Thyroglobulin and Low-Dose Iodine-131 and Technetium-99m-Tetrofosmin Whole-Body Scintigraphy in Differentiated Thyroid Carcinoma

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Determination of thyroglobulin (Tg) levels, determined under endogenous thyroid-stimulating hormone stimulation after withdrawal of L-thyroxin treatment (off-T4), has been proven to be the most sensitive method for evaluation of patients with recurrent malignancy or distant metastases. This study uses a comparative approach between low-dose ^{131}I scan and the previously reported highly sensitive ^{99m}Tc-tetrofosmin whole-body scintigraphy, using Tg-off-T4 as a basis for comparison. **Methods:** Fifty-eight consecutive patients of our follow-up program with primary thyroid carcinoma ablated with thyroidectomy and radioiodine therapy were examined after L-thyroxin withdrawal over 3–4 wk with ^{131}I (185 MBq) and ^{99m}Tc-tetrofosmin whole-body scintigraphy and Tg determination (off-T4) within 5 days. Patients with Tg levels above 0.5 ng/ml were defined as Group A (n = 29). Group B (n = 29) comprised patients who had Tg levels (off-T4) below 0.5 ng/ml. **Results:** Iodine-131 revealed only 19 of 44 tumor sites (43.18%). Additionally, three remnants could be demonstrated. Sensitivity showed decreasing values for local recurrences (4 of 7, 57.1%), bone lesions (7 of 13, 53.85%) and mediastinal (2 of 4, 50%), lung parenchymal (3 of 7, 42.85%) and lymph node (2 of 9, 22.2%) metastases. Whole-body scintigraphy with ^{99m}Tc-tetrofosmin revealed a total of 39 of 44 malignant lesions (88.6%). Sensitivity was superior for lung parenchymal metastases (9 of 9, 100%), mediastinum (4 of 4, 100%) and lymph nodes (9 of 10, 90%) and inferior for bone metastases (11 of 13, 84.6%). Local recurrences could be detected in 6 of 7 patients (85.7%), and thyroid remnants were detected in 2 cases (2 of 11, 18.2%). One liver metastasis could not be detected because of the physiologic tracer distribution of ^{99m}Tc-tetrofosmin. Thyroglobulin-off-T4 detected malignant recurrence or metastases in 18 of 19 patients (94.7%) when a cutoff of 3 ng/ml was used and in 16 of 19 patients (84.2%) when a cutoff of 10 ng/ml was used. Specificity was calculated as 71.8% when a cutoff of 0.5 ng/ml was used, 89.7% when a cutoff of 3 ng/ml was used and 100% when a cutoff of 10 ng/ml was used. **Conclusion:** Scintigraphy with ^{99m}Tc-tetrofosmin showed clear advantages concerning sensitivity in most metastatic lesions when compared with low-dose ^{131}I scan. Despite a slight lower specificity, ^{99m}Tc-tetrofosmin whole-body scintigraphy has, therefore, been proven to be a useful tool in the assessment of metastatic lesions in differentiated thyroid carcinoma.

Key Words: thyroid carcinoma; iodine-131; technetium-99m-tetrofosmin; whole-body scan

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Over the past few years, several studies concerning the usefulness of alternative tracers in the follow-up of thyroid carcinoma have been released (*1–9*). The main problem with these studies is that most studies that are based on thyroglobulin (Tg) level elevation cannot be compared because they are performed under different conditions of endogenous thyroid-stimulating hormone (TSH) stimulation. The aim of this study was to compare low-dose ^{131}I scan and the previously reported highly sensitive ^{99m}Tc-tetrofosmin whole-body scintigraphy using Tg after withdrawal of L-thyroxin treatment (off-T4) as a basis for comparison.

