Prediction of Posttransplantation Recurrence of Hepatocellular Carcinoma Using Metabolic and Volumetric Indices of ^{18}F-FDG PET/CT

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^{18}F-FDG PET is an effective method of predicting recurrence of hepatocellular carcinoma (HCC) after liver transplantation. We compared recently introduced metabolic and volumetric ^{18}F-FDG PET/CT indices with the current clinicopathologic predictors for ability to predict recurrence. **Methods:** In total, 110 HCC patients who underwent ^{18}F-FDG PET and liver transplantation were enrolled. On PET, SUVs and tumor-to-background ratios (TBRs) were measured as metabolic activity indices. Various metabolic tumor volumes and uptake-volume products (UVP) were also measured as volumetric indices. The ability of these indices and other clinicopathologic factors to predict recurrence was compared. **Results:** All metabolic and volumetric indices were significant for recurrence prediction on receiver-operating-characteristic curve analyses ($P < 0.001$). On univariate survival analyses, all PET indices—as well as tumor size, tumor number, the Milan criteria, tumor grade, vascular invasion, and T-stage—were significant factors. However, on multivariate analyses, tumor size, tumor grade, maximum TBR, and UVP calculated by inferior vena cava activity were significant factors ($P = 0.004$, 0.014, 0.009, and 0.021, respectively). When the Milan criteria and PET factors were included in the multivariate analysis, the Milan criteria ($P = 0.029$), maximum TBR ($P < 0.001$), and UVP ($P = 0.016$) were significant. **Conclusion:** Volumetric and metabolic activity indices of ^{18}F-FDG PET are effective predictors of posttransplantation HCC recurrence. In addition to clinicopathologic factors, these indices need to be considered in the selection of candidates for liver transplantation.

Key Words: hepatocellular carcinoma; liver transplantation; positron emission tomography; recurrence; metabolic tumor volume

J Nucl Med 2016; 57:1045–1051
DOI: 10.2967/jnumed.115.170076

Liver transplantation is the best option for radical treatment of early but unresectable hepatocellular carcinoma (HCC), particularly in the setting of liver cirrhosis (*1,2*). However, HCC recurs after liver transplantation in approximately 20%–30% of patients, and recurrence is difficult to treat and is the rate-limiting factor for long-term survival (*3–5*). For prediction of HCC recurrence and selection of appropriate candidates for liver transplantation, the Milan criteria, which consider size and number of tumors, have performed well (*6*), and some other pathologic factors also have been shown to be significant prognostic factors for posttransplantation recurrence (*7,8*). However, exact assessment of the Milan criteria and pathologic factors is not possible before liver transplantation, and thus, use of other laboratory tests or radiologic factors for selecting candidates has been attempted (*8,9*).

Currently, PET/CT using ^{18}F-FDG is widely applied in oncologic clinical practice. With regard to HCC, PET/CT is effective in initial staging, prediction of treatment response, and detection of recurrence (*10–12*). Additionally, PET/CT has been reported to be effective in predicting posttransplantation recurrence using visual analysis or semiquantitative indices such as SUV or tumor-to-background ratio (TBR) (*13,14*).

In recent years, the use of volumetric indices in PET/CT has been increasing because they can reflect tumor burden as well as metabolic activity. Metabolic tumor volume (MTV) and total lesion uptake on PET/CT are effective indices, particularly in terms of prognosis prediction and treatment response monitoring (*15–18*). These volumetric indices are also expected to be effective in recurrence prediction after liver transplantation for HCC, because the indices consider tumor burden. However, to our knowledge, use of volumetric indices has not been attempted for prediction of HCC recurrence after liver transplantation.

In this study, we investigated the prognostic value of volumetric indices of PET/CT in predicting posttransplantation recurrence of HCC. Various methods of using volumetric indices were tested to determine those that are optimal, and their prognostic value was compared with that of clinicopathologic factors.

