: Patient characteristics

Characteristic	Number of patients (n=42), n (%)
Age (years)	
Mean±SD	55.33±10.71
Range	32-80
Sex	
Male	34 (80.95)
Female	8 (19.04)
Primary tumor site	
Right side	24 (57.14)
Left side	18 (42.85)
Histopathology	
NSCLC (NOS)	6 (14.28)
Squamous cell carcinoma	16 (38.09)
Adenocarcinoma	20 (47.61)
ECOG	
0	2 (4.76)
1	30 (71.42)
2	7 (16.66)
3	3 (7.1)
Smoking history	
Nonsmokers	10 (23.80)
Smokers	32 (76.19)
Smoking index (mean±SD)	377.74±453.224
TNM stage	
T stage	
T1c	3 (7.1)
T2c	1 (2.38)
T3	5 (11.90)
T4	33 (78.57)
N stage	
N0	3 (7.1)
N1	1 (2.38)
N2	7 (16.66)
N3	31 (73.80)
M stage	
M0	8 (19.04)
M1a	11 (26.19)
M1b	8 (19.04)
M1c	15 (35.71)
Overall stage	
IIIA	3 (7.14)
IIIB	1 (2.38)
IIIC	4 (9.5)
IVA	19 (45.23)
IVB	15 (35.71)

NSCLC: Nonsmall cell lung carcinoma, NOS: Not otherwise specified, ECOG: Eastern co-operative oncology group, TNM: Tumor node metastasis, SD: Standard deviation

Discussion

The median survival time of untreated advanced-stage NSCLC is 4–5 months with a 1-year survival rate of only 10%.^[23] However, it has been demonstrated in the previous study that, as compared with best supportive care, chemotherapy improves survival in patients with

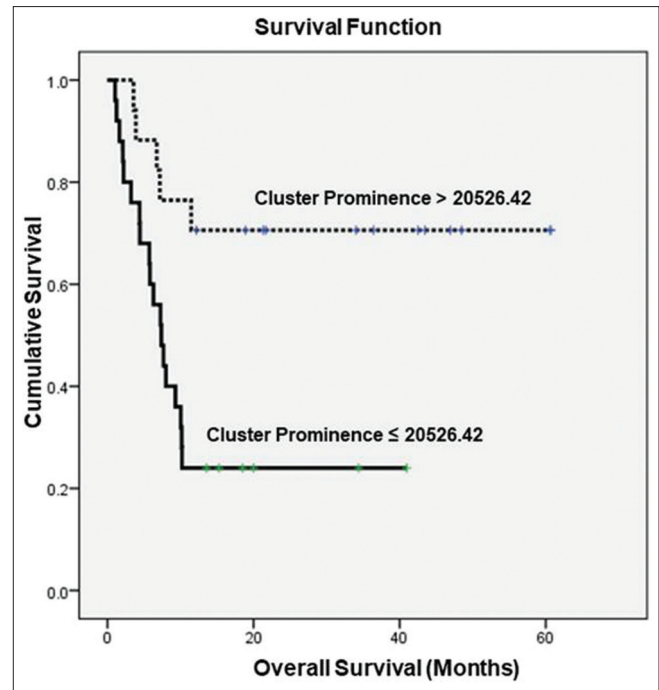


Figure 2: Kaplan-Meier curve of cluster prominence (most significantly associated with 1-year survival) *Kaplan-Meier curves of other significant parameters are given as supplementary data

advanced NSCLC.^[24] Moreover, newer chemotherapy combinations resulted in a median survival time of 7.9–11.3 months.^[25,26] In this study, we evaluated the potential of texture parameters and conventional metabolic parameters of F-18 FDG PET/CT in the prediction of 1-year survival in NSCLC patients. Out of 42 patients, maximum patients (n = 34) had stage IV NSCLC followed by stage IIIB and IIIC (n = 5) and only 3 patients were with IIIA stage of disease. All patients underwent platinum-based chemotherapy as first-line treatment.

