Int J Clin Exp Med 2019;12(9):11859-11863
www.ijcem.com /ISSN:1940-5901/IJCEM0096309

Original Article

Value of whole-body diffusion weighted imaging in metastatic lung cancer

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Received April 29, 2019; Accepted July 11, 2019; Epub September 15, 2019; Published September 30, 2019

Abstract: Objective: The goal of this study was to compare the diagnostic value of whole-body diffusion-weighted imaging (WB-DWI) with computed tomography (CT) combined with magnetic resonance imaging (MRI) in metastatic lung cancer. Methods: A total of 76 patients with lung tumors treated in Qianfo Hill Hospital of Shandong Province from June 2011 to June 2016 were selected as subjects, and after admitted, they all received WB-DWI test, CT and MRI examination for the diagnosis of cancer metastasis, which were confirmed via pathologic examination or follow-up for at least 6-months. The detection rate, sensitivity, specificity, positive predictive value, negative predictive value and accuracy of these two methods and their combination were analyzed and compared. Results: Kappa test showed that there was low consistency between WB-DWI and CT/MRI (Kappa = 0.385). There were significant differences in sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy rate among WB-DWI, CT/MRI and WB-DWI combined with CT/MR in the diagnosis of metastatic tumor from lung cancer (all P<0.001). Conclusion: Compared with using CT and MRI only, WB-DWI was characterized by higher accuracy, convenience, and efficiency in diagnosis of tumor metastases, especially when combined with routine CT and MRI, which is worthy of clinical study and application.

Keywords: WB-DWI, CT scan, magnetic resonance imaging, lung cancer, metastases

Introduction

Lung cancer is a malignant tumor with a high incidence rate, which is an invisible killer that threatens the health and safety of human beings [1]. According to statistics, the incidence rate of lung cancer has been greatly increased since 2006 [2]. Lung cancer in late stage appears metastasis in the whole body, which bring great pain to the patient, even threaten their life. Therefore, accurate diagnosis of metastatic lesions in lung cancer patients is very important.

Computed tomography (CT) scan is the most common methods used for the diagnosis of tumor and metastatic lesion, which has relative higher density resolution and could provide high quality images, however, it has obvious limitations [3, 4]. For example, CT scan is easy to misdiagnosis for the lung cancer with enlarged posterior mediastinal lymph nodes and the intraluminal bronchial carcinoma. Magnetic resonance imaging (MRI) can provide more imaging parameters, thus to help the doctor make an accurate diagnosis. Studies have reported that compared with CT, MRI showed better accuracy, sensitivity, and specificity in the diagnosis. For example, Huang et al. and Xiao et al. found that MRI and CT had good application value in the diagnosis of lymph node metastasis and bone metastasis in lung cancer, respectively; Ohno et al. also reported the predictive capability of MRI and CT in lung cancer patients [5-7]. Moreover, MRI also has a high imaging resolution in the diagnosis of tumors in trachea, the central pulmonary vascular and para-lymph nodes, which can be used as an auxiliary technique for CT imaging [8]. However, according to some studies, if the patients already had metastatic lesions, the detection accuracy was limited by using CT and MRI, while whole-body diffusion-weighted imaging (WB-DWI) was a better choice [9-12].

WB-DWI, a type of whole-body imaging method, can reflect the changes of tissue structure and pathology at the cellular level, which is characterized by low cost and is radiation-free, showing a great potential in the diagnosis of tumor

lesions in the whole body [13]. A large number of animal experiments have shown that WB-DWI has a significant value in predicting tumor response to treatment [14]. Especially, WB-DWI is more sensitive in the diagnosis of adrenal, bone marrow, liver and brain parenchyma metastases [15]. Therefore, this study aimed investigate the application value of WB-DWI in the diagnosis of metastases from lung cancer by comparing with CT/MRI.

Materials and methods

Subjects

A total of 76 patients with lung cancer treated in Qianfo Hill Hospital of Shandong Province from June 2011 to June 2016 were selected in this study. There were 46 males and 30 females, with the average age of 53.7±11.4 and median body mass index of 23.19±9.45. After the patients were admitted to the hospital, they all received WB-DWI test and they underwent whole body MRI and CT examination within a week for the diagnosis of cancer metastasis, which were confirmed via pathologic examination or follow-up for 6-month at least. All objects signed the informed consent. The Ethics Committee of Qianfo Hill Hospital of Shandong Province approved our study.