MATERIALS AND METHODS

Patients

From April 2008 to November 2012, liver transplantation was performed on 249 consecutive patients at our institution. Those patients who underwent liver transplantation because of HCC were

Received Nov. 18, 2015; revision accepted Feb. 2, 2016.
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Published online Mar. 16, 2016.

retrospectively enrolled in this study with the following inclusion criteria; pathologically confirmed HCC before liver transplantation, ^{18}F-FDG PET/CT performed within 4 mo before liver transplantation, and follow-up more than 24 mo after liver transplantation in cases of nonrecurrence. At our institution, candidates for liver transplantation are selected on the basis of the Milan criteria. However, liver transplantation is also performed when the Milan criteria are not met if a patient strongly desires transplantation from a living donor and there is neither major vascular invasion nor extrahepatic metastasis. Patients are routinely followed up using contrast-enhanced CT every 3 mo during the first year after liver transplantation and every 6 mo thereafter. MRI is complementarily used in some cases. Serum α-fetoprotein level is measured every 2–3 mo. Additional imaging studies are performed when the level is increased or other suggestive symptoms or signs appear. Recurrence of a lesion is confirmed by follow-up imaging studies.

The study design was approved, and the need for informed consent waived, by our Institutional Review Board (H-1508-030-696).

^{18}F-FDG PET/CT and Image Analysis

^{18}F-FDG (5.18 MBq/kg) was injected intravenously after the patient had fasted for at least 6 h, and imaging was performed 1 h later using a PET/CT scanner (Biograph 40 TruePoint; Siemens Healthcare) with an imaging resolution of 0.4 mm for CT and 4.2 mm for PET. CT images were acquired from the skull base to the upper thigh for creation of an attenuation map and localization of lesions (50 mA, 120 kVp, 5-mm section width). After the CT scan, PET images of the same area were acquired in 3-dimensional mode at 6–7 bed positions. Images were reconstructed on 128 × 128 matrices using an iterative algorithm and analyzed using a dedicated workstation and software (Syngo.via; Siemens Healthcare).

The images were visually analyzed first by two experienced image specialists working in consensus; the patient's HCC was classified as hypermetabolic (discernible from the background liver) or nonhypermetabolic (not discernible from the background liver). For quantitative analysis of the PET images, SUV was measured. Additionally, TBR—defined as the ratio between the maximum SUV of a target lesion and background tissue—was calculated, adopting the inferior vena cava (IVC) or normal liver as the background tissue. Cylindric volumes of interest (VOIs; 1 cm^3) were drawn on 3 levels of the abdominal IVC, and SUV_{mean} was measured. Spheric VOIs (20 cm^3) were drawn on 3 sites of normal liver, and SUV_{mean} was measured (Fig. 1). TBRs calculated using IVC activity and normal-liver activity were defined as TBR_{IVC} and TBR_{NL}, respectively. For tumor lesions, SUV_{max} and TBR_{max} (TBR_{IVCmax} or TBR_{NLmax}) were measured as indices of metabolic activity.

MTV and uptake–volume product (UVP), indices of metabolic tumor burden, were measured from tumor VOIs defined by isoactivity contours. A spheric VOI was manually drawn with reference to the enhanced CT images to include the entire lesion, and an isoactivity contour was automatically drawn by setting a certain margin threshold around the lesion. Two margin thresholds were adopted on the basis of a pilot study (Supplemental Table 1, available at http://jnm.snmjournals.org): TBR_{IVC} 2.0 and TBR_{NL} 1.5. In a tumor VOI, MTV was defined as the volume (cm^3), and UVP was defined as the product of TBR_{mean} and MTV. Values that were measured using thresholds for TBR_{IVC} were defined as MTV_{IVC} and UVP_{IVC}, and those measured using thresholds for TBR_{NL} were defined as MTV_{NL} and UVP_{NL}.

Clinicopathologic Factors and Statistical Analysis

Clinicopathologic information was obtained from medical record review. Sex, age, pretransplantation α-fetoprotein level, viral infection status, and donor type were analyzed as clinical factors. The Milan criteria, tumor size (the largest diameter, in cm), tumor number, necrotic portion of tumors (%), tumor grade, vascular invasion, and T-stage were analyzed as pathologic factors.

Clinicopathologic factors and image indices were compared between the recurrence and nonrecurrence groups using the χ^2 test for categoric data, the Student t test for continuous data, and the Mann–Whitney test for nonparametric analysis. For predicting recurrence, the receiver-operating-characteristic curves for quantitative indices of PET/CT were analyzed. For predicting recurrence-free survival, Kaplan–Meier curve and stepwise Cox regression analysis was performed. In survival analysis, optimal cutoffs for quantitative factors were determined using an algorithm (*19*) that selects the cutoff that maximizes significance. All statistical analyses were performed using commercialized statistical software packages (SPSS, version 18.0 [SPSS Inc.], and MedCalc, version 15.8 [MedCalc Software bvba]). Continuous variables were expressed as mean ± SD, and P values of less than 0.05 were considered significant.

