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The Added Value of SPECT/CT with Radioactive Iodine Whole Body Scanning in Patients with Differentiated Thyroid Cancer and its Impact on TNM Staging.

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ABSTRACT:

Aim: To determine the impact of SPECT/CT in lesion detection and its influence on TNM staging, when associated with whole-body radioiodine (WBI) scans in differentiated thyroid cancer (DTC) patients. **Material and Methods:** Patients with pathologically proven DTC who underwent thyroidectomy with or without LN dissection and who have WBI imaging with SPECT/CT were enrolled in this study. Records were reviewed for patients' demographics, serum TSH, TG and TG antibodies levels, prior radioiodine ablation, histopathology and imaging results. After excluding physiological tracer distribution, radioiodine uptake was classified as positive, or equivocal in thyroid bed (TB), cervical lymph nodes (LN), or distant metastases (DM). SPECT/CT results were analyzed for added or excluded lesions and translated to changes in TNM staging. **Results:** We included 48 patients (mean age; 46.9±18.7 years). In 20 patients, SPECT/CT was able to detect/confirm additional 45 lesions (4 TB, 22 LN, and 19 DM). SPECT/CT decreased number of equivocal results by 87% from 54 lesions to only 7 lesions, achieving definitive diagnosis in 41 patients (85.4%) compared to only 10 patients (20.8%) on planar images ($p<0.0001$). This was translated to TNM up-staging in 8 patients, and down-staging in 7 patients. Both TG and age were positively correlated to number of SPECT/CT added lesions (0.601; $p<0.0001$ and 0.375; $p=0.009$ respectively).

Cutoff values of Tg≥3.4 ng/ml and age>45 years were the best to predict additional lesions on SPECT/CT with sensitivity, specificity, and accuracy of 95, 75, & 87.5% and 80, 71.4, & 75% respectively (p<0.01 for both). No TNM up-staging was noted in patients with TG<3.4 ng/ml. **Conclusion:** SPECT/CT imaging was found to be superior to planar imaging in terms of detecting additional lesions, improving sensitivity and reducing number of equivocal lesions, improving specificity. SPECT/CT was able to significantly influence the TNM staging, with no up-staging noted in patients with TG<3.4.

Key Words: differentiated thyroid cancer, SPECT/CT, radioiodine whole body imaging, serum thyroglobulin, TNM staging.

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INTRODUCTION:

Thyroid cancer (TC) incidence is about 3.1% of all cancers worldwide [(1)]. About 94% of thyroid carcinomas are DTC, including papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC) and their mixed variants [(2)]. The prognosis of DTC is generally favorable; however, lifetime follow-up is mandatory in most cases. Radioiodine imaging using iodine-123 (I-123) or iodine-131 (I-131) is frequently performed, for follow-up after the first surgery and ablation of residual thyroid tissue by I-131 therapy. It is also used for staging and risk stratification, as well as for long-term follow-up of DTC patients. Proper staging and localization of radioiodine-avid metastatic lesions can be challenging due to the lack of anatomical details on planar imaging or due to overlap by areas with physiologically increased radioiodine uptake, which can lead to false positive or false negative results, and consequently over or under-treatment of patients [(3)]. SPECT/CT is currently more frequently employed in addition to planar imaging, to evaluate patients with TC. Co-registration of anatomical and functional data is made possible by SPECT/CT, which can offer precise patient-specific attenuation correction and more realistic trace distribution within the body [(4)].

This allows for more accurate anatomical localization and better characterization of radiotracer avid foci. The accuracy of DTC staging and subsequent patient care can be improved by both confirming and better localization of iodine avid lesions as well as by successfully excluding equivocal findings related to benign non-specific uptake or atypical physiological uptake [5]. The aim of this study is to determine the impact of SPECT/CT over planar WBI imaging and its influence on TNM staging in DTC patients, stratified by various clinical and laboratory variables, including serum TG level.

MATERIALS and METHODS:

This study was performed in accordance with ethical standards of the ***Helsenki*** Declaration (1964) and its later amendments, and was approved by Institutional Review Board that waived the requirement for an informed consent, based on the retrospective nature of the study. **Patients:** Patients at Prince Sultan Military Medical City with histo-pathologically confirmed thyroid cancer, which had prior total or near total thyroidectomy with or without regional lymph node dissection and at least one radioiodine whole body scan associated with SPECT/CT imaging (between October 2016 and September 2018), were retrospectively included. Studies without SPECT/CT imaging or studies with markedly poor or uninterpretable quality were excluded. Patient demographics, TSH levels, thyroglobulin levels (TG) and TG antibodies levels, information on prior radioiodine ablation, surgical and histological results, planer and SPECT/CT results, and patient demographics were also obtained. Patients' TNM staging was performed according to the American Joint Committee on Cancer (AJCC) eighth edition and were stratified based on the American Thyroid Association (ATA) risk classification system [6, 7].