Inclusion criteria: Patients with lung cancer, which was diagnosed via fiberoptic bronchoscopy or lung biopsy; patients aged under 70 years old.

Exclusion criteria: Patients had other types of tumors other than lung cancer; patients had contraindications of MRI, such as having cardiac pacemaker or claustrophobia; patients with mental disease, cognitive disorder and communication disorder.

WB-DWI

WB-DWI scanner was used for scanning, and the radio-frequency pulse generated by body coil was used for signal acquisition. The scan sequence was WB-DWI (TR 3, 900 ms, TE 101 ms, matrix 128*128, NEX 4, FOV 40 cm*40 cm, layer thickness of 6mm, interlayer spacing 0, and diffusion coefficient b value = 600). Subjects were allowed free breathing on a detection bench under the supine position scanning from head to knee. After scanning, the image was preliminarily superimposed and treated using SUB software, followed by data processing and 3D post-processing via the workstation [16].

MRI scan

After admission, all the patients received whole body routine axial, sagittal and coronal MRI scans using T1 weighted image (T1WI) and T2 weighted image (T2WI), or T2WI/STIR sequence. The suspicious lesions received contrast-enhanced MRI [17].

CT scan

All patients received whole body routine CT flat sweeping scan after admitted (layer thickness of 7.5 cm, 25.0 mA and 120.0 kV). The lung nodules found in examination were reconstructed in thin-slice with the thickness of about 1.25 cm, followed by enhanced scanning of suspicious lesions (layer thickness of 5.0 mm, 220.0 mA and 120.0 kV). After the scan reconstruction, the image information was sent to the workstation for surface reconstruction, thin-slice multi-planar reconstruction and volume reconstruction, etc. [18].

Statistical analysis

The images obtained via the two diagnostic methods were all read by senior physicians working for more than 5 years in Qianfo Hill Hospital of Shandong Province.

SPSS 17.0 statistical software was used for statistical analysis of all data in this study. Chi-square test was used for comparison of enumeration data which is presented as a percentage. Kappa test was used for the consistency analysis. The detection rate, sensitivity, specificity, positive predictive value, negative predictive value and accuracy of the two diagnostic methods were calculated by referring to the results of pathological measurement and follow-up. $P<0.05$ suggested that the difference was statistically significant between the two groups.

Results

Comparison of two diagnostic methods in different parts

Among the 76 enrolled patients, there were 354 suspected metastatic tumors. The results of pathology or follow-up showed that there were 302 metastatic tumors, which is the gold standard in the metastasis diagnosis. The WB-

Table 1. Sensitivity of metastatic tumors from lung cancer by WB-DWI

Location of metastasis	WB-DWI			Detection rate (%)
	True positive	False negative	False positive	
Bone	132	3	8	97.78
Lymph gland	64	6	5	91.42
Brain	35	2	4	95.59
Liver	21	1	1	95.45
Adrenal gland	32	1	0	96.96
Others	16	1	2	94.12
Total	288	14	20	95.36

Note: WB-DWI: whole body diffusion-weighted imaging.

Table 2. Sensitivity of metastatic tumors from lung cancer by CT/MRI

Location of metastasis	CT/MRI			Detection rate (%)
	True positive	False negative	False positive	
Bone	88	39	6	69.29
Lymph gland	34	36	17	48.57
Brain	21	19	3	52.50
Liver	14	11	1	56.00
Adrenal gland	11	14	1	44.00
Others	8	7	4	53.33
Total	176	126	32	58.27

Note: CT: computed tomography; MRI: magnetic resonance imaging.

Table 3. Detection rate of metastatic tumors from lung cancer by WB-WDI combined with CT/MRI

WB-DWI+CT/MRI	Gold Standard		Total
	+	-	
+	294	4	298
-	8	48	52
Total	302	52	354

Note: WB-DWI: whole body diffusion-weighted imaging; CT: computed tomography; MRI: magnetic resonance imaging.

DWI showed there were 298 areas with abnormal signal, while CT/MRI showed there were 208 areas with abnormal signal. The sensitivity of WB-DWI, CT/MRI, and WB-DWI combined with CT/MRI in bone, lymph gland, brain, liver, adrenal gland, and other organs are listed in **Tables 1**-**3**, respectively.

