European Journal of Radiology 81 (2012) 2417–2422

Contents lists available at SciVerse ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Review

18F-FDG PET or PET/CT for detecting extrahepatic metastases or recurrent hepatocellular carcinoma: A systematic review and meta-analysis

Chun-Yi Lin[a,1], Jin-Hua Chen[b,1], Ji-An Liang[c,d], Cheng-Chieh Lin[d,e], Long-Bin Jeng[d,f], Chia-Hung Kao[d,g,*]

[a] Department of Nuclear Medicine, Show Chwan Memorial Hospital, Changhua, Taiwan
[b] Biostatistics Center and Graduate Institute of Biostatistics, Taichung, Taiwan
[c] Department of Radiation Oncology, China Medical University Hospital, Taichung, Taiwan
[d] School of Medicine, China Medical University, Taichung, Taiwan
[e] Department of Community Medicine and Health Examination Center, China Medical University Hospital, Taichung, Taiwan
[f] Organ Transplantation Center, China Medical University Hospital, Taichung, Taiwan
[g] Department of Nuclear Medicine and PET Center, China Medical University Hospital, Taichung, Taiwan

ARTICLE INFO

Article history:
Received 16 May 2011
Received in revised form 28 July 2011
Accepted 4 August 2011

Keywords:
FDG PET
Metastatic HCC
Recurrent HCC
Systematic review
Meta-analysis

ABSTRACT

Aim: Positron emission tomography (PET) using F18-flurodeoxy-glucose (FDG) has been widely used for reflecting cellular metabolism. However, the feasibility of FDG PET in the diagnosis of hepatocellular carcinoma (HCC) is limited. The aim of the study was to assess the ability of FDG PET (PET/CT) in the detection of extrahepatic metastases or recurrent HCC.
Materials and methods: We conducted MEDLINE, EMBASE and COCHRANE searches (last update, April 2011). Eight eligible articles were identified evaluating F18-FDG PET (PET/CT) in extrahepatic metastases or recurrent HCC. Two authors independently evaluated the methodological quality of each study. We estimated pooled sensitivities, specificities, summary receiver-operating-characteristic (SROC) curves, and summary likelihood ratios.
Results: Eight eligible studies were enrolled in this study. The pooled estimates of sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of FDG PET (PET/CT) in the detection of metastatic HCC were 76.6%, 98.0%, 14.68, and 0.28, respectively. The pooled estimates of sensitivity, specificity, LR+ and LR− of FDG PET (PET/CT) in the detection of recurrent HCC were 81.7%, 88.9%, 4.72, and 0.19, respectively.
Conclusion: Based on the results of this systematic review, F-18 FDG PET (PET/CT) was useful in ruling in extrahepatic metastases of HCC and valuable for ruling out the recurrent HCC.

Hepatocellular carcinoma (HCC) is one of the 6th most common malignancies worldwide. Of all cancers, HCC is the 3rd leading cause of cancer related death globally. China is the country with the highest incidence (>20 per 100,000) of HCC globally. The 5-year survival rate for HCC patients in China is 2–16% [1–4].

Extrahepatic metastases from HCC are not rare. The incidence of extrahepatic metastases was reported in 37% of patients. Although the most metastatic HCC occur in patients at the advanced stage, accurately diagnosis of metastatic HCC is important to manage the disease and decide the treatment strategy [5–8]. HCC has a high recurrence rate (51–90%) even after curative resection. Therefore, accurately early diagnosing recurrence is critical [9–11].

Positron emission tomography (PET) using F18-flurodeoxy-glucose (FDG) has been well established as a noninvasive diagnostic tool for the detection of a variety of malignancies. However, the feasibility of FDG PET in the diagnosis of hepatocellular carcinoma (HCC) is limited. Several investigators have reported that the sensitivity of FDG PET in early diagnosis of HCC was about 50–55% [1,4,12–15].

The aim of the study was to assess the ability of F-18 FDG PET (PET/CT) in the detection of extrahepatic metastatic or recurrent HCC.