The survival rate at 1 year in our study was 57.14% and the results demonstrated that among the metabolic parameters. Among metabolic parameters, only MTVwb was able to predict 1-year survival in these patients. Moreover, texture parameters performed better than metabolic parameters. Among the texture parameters “cluster prominence” was the independent predictor of 1-year survival.

SUVmax and routinely used clinical parameters were not significantly associated with OS in our study.

SUVmax is the most routinely used parameter of F-18 FDG PET/CT and its prognostic value was previously evaluated in various studies.^[9-13] Some studies showed SUVmax as a significant prognostic marker in NSCLC,^[9-11] while other studies showed no association of SUVmax with survival.^[12,13] In the present study also, SUVmax was not associated with OS. Clinical parameters are also the proven prognostic markers in NSCLC and the most important among them are the stage of disease at diagnosis, performance status, weight loss, and sex.^[6,27] In our study,

Table 3: Descriptive and receiver operating characteristic curve analysis results of parameters which were significantly different among two groups

Parameters	Median (range)		P (Mann-Whitney U)	AUROC (95% CI)	Cut-offs
	<1 year (n=18)	≥1 year (n=24)			
Metabolic parameters					
MTVwb	218.89 (16.35-886.30)	132.87 (14.43-480.460)	0.035	69.2 (53.0-85.4)	158.56
First order-texture parameters					
Mean	9.92 (6.398-11.695)	10.67 (7.500-11.66)	0.047	68.1 (51.4-84.7)	10.25
Median	11.00 (6-14)	13.00 (7-14)	0.001	68.8 (52.3-85.2)	11.50
RMS	10.79 (7.86-12.32)	11.51 (8.99-12.28)	0.029	69.9 (53.9-86.0)	11.27
Second order-texture parameters					
Mean	10.05 (6.43-11.80)	10.79 (7.64-11.83)	0.042	68.5 (52.0-85.1)	10.45
Auto correlation	118.57 (62.02-153.38)	133.71 (82.35-153.28)	0.031	69.7 (53.6-85.8)	128.70
Cluster prominence	17,628.72 (6053.99-31,387.81)	21,770.87 (12,225.06-28,104.16)	0.027	70.1 (53.7-86.6)	20526.42
Cluster shade	-914.79 (-1458.09--112.53)	-1025.14 (-1392.82--522.42)	0.047	68.1 (51.4-84.7)	-983
Sum average	21.23 (14.62-24.60)	23.03 (16.73-25.448)	0.035	69.2 (52.8-85.6)	22.51
Sum variance	427.22 (213.53-548.35)	491.55 (283.25-579.98)	0.015	72.2 (56.6-87.9)	454.39

AUROC: Area under the receiver operating characteristic, CI: Confidence interval, MTVwb: Metabolic tumor volume whole-body, RMS: Root mean square

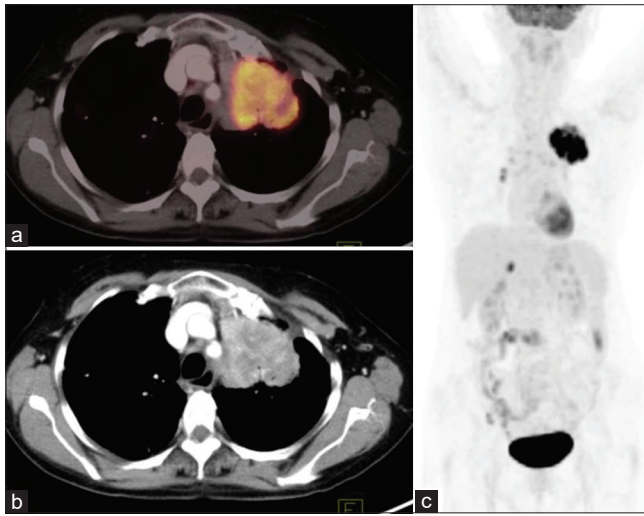


Figure 3: (a-c) are ^{18}F fluorodeoxyglucose positron emission tomography/computed tomography images of 69-year-old female with squamous cell carcinoma. OS of the patient was 43 months. Metabolic tumor volume whole-body was 14.43 cm³. Intensity histogram-based first-order mean, median and restricted mean survival were 11.13, 14, and 11.94, respectively. Gray level co-occurrence matrix based second-order mean, auto correlation, cluster prominence, cluster shade, sum average and sum variance were 11.24, 144.165, 21985, -1137.48, 24.37 and 541.32, respectively