MATERIALS AND METHODS

Patients

Fifty-eight consecutive patients of our follow-up program with proven thyroid carcinoma of different histologic types after World Health Organization classification (12 follicular, 5 poorly differentiated follicular subtype, 2 papillary oxyphilic subtype, 36 papillary, 1 mixed papillary-medullary and 2 not classified) were examined off-T4 over 3–4 wk (basal TSH > 30 mU/liter). After primary therapy with total thyroidectomy, all patients had at least one high-dose ^{131}I ablation (2960–3700 MBq) of the remnants and TSH-suppressive treatment with L-thyroxin. After tumor-node-metastasis (TNM) classification, 2 patients were staged pT_1N_1, 15 were pT_2, 6 were pT_3 and 24 were pT_4. Nine patients had N stages and 2 had M stages at the time of surgery. Ten patients were not classified after TNM. Patients with a Tg level of greater than 0.5 ng/ml determined off-T4 were defined as Group A (n = 29, 21 women, 8 men; mean age = 60.5 yr). Group B (n = 29, 23 women, 6 men; mean age = 52.5 ± 12.7) comprised patients who had a Tg level (off-T4) of <0.5 ng/ml, which excludes significant tumor mass in distant location. In each patient in our study, whole-body scintigraphy with ^{131}I (185 MBq) and ^{99m}Tc-tetrofosmin, ultrasonography of the neck and Tg determination (off-T4) were performed within 5 days.

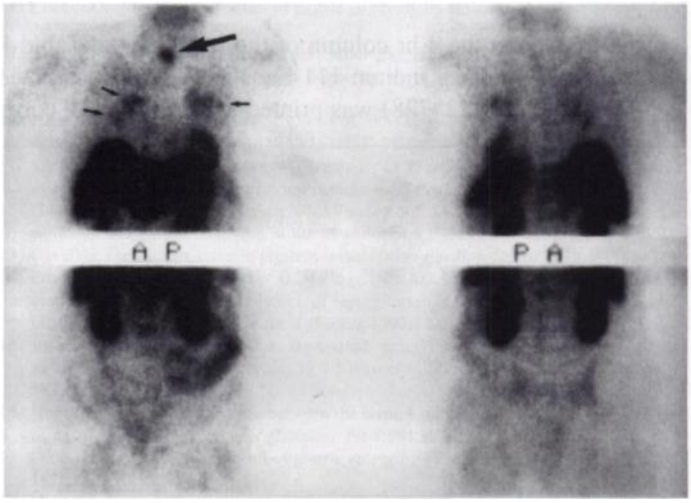

FIGURE 1. Technetium-99m-tetrofosmin scan of a patient with follicular carcinoma showing local recurrence, multiple lung parenchymal metastases and suspected tumor site in the ileosacral joints.

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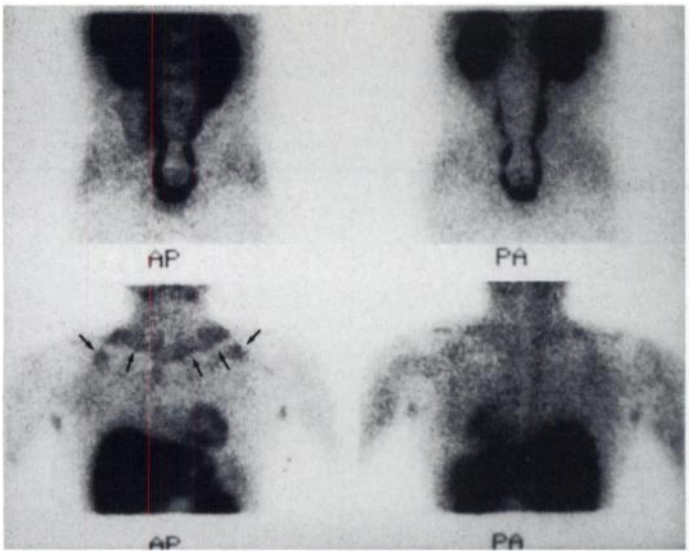

FIGURE 2. Technetium-99m-tetrofosmin scan demonstrating multiple cervical and mediastinal lymph node metastases in a 32-yr-old man with papillary carcinoma, stage $pT_{2b}N_1$ (Tg-off-T4 = 186 ng/ml).

Imaging Procedures

On the first day, after an early static abdominal scan (300,000 counts, beginning at 5 min postinjection), static whole-body scintigraphs with 370 MBq of ^{99m}Tc-tetrofosmin (Myoview; Amersham, Buckinghamshire, UK) were taken simultaneously in anterior and posterior projection using the Elscint Helix HR (Haifa, Israel) with a low-energy, high-resolution collimator (10 cm/min, 512 × 512 pixel matrix, 10% window at 140-keV peak). Quality control for labeling was performed with the chromatographic method and revealed a radiochemical purity over 94%. SPECT (64 × 64 matrix, 6° step and shoot, Hanning filter with a cutoff of 1.0 cm^{-1}) was performed only in cases with uncertain pulmonary lesions, to exclude thorax wall artifacts.

