

Diagnostic Accuracy and Prognostic Value of ^{18}F -FDG PET in Hürthle Cell Thyroid Cancer Patients

Daniel A. Pryma^{1,2}, Heiko Schöder¹, Mithat Gönen³, Richard J. Robbins⁴, Steven M. Larson¹, and Henry W.D. Yeung¹

¹Nuclear Medicine Service, Memorial Sloan-Kettering Cancer Center, New York, New York; ²Department of Radiology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; ³Epidemiology and Biostatistics Department, Memorial Sloan-Kettering Cancer Center, New York, New York; and ⁴Endocrinology Service, Memorial Sloan-Kettering Cancer Center, New York, New York

Hürthle cell carcinoma is an uncommon and occasionally aggressive differentiated thyroid cancer associated with increased mortality compared with other differentiated thyroid malignancies. Because it generally has lower iodine avidity, ^{18}F -FDG PET has been suggested as a more accurate imaging modality. However, there is limited information with regard to the true diagnostic accuracy and prognostic value of ^{18}F -FDG PET in this disease. **Methods:** All patients with Hürthle cell thyroid cancer who underwent their first ^{18}F -FDG PET scan between May 1996 and February 2003 were identified retrospectively. ^{18}F -FDG PET scans were reviewed and compared with all available imaging studies, including CT, ultrasound, and radioiodine scintigraphy (RIS). Abnormal ^{18}F -FDG uptake was assessed visually and by measuring the maximum standardized uptake value (SUVmax) of the most intense lesion. Clinical follow-up for at least 1 y or until death was required for inclusion. **Results:** Forty-four patients met inclusion criteria. The median follow-up was 2.9 y. There were 24 positive and 20 negative ^{18}F -FDG PET scans with 1 false-positive and 1 false-negative study, resulting in a diagnostic sensitivity of 95.8% and a specificity of 95%. In 5 of 11 patients who had both positive CT and ^{18}F -FDG PET findings, ^{18}F -FDG PET revealed additional sites of disease. Furthermore, ^{18}F -FDG PET correctly classified as negative 3 patients with false-positive CT findings. In 3 of 6 patients with positive RIS, ^{18}F -FDG PET revealed additional sites of metastatic disease. Ten patients with positive ^{18}F -FDG PET had negative RIS. Only 1 patient with negative ^{18}F -FDG PET had positive RIS. The SUVmax also provided prognostic information: In a stepwise fashion, each increase in intensity by SUVmax unit was associated with a 6% increase in mortality ($P < 0.001$). The 5-y overall survival in patients with SUVmax < 10 was 92%; it declined to 64% in those with SUVmax > 10 ($P < 0.01$). **Conclusion:** ^{18}F -FDG PET has excellent diagnostic accuracy in Hürthle cell thyroid cancer patients, improving on CT and RIS. Intense ^{18}F -FDG uptake in lesions is an indicator of a poor prognosis. Our data suggest that all patients with Hürthle cell thyroid cancer should undergo ^{18}F -FDG PET as part of their initial postoperative staging and pe-

riodically to screen for occult recurrence, particularly in patients with elevated serum thyroglobulin.

Key Words: thyroid cancer; ^{18}F -FDG PET; Hürthle cell thyroid cancer; CT; radioactive iodine scintigraphy

J Nucl Med 2006; 47:1260–1266

Hürthle cell thyroid cancer is an uncommon and occasionally aggressive differentiated thyroid malignancy (1), particularly when the primary tumor is widely invasive (2,3). Approximately 3.6% of thyroid cancers are of the Hürthle cell subtype (4), though there has been significant controversy among pathologists as to the exact definition of Hürthle cell thyroid cancer (5). When clearly defined histopathologically as an invasive tumor, Hürthle cell thyroid cancer has a higher incidence of distant metastasis (33%) than other differentiated thyroid cancers (range, 10%–22% in papillary or follicular thyroid cancers) (6,7). Invasive Hürthle cell thyroid cancer also has a worse prognosis: Shaha et al. reported a 20-y survival of 65%, which is significantly lower than the 87% seen in papillary thyroid cancer and 81% in follicular thyroid cancer (7). However, some studies with shorter follow-up have not shown such a striking difference in survival between Hürthle cell and follicular thyroid cancers (8,9).

For most patients with differentiated thyroid cancer and poor prognostic factors (older age, large primary tumor, extrathyroidal or vascular invasion, lymph node involvement (10)), the postsurgical management centers around therapy with radioiodine. The combination of serum thyroglobulin (Tg) measurements and radioiodine scintigraphy (RIS) is commonly used for the detection of residual or metastatic disease. However, Hürthle cell thyroid cancer presents a unique clinical dilemma because of its generally low iodine avidity (11). Indeed, the sensitivity of diagnostic RIS using ^{131}I has been reported to be as low as 18% (12). Furthermore, medical redifferentiation therapies to increase iodine avidity have had generally disappointing results (13,14).

Received Mar. 21, 2006; revision accepted May 8, 2006.

For correspondence or reprints contact: Daniel A. Pryma, MD, Department of Radiology, University of Pittsburgh Medical Center, Room E-177, 200 Lothrop St., Pittsburgh, PA 15213.

