Prognostic Ability of ^{18}F-FDG PET/CT in the Assessment of Colorectal Liver Metastases

Vijayaragavan Muralidharan[1], Marco Kwok[1], Sze Ting Lee[2,3], Lawrence Lau[1], Andrew M. Scott*[2,3], and Christopher Christophi*[1]

[1]Department of Surgery, Austin Hospital, University of Melbourne, Victoria, Australia; [2]Department of Nuclear Medicine and Centre for PET, Austin Hospital, University of Melbourne, Victoria, Australia; and [3]Ludwig Institute for Cancer Research, Austin Hospital, University of Melbourne, Victoria, Australia

Modern multidisciplinary therapy for colorectal liver metastases (CRLM) is associated with significant morbidity and must be adapted to the patient's relative risk. The tools currently available to risk-stratify patients are limited. This study assessed the prognostic utility of metabolic measurements derived from ^{18}F-FDG PET compared with previously proposed prognostic scoring systems. **Methods:** Preoperative ^{18}F-FDG PET/CT studies from a series of 30 patients who underwent liver resection for CRLM after neoadjuvant chemotherapy were evaluated. Quantitative ^{18}F-FDG PET analysis calculated the maximum and mean standardized uptake value, metabolic tumor volume (MTV), and tumor glycolytic volume (TGV) as measures of the metabolic activity of tumors. The predictive value of these parameters was compared with that of 4 prognostic scores developed by Fong, Iwatsuki, Nordlinger, and Rees. **Results:** High MTV and TGV in patients before metastasectomy were significantly associated with poorer overall survival (MTV: $P = 0.001$; TGV: $P = 0.004$) and recurrence-free survival (MTV: $P = 0.001$, TGV; $P = 0.002$). Maximum and mean standardized uptake value did not show any significant predictive ability. Of the prognostic scores, prediction of outcome was most accurate using the Basingstoke index (area under the curve, 0.898). **Conclusion:** Assessment of metabolic tumor burden with volumetric ^{18}F-FDG PET parameters appears to be a valuable adjunct in determining the biology of CRLM before surgical resection and may enable better risk stratification of patients.

Key Words: colorectal liver metastases; ^{18}F-FDG PET/CT; prognostic scoring system; MTV; TGV

J Nucl Med 2012; 53:1345–1351
DOI: 10.2967/jnumed.112.102749

Colorectal cancer is among the most common malignancies affecting both men and women worldwide (*1*). Although screening initiatives have successfully enabled earlier detection of this cancer, metastatic disease to the liver remains the most frequent cause of mortality. Treatment of colorectal liver metastases (CRLM) with a combination of surgical resection and systemic chemotherapy results in 5-y survival rates of 30%–50% in patients undergoing the procedure (*2,3*). However, despite substantial survival benefit, surgical resection can be offered only to 20%–30% of patients (*4*) because of the presence of extrahepatic or bilobar disease or the lack of patient fitness for major surgery. Although technical advances have allowed major liver resections to be conducted safely, with perioperative mortality below 2%, liver resection remains a major undertaking carrying a postoperative morbidity as high as 35% (*5*). There is an urgent need for the treatment of CRLM to be risk-adapted such that patients with a predicted poor prognosis may be spared invasive surgery, and major interventions may be targeted at those who are likely to significantly benefit.

Previous investigators have developed clinicopathologic prognostic scoring systems (*6–9*) in an effort to delineate risk categories in patients before the onset of treatment (Table 1). The accuracy of these predictive models has, however, been questioned in follow-on studies when evaluated in independent patient cohorts (*10,11*). One potential reason for these inconsistencies may be that the clinicopathologic factors scored in these systems are an inadequate surrogate for the overall burden and biologic aggressiveness of the tumor (*12*), both of which impact heavily on patient outcomes.

PET has been widely used and has become an integral part of staging of CRLM (*13*). PET has progressively come to the forefront as a minimally invasive method of studying functional and metabolic processes in tumors. Increased glucose utilization is a feature of many malignancies and can be identified on PET using the radiotracer ^{18}F-FDG. Recent studies have correlated high ^{18}F-FDG uptake in tumors with poorer patient survival in a range of tumors including lung (*14*), breast (*15*), head and neck (*16*), and esophageal cancers (*17*). Despite growing interest in the biology of tumors as a predictor of outcome, there is a general lack of tools to assess tumor biology in CRLM. In this study, we investigated the predictive ability of quantitative measurements of tumor

Received Jan. 23, 2012; revision accepted Apr. 2, 2012.
For correspondence or reprints contact: Vijayaragavan Muralidharan, Department of Surgery, Austin Health, University of Melbourne, Heidelberg, Victoria, 3084, Australia.
E-mail: surgery-armc@unimelb.edu.au
Published online Jul. 13, 2012.
*Contributed equally to this work.