1. Materials and methods

1.1. Literature search

We conducted MEDLINE, EMBASE and COCHRANE searches (last update, April 2011). We used the following algorithm: “FDG” AND “positron emission tomography” AND “hepatocellular” AND “car-

* Corresponding author at: Department of Nuclear Medicine and PET Center, China Medical University Hospital, No. 2, Yuh-Der Road, Taichung 404, Taiwan. Tel.: +886 4 22052121x7412; fax: +886 4 22336174.
E-mail address: d10040@mail.cmuh.org.tw (C.-H. Kao).
[1] These authors contributed equally to this work.

0720-048X/$ – see front matter © 2011 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ejrad.2011.08.004

Table 1
Criteria list used to assess the methodological quality of the studies.

Criteria of validity		Positive score
Internal validity		
IV 1	Valid reference test	Histology, clinical and radiologic follow-up
IV 2	Blind measurement of FDG-PET without knowledge of reference test	
IV 3	Blind measurement of reference test without of knowledgement of FDG PET	
IV 4	Avoidence of verification bias	Assessment by reference test independent of FDG-PET results
IV 5	FDG-PET interpreted indendently of all clinical information	Mentioned in publication
IV 6	Prospective study	Mentioned in publication
External validity		
EV 1	Spectrum of disease	Metastatic or recurrent HCC
EV 2	Demographic information	Age and sex information given
EV 3	Inclusion criteria	Metioned in the publication
EV 4	Exclusion criteria	Metioned in the publication
EV 5	Avoidence of selection bias	Consecutive series of patients
EV 6	Standard execution of FDG-PET	Type of camera, dose FDG, time interval, reconstruction

cinoma". Searches were limited to human subjects. No language restriction or date limitation was applied. To be sure that re-sampling of the same patients did not occur, if overlapping patient cohort were used among multiple studies, only the latest or the largest study was included.

1.2. Selection criteria

Studies were eligible for inclusion based on the following criteria: (a) histological assessment, clinical follow-up or radiographic techniques confirmed metastatic HCC or recurrent HCC, (b) diagnostic performed by F-18 FDG PET or F-18 FDG PET/CT, (c) 2×2 tables can be derived from the provided data. Abstract presented at congresses, unpublished data, case report, meta-analysis, reviews, letter, editorials and comments were excluded. Duplicated studies with overlapping patient populations as well as studies evaluated less than 10 patients were excluded. To avoid the potentially useful papers for the present meta-analysis were lost from the analysis, the abstracts were doubled checked up by at least two authors to make sure that they fitted the included criteria or did not related to the topic of this study.

1.3. Quality assessment and data extraction

The methodological quality of the selected studies was evaluated by the two authors (C.Y.L. and C.H.K.) independently, discussed discrepancies, and reach consensus for all items. Cochrane Methods Working Group on Systematic Review of Screening and Diagnostic Tests was used as the criteria list. Some items on the list were modified for the specific review. The complete criteria list used in this study is presented in Table 1. Internal validity criteria (IV) were scored as positive (adequate methods), negative (inadequate methods, potential bias, or insufficient information had been provided on s specific item). Unclear responses were interpreted as the quality item was not met. External validity criteria (EV) were used to evaluate generalizability. Standard performance of FDG PET or PET/CT was scored positive when the type of PET or PET/CT camera, the dose of FDG, the time between injection and scanning, and the methods of reconstruction were described. The criteria for external validity were score positive when sufficient information was provided to judge generalizability of findings. Agreement between both authors was quantified by Cohen's κ [16]. Quality scores were expressed as a percentage of the maximum score. Subtotals were calculated for internal (maximum 6) and external (maximum 6) validity separately.

For each report, we recorded the number of true-positive, false-positive, true negative, and false-negative findings for F18-FDG PET (PET/CT) in diagnosing metastatic or recurrent HCC.

