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Fluorodeoxyglucose positron emission tomography in leiomyosarcoma: imaging characteristics

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Abstract

Leiomyosarcoma, a malignant neoplasm of smooth muscle, accounts for 7% of the sarcomas. Patients with leiomyosarcoma tumors have an average survival of 5 years. These tumors, which are derived from mesenchymal tissues, are difficult to diagnose and treatment options remain controversial. The relatively rare incidence of this soft tissue sarcoma subtype has limited the number of patients available for studies and research. This study examines whether the imaging characteristics of positron emission tomography (PET) with radiolabeled fluorodeoxyglucose (FDG) provide a reliable, noninvasive means to predict tumor behavior in patients with leiomyosarcomas. 18F-FDG PET was performed on the tumors of participating patients before the neoadjuvant chemotherapy or resection, and a maximum tumor standard uptake value (SUV_{max}) was calculated. The SUV_{max} was correlated with tumor grade ($P=0.001$) and tumor size as greatest dimension ($P\lambda=\lambda 0.004$). Analysis of this data indicated the potential effectiveness of FDG PET imaging in predicting tumor grade. In leiomyosarcoma, the SUV_{max} from FDG PET is a likely predictor of tumor behavior. Improvements made in the clinical treatment of leiomyosarcomas by use of FDG PET imaging data may lead to an increase in patient survival.

Keywords

fluorodeoxyglucose positron emission tomography; leiomyosarcoma; sarcoma; maximum tumor standard uptake value

Introduction

The malignant neoplasm leiomyosarcoma accounts for 7% of the sarcomas. Patients with these tumors have an approximately 5-year survival, and a lack of leiomyosarcoma research continues to result in poor patient prognosis for this group [1–3]. Leiomyosarcomas are characterized histologically as epithelial, myxoid, and rhabdoid, containing osteoclast-like giant cells which may account for variable clinical behavior within this histologic classification [4]. These tumors are usually treated with neoadjuvant chemotherapy; however, despite complete resection and adjuvant radiotherapy, disease progression often results in widespread metastatic disease that includes lung metastases.

Previous research identifies tumor characteristics that are used to predict the outcome of patients with all types of sarcomas [5–12]. In earlier studies, primary tumor size, tumor

histologic grade, and tumor anatomic locations have been shown to correlate with patient outcome in general sarcoma tumor populations. These components of tumor grade would also be expected for leiomyosarcoma patients.

Use of fluorodeoxyglucose positron emission tomography (FDG-PET) to image tumor metabolism is becoming more readily available in clinical practice. Tumor uptake as described by the maximum tumor standard uptake value (SUV_{max}) [13] has proven useful in other studies as a parameter for grading sarcomas and describing their behavior on a histological basis [6–8,10]. In studies examining patients with chondrosarcoma, liposarcoma, and synovial sarcoma, tumor SUV_{max} has correlated with tumor grade and disease progression [9,14,15].

Few reports have been made on the relationship between FDG-PET SUV_{max} and tumor size and histologic grade in leiomyosarcoma. These reports mainly emphasize case reports involving leiomyosarcoma or uterine leiomyosarcoma [16–18]. Uterine leiomyosarcomas and leiomyosarcomas in case reports may not exhibit the same behavior as leiomyosarcomas in nonuterine or extremity locations. Based on the findings reported for other sarcomas, it would be expected that FDG-PET SUV_{max} would correlate with tumor size, tumor grade denoted by the French Federation Nationale des Centres de Lutte Contra le Cancer System, and possibly anatomic location because leiomyosarcoma tumors are a subset of the general sarcoma population. The primary aim of this study was to test for those correlations to assess the diagnostic value of the FDG-PET SUV_{max} for patients with leiomyosarcoma. FDG-PET may play an important role in diagnosis and treatment assessment for patients with this tumor type.

Materials and methods

Patients in this study analysis were enrolled in a prospective FDG-PET study for patients with sarcoma. Data for some of these patients has been included in reports of the larger sarcoma groups. This is an analysis of leiomyosarcoma patients separately from the group [6]. The remainders are more recent study patients accrued since that report. Thirty-nine consecutive patients presenting with leiomyosarcoma treated at the University of Washington Sarcoma Clinic between April 1994 and May 2005 were imaged with FDG-PET. Informed consent was obtained from all patients in this study by signing University of Washington Human Subjects and Radiation Safety Committee approval forms. Patients were excluded from the study if they received any type of treatment for their tumor before the their clinical PET scan, had an FDG-PET performed and read at an institution other than the University of Washington, or were not a candidate for chemotherapy.