TABLE 1
Summary of Criteria of Previously Proposed Prognostic Scoring Systems

Prognostic score	Prognostic variable
Memorial Sloan-Kettering Cancer Center clinical risk score (Fong et al. (*6*))	Node-positive primary tumor Disease-free interval from primary tumor Number of liver metastases Preoperative CEA level Diameter of largest tumor
Pittsburgh system (Iwatsuki et al. (*7*))	Bilobar tumors Disease-free interval from primary tumor Number of liver metastases Diameter of largest tumor Extrahepatic metastatic disease Positive surgical margins
Nordlinger score (Nordlinger et al. (*8*))	Age Diameter of largest tumor Extension of primary cancer to serosa Node-positive primary tumor Disease-free interval from primary tumor Surgical margin
Basingstoke index (Rees et al. (*9*))	Node-positive primary tumor Differentiation of primary tumor Number of liver metastases Preoperative carcinoembryonic antigen level Diameter of largest tumor Extrahepatic metastatic disease Hepatic resection margins

metabolic uptake using ^{18}F-FDG PET as a prognostic tool before surgical resection for CRLM. Four measures of tumor glucose uptake were studied in this setting: the maximum and mean standardized uptake value (SUV_{max} and SUV_{mean}), which are semiquantitative measures of ^{18}F-FDG concentration in the tumor, and the metabolic tumor volume (MTV) and tumor glycolytic volume (TGV), which are 3-dimensional measurements that may enable more accurate representation of the metabolically active tumor burden.

MATERIALS AND METHODS

Patients

Patients admitted for surgical resection of CRLM between January 2004 and December 2007 were identified from the database maintained by the Hepato-Pancreato-Biliary and Transplant Unit at the Austin Hospital, Australia. Patient selection was standardized by including only those receiving neoadjuvant chemotherapy before surgery followed by adjuvant chemotherapy after surgery. The availability of ^{18}F-FDG PET/CT scans after completion of chemotherapy and immediately before liver surgery was also a criterion for inclusion. Ethics approval from Austin Hospital was obtained for prospective analysis (approval no. H2011/04301).

Patient data were collected from the prospective database of the Hepato-Pancreato-Biliary and Transplant Unit, with additional information gathered from the hospital medical records and from discussions with treating clinicians. The data included patient demographics (age and sex), details of the liver and colorectal operations, histopathologic features of the resected liver metastasis and the primary colorectal tumor, perioperative blood transfusion, blood carcinoembryonic antigen levels, and chemotherapy received. From these factors, prognostic scores were calculated according to the systems developed by Fong et al. (Memorial Sloan-Kettering Cancer Center) (*6*), Iwatsuki et al. (Pittsburgh) (*7*), Nordlinger et al. (*8*), and Rees et al. (Basingstoke index) (*9*), which have been described in Table 1.

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

In preparation for the imaging study, patients fasted for 6 h before intravenous injection of approximately 5 MBq of ^{18}F-FDG per kilogram of body weight according to the standard protocol. All patients were then scanned from base of skull to upper thighs on a PET/CT system (Philips) after a 60-min uptake period. The scan included a low-dose 30 mA/slice CT component for attenuation correction and anatomic localization. The duration of the ^{18}F-FDG PET emission scan was 3 min/bed position, and the patients were scanned with their arms above their heads. The scans were processed with 3-dimensional iterative reconstruction.

The PET scans were reanalyzed by a nuclear medicine physician who was masked to the clinical and survival data of the patients. Software previously validated for assessing 3-dimensional glycolytic volume (*18*) was used to define a volume of interest for each metabolically active liver lesion. The software uses a semiautomated threshold-based 3-dimensional seed-growing algorithm that is determined by the current mean activity, the activity in neighboring pixels, and the maximum normal background level. A threshold of SUV_{mean} plus 2 SDs was used, and separate seeds were applied for each noncontiguous liver metastasis. The MTV and TGV were then calculated from the volume of interest. SUV_{max} and SUV_{mean} were also measured and recorded, using standard methods involving injected dose, blood glucose level, and normalization by the patient's body weight. TGV, being a composite of metabolic activity and volume, was measured as SUV·mL. MTV was recorded as cubic centimeters because it is defined as the physical volume of metabolically active tumor.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics, version 17 (IBM). Overall survival was calculated as the number of months from liver resection until death. Recurrence-free survival was defined as the interval from hepatectomy to the time of the first evidence of tumor recurrence found by either PET or CT. Patients were censored on the date of last follow-up if they were still alive or had no evidence of disease recurrence.