Preparation and Dosing: All radioiodine imaging studies were performed as per our local protocols. The thyroid hormone was stopped for at least 4 weeks, to allow for an adequate rise in the TSH level (> 30 mIU/L) or alternatively Thyrogen was administered as two injections of 0.9 mg intramuscularly on each of two consecutive days before the radioiodine (I-123 or I-131) dosing. Contrast agents and iodine-containing drugs were avoided for a reasonable number of weeks or months with IV contrast agents avoided for at least 3 weeks [8].

Laboratory investigations (TSH, TG, and TG-Abs), renal function tests , and blood pictures were performed before ablative doses. Female patients in childbearing age unless on period, had HCG pregnancy test 1-2 days before the administration of radioiodine with acceptable result being HCG <= 2 mIUml according to our procedural protocol. Patients fasted for 4 hours prior and 2 hours following oral radioiodine administration. For I-123 radioiodine scan, a dose of approximately 185 MBq diluted in water is administered orally and imaging is performed in the next day. According to imaging protocol based on ATA guidelines, post-ablation / post-therapy scan was obtained 7±3 days (typically 7 days) following oral administration of the I-131 therapeutic/ablative dose [7].

Imaging Procedure:

- ***Whole-body planar imaging:*** WBI scan was obtained in anterior and posterior views, using a GE Discovery NM/CT 670 dual-head γ-camera, fitted with a parallel-hole high energy collimator for I-131 scans and extended low energy general purpose collimator for I-123 scans. A 20% energy window was set at 364 keV or 159 keV photo peaks of I-131 or I-123 respectively.
- The table speed was set at 7 cm/min. The used matrix size was 128 x 128. Anterior & posterior static images including the neck and upper chest were acquired for all patients, for at least 150 K counts or equivalent time, and whenever required, imaging for other body regions were obtained on case-by-case bases.
- ***SPECT/CT Imaging:*** SPECT/CT images of the neck and upper chest as well as additional suspected sites were obtained following the review of planar images by the attending nuclear medicine physician. SPECT images were acquired for 40 sec/frame, using a step and shoot mode, for 30 stops/head (total 60 stops) using a 360º noncircular orbit, for diagnostic and post-ablation / post-therapy imaging.

A matrix size of 128 x 128 was used and iterative reconstruction using OSEM was performed. Attenuation correction using the low dose CT data as well as scatter correction was applied. A low-dose non-contrast CT was obtained using a tube voltage of 120 kV and current of 80 mA, slice thickness 3.75 as our standard protocol for adult patients. Image processing and reconstruction was performed using the software provided by the vendor.

Images interpretation: Images interpretation and analysis were performed, independently, by two experienced nuclear medicine physicians. After exclusion of the known physiological uptake sites as in salivary glands, gastrointestinal tract, and urinary bladder, results were reported as positive, negative, or equivocal at thyroid bed (TB), cervical lymph nodes (LN), or distant metastases (DM), for both planar and SPECT/CT images. For positive-negative classification, equivocal results were included with the negative group. Clinical assessment, other imaging studies as neck ultrasound (US), CT, MRI or PET/CT if available, as well as laboratory studies (TG & TG-Antibodies) were used to validate the image findings. Changes in patients TNM (Tumor-Node-Metastasis) classification and stage on addition of SPECT/CT imaging, were interpreted based on the AJCC TNM staging manual (8^{th} edition) **(8)**. TNM up or down staging was considered according to the following algorithm:

Patients <55 years old:

- Up-staging if SPECT/CT detects or confirms DM in patients with no or equivocal/uncertain DM on planar images.
- Down-staging if SPECT/CT excludes DM in patients with equivocal/uncertain DM on planar images and otherwise not known to have other DM.

- Patients ≥55 years old:
- Up-staging if SPECT/CT detects or confirms LN metastases in patients with no or uncertain LN on planar images and otherwise not known to have DM.
- SPECT/CT detects or confirms DM in patients with no or uncertain DM on planar images.
- SPECT/CT detects thyroid bed recurrence, with obvious invasion of nearby extra thyroidal tissues.
- Down-staging if SPECT/CT excludes LN metastases in patients with equivocal/uncertain LN on planar images and otherwise not known to have other LN metastases or DM.
- SPECT/CT excludes DM in patients with equivocal/uncertain DM on planar images and otherwise not known to have other DM.
- The presence of iodine avid tissue in thyroid bed, if consistent with recurrent or residual tumor, unless with obvious invasion of nearby extra thyroidal tissues, was considered equivalent to T1 or T2 with no influence on staging in patients ≥55 years old while in patients <55 years old was not accounted for, to up or down-staging.