RESULTS

Clinicopathologic Characteristics and Follow-up

Of the 249 patients who underwent liver transplantation during the study interval, the cause was HCC in 215; of those 215, ^{18}F-FDG PET/CT was performed beforehand in 121; of those 121, the inclusion criteria were met by 110 (89 men and 21 women; age 54 ± 9 y, range 22–72 y). Their clinical characteristics are summarized in Table 1.

During the follow-up period (45.6 ± 18.0 mo; range, 7.4–83.1 mo), HCC recurred in 30 patients (27%) at 11.5 ± 9.0 mo after liver transplantation (range, 0.9–36.2 mo), involving extrahepatic organs in 20 patients, only liver in 2 patients, and both liver and extrahepatic organs in 8 patients. None of the analyzed clinical factors significantly differed between the recurrence and nonrecurrence groups. In contrast, most of the pathologic factors differed significantly; the recurrence group had larger tumor size ($P = 0.001$), more tumor multiplicity ($P = 0.011$), more vascular invasion ($P < 0.001$), higher T-stage ($P = 0.002$) (Table 1), and fewer patients within the Milan criteria ($P = 0.003$).

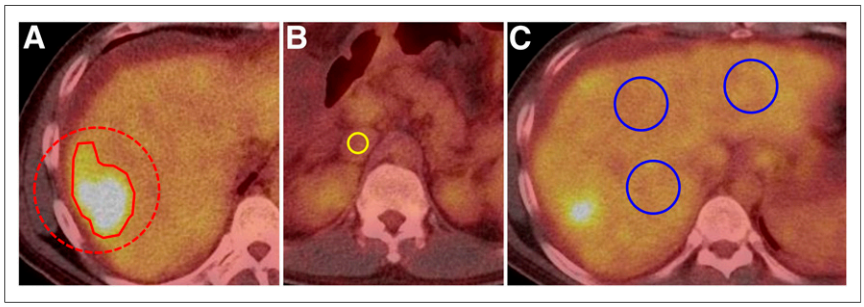

FIGURE 1. Measurement methods using ^{18}F-FDG PET/CT indices. Spheric VOI (dashed circle) was manually drawn to include entire tumor, and isoactivity contour (solid line) was automatically drawn by setting a certain threshold (A). For background activity, 1-cm^3 cylindric VOIs (yellow circle) were drawn on IVC (B) and 20-cm^3 spheric VOIs (blue circles) were drawn on normal liver (C).

TABLE 1
Clinicopathologic Characteristics According to Recurrence

Characteristic	Overall	Recurrence	Nonrecurrence	*P*
Patients (*n*)	110	30	80	
Sex (*n*)	89 M:21 F	24 M:6 F	6 M:15 F	0.882
Age, mean (y)	54 ± 9 (range, 22–72)	53 ± 12 (range, 22–72)	55 ± 7 (range, 33–71)	0.301
Follow-up time, mean (mo)	45.6 ± 18.0 (range, 7.4–83.1)	22.9 ± 35.0 (range, 7.4–64.2)	48.6 ± 55.0 (range, 27.5–83.1)	<0.001
Viral status				
HBV	86 (78%)	22 (73%)	64 (80%)	
HCV	16 (15%)	4 (13%)	12 (15%)	
Neither HBV nor HCV	8 (7%)	4 (13%)	4 (5%)	
Pretransplantation α-fetoprotein, median (ng/mL)	22.2 (range, 1.0–1,708,000)	141.9 (range, 1.0–1,708,000)	15.2 (range, 1.5–1597)	0.215
Donor (*n*)				0.706
LDLT	93 (85%)	26 (87%)	67 (84%)	
DDLT	17 (15%)	4 (13%)	13 (16%)	
Tumor size, mean (cm)	3.8 ± 3.6	6.6 ± 5.5	2.7 ± 1.6	0.001
Tumor number (*n*)				0.011
Single	37 (34%)	4 (13%)	33 (41%)	
Multiple	73 (66%)	26 (87%)	47 (59%)	
Milan criteria (*n*)				0.003
Within	55 (50%)	8 (27%)	47 (59%)	
Beyond	55 (50%)	22 (73%)	33 (41%)	
Tumor necrosis, mean (%)	37.5 ± 41.8	41.6 ± 40.1	36.0 ± 42.6	0.535
Tumor grade (*n*)				0.003
1/2	45 (41%)	5 (17%)	40 (50%)	
3/4	65 (59%)	25 (83%)	40 (50%)	
Vascular invasion (*n*)				<0.001
No	84 (76%)	14 (47%)	70 (88%)	
Yes	26 (24%)	16 (53%)	10 (13%)	
T-stage (*n*)				0.002
T1/T2	45 (41%)	5 (17%)	40 (50%)	
T3/T4	65 (59%)	25 (63%)	40 (50%)	

