PET Scan in Thyroid Cancer

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KEYWORDS

• PET • Differentiated thyroid carcinoma • ^{18}F-fluorodeoxyglucose • ^{124}I • ^{18}F-DOPA • ^{68}Ga-DOTATOC

KEY POINTS

- The most widely advocated indication of fluorodeoxyglucose (FDG)-PET in differentiated thyroid cancer is in evaluating patients with high thyroglobulin level when radioiodine whole-body scan is negative.
- FDG-PET imaging can provide prognostic information and thus may be useful in identifying the patients at higher risk of recurrent and metastatic disease.
- The role of novel PET tracers such as 18F-dihydroxyphenylalanine and ^{68}Ga-DOTA-NOC/^{68}Ga-DOTA-TATE in medullary thyroid carcinoma and use of ^{124}I in differentiated thyroid carcinoma (especially for lesional dosimetry) continues to evolve with promising results.

INTRODUCTION

Thyroid cancer is a group of tumors with different histologic and behavioral features including follicular cell–derived papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC), and Hürthle cell thyroid carcinoma (HTC). Medullary thyroid carcinoma (MTC) originates from parafollicular C cells scattered around the follicular epithelium in thyroid gland. Thyroid cancer accounts for approximately 1% to 3% of all cancer cases; however, its incidence has increased significantly around the world in the past 3 decades. The age-adjusted incidence was 11.6 per 100,000 per year. It has been estimated that approximately 56,500 men and women will be diagnosed with thyroid cancer, and about 1800 of them will die of the disease in 2012. PTC comprises most of the thyroid cancer cases (up to 80%) and more than 70% of patients are women. The median age at diagnosis for thyroid cancer was 50 years of age.[1] The risk for developing thyroid cancer increases in patients receiving external beam radiation to the head and neck, especially in childhood. Also at risk are those who have been irradiated internally following radioactive fallout and those with a family history of thyroid malignancy.[2] The incidence of thyroid cancer and the dose of irradiation have been closely correlated with exposures up to 1500 cGy, but the cancer risk is not increased at higher doses, probably because of the cell death from the radiation. Another factor for developing thyroid cancer is the iodine supply: follicular or anaplastic subtype of thyroid cancer is frequently seen in countries with low iodine intake, whereas there is a tendency to PTC in populations in which dietary iodine ingestion is adequate.

Differentiated thyroid cancer (DTC) has a favorable prognosis with overall 10-year survival rates of about 80% to 93%. However, recurrent disease in the neck may develop in up to 40% of patients, most commonly in the first 2 years following initial treatment with the following risk factors: incomplete surgery, an aggressive histologic subtype (tall cell, columnar cell), age greater than 45 years at initial diagnosis, tumor size more than 4 cm, extrathyroidal extension of the primary tumor, and

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lymph node involvement.[3] Mortality is about 8% and the underlying cause of death is usually local compression of the trachea and vasculature in the neck.

The thyroid tumors usually retain many of the characteristics of their normal progenitor cells such as iodine avidity, capacity to secrete thyroid hormones, and capacity to synthesize thyroglobulin (Tg). In the surveillance period, radioiodine scanning has been a well-established procedure in detecting recurrent or metastatic disease in patients with differentiated thyroid carcinoma when serum Tg level is increased, but the non–iodine-avid thyroid tumor poses a diagnostic and therapeutic challenge. The persistent tumor should be localized precisely and treated with either surgery or external beam radiation treatment because it will gain no benefit from ^{131}I treatment.[4] However, recurrent or metastatic tumor is seldom localized precisely with anatomic imaging modalities including ultrasound, computerized tomography (CT), and magnetic resonance (MR) imaging. In particular, ultrasound of the neck is useful for detecting small cervical adenopathy; however, it is often inconclusive in discriminating between malignant lesions and nonspecific tissue changes in the postsurgical neck.

FLUORODEOXYGLUCOSE-PET AND PET/CT SCAN IN PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA

Radioiodine whole-body scanning (WBS) has been well established in the management of patients with thyroid carcinoma provided that the original tumor cells are well differentiated and have the ability to concentrate radioiodine. However, in up to 30% of patients with differentiated thyroid carcinoma, tumor cells lose the ability to take up radioiodine, which impairs the clinical role of iodine isotopes and limits their use for diagnostic and therapeutic purposes.

Metabolic imaging with PET using [^{18}F]fluorodeoxyglucose (^{18}F-FDG) seems to be a valuable diagnostic tool in patients with non–iodine-avid thyroid tumor, particularly in the setting of high and gradually increasing Tg levels (**Fig. 1**). An ^{18}F-FDG-PET scan provides unique metabolic information and complements anatomic imaging findings in the characterization of non–iodine-avid thyroid tumor and leads the patients to alternative treatments including surgical intervention and external beam radiation. In a multicenter trial by Grünwald and colleagues,[5] the sensitivity of FDG-PET was 75% in the whole group and 85% in the subgroup of patients with negative ^{131}I WBS. Integrated PET/CT or PET/MR imaging devices provides additional structural information in the same session that helps in discriminating persistent or recurrent thyroid cancer from nonspecific FDG uptake in the neck and improves the diagnosis of persistent or recurrent thyroid cancer .[6–9]

FDG-PET has been most useful in patients with poorly differentiated or anaplastic thyroid carcinoma, which are known to have increased glucose metabolism and limited or no radioiodine uptake (**Fig. 2**). More than 80% of patients with HTC have negative radioiodine scanning, whereas FDG uptake by tumor cells has been reported to be high. It is more aggressive than other types of DTC and has a worse prognosis, especially when the primary tumor is widely invasive. HTC has higher incidence of distant metastasis, and cervical lymph node metastasis is frequent at initial diagnosis. The combination of serum Tg measurement and radioiodine WBS is used for the detection of recurrent or metastatic HTC, but the sensitivity of diagnostic radioiodine scanning has been as low as 18%.[10] Accurate localization of the disease site is essential; surgical intervention and external beam radiation treatment are the only options for cure because non–iodine-avid tumor cells do not benefit from high-dose radioiodine treatment. PET scanning often provides additional information compared with conventional imaging and contributes to localizing the tumor in patients with a clinical suspicion of recurrent or metastatic tumor because of increasing Tg levels. FDG-PET has a sensitivity, specificity, and accuracy of 92%, 80%, and 89%, respectively, reported in a meta-analysis by Plotkin and colleagues.[11] If the tumor secretes no Tg, which is an important marker for early detection of recurrent and metastatic thyroid cancer, FDG-PET remains the only diagnostic tool to diagnose persistent disease after initial thyroidectomy. Furthermore, thyroid tumors contain both differentiated and undifferentiated tumor cells, so FDG-PET should not be limited to only ^{131}I WBS–negative patients. The accuracy of FDG-PET scan increases when it is used together with ^{131}I scanning. Using this combination, tumor sites were missed in only 7% of all thyroid cancer cases.[12,13]

It has been postulated that cellular metabolism is stimulated with recombinant thyroid-stimulating hormone (TSH) (rhTSH) and thus more FDG is accumulated inside the thyroid cancer cells. Some investigators suggested that the sensitivity of FDG-PET is higher when it is performed under TSH stimulation (rhTSH) compared with TSH suppression, and that more FDG-avid lesions are detected because of better resolution of the PET instrument. However, some investigators reported no significant impact of TSH stimulation on scan interpretation.[14,15] The potential benefits and the