The ^{131}I scan was performed under endogenous TSH stimulation (>30 mU/liter) 72 hr after a diagnostic (185 MBq) oral dose of ^{131}I with planar anterior and posterior projections (Elscint SP6, high-energy, all-purpose collimator, 10 min/projection, 256 × 256 matrix, 20% window) at Day 4. The time interval between the ^{131}I and ^{99m}Tc-tetrofosmin scans was 4 days. An ingestion of stable iodine (>250 μg of iodine per g of creatinine) was excluded in cases with no iodine uptake and high Tg level by measuring urine iodine excretion in a single-spot sample using a modified cerarsenate method (*10*).

Thyroglobulin

Thyroglobulin levels were determined by immunoradiometric assay (immunoradiometric assay coated tube, SELCO, Tg, Medipan) with a functional assay sensitivity of 0.5–1.0 ng/ml Tg (10% intra-assay or 20% interassay coefficient) taking recovery (70%–130%) and possible Tg autoantibodies into account.

Criteria for Positivity

All scans were reviewed independently by two nuclear physicians for a qualitative evaluation: + = positive; (+) = possibly positive; − = negative. The concordance between the two examiners was 96.5% (56 of 58 patients).

A scan was considered true-positive when it was confirmed by either the ^{131}I scan or other imaging modalities in correspondence with high Tg level and clinical observation. Histologic confirmation was received in only five patients. If it was not possible to verify lesions histologically, other imaging methods (CT, MRI, x-rays and bone scintigraphy), together with Tg levels, were used as a basis for comparison and confirmation. Thyroid bed uptake was only considered as pathologic when it reappeared after a first negative diagnostic scan after primary ^{131}I ablation.

RESULTS

Twenty-nine patients (21 women, 8 men; mean age = 60.5 yr) were delegated to Group A with suspicion of recurrence or metastases because of elevated Tg levels (>0.5 ng/ml off-T4). This group consisted of 13 papillary (1 oxyphilic subtype), 11 follicular and 5 poorly differentiated follicular carcinomas. After TNM classification, 7 patients were characterized as pT_2, 4 were pT_3, 7 were pT_4 and 10 were not classified at the time of operation. Thyroglobulin levels (off-T4) of these patients were in a range of 0.66–73,071 ng/ml (mean = 3,227.1, median = 21.12 ng/ml). Twenty-two patients in this group received high-dose radioiodine therapy (>2960 MBq) more than once due to persistent iodine retention after postoperative remnant ablation with 2960 MBq of ^{131}I. All patients with thyroid remnants had Tg levels below 10 ng/ml. Patient 10, who had a poorly differentiated follicular carcinoma, showed a histologically proven local recurrence with only slight elevated Tg levels (3.2 ng/ml). All other patients in this group with malignancy recurrence or metastases showed clear elevated Tg levels above 10 ng/ml.

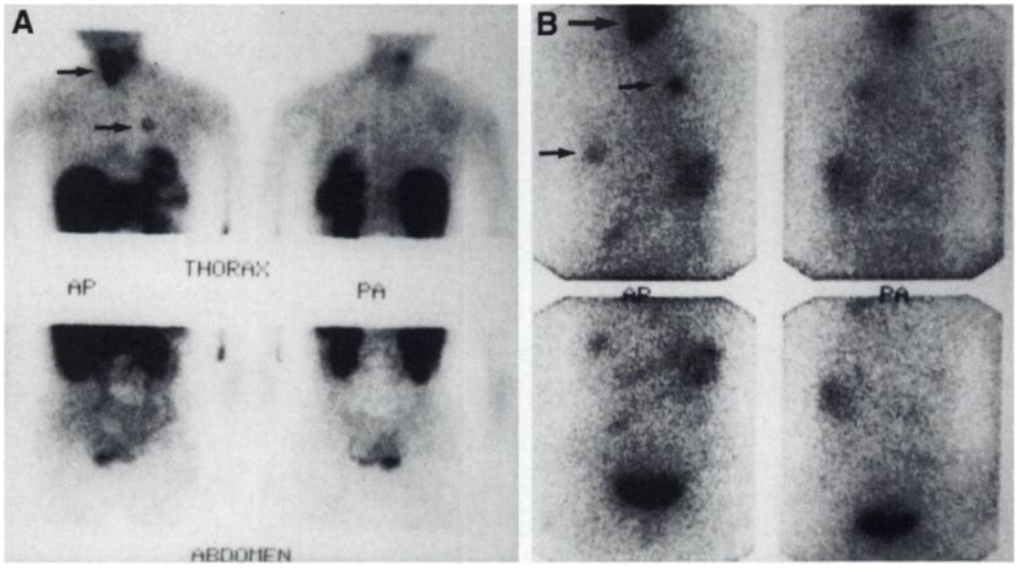

FIGURE 3. (A) Technetium-99m-tetrofosmin scan demonstrating local recurrence and solitary lung parenchymal metastasis in Patient 25 with follicular carcinoma oxyphilic subtype (Tg = 11,910 ng/ml). (B) Liver metastasis in this patient could only be visualized with ^{131}I.