HBV = hepatitis B virus; HCV = hepatitis C virus; LDLT = living donor liver transplantation; DDLT = deceased donor liver transplantation.

PET/CT Indices and Recurrence

^{18}F-FDG PET/CT was performed 0.7 ± 0.6 mo (range, 0.0–3.7 mo) before liver transplantation. On visual analysis of PET/CT images, the rate of hypermetabolic lesions was higher in the recurrence group ($P < 0.001$). On quantitative analysis, SUV_{max}, TBR_{IVCmax}, and TBR_{NLmax} were significantly higher in the recurrence group ($P < 0.001$ for all). Additionally, MTV and UVP were significantly higher in the recurrence group for both of the thresholds used for isoactivity contour drawing (Table 2).

On receiver-operating-characteristic curve analysis, all PET/CT indices were significantly predictive of recurrence ($P < 0.001$ for all; Table 3). However, the indices calculated by IVC activity (TBR_{IVCmax}, MTV_{IVC}, and UVP_{IVC}) had higher areas under the curve than those calculated by normal-liver activity (TBR_{NLmax}, MTV_{NL}, and UVP_{NL}). Among the metabolic activity indices, TBR_{IVCmax} had the highest area under the curve, 0.913, with sensitivity and specificity of 83.3% and 88.7%, respectively, at the 1.16 cutoff. Among the metabolic burden indices, UVP_{IVC} exhibited the highest area under the curve, 0.896, with sensitivity

TABLE 2
PET/CT Findings According to Recurrence

Characteristic	Overall	Recurrence	Nonrecurrence	*P*
Visual findings (*n*)				<0.001
Nonhypermetabolic	71 (65%)	5 (17%)	66 (83%)	
Hypermetabolic	39 (35%)	25 (63%)	14 (18%)	
Quantitative indices, mean				
SUV_{max}	4.01 ± 1.51	5.26 ± 2.24	3.54 ± 0.69	<0.001
TBR_{IVCmax}	2.38 ± 0.85	3.25 ± 1.17	2.06 ± 0.30	<0.001
TBR_{NLmax}	1.74 ± 0.56	2.29 ± 0.81	1.54 ± 0.16	<0.001
MTV_{IVC}	24.5 ± 109.5	85.8 ± 199.0	1.5 ± 4.8	<0.001
MTV_{NL}	16.3 ± 78.3	58.8 ± 143.1	0.4 ± 1.3	<0.001
UVP_{IVC}	47.4 ± 214.9	168.5 ± 390.5	2.0 ± 7.6	<0.001
UVP_{NL}	29.9 ± 134.3	108.5 ± 242.8	0.5 ± 1.6	<0.001

and specificity of 90.0% and 81.2% at the 0.73 cutoff. Based on these results, IVC-based quantitative PET/CT indices were used in the survival analysis.

Survival Analysis

Among clinicopathologic factors, tumor size (cutoff, 6.7 cm), tumor number (1 vs. ≥2), Milan criteria (within vs. beyond), tumor grade (1/2 vs. 3/4), vascular invasion (yes vs. no), and T-stage (T1/T2 vs. T3/T4) were included in the univariate survival analysis, and all were significantly predictive of recurrence (Table 4). Among PET/CT factors, visual findings (hypermetabolic vs. nonhypermetabolic), SUV_{max} (cutoff, 5.16), TBR_{IVCmax} (cutoff, 1.25), MTV_{IVC} (cutoff, 18.3), and UVP_{IVC} (cutoff, 14.3) were also significant for predicting recurrence ($P < 0.001$ for all). TBR_{IVCmax} and UVP_{IVC} exhibited hazard ratios of 13.65 and 12.49, respectively (Fig. 2).