FDG-PET imaging was performed in all patients, before the surgical resection or neoadjuvant chemotherapy. Methods for PET imaging of sarcoma patients have been previously published [6]. Briefly, the imaging studies were performed on an Advance Tomograph or Discovery LS PET/CT (General Electric Medical Systems, Waukesha, Wisconsin, USA) operating in a two-dimensional high sensitivity mode. All patients fasted for at least 12h before the intravenous injection of 370MBq FDG. After the patients were positioned in the tomograph, a 15-min attenuation scan over the tumor site was acquired on the PET, or a low dose computer tomography (CT) attenuation scan was performed on the PET/CT, followed by an emission scan of the tumor site at 45–60 min after tracer injection. Circular or elliptic regions of interest (ROI) were placed over the tumor site on sequential transaxial images on the Advance scans. Sagittal and coronal image planes were performed to ensure correct ROI placement. In PET/CT scans, a volume ROI was placed over the tumor with reference to the tumor volume on FDG and CT images. ROI placement was performed by the study principle investigator, who identified ROI for SUV determination independent of the technical staff. The SUV_{max} for each ROI was automatically calculated by the tomograph software according to the following expression:

$$\text{SUV}_{\text{max}} = \frac{\text{A}}{\text{ID} / \text{m}}$$

Where A is the maximum tissue activity within the ROI (in mCi/ml), ID is the injected dose (in mCi), and m is the patient body weight (in kg) [13]. The maximum SUV in the tumor volume was reported. The SUV_{max} value obtains the tumor uptake variable, but is not influenced by the tumor size or spatial heterogeneity in FDG uptake, as the entire tumor volume independent of surrounding normal tissues is examined.

Tumor size, histologic grade, and anatomic location were recorded for each patient and tumor size was reported as the greatest dimension from pretreatment CT, MRI, or gross pathology measurements. Tumor grade was designated according to the Federation Nationale des Centres de Lutte Contra le Cancer grading system for soft tissue sarcomas. Anatomic location was defined as extremity (any tumors occurring within the limbs), pelvis (any tumors occurring within the pelvis or groin), or trunk (any tumors occurring within the thorax, retroperitoneum, paraspinal muscles, or axilla).

The correlation between SUV_{max} and tumor greatest dimension, grade, and anatomical location was evaluated with both univariate and multivariate analysis. Univariate analysis on the study data was performed to assess the correlation of investigated variables with SUV_{max} . Multivariate analysis was performed to identify independent variable correlation with SUV_{max} .

Results

Thirty-nine patients were enrolled in this study. These patients are described in Tables 1 and 2. Patients ranged in ages from 33.2 to 82.7 years with a mean age of 53.0 years. Tumor SUV_{max} ranged from 2.8 to 26.1 with a median of 9.3. Tumor greatest dimension ranged from 3.5 to 20.2 cm with a median of 10.2 cm. Tumor grade ranged from low (I) to high (III) grade: 19 patients (48.7%) presented with a high grade (III) tumor, 16 patients (41.0%) presented with an intermediate grade (II) tumor, and four patients (10.3%) presented with a low grade (I) tumor. Of those who presented with intermediate tumors, six patients (37.5%) presented with intermediate grade tumors greater than 9 cm. Twenty-one patients (53.8%) presented with a tumor located in the extremity, whereas 18 patients (46.2%) presented with a tumor located in the pelvis or trunk.

From univariate regression analysis, it was found that a correlation exists between tumor SUV_{max} and both tumor greatest dimension ($P < 0.004$) and tumor grade ($P < 0.001$) (Table 3). Owing to the large number of intermediate grade tumors (16) and a low number of low-grade tumors (4), grade was recategorized so that there were only two groups (intermediate tumors > 9 cm and high grade and smaller intermediate tumors and low grade). A correlation between tumor SUV_{max} and anatomic location was not identified in the pelvis ($P = 0.42$) or trunk ($P = 0.43$) (Table 3).

The multivariate regression analysis allows us to determine the independent association of tumor grade and greatest dimension SUV_{max} . Both of these are found to be somewhat significant ($P = 0.08$ and $P = 0.017$, respectively in Table 4). No other variables were found to correlate with SUV_{max} in this multivariate analysis: tumor location (pelvis $P = 0.67$ and trunk $P = 0.69$) did not correlate with SUV_{max} (Table 4).

Discussion

A lack of leiomyosarcoma data to date supports the need to identify a reliable means to characterize this tumor type for treatment selection. From this study, two possible variables

have been found to correlate with the tumor imaging value FDG-SUV_{max}, a measure of tumor metabolic activity. From both the univariate and multivariate analyses, a higher SUV_{max} correlated with both tumor grade and tumor greatest dimension. This correlation was not found for anatomic location. In the multivariate analysis, tumor size was not found to be an independent variable that correlates with tumor prognosis either.