Statistical tests: SPSS 21.0 and MedCalc 11.0 software were used for data analysis. Qualitative data were expressed as frequencies and percentages. Quantitative data were summarized and expressed as mean ± SD. Pearson correlation was used to measure the magnitude of correlations between the number of SPECT/CT added lesions and Tg level or age, where the strength of correlation was classified based on correlation coefficient (r) as; low (r= 0-0.25), moderate (r= 0.25-75), and high (r= 0.75-1.0). Student T-test was used to compare the mean values of continuous variables between study groups. McNemar test was applied to compare the frequency of definitive versus equivocal results as paired data, between planar and SPECT/CT studies. Fissure Exact test was used to compare the frequency of added SPECT/CT lesions between the study groups stratified according to TG level or age. The cutoff for TG and age that best differentiate positive from negative scans was determined based on ROC analysis, where the area under the curve (AUC) was considered as negligible if <0.55, small if 0.56-0.63, moderate if 0.64-0.7 and strong if ≥0.71. Logistic regression was performed to detect independent predictors of SPECT/CT additional lesions, using a forward stepwise method with entry significance level of $p < 0.05$ and removal significance level of $p > 0.10$. A p-value was considered significant if less than 0.05.

RESULTS:

This study included total of 48 patients [average age 46.9 ± 18.7 years; 30 females (62.5 %)]. Histopathology revealed papillary carcinoma in 43 cases, follicular carcinoma in 4 patients, and Hürthle cell carcinoma in 1 patient. Sixteen patients (33.3%) had received at least one prior ablative/therapy dose of radioiodine (I-131), at least 6 months from the radioiodine imaging procedure included in the study.

Fifteen WBI scans were performed using I-123 while 33 scans were performed post I-131ablation/therapy. Thyrogen preparation was used in 26 (54%) patients. Most patients were AJCC stage I or II (83.3%). The majority of patients were classified as intermediate risk (41.7%) or high risk (35.4%), bases on the ATA clinic-pathologic risk stratification system. Patient's demographic and histopathological characteristics are illustrated in ***Tables (1 & 2)***.

Table (1): Demographic and histopathological characteristics of the study populations.

		Frequency (%)
Sex	Male	18 (37.5 %)
	Female	30 (62.5 %)
Age Group	< 45	24 (50.0%)
	≥ 45	24 (50.0%)
	< 55	17 (35.4%)
	≥ 55	31 (64.6%)
TNM Classification	T1a	6 (12.5%)
	T1b	11 (22.9%)
	T2	8 (16.7%)
	T3a	5 (10.4%)
	T3b	17 (35.4%)
	T4a	1 (2.1%)
	N0	30 (62.5)
	N1a	7 (14.6%)
	N1b	11 (22.9%)
	M0	36 (75.0%)
	M1	12 (25.0%)
AJCC Stage	I	27 (56.3%)
	II	13 (27.1%)
	III	1 (2.1%)
	IVb	7(14.6%)
Tumor Histology	Papillary carcinoma	43 (89.6%)
	Follicular carcinoma	4 (8.3 %)
	Hurthle cell carcinoma	1 (2.1 %)
ATA Risk	Low	10 (20.8%)
	Intermediate	18 (37.5%)
	High	20 (41.7%)
Prior Radioiodine Ablation (≥ 6 months before imaging)		16 (33.3%)
Type of Scan	Post Ablation WBS	33 (68.8 %)
	Diagnostic WBS	15 (31.3 %)
Uptake on WBS or SPECT/CT	Yes	43 (89.6 %)
	No	5 (10.4 %)

Table (2): Descriptive Statistics of the laboratory investigations.

	Minimum	Maximum	Mean ± SD
TSH level (mIu/ml)	55	839	166 ± 157
TG level (ng/ml)	0.1	5396	523 ± 1331
TG antibodies (IU/ml)	2	905	106±219
Ablative dose of I-131(MBq)	1733	7489	3994±1291

Based on both planar and SPECT/CT images, there were 43 (89.6%) positive and 5 (10.4%) negative scans. Positive scans had 38 patients with TB uptake, 18 with LN uptake, and 12 with DM. SPECT/CT was able to add a total of 45 lesions in 20 patients by either detecting new lesions or confirming prior equivocal lesions (4 in TB, 22 LN, and 19 DM) (41.7%) **(*Table 3)***.

In addition, SPECT/CT was able to rule out 20 equivocal lesions in 19 patients (13 suspected LN and 7 suspected DM) with only 7 equivocal lesions left in 7 patients. Excluded lesions included non-specific radioiodine uptake associated with dental infection or inflammation related to recent dental procedure or dental implant (usually misinterpreted as cervical lymph nodes), foot infection, skin inflammation/infection, faint uptake in mediastinum revealed to be thymus gland activity, non-specific uptake in pericardium or pericardial fat, diverticulitis, atypical focal esophageal activity, atypical gastric or bowel uptake, uterine or adnexal activity related to inflammation/infection, menstrual endometrium, uptake within uterine lesion or fibroid, as well as contamination of skin, hair or clothes.

Table (3): Frequency of definitive and equivocal lesions in planar and SECT/CT according to site.