we evaluated histopathology, age, sex, performance status, and stage at diagnosis. Among them, none of the clinical parameters were found to be associated with OS. The result of our study is in accordance with the study done by Liao *et al.* and Yoo *et al.*^[28,29] In both of these studies, neither SUVmax nor the other clinical parameters were found to be associated with survival.

SUVmax is robust and easily reproducible but it does not take into account the metabolically active tumor size and volume. MTV-based parameters evaluated from F-18 FDG PET/CT reflect the tumor volume and are recently been studied for response assessment and prediction of

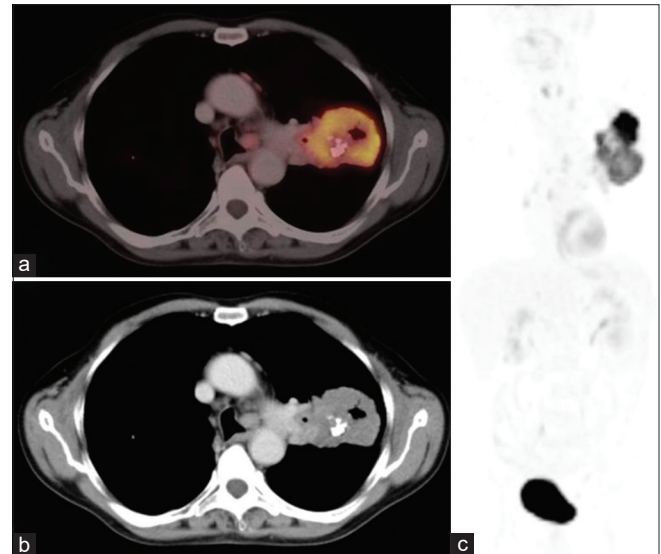


Figure 4: (a-c) ^{18}F fluorodeoxyglucose positron emission tomography/computed tomography images of 60-year-old male with squamous cell carcinoma. OS of the patient was 8 months. Metabolic tumor volume whole-body was 161.19 cm³. Intensity histogram based first-order mean, median, and restricted mean survival were 9.258, 12, and 10.21, respectively. Gray level co-occurrence matrix-based second-order mean, autocorrelation, cluster prominence, cluster shade, sum average, and sum variance were 9.44, 105.99, 14,756, -827.27, 20.629, and 384.95, respectively

prognosis in various tumors. We previously showed that MTV-based parameters are better predictors of OS in NSCLC in patients receiving platinum-based chemotherapy as first-line treatment.^[16] The same has been reported in few other studies.^[30-33] In the present study also, MTVwb came out as the predictor of OS but it has limitation as its evaluation requires the assessment of whole-body tumor lesions which is a time-consuming task.

Nowadays texture analysis has become the area of interest for all clinical imaging as texture parameters quantify the variability of grey-scale levels in the area of interest