Receiver-operating-characteristic analysis was conducted to assess the discriminative performance of each PET parameter (SUV_{max}, SUV_{mean}, MTV, and TGV) and the proposed prognostic score (Iwatsuki, Fong, Nordlinger, and Basingstoke) for death and tumor recurrence at 30 mo as endpoints (duration of minimum follow-up). Areas under the curve (AUCs) were derived from these plots and compared on the conventional scale ranging from 0.5 (discriminative ability no better than chance) to 1.0 (perfect discrimination). A separate AUC analysis was performed excluding patients with non–^{18}F-FDG-avid tumors to investigate survival in only patients with tumors that had metabolic uptake observable on ^{18}F-FDG PET. Survival curves were produced by the Kaplan–Meier method and compared using the log-rank test. The prognostic value of demographic, clinicopathologic, and tumor metabolic parameters were examined on univariate and multivariate analysis with the Cox proportional hazards regression model, which calculated the hazard ratio and a 95% confidence interval. Statistical significance was regarded as a P value of less than 0.05.

RESULTS

Patient Characteristics

A total of 30 patients with histologically proven CRLM were included in the study. The median follow-up time for surviving patients was 37 mo (range, 30–83 mo). Patient demographics and clinical characteristics are summarized in Table 2.

All patients had been assessed by a multidisciplinary team consisting of radiologists, hepatobiliary surgeons, oncologists, and nuclear physicians before the commencement of treatment. Standard indications for liver resection for CRLM were followed after exclusion of extrahepatic metastases by multidetector CT of the chest and triple-phase multidetector CT of the abdomen and pelvis in addition to whole-body ^{18}F-FDG PET/CT. Patients received a combination chemotherapy regimen involving oxaliplatin (folinic acid/fluorouracil/oxaliplatin or capecitabine/oxaliplatin) or irinotecan (folinic acid/fluorouracil/irinotecan). It is well established that the efficacy of all these treatment regimens in advanced colorectal cancer is comparable (*19*).

Of the thirty ^{18}F-FDG PET/CT scans evaluated, 4 involved tumors with no observable ^{18}F-FDG uptake. Extrahepatic metastases involving the lung were found in 1 patient on preoperative ^{18}F-FDG PET/CT staging, who underwent staged liver resection and subsequent lung resection. No perioperative deaths occurred in this series of patients, but surgical resection margins were proven histologically positive in 5 patients (16.7%). At the completion of follow-up, 20 (66.7%) of the 30 patients were found to have tumor recurrences, and the median overall survival was calculated to be 58 mo (95% confidence interval, 42.25–73.75) using the Kaplan–Meier method.

TABLE 2
Demographic and Clinical Characteristics

Variable	Value
Age (y)	59 (36–80)
Sex (male:female)	3:2
Number of liver metastases	2 (1–8)
Diameter of liver metastases (mm)	30 (10–80)
SUV_{mean}	3.22 (0–4.91)
SUV_{max}	4.51 (0–10.51)
MTV (cm^3)	11.54 (0–77.31)
TGV (SUV·mL)	36.94 (0–343.16)
Procedure performed	
Subsegmental	5 (16.7%)
Segmental	15 (50%)
Hemihepatectomy or more	10 (33.3%)

Data are median followed by range in parentheses or *n* followed by percentage in parentheses.

Receiver-Operating-Characteristic Analysis

SUV_{mean} (AUC, 0.531) and SUV_{max} (AUC, 0.580) were poor predictors of patient mortality at 30 mo on receiver-operating-characteristic analysis. However, the volumetric parameters MTV (AUC, 0.760) and TGV (AUC, 0.753) exhibited high predictive power that showed further improvement when only patients with ^{18}F-FDG-avid tumors were analyzed (MTV: AUC, 0.886; TGV: AUC, 0.876). Similarly, in the prediction of tumor recurrence as an outcome, MTV (AUC, 0.804) and TGV (AUC, 0.786) outperformed SUV_{mean} (AUC, 0.577) and SUV_{max} (AUC, 0.673) (Fig. 1).