	Planar Detected Lesions		SPECT/CT Detected Lesions		SPECT/CT Added Definitive Lesions	
	Definitive	Equivocal	Definitive	Equivocal		p- Value
TB	34	2	38	0	4	0.125
LN	5	33	27	5	22	<0.0001
DM	16	19	35	2	19	<0.0001
Total	55	54	100	7	45	<0.0001

TB; thyroid bed, LN; lymph node, and DM; distant metastasis.

Adding SPECT/CT reduced the equivocal results by accurate localization of uptake sites, differentiating lymph nodes from thyroid bed uptake, and excluding false positives due to unexpected or atypical physiological uptake patterns (e.g. in salivary glands) or benign non-specific radioiodine uptake, frequently related to sites of infections or inflammation. SPECT/CT by confirming or excluding equivocal lesions reduced the number of equivocal lesions by 87% from 54 lesions (2 TB, 33 LN and 19 DM) to only 7 (5 LN, and 2 DM) and achieved definitive diagnosis in 41 patients (85.4%) compared to only 10 patients (20.8%) on planar images ($p<0.0001$).

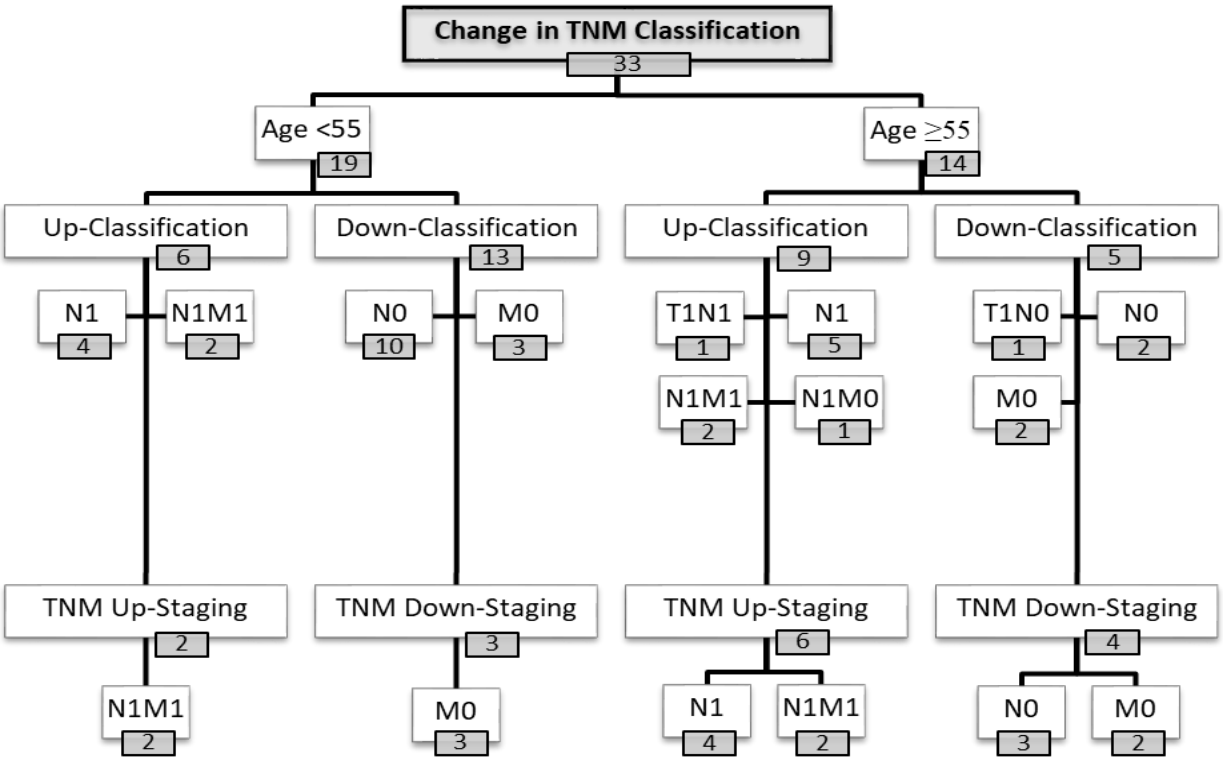

Figure (1): SPECT/CT imaging induced changes in TNM classification and TNM staging as compared to planar imaging in patient <55 and ≥55 years old (number of patients written in grey boxes). *Abbreviations: T1, thyroid bed recurrence; N1, nodal metastases detected; N0, nodal metastases excluded; M1, distant metastases detected; M0, distant metastases excluded.*

SPECT/CT changed TNM classification in 33/48 patients (68.8%) of whom 19 (39.6%) are <55 years old and 14 (29.2%) are ≥55 years old. Up-classification was noted in 15 (32.6%) patients due to detection of nodal and/or distant metastases that were not detected on planar images, while 18 (37.5%) patients had down-classification due to exclusion of suspected lymph nodes or distant metastases. The changes in TNM classification were translated into change in TNM stage in only 15 (31.3%) patients, with up-staging in 8 (16.7%) patients, and down-staging in 7 (14.6%) patients. Out of 19 patients <55 years old, TNM stage changed in only 5 patients with up-staging in 2 and down-staging in 3, while in remaining 14 patients the TNM stage was not affected (4 patients with SPECT/CT detected lymph nodes metastases and 10 patients with excluded lymph nodes metastases), and such patients continued to be classified as stage I or stage II, according to 8th edition of TNM thyroid cancer staging system.

