Original Article

Role of single photon emission computed tomography/computed tomography in diagnostic iodine-131 scintigraphy before initial radioiodine ablation in differentiated thyroid cancer

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ABSTRACT

Objectives: The study was performed to evaluate the incremental value of single photon emission computed tomography/computed tomography (SPECT/CT) over planar radioiodine imaging before radioiodine ablation in the staging, management and stratification of risk of recurrence (ROR) in differentiated thyroid cancer (DTC) patients. **Materials and Methods:** Totally, 83 patients (21 male, 62 female) aged 17–75 (mean 39.9) years with DTC were included consecutively in this prospective study. They underwent postthyroidectomy planar and SPECT/CT scans after oral administration of 37–114 MBq iodine-131 (I-131). The scans were interpreted as positive, negative or suspicious for tracer uptake in the thyroid bed, cervical lymph nodes and sites outside the neck. In each case, the findings on planar images were recorded first, without knowledge of SPECT/CT findings. Operative and pathological findings were used for postsurgical tumor–node–metastasis staging. The tumor staging was reassessed after each of these two scans. **Results:** Single photon emission computed tomography/computed tomography localized radioiodine uptake in the thyroid bed in 9/83 (10.8%) patients, neck nodes in 24/83 (28.9%) patients and distant metastases in 8/83 (9.6%) patients in addition to the planar study. Staging was changed in 8/83 (9.6%), ROR in 11/83 (13.2%) and management in 26/83 (31.3%) patients by the pretherapy SPECT/CT in comparison to planar imaging. SPECT/CT had incremental value in 32/83 patients (38.5%) over the planar scan. **Conclusion:** Single photon emission computed tomography/computed tomography is feasible during a diagnostic I-131 scan with a low amount of radiotracer. It improved the interpretation of pretherapy I-131 scintigraphy and changed the staging and subsequent patient management.

Keywords: Differentiated thyroid cancer, iodine-131 scan, pretherapy, single photon emission computed tomography/computed tomography

INTRODUCTION

Differentiated thyroid cancer (DTCs) account for 80% of all thyroid cancers and generally affected patients have a good prognosis.[1,2] While cancer-specific mortality of low risk (tumor–node–metastasis [TNM] stage I) patients is approximately 1% at 20 years, this increases to 25–45% at 10 years after diagnosis for high-risk (TNM stage III/IV) patients.[3] Conventional planar iodine-131 (I-131) whole-body scintigraphy (WBS), in association with serum thyroglobulin measurement is used in patients with DTCs after thyroidectomy to detect residual thyroid tissue as well as local and distant metastases and to estimate the dose of I-131 to be administered subsequently.[4]

However, planar I-131 scans demonstrate poor anatomical information. Physiological uptake by the salivary glands, stomach, gastrointestinal tract, liver, esophagus and urinary bladder add to the difficulty in image interpretation.[5] Single photon emission computed tomography/computed tomography (SPECT/CT) is often used to overcome the limitations of planar images and accurately localizes the uptake of tracer.[6-11] Several studies have

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also demonstrated the incremental value of SPECT/CT over planar imaging in DTC patients, in imaging performed after administration of a therapeutic dose of I-131.[12-15] However, correct anatomical localization and characterization of lesions before high dose I-131 ablation may be more useful in tailoring the administered dose with the option of surgery or external radiotherapy when indicated. The impact of SPECT/CT on diagnostic imaging using a low amount of radioactivity of I-131 has not been investigated adequately. This prospective study was designed to evaluate the incremental value of SPECT/CT over planar imaging before ablative radioiodine therapy in staging, management and stratification of risk of recurrence (ROR) in postthyroidectomy DTC patients.

MATERIALS AND METHODS

A total of 83 consecutive thyroidectomized patients with histopathologically proven DTC from July 2010 to December 2011 were included in this prospective study after approval by the ethics committee of the institute. There were 21 male and 62 female patients (age range 17–75 years; mean age 39.9 years). Written informed consent was obtained from all the included patients.