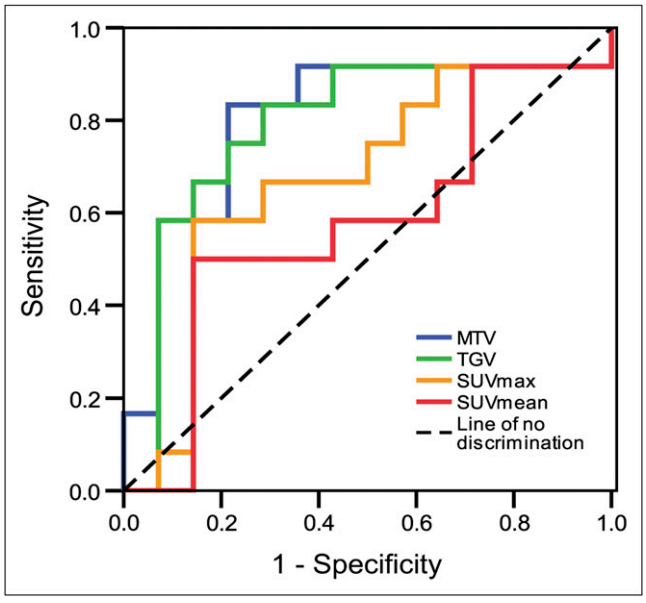

FIGURE 1. Receiver-operating-characteristic curves of ^{18}F-FDG PET metabolic parameters in predicting tumor recurrence at 30 mo. Dotted line represents line of no discrimination, where a test is no better than a random guess.

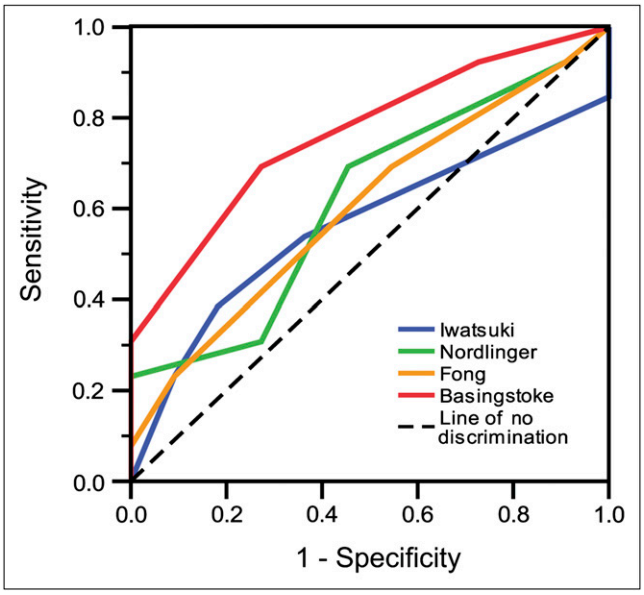

FIGURE 2. Receiver-operating-characteristic curves of prognostic scores in predicting tumor recurrence at 30 mo. Dotted line represents line of no discrimination, where a test is no better than a random guess. Shown are prognostic scores calculated according to systems of Fong (*6*), Iwatsuki (*7*), Nordlinger (*8*), and Rees (*9*).

Prognostic scores were also good predictors of medium-term mortality. The most accurate prediction was seen with the Basingstoke index (AUC, 0.898), and the Iwatsuki (AUC, 0.824), Nordlinger (AUC, 0.884) and Fong (AUC, 0.787) scores achieved AUCs comparable to those of MTV and TGV. However, unlike volumetric PET parameters, prediction of tumor recurrence using the scoring systems was limited (Fig. 2), with low AUCs for the Iwatsuki (AUC, 0.563), Memorial Sloan-Kettering Cancer Center (AUC, 0.605), and Nordlinger (AUC, 0.619) scores. The Basingstoke index (AUC, 0.766) once again demonstrated the best predictive performance of all scoring systems, achieving an AUC only slightly lower than that of the volume-based PET parameters.

Cutoffs that maximized the sensitivity and specificity of each PET metabolic measurement were then established. There was again a noticeable increase in predictive power when patients with ^{18}F-FDG–avid tumors were analyzed separately. MTV above a cutoff of 15.58 cm^3 correctly identified all patients who would not survive up to 30 mo (sensitivity, 100%), and below this threshold approximately 7 of 10 surviving patients were classified appropriately (specificity, 73.3%). A similar level of performance was seen with TGV at a cutoff of 64.97 SUV·mL (sensitivity, 100%; specificity, 76.2%).

Survival Analysis

Using these cutoff thresholds, PET parameters were dichotomized to generate Kaplan–Meier survival plots (Fig. 3). The log-rank test demonstrated significant survival differences between patients with high and low MTV ($P = 0.015$) and TGV ($P = 0.001$), but not when SUV_{mean} ($P = 0.859$) and SUV_{max} ($P = 0.165$) were used as measures of metabolic activity. For TGV, the 3-y survival rate was 40.0% in the group with high metabolic uptake, compared with 88.7% in the low-uptake group. Corresponding values for MTV were 45.5% in the high-uptake group and 88.0% in the low-uptake group.