E-mail: pryma@upmc.edu

COPYRIGHT © 2006 by the Society of Nuclear Medicine, Inc.

Serum Tg is very sensitive in detecting the presence of residual disease and the absolute Tg level may be associated with the site of metastasis (15). However, accurate localization of disease is essential in Hürthle cell thyroid cancer because surgery and external beam radiation therapy may be beneficial (16). There have been multiple attempts at imaging Hürthle cell thyroid cancer, including CT, ultrasound (US), radiolabeled somatostatin analogs, radiolabeled anticarcinoembryonic antigen antibodies, ^{201}Tl chloride, and $^{99\text{m}}\text{Tc}$ -sestamibi (17–22). Although many of these modalities show increased diagnostic sensitivity compared with RIS, none of them has excellent sensitivity or specificity in detecting residual or recurrent disease.

To improve detection of Hürthle cell thyroid cancer, investigators have examined imaging of ^{18}F -FDG (23–26). ^{18}F -FDG PET, including semiquantitative analysis using standardized uptake values (SUVs), is of proven value in the staging and detection of recurrent disease in many malignancies (27–29), including differentiated thyroid carcinoma (30). For instance, in a group of 125 high-risk differentiated thyroid cancer patients, including 12 patients (9.6%) with Hürthle cell cancer, Wang et al. showed that a positive ^{18}F -FDG PET scan, maximum SUV (SUV_{max}), and volume of ^{18}F -FDG-avid disease all have important prognostic value (30). More recently, Robbins et al. reported further evidence that ^{18}F -FDG PET can accurately stratify thyroid cancer patients into high and low risk of cancer-specific mortality (31).

There is limited published experience with ^{18}F -FDG PET in the management of Hürthle cell carcinoma. The largest study to date included 17 patients along with a meta-analysis involving a total of 35 patients (26). In a group of 12 patients, Lowe et al. reported an excellent sensitivity of 92% for the detection of Hürthle cell cancer using ^{18}F -FDG PET. However, 10 of the 12 patients had known or suspected active disease at the time of PET. In that report, the results affected patient care choices in 50% of cases (25). In the present study, we describe our own experience with ^{18}F -FDG PET in a larger population of Hürthle cell cancer patients to verify the diagnostic accuracy of this test compared with other imaging modalities. We also investigated the prognostic value of ^{18}F -FDG PET in this disease.

MATERIALS AND METHODS

Patients

In accordance with institutional practices, from our Memorial Sloan-Kettering Cancer Center PET database, we identified all patients with Hürthle cell thyroid cancer who underwent their first ^{18}F -FDG PET scan between May 1996 and February 2003. All patients had previously undergone total thyroidectomy and pathologic diagnosis was confirmed by a Memorial Sloan-Kettering Cancer Center pathologist. Patients had been referred for ^{18}F -FDG PET because of an elevated Tg, abnormal conventional imaging findings, or high-risk histopathologic findings (2). Patient charts were reviewed retrospectively for imaging and laboratory data in addition to clinical follow-up for at least 1 y or until death.

Imaging and laboratory studies done within 60 d of the ^{18}F -FDG PET were included for analysis. Imaging studies reviewed included all available CT, US, and RIS (including posttherapy scans when available). Laboratory results, with specific attention to serum Tg (15) and clinical follow-up, including biopsies from suspected sites of recurrence or metastasis when available, were all considered. An elevated Tg (≥ 10 ng/mL during thyroid suppression therapy), even in the absence of positive imaging, was considered positive for metastatic disease. However, a mildly elevated suppressed Tg (< 10 ng/mL), which remained stable or decreased on follow-up, was considered equivocal in the presence of negative imaging. At least 1 y of clinical follow-up after ^{18}F -FDG PET (or death within the first year with clinical follow-up until the time of death) was necessary for inclusion into the study.

PET

Patients fasted for at least 6 h before ^{18}F -FDG injection, but liberal water intake was encouraged. Patients were instructed to sit quietly after intravenous injection of a median dose of 385 MBq (range, 337–592 MBq [10.4 mCi; range, 9.1–16 mCi]) ^{18}F -FDG. A blood sample was drawn at the time of injection for blood glucose measurement and was confirmed to be in the acceptable range, with a median value of 91 mg/dL (range, 67–205 mg/dL).

PET studies were performed on an Advance PET (GE Healthcare; 29 patients), ECAT HR+ PET (Siemens/CTI; 3 patients), Discovery LightSpeed Plus (LS) PET/CT (GE Healthcare; 3 patients), or lutetium oxyorthosilicate (LSO) Biograph PET/CT (Siemens/CTI; 9 patients). The Advance PET was used in 2-dimensional mode and has an axial field of view (FOV) of 15.2 cm and a transaxial resolution of 4.2-mm full width at half maximum (FWHM) at the center. The ECAT HR+, using 3-dimensional acquisition, has an axial FOV of 15.5 cm and a transaxial resolution of 4.1-mm FWHM at the center. The Discovery LS PET/CT includes a 4-slice LightSpeed CT with a tube voltage of 120 kVp and a tube current of 40–85 mA, depending on patient weight. The PET component is the same as in the Advance scanner. Finally, the LSO Biograph PET/CT includes a dual-slice SOMATOM Emotion CT operated at a tube voltage of 130 kVp and a tube current of 40–85 mA, depending on patient weight. The PET component uses 3-dimensional acquisition and includes an axial FOV of 15.5 cm and a transaxial resolution of 4.5 mm at 1 cm from the center.