Table 4: Results of univariate survival analysis

Variables	Cumulative survival proportion at 1 year	Log-rank test <i>P</i>	HR (95% CI)	P-value (Cox-regression)
Metabolic parameters				
MTVwb				
≥158.56 (<i>n</i> =23) versus	26.1	0.032	2.542 (1.050-6.158)	0.039
<158.56 (<i>n</i> =19)	63.2			
Texture parameters (first order)				
Mean				
≤10.25 (<i>n</i> =22) versus	27.3	0.029	2.509 (1.070-5.884)	0.034
>10.25 (<i>n</i> =20)	60.0			
Median				0.05
≤11.50 (<i>n</i> =19) versus	26.3	0.04	2.259 (1.00-5.104)	
>11.50 (<i>n</i> =23)	56.5			
RMS				
≤11.27 (<i>n</i> =22) versus	27.3	0.029	2.509 (1.070-5.884)	0.034
>11.27 (<i>n</i> =20)	60.0			
Texture parameters (s order)				
Mean				
≤10.45 (<i>n</i> =22) versus	27.3	0.029	2.509 (1.070-5.884)	0.034
>10.45 (<i>n</i> =20)	60.0			
Auto-correlation				
≤128.70 (<i>n</i> =22) versus	27.3	0.029	2.509 (1.070-5.884)	0.034
>128.70 (<i>n</i> =20)	60.0			
Cluster prominence				
≤20,526.42 (<i>n</i> =25) versus	24.0	0.004	3.929 (1.455-10.611)	0.007
>20,526.42 (<i>n</i> =17)	70.6			
Cluster shade				
≥-983 (<i>n</i> =23) versus	26.1	0.013	2.903 (1.198-7.034)	0.018
<-983 (<i>n</i> =19)	63.2			
Sum average				
≤22.51 (<i>n</i> =23) versus	26.1	0.012	2.954 (1.219-7.156)	0.016
>22.51 (<i>n</i> =19)	63.2			
Sum variance				
≤481.82 (<i>n</i> =21) versus	23.8	0.010	2.906 (1.237-6.825)	0.014
>481.82 (<i>n</i> =21)	61.9			

HR: Hazard ratio, CI: Confidence interval, MTVwb: Metabolic tumor volume whole-body, RMS: Root mean square

which in turn reflects the measure of heterogeneity in the area of interest. It actually facilitates in detecting features and patterns that otherwise would go unnoticed to the human eye. Many studies have shown significant role of tumor heterogeneity evaluated from texture analysis in differentiating benign from malignant tumors, prediction of prognosis, response assessment in various tumors.^[17,19,33-38] In the present study, IH based first-order mean, median, RMS, and GLCM-based second-order mean, autocorrelation, cluster prominence, cluster shade, sum average, sum variance were significant in the prediction of survival of NSCLC patients who underwent platinum-based chemotherapy. Among all these parameters, cluster prominence was the independent predictor of 1-year survival. Cluster Prominence is a measure of skewness and asymmetry of the GLCM which indirectly reflects the measure of heterogeneity in tumor. In our study sample the cluster prominence was higher in

patients with OS ≥1-year whereas, lesser in patients with OS <1-year.

A few studies have shown the prognostic value of texture parameters in disease control and survival in early-stage NSCLC patients treated with Stereotactic body radiation therapy (SBRT). Pyka *et al.* reported that entropy, correlation, and busyness were significant predictors for local recurrence and/or disease-specific survival.^[35] and Lovinousse *et al.* reported dissimilarity as the most significant predictor of disease-specific survival.^[19] Wu *et al.* reported that the combination of Gauss cluster shade and other known parameters improved the prediction for distant metastasis in 101 lung cancer patients.^[17] Oikonomou *et al.* quantify the contribution of radiomics and SUVmax at PET/CT to predict clinical outcomes in lung cancer patients treated with SBRT. Radiomics remained the only predictor of OS, disease-specific survival, and regional control.^[37]

Cook *et al.* studied the role of texture parameters. i.e. coarseness, contrast, busyness, and complexity in OS prediction of stage I, II, and III NSCLC who underwent radiotherapy and concurrent chemotherapy as first-line treatment. Coarseness came out as the most significant parameter for OS prediction.^[39]

Notable limitations of the study include the retrospective analysis of patient data and the small sample size. As the preliminary work done in the present study has given us promising results, so in future we will attempt to perform texture analysis as a prospective study with the large number of patients and will further validate the results of texture analysis so that they can be used routinely in the management of NSCLC patients.

Conclusion

Texture analysis based on F-18 FDG PET/CT is potentially beneficial in the prediction of OS ≥ 1 year in NSCLC patients undergoing platinum-based chemotherapy as first-line treatment. Thus, can be used to stratify the patients which will not be benefitted with platinum-based chemotherapy and essentially needs to undergo some other therapy option.

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Conflicts of interest

There are no conflicts of interest.

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