Frozen section and fine needle aspiration biopsy in thyroid surgery – needles and sections

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Abstract

Purpose To review our own experience with fine needle aspiration biopsy (FNAB) and frozen section (FS) in thyroid surgery and to assess the value of FNAB and FS in predicting malignancy in patient with thyroid disease.

Methods The records of 300 patients who underwent thyroid surgery between April 2001 and June 2006 were analyzed.

Results Of the 153 patients who had preoperative FNABs performed, 8 (5.22%) were reported as indeterminate, 100 (65.35%) were read as benign, and 3 (1.96%) were read as malignant. Forty two of the FNABs were inadequate for evaluation (27.45%). When occult papillary carcinomas were excluded, sensitivity, and accuracy rates for FNAB reached 100%. One hundred and ninety one patients had FSs performed. 184 (96.33%) of these were reported as benign, 4 (2.09%) were reported as malignant, 3 (1.57%) were deferred to permanent paraffin (PP) sections. When occult papillary carcinomas were excluded, sensitivity, and accuracy rates for FS were 42.85%, 43%, and 97.28% respectively.

Conclusions Our data supports the use of FNAB in the confirmation of malignancy and the need for operation. The routine use of FS is not warranted. Selective use of FS when FNAB is nondiagnostic or indeterminate may provide additional information. Both FNAB and FS fail to reveal occult carcinomas of thyroid.

Keywords Thyroid · Frozen section · Fine-needle aspiration biopsy.

Introduction

Due to their high incidence and malignant potential, thyroid nodules represent a significant problem in the current clinical and surgical practice. Despite that most thyroid nodules represent benign lesions, 5–20 percentage of them are malignant [1–3]. Careful evaluation is required in order to avoid both over treatment (unnecessary surgery) as well as under treatment of these potentially malignant, but highly curable lesions.

Frozen section (FS) biopsy of a thyroid nodule is performed to obtain an intraoperative pathological diagnosis of malignant nodule at the time of operation which may alter surgical strategy. In case of malignancy total thyroidectomy should be the option of surgical choice in order to protect patient from the risk of a second intervention which might possess increased morbidity and complication rates. On the other hand, according to the accurate diagnosis of a benign thyroid disease the impact of FS could alter operative management from aggressive to conservative surgery [4–6].

Fine-needle aspiration biopsy (FNAB) of thyroid nodules is considered to be the most reliable test for the diagnosis of malignancy and is now widely recommended for preoperative selection of patients who are appropriate candidates for surgery and FNAB replaced the need for FS

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in many centers. Unfortunately, FNAB is not sufficient in differentiating benign from malignant follicular nodules, which represent the major debate of concern for surgeons [7].

Gibb and Paieka [8] suggest that each institution must determine for itself the usefulness of both the FNAB and FS in the surgical management of thyroid nodules. As a consequence of this major point of discussion, we decided to review our own experience with FNAB and FS in thyroid surgery and to assess the value of FNAB and FS in predicting malignancy in patient with thyroid disease in our endemic region.

Methods

A retrospective review of all patients, who underwent thyroid surgery in our university hospital between April 2001 and June 2006 was performed. We collected the following data: age, sex, date and type of operation, results of FNAB and/or FS and the permanent paraffin (PP) section histology. Patients with completion thyroid resections, thyroglossal duct cysts excision, and incidental thyroid resections as a part of laryngectomy were excluded.

The FNAB results were reclassified and described as benign, malignant, indeterminate, and nondiagnostic. FNAB results were considered benign if the definite diagnosis was reported to be clearly benign. In cases, which either predicted to possess malignancy suspicion or achieve the definite diagnosis of malignancy by FNAB were reclassified as malignant. The term indeterminate was used for both follicular lesions and Hürthle cell lesions. Inadequate sample for evaluation was mentioned as non-diagnostic.

FS biopsy findings were categorized as benign, malignant, and deferred until PPs. The PP results were either benign or malignant. The dominant nodule of multinodular goitre or a solitary nodule was sampled by FNAB preoperatively and FS intraoperatively. The maximum diameter of the tumour in PP was recorded for all malignant lesions. Occult microcarcinomas of the thyroid are defined as tumours 1 cm or smaller in dimension without evidence of capsular invasion and not associated with lymph-node metastases [9, 10]. Sensitivity, specificity, diagnostic accuracy, positive predictive value (PPV), and negative predictive value (NPV) for both FS and FNAB were assessed separately, including and excluding occult carcinomas.

These are defined as sensitivity (true positives/true positives + false negatives), specificity (true negatives/true negatives + false positives), accuracy (true positives + true negatives/true positives + true negatives + false positives + false negatives), PPV (true positives/true positives + false positives), and NPV (true negatives/true negatives + false negatives).

Results

Patient data

Three-hundred patients who underwent thyroid surgery were included in this study. The median age was 45.4 years (range 20–76). There were 87 (29%) male and 213 (71%) female patients. Malignant disease was encountered in 18 patients (6%). 16 of which were papillary, 1 was follicular, and the other was medullary carcinoma. 6 of the 16 papillary carcinomas were occult micro carcinomas. FS was performed in 191 operations and FNA reports were available in 153 patients. In 104 patients both FS and FNA reports were present. PP section reports were available in all cases.