Finally, the prognostic influence of demographic, clinicopathologic, and tumor metabolic factors on overall and recurrence-free survival was examined (Table 3). On univariate analysis, MTV, TGV, Basingstoke score, and the size of the largest metastases were all found to be predictive of both endpoints, and the Fong score predicted only recurrence-free survival at a statistically significant level. Multivariate analysis of these variables found that all prognostic factors remained significant even when adjusted for age and sex. Table 4 shows the hazard ratios calculated for each of these variables.

DISCUSSION

Management of CRLM has long suffered from a lack of viable prognostic tools. This drawback limits the commu-

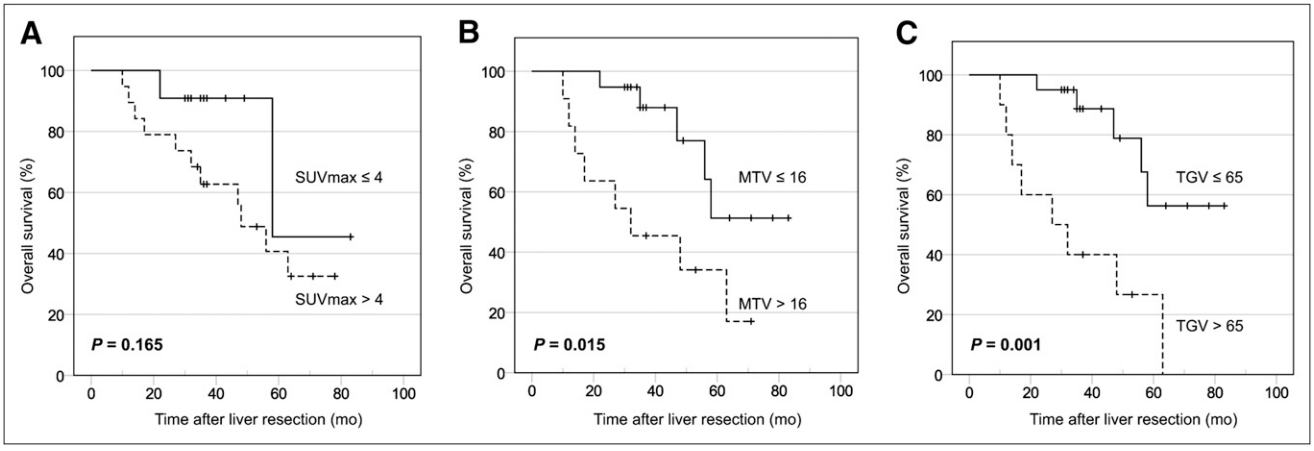

FIGURE 3. Kaplan–Meier survival plots illustrating differences in overall survival in patients with low metabolic uptake and high metabolic uptake when classified by SUV_{max} (A), MTV (B), and TGV (C).

TABLE 3
Univariate Cox Regression Analysis of Risk Factors Associated with Overall and Recurrence-Free Survival

Variable	*n*	Overall survival			Recurrence-free survival		
		Hazard ratio	95% CI	*P*	Hazard ratio	95% CI	*P*
Age	30	0.966	0.921–1.014	0.159	0.961	0.927–0.997	0.032
Sex							
Male	18	1.890	0.505–7.065	0.344	1.450	0.577–3.643	0.429
Female	12	—	—	—	—	—	—
PET metabolic parameters							
TGV	30	1.007	1.002–1.011	0.004	1.006	1.002–1.010	0.002
MTV	30	1.035	1.013–1.058	0.001	1.031	1.013–1.049	0.001
SUV_{max}	30	1.062	0.883–1.277	0.522	1.048	0.887–1.240	0.580
SUV_{mean}	30	1.084	0.733–1.604	0.686	1.013	0.715–1.436	0.941
Clinicopathologic factors							
Number of metastases	30	1.269	0.918–1.753	0.149	1.261	0.961–1.654	0.095
Diameter of largest metastasis (mm)	30	1.054	1.020–1.088	0.001	1.040	1.015–1.065	0.001
Bilobar metastases							
Yes	9	2.576	0.858–7.732	0.092	1.532	0.582–4.031	0.388
No	21	—	—	—	—	—	—
Synchronous metastases							
Yes	4	0.505	0.066–3.893	0.512	0.526	0.121–2.290	0.392
No	26	—	—	—	—	—	—
Preoperative CEA (μg/L)	28	1.011	0.982–1.040	0.468	1.025	0.998–1.052	0.067
Resection margin (mm)	27	0.958	0.894–1.027	0.223	0.990	0.941–1.042	0.700
Site of primary tumor							
Rectal	14	1.457	0.487–4.356	0.500	1.535	0.636–3.709	0.341
Colonic	16	—	—	—	—	—	—
Node status of primary tumor							
Positive	18	3.250	0.885–11.936	0.076	2.320	0.887–6.063	0.086
Negative	12	—	—	—	—	—	—
Prognostic scores							
Iwatsuki (Pittsburgh)	30	1.295	0.927–1.809	0.130	1.291	0.973–1.712	0.076
Fong (MSKCC)	28	1.467	0.840–2.564	0.178	1.830	1.045–3.205	0.034
Nordlinger	27	1.665	0.935–2.964	0.083	1.236	0.765–1.996	0.386
Rees (Basingstoke)	27	1.614	1.232–2.116	0.001	1.512	1.192–1.918	0.001