On the other hand, out of 14 patients aged ≥55 years old, TNM stage changed in 10 patients with up-staging in 6 and down-staging in 4 ***(Figure 1)***. We noted new appearance of thyroid bed activity on SPECT/CT in 2 patients ≥55 years old, previously free of disease for several years, concordant with local recurrence. In both patients the lesions are localized and small in size with no frank evidence to suggest involvement of any extra-thyroidal structures, and were considered equivalent to T1 with no influence on TNM staging. In 4 patients >55 years old, with confirmed distant metastases to bone and/or lungs (TNM stage IVB), SPECT detected nodal metastases in 3 patients and excluded nodal metastases in 1 patient, though with no change in TNM score. The additional use of SPECT/CT imaging, resulted in a significantly higher frequency of TNM up-staging and overall change in TNM stage in patients' group aged ≥55 years compared to those < 55 years old. The frequency of TNM down-staging, tends to be relatively higher, as well in the older age group, however, did not reach a statistically significant level ***(Table 4)***.

Table (4): Frequency of changes in TNM staging on SECT/CT compared to planar imaging.

	Age		
	<55 y (n=31)	**≥55 y (n=17)**	**p- Value**
TNM Up-staging (n=8)	2 (6.5%)	6 (35.3%)	0.010
TNM Down-staging (n=7)	3 (9.7%)	4 (23.3%)	0.193
Total Change in TNM (n=15)	5 (16.15)	10 (58.8%)	0.002

Patients group with SPECT/CT added lesions had higher mean serum TG level (1190.5±1872.9 vs. 46.8±225.4; p<0.01) and an older mean age (58.3±16.9 vs. 38.8±15.6; p<0.01). Both TG and age showed a significant positive correlation of a moderate magnitude to the number of SPECT/CT added lesions (r=0.601; p<0.01 and 0.375; p=0.009, respectively) ***(Figure 2)*.**

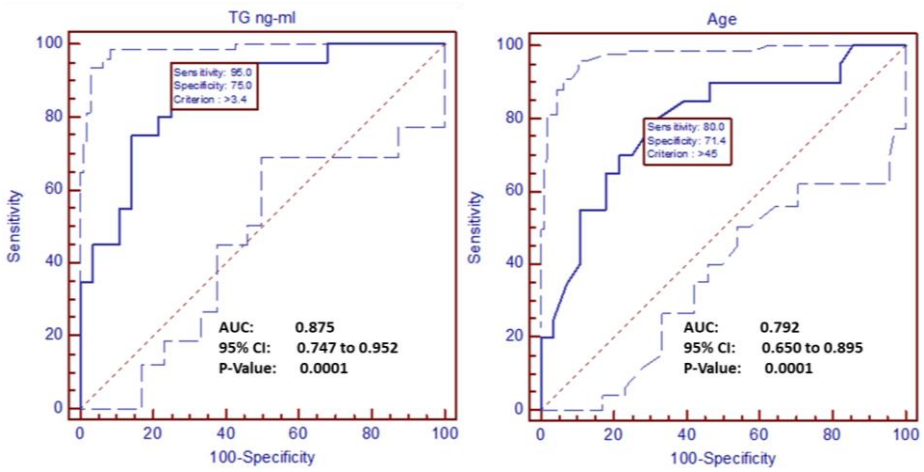

Figure (2): Scatter Dot Plots of SPECT/CT added lesions according to TG level (left) and according to age (right).

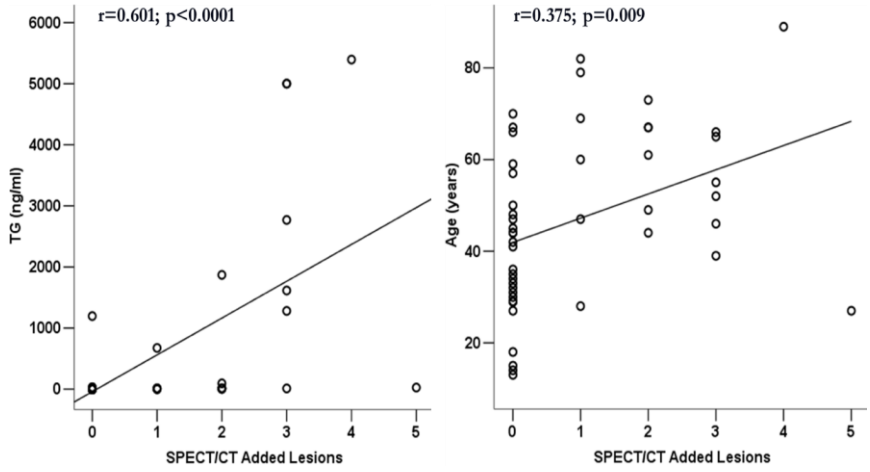

Figure (3): ROC Analysis of the added lesions on SPECT/CT according to TG (left) and according to age (right).

