

FNA Cytology and Frozen Section Examination in Patients with Follicular Lesions of the Thyroid Gland*

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Abstract. Patients with solitary thyroid nodules should have fine-needle aspiration (FNA) cytology as the initial screening test, but the most of those referred to a surgeon usually undergo frozen section examination (FS). The aim of this retrospective study was to assess the usefulness of FNA cytology and FS together in patients with a solitary thyroid nodule (TN). Two-hundred and ten patients with a TN and FNA cytology suggesting follicular neoplasm underwent intraoperative FS and subsequent hemithyroidectomy or total thyroidectomy. There were 47 (22.4%) men and 163 (77.6%) women, with a median age of 43 years (range 18-76 years). In all patients, ultrasound-guided FNA was successfully performed using 22-G needle prior to surgery. Smears of the FNA samples were stained by May-Grünwald-Giemsa stain and evaluated immediately by the cytologist. Final histology was follicular carcinoma in 23 (10.9%), follicular adenoma in 181 (86.2%), and hyperplasia in 6 (2.9%) patients. No difference ($p=NS$) in age of the patients, and greatest diameter on the TN was found between groups. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 13.0%, 97.3%, 37.5%, 90.0%, and 88.1% for FNA cytology, and 17.4%, 100%,

100%, 90.8%, and 91.0% for FS, respectively. The combination of FNA plus FS did not significantly improve the results. In conclusion, both FNA cytology and FS are highly specific tests, but their sensitivity is low, even when they are used in combination. Thus, in patients with smears suggesting follicular neoplasm, FS should be considered unnecessary because it does not affect the intraoperative decision making. FS is most useful in those cases that are diagnosed as suspicious for papillary carcinoma by FNA.

The estimated prevalence of palpable thyroid nodules (TN) is 5%, but using neck ultrasonography one half of population may have a thyroid nodule (1, 2). All patients with solitary TN should have fine-needle aspiration (FNA) cytology as the initial screening test but, unfortunately, up to 30% of patients with nodular thyroid disease will receive an FNA report that reads follicular lesion, or suspicious (3). Thus, most patients with follicular lesions will require surgical management with the aim of having a permanent histological record, and the intraoperative decision-making for such patients may require frozen section examination (FS). The aim of this retrospective study was to determine the clinical utility of FNA and FS in patients with follicular lesions.

Patients and Methods

Two-hundred and ten patients with a TN and FNA cytology suggesting follicular neoplasm underwent intraoperative FS and subsequent hemithyroidectomy or total thyroidectomy. There were 47 (22.4%) men and 163 (77.6%) women, with a median age of 43 years (range 18-76 years). The median size of the nodules on neck high-resolution ultrasonography (US) was 17 mm (range 9-21 mm). In all patients, US-guided FNA was successfully performed prior to surgery, according to the technique previously reported (4). Smears of the FNA samples were stained by May-Grünwald-Giemsa stain

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Table I. Results of the study.

Parameter	FNAC	FS	FNAC+FS
TP	3	4	6
FN	20	19	17
TN	182	187	187
FP	5	0	0
Sensitivity	13%	17%	26%
Specificity	97%	100%	100%
Accuracy	88%	91%	92%
PPV	37%	100%	100%
NPV	90%	91%	91%

FNAC, fine-needle aspiration cytology; FS, frozen section examination; TP, true positive; FN, false negative; TN, true negative; FP, false positive; PPV, positive predictive value; NPV, negative predictive value.

and evaluated immediately by the cytologist. Inadequate smears were repeated and nondiagnostic specimens excluded. Freezing the tissue in liquid nitrogen or in cooled isopentane (methylbutane) resulted in fewer artefacts than when the tissue was frozen on the cryostat stage, and we preferred haematoxylin-eosin stain, because of the quality of the preparation and its better correlation with the permanent sections (5). The reported data are expressed as mean±standard deviation (SD) and comparisons between groups were performed using the chi-square (χ^2) test corrected by Yates and Student's *t*-test, when required. The differences were considered significant at a *p*-value <0.05. Sensitivity was defined as true-positives (TP)/TP + false-negatives (FN), specificity as true-negatives (TN)/TN + false-positives (FP), positive predictive values (PPV) as TP/(TP + FP), negative predictive values (NPV) as TN/(TN + FN), and accuracy as (TN + TP)/overall patients.