On multivariate analysis, when all clinicopathologic factors (except the Milan criteria) and PET/CT quantitative indices were included, tumor size, tumor grade, TBR_{IVCmax}, and UVP_{IVC} were found to be significant ($P = 0.004$, 0.014, 0.009, and 0.021, respectively). When PET/CT indices with the Milan criteria alone were included, the Milan criteria ($P = 0.029$), TBR_{IVCmax} ($P < 0.001$), and UVP_{IVC} ($P = 0.016$) were significant (Table 4). The hazard ratios for these factors were 2.54, 6.75, and 3.16, respectively. Images of representative cases are shown in Figure 3.

DISCUSSION

In this study, we demonstrated that ^{18}F-FDG PET/CT can provide effective predictors of HCC recurrence after liver transplantation. On comparing several methods of producing metabolic indices on ^{18}F-FDG PET/CT, we found TBR_{IVCmax} and UVP_{IVC} to be significant prognostic factors and to exhibit higher predictive power than the other indices; both were found to be significant prognostic factors on multivariate analysis.

Because liver transplantation requires a limited resource—donor organs—and is expensive, selection of candidates who have a low likelihood of HCC recurrence is of the utmost importance. Several methods, including the Milan criteria, are currently used to select candidates, and most of these methods are based on the size and number of intrahepatic tumors. Although such methods can be effective in predicting recurrence and in selecting candidates (*20*), their predictive power needs to be enhanced. Moreover, the precise evaluation of pathologic factors such as tumor size, tumor number, vascular invasion, and tumor grade is possible only when the explanted liver is available. Thus, ^{18}F-FDG PET/CT imaging,

TABLE 3
Receiver-Operating Characteristic Curve Analysis of PET/CT Quantitative Indices in Predicting Recurrence

Index	Area under curve	*P*	Sensitivity (%)	Specificity (%)	Cutoff
SUV_{max}	0.762 (0.671–0.838)	<0.001	53.3	93.7	4.77
TBR_{IVCmax}	0.913 (0.844–0.958)	<0.001	83.3	88.7	1.16
TBR_{NLmax}	0.869 (0.792–0.926)	<0.001	73.3	88.7	1.13
MTV_{IVC}	0.891 (0.818–0.943)	<0.001	90.0	78.7	0.51
MTV_{NL}	0.862 (0.783–0.920)	<0.001	80.0	83.7	0.29
UVP_{IVC}	0.896 (0.824–0.946)	<0.001	90.0	81.2	0.73
UVP_{NL}	0.863 (0.784–0.921)	<0.001	80.0	83.7	0.33

Data in parentheses are 95% confidence interval.

TABLE 4
Results of Survival Analyses

Factor	Univariate analysis		Multivariate analysis: With all factors		Multivariate analysis: With Milan criteria and PET indices	
	Hazard ratio	*P*	Hazard ratio	*P*	Hazard ratio	*P*
Tumor size	12.30 (5.72–26.46)	<0.001	3.62 (1.52–8.63)	0.004		NA
Tumor number	3.84 (1.35–10.94)	0.012		NS		NA
Milan criteria	3.27 (1.46–7.33)	0.004		NA	2.54 (1.11–5.83)	0.029
Tumor grade	3.93 (1.91–8.07)	0.003	3.39 (1.29–8.92)	0.014		NA
Vascular invasion	5.63 (2.75–11.55)	<0.001		NS		NA
T-stage	7.66 (3.70–15.85)	<0.001		NS		NA
Visual PET finding	14.11 (5.40–36.89)	<0.001		NA		NA
SUV_{max}	12.98 (6.12–27.54)	<0.001		NS		NS
TBR_{IVCmax}	13.65 (6.31–29.53)	<0.001	4.62 (1.48–14.41)	0.009	6.75 (2.53–18.02)	<0.001
MTV_{IVC}	13.72 (6.22–30.29)	<0.001		NS		NS
UVP_{IVC}	12.49 (5.97–26.13)	<0.001	3.39 (1.21–9.55)	0.021	3.16 (1.24–8.06)	0.016

NA = not assessed; NS = not selected as significant factor.
Data in parentheses are 95% confidence interval.

which shows the metabolic activity of a tumor, has been used to predict HCC recurrence after liver transplantation.

In some previous studies, the metabolic status of HCC as seen on ^{18}F-FDG PET was the only significant factor predicting long-term survival (*21*) and early recurrence (<6 mo) after liver transplantation (*22*). Other studies found some additional factors to be significant, such as the metabolic status of the HCC, the extent of vascular invasion (*23,24*), and the degree of differentiation (*23,24*). Aside from one discordant result (*25*), the use of ^{18}F-FDG PET/CT TBR as a metabolic activity index has been reported to be efficacious in predicting HCC recurrence after liver transplantation (*14*).

