Usefulness of $^{99m}$Tc-pertechnetate Scintigraphy and Fine-needle Aspiration Cytology in Patients with Solitary Thyroid Nodules and Thyroid Cancer*

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Abstract. The aim of this study was to evaluate the accuracy of fine-needle aspiration (FNA) cytology and thyroid scintigraphy (TS) in patients with solitary thyroid nodules. We retrospectively reviewed a series of 657 consecutive patients (531 (80.8%) women and 126 (19.2%) men, median age 45 years, range 16-81 years) with solitary thyroid nodules. Prior to surgery, all patients underwent FNA cytology whilst $^{99m}$Tc-pertechnetate TS was performed in 496 (75.5%) patients. Final histopathology showed 533 (81.1%) benign nodules, including 251 (38.2%) follicular adenomas and 124 (18.9%) thyroid carcinomas. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy in the detection of thyroid cancer were 95.8%, 21.1%, 22.6%, 95.5% and 35.7% for TS, and 81.4%, 99.4%, 97.1%, 95.8% and 96.0% for FNA cytology. The presence of thyroid cancer was confirmed in 92 out of 407 (22.6%) patients with a "cold" nodule, in 4 (4.5%) patients who had normal or increased uptake on TS, in 101 out of 104 (97.1%) patients with smears suggesting malignancy, and in 3 out of 533 (0.6%) smears suggesting benign lesions. In conclusion, the specificity of TS is low and this technique should be abandoned as a routine test in patients with nontoxic thyroid nodules. However, a more careful evaluation should be suggested for patients with cold thyroid nodules and a FNA cytology that reads follicular neoplasm.

The prevalence of thyroid nodules has been estimated to be 4% of the population, with an incidence of 5% in persons over age 60 (1). In contrast to thyroid nodules, thyroid cancer is a rare condition, accounting for only 1% of all reported malignancies (2). Thus, the majority of patients with thyroid nodules do not have cancer. They may be carefully followed-up by using serum TSH measurement, ultrasonography (US) and fine-needle aspiration (FNA) cytology, with the aim of early diagnosing hyperthyroidism and thyroid cancer, respectively. $^{99m}$Tc-pertechnetate thyroid scintigraphy (TS) is usually performed in patients with a low TSH level, but several patients have undergone TS since 15-20% of "cold" nodules may be malignant (1). The objective of this study was to evaluate the usefulness of FNA and TS in patients with solitary solid thyroid nodules undergoing surgery and to correlate the results of each test with final histopathology.

Patients and Methods

Study population. We retrospectively reviewed a series of 657 consecutive patients with solitary thyroid nodule who underwent surgery and subsequently histological examination of the thyroid gland. There were 531 (80.8%) women and 126 (19.2%) men, with an overall median age of 45 years (range 16-81 years). Once the patients had given their informed consent, all patients underwent US-guided (N=308, 46.9%) or manually-guided (N=349, 53.1%) FNA cytology. TS was performed in 496 (75.5%) patients. CT-scan and MRI were not routinely used as a primary imaging modality. The extension of the thyroid resection was decided according to the results of both preoperative ultrasonographic features, and
intrathecal administration (MIBG). Scintigrams were acquired by
matrix was obtained, 20 minutes after intravenous administration
supine position. One planar image of the neck in a 256 x 256 pixel
L-thyroxin) was excluded. Patients were examined in a normal
recent use of iodine-containing preparations (contrast media,
NPV = negative predictive value.
FNA = fine-needle aspiration, PPV = positive predictive value,
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Table I. Results of 99mTc-pertechnetate scintigraphy and FNA cytology in
differentiating between benign thyroid nodules and thyroid tumours.

<table>
<thead>
<tr>
<th>Results</th>
<th>Scintigraphy</th>
<th>FNA cytology</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>True-positives</td>
<td>334</td>
<td>353</td>
<td></td>
</tr>
<tr>
<td>False-negatives</td>
<td>41</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>True-negatives</td>
<td>48</td>
<td>279</td>
<td></td>
</tr>
<tr>
<td>False-positives</td>
<td>73</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Number of patients</td>
<td>496</td>
<td>657</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>89.1%</td>
<td>94.1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Specificity</td>
<td>39.7%</td>
<td>98.9%</td>
<td></td>
</tr>
<tr>
<td>PPV</td>
<td>82.1%</td>
<td>99.1%</td>
<td>0.008</td>
</tr>
<tr>
<td>NPV</td>
<td>53.9%</td>
<td>92.7%</td>
<td>0.008</td>
</tr>
<tr>
<td>Accuracy</td>
<td>77.0%</td>
<td>96.2%</td>
<td>0.013</td>
</tr>
</tbody>
</table>

FNA = fine-needle aspiration, PPV = positive predictive value,
NPV = negative predictive value.

The age of the patients did not differ significantly between
men and women (44.8±13.1 vs. 43.2±12.2 years; p=0.19).
Overall, the size of the removed thyroid nodule ranged from
8 to 60 mm (median 16 mm). There was no relationship
between the age of the patient and size of the thyroid nodule. Normal or increased uptake of 99mTc-
pertechnetate was found in 89 out of 496 (17.9%) nodules, whilst 407 (82.1%) patients had a "cold"
thyroid nodule. The final histopathology showed 533 (81.1%) benign nodules,
including 251 (38.2%) follicular adenomas, and 124 (18.9%)
thyroid carcinomas, of which 32 (25.8%) and 92 (74.2%)
were in male and female patients, with a prevalence of
25.4% and 17.3% (χ²=2.84, p=0.12), respectively. Overall,
there were 91 (73.4%) papillary, 24 (19.4%) follicular, 5
(4.0%) anaplastic and 4 (3.2%) medullary carcinomas.