Results

Final histology was follicular carcinoma in 23 (Group A, 10.9%), follicular adenoma in 181 (Group B, 86.2%) patients. No difference in age of the patients (43.9±11.8 vs. 42.7±12.4 years, *p*=0.66) and greatest diameter on the TN (16.3±1.8 vs. 17.1±1.4 mm, *p*=0.13) was found between groups. In six (2.9%) patients, the final histology showed simply hyperplasia. Neither age nor size differed significantly between men and women. The overall results are reported in Table I. Overall, there were 187 (89%) cases of benign lesions. We obtained few TP results by both FNA and FS: only 6 (26.1%) follicular carcinoma were correctly detected by FNA and FS together. However, we found only 5 FN results on FNA cytology and no FP results on FS. The sensitivity was very low, but the specificity was 100% with FS and the accuracy ranged between 88% and 92%. The combination of FNA cytology plus FS did not improve significantly (*p*=NS) the results.

Table II. Results of fine-needle aspiration cytology in different studies.

Results of FNAC	Year (reference)			
	1993 (14)	2000 (15)	2001 (3)	2004 (6)
Cases	18,183 ^a	4,049	329	606
Suspicious ^b	27% ^c	23%	44%	37%
Malignant	4%	13%	28%	17%

FNAC, fine-needle aspiration cytology; ^aMeta-analysis from 7 series; ^bincluded indeterminate specimens; ^cincluded 17% nondiagnostic specimens.

Discussion

Thyroid cancer is a rare malignancy, occurring in fewer than 1% of all cancer patients, while its incidence per 100,000 in 2002 was 13.4 for women and 2.5 for men in the United States (1, 6, 7). Adenocarcinoma is the most common histological type seen in the thyroid gland (8). However, the incidence of thyroid cancer is increasing: from 8,000 to 26,000 cases per year in the United States in from 1975 to 2006, respectively (9). In this review, 16% were follicular or Hürthle cell carcinomas. Patients with follicular carcinoma have a higher incidence of metastasis than those with papillary carcinoma (10). As many as 95% of thyroid tumors present as a solitary TN and up to 30% may harbour malignancy (11, 12). Ultrasound-guided FNA cytology has long been used in the management of TN, allowing a better selection of patients requiring surgery (7, 13). The results of FNA cytology show different incidences of thyroid cancer. In 1993, a meta-analysis of more than 18,000 cases (14) showed only 4% thyroid cancer, but more recently, the percentage of cancer discovered by FNA is significantly higher, depending on the type of study and the criteria for patient selection (Table II). In differentiating between neoplasia and hyperplasia, the overall results of FNA cytology are good, with a sensitivity, specificity and accuracy ranging between 57-86%, 60-100% and 65-100%, respectively (6, 11, 12, 16, 17). FS shows usually similar sensitivity (32-87%) and accuracy (65-96%), but higher specificity (96-100%). However, in the presence of follicular lesions the sensitivity, specificity and accuracy range between 17-82%, 97-100% and 82-96%, respectively (11, 12, 18, 19). Our results are consistent with these results, with 13% and 17% sensitivity and 97% and 100% specificity for FNA cytology and FS, respectively. Ideally, the surgeon and the pathologist should have discussed the case beforehand and the pathologist should be prepared to advise the surgeon as to the best area to biopsy, with the aim of selecting from the specimen received the portion to be examined microscopically (5). Thus, different suggestions are given in the literature: FS

is specific and cost effective (7, 12, 19-22), or adds little to the management of the lesion (3, 17, 23). When FNA and FS are combined, an improvement of the results was shown in some studies (21, 24), while the usefulness of FNA and FS together was limited in others (20, 22, 25).

In conclusion, both FNA cytology and FS are highly specific tests, but their sensitivity is low even when they are used in combination. Thus, in patients with smears suggesting follicular neoplasm, FS should be considered unnecessary because it does not affect the intraoperative decision making. FS is most useful in those cases that are diagnosed as suspicious for papillary carcinoma by FNA (6).

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