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Research Article

Detection of Hepatic Metastases by 18F-FDG PET/CT and MRI

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Abstract

Objectives: The purpose of this study was to evaluate the performance of 18F-fluorodeoxy-glucose positron emission tomography / computed tomography (18F-FDG PET/CT) and magnetic resonance imaging (MRI) in the detection of hepatic metastases.

Methods: Fifteen patients harboring an extrahepatic primary malignancy, with suspected hepatic metastases on clinico-radiological examination were enrolled prospectively. Each patient underwent contrast-enhanced and diffusion weighted MRI and 18F-FDG PET/CT within 10 days of each other, reported by an experienced radiologist and nuclear medicine specialist, respectively in a blinded manner. MRI and PET-CT findings were compared and analyzed. Final diagnosis was based on histology and/or follow-up (ranging from 6 to 12 months).

Results: The sensitivity, specificity and accuracy of PET/CT in the detection of hepatic metastasis was 90.3%, 85.7% and 89.8% respectively, whereas that of MRI was 100%, 85.7% and 98.5% respectively. The improved performance of MRI was largely owing to its ability to detect lesions less than 1 cm in size.

Conclusion: MRI appears to be superior to 18F-FDG PET/CT in the detection of hepatic metastases from primary neoplasm. It may therefore be worthwhile to consider the use of MRI in cases wherein metastasis to the liver is suspected.

Key Words: 18F-FDG PET/CT; Contrast enhanced MRI; Diffusion weighted MRI; hepatic metastases

Introduction

The liver is the most common site of haematogenous metastatic spread. Liver metastases are 18-40 times more common than primary liver cancer [1]. Although metastases to the liver result from a variety of primary neoplasm, the commonest primaries arise from colorectal, bronchogenic, breast, pancreatic cancers and melanomas [2,3]. The presence of hepatic metastasis often significantly alters treatment plan; hence accurate diagnosis is a vital pre-requisite to appropriate management. MRI is generally regarded as an excellent modality for imaging of the liver. Dynamic contrast enhanced MRI (CEMR) of the liver is a vital part of the imaging protocol due to its high diagnostic accuracy. Given the distinctive liver physiology and its dual blood supply, dynamic CEMR can narrow the differential diagnosis and helps in the detection of more lesions. Diffusion weighted (DW) MR imaging assesses in vivo changes in random motion of protons in water and can contribute to accurate diagnosis and discrimination between benign and malignant hepatic masses. Overall, FDG PET has an excellent detection rate for liver metastases. Liver metastases are generally FDG avid and therefore are detected easily by FDG PET. So there is a need to investigate further the role of contrast enhanced MRI and DW (diffusion weighted) MRI in evaluation of metastatic disease and to compare the same with FDG-PET/CT.

Methodology

15 cases suspected to have hepatic metastases, based on clinico-radiological findings were enrolled for this prospective study. All cases had discrete focal lesions in the liver, suspected to be metastases on other (non-MRI) imaging modalities. All patients subsequently underwent both18F-FDG PET/CT and MRI (in either order), within 10 days of each other. None of the patients

had undergone prior therapy for hepatic metastases. The patients were subjected to histopathological confirmation of diagnosis, on at least one lesion. They were followed up for a period extending from 2 to 12 months. Patients with underlying hepatic parenchymal disease were excluded from the study. Other exclusion criteria were inability to sustain a breath-hold, presence of ferromagnetic implants in situ, claustrophobia, pregnancy, lactation and uncontrolled diabetes. Written informed consent was taken from all patients. The institutional board approved of the study.

Image acquisition

MRI data was collected on a Siemens Skyra 3.0T scanner with a torso phased-array coil. A 22-gauge IV catheter was placed in an arm vein and attached to an MRI-compatible power injector. (Medrad, Spectris Solaris EP). Routine MR Sequences were first performed. This included a single shot fast spin echo T2-weighted sequence, HASTE (TR-1400, TE-91, Slice thickness-5mm, No. of slices-30, FOV-400X400,Matrix-320X320, Matrix Pulse Bandwidth- 710Hz,No. of averages-1) in the axial and coronal plane. This was followed by a fast spin echo fat-saturated T2 weighted sequence in the axial plane. Diffusion-weighted magnetic resonance imaging was then performed with b-factors of 50, 400 and 800 s/mm2 using a single-shot spin-echo echo-planar sequence with chemical shift selective fat-suppression technique (TR-1900, TE-50, Slice thickness-5mm, FOV-285X380, Matrix-78X128, Matrix Pulse Bandwidth-2442). DWI was followed by multiphase dynamic contrast- enhanced imaging with 3D spoiled gradient-echo sequences in the arterial, portal venous and equilibrium phases. The volumetric interpolated breath-hold examination (VIBE), a 3D spoiled gradient-echo sequence was used for dynamic contrast imaging (TR-4.58, TE-1.32, No. of averages-1, Slab-1, No. of slices per slab-64, FOV-297X380, Matrix-188X320, Bandwidth-980, Breath-hold time 24 sec) in axial and coronal sections. Before this, a pre-contrast VIBE was done in axial sections (TR-4.30, TE-1.89, Slab-1, No. of slices per slab-60, FOV-273X380, Matrix-173X320, and No. of averages-1).