Inclusion criteria

- Histopathologically proven DTC (papillary/follicular/Hurthle cell type)
- Patient having undergone subtotal, near total or total thyroidectomy
- No previous history of radioactive iodine treatment.

Exclusion criteria

- Pregnancy and lactation
- Refusal to give written informed consent.

Scintigraphy protocol

The diagnostic I-131 scan was performed 4–6 weeks after total thyroidectomy. Levothyroxine was stopped for 4–6 weeks with physician's advice. A low iodine diet was also followed for 2 weeks before and up to 24 h after the scan. After oral administration of 37-114 MBq (mean 49.2 MBq) of I-131 (supplier: BRIT, BARC, Mumbai, India), whole-body images followed by SPECT/CT of the neck and thorax were obtained in all patients at 48 h. SPECT/CT was also performed for any other areas of abnormally increased I-131 uptake detected on planar imaging.

Planar I-131 whole-body imaging was performed in both anterior and posterior projections at a table speed of 10 cm/min on a dual head gamma camera (Infinia Hawkeye 4, GE, USA) using a medium energy collimator, with a 20% energy window centered on a 364 keV photopeak. Emission SPECT images were acquired in a 128 × 128 matrix over 360° with a 6° angular step (30 s/step) using a 364 keV photopeak and ± 10% energy window. The body contouring system was used to minimize the distance between the patient and the collimator. The SPECT examination was followed by a low dose CT scan (2.5 mA) for anatomical localization on the same instrument. SPECT images were reconstructed with the iterative method and fused with CT images using a dedicated software package (Xeleris, GE Healthcare, USA).

Scan interpretation

Two experienced nuclear medicine physicians interpreted the scans. The scans were read as positive, negative or equivocal for abnormal I-131 uptake in the thyroid bed, regional neck lymph nodes and sites outside the neck (distant sites). The uptake of tracer in the planar scans was considered positive when abnormal tracer uptake was clearly seen in a particular site beyond any doubt. The uptake of tracer was considered suspicious for involvement of a particular site when it was difficult to ascertain the anatomic location or to characterize the uptake. Any uptake was characterized as negative when it was seen at the known physiological sites like salivary glands or the gastrointestinal or urinary tract. Similarly, SPECT/CT scans were also recorded as positive, negative or suspicious for involvement of the thyroid bed, regional lymph nodes and distant sites. In each case, findings on the planar images were recorded first, without knowledge of the SPECT/CT findings.

Data analysis

Surgical operative notes and pathology reports of the patients were reviewed. The size of the primary thyroid tumor, capsular penetration, extension into surrounding tissues, regional nodal involvement and known distant metastases from other imaging investigations like ultrasonography/CT were recorded and postsurgical staging for each patient was determined using these data. The 7th edition of the Cancer Staging Manual of the American Joint Committee on Cancer was used for staging DTC in these patients. The TNM stage was reassessed for each patient after each scan to obtain the planar and SPECT/CT imaging TNM stage for each patient. Any suspicious uptake for a particular site was considered positive for the purpose of staging. While assigning a stage for each patient, age, sex, clinical and pathological findings were also considered. The stage was not graded lower than the surgical or pathological grade, on the basis of scan findings alone.

The thyroid bed, regional lymph node and distant metastatic uptake on the planar scans were compared with the SPECT/CT scan findings. Comparison was also made for any change in staging of cancer between these two scans. An incremental value was assigned to the SPECT/CT studies (with respect to planar I-131 whole-body studies) when they provided more accurate anatomic localization and characterization of the uptake foci. Change in patient management (particularly the need for further tests, imaging studies and change in I-131 dose) resulting from the SPECT/CT scan compared to planar findings was evaluated for each patient.

Statistical analysis

Statistical analysis using the Chi-square test was used to determine any statistically significant difference between I-131 uptake in the thyroid bed, regional lymph nodes and distant metastatic

sites detected on the planar scans as compared to SPECT/CT studies. The Chi-square test was also used to determine if there was any statistically significant difference between staging of the disease as defined by the planar scan against that by SPECT/CT. All statistical computations were performed using statistical software (SPSS, version 16.0.0; SPSS, Chicago, IL, USA).