TABLE 1
Group A Patient Data

Patient	Age (yr)	Sex	Histology	TNM stage	Total radiation dose (MBq)	Tg (ng/ml)	Localization	^{131}I	^{99m}Tc-tetrofosmin	Confirmation
10	53	F	Follicular-PD	T_3	9,252	3.2	Local recurrence	P	P	US, ^{131}I, H
11	46	F	Papillary	T_2	2,960	6.6	Thyroid remnant	P	N	US
12	61	M	Papillary	T_4	10,360	228	Thoracic spine 9	P	N	^{131}I, CT
							Thoracic spine 10	P	N	
17	58	F	Follicular		22,604	1.4	Thyroid remnant	N	N	US
18	61	M	Follicular	T_4NM_1	8,436	1,413	Lung left middle field	P	P	CT, ^{131}I
19	74	F	Papillary	T_3	27,010	701	Thoracic spine 8	P	P	^{131}I, XR
							Pelvis right	P	P	
							Calvaria right parietal	N	P	
24	45	F	Papillary	T_2	2,960	1.49	Thyroid remnant	N	N	US
25	82	F	Follicular		27,380	11,910	Local recurrence	P	P	^{131}I, US
							Lung	P	P	XR, ^{131}I, CT
							Liver	P	N	US, ^{131}I
27	67	M	Follicular-PD	T_4	3,320	7.2	Mediastinum	P	P	CT, ^{131}I
28	83	F	Follicular-PD	T_4	10,135	223.81	Mediastinum	P	P	CT, ^{131}I
29	75	F	Papillary		12,310	529	Mediastinum	N	P	CT
30	73	F	Follicular-PD	T_3	7,400	2.77	Thyroid remnant	P	N	US
32	55	M	Follicular		48,100	73,051	Left iliosacral joint	P	P	MRI, CT, BSC, H
							Crista iliaca right	P	P	
							Acetabulum right	N	P	
							Trochanter major right	N	P	
							Femur right	N	P	
							Trochanter major left	N	P	
							Lung-hilus right	N	P	
							Lung-hilus left	N	P	
							Lymph node infraclavicular right	N	P	
34	45	M	Papillary	T_4	6,660	6.12	Thyroid remnant	P	P	US
38	50	M	Papillary	T_4	18,900	16.9	Lung left middle field	N	P	CT, ^{131}I
							Lung left lower field	N	P	
							Lung right upper field	N	P	
39	41	F	Follicular	TxM_1	18,500	3,810	Lumbar spine 2	P	P	CT
40	50	M	Papillary	T_2	2,960	0.95	Thyroid remnant	N	P	US
42	72	F	Papillary	T_4N_1	4,220	1.07	Thyroid remnant	N	N	US
44	56	F	Papillary		10,410	66.9	Local recurrence	N	P	US, MRI
47	50	F	Papillary oxyphilic	T_2	2,960	4.3	Thyroid remnant	N	N	US
48		F	Follicular		7,183	173	Lung diffuse	P	P	CT
							Mediastinum right	N	P	
							Local recurrence	N	P	US
49	55	F	Follicular		5,926	50.5	Local recurrence	N	P	US, ^{131}I
53	57	F	Follicular	T_3	11,160	423	Local recurrence	N	N	
54	81	F	Follicular		28,456	3.2	Thyroid remnant	N	N	US
20	45	F	Follicular	T_2	2,960	0.66	Thyroid remnant	N	N	US
43	72	F	Papillary	T_2	2,960	0.73	Thyroid remnant	N	N	US
56	73	F	Follicular		9,684	21.12	Local recurrence	P	P	H
							Local recurrence	P	P	
57	82	F	Follicular-PD		18,870	743	Sacrum	N	P	MRI
58	32	M	Papillary	$T_{2b}N_1$	3,700	186	Lymph node cervical	P	P	MRI, CT, H
							Lymph node mediastinum	P	P	
							Lymph node mediastinum	N	P	
							Lymph node mediastinum	N	P	
							Lymph node infraclavicular	N	P	
							Lymph node infraclavicular	N	P	
							Lymph node infraclavicular	N	P	
							Lymph node infraclavicular	N	P	

PD = poorly differentiated; P = positive; N = negative; US = ultrasonography; H = histology; XR = x-ray; BSC = bone scintigraphy; TNM = tumor-node metastasis.