Images were acquired at approximately 60 min (range, 40–98 min) after intravenous injection of the radiotracer. In 25 patients, ^{18}F -FDG PET was done from the base of the skull to the proximal thighs; in 17 patients, imaging was done from the base of the skull to midabdomen. In an additional 2 patients, who were evaluated in the early phase of clinical PET at this institution, only a limited area of interest was assessed (lower neck and chest in 1 patient; pelvis and proximal femora in 1 patient).

Images were reconstructed using ordered-subset expectation maximization. Attenuation correction was done using either rod source (GE Advance and ECAT HR+) or CT (GE Discovery LS and Siemens LSO Biograph) transmission scans. ^{18}F -FDG PET scans were reviewed in 3 orthogonal planes and a maximum-intensity-projection image. CT, when available, was used for anatomic localization. Images were interpreted by 2 nuclear medicine physicians who were unaware of the results of correlative imaging. Findings were categorized as consistent with presence or absence of disease. A study was considered positive when focal ^{18}F -FDG uptake was greater than background blood-pool activity and located outside of organs that show physiologic tracer uptake,

such as the liver, or greater than background physiologic activity within an organ. Circular regions of interest were placed over all areas of abnormal ^{18}F -FDG uptake and the SUVmax (corrected for body weight) was calculated. In each patient, the SUVmax of the lesion with the most intense ^{18}F -FDG uptake was recorded.

Statistics

Categoric variables are summarized using proportions and numeric variables are presented as median and range. Survival probabilities were calculated using the Kaplan–Meier method and compared using the log-rank test (32). The association between survival times and SUVmax, age, sex, tumor extension, and cervical node status was modeled using proportional hazards regression (32). SUVmax was grouped into patients with SUVmax < 10 and ≥ 10 and survival probabilities are presented for each group. A *P* value of <0.05 was considered significant.

RESULTS

Forty-four patients with Hürthle cell thyroid cancer patients met study inclusion criteria and underwent their first ^{18}F -FDG PET scan during the study interval. Studies were ordered at the discretion of the referring endocrinologist. In retrospect, 22 patients with no known disease were referred for an ^{18}F -FDG PET scan to determine the extent of the disease. Referral was based on earlier clinical observation that ^{18}F -FDG PET can provide diagnostic and prognostic information in patients with other entities of differentiated thyroid cancer (30). Twenty patients were referred because of clinical suspicion of disease after physical examination and Tg measurement, 1 patient for staging in light of antibodies interfering with the measurement of Tg, and 1 patient because of suggestive CT findings on follow-up. Patient characteristics are listed in Table 1.

Tg measurements, obtained within 60 d of ^{18}F -FDG PET, were available for 39 patients (4 of the remaining 5 patients had no sample drawn during this time interval, whereas 1 had antibodies interfering with Tg measurement). The median Tg was 6.5 ng/mL (range, 0–214,000 ng/mL).

Fifteen patients underwent CT of the neck or chest, 33 underwent RIS (24 posttherapy scans and 9 diagnostic scans), and 3 underwent US. Forty-two patients continued suppressive thyroid hormone therapy at the time of the ^{18}F -FDG PET scan.

TABLE 1
Patient Characteristics

Patient characteristic	Result
Median age at time of ^{18}F -FDG PET (y)	62 (range, 24–81)
No. of females (%)	21 (48)
Median time from diagnosis to ^{18}F -FDG PET (y)	1.5 (range, 0.1–37.5)
Median Tg (ng/mL)	6.5 (range, 0–214,000)
Median Tg with positive ^{18}F -FDG PET (ng/mL)	348 (range, 0–214,000)
Median Tg with negative ^{18}F -FDG PET (ng/mL)	1 (range, 0–7)
Median follow-up (y)	2.9 (range, 0–8.8)

Two patients were scanned while in the hypothyroid state (thyroid-stimulating hormone > 30 $\mu\text{IU/mL}$), both of whom had true-negative ^{18}F -FDG PET findings.

There were 24 positive and 20 negative ^{18}F -FDG PET scans. There was 1 false-positive and 1 false-negative scan, resulting in a sensitivity of 95.8% (95% confidence interval, 80%–100%), a specificity of 95% (76%–100%), and an overall accuracy of 95.5% (78%–100%). On long-term follow-up, 3 patients with initially negative ^{18}F -FDG PET scans had disease recurrence at 3.2, 4.1, and 5.7 y, respectively. These recurrences all initially manifested as rising Tg levels on routine surveillance. Incidentally, in all 3 patients, follow-up ^{18}F -FDG PET done shortly after detection of the rising Tg levels accurately localized the disease. Among patients with positive ^{18}F -FDG PET scans, the median SUVmax was 17.6 (range, 2.1–64.9). Furthermore, when excluding the 8 patients with low-volume disease (all tumor deposits were <2 cm in maximal dimension), in whom SUVmax is likely underestimated because of volume averaging, the median SUVmax increased to 26.