RESULTS

Of 83 patients, 74 had papillary carcinoma, 8 had follicular carcinoma and 1 had Hurthle cell carcinoma. Before the diagnostic I-131 scan, 55, 5, 5, 10, 3 and 5 patients had stage I, II, III, IVA, IVB and IVC disease respectively. Table 1 summarizes the patient characteristics.

The planar scan was positive or was suspicious for uptake in the thyroid bed in 71 patients, in the regional lymph node in 53 patients and at distant sites in 10 patients. SPECT/CT was positive for uptake in the thyroid bed in 69 patients, in the regional lymph nodes in 47 patients and at distant sites in 7 patients. SPECT/CT changed the planar scan interpretation or increased reader confidence of planar imaging interpretation for residual functioning tissue in the thyroid bed in 9/83 (10.8%) patients ($P < 0.001$), neck node metastases in 24/83 (28.9%) patients ($P < 0.001$) and distant metastases in 8/83 (9.6%) patients ($P < 0.001$). While SPECT/CT also detected additional foci of I-131 uptake in the cervical lymph nodes in two patients, there were no equivocal findings. The differences in I-131 uptake in the thyroid bed, regional lymph nodes and sites outside the neck as detected separately on planar and SPECT/CT imaging are shown in Figures 1-3. Representative pretherapy planar and SPECT/CT I-131 scans of the patients with papillary and follicular thyroid carcinoma are shown in Figures 4-7.

Comparison of staging by planar and single photon emission computed tomography/computed tomography imaging

In patients below 45 years of age, the planar scan categorized 46 patients to stage I and 7 to stage II. SPECT/CT changed the staging in 4/53 (7.54%) patients in this group ($P < 0.001$). In patients above 45 years of age, the planar scan categorized 2, 7, 13, 3, and 5 patients to stage II, III, IVA, IVB, and IVC respectively. SPECT/CT changed the stage in 4/30 (13.33%) patients in this group ($P < 0.001$). Thus, staging was changed in 8/83 (9.63%) patients on the basis of the I-131 scan. Two patients were upstaged (one from stage III to IVA and another from IVA to IVC) and six downstaged by SPECT/CT (four from stage II to I, one from III to I and one from IVA to III).

Change in risk stratification

In patients below 45 years of age, the planar scan categorized 12, 27 and 14 patients to high, intermediate and low ROR categories respectively. SPECT/CT changed the ROR in 8/53 (15.1%) patients in this patient group ($P < 0.001$). In patients above 45 years of age, the planar scan categorized 10, 19 and 1 patient to high, intermediate and low ROR categories respectively. SPECT/CT changed the ROR in 3/30 (10.0%) patients in this group ($P < 0.001$). ROR was changed in 11/83 (13.2%) of the whole patient population ($P < 0.001$). The differences in ROR based on planar and SPECT/CT imaging are shown in Table 2.

Change in management by single photon emission computed tomography/computed tomography over the planar scan

The SPECT/CT scan had incremental value in 32/83 (38.5%) patients over the planar scan, of whom 17/53 (32.0%) were aged less than 45 years and 15/30 (50.0%) above 45 years of age. Management was changed in 15/53 (28.3%) patients below 45 years of age and in 11/30 (36.6%) patients aged above 45 years. Overall management was changed in 26/83 (31.3%) patients by SPECT/CT over planar imaging.