Cutoff values of >3.4 ng/ml for TG and >45 years old for age were the best to predict additional lesions on SPECT/CT with AUC = 0.875 (95% CI: 0.747 - 0.952) and 0.792 (95% CI: 0.650 to 0.895) respectively, with sensitivity, specificity, PPV, NPP, and accuracy of 95, 75, 73.1, 95.5 & 87.5% and 80, 71.4, 66.7, 83.3 & 75% respectively with P= 0.001 for both ***(Figure 3)***.

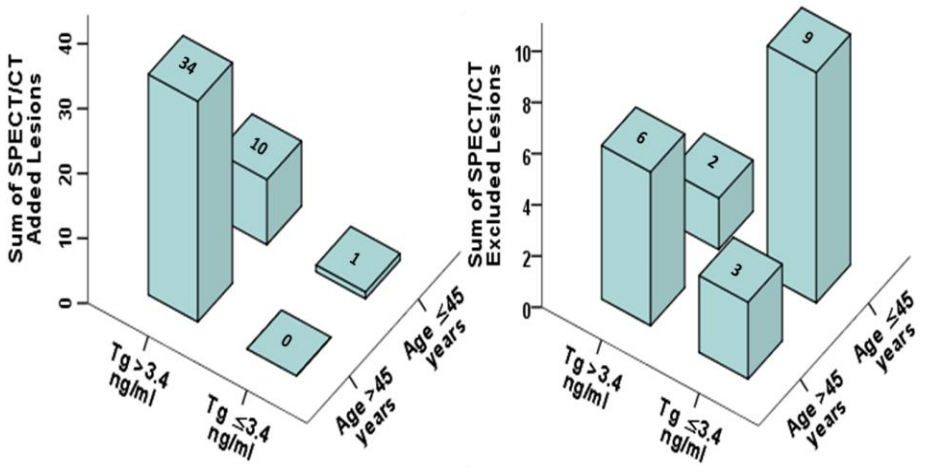

Figure (4): Bar charts showing number of SPECT/CT added lesions (left panel) and excluded lesions (right panel), stratified according to both TG >3.4 ng/ml and age >45 years.

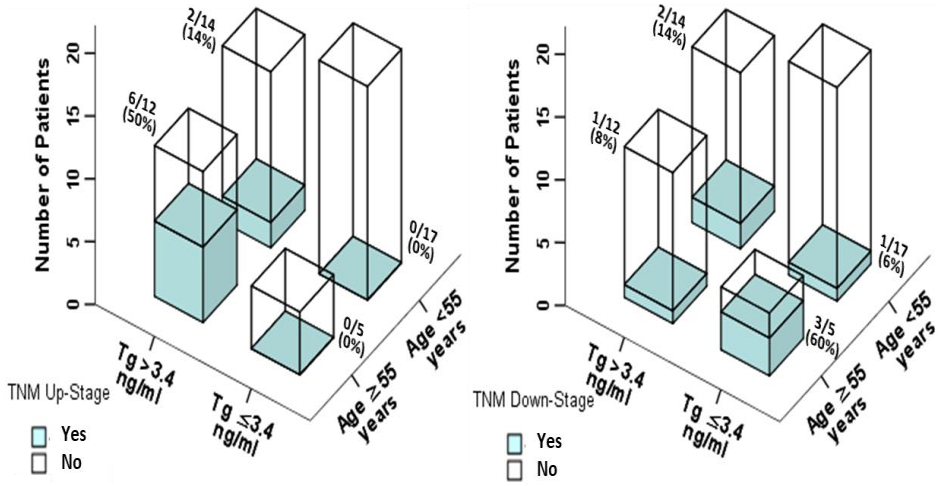

Figure (5): Bar charts showing number of patients with SPECT/CT up-staging (left panel) and down-staging (right panel), stratified according to both TG >3.4 ng/ml and age ≥55 years.

Out of 22 patients with TG <3.4 ng/ml, SPECT/CT added only 1 lesion (a lymph node) in 1 (4.5%) patient. Despite to this added LN, the 28-year-old patient continues to be classified as TNM stage 1, and none of the patients with TG <3.4 had been up-staged, based on the 8th edition of AJCC TNM staging system. On the other hand, out of 26 patients with TG ≥3.4 ng/ml, 44 added lesions were detected on SPECT/CT in 19 patients with TNM up-staging noted in 8 (30.8%) patients (p value = 0.010) ***(Figure 4 & 5)***.