1.4. Statistical analysis

Data in the diagnostic performance of F18 FDG PET (PET/CT) in the detection of metastatic HCC or recurrent HCC were combined quantitatively across eligible studies. First, we combined independently sensitivities and specificities across studies. Second, we constructed summary receiver-operating-characteristic (SROC) curves. Third, we estimated the weighted positive likelihood ratio (LR+), and negative Likelihood ratio (LR−) across studies using fixed effects model

For a diagnostic test, the sensitivity and specificity are related to each other. It is not totally correct to estimate these two quantities independently. One may use the SROC method to bypass this problem. The SROC curve shows the trade-off between sensitivity and specificity across the included studies [17].

Likelihood ratios are also metrics that combine sensitivity and specificity in the calculations. The ratio of sensitivity over 1 – specificity is defined as LR+. The ratio of 1 – sensitivity over specificity is defined as LR−. The discrimination ability is better with higher LR+ and lower LR−. In the previous papers, a clinically useful test was defined when a LR+ was greater than 5.0 and LR− was less than 0.2 [18]. Analyses were conducted by free software Meta-DiSc (version 1.4) [19].

2. Results

2.1. Literature search

A total of 149 studies about HCC with F18-FDG PET (PET/CT) were yielded initially. 136 articles were excluded up front on the basis of their abstracts. These studies included HCC not related to metastases or recurrence, duplicated studies, case reports, reviews, letter, editorials, comments, studies evaluated less than 10 patients, secondary liver tumors, studies reporting on the mechanism of varying FDG uptake in human tumor cells, reporting on the different scanning protocol effects on the image quality.

We screened 13 articles in full-text. Two studies were excluded because of insufficient information to construct a 2×2 table [20,21]. One study was excluded because the results of the sensitivity and specificity of this study were lesions-based [22]. Two studies were excluded because the results of the diagnostic performance of FDG PET in different metastatic lesions of HCC were analyzed individually, and thus the overall sensitivity and specificity of these studies cannot be estimated [23,24]. Finally, eight eligible studies [25–32] were enrolled in this systematic review (Fig. 1).

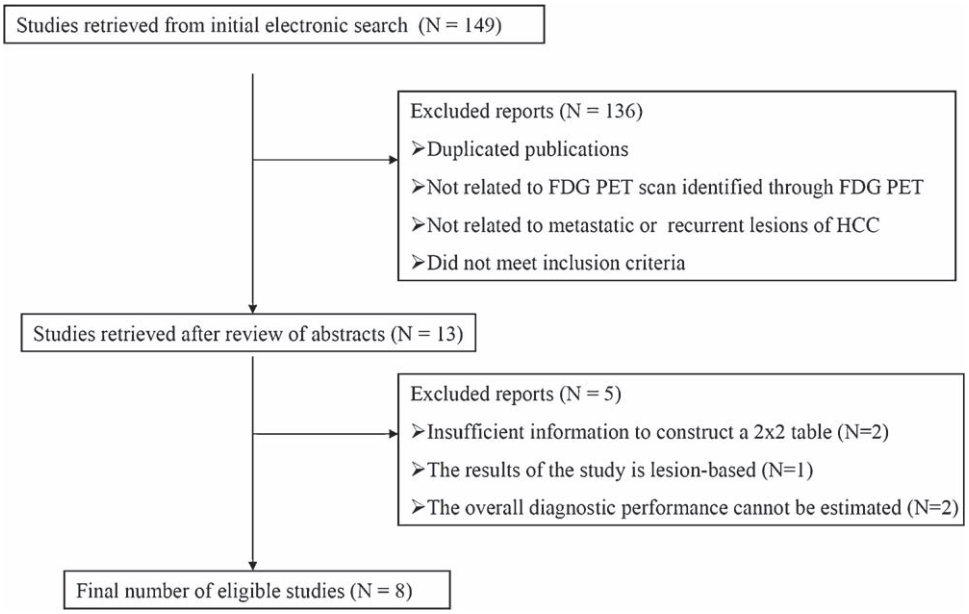

Fig. 1. Flow chart of selection processes for eligible studies.

2.2. Study characteristics

The characteristics of the eligible studies are summarized in Table 2. One of the studies was prospective, [27] and the others were retrospective. In all studies, the results of the diagnostic performance were patient-based. Three of the studies were performed by FDG PET scan, [25,28,30] and five studies were performed by FDG PET/CT scan [26,27,29,31,32]. The dose of FDG ranged considerably across studies. One study used quantitative methods, which standardized uptake values (SUVs) > 2.0 as the cut-off for positive [26].