The 1 patient with a false-positive ^{18}F -FDG PET scan had an enlarged left supraclavicular lymph node with SUVmax of 3.5. The node was also consistent with metastatic disease on a CT scan of the neck (Fig. 1). However, subsequent biopsy revealed granuloma and *Mycoplasma avium* grew in culture. The patient with false-negative ^{18}F -FDG PET was shown to have iodine-avid disease in the right lung and chest wall on RIS (Fig. 2). CT of the neck and chest was also negative. After 2 annual treatments with 11.1 GBq (300 mCi) Na^{131}I , his Tg decreased and he remains without clinical evidence of residual disease.

Fifteen patients underwent concurrent ^{18}F -FDG PET and CT. Both imaging studies were positive in 11 of the 15 patients, but in 5 individuals ^{18}F -FDG PET revealed additional sites of disease (4 patients with bone metastases not seen on CT and 1 patient with a cervical lymph node not seen on CT; Fig. 3). In 3 patients with true-negative PET findings, the CT was false-positive, suggesting lymphadenopathy that biopsy and follow-up revealed to be benign (Fig. 4). Finally, in 1 patient both ^{18}F -FDG PET and CT were true-negative.

Thirty-three patients underwent RIS within 60 d of ^{18}F -FDG PET. Twenty-four of these imaging studies were posttherapy scans, which had a sensitivity of 72% in detecting at least 1 site of disease in a given patient, using

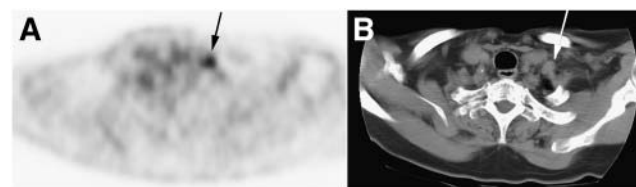


FIGURE 1. False-positive PET and CT. (A) Increased ^{18}F -FDG uptake is seen in left supraclavicular lymph node (black arrow) on ^{18}F -FDG PET. (B) Lymph node was also interpreted as malignant on dedicated CT (white arrow). Excisional biopsy showed granuloma and *Mycoplasma avium* grew in culture.

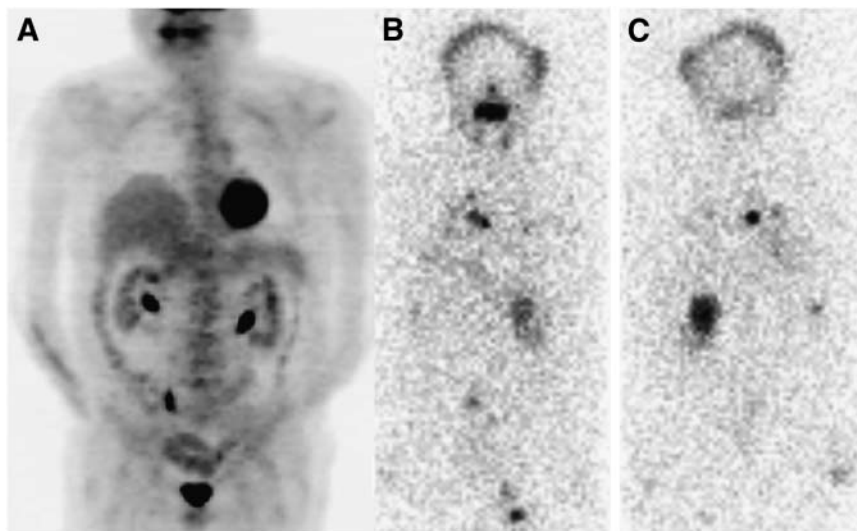


FIGURE 2. (A) Negative ^{18}F -FDG PET before receiving 11.1 GBq (300 mCi) Na^{131}I . Concurrent CT of neck and chest (not shown) was also negative. Anterior (B) and posterior (C) images from post-therapy scan 1 wk after radioiodine therapy show iodine-avid disease in neck and chest. Increased activity along the scalp was confirmed to be surface contamination. After 2 annual doses of 11.1 GBq Na^{131}I , patient has no evidence of disease.

the clinical follow-up and the result of conventional imaging as the gold standard. The remaining 9 studies were diagnostic scans, which had a sensitivity of 50%. Six patients had positive ^{18}F -FDG PET and RIS scans (all posttherapy). However, in 3 of the 6 patients, ^{18}F -FDG PET revealed multiple additional sites of uptake. Ten patients had positive ^{18}F -FDG PET in the face of negative RIS (5 posttherapy scans and 5 diagnostic scans), including 1 false-positive ^{18}F -FDG PET scan. Only 1 patient had false-negative ^{18}F -FDG PET with positive posttherapy RIS. Finally, in 16 patients, ^{18}F -FDG PET and RIS were both negative.

