The role of ^{18}F-FDG PET/CT predicting microvascular tumor invasion in patients with hepatocellular carcinoma

PET/CT and hepatocelular carcinoma

Hikmet Aktas

Acibadem Bursa Hospital, Department of Organ Transplantation, Bursa, Turkey

Abstract

Aim: Microvascular tumor invasion is one of the significant factors affecting recurrence risk following liver transplantation in patients with hepatocellular carcinoma. However, detecting the presence of microvascular invasion with tumor biopsy or radiological methods is troublesome before transplantation. The present study aims to determine the predictive value of ^{18}F-FDG PET/CT for microvascular invasion.

Materials and Methods: Between August 2012 and January 2018, 118 patients with HCC underwent liver transplantation. Data were collected retrospectively. Sixteen patients who have no PET/CT and/or whose follow-up time was less than one year were excluded from the study. The clinical characteristics of patients, the uptake analysis of PET/CT, the presence of microvascular invasion in pathological examination after surgery were main variables. The association between preoperative PET/CT examination and microvascular invasion were evaluated.

Results: Sixty patients (58,8%) had microvascular invasion (MVI) and 84 patients (82,3%) significant ^{18}F-FDG uptake on PET/CT. Of 84 patients with significant ^{18}F-FDG uptake, 47 patients had MVI (56%) and 37 patients had no MVI (44%). Besides that, 13 patients with MVI had negative ^{18}F-FDG uptake. There was no statistical relationship between ^{18}F-FDG uptake and the presence of MVI (p = 0.2).

Discussion: ^{18}F-FDG uptake on PET/CT is not sufficient alone to predict MVI in patients with HCC before liver transplantation.

Keywords

Liver Transplantation; Hepatocellular Carcinoma; ^{18}F-fluorodeoxyglucose; Microvascular Invasion

Introduction

Liver transplantation (LT) became a standard treatment for patients with hepatocellular carcinoma (HCC) in liver cirrhosis. In last decade, it is shown that the biological features of HCC have more effect on postoperative outcomes compared to the macromorphological characteristics. Thus, the studies are focused on searching for tools to determine biological features before surgery [1,2].

The existence of microvascular invasion (MVI) has significant influence on recurrence of HCC following LT. Therefore, determining the presence of MVI of tumor is very important. As well known, the role of biopsy is restricted in HCC. In this retrospective study, we report the predictive role of ^{18}F-FDG uptake on PET/CT defining the MVI.

Material and Methods

The design of the study was retrospective in its nature. It was approved by the local ethics committee with protocol number 2018-17/4. We performed 118 LTs for HCC between May 2012 and June 2018 at our institution. The patients were reviewed on a retrospective basis, and the characteristics of the patients were recorded. Postoperative pathological features and preoperative PET/CT results were investigated. The association between ^{18}F-FDG uptake on PET/CT and the presence of MVI was evaluated.

Computerized tomography angiography and magnetic resonance angiography were used to evaluate tumour features and any macrovascular invasions. PET/CT imaging has been established to asses metastases of HCC.

Unfortunately, we could not obtain the PET/CT results of 16 patients and therefore 102 patients were enrolled in the study. Statistical Analysis

Comparisons were analyzed using the Chi-square test for categorical variables. A p-value of $p<0.05$ was considered statistically significant in all analyses.

Results

Ninety patients were male (88.2%) and 12 patients were female (11.8%). The mean age was 57.1±8.2 years. According to final pathology findings, 60 patients had MVI (58.8%) and 42 patients had no MVI (41.2%). In regard to PET/CT results, SUVmax greater than 5 was accepted positive. The tumor has not ^{18}F-FDG uptake on PET/CT in 18 patients (17.6%) and PET/CT were positive in 84 patients (82.4%).

The statistical analysis of relationship between the presence of MVI and PET/CT examination was not significant (Table 1).