Whole-body scintigraphy with ^{99m}Tc-tetrofosmin revealed a total of 39 of 44 (88.6%) malignant lesions. Sensitivity was superior for lung parenchymal metastases (9 of 9, 100%), mediastinum (4 of 4, 100%) and lymph nodes (9 of 10, 90%) and inferior for bone metastases (11 of 13, 84.6%) (Figs. 1 and 2). Local recurrences could be detected in six of seven patients (85.7%), and thyroid remnants could be detected in two cases (2 of 11, 18.2%). One liver metastasis in Patient 25 could not be detected because of the physiologic tracer distribution of ^{99m}Tc tetrofosmin with high hepatobiliary uptake (Fig. 3). Patient 53,

TABLE 2
Group B Patient Data

Patient	Age (yr)	Sex	Histology	TNM stage	Total radiation dose (MBq)	Tg (ng/ml)	^{131}I	^{99m}Tc-tetrofosmin	Localization
1	54	M	Papillary	T_4	2,960	0.5	N	N	
2	57	F	Papillary	T_3	2,960	0.5	N	N	
3	48	F	Papillary	T_4	2,960	0.5	N	N	
4	59	M	Papillary	T_4	2,960	0.5	N	FP	Thoracic wall
5	62	F	Papillary	T_2	2,960	0.5	N	N	
6	35	F	Papillary	T_4	3,007	0.5	FP	N	Pharyngeal salivary retention
7	55	F	Papillary	T_2	3,060	0.5	N	N	
8	44	F	Papillary	T_{4b}	3,870	0.5	N	N	
9	27	F	Papillary	T_2N_{1b}	2,960	0.5	N	N	
13	34	F	Follicular	T_2	2,960	0.5	N	N	
14	48	F	Papillary	T_1N_{1b}	2,960	0.5	P	P	Thyroid remnant
15	50	F	Papillary	T_4	2,960	0.5	P	P	Thyroid remnant
16	62	F	Papillary	T_1	2,960	0.5	N	N	
21	54	F	Papillary	T_3	27,750	0.5	N	N	
22	66	M	Papillary	T_4N_1	3,880	0.5	FN	FN	Lymph node left cervical
23	66	F	Papillary	T_4	2,960	0.5	N	N	
26	42	F	Papillary	T_4	3,700	0.5	N	N	
31	73	M	Follicular	T_2	3,230	0.5	N	FP	Right thoracic wall
33	54	F	Papillary	T_{4b}	3,700	0.5	N	N	
35	75	F	Papillary	T_4N_1	2,960	0.5	N	N	
36	63	F	Follicular	T_4	2,960	0.5	N	FP	Thoracic wall
37	34	F	Papillary	T_2	2,960	0.5	N	N	
41	44	F	Papillary	T_4N_1	3,070	0.5	N	N	
45	50	F	Papillary	T_4	3,760	0.5	N	N	
46	60	F	Papillary	T_2	3,515	0.5	N	N	
50	31	F	Papillary	T_4	2,960	0.5	N	N	
51	67	F	Papillary oxyphilic	T_2	2,997	0.5	N	N	
52	64	M	Papillary	T_4N_{1b}	5,550	0.5	N	N	
55	44	M	Papillary	T_4	2,960	0.5	N	N	

P = positive; N = negative; FP = false-positive; FN = false-negative; TNM = tumor-node metastasis.

who had local recurrence of follicular carcinoma (423 ng/ml Tg) and numerous previous radioiodine doses (in all, 11.16 GBq of ^{131}I) demonstrated false-negative results on both ^{99m}Tc-tetrofosmin and ^{131}I scans.