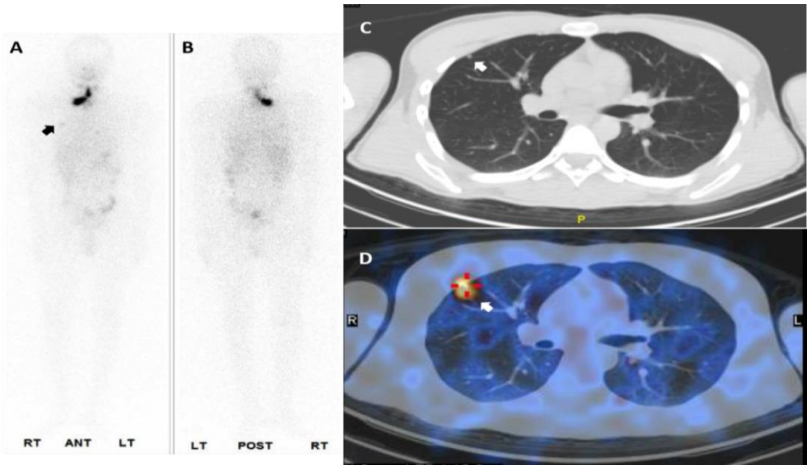

Figure (4): Case 1: 27 years old male with papillary thyroid carcinoma post total thyroidectomy. On WB images (A &B), tracer uptake is seen in thyroid bed together with small faint activity in right anterior chest (black arrow). SPECT/CT imaging (C & D) revealed a tiny pleural based metastatic pulmonary nodule in anterior segment of right upper lobe with significant activity.

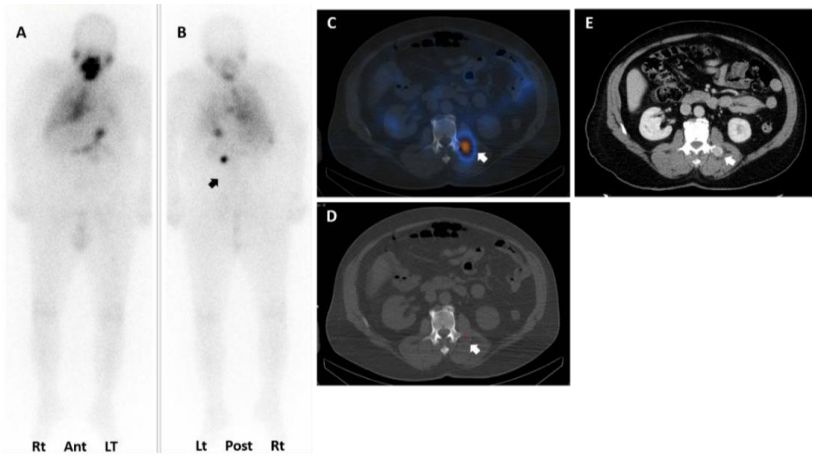

Figure (5): Case 2: 65 years old male with papillary thyroid carcinoma post total thyroidectomy. Apart from iodine avid residual thyroid tissue and right lung uptake noted on whole body images (A & B), a focal uptake is seen in abdominal left paramedian region (black arrow). SPECT/CT imaging (C, D & E) revealed a metastatic osseous lesion in left transverse process of L2 vertebra (white arrow).

Table (4): Logistic regression model including TG >3.4 ng/ml and Age >45 years as independent predictors of additional lesions on SPECT/CT compared to planar imaging.

	Chi-square	p-value	Coefficient	Std. Error	p-value	OR	95% C.I.
TG > 3.4	26.777	<0.0001	3.7758	1.1583	0.001115	43.634	4.506 - 422.498
Age > 45	4.859	0.0275	1.8926	0.8886	0.03319	6.6346	1.1628 - 37.874
Total Model	31.636	<0.0001					

Logistic regression analysis revealed a regression model with TG > 3.4 ng/ml and Age > 45 years as independent predictors of additional lesions on SPECT/CT compared to planar imaging with AUC of 0.911 (95% CI: 0.792 - 0.973). This model was able to correctly identify patients with or without additional lesions in 42/48 patients, consistent with 87.5% accuracy ***(Table 4)***.

DISCUSSION:

Radioactive iodine therapy with iodine-131 is a well-accepted treatment for DTC following complete thyroidectomy. According to the guidelines, the goals of RAI therapy fall into three categories: ablation of residual thyroid tissue to facilitate follow-up using serum TG, adjuvant therapy for microscopic lesions to reduce the risk of recurrence or distant metastasis, and treatment for residual or metastatic disease [(7)]. Overall, the prognosis for DTC is good; though, in many cases, lifetime follow-up is required. The gold standard for follow-up following surgery and radioiodine ablation of remaining thyroid tissue using I-131 therapy is through TG serum level monitoring as well as radioiodine imaging using I-123 or I-131. Occasionally proper diagnosis and localization of radioiodine-avid metastatic disease can be difficult due to lack of anatomical details on planar imaging, superimposition by areas with increased physiological uptake or areas of benign non-specific uptake, leading to false positive or false negative results and consequently over or under treatment of such patients. SPECT/CT imaging lately had been frequently utilized to overcome this obstacles [(3)].