PET/CT data was collected using an 18F-FDG PET CT scan performed on a whole body full ring PET/CT camera (Discovery STE 16, GE). 370 MBq of 18F-FDG was administered intravenously. Patients were made to rest in a dimly lit room for an hour after administration. A low-dose non-contrast CT scan was then performed, followed by the PET acquisition. Images were reconstructed by 3D VUE algorithm (GE) and viewed on a Xeleris workstation (GE) using the volumetric protocol.

Results

Of the 15 patients (6 males, 9 females; age range 49-78 years) included in this study, the primary site of involvement was breast (six cases), colorectal (five cases), bronchogenic (two cases), esophageal (one case) and unknown primary (one case) (Table 1). A total of 69 hepatic lesions were detected, of which 62 were metastatic based on histology and/or follow-up. All 15 patients underwent chemotherapy after the initial imaging studies were undertaken. Of these, 8 patients showed a good response to chemotherapy, with diminution in size or disappearance of the lesions, thereby confirming the fact that they were indeed metastatic. In 3 cases, there was progression of lesions, both in size and number. The new lesions were similar in morphology to the previous ones. 3 cases succumbed to the disease during the follow-up period. The remaining 2 patients were lost to follow-up.

The sensitivity, specificity and accuracy of PET/CT in the detection of hepatic metastasis was 90.3%, 85.7% and 89.8% respectively, whereas that of MRI was 100%, 85.7% and 98.5% respectively (Table 2,3).

S. No.	Primary Site	PET/CT (number of metastases, mean SUV max)	MRI (number of metastases)
1	Breast	Solitary (5.1)	Solitary
2	Colorectal	Multiple (2, 6.5)	Multiple (2)
3	Breast	Multiple (6, 9.1)	Multiple (7)
4	Breast	Multiple (3, 5.6)	Multiple (3)
5	Esophagus	Multiple (4, 7.2)	Multiple (4)
6	Bronchogenic	Solitary (4.9)	Solitary
7	Breast	Multiple (3, 5.8)	Multiple (3)
8	Unknown	Solitary (6.2)	Solitary
9	Colorectal	Multiple (4, 6.4)	Multiple (4)
10	Breast	Solitary (5.2)	Solitary
11	Colorectal	Multiple (7, 7.5)	Multiple (8)
12	Colorectal	Solitary (5.8)	Solitary
13	Bronchogenic	Multiple (19, 8.1)	Multiple (23)
14	Breast	Multiple (2, 7.9)	Multiple (2)
15	Colorectal	Solitary (5.8)	Solitary

Table 1: Hepatic metastases in patients evaluated with PET/CT and MRI

PET/CT Result	Metastases present	Metastases absent
Positive	56 (True positive)	01 (False positive)
Negative	06 (False negative)	06 (True negative)

Table 2: PET/CT findings in hepatic metastases

MRI Result	Metastases present	Metastases absent
Positive	62 (True positive)	01 (False positive)
Negative	0 (False negative)	06 (True negative)

Table 3: MRI findings in hepatic metastases

In the diagnosis of hepatic metastases, PET/CT and MRI were concordant in 10 (66.6 %) cases. The findings on these imaging modalities have been summarized in Table 1. In 3 cases, MRI picked up more metastatic lesions (both on DWI and on contrast enhanced MRI) as compared to PET/CT (Figure 1 and 2). In all 3 cases, the lesions missed on PET/CT measured less than 10 mm in size. One case had a PET positive lesion which later proved to be an abscess cavity. This was correctly characterized as an abscess on MR. In another case, MR depicted a small (subcentimeter size) lesion, which could not be conclusively characterized, hence possibility of metastases could not be excluded. This lesion was negative on the PET scan, appeared hyperechoic on ultrasound and remained unchanged on follow-up study at 9 months, thus pointing towards a small haemangioma.