CEA = carcinoembryonic antigen; CI = confidence interval; MSKCC = Memorial Sloan-Kettering Cancer Center.

nication of risk between clinicians and patients and hampers decision making regarding the most appropriate treatment strategy for patients in terms of their likely outlook. Accumulating evidence indicates the biology of the tumor to be a major determinant of clinical outcome (*20,21*). Traditionally, the biologic aggressiveness of the tumor has been assessed by radiologic and clinical staging and by histopathologic features. Several investigators have developed clinicopathologic scoring systems to predict the long-term outcomes of patients undergoing metastasectomy. However, there has been uncertainty about the prognostic value of these scoring systems when applied to the wider population. In a study at the Mayo clinic in which 3 proposed risk scores (Fong, Iwatsuki, and Nordlinger) were applied retrospectively to 662 patients, Zakaria et al. reported that none of these scores were able to successfully stratify patients into distinct risk categories (*11*). On the other hand, several studies have identified the Fong and Iwatsuki scores to be predictive of recurrence-free survival (*10,22*). In our own survival analysis, the Fong score accurately predicted the risk of recurrence after resection and was one of the simpler systems to score. However, its performance appeared to be outclassed by the more recently developed Basingstoke index, which was found to predict both overall and recurrence-free survival.

Although these prognostic scores have been fundamental in establishing clinical risk factors for CRLM, they are likely to face significant challenges in the future. Validation of many of these scoring systems in independent patient populations is still limited. Meanwhile, the growing trend toward molecular targeted therapies may require an entirely new repertoire of biomarkers directly related to novel treatments. Prognostic models will need to be flexible enough to accommodate these newer factors and concise enough to be applied in the clinical setting.

With these considerations in mind, the present paper describes an alternative approach to the prognostication of CRLM using ^{18}F-FDG PET. In our analysis, we identified the volume-based metabolic parameters MTV and TGV as important predictors of overall and recurrence-free survival when measured before liver resection. This is the first study to our knowledge assessing such an association in CRLM.

TABLE 4
Multivariate Cox Regression Analysis* Adjusted for Age and Sex

Variable (by unit increase)	Overall survival			Recurrence-free survival		
	Hazard ratio	95% CI	*P*	Hazard ratio	95% CI	*P*
TGV	1.010	1.004–1.016	0.001	1.006	1.002–1.010	0.002
MTV	1.035	1.013–1.058	0.001	1.031	1.013–1.049	0.001
Size of largest metastasis (mm)	1.054	1.020–1.088	<0.001	1.061	1.028–1.096	<0.001
Basingstoke index	1.614	1.232–2.116	0.001	1.569	1.206–2.041	0.001
Fong (MSKCC) score	—	—	—	1.830	1.045–3.205	0.034

*Forward-stepwise method.
CI = confidence interval, MSKCC = Memorial Sloan-Kettering Cancer Center.

From our findings, an increase of MTV and TGV by 1 unit increased the hazard of death by 3.5% and 1%, respectively. Considering that MTV and TGV measurements ranged by up to 77.31 cm^3 and 343.16 SUV·mL, respectively, the survival advantage of patients with a low metabolically active tumor burden appears to be quite substantial.