Only 3 patients underwent US of the neck within 60 d of ^{18}F -FDG PET. All 3 of the patients had negative neck ultrasound and no abnormal ^{18}F -FDG uptake in the neck. Of note, 1 of the patients had widespread pulmonary metastases on ^{18}F -FDG PET.

During the follow-up interval, 9 patients died of thyroid cancer. All had a positive ^{18}F -FDG PET scan. One patient with negative ^{18}F -FDG PET findings died from complications of an unrelated surgery. Among patients dying from thyroid cancer, 2 died within 18 and 61 d after the ^{18}F -FDG PET. Both had widespread metastatic disease. Among the remaining patients, the median follow-up after PET was 2.9 y (range, 1.2–8.8 y). Patients with $\text{SUV}_{\text{max}} \geq 10$ had 5-y all-cause survival of 64% compared with 92% in those with $\text{SUV}_{\text{max}} < 10$ ($P < 0.01$; Figure 5). Each increase in ^{18}F -FDG uptake by 1 SUV_{max} unit was associated with a 6% increase in mortality ($P < 0.001$). In univariate analysis, there was no significant difference in survival for male sex ($P = 0.99$), age > 45 y ($P = 0.31$), or degree of

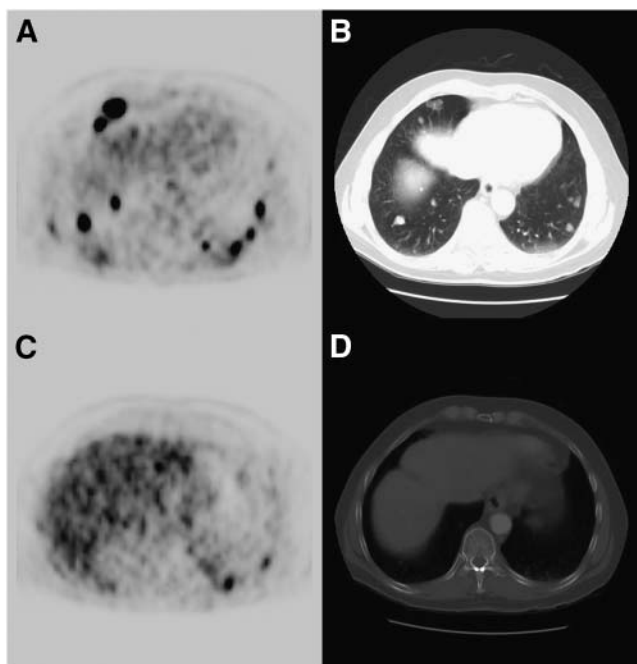


FIGURE 3. Patient with widely metastatic Hürthle cell thyroid cancer. ^{18}F -FDG PET (A) and CT (B) both revealed pulmonary metastases, whereas left rib metastases seen on ^{18}F -FDG PET (C) appear unremarkable on CT (D).

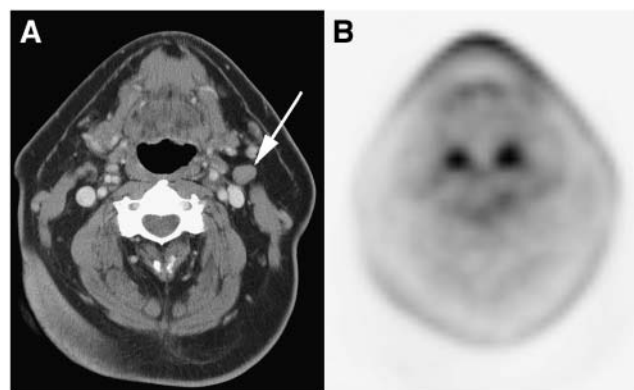


FIGURE 4. Contrast-enhanced diagnostic CT of the neck (A) shows a left level II cervical lymph node interpreted as consistent with metastatic disease (white arrow). (B) ^{18}F -FDG PET shows no uptake in this node. Long-term follow-up demonstrated no evidence of disease.

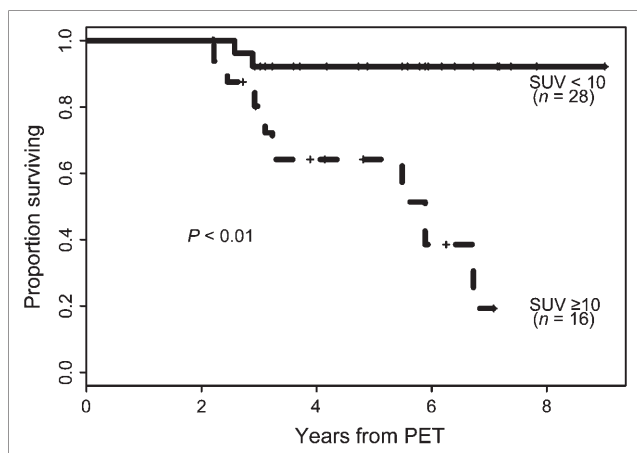


FIGURE 5. Kaplan-Meier survival curve. Dashed line: Patients with SUVmax ≥ 10 have 5-y all-cause mortality of 64%. Solid line: Patients with SUVmax < 10 have 5-y all-cause mortality of 92% ($P < 0.01$).

extrathyroidal extension ($P = 0.10$). In contrast, cervical node metastasis, when sampled, did show significant correlation with mortality, wherein 5-y survival in node-negative patients was 100% compared with 31% in node-positive patients ($P = 0.01$). However, only 15 of 44 patients underwent cervical node sampling.