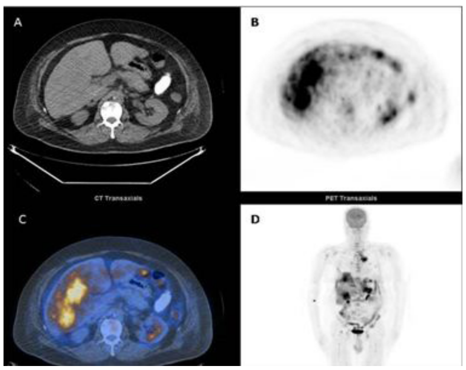

Figure 1: PET/CT of 56 year old male with bronchogenic carcinoma. Non-contrast CT scan (a) shows areas of subtle hypo density. Multiple hepatic metastases seen on PET image (b), fused PET/CT image (c) and MIP image (d)

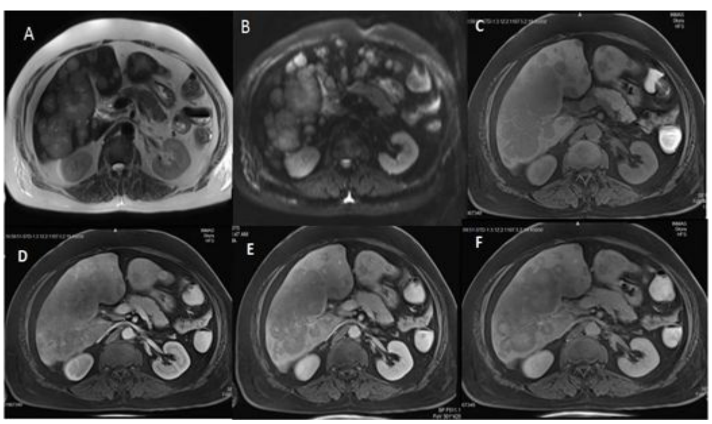

Figure 2: MRI of 56 year old male with bronchogenic carcinoma shows multiple hepatic metastases on (a) HASTE (half-Fourier acquisition single shot turbo spin echo), (b) DW (diffusion weighted) images, (c) non-contrast VIBE (volumetric interpolated breath-hold examination), (d) arterial phase, (e) portal venous phase and (f) interstitial phase contrast-enhanced images

Discussion

The liver is the most common site for metastatic disease. An accurate staging and thorough tumour surveillance are essential in patients with neoplastic disease to assess prognosis and to decide the most appropriate therapeutic options. A variety of imaging techniques have been employed in the diagnosis of hepatic metastases, notably ultrasonography, CT, MRI, SPECT and PET/CT. Choosing an imaging modality with the highest sensitivity at an acceptable rate of specificity is of the utmost importance.

Several studies addressing different tumour entities have suggested an advantage of PET/CT over morphological procedures alone. There is an increasing amount of evidence of the incremental value of PET/CT in a multitude of solid tumours [4]. Many studies have been conducted on the impact of FDG PET/CT in the evaluation of hepatic metastases, especially from colorectal primary. In recent years, MRI has been widely acclaimed as an excellent modality for detection and characterization of hepatic masses. It is playing an increasingly important role in the evaluation of patients with liver disease because of its high contrast resolution, lack of ionizing radiation, and the possibility of performing functional imaging sequences. The use of dynamic contrast enhanced MRI with images acquired in three phases following contrast administration: a predominant arterial (or late arterial) phase, portal phase, and a delayed (equilibrium) phase, is a very useful tool in lesion characterization. DW MR imaging is an attractive technique for multiple reasons: it can potentially add useful qualitative and quantitative information to conventional imaging sequences; it is quick (performed within a breath hold) and it is a non enhanced technique (performed without the use of gadolinium-based contrast media). DW MR imaging represents a new functional tool for the characterization of liver metastases, which can contribute to accurate diagnosis and discrimination between benign and malignant hepatic masses. It is based on the randomized microscopic movement of water molecules within the tissue. DW MR imaging of the liver offers functional and even quantitative information about hepatic tissue that can be used in conjunction with other MRI sequences to enhance the diagnosis of metastases, aid in treatment planning, and assess treatment success and recurrence. There is a need to determine the role of 18F- FDG PET/CT in comparison to contrast enhanced MRI and DW MRI in the evaluation of metastatic disease.

FDG PET/CT has been shown to be very accurate and sensitive in the detection of liver metastases derived from a wide range of primary cancers. Colorectal carcinoma (CRC) is the most common cause for hepatic metastases. Therefore, a majority of studies evaluate the value of 18F-FDG-PET in the detection of hepatic metastases from CRC. The sensitivity and specificity of PET for detection of hepatic metastases from CRC have been found to be 88-96% and 75-96% respectively [5,6]. Similarly, Lai et al [7] found a high sensitivity (29/31 lesions [94%]) of FDG PET for detecting hepatic metastases. The findings of the present study are also in conformity with these studies, wherein a high sensitivity of 90.3 % and specificity of 85.7 % was found on PET/CT. PET/CT has been found superior to contrast-enhanced CT in the detection of untreated hepatic metastases in a prospective study evaluating 45 patients with suspected liver metastases from various primary cancers [8].