It had been employed in conjunction with WBS planar imaging in DTC in recent years, resulting in major diagnostic and localization benefits [10].

In our cohort adding SPECT/CT helped to reduce the number of equivocal results by accurate localization of uptake sites, differentiating lymph nodes from thyroid bed uptake or physiological salivary gland activity, and excluding false positive results due to underlying unexpected physiological uptake. The use of SPECT/CT reduced the number of studies with equivocal results by 64.6% from 38/48 patients (79.2%) to only 7/48 patients (14.6%). ***Şimşek et al.*** found that SPECT-CT affected therapy management in 23.3% of patients; the discrepancy in the rate may be attributed to the fact that in the current study, the included patients are those patients for whom SPECT/CT was added based on equivocal findings on their planar images and was not performed upfront on routine bases. Also the different sample size in both studies (325 patients vs. 48 patients in our cohort) [11].

Various published studies have demonstrated the superiority of SPECT/CT over planar imaging for detection of metastatic lymph nodes, distant metastases, and the management of DTC patients [12, 13].

Al Hatmi et al. found a disagreement in nodal metastases between planar and SPECT/CT images (P <0.01) where SPECT/CT downgraded the false-positive nodes on planar imaging, the authors found that both the false positive and equivocal nodal lesions in the planar images corresponded to residual thyroid tissue in the SECT/CT images. Overall, 34% of lymph nodal lesions were changed with SPECT/CT, and this comes in line with our results where SPECT/CT reduced the number of equivocal nodal lesions from 33 to only 5 [14].

Several studies concluded that SPECT/CT decreased the number of indeterminate metastatic foci and also discriminated benign physiological uptake from pathological uptake [14, 15 and 16] , in our study SPECT/CT was able to rule out DM in 5 cases, where 3 cases with pelvic uptake seen in planar imaging were corresponded to uterine fibroid or adnexal lesions in the SPECT/CT images, one case with abdominal uptake in the planar images corresponded to diverticulitis on SPECT/CT images, and one case with uptake in the head and SPECT/CT revealed a contamination.

Measurement of serum TG is a crucial step in assessing risk stratification. TG is a glycoprotein that is expressed only in normal thyroid tissues and in DTC, and it's clear organ specificity makes it a valuable biomarker for monitoring DTC patients and detection of residual/recurrence [7, 17]. In our study, we found higher mean TG values in patients with SPECT/CT added lesions and that TG positively correlated with the number of SPECT/CT added lesions. We found that in patients with TG <3.4 ng/ml, SPECT/CT added only 1 nodal lesion in 1 patient (4.5%) with no TNM up-staging in any patient, according to the 8th edition of AJCC TNM staging system. However, in 26 patients with TG ≥3.4 ng/ml, SPECT/CT added 44 lesions in 19 patients, which was translated into TNM up-staging in 8 (30.8%) patients. The 7th edition of AJCC TNM staging grouped the DTC patients by age using a cutoff of 45 years [18]. However, the cut-off point of 45 was controversial. Cao et al. reported that patient age is significantly related to disease-free survival (DFS) and that patients >45 years old are at higher risk of postoperative DFS-related adverse events than younger patients [19]. Although the age threshold had been increased in the 8th edition of TNM staging system, from 45 to 55 years old [8], in the current population ROC analysis revealed that age >45 years old was the best age cutoff point to predict higher number of SPECT/CT added lesions. Moreover, we detected significant positive correlation between age and number of SPECT/CT added lesions.

Limitations: The relatively small sample size, different tracers used (I-123 / I-131), and probably heterogeneous patient sample at different stages of disease and patients with or without previous ablation, may be considered as potential limitations of the current study. In addition, the current population tends to have more equivocal or suspicious lesions, since SPECT/CT was not routinely performed for every patient, but was selectively added depending on nuclear medicine physician judgment after reviewing planar images.

CONCLUSION:

Adding SPECT/CT to the WBI scans, detected new lesions and significantly reduced equivocal results, achieving definitive results in most cases. SPECT/CT either added/confirmed or excluded lesions in about 73% of patients, which was more pronounced particularly for LN involvement or DM in patients with higher serum TG (>3.4 ng/ml) and in older age groups. SPECT/CT was able to change the TNM staging in 31% of patients, with no up-staging in any patient having TG <3.4 ng/ml of the current population. The current findings implies that SPECT/CT may not considerably add to the sensitivity of the study in patients with low TG levels, even though can be selectively added in imaging of these patients to improve specificity, whenever suspicious or equivocal findings are noted on planar images.

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