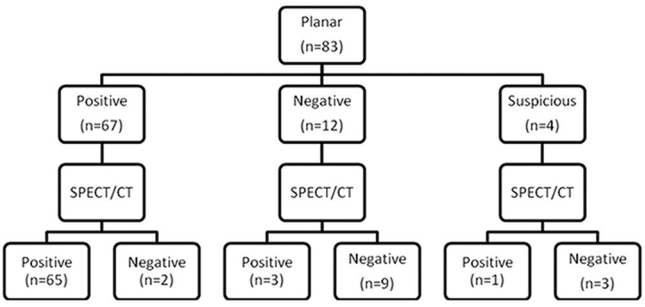

Figure 1: Flow diagram demonstrating planar and single photon emission computed tomography/computed tomography findings in the thyroid bed

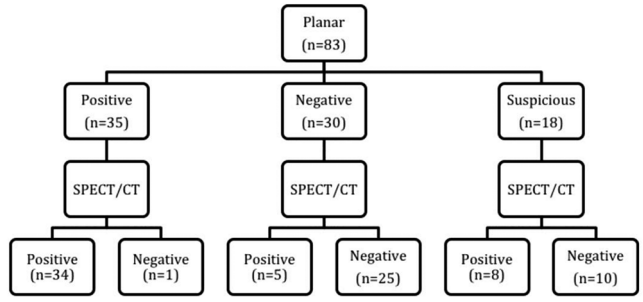

Figure 2: Flow diagram demonstrating planar and single photon emission computed tomography/computed tomography findings in cervical lymph nodes

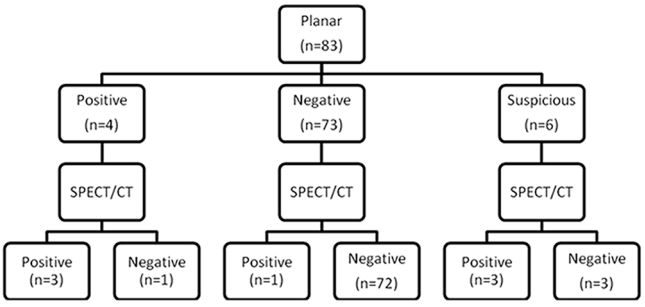

Figure 3: Flow diagram demonstrating planar and single photon emission computed tomography/computed tomography findings at sites other than the neck

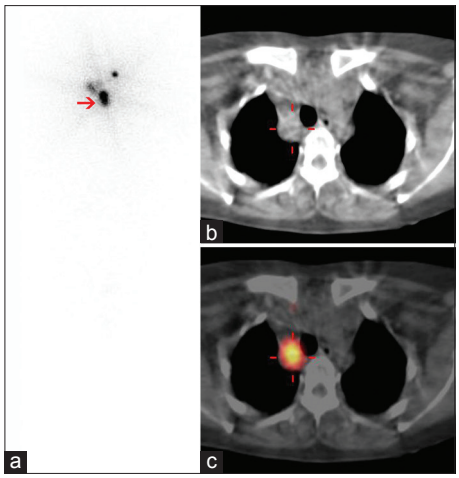

Figure 4: Pretherapy I-131 planar whole-body anterior view image (a) of a 50-year-old female patient with papillary thyroid cancer showing an intense focus of tracer uptake in the midline in the neck (arrow), interpreted as residual thyroid bed uptake. Three other laterally located foci were interpreted as uptake in regional lymph nodes. Transaxial CT (b) and corresponding transaxial fused single photon emission computed tomography/computed tomography (SPECT/CT) images (c) of the thorax localized the most intense focus to the right paratracheal lymph node (cursor), consistent with distant metastasis. Thus, SPECT/CT changed the staging and management of the disease

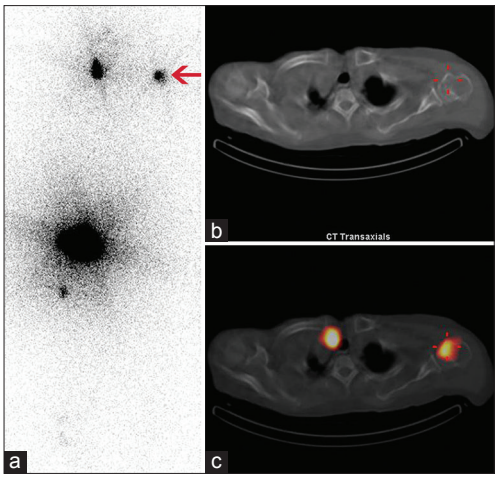

Figure 5: Pretherapy I-131 planar whole-body anterior view image (a) of a 65-year-old female patient with follicular thyroid cancer showed intense tracer uptake at the thyroid bed. Increased foci of tracer uptake were also noted in the left shoulder region (arrow), pelvic and right thigh region. Transaxial CT (b) and corresponding transaxial fused single photon emission computed tomography/computed tomography images (c) of the thorax localizes foci of tracer uptake to the thyroid bed and left humerus (cursor)