In a prospective comparison of contrast enhanced ultrasound, contrast enhanced CT, PET/CT, and contrast enhanced MRI for the detection of hepatic metastases from colorectal cancer, it was observed that contrast enhanced MRI appeared to be the most accurate modality [9]. Several meta-analyses have been published in the literature pertaining to the performance of PET vis-à-vis other imaging modalities in the detection of hepatic metastases. FDG PET was found to be the most sensitive (90–94.6%) imaging modality in the diagnosis of liver metastases [10-12]. FDG PET outperformed other imaging techniques, with a reported sensitivity of 94.6% compared to 60.2% for non helical CT, 64.7% for helical CT (n = 621) and 75.8% for 1.5-T MRI [11].

The use of FDG PET/CT has been stated to have a significant impact on the staging and selection of candidates for liver metastasis resection, based on the fact that it resulted in restaging and a change in therapy in 12 of 43 patients (28%) of patients with known solitary liver metastasis from various primaries [13]. Another study demonstrated a change in clinical management in 31.6% of patients suspected to have hepatic metastases from colorectal cancer, most commonly by upstaging [6]. Based on the additional value of PET/CT, routinely performing PET/CT in all patients being evaluated for liver resection for metastatic colorectal cancer has been recommended by some authors [14].

Despite the fact that higher sensitivity of FDG-PET (94.1%) for detecting hepatic metastases from colorectal carcinoma, as compared to MR (88.2%) and CT (83.6%) has been demonstrated in several meta-analysis [12], nevertheless for lesions smaller than 10mm in diameter, the sensitivity of FDG PET was found to be lower [15,16]. Other studies have also shown the accuracy of PET to be limited in the detection of hepatic metastases smaller than 10mm [17,18]. In a landmark meta-analysis of thirty-nine articles (3391 patients included) published from January 1990 to January 2010, Niekel et al [12] ascertained that on a per-patient basis, the pooled sensitivities of CT, MR imaging, and FDG PET were 83.6%, 88.2%, and 94.1%, respectively. The sensitivity of MR imaging increased significantly after January 2004 in this meta-analysis. For lesions smaller than 10 mm, the sensitivity estimates for MR imaging were definitely higher. The authors concluded that MR imaging is the preferred first-line modality for evaluating hepatic metastases as it has a high detection rate, even for lesions smaller than 10 mm. In patients requiring further work-up, FDG PET can be used as a second-line modality because both sensitivity and specificity were high and FDG PET plays a role in detecting extrahepatic disease.

A recent study using contrast enhanced MRI on a 3-T system as well as contrast enhanced PET/CT, found a superior performance of the former modality, especially for the detection of small (≤1.0 cm) lesions [19]. Patient-based analysis revealed that MRI had a higher sensitivity and negative predictive value than contrast enhanced PET/CT. The sensitivity, specificity, positive predictive values, and negative predictive value on a patient basis were 100%, 71%, 97%, and 100% for MRI and 93%, 71%, 97%, and 57% for contrast enhanced PET/CT, respectively. Another multimodality study which compared the diagnostic performance of MDCT, PET/CT and contrast- enhanced MRI in patients with colorectal liver metastases being considered for hepatic resection, also demonstrated the superior performance of MRI with a sensitivity of 96% and PPV 0.91 [20]. The results of our study are in concordance with previous studies with the sensitivity, specificity and accuracy of PET/CT at 90.3%, 85.7% and 89.8% respectively, whereas that of MRI was 100%, 85.7% and 98.5% respectively. Another study which assessed the diagnostic accuracy of diffusion weighted MRI to FDG PET/CT in the assessment of early response of liver metastases to Y-90 radioembolization, found the former to have a superior diagnostic performance [21].

The incorporation of PET/MRI in the diagnostic arena is believed to offer a significant advantage over the use of either modality in isolation. Recent studies have shown that PET/MRI provides higher lesion conspicuity and diagnostic confidence compared to PET/CT and should be considered the procedure of choice in the detection of liver metastatic lesions from colorectal cancer [22,23]. However, bearing in mind the limited availability and affordability of PET/MRI, the other available modalities, namely MRI and PET/CT should be wisely and judiciously used to optimize diagnostic performance.

Conclusion

MRI appears to be superior to 18F-FDG PET/CT in the detection of hepatic metastases from primary neoplasm. It may therefore be worthwhile to consider the use of MRI in cases wherein metastasis to the liver is suspected.

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