These characteristics likely lead to a larger tumor that develops higher levels of metabolic activity (SUV_{max}); a higher SUV_{max} value correlates with larger tumors and higher-grade tumors. This is expected as there is a pathological correlation between tumor greatest dimension or tumor grade as high-grade tumors feature rapid growth and invasion. In practice, this is the clinical risk assessment grouping for treatment decision making. Tumors with intermediate grade greater than 5–7 cm in diameter are considered to have the same high clinical risk for poor outcome as high-grade tumors. Our data analysis shows that a large intermediate leiomyosarcoma tumors greater than 9 cm should undergo the same treatment as a high-grade tumor with a high risk for metastasis, supporting this clinical practice.

Tumor greatest dimension provides spatial information, but tumor volume may be more precise. By calculating the volume of a tumor from three dimensions obtained from pretreatment imaging, a more accurate description of the tumor can be obtained. For tumors that had fewer than three dimensions provided, this variable's accuracy is, however, limited. Making certain that all tumor dimensions are recorded is one method to ensure a greater accuracy, but the use of measuring tumor volume through a discrete volume representation such as image voxels would increase accuracy. By obtaining volume data easily calculated through computer, a more precise volume measurement would result. With more accurate tumor volume measurements, a strong correlation between tumor SUV_{max} and tumor volume might be found as it has been found between SUV_{max} and tumor greatest dimension.

In recent reports on synovial and other sarcomas, tumor size, tumor grade, and anatomic tumor location were correlated with SUV_{max} [7–10]. These studies used a large sample size of tumors that were imaged by FDG PET with a constant methodology at similar times before treatment initiation in a progressive imaging protocol. In leiomyosarcomas, there are few studies that correlate tumor size, tumor grade, and anatomic location with SUV_{max}.

FDG-PET continues to be investigated as a noninvasive way to image and characterize tumors as well as potentially predict patient survival. This retrospective analysis has identified two potential markers with which SUV_{max} can be correlated in leiomyosarcoma: tumor greatest dimension and tumor grade. The clinical significance of tumor grade is that a set of tumor histologic features can predict histologic behavior of the malignant process. This suggests that a large (by greatest dimension) intermediate grade tumor is expected to have the same predicted outcome as a high-grade tumor and should be treated in the same manner, as they share the same prognosis by definition of tumor grade. By identifying these features of leiomyosarcoma that correlate with FDG SUV_{max}, we have found tumor characteristics that are predictive of tumor behavior and probably patient outcome. The use of FDG PET can contribute to individualized patient diagnosis and treatment planning and improved patient treatment response evaluation.

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Table 1

Patient characteristics

Variable	Mean	Standard deviation	<i>n</i>
λAge	53.0	11.6	38
Greatest dimension	10.2	4.6	38
FDG SUV _{max}	9.3	3.7	38

FDG, fluorodeoxyglucose; SUV_{max}, maximum tumor standard uptake value.

Table 2

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Variable	Number (percent)
λSex	
vMale	17 (45)
vFemale	21 (55)
Grade	
vHigh/intermediate >9λcm	25 (66)
vLow/intermediate ≤9λcm	13 (34)
Location	
vPelvis	8 (21)
vExtremity	21 (55)
vTrunk	9 (24)

Table 3Summary of univariate statistics for simple linear regression model of FDG SUV_{max} on explanatory variables

Variable	Coefficient	<i>P</i> value
λAge	−0.08	0.13
Greatest dimension	0.36	0.004
Sex	2.11	0.08
Grade (High/Int>9 vs. Low/Int≤9)	3.95	<0.001
Location		
vPelvis	−1.27	0.42
vTrunk	−1.19	0.43

FDG, fluorodeoxyglucose; SUV_{max}, maximum tumor standard uptake value; Int, intermediate.

Table 4

Summary of statistics for multivariate regression model of FDG SUV_{max} model including both greatest dimension and grade^a

Variable	Coefficient	P value
λGreatest dimension	0.25	0.08
Grade	3.49	0.017
Age	−0.05	0.29
Sex	0.98	0.37
Location		
vPelvis	−0.57	0.67
vTrunk	−0.52	0.69

^a Other variables when added individually to the above model in a stepwise manner (i.e. greatest dimension, grade and the variable of interest were each added individually to the base model with greatest dimension and grade).

FDG, fluorodeoxyglucose; SUV_{max}, maximum tumor standard uptake value.