2.3. Quality assessment

Methodological quality was assessed by 12 items for each of the 8 selected articles. There was disagreement in 28 of 96 scores with a Cohen's κ of 0.70. Main disagreement was in the questions of IV5 and EV4. Disagreements were caused by differences in interpretation and reading errors. The scores for internal and external validity of the 8 selected studies were presented in Table 3. All of the selected studies had a valid reference test, verification bias was avoided because of patients were selected for assessment by the reference test independently of

Table 2
Study characteristics.

Author	Reference	Year	No. of patients	Mean age	Design	Data type	Equipment	F18-FDG dose	Measures
Metastatic HCC									
Sugiyama et al.	[25]	2004	19	69 years	Retrospective	Patient-based	PET	300–400 MBq	Qualitatively
Ho et al.	[26]	2007	121	58.6 years	Retrospective	Patient-based	PET/CT	370–550 MBq	SUV
Park et al.	[27]	2008	99	57.6 years	Prospective	Patient-based	PET/CT	444–740 MBq	Qualitatively
Recurrent HCC									
Chen et al.	[28]	2005	31	60.9 years	Retrospective	Patient-based	PET	370 MBq	Qualitatively
Wang et al.	[29]	2006	11	47.2 years	Retrospective	Patient-based	PET/CT	259–444 MBq	Qualitatively
Paudyal et al.	[30]	2007	24	65.8 years	Retrospective	Patient-based	PET	5–6 MBq/kg	Qualitatively
Han et al.	[31]	2009	18	55.4 years	Retrospective	Patient-based	PET/CT	370 MBq	NR
Sun et al.	[32]	2009	25	51.6 years	Retrospective	Patient-based	PET/CT	370–666 MBq	Qualitatively

Table 3
Quality assessment.

Study	Year	IV						EV						Total IV score	Total EV score	% of maximum score
		IV 1	IV 2	IV 3	IV 4	IV 5	IV 6	EV 1	EV 2	EV 3	EV 4	EV 5	EV 6			
Metastatic HCC																
Sugiyama et al.	2004	+	+	–	+	–	–	+	+	+	–	+	+	3	5	66.7
Ho et al.	2007	+	+	–	+	–	–	+	+	+	–	+	+	3	5	66.7
Park et al.	2008	+	+	+	+	–	+	+	+	+	+	+	+	5	6	91.6
Recurrent HCC																
Chen et al.	2005	+	+	–	+	–	–	+	+	+	–	+	+	3	5	66.7
Wang et al.	2006	+	–	–	+	–	–	+	+	+	–	–	+	2	4	50.0
Paudyal et al.	2007	+	–	+	+	–	–	+	+	+	–	+	+	3	5	66.7
Han et al.	2009	+	+	–	+	–	–	+	+	+	–	+	+	3	5	66.7
Sun et al.	2009	+	+	–	+	–	–	+	+	+	–	+	+	3	5	66.7

