Translational Oncology
www.transonc.com

Volume 11 Number xx Month 2018 pp. 31–36 31

Diagnosis of Distant Metastasis of Lung Cancer: Based on Clinical and Radiomic Features

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Abstract

OBJECTIVES: To analyze the distant metastasis possibility based on computed tomography (CT) radiomic features in patients with lung cancer. *METHODS:* This was a retrospective analysis of 348 patients with lung cancer enrolled between 2014 and February 2015. A feature set containing clinical features and 485 radiomic features was extracted from the pretherapy CT images. Feature selection via concave minimization (FSV) was used to select effective features. A support vector machine (SVM) was used to evaluate the predictive ability of each feature. *RESULTS:* Four radiomic features and three clinical features were obtained by FSV feature selection. Classification accuracy by the proposed SVM with SGD method was 71.02%, and the area under the curve was 72.84% with only the radiomic features extracted from CT. After the addition of clinical features, 89.09% can be achieved. *CONCLUSION:* The radiomic features of the pretherapy CT images may be used as predictors of distant metastasis. And it also can be used in combination with the patient's gender and tumor T and N phase information to diagnose the possibility of distant metastasis in lung cancer.

Translational Oncology (2018) 11, 31–36

Introduction

Lung cancer is one of the most common malignant tumors with the highest morbidity and mortality, which is a considerable threat to people's health and life [1]. Advanced lung cancer is likely to metastasize, which may lead to corresponding symptoms in patients with great pain, and are even life-threatening. This phenomenon is referred to as the distant metastasis of lung cancer, which is represented by the M staging in the TNM staging system [2].

Metastatic tumors are very common in the later stages of cancer. The spread of metastasis may occur through blood or lymphatic vessels or both pathways. The most common sites of metastases are the lungs, liver, brain, and bone. Because of the metastasis of cancer cells to various parts of the body, treatment becomes more difficult, surgery is almost impossible, and in most cases, only wide-range radiation therapy or chemotherapy may be used to inhibit cancer cell growth [3].

Computed tomography (CT) imaging is a widely used method for the evaluation of tumor prognosis. Based on the analysis of the CT image of the tumor, the image texture feature description can be extracted.

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Received 14 September 2017; Revised 24 October 2017; Accepted 26 October 2017

1936-5233
https://doi.org/10.1016/j.tranon.2017.10.010

Doctors can diagnose the distant metastasis of the tumor using CT or positron emission tomography (PET)-CT of secondary tumors (metastatic tumors). Quantitative analysis has been employed to study the characteristics of various types of tumor metastases to predict the therapeutic effect [4,5]. The clinical features of these cases can be used to predict the survival time of patients [6,7]. However, there is lack of evidence regarding the prediction of distant metastasis based on the tumor. [8] In this paper, we employed radiomic methods to predict the possibility of distant metastasis of lung cancer based on the information of the tumor and the clinical features.

Radiomic refers to the comprehensive quantification of tumor phenotype using a large number of image features [9–12]. It is defined as the conversion of image data to higher dimensional space and the subsequent mining of these data for improved decision support [13]. The radiomic method has been widely used in diagnosis [14], such as survival analysis [15], or lymph node metastasis prediction [16].

Diagnosis based on radiomic features has been used in the literature [16–18], but for the analysis of the prediction of M stage tumors, it remains inadequate. The aim of our study was to analyze the possibility of tumor metastasis from two aspects: clinical features and radiomic features extracted by CT, to investigate the relationship between the two kinds of features and the occurrence of distant metastasis.

Materials and Methods

Patients

The study was approved by the West China Hospital, Sichuan University. Approximately 404 patients with lung cancer (enrolled from West China Hospital, Sichuan University) were enrolled in this study. These data include small cell carcinoma and non–small cell carcinoma patients; tumor histological subtypes include squamous cell carcinoma, adenocarcinoma, and small cell carcinoma. Patient data registration time ranged from 2014 to February 2015. Patients with missing data were excluded, and the remaining 348 data sets were used in the study. The demographic and tumor characteristics of all patients are summarized in Table 1. The study design was approved by the appropriate ethics review boards.

CT Images and Tumor Segmentation

Tumor segmentation and CT images were provided by the hospital (West China Hospital, Sichuan University). CT images were loaded into the ITK-SNAP software (version 2.2.0; www.itksnap.org) for three-dimensional manual segmentation. A radiologist with 8 years of experience with CT performed the tumor segmentations in all patients. The following parameters were used to obtain the CT images: collimator with 64 × 0.6 mm, voxel spacing 0.638672 × 0.638672 × 5 mm, and tube voltage of 100 kV. The tube current is calculated according to the individual's weight, height, and body mass index. The tube current was 220 mA for body mass index <25 kg/m^2 and 330 mA for body mass index >25 kg/m^2. The region of interest in the CT images can be extracted based on the segmentation.

Feature Extraction and Analysis

A complete lung cancer tumor radiomic features set included its volume, texture [19,20], and Gabor and wavelet features. According to a previous study [9], the 485 radiomic features could be divided into four groups based on the tumor's intensity, shape, texture, and wavelet. The first group's quantified tumor intensity characteristics were calculated from the histogram of tumor voxel intensity values by using first-order statistics. Group 2 consisted of features based on the shape of the tumor, such as volume, surface area, and sphericity. Group 3 was composed of intratumor texture features, using "gray-level nonuniformity" to measure intratumor heterogeneity. Group 4 included the calculated intensity and textural features from the wavelet decomposition of the original image. We used the gray-level co-occurrence matrix and gray-level run length matrix (GLRLM) features as used in the study [9], and added the Gabor descriptor (we use six different angles of Gabor function for convolution of the image to obtain the features) to represent it in

Table 1. Patient Demographics and Clinic Pathological Characteristics of the Training and Validation Set for the Metastasis Analysis

Demographic or Clinic pathological Characteristics			Training Set		Validation Set	
			Without Metastasis	Metastasis	Without Metastasis	Metastasis
Total			149	92	66	41
Gender, no. (%)	Male		105 (70.5)	59 (64.1)	45 (68.2)	22 (53.7)
	Female		44 (29.5)	33 (35.9)	21 (31.8)	19 (46.3)
Age (years), no. (%)	≤60		64 (43.0)	38 (41.3)	19 (28.8)	10 (24.4)
	>60		85 (57.0)	54 (58.7)	47 (71.2)	31 (75.6)
Smoking status	Smoker		82	41	34	16
Stage, no. (%)	I		46 (30.9)		19 (28.8)	
	II		32 (21.5)		11 (16.7)	
	III		71 (47.6)		36 (54.5)	
	IV			92 (1)		41 (1)
Histological subtype	Squamous cell carcinoma		75	30	31	2
	Adenocarcinoma		66	50	34	33
	Small cell carcinoma		12	8	1	6
TNM no. (%)	T	T1	33 (22.1)	1 (1.0)	10 (15.2)	2 (4.9)
		T2	61 (41.0)	31 (33.7)	28 (42.4)	11 (26.8)
		T3	29 (19.5)	11 (12.0)	12 (18.2)	7 (17.1)
		T4	26 (17.4)	49 (53.3)	16 (24.2)	21 (51.2)
	N	N0	73 (49.0)	11 (12.0)	31 (47.0)	1 (2.4)
		N1	21 (14.1)	3 (3.3)	8 (12.1)	5 (12.2)
		N2	48 (32.2)	54 (58.7)	18 (27.3)	27 (65.9)
		N3	7 (4.7)	24 (26.0)	9 (13.6)	8 (19.5)