The presence of a thyroid carcinoma was confirmed in 92
out of 407 (22.6%) patients with a "cold" thyroid nodule. The
sensitivity was defined as TP/(TP + FN), specificity as
TN/(TN + FN), positive predictive value (PPV) as TP/(TP + FP),
negative predictive value (NPV) as TN/(TN + FN), and accuracy
as (TN + TP)/overall patients.

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cytology reached 98.9% sensitivity. There were no FP results on FSE, but the majority of the patients with a follicular carcinoma (22 out of 24, 91.7%) had an indefinite FSE. Thus, the sensitivity of FSE and FNA cytology in detecting follicular cancer was similar (p=NS), and the combination of FNA cytology and FSE did not significantly improve (p=NS) the sensitivity of the single tests. FSE showed cancer in only 4 out of 23 (17.4%) patients with negative FNA cytology, while FNA cytology did not suggest the presence of thyroid cancer in patients with negative FSE.

**Discussion**

Although thyroid cancer accounts for 90% of all endocrine malignancies, it causes only 0.4% of all cancer deaths (5). The prevalence of thyroid cancer in our series (124 out of 657, 18.9%) was overestimated because of the selection of the patients, who had been previously scheduled for surgery. Usually, less than 10% of patients with a solitary thyroid nodule may have thyroid cancer.

Patients with solitary thyroid nodules should have FNA as the initial screening test, while radionuclide imaging by using $^{123}$I- or $^{99m}$Tc-pertechnetate is usually used for determining the functional activity of the thyroid gland (1). Unfortunately, up to 30% of patients with a solitary thyroid nodule receive a FNA that reads follicular neoplasm or suspicious lesion, and thus they require further evaluation before surgery, and usually undergo thyroidectomy (6).

$^{99m}$Tc-pertechnetate is the most readily available radiopharmaceutical employed for routine thyroid imaging. Pertechnetate ions are trapped by the thyroid gland although they are not organified, and thus the thyroid radiation dose is lower (0.6 vs. 2.6 rads) than that obtained by using $^{123}$I (4). However, early imaging following $^{99m}$Tc-pertechnetate administration is associated with high background activity requiring a carefully evaluation of the images. $^{123}$I is cyclotron-produced, it has a relatively short half-life but is expensive and is rarely used for standard thyroid imaging (4). In the majority of cases, thyroid cancer presents as a “cold” nodule on both radioiodine and pertechnetate scans (7).

Belfiore et al. (8) found that patients with cold thyroid nodules living in an iodine-deficient area had a lower risk of having thyroid cancer in comparison to those living in an iodine-sufficient area (2.7% vs. 5.3%), and that the frequency of cancer was higher in males. We did not find significant differences between men and women. In our experience, TS, FNA cytology and FSE showed FN results in 4 out of 96 (4.2%), 23 out of 124 (18.5%) and 22 out of 124 (17.7%) patients with thyroid cancer, respectively. Duquelle et al. (9) obtained similar results: the sensitivity, specificity, PPV and NPV were 94.3%, 80.5%, 35.9% and 99.2% for FNA cytology, and 95.6%, 10.5%, 11.7% and 95.0% for TS. It has also been stated that the probability of malignancy in patients with smears suggesting follicular adenoma is 15% and that, potentially, the risk of FN diagnoses following adequate sampling may reach 1% (10).

Recently, Roach et al. (11) found that 95% of the patients with FNA results suggestive of papillary cancer had correct diagnosis according to the final pathological examination. Although both FNA cytology and TS may help with the selection of patients requiring surgery, these techniques are rarely useful in determining the extent of thyroid resection (12). Follicular neoplasms are common in patients with a solitary TN and cause diagnostic problems for both the cytologist and pathologist in FSE specimen (13). McHenry et al. (14) showed that the sensitivity, specificity and accuracy were 88%, 89% and 91% for FNA cytology, and 93%, 100% and 97% for FSE, respectively (p=NS). FSE does not affect the intraoperative decision-making when an adequate FNA cytology suggesting malignancy is available, and rarely yields useful information for surgical planning (15).

In conclusion, the specificity of TS is low, and this technique should be abandoned as a routine test in patients with nontoxic solitary thyroid nodules. However, in patients with indeterminate FNA cytology, TS may be useful in suggesting a more careful evaluation. In our experience, the sensitivity of combined TS and FNA cytology was 98.9%. Moreover, $^{99m}$Tc-pertechnetate scintigraphy should be performed in all patients with a cytologically benign solitary TN when the TSH serum level is low (9). Although TS does not distinguish between benign and malignant lesions, it is useful if a hot nodule is considered in the differential diagnosis (13). Patients with cold thyroid nodules and a FNA cytology that reads follicular neoplasm should undergo thyroidectomy, and FSE rarely may have an influence on extension of surgery.

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**References**


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