In addition to metabolic activity indices such as SUV and TBR, volumetric indices are now widely used to analyze ^{18}F-FDG PET/CT results for various cancers (*15–18*). MTV is defined as the volume of tissue that exhibits a higher metabolism over a certain threshold, and total lesion uptake, or total lesion glycolysis, is defined as MTV multiplied by SUV_{mean}. In the present study, UVP, an index of total lesion uptake, was calculated as MTV multiplied by mean uptake expressed in TBR. Although SUV_{max} and TBR_{max} reflect the metabolic activity of the most malignant component of a tumor, volumetric indices reflect both metabolic activity and tumor burden, that is, the size of the entire tumor. In liver transplantation for HCC, the size and number of tumors—which are considered in the Milan criteria—relate to tumor burden, and thus we tested the predictive values of these volumetric indices in comparison with metabolic activity indices.

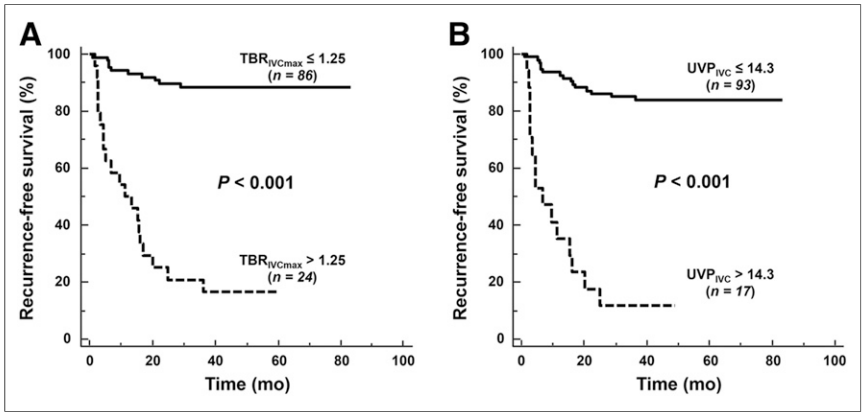

FIGURE 2. Kaplan–Meier survival analysis with regard to TBR_{IVCmax} and UVP_{IVC}. (A) Patients with low TBR_{IVCmax} (≤1.25) showed significantly longer recurrence-free survival than those with high TBR_{IVCmax} (>1.25). (B) Patients with low UVP_{IVC} (≤14.3) showed significantly longer recurrence-free survival than those with high UVP_{IVC} (>14.3).

Despite the potential value of volumetric indices, there is no single optimal method for metabolic volumetry. Currently, a certain SUV or a certain percentage of SUV_{max} is commonly used as a threshold for volumetry (*26*). However, although SUV is often prone to measurement errors, TBR is relatively robust because it is based on the activity of reference tissue in the same image of a patient. We compared several metabolic activity and volumetric indices and, similar to a previous report (*14*), found that TBR_{max} exhibited greater significance than SUV_{max} in predicting posttransplantation recurrence. Thus, TBR was used for measuring volumetric indices with varying thresholds, and UVP was used instead of the commonly used volumetric index, total lesion glycolysis. In the pilot study, we tested various thresholds in the measurement of MTV,