Iodine-131 revealed only 19 of 44 tumor sites (43.18%). Additionally, three remnants could be demonstrated. Sensitivity showed decreasing values for local recurrences (4 of 7, 57.1%), bone lesions (7 of 13, 53.85%) and mediastinal (2 of 4, 50%), lung parenchymal (3 of 7, 42.85%) and lymph node (2 of 9, 22.2%) metastases. One liver metastasis in Patient 25 could be exclusively detected with ^{131}I (Table 1 and Fig. 3). Mean ablative doses of ^{131}I demonstrated no significant difference between patients with ^{131}I retention (mean ± s.d. = 15,255 ± 13,071 MBq) and patients without retention on radioiodine whole-body scintigraphy (18,044 ± 13,018 MBq; not significant). Also concerning Tg level, no significant difference could be found between both groups (means = 7644 and 7594 ng/ml, respectively; not significant).

Group B consisted of 29 patients (23 women, 6 men; mean age = 52.5 ± 12.7) with a Tg level below 0.5 ng/ml. Histologically, 25 patients had a papillary, 3 had a follicular and 1 patient had a mixed papillary-medullary carcinoma. After TNM classification, 2 carcinomas were classified as pT_1, 8 as pT_2, 2 as pT_3 and 17 as pT_4. Six patients had a N_1 stage (three N_{1b}). Twenty-seven patients were postoperatively treated once with 2960–3880 MBq of ^{131}I, 1 patient (Patient 52) was treated twice with 5550 MBq and 1 patient (Patient 21) who had papillary carcinoma had numerous therapies with a cumulative dose of 27,750 MBq. Correct negative results were obtained with ^{131}I in 25 cases and with ^{99m}Tc-tetrofosmin in 23 cases. A 14 × 9 mm (in diameter), histologically proven cervical lymph node metastasis in Patient 22 accounted for a false-negative result with both methods. Three false-positive retentions were found with ^{99m}Tc-tetrofosmin (all thoracic wall), and one was found by ^{131}I (pharyngeal salivary retention). In two patients (Patients 14 and 15), ^{131}I and ^{99m}Tc-tetrofosmin showed concordant retention in the thyroid bed (Table 2). Specificity is calculated with 96.1% for ^{131}I (185 MBq) and with 88.5% for ^{99m}Tc-tetrofosmin (Table 3).

Thyroglobulin-off-T4 detected malignancy recurrence or metastases in 18 of 19 patients (94.7%) when a cutoff of 3 ng/ml was used and in 16 of 19 patients (84.2%) when a cutoff of 10 ng/ml was used. Specificity was calculated as 71.8% when a cutoff of 0.5 ng/ml was used, 89.7% when a cutoff of 3 ng/ml was used and 100% when a cutoff of 10 ng/ml was used (Fig. 4).

TABLE 3
Comparison Between Tg and Low-Dose Iodine-131 and Technetium-99m-Tetrofosmin Whole-Body Scintigraphy

	Sensitivity (%)	Specificity (%)
Tg-off-T4 (cutoff = 3 ng/ml)	94.7	89.7
^{131}I whole-body scintigraphy (185 MBq)	43.18	96.1
^{99m}Tc-tetrofosmin whole-body scintigraphy	88.6	88.5

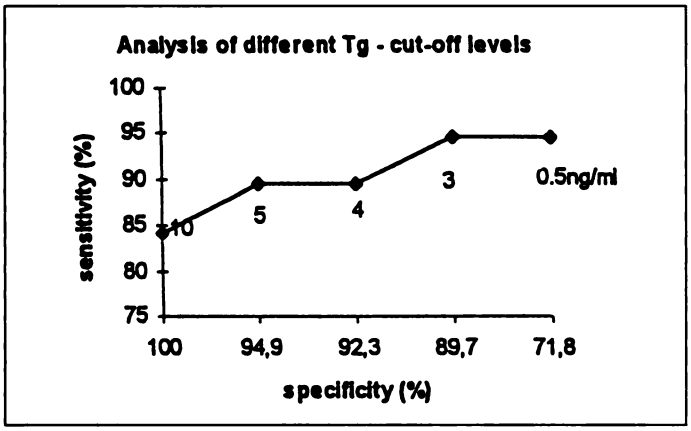

FIGURE 4. Analysis of different Tg-cutoff levels.

DISCUSSION

Our previous results with ^{99m}Tc-tetrofosmin in the follow-up of differentiated thyroid carcinoma (DTC) demonstrated that ^{99m}Tc-tetrofosmin, as an alternative tracer to low dose ^{131}I scan, is a very useful tool in the assessment of malignancy recurrence or metastases of DTC and could easily be performed under TSH-suppressive L-thyroxin therapy (on-T4) (*3,5*).