DISCUSSION

Our study demonstrated that ^{18}F -FDG PET had excellent sensitivity for disease detection and localization in our cohort of patients with Hürthle cell thyroid cancer. In addition, the intensity of ^{18}F -FDG uptake in metastatic lesions provides important prognostic information about overall survival. Although ^{18}F -FDG is known to be a nonspecific tracer (particularly in the face of infection or inflammation), this is mitigated by the very intense ^{18}F -FDG uptake by most Hürthle cell thyroid cancers. Indeed, the median SUVmax per patient was 17.6 in our study and a higher SUVmax correlated strongly with an increased risk of mortality.

In a study of 12 patients with Hürthle cell thyroid cancer from the Mayo Clinic, Lowe et al. (25) reported a 92% diagnostic sensitivity for ^{18}F -FDG PET. Here, we confirm their preliminary data in a larger patient population: Indeed, ^{18}F -FDG PET has an excellent diagnostic accuracy in the detection of residual Hürthle cell thyroid cancer. Our results also demonstrate that ^{18}F -FDG PET has better sensitivity and specificity than CT on a per patient basis. In 45% of patients with both positive CT and ^{18}F -FDG PET, the ^{18}F -FDG PET revealed additional metastatic lesions not seen on CT. Because local therapies such as surgery and external beam radiation are often pursued in metastatic Hürthle cell thyroid cancer, accurately identifying all metastatic lesions is of great clinical importance.

US was not widely used in our patient population. Indeed, only 3 patients were referred for US and all 3 had negative

studies. Although US provides an excellent evaluation of the neck, few of our patients had significant morbidity or mortality from local disease in the neck. A small series examining the cause of mortality among all thyroid cancers showed that 80% of the patients died of distant metastases and only 20% died of local complications (33). Ultrasound studies of the neck were not systematically performed during follow-up of these patients. However, the correlation between cervical lymph node status at the time of thyroidectomy and mortality (though cervical nodal sampling was not done routinely) suggests that cervical nodal status may have a prognostic value in patients with Hürthle cell carcinoma. It is conceivable that ultrasound during follow-up would also add diagnostic and perhaps prognostic information. However, our retrospective study was not designed to specifically address the value of US in this patient population.

The sensitivity of RIS in our series was 65%, which is better than the 18% reported by Yen et al. (12). This is likely due, at least in part, to the fact that we included posttherapy scans when available, which have a higher sensitivity (72% in this population) than diagnostic RIS (50%). Despite this, in 50% of the positive studies, RIS underestimated the disease burden compared with ^{18}F -FDG PET. However, though Hürthle cell thyroid cancer generally has poor iodine avidity compared with other differentiated thyroid cancers, those 50% of patients with positive iodine scans could potentially benefit from treatment with radioactive iodine. Therefore, therapy with radioactive iodine should be considered at least once in all patients (especially in light of the dearth of other effective systemic therapies). This is particularly appropriate considering the case of our patient with metastatic Hürthle cell thyroid cancer that has remained ^{18}F -FDG PET negative and has had complete clinical response of his metastatic disease after therapy with radioactive iodine.

Even among high-risk patients with suspected or known metastatic disease, ^{18}F -FDG PET had a striking contribution over conventional imaging modalities. We found that an SUVmax of 10 distinguishes between subsets of patients with relatively good prognosis and those with poor prognosis. We have chosen to use an SUVmax cutoff of 10, building on the work of Wang et al., who showed that this SUV number differentiates between good and poor prognosis in a larger population of all differentiated thyroid cancers (30). Furthermore, age, sex, tumor extension, and cervical node status were examined, as their prognostic significance had been assessed previously in a series of 555 patients with Hürthle cell thyroid cancer (8). We found that age, sex, and primary tumor extension were not correlated with survival, whereas cervical node status did correlate with survival.

Three of 20 patients with negative ^{18}F -FDG PET scans did develop recurrent disease an average of 4.1 y after their initial ^{18}F -FDG PET. However, these 3 patients all had positive ^{18}F -FDG PET findings shortly after recurrence was suspected because of rising Tg levels. No foreseeable imaging modality can detect microscopic disease, but these

data suggest that ^{18}F -FDG PET may detect disease sooner than other imaging modalities.

We have reported the SUVmax of only the most intense lesion in each patient because it is likely that prognosis and therapeutic options are determined by the most aggressive disease in a given patient. Furthermore, the most intense lesions tend to be the largest lesions, which minimizes the effects of volume averaging. Additionally, as each patient may have a spectrum of disease, reporting the SUVmax for each hypermetabolic lesion would likely cause more overlap among patients, possibly obscuring the significance of our findings.