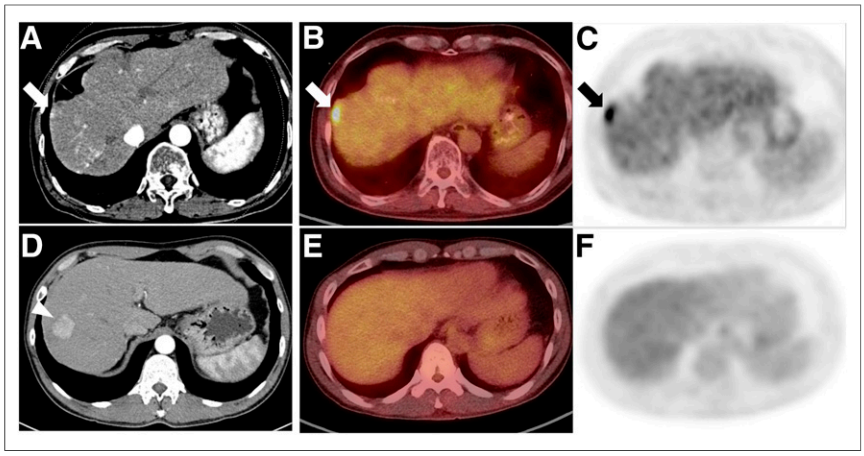

FIGURE 3. Images of representative cases. (A–C) 65-y-old man who presented with hepatic tumor (arrows) on enhanced CT (A), which showed high TBR_{IVCmax} (2.59) and UVP_{IVC} (18.91) on ^{18}F-FDG PET/CT (B) and PET (C). Although patient was within Milan criteria (3 tumors, with largest being 2.5 cm, and no vascular invasion), tumor recurred 16 mo after transplantation. (D–F) In contrast, 54-y-old man with hepatic tumor (arrowhead) on enhanced CT (D) showed low TBR_{IVCmax} (1.09) and UVP_{IVC} (13.54) on ^{18}F-FDG PET/CT (E) and PET (F). Although he was beyond Milan criteria (3 tumors, with largest being 3.3 cm), he exhibited no tumor recurrence until 41.7 mo after transplantation.

and we selected TBR_{IVC} 2.0 and TBR_{NL} 1.5 on that basis. Intriguingly, the indices based on IVC activity were slightly more predictive than those based on normal-liver activity. It is speculated that IVC is a more reliable background than normal liver because normal liver tissue shows varying SUVs of 1.4–5.0 in HCC (*27*). Additionally, many HCC patients have underlying viral hepatitis and liver cirrhosis, which may influence ^{18}F-FDG uptake in normal liver tissue.

TBR_{IVCmax} had the highest area under the receiver-operating-characteristic curve and the highest hazard ratio on multivariate analysis. This finding suggests that the metabolic activity of the most malignant component of the tumor is a significant prognostic factor in liver transplantation for HCC. In contrast to treatments such as chemotherapy, radiotherapy, and some excisional surgeries, the entire primary organ of the tumor is removed in liver transplantation. All but two of our study patients experienced recurrence in extrahepatic organs. We thus speculate that the potential for distant metastasis relates closely to posttransplantation recurrence and that TBR_{IVCmax} is a marker for metastatic potential. However, UVP_{IVC} also was a significant prognostic factor, suggesting that overall metabolic tumor burden is another independent prognostic factor for metastasis. Further studies on large, prospective patient cohorts are warranted to determine the potential of volumetric indices to complement or add to the prognostic role of metabolic activity indices.

Among the clinicopathologic factors, tumor size was found to be significant on multivariate analysis, in addition to TBR_{IVCmax} and UVP_{IVC}. We adopted a tumor size cutoff that was optimized for our dataset. The cutoff was somewhat different from that established in the Milan criteria, and thus, multivariate analysis was performed again including the Milan criteria as a clinicopathologic factor, with the result being that TBR_{IVCmax} and UVP_{IVC}, as well as the Milan criteria, were still significant prognostic factors. Further studies are required to establish optimal criteria for selection of HCC liver transplantation candidates—criteria combining all significant clinicopathologic and PET/CT factors that are preoperatively available.

The present study had several limitations. It was retrospective, and its protocol was not strictly controlled. The relatively large variation in interval between ^{18}F-FDG PET/CT and liver transplantation may have been a bias factor, even if not a critical one. Additionally, the retrospective design resulted in some missing clinicopathologic data, such as the Child–Pugh score before transplantation (*6*) and pathologic findings of satellitosis and giant cells (*7*).

CONCLUSION

In addition to clinicopathologic factors such as tumor size and the Milan criteria, ^{18}F-FDG PET/CT indices such as volumetric and metabolic activity are effective predictors of HCC recurrence after liver transplantation. Among the various PET/CT indices, TBR_{IVCmax} and UVP_{IVC} are significant. It is expected that prediction of HCC recurrence and selection of candidates for liver transplantation can be optimized through a combination of both clinicopathologic factors and PET/CT indices.

DISCLOSURE

The costs of publication of this article were defrayed in part by the payment of page charges. Therefore, and solely to indicate this fact, this article is hereby marked "advertisement" in accordance with 18 USC section 1734. This research was supported by grants HI14C1277 and HI14C1072 from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health and Welfare, Republic of Korea. No other potential conflict of interest relevant to this article was reported.

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