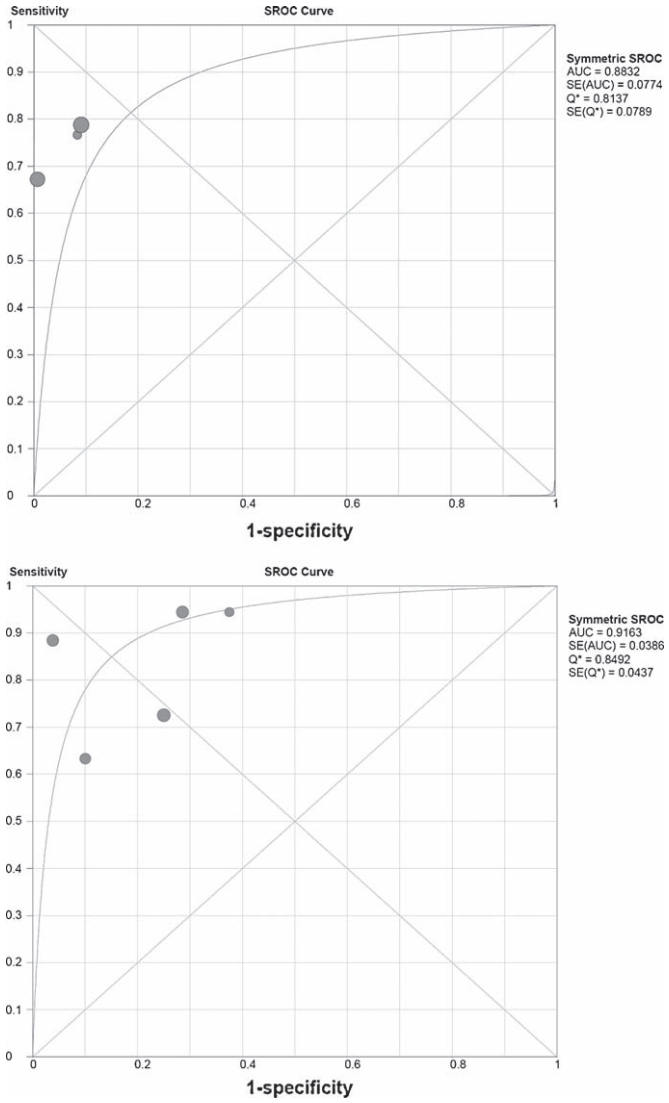

Fig. 2. Summary ROC curves of diagnostic performance of F-18 FDG PET (PET/CT) in evaluation of metastatic HCC (upper) and recurrent HCC (lower).

the FDG PET results (IV4). One study was prospective, and in other seven studies, patients entered the study consecutively. All of the selected studies described inclusion criteria, but only one study described exclusion criteria [30]. The total score for the combined internal and external validity, expressed as a fraction of the maximum score, ranged from 50% to 91.6%, with a mean of 67.7%. Seven of the eight studies had a total score above 60%.

2.4. Diagnostic performance

The data of each study and the results of the statistical pooling are presented in Table 4. The pooled estimates of sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of FDG PET (PET/CT) in the detection of extrahepatic metastases of HCC were 76.6% (95% CI: 68.7–83.3%), 98.0% (95% CI: 92.8–99.8%), 14.68 (95% CI: 5.5–39.14), and 0.28 (95% CI: 0.20–0.40), respectively. The summary receiver-operating-characteristic (SROC) curve for metastatic HCC was presented in Fig. 2 (upper). The pooled estimates of sensitivity, specificity, LR+ and LR− of FDG PET (PET/CT) in the detection of recurrent HCC were 81.7% (95% CI: 71.6–89.4%), 88.9% (95% CI: 70.8–97.6%), 4.72 (95% CI: 2.21–10.07), and 0.19 (95% CI: 0.10–0.35), respectively. The SROC curve for recurrent HCC was presented in Fig. 2 (lower).

3. Discussion

PET with F18-FDG is a well known functional diagnostic oncologic imaging technique. However, FDG PET is not sensitive enough in detection of HCC, especially in cases of low-grade HCC. Because of the enzyme activity of low-grade HCC resembles that of normal hepatocytes and results in low FDG uptake in these tumors [33]. If there are no extrahepatic metastases in advanced HCC, aggressive locoregional intervention is possible. Nevertheless, once there is extrahepatic spread from HCC, the treatment for is limited and the prognosis is poor. Extrahepatic metastases of HCC are not rare. Hence accurate staging of HCC is important [24]. Sun et al. [34] reported that FDG PET is helpful in discriminating between benign and malignant portal vein thrombi in HCC patients. Ho et al. [26] reported that FDG PET is useful in the evaluation of HCC metastases. Park et al. [27] reported that the overall sensitivity of FDG PET for metastatic HCC was 85.7%.