Our data are limited by the fact that this is a retrospective study. There may have been referral bias, particularly among the earliest patients. On the basis of the initial clinical data, all patients with Hürthle cell thyroid cancer now undergo at least one ^{18}F -FDG PET study shortly after thyroidectomy and before postsurgical radioiodine therapy. This regimen was followed in about half of the study population, whereas in earlier cases ^{18}F -FDG PET was done at the discretion of the referring endocrinologist. Furthermore, it would be preferable to have all correlative imaging and laboratory tests performed in a narrower time range than 60 d of ^{18}F -FDG PET. However, because of scheduling constraints, many patients could not have these tests completed more expeditiously. We initially hoped to discuss the impact of the ^{18}F -FDG PET studies on subsequent patient care decisions. However, most patients returned to their referring physician after all imaging and laboratory studies were done. Therefore, the referring physician's note after the ^{18}F -FDG PET study did not specifically address the impact of ^{18}F -FDG PET but, rather, synthesized all available data. We decided that a retrospective analysis of the likely impact of the ^{18}F -FDG PET scan would require too much inference. Instead, we chose to concentrate on the accuracy of ^{18}F -FDG PET and its prognostic implications in this patient population. Ideally, the true prognostic value and impact of ^{18}F -FDG PET in Hürthle cell thyroid cancer should be assessed in a prospective study. Such a study would require long-term follow-up because of the protracted time course of many thyroid cancers.

CONCLUSION

Hürthle cell thyroid cancer tends to be ^{18}F -FDG avid with very intense, conspicuous uptake on ^{18}F -FDG PET. ^{18}F -FDG PET has excellent diagnostic accuracy in Hürthle cell thyroid cancer and often provides additional information over conventional imaging. In patients with a clinical suspicion of recurrent disease because of rising Tg levels, ^{18}F -FDG PET is likely the most accurate imaging test in localizing metastatic disease. Finally, ^{18}F -FDG PET conveys important prognostic information that may potentially alter patient management. We suggest that all patients with Hürthle cell thyroid cancer should undergo ^{18}F -FDG PET as part of their initial postoperative staging and during

follow-up when there is a rising Tg level or other clinical suspicion of recurrent disease.

REFERENCES

1. Azadian A, Rosen IB, Walfish PG, Asa SL. Management considerations in Hürthle cell carcinoma. *Surgery*. 1995;118:711–714.
2. Stojadinovic A, Ghossein RA, Hoos A, et al. Hürthle cell carcinoma: a critical histopathologic appraisal. *J Clin Oncol*. 2001;19:2616–2625.
3. Stojadinovic A, Hoos A, Ghossein RA, et al. Hürthle cell carcinoma: a 60-year experience. *Ann Surg Oncol*. 2002;9:197–203.
4. Hundahl SA, Cady B, Cunningham MP, et al. Initial results from a prospective cohort study of 5583 cases of thyroid carcinoma treated in the United States during 1996: U.S. and German Thyroid Cancer Study Group—an American College of Surgeons Commission on Cancer Patient Care Evaluation study. *Cancer*. 2000;89:202–217.
5. Tallini G, Carcangiu ML, Rosai J. Oncocytic neoplasms of the thyroid gland. *Acta Pathol Jpn*. 1992;42:305–315.
6. Shaha AR, Ferlito A, Rinaldo A. Distant metastases from thyroid and parathyroid cancer. *ORL J Otorhinolaryngol Relat Spec*. 2001;63:243–249.
7. Shaha AR, Shah JP, Loree TR. Patterns of nodal and distant metastasis based on histologic varieties in differentiated carcinoma of the thyroid. *Am J Surg*. 1996;172:692–694.
8. Bhattacharyya N. Survival and prognosis in Hürthle cell carcinoma of the thyroid gland. *Arch Otolaryngol Head Neck Surg*. 2003;129:207–210.
9. Hundahl SA, Fleming ID, Fremgen AM, Menck HR. A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the U.S., 1985–1995. *Cancer*. 1998;83:2638–2648.
10. Lopez-Penabad L, Chiu AC, Hoff AO, et al. Prognostic factors in patients with Hürthle cell neoplasms of the thyroid. *Cancer*. 2003;97:1186–1194.
11. Yutan E, Clark OH. Hürthle cell carcinoma. *Curr Treat Options Oncol*. 2001;2:331–335.
12. Yen TC, Lin HD, Lee CH, Chang SL, Yeh SH. The role of technetium-99m sestamibi whole-body scans in diagnosing metastatic Hürthle cell carcinoma of the thyroid gland after total thyroidectomy: a comparison with iodine-131 and thallium-201 whole-body scans. *Eur J Nucl Med*. 1994;21:980–983.
13. Grunwald F, Menzel C, Bender H, et al. Redifferentiation therapy-induced radioiodine uptake in thyroid cancer. *J Nucl Med*. 1998;39:1903–1906.
14. Short SC, Suovuori A, Cook G, Vivian G, Harmer C. A phase II study using retinoids as redifferentiation agents to increase iodine uptake in metastatic thyroid cancer. *Clin Oncol (R Coll Radiol)*. 2004;16:569–574.
15. Robbins RJ, Srivastava S, Shaha A, et al. Factors influencing the basal and recombinant human thyrotropin-stimulated serum thyroglobulin in patients with metastatic thyroid carcinoma. *J Clin Endocrinol Metab*. 2004;89:6010–6016.
16. Foote RL, Brown PD, Garces YI, McIver B, Kasperbauer JL. Is there a role for radiation therapy in the management of Hürthle cell carcinoma? *Int J Radiat Oncol Biol Phys*. 2003;56:1067–1072.
17. Abdel-Nabi H, Hinkle GH, Falko JM, Kelly D, Olsen JO, Martin EW Jr. Iodine-131 labeled anti-CEA antibodies uptake by Hürthle cell carcinoma. *Clin Nucl Med*. 1985;10:713–715.
18. Boi F, Lai ML, Deias C, et al. The usefulness of $^{99\text{m}}\text{Tc}$ -sestamibi scan in the diagnostic evaluation of thyroid nodules with oncocytic cytology. *Eur J Endocrinol*. 2003;149:493–498.
19. Christian JA, Cook GJ, Harmer C. Indium-111-labelled octreotide scintigraphy in the diagnosis and management of non-iodine avid metastatic carcinoma of the thyroid. *Br J Cancer*. 2003;89:258–261.
20. Gulec SA, Serafini AN, Sridhar KS, et al. Somatostatin receptor expression in Hürthle cell cancer of the thyroid. *J Nucl Med*. 1998;39:243–245.
21. Kostoglou-Athanassiou I, Pappas A, Gogou L, Kaldrymides P. Scintigraphy with [^{111}In]octreotide and ^{201}Tl in a Hürthle cell thyroid carcinoma without detectable radio-iodine uptake: report of a case and review of the literature. *Horm Res*. 2003;60:205–208.
22. Valli N, Catargi B, Ronci N, et al. Evaluation of indium-111 pentetreotide somatostatin receptor scintigraphy to detect recurrent thyroid carcinoma in patients with negative radioiodine scintigraphy. *Thyroid*. 1999;9:583–589.
23. Blount CL, Dworkin HJ. F-18 FDG uptake by recurrent Hürthle cell carcinoma of the thyroid using high-energy planar scintigraphy. *Clin Nucl Med*. 1996;21:831–833.
24. Grunwald F, Menzel C, Bender H, et al. Comparison of ^{18}F -FDG-PET with ^{131}I iodine and $^{99\text{m}}\text{Tc}$ -sestamibi scintigraphy in differentiated thyroid cancer. *Thyroid*. 1997;7:327–335.