Comparisons of specificity, positive predictive value, negative predictive value and accuracy among three methods in the diagnosis of metastatic tumor from lung cancer

There were significant differences in sensitivity, specificity, accuracy, positive predictive value, and negative predictive value among the three methods, WB-WDI only, CT/MRI only, and WB-WDI combined CT/MRI, in the diagnosis of metastatic lung cancer (all $P<0.001$, **Table 4**). Kappa test showed that there was low consistency between WB-DWI and CT/MRI (Kappa = 0.385, **Table 5**).

Discussion

Brain, bone, and lymphatic nodes are common targets of metastases from lung cancer. About 20% of patients with small cell lung cancer have brain metastasis at the time of diagnosis, and the incidence of brain metastasis is as high as 80% [19]. Bone is the most common metastatic site of lung cancer, especially for small cell lung cancer and poorly differentiated non-small cell lung cancer, with an incidence of 30% to 70% [20]. This study also found that patients with lung cancer had higher metastatic rates in bone and brain than other parts, which is consistent with the previous reports. Particularly, in the early stage, bone metastasis from lung cancer does not have any clinical symptoms, and in the late stage, it mainly manifested as local pain and joint dysfunction, and the related respiratory symptoms are mild,

Table 4. Comparisons of sensitivity, specificity, accuracy, positive predictive value and negative predictive value among three methods in the diagnosis of metastatic lung cancer

Method	Sensitivity	Specificity	Accuracy	Positive predictive value	Negative predictive value
WB-DWI	95.36% (288/302)	84.62% (44/52)	93.78% (332/354)	97.30% (288/296)	64.70% (44/68)
CT/MRI	58.28% (176/302)	38.46% (20/52)	55.36% (196/354)	84.62% (176/208)	13.70% (20/146)
WB-DWI+CT/MRI	97.35% (294/302)	92.31% (48/52)	96.61% (342/354)	98.66% (294/298)	92.31% (48/52)
χ^2	35.32	43.56	253.8	53.59	116.3
P	<0.001	<0.001	<0.001	<0.001	<0.001

Note: WB-DWI: whole body diffusion-weighted imaging; CT: computed tomography; MRI: magnetic resonance imaging.

Table 5. Comparison between WB-DWI and CT/MRI in detection rate of metastatic tumors from lung cancer

CT/MRI	WB-DWI		Total	Kappa
	+	-		
+	176	32	208	0.385
-	112	34	146	
Total	288	66	354	

Note: WB-DWI: whole body diffusion-weighted imaging; CT: computed tomography; MRI: magnetic resonance imaging.

which leads to a high possibility of misdiagnosis [21]. Hence, it is necessary to apply a more sensitive, specific and accurate method to diagnose the metastatic lesion for cancer patients.

WB-DWI can diagnose patients with cancer more rapidly than CT or MRI technique, which is characterized by less time and better imaging effect [9]. Moreover, it measures the activity of water molecules inside the human body, so it will not cause radiation damage to the patient's body, significantly reducing the incidence rate of complications and improving the safety [10]. Most importantly, WB-DWI is less expensive without causing financial stress to the patients, which is more effective and cost-effective [11, 12]. The results also confirmed the advantages of WB-WDI.

This study reports that the sensitivity of WB-DWI is higher than CT/MRI. Additionally, the specificity, positive predictive value, negative predictive value, and diagnostic accuracy were all significantly higher than CT/MRI. Wang J found that WB-DWI had the advantages of short time-consuming, low cost, high efficiency in the clinical tumor lesion diagnosis; they recruited 16 malignant tumor patients who had systemic metastases and 16 healthy volunteers and these subjects all received WB-DWI. Finally, they found that the WB-DBI could discover all the tumor lesions and metastatic lymph nodes [14]. Wang et al. also reported that WB-DWI had good value in the diagnosis of bone metastatic tumor, which is more sensitive in the detection of lumbar, sacral, pelvic, rib and femur lesions than radionuclide bone imaging (87.50% vs. 63.89%) [15]. All these reports are in accordance with our findings.

Although WB-DWI has defects such as lower spatial resolution and unclear anatomical location, it can solve the above problems combined with other diagnostic methods. In this study, when WB-DWI combined with CT/MRI, the sensitivity, specificity, positive predictive value, negative predictive value and accuracy were obviously improved. Moreover, this diagnostic technique is still in constant development and improvement, so it will certainly play a greater role in the diagnosis and treatment of patients with malignant tumors in the future.

In conclusion, WB-DWI is characterized by high accuracy, convenience, and efficiency in diagnosis of tumor metastases, especially when combined with routine CT and MRI, which is worthy of additional clinical development.

Disclosure of conflict of interest

None.

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