Table 1. Association between microvascular invasion and PET/CT

microvascular invasion	^{18}F-FDG uptake on PET/CT		
	positive	negative	
existent	47	13	60 (58.8%)
nonexistent	37	5	42 (41.2%)
	84 (82.4%)	18 (17.6%)	
Chi-squared test: p=0.2, not significant			

Discussion

Microvascular invasion on explant pathology has been recognized as the gold standard to predict poor outcome following LT. Unfortunately, the biopsy has a limited role depending on biological structure of HCC and the risk of tumor seeding is still a problem. The mechanism of PET/CT is mainly based on estimating the glucose metabolism of tumor cells. However, HCC shows various feature and the sensitivity is PET/CT relative low. Nevertheless, there are remarkable studies in the literature pointing the role of PET/CT to define MVI in patients with HCC who underwent LT. However, these studies were based on experiences with small sample size. Besides, there is a wide range of sensitivity, specificity, positive predictive value and negative predictive value for MVI [3,4,5].

Kornberg et al. [3] reported high positive and negative predictive values (87.5%, 88.5%) with 88.1% accuarcy value. In spite of that, Hsu et al. [6] reported low positive and negative predictive values (56.7%, 66.7%) with 64.6% accuarcy value. Our results demonstrated that positive and negative predictive values for PET/CT are 57.1% and 26.8%, respectively. It is clear that the negative and positive predictive values of PET/CT for MVI are heterogeneous.

This heterogeneity prompted researchers to determine another predictive tool. Some studies have focused on hybrid criteria combining PET/CT with another parameter like alpha-fetoprotein level [7,8]. It seems that using combine parameters has more prognostic value for determining MVI.

It is clear that PET/CT is helpful to identify patients with poor prognosis following LT. However, the current PET/CT technique is not sufficient alone to establish MVI. Novel PET/CT methods paying regard to biological features of HCC might be more forceful.

Conclusion

This study demonstrated that PET/CT alone has no predictive value to determine MVI in HCC patients. It might be useful to use more than one tool for determining MVI which is clearly an independent risk factor for recurrence of HCC.

References
1. Mehta N, Dodge JL, Roberts JP, Yao FY. Validation of the prognostic power of the RETREAT score for hepatocellular carcinoma recurrence using the UNOS database. Am J Transplant. 2018;18(5):1206-13.
2. Ahn SY, Lee JM, Joo I, Lee ES, Lee SJ, Cheon GJ, et al. Prediction of microvascular invasion of hepatocellular carcinoma using gadoxetic acid-enhanced MR and (18) F-FDG PET/CT. Abdom Imaging. 2015;40(4):843-51.
3. Kornberg A, Freesmeyer M, Bärthel E, Jandt K, Katenkamp K, Steenbeck J, et al. 18F-FDG-uptake of hepatocellular carcinoma on PET predicts microvascular tumor invasion in liver transplant patients. Am J Transplant. 2009;9(3):592-600.

4. Lin CY, Liao CW, Chu LY, Yen KY, Jeng LB, Hsu CN, et al. Predictive Value of 18F-FDG PET/CT for Vascular Invasion in Patients With Hepatocellular Carcinoma Before Liver Transplantation. Clin Nucl Med. 2017;42(4):e183-7.

5. Lee JW, Paeng JC, Kang KW, Kwon HW, Suh KS, Chung JK, et al. Prediction of tumor recurrence by 18F-FDG PET in liver transplantation for hepatocellular carcinoma. J Nucl Med. 2009;50(5):682-7.

6. Hsu CC, Chen CL, Wang CC, Lin CC, Yong CC, Wang SH, et al. Combination of FDG-PET and UCSF criteria for predicting HCC recurrence after living donor liver transplantation. Transplantation. 2016;100:1925–32.

7. Hong G, Suh KS, Suh SW, Yoo T, Kim H, Park MS, et al. Alpha-fetoprotein and (18)F-FDG positron emission tomography predict tumor recurrence better than Milan criteria in living donor liver transplantation. J Hepatol. 2016;64:852–9.

8. Takada Y, Kaido T, Shirabe K, Nagano H, Egawa H, Sugawara Y, et al. Significance of preoperative fluorodeoxyglucose-positron emission tomography in prediction of tumor recurrence after liver transplantation for hepatocellular carcinoma patients: a Japanese multicenter study. J Hepatobiliary Pancreat Sci. 2017;24(1):49-57.