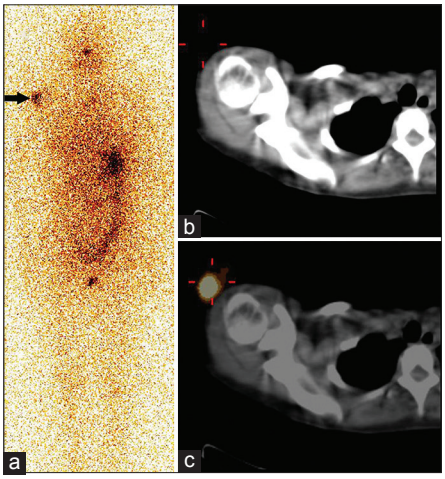

Figure 6: Pretherapy I-131 planar whole-body anterior view image (a) of a 26-year-old female patient with papillary thyroid cancer demonstrated intense tracer uptake in the right arm region (arrow) with physiological tracer uptake in the stomach, bowel and bladder. Transaxial CT (b) and corresponding transaxial fused single photon emission computed tomography/computed tomography images (c) of right arm showing tracer activity outside the body confirming this as surface contamination

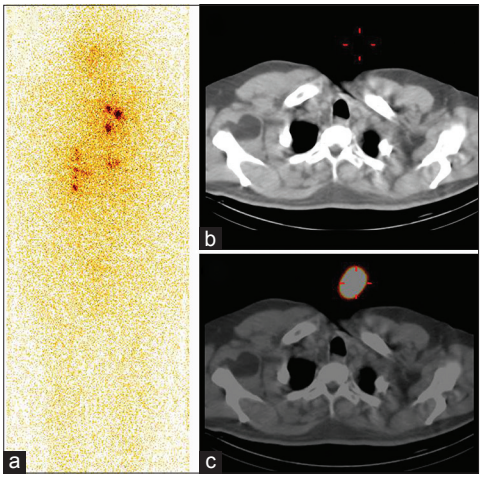

Figure 7: Pretherapy I-131 planar whole-body anterior view image (a) of a 64-year-old male patient with papillary thyroid cancer demonstrated multiple foci of tracer uptake projected over the chest and abdomen, which could be due to lung and liver metastases. Transaxial CT (b) and corresponding transaxial fused single photon emission computed tomography/computed tomography (SPECT/CT) images (c) of chest localizes the tracer uptake outside the body confirming these as surface contamination. In this case, SPECT/CT avoided unnecessary treatment of the patient

DISCUSSION

Conventional planar I-131 WBS is a routine diagnostic procedure in patients with DTCs after thyroidectomy for detection of local and distant metastases. However, there is growing interest in the utility of SPECT/CT technology and increasing evidence in the literature regarding the superior performance of SPECT/CT over planar and SPECT imaging in various cancers.[6-11] This study was conducted to assess the impact of SPECT/CT in addition to planar imaging in postoperative patients with differentiated thyroid cancer using a low amount of I-131.

Even after total thyroidectomy, some residual thyroid tissue may remain in the neck and appear as focal central neck activity on the I-131 scan. It is often difficult to accurately differentiate uptake within the thyroid remnant and the cervical lymph nodes on planar images. The use of SPECT/CT facilitates the characterization of central neck activity as either normal residual thyroid tissue or cervical lymph node metastases. Physiological activity in the salivary glands, stomach, bowel, kidney, bladder and thymus, may also mimic disease. A retrospective study of 500 whole-body radioiodine scans showed diagnostic pitfalls leading to additional imaging or diagnostic procedures in 59% of patients.[16] The detection of physiological variants and