It has been reported that early re-section correlated with better post-recurrent survival rate, so early detection of recurrent HCC is critical [11]. The previous studies were promising for the use of FDG PET as an indicator of tumor viability after therapy. Chen et al [28] reported that when conventional examinations are normal, FDG PET is a valuable imaging tool in patients with rising alpha-fetoprotein (AFP) after HCC treatment. Han et al. [31] also found that FDG PET/CT was valuable to reveal recurrent tumor in patients with AFP elevation after interventional therapy for HCC. Wang et al. [29] described that with the advantage of whole body scanning and high sensitivity of tumor detection, FDG PET/CT can be instrumental in postoperative early detection of recurrent tumors in patients with liver transplantation for HCC.

The diagnostic performance of the eight studies discussed in the present review was patient-based. The pooled estimates of sensitivity, specificity, positive likelihood ratio (LR+), and negative likelihood ratio (LR−) of FDG PET (PET/CT) in the detection of metastatic HCC were 76.6%, 98.0%, 14.68, and 0.28, respectively. Generally speaking, for patients who have a positive result, LR+ of more than 10 significantly increased the probability of disease ("rule in" disease) [35]. The pooled estimates of sensitivity, specificity, LR+ and LR− of FDG PET (PET/CT) in the detection of recurrent HCC were 81.7%, 88.9%, 4.72, and 0.19, respectively. A low LR− (less than 0.2) is clinically useful for ruling out the chance that a person has the disease [18]. The results of this systematic review indicated that FDG PET (PET/CT) has a good diagnostic performance in metastatic HCC or recurrent HCC.

There are some potential limitations in this study. First, the number of selected papers is relatively small resulting in the variability in reported specificity and specificity values are variable as well as the different interpretation criteria. The little number of evaluated study and the variability among them may have impaired the strength of the present meta-analysis study. Second, the clinical heterogeneity may affect the generalizability of the results. Third, biopsy results were available in only some lesions. Other lesions rely on the clinical follow-up which may have variety of imaging modalities and clinical examinations. Not all of clinical follow-up were performed in the same manner in all the studies. Fourth, the variability in the quality of the primary studies may introduce important limitations for the interpretation of this review study. Fifth, selection bias may have been introduced because of the retrospective nature of the studies. In addition,

Table 4
Diagnostic performance of F-18 FDG PET or PET/CT in detection of metastatic or recurrent HCC.

Study	No. of patients	TP	FP	TN	FN	Sensitivity (%)		Specificity (%)		Likelihood ratios			
										LR+		LR−	
						Value	95% CI	Value	95% CI	Value	95% CI	Value	95% CI
Metastatic HCC													
Sugiyama et al.	19	11	0	5	3	78.6	49.2–95.3	1.0	47.8–1.00	9.2	0.64–132.64	0.26	0.10–0.66
Ho et al.	121	78	2	20	21	78.8	69.4–86.4	90.9	70.8–0.99	8.7	2.30–32.62	0.23	0.16–0.35
Park et al.	99	19	0	71	9	67.9	47.6–84.1	1.0	94.9–1.00	96.8	6.04–1551.2	0.33	0.20–0.56
Pooled data						76.6	68.7–83.3	98.0	92.8–99.8	14.7	5.50–39.14	0.28	0.20–0.40
Recurrent HCC													
Chen et al.	31	22	0	1	8	73.3	54.1–87.7	1.0	2.5–1.0	2.9	0.26–32.33	0.37	0.14–0.98
Wang et al.	11	8	1	2	0	1.0	63.1–1.0	66.7	9.4–99.2	2.5	0.70–9.01	0.09	0.005–1.46
Paudyal et al.	24	11	0	12	1	0.92	61.5–1.0	1.0	73.5–1.0	23.0	1.51–350.92	0.12	0.03–0.54
Han et al.	18	9	0	4	5	0.64	0.35–0.87	1.0	39.8–1.0	6.3	0.44–90.33	0.41	0.20–0.84
Sun et al.	25	17	2	5	1	0.94	0.73–1.0	71.4	29.0–96.3	3.3	1.02–10.72	0.08	0.01–0.55
Pooled data						81.7	71.6–89.4	88.9	70.8–97.6	4.72	2.21–10.07	0.19	0.10–0.35

HCC is not common in the Western, so very few English publications with enough study cases were found for this meta-analysis study.