Low-dose ^{131}I whole-body scintigraphy (111–185 MBq of ^{131}I) is the most specific modality but shows a clear dose-dependent sensitivity (*11–14*). However, post-therapeutic scan after a high dose of ^{131}I may reveal new lesions not previously seen on diagnostic scan in up to 10%, especially in patients with previous radioiodine therapy (*13*). Even in our study, post-therapeutic ^{131}I scan detected three lung parenchymal metastases in Patient 38 and local recurrence in Patient 49, which was negative on diagnostic low-dose scan.

Thyroglobulin, determined under endogenous TSH stimulation off-T4, has been proven to be the most sensitive method for evaluation of patients with residual thyroid tissue or recurrent malignancy (*8,15*). The cutoff of Tg cannot be drawn without difficulties in overlapping between thyroid remnants or recurrence because particularly small lymph node metastases release only slight quantities of Tg.

In either case, the reason for elevated Tg must be localized. Ultrasonography of the neck often reveals residual tissue that is not distinguishable from scarred tissue, which is only provable by thyroid bed uptake on ^{131}I scans in these cases, but sometimes the reason for Tg elevation remains unclear. In our study, all but one case with elevated Tg could explained by either ^{131}I or ^{99m}Tc-tetrofosmin scintigraphy or ultrasonography. Only in one case (Patient 53), with previous high-dose (7400 MBq) radioiodine therapy because of local recurrence 4 mo prior to the study, did the reason for persistent Tg elevation (423 ng/ml, recovery = 76%) remain unclear, even with post-therapeutic ^{131}I scan after another dose of 7400 MBq. One small lymph node metastasis in Patient 22 could not be detected by Tg elevation or ^{99m}Tc-tetrofosmin or ^{131}I whole-body scintigraphy but could be detected with ultrasonography and CT of the neck. Histology gave evidence of malignancy in this case.

In our actual study, ^{99m}Tc-tetrofosmin was proven to have a better sensitivity in detection of all metastatic lesions compared to low-dose ^{131}I, except liver metastasis in Patient 25, because of physiologic hepatobiliary excretion of this tracer. Clear superiority over ^{131}I could be demonstrated for lung parenchymal, mediastinal and lymph node but also for bone metastases.

Of course, all but seven of the radioiodine-negative patients had more than one high-dose ^{131}I ablation before ^{131}I whole-body scintigraphy became negative, so one might well argue that this is a problem not of lower sensitivity but of a therapy-induced, selected population with less differentiated tumors. In case of elevated Tg levels, mean ablative doses of ^{131}I were not significantly different in ^{131}I-negative or -positive patients in our population.

Technetium-99m-tetrofosmin whole-body scintigraphy demonstrated a lower sensitivity for bone metastases compared with pulmonary or soft-tissue lesions, as could be previously demonstrated under TSH-suppressive condition (*5*). In case of Tg elevation and negative ^{99m}Tc-tetrofosmin and ^{131}I whole-body scintigraphy, a bone scan would be probably the next step in the evaluation for that reason.

Because the uptake of cationic tracers in tumor cells shows no dependence on TSH levels, no significant difference in sensitivity should be expected if whole-body scintigraphy is performed on- or off-T4. This is supported by the similar values for sensitivity obtained under TSH suppression (86%) and endogenous TSH stimulation (88.6%) (*5*).

The usefulness of ^{99m}Tc-tetrofosmin for detection of breast cancer (*16,17*) also makes it clear that, despite a high specificity (88.5%) in our study, the specificity of ^{131}I cannot be achieved by such a nonspecific but highly sensitive tracer. In Group B, we observed false-positive retentions in three patients, all contributed to the thoracic wall, demonstrated with SPECT.

Thyroglobulin, determined off-T4 over 3–4 wk, was proven to be the most sensitive method (94.7%) concerning detection of malignancy recurrence when a cutoff of 3 ng/ml was used. At this cutoff level, a specificity of 89.7% can be expected for the clinician. For that reason, elevated Tg levels have to be confirmed by imaging modalities (ultrasonography, ^{131}I and whole-body scintigraphy with an alternative tracer such as ^{99m}Tc-sestamibi or ^{99m}Tc-tetrofosmin) to decide whether therapy is indicated and to get an accurate base for therapy planning.

