



Performance of ^{18}F -FDG PET/TC in the differential diagnosis of adrenal masses in noncancer patients

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Introduction

Adrenal incidentalomas are lesions detected accidentally in the course of imaging performed for unrelated reasons. Their incidence increases gradually with age, and may reach 10% among individuals over the age of 70 years. The diagnostic approach to an adrenal incidentaloma involves (1):

- History and physical examination.
- Search for hormonal hypersecretion: morning cortisol following 1 mg Dexamethasone the night before, ACTH, aldosterone/renin ratio (renin being measured directly or as plasma renin activity), urinary metanephrines, and adrenal androgens.
- Differentiation between benign and malignant masses, on the basis of the results provided by CT and/or MRI (table).

CT and/or MRI characteristics which may inform the diagnosis of an adrenal incidentaloma		
Criteria	Benign	Malignant
Size	<4 cm	>4 cm
Borders	Regular	Irregular
Structure	Homogeneous	Heterogeneous
Contrast wash-out	Early	Delayed
Signal attenuation on non contrast CT	<10 HU	>10 HU
Signal intensity on opposed phase T1-weighted MRI	Signal loss	Signal persistence

In the past few years, masses non-characterized by CT and/or MRI, particularly if suspicious for primary or metastatic adrenal cancer, have been investigated by PET with ^{18}F -Fluorodeoxyglucose (^{18}F -FDG), combined with CT to improve spatial resolution. Utilization of ^{18}F -FDG PET/CT in patients with an adrenal incidentaloma but no history of cancer remains a source of debate.

Patients and methods

A recent French multicenter prospective study (2) has evaluated the role of ^{18}F -FDG PET/CT in detecting malignancy in 87 patients with no previous history of cancer (53 women, average age 55 years) with 87 adrenal masses (none bilateral):

- 56 masses with a diameter >4 cm
- 31 masses with diameter <4 cm but of undetermined nature on CT (>10 HU and delayed contrast wash-out).

Exclusion criteria:

- Pregnancy or breastfeeding
- Pathologic increase of plasma or urinary metanephrines
- CT features suggestive of myelolipoma, simple cyst or hematoma
- Previous history of clear cell renal carcinoma or any other cancer not in remission
- Adrenal cancer with loco-regional or systemic spread.

Fourteen patients presented manifestations of hypercortisolism.

All enrolled patients underwent ^{18}F -FDG PET/CT and 63 an adrenalectomy. Diagnosis of malignancy was based on histology (available for all the patients undergoing surgery and in one patient who underwent biopsy). In the remaining 23 patients, the mass was judged benign if stable on CT follow-up at 12 months.

Results

The 87 incidentalomas have produced the following results:

- Benign in 72 cases, 49 of which with an histological diagnosis: 34 cortico-adenomas, 4 oncocytomas, 2 pheochromocytomas, 2 hematomas, 2 cysts, and one each of nodular hyperplasia, ganglioneuroma, lymphangioma, schwannoma, and myelolipoma.
- Malignant in 15 cases: 11 adrenocorticocarcinomas, 2 leiomyosarcomas, 1 liposarcoma, and 1 lung cancer metastasis.

In comparison to benign incidentalomas, malignant masses were significantly larger, with higher attenuation values, more delayed wash-out, and higher capture of ^{18}F -FDG.

No incidentaloma with an attenuation value less than 10 HU turned out to be malignant. Secreting and non-secreting masses could not be differentiated on the basis of the ability to capture ^{18}F -FDG.

A comparison was made between the highest standardized uptake value (SUV) in the adrenal mass (T_{\max}) and the highest SUV in a homogeneous area of the 8th segment of the liver (L_{\max}). A ratio > 1.5 showed a sensitivity and specificity of 86% in differentiating benign and malignant lesions, and a negative predictive value of 96.9% in ruling out cancer. However, two of the lesions with a T_{\max}/L_{\max} less than 1.5 were cancers (a liposarcoma and a corticocarcinoma), while 4 of the lesions with a $T_{\max}/L_{\max} > 1.5$ were oncocytomas.

Conclusions

This study explores the potential role of ^{18}F -FDG PET/CT in defining the nature of large adrenal masses, which remain non-characterized after CT and/or MRI. Besides the routine evaluation of the SUV of the lesion, a T_{\max}/L_{\max} ratio seems to be more specific for defining malignancy than the visual assessment of the uptake. However, clinical judgment remains paramount as some adrenal masses may present misleading T_{\max}/L_{\max} ratios, as exemplified by the false negative reports in cases of adrenocortical carcinomas or retroperitoneal sarcomas. The best approach to diagnosis relies on the integration of the history with the biochemical and imaging data, and, when needed, a close follow-up.

References

1. Fassnacht M, Arlt W, Bancos I, et al. Management of adrenal incidentalomas: European Society of Endocrinology Clinical Practice Guideline in collaboration with the European Network for the Study of Adrenal Tumors. *Eur J Endocrinol* [2016, 175: G1-34](#).
2. Guerin C, Pattou F, Brunaud L, et al. Performance of ^{18}F -FDG PET/CT in the characterization of adrenal masses in noncancer patients: a prospective study. *J Clin Endocrinol Metab* [2017, 102: 2465-72](#).