4. Conclusion

Based on the results of this systematic review, F-18 FDG PET (PET/CT) was useful in ruling in extrahepatic metastases of HCC and valuable for ruling out the recurrent HCC. F-18 FDG PET (PET/CT) could contribute to the proper management of HCC patients and provide useful information about accurate staging to HCC patients suspected of having extrahepatic metastases or recurrent HCC.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

Acknowledgements

The grant supported by the study projects (DMR-98-052 and DMR-98-087) of our hospital and Taiwan Department of Health Clinical Trial and Research Center for Excellence (DOH100-TD-B-111-004) and Taiwan Department of Health Cancer Research Center for Excellence (DOH100-TD-C-111-005).

References

[1] Khan MA, Combs CS, Brunt EM, et al. Positron emission tomography scanning in the evaluation of hepatocellular carcinoma. J Hepatol 2000;32:792–7.
[2] Venook AP, Papandreou C, Furuse J, et al. The incidence and epidemiology of hepatocellular carcinoma: a global and regional perspective. Oncologist 2010;15(Suppl. 4):5–13.
[3] He YX, Guo QY. Clinical applications and advances of positron emission tomography with fluorine-18-fluorodeoxyglucose (18F-FDG) in the diagnosis of liver neoplasms. Postgrad Med J 2008;84:246–51.
[4] Jeng LB, Changlai SP, Shen YY, et al. Limited value of 18F-2-deoxyglucose positron emission tomography to detect hepatocellular carcinoma in hepatitis B virus carriers. Hepatogastroenterology 2003;50:2154–6.
[5] Nakashima T, Okuda K, Kojiro M, et al. Pathology of hepatocellular carcinoma in Japan. 232 Consecutive cases autopsied in ten years. Cancer 1983;51:863–77.
[6] Yuki K, Hirohashi S, Sakamoto M, et al. Growth and spread of hepatocellular carcinoma. A review of 240 consecutive autopsy cases. Cancer 1990;66:2174–9.
[7] Fukutomi M, Yokota M, Chuman H, et al. Increased incidence of bone metastases in hepatocellular carcinoma. Eur J Gastroenterol Hepatol 2001;13:1083–8.
[8] Katyal S, Oliver 3rd JH, Peterson MS, et al. Extrahepatic metastases of hepatocellular carcinoma. Radiology 2000;216:698–703.
[9] Nagasue N, Uchida M, Makino Y, et al. Incidence and factors associated with intrahepatic recurrence following resection of hepatocellular carcinoma. Gastroenterology 1993;105:488–94.
[10] Arii S, Teramoto K, Kawamura T, et al. Characteristics of recurrent hepatocellular carcinoma in Japan and our surgical experience. J Hepatobiliary Pancreat Surg 2001;8:397–403.
[11] Chen WT, Chau GY, Lui WY, et al. Recurrent hepatocellular carcinoma after hepatic resection: prognostic factors and long-term outcome. Eur J Surg Oncol 2004;30:414–20.
[12] Kashiwagi T. FDG-PET and hepatocellular carcinoma. J Gastroenterol 2004;39:1017–8.
[13] Okazumi S, Isono K, Enomoto K, et al. Evaluation of liver tumors using fluorine-18-fluorodeoxyglucose PET: characterization of tumor and assessment of effect of treatment. J Nucl Med 1992;33:333–9.
[14] Trojan J, Schroeder O, Raedle J, et al. Fluorine-18 FDG positron emission tomography for imaging of hepatocellular carcinoma. Am J Gastroenterol 1999;94:3314–9.
[15] Shin JA, Park JW, An M, et al. Diagnostic accuracy of 18F-FDG positron emission tomography for evaluation of hepatocellular carcinoma. Korean J Hepatol 2006;12:546–52.
[16] Brennan P, Silman A. Statistical methods for assessing observer variability in clinical measures. BMJ 1992;304:1491–4.