However, these survival differences were not observed when SUV variables were used as a measure of tumor metabolic activity. This finding is in keeping with earlier studies of other cancers in which authors found volumetric PET variables to be of prognostic value in lung and esophageal cancer but failed to demonstrate an association between SUV and survival (*23,24*). It is believed that use of the volumetric parameters MTV and TGV enables a more global representation of tumor metabolism, in contrast to SUV_{max}, which depicts only the most intense metabolic region of a tumor. However, SUV has been shown previously to be predictive of survival in a study conducted by de Geus-Oei et al., of both palliatively and curatively treated CRLM patients (*25*). Our failure to detect this association may be attributable to the narrower range of SUVs of this cohort, which consisted of only patients who underwent surgical resection and excluded those treated with a palliative intent. Nonetheless, the results of our receiver-operating-characteristic analysis suggest that volumetric parameters may be the more powerful prognostic tool. A single measurement of either MTV or TGV was able to predict outcome with accuracy similar to or better than the 4 prognostic scores analyzed. Furthermore, performance was consistently high for predicting both the risk of recurrence and mortality. Although a recent study (*26*) has shown that metabolic volumes should ideally be performed on ^{18}F-FDG PET scans that were acquired in list mode using arterial input data, this method is not clinically feasible as it limits the scan to a single field of view. The method that we have used has been previously used and validated by prior studies (*18,27*).

Volumetric PET parameters have several features apart from their prognostic capacity that allow them to perform either as a simple stand-alone prognostic tool or as an addition to future prognostic models. In contrast to more complicated assessments of tumor biology such as tumor doubling time (*28*), the calculation of volumetric PET variables is less time-consuming and may be undertaken with routine preoperative staging studies. There are also many opportunities for this technique to be further enhanced and refined. For instance, assessing volumetric PET variables before the onset of chemotherapy may be an additional predictor of prognosis. As well, the differential change in volumetric PET variables in response to systemic chemotherapy may be an even better predictor of outcome than a single-time-point measurement. Finally, new radiotracers allow a whole array of biologic features to be studied. In particular, fluoromisonidazole is a marker for hypoxia that has garnered attention due to its possible relevance to tumor behavior and the prediction of response to chemoradiotherapy (*29*). Volumetric PET variables using such tracers may allow greater stratification of tumors in relation to long-term prognosis.

CONCLUSION

This pilot study demonstrated the predictive value of volumetric PET variables in a group of patients undergoing potentially curative liver resection. Although the retrospective nature of this study created limitations, many of our findings were consistent with prior studies investigating the role of PET parameters in other malignancies. A prospective study at our center to expand on these results is currently under way. Meanwhile, our current findings suggest that volumetric ^{18}F-FDG PET parameters have the prognostic potential to guide the selection of therapy in order to optimize outcomes in patients with CRLM.

DISCLOSURE STATEMENT

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.

ACKNOWLEDGMENTS

We thank the members of the Hepato-Pancreato-Biliary and Transplant Unit, Austin Hospital, including Roger Berry, Michael Fink, Mehrdad Nikfarjam, Robert Jones,

and Mark Goodwin from the Department of Radiology and Niall Tebbutt from GI Oncology, for their clinical contribution to this study, as well as the staff of the Centre for PET, Austin Hospital. This study was supported in part by NHMRC Program Grant 487922 and OIS funding from the Victorian Government. No other potential conflict of interest relevant to this article was reported.