Table 1: Patients Demographics

Parameters	Number (*N*= 83)
Participant age, years	
Mean	39.92
Range	17-75
Sex	
Female	62
Male	21
Histopathology	
Papillary thyroid cancer	74
Follicular thyroid cancer	8
Hurthle cell cancer	1
Stage at diagnosis	
I	55
II	5
III	5
IV	18

Table 2: Change in ROR after pretherapy planar versus pretherapy SPECT/CT

ROR after planar imaging	ROR after SPECT/CT imaging	Number of Patients (*N*=11)
High	Intermediate	2
High	Low	1
Intermediate	Low	4
Intermediate	High	1
Low	Intermediate	3
ROR Risk of Recurrence		

accurate localization of foci of tracer uptake can potentially change the dose of radioiodine to be administered. However, the limited use of SPECT/CT during a diagnostic I-131 WBS may be due to the low amount of radiotracer used for the scan.

A few studies in the literature have demonstrated the impact of SPECT/CT over planar imaging prior to I-131 treatment. Three studies have reported the role of SPECT/CT in mixed groups of posttherapy and diagnostic radioiodine scans[14,15,17] and only one study has reported the use of SPECT/CT for patients undergoing diagnostic I-131 imaging.[18] Wong *et al.* studied the incremental value of pretherapy I-131 SPECT/CT imaging over planar imaging in 53 postthyroidectomy patients with DTC.[17] They showed that incremental diagnostic value of SPECT/CT over planar imaging was 47.6%, including 40.8% of neck foci and 100% of distant foci. They retrospectively evaluated the data of only selected patients who had undergone SPECT/CT imaging for indeterminate findings on the planar scan. This patient selection bias may be a probable reason for the slightly higher incremental value with SPECT/CT in this study than that observed in our study (38%).

In a retrospective study, Barwick *et al.* assessed the diagnostic performance of co-registered SPECT/CT compared to I-123 whole-body planar imaging and to SPECT alone in 79 patients with DTC.[19] SPECT/CT provided additional diagnostic information in 42% of cases, with the change in management in 11%. However, I-123 imaging was performed in patients with rising thyroglobulin levels after radioiodine ablation. Normally, relatively higher amount (~370 MBq) of I-123 radiotracer is used for the scans compared to I-131 tracer activity used for diagnostic scan in our study. We used lower activity of I-131 (37–114 MBq) as suggested for diagnostic I-131 whole-body study by guidelines to avoid stunning.[20] Wong *et al.* evaluated the feasibility of staging before initial radioiodine therapy using diagnostic I-131 scintigraphy with SPECT/CT in 48 DTC patients.[18] They showed that SPECT/CT changed the stage in 8% of patients over planar imaging. This correlates well with our study, which showed a change in staging in 9% of patients. In the present study, staging was found to change in 7.5% of younger patients but in 13% of the older group. This may be because in the AJCC classification of thyroid cancer, younger patients are categorized into only two stages. Similarly, ROR and further patient management was changed by SPECT/CT in 13% and 31% respectively in the two groups over planar imaging.

Our study has several limitations. First, the SPECT-CT findings were not confirmed by histopathology due to logistical and ethical issues. However, the patients were followed with clinical examination, thyroglobulin levels and imaging follow-up in all cases confirming the findings of SPECT-CT. Second, we used a low dose CT in SPECT/CT, which was not of diagnostic image quality although the CT images provided valuable anatomical information and localized the abnormal radio-iodine uptake. More recently, SPECT/CT systems are incorporating diagnostic multi-slice CT, which may permit even better lesion characterization and as such, further reduce the need for subsequent diagnostic studies. The absorbed dose of radiation in cancer tissue is the best predictor of the response to radioiodine therapy in thyroid cancer. Thus, SPECT/CT could be used to measure volumes of tumor targets, perform dosimetry and determination of radioactivity required for successful tumor ablation.[21]

CONCLUSION

Single photon emission computed tomography/computed tomography significantly improved the interpretation of I-131 planar WBS, leading to change in staging and further management before prescribing the initial radioiodine therapy.

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