[17] Moses LE, Shapiro D, Littenberg B. Combining independent studies of a diagnostic test into a summary ROC curve: data-analytic approaches and some additional considerations. Stat Med 1993;12:1293–316.
[18] Kang S, Kim SK, Chung DC, et al. Diagnostic value of (18)F-FDG PET for evaluation of paraaortic nodal metastasis in patients with cervical carcinoma: a metaanalysis. J Nucl Med 2010;51:360–7.
[19] Zamora J, Abraira V, Muriel A, et al. Meta-DiSc: a software for meta-analysis of test accuracy data. BMC Med Res Methodol 2006;6:31.
[20] Cheng MF, Wu YW, Tzen KY, et al. Whole-body F-18 FDG PET for hepatocellular carcinoma patients after interventional treatment. Neoplasma 2007;54:342–7.
[21] Kim YK, Lee KW, Cho SY, et al. Usefulness 18F-FDG positron emission tomography/computed tomography for detecting recurrence of hepatocellular carcinoma in posttransplant patients. Liver Transpl 2010;16:767–72.
[22] Ho CL, Chen S, Cheng TK, et al. PET/CT characteristics of isolated bone metastases in hepatocellular carcinoma. Radiology 2011;258:515–23.
[23] Kawaoka T, Aikata H, Takaki S, et al. FDG positron emission tomography/computed tomography for the detection of extrahepatic metastases from hepatocellular carcinoma. Hepatol Res 2009;39:134–42.
[24] Yoon KT, Kim JK, Kim do Y, et al. Role of 18F-fluorodeoxyglucose positron emission tomography in detecting extrahepatic metastasis in pretreatment staging of hepatocellular carcinoma. Oncology 2007;72(Suppl. 1):104–10.
[25] Sugiyama M, Sakahara H, Torizuka T, et al. 18F-FDG PET in the detection of extrahepatic metastases from hepatocellular carcinoma. J Gastroenterol 2004;39:961–8.
[26] Ho CL, Chen S, Yeung DW, et al. Dual-tracer PET/CT imaging in evaluation of metastatic hepatocellular carcinoma. J Nucl Med 2007;48:902–9.
[27] Park JW, Kim JH, Kim SK, et al. A prospective evaluation of 18F-FDG and 11C-acetate PET/CT for detection of primary and metastatic hepatocellular carcinoma. J Nucl Med 2008;49:1912–21.
[28] Chen YK, Hsieh DS, Liao CS, et al. Utility of FDG-PET for investigating unexplained serum AFP elevation in patients with suspected hepatocellular carcinoma recurrence. Anticancer Res 2005;25:4719–25.
[29] Wang XL, Li H, Wang QS, et al. Clinical value of pre-and postoperative 18F-FDG PET/CT in patients undergoing liver transplantation for hepatocellular carcinoma. Nan Fang Yi Ke Da Xue Xue Bao 2006;26:1087–91, 1095.
[30] Paudyal B, Oriuchi N, Paudyal P, et al. Early diagnosis of recurrent hepatocellular carcinoma with 18F-FDG PET after radiofrequency ablation therapy. Oncol Rep 2007;18:1469–73.

[31] Han AR, Gwak GY, Choi MS, et al. The clinical value of 18F-FDG PET/CT for investigating unexplained serum AFP elevation following interventional therapy for hepatocellular carcinom. Hepatogastroenterology 2009;56:1111–6.
[32] Sun L, Guan YS, Pan WM, et al. Metabolic restaging of hepatocellular carcinoma using whole-body F-FDG PET/CT. World J Hepatol 2009;1:90–7.
[33] Yamamoto Y, Nishiyama Y, Kameyama R, et al. Detection of hepatocellular carcinoma using 11C-choline PET: comparison with 18F-FDG PET. J Nucl Med 2008;49:1245–8.
[34] Sun L, Guan YS, Pan WM, et al. Highly metabolic thrombus of the portal vein: 18F fluorodeoxyglucose positron emission tomography/computer tomography demonstration and clinical significance in hepatocellular carcinoma. World J Gastroenterol 2008;14:1212–7.
[35] Akobeng AK. Understanding diagnostic tests 2: likelihood ratios, pre- and post-test probabilities and their use in clinical practice. Acta Paediatr 2007;96:487–91.