REFERENCES

1. Garcia M, Jemal A, Ward E, et al. *Global Cancer Facts & Figures 2007*: American Cancer Society. 2007.
2. Primrose JN. Surgery for colorectal liver metastases. *Br J Cancer.* 2010;102: 1313–1318.
3. Malafosse R, Penna C, Sa Cunha A, Nordlinger B. Surgical management of hepatic metastases from colorectal malignancies. *Ann Oncol.* 2001;12:887–894.
4. Simmonds PC, Primrose JN, Colquitt JL, Garden OJ, Poston GJ, Rees M. Surgical resection of hepatic metastases from colorectal cancer: a systematic review of published studies. *Br J Cancer.* 2006;94:982–999.
5. Doci R, Gennari L, Bignami P, et al. Morbidity and mortality after hepatic resection of metastases from colorectal cancer. *Br J Surg.* 1995;82:377–381.
6. Fong Y, Fortner J, Sun RL, Brennan MF, Blumgart LH. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. *Ann Surg.* 1999;230:318–321.
7. Iwatsuki S, Dvorchik I, Madariaga JR, et al. Hepatic resection for metastatic colorectal adenocarcinoma: a proposal of a prognostic scoring system. *J Am Coll Surg.* 1999;189:291–299.
8. Nordlinger B, Guiguet M, Vaillant JC, et al. Surgical resection of colorectal carcinoma metastases to the liver: a prognostic scoring system to improve case selection, based on 1568 patients. Association Francaise de Chirurgie. *Cancer.* 1996;77:1254–1262.
9. Rees M, Tekkis PP, Welsh FK, O'Rourke T, John TG. Evaluation of long-term survival after hepatic resection for metastatic colorectal cancer: a multifactorial model of 929 patients. *Ann Surg.* 2008;247:125–135.
10. Merkel S, Bialecki D, Meyer T, Muller V, Papadopoulos T, Hohenberger W. Comparison of clinical risk scores predicting prognosis after resection of colorectal liver metastases. *J Surg Oncol.* 2009;100:349–357.
11. Zakaria S, Donohue JH, Que FG, et al. Hepatic resection for colorectal metastases: value for risk scoring systems? *Ann Surg.* 2007;246:183–191.
12. Neal CP, Garcea G, Doucas H, et al. Molecular prognostic markers in resectable colorectal liver metastases: a systematic review. *Eur J Cancer.* 2006;42:1728–1743.
13. Scott AM, Gunawardana DH, Kelley B, et al. PET changes management and improves prognostic stratification in patients with recurrent colorectal cancer: results of a multicenter prospective study. *J Nucl Med.* 2008;49:1451–1457.
14. Downey RJ, Akhurst T, Gonen M, et al. Preoperative F-18 fluorodeoxyglucose-positron emission tomography maximal standardized uptake value predicts survival after lung cancer resection. *J Clin Oncol.* 2004;22:3255–3260.
15. Oshida M, Uno K, Suzuki M, et al. Predicting the prognoses of breast carcinoma patients with positron emission tomography using 2-deoxy-2-fluoro[^{18}F]-D-glucose. *Cancer.* 1998;82:2227–2234.
16. Minn H, Lapela M, Klemi PJ, et al. Prediction of survival with fluorine-18-fluorodeoxyglucose and PET in head and neck cancer. *J Nucl Med.* 1997;38:1907–1911.
17. Chatterton BE, Ho Shon I, Baldey A, et al. Positron emission tomography changes management and prognostic stratification in patients with oesophageal cancer: results of a multicentre prospective study. *Eur J Nucl Med Mol Imaging.* 2009;36:354–361.
18. Francis RJ, Byrne MJ, van der Schaaf AA, et al. Early prediction of response to chemotherapy and survival in malignant pleural mesothelioma using a novel semiautomated 3-dimensional volume-based analysis of serial ^{18}F-FDG PET scans. *J Nucl Med.* 2007;48:1449–1458.
19. Tournigand C, Andre T, Achille E, et al. FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: a randomized GERCOR study. *J Clin Oncol.* 2004;22:229–237.
20. Ludwig JA, Weinstein JN. Biomarkers in cancer staging, prognosis and treatment selection. *Nat Rev Cancer.* 2005;5:845–856.
21. Maithel SK, Gonen M, Ito H, et al. Improving the clinical risk score: an analysis of molecular biomarkers in the era of modern chemotherapy for resectable hepatic colorectal cancer metastases. *Surgery.* 2012;151:162–170.
22. Reissfelder C, Rahbari NN, Koch M, et al. Validation of prognostic scoring systems for patients undergoing resection of colorectal cancer liver metastases. *Ann Surg Oncol.* 2009;16:3279–3288.
23. Lee P, Weerasuriya DK, Lavori PW, et al. Metabolic tumor burden predicts for disease progression and death in lung cancer. *Int J Radiat Oncol Biol Phys.* 2007;69:328–333.
24. Hyun SH, Choi JY, Shim YM, et al. Prognostic value of metabolic tumor volume measured by ^{18}F-fluorodeoxyglucose positron emission tomography in patients with esophageal carcinoma. *Ann Surg Oncol.* 2010;17:115–122.
25. de Geus-Oei LF, Wiering B, Krabbe PF, Ruers TJ, Punt CJ, Oyen WJ. FDG-PET for prediction of survival of patients with metastatic colorectal carcinoma. *Ann Oncol.* 2006;17:1650–1655.
26. Cheebsumon P, van Velden FH, Yaqub M, et al. Measurement of metabolic tumor volume: static versus dynamic FDG scans. *EJNMMI Res.* 2011;1:35.
27. Feigen M, Lee ST, Lawford C, et al. Establishing locoregional control of malignant pleural mesothelioma using high-dose radiotherapy and ^{18}F-FDG PET/CT scan correlation. *J Med Imaging Radiat Oncol.* 2011;55:320–332.
28. Tanaka K, Shimada H, Miura M, et al. Metastatic tumor doubling time: most important prehepatectomy predictor of survival and nonrecurrence of hepatic colorectal cancer metastasis. *World J Surg.* 2004;28:263–270.
29. Lee ST, Scott AM. Hypoxia positron emission tomography imaging with ^{18}f-fluoromisonidazole. *Semin Nucl Med.* 2007;37:451–461.