CONCLUSION

Scintigraphy with ^{99m}Tc-tetrofosmin showed clear advantages concerning sensitivity in most metastatic lesions when compared to the low-dose ^{131}I scan. Despite having a slightly lower specificity, ^{99m}Tc-tetrofosmin whole-body scintigraphy has, therefore, been proven to be a useful tool in the assessment of metastatic lesions or local recurrence in the follow-up of DTC. In case of elevated Tg levels and no retention on ^{131}I scan, the use of a nonspecific tracer such as ^{99m}Tc-tetrofosmin or ^{99m}Tc-sestamibi should be considered.

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Clinical Usefulness of Technetium-99m-HMPAO-Labeled Leukocyte Scan in Prosthetic Vascular Graft Infection

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The infection of a prosthetic vascular graft (PVGI), although rare, is the most severe complication in reconstructive vascular surgery. The early diagnosis of this complication reduces the death rate from surgery. Aortofemoral graft infections differ clinically from peripheral graft infections in significant ways. The aim of this article is to evaluate separately the reliability of the ^{99m}Tc-HMPAO-labeled leukocyte scan or white blood cell count (WBC) in the early detection of both aortofemoral and peripheral graft infections. **Methods:** One hundred sixty-two WBCs were performed on 129 consecutive patients with suspected aortofemoral (122 scans) and peripheral (40 scans) graft infection and in a 12-patient control group. Patients with suspected PVGI were categorized into three groups on the basis of their signs and symptoms on readmission: (a) patients with specific signs of graft infection (Group A); (b) patients with nonspecific signs of graft infection (Group B); and (c) patients with anastomotic aneurysms (Group C). Gram's stains of the perigraft exudate and graft cultures were performed and used as the gold standard in patients who underwent surgery. An 18-mo clinical follow-up was done to assess the presence or absence of graft infection in patients who did not have surgery. **Results:** In patients with suspected aortofemoral graft infections, the overall sensitivity, specificity and accuracy of WBCs (Groups A, B, C) were 100%, 92.5% and 97.5%, respectively, whereas sensitivity, specificity and accuracy calculated in the patients with nonspecific signs of graft infection (Groups B, C) were 100%, 92.3% and 96.9%, respectively. In patients with suspected peripheral graft infections, sensitivity, specificity and accuracy were 100%. **Conclusion:** The white blood cell scan seems a reliable diagnostic method for early diagnosis of PVGI, and it is more useful in aortofemoral graft infections.

Key Words: vascular graft; infection; technetium-99m-HMPAO-labeled leukocyte scan

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In the last ten years, the white blood cell count (WBC) scan has been used widely in the diagnosis of prosthetic vascular graft infection. The reported sensitivity and specificity values of this procedure were over 90% in almost all the studies (*1–6*) regardless of the radiopharmaceutical used to perform the leukocyte labeling (^{111}In-oxine or ^{99m}Tc-HMPAO). The recurrent problem in assessing vascular graft infection is making a diagnosis given the absence of specific clinical signs and symptoms. Therefore, an aortofemoral graft differs significantly from a peripheral one. Patients with extremity vascular prostheses often have cutaneous signs of infection such as draining sinuses or nonhealing wounds. These signs are not usually found in aortofemoral grafts, which are located wholly in the abdominal cavity. An evaluation of the clinical usefulness of the WBC scan in prosthetic vascular graft infections requires a separate assessment of its reliability for aortofemoral and peripheral grafts. The complications of advanced aortofemoral graft infection, such as retroperitoneal abscess or aortoenteric fistula, are characterized by a high death rate, while low-grade infections cause fewer deaths (*7–14*). The helpfulness and widespread use of these scintiscan techniques depend on their ability to identify low-grade infections and permit patient treatment under optimal surgical conditions.

We evaluated the clinical usefulness of the ^{99m}Tc-hexametazime (HMPAO)-labeled leukocyte scan or WBC in relation to the type of vascular graft and, more important, to the presence or absence of specific clinical signs and symptoms of infection.

MATERIALS AND METHODS

One hundred sixty-two scans with ^{99m}Tc-HMPAO-labeled leukocytes were obtained from 129 consecutive patients (4 women, 125 men; age range 36–77 yr; mean age 62 yr) with suspected graft infections and then reviewed. The type and the number of the studied grafts are shown in Table 1.

All patients had undergone previous reconstructive surgery with knitted Dacron or polytetrafluoroethylene (PTFE) grafts for either obstructive vascular diseases (98 patients) or an aortic aneurysm