25. Lowe VJ, Mullan BP, Hay ID, McIver B, Kasperbauer JL. ^{18}F -FDG PET of patients with Hurthle cell carcinoma. *J Nucl Med*. 2003;44:1402–1406.
26. Plotkin M, Hautzel H, Krause BJ, et al. Implication of 2-18fluor-2-deoxyglucose positron emission tomography in the follow-up of Hurthle cell thyroid cancer. *Thyroid*. 2002;12:155–161.
27. 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.
28. Vansteenkiste JF, Stroobants SG, Dupont PJ, et al. Prognostic importance of the standardized uptake value on ^{18}F -fluoro-2-deoxy-glucose-positron emission tomography scan in non-small-cell lung cancer: an analysis of 125 cases—Leuven Lung Cancer Group. *J Clin Oncol*. 1999;17:3201–3206.
29. Wong RJ, Lin DT, Schoder H, et al. Diagnostic and prognostic value of [^{18}F]fluorodeoxyglucose positron emission tomography for recurrent head and neck squamous cell carcinoma. *J Clin Oncol*. 2002;20:4199–4208.
30. Wang W, Larson SM, Fazzari M, et al. Prognostic value of [^{18}F]fluorodeoxyglucose positron emission tomographic scanning in patients with thyroid cancer. *J Clin Endocrinol Metab*. 2000;85:1107–1113.
31. Robbins RJ, Wan Q, Grewal RK, et al. Real-time prognosis for metastatic thyroid carcinoma based on 2- [^{18}F]fluoro-2-deoxy-D-glucose-positron emission tomography scanning. *J Clin Endocrinol Metab*. 2006;91:498–505.
32. Altman DG. *Practical Statistics for Medical Research*. 1st ed. New York, NY: Chapman and Hall; 1992.
33. Beasley NJ, Walfish PG, Witterick I, Freeman JL. Cause of death in patients with well-differentiated thyroid carcinoma. *Laryngoscope*. 2001;111:989–991.

Erratum

The “Results” section of the article “Dual-Time-Point ^{18}F -FDG PET for the Evaluation of Gallbladder Carcinoma” by Nishiyama et al. (*J Nucl Med*. 2006;47:633–638) contained 3 errors. The fifth sentence of the second paragraph should read “Overall, for visual analysis of gallbladder carcinoma, delayed PET improved the diagnosis in 2 patients (6%).” The second sentence of the third paragraph should read “The sensitivity of diagnosis of gallbladder carcinoma using semiquantitative analysis of PET images was improved for delayed imaging and combined early and delayed imaging—in 3 patients (13%) and 4 patients (17%), respectively.” The second sentence of the fourth paragraph should read “CRP levels were measured in all patients except two.”