FNAB results

Of the 153 patients who had preoperative FNABs performed, 8 (5.22%) were reported as indeterminate, 100 (65.35%) were read as benign, 3 (1.96%) were read as malignant. 42 of the FNABs were inadequate for evaluation (27.45%). Four (4%) patients with a benign diagnosis was found to achieve malignancy on permanent histopathological interpretation. All of them were occult papillary microcarcinomas. Table 1 shows FNAB results and their correlation with PP sections.

The sensitivity, specificity, accuracy, PPV and NPV for malignancy by FNAB were 42.85%, 96%, 96.11%, 100%, and 96%, respectively. When occult papillary carcinomas were excluded, sensitivity, accuracy, and PPV rates for FNAB reached 100% for all. There were no change in specificity and NPV rates (Table 1).

FS results

FS biopsies had been performed in 191 cases. 184 (96.33%) of these were reported as benign, 4 (2.09%) were reported as malignant, and 3 (1.57%) were deferred to PP sections. Although a benign diagnosis was rendered on 184

Table 1 Correlation of fine needle aspiration diagnoses with permanent paraffin section diagnoses.

FNAB (n)	PP	
	Benign (n)	Malignant (n)
Benign (n = 100)	96	4*
Malignant (n = 3)	0	3
Indeterminate (n = 8)	4	4
Non diagnostic (n=42)	39	3
Total (n = 153)	139	14

FNAB, fine needle aspiration biopsy; PP, permanent paraffin

* PP reports of four cases were occult papillary micro carcinoma.

specimens, the permanent histopathological diagnosis was turned to malignant in 8 cases, 4 of which were verified to be occult papillary carcinoma. Table 2 shows FS results and their correlation with FP sections. Among the 4 patients reported as having malignant nodules by FS, the permanent histopathological examination diagnosed benign disease in 1 of these.

The sensitivity, specificity, accuracy, PPV, and NPV for malignancy by FS were 27.27%, 99.43%, 95.21%, 75%, and 95.65% respectively. When occult papillary carcinomas were excluded, sensitivity, accuracy, and NPV rates for FS reached 42.85%, 97.28%, 97.77% respectively. There were no change in specificity and NPV rates (Table 2).

Table 2 Correlation of frozen section diagnoses with permanent paraffin section diagnoses.

	PP	
	Benign (n)	Malignant (n)
FNAB (n)		
Benign (n = 184)	176	8*
Malignant (n = 4)	1	3
Deferred (n = 3)	3	0
Total (n = 191)	180	11

FS, frozen section; PP, permanent paraffin

* PP reports of four cases were occult papillary microcarcinoma.

Table 3 Correlation of fine needle aspiration and frozen section diagnoses with permanent paraffin section diagnoses.

Permanent paraffin diagnosis	FNAB diagnoses/FS diagnoses											
	B/B (n)	B/M (n)	B/Def (n)	M/B (n)	M/M (n)	M/Def (n)	Ind/B (n)	Ind/M (n)	Ind/Def (n)	Nd/B (n)	Nd/M (n)	Nd/Def (n)
Benign (n = 94)	66	0	2	0	0	0	3	1	0	22	0	0
Malignant (n = 10)	2*	0	0	0	2	0	3	1	0	2*	0	0
Total	104	68	2	0	2	0	6	2	0	24	0	0

B, benign; M, malignant; Ind, indeterminate; Nd, nondiagnostic; Def, deferred; FNAB, fine needle aspiration biopsy; FS, frozen section; PP, permanent paraffin

*PP reports of all cases were occult papillary microcarcinoma.

Table 4 Sensitivity, specificity, diagnostic accuracy, positive predictive value, and negative predictive value for both FS and FNAB were assessed separately, including and excluding occult carcinomas.

	FNAB (%)	FS (%)	Concordant FNAB and FS (%)	Occult carcinomas excluded		
				FNAB (%)	FS (%)	Concordant FNAB and FS (%)
Sensitivity	42.85	27.27	50	100	42.85	100
Specificity	96	99.43	100	96	99.43	100
Accuracy	96.11	95.21	97.14	100	97.28	100
PPV	100	75	100	100	75	100
NPV	96	95.65	97.05	100	97.77	100

FNAB, fine needle aspiration biopsy; FS, frozen section

Concordant FNAB and FC

The correlation of FNAB/FS with permanent histological diagnosis is shown table 3. When FNAB and FS diagnosis were concordant (Benign/Benign and Malignant/Malignant); sensitivity, specificity, accuracy, PPV, and NPV for malignancy were 50%, 100%, 97.14%, 100%, 97.05% respectively. When occult carcinomas were excluded sensitivity, specificity, accuracy, PPV, and NPV reached 100% for all (Table 4).

Discussion

Since the introduction of FNAB, the use of FS has been questioned. Some surgeons still perform intraoperative FS on all thyroid nodules, while others have completely abandoned the procedure [5]. There is a large body of literature discussing the success of FNAB for the preoperative identification of malignancy [6, 10–15]. FNAB is a safe, cost effective and accurate test in preoperative evaluation of thyroid nodules [11]. Unfortunately, FNAB has some limitations in the diagnosis of follicular thyroid cancer, as a consequence of being deficient to identify the hallmark features of malignancy, including vascular and capsular invasion [12, 13].

In our series, the sensitivity, specificity, accuracy, NPV, and PPV of thyroid FNABs were 42.85%, 96%, 96.11%, 100%, and 96%, respectively. When occult papillary carcinomas were excluded, sensitivity, accuracy, and PPV rates for FNAB reached 100%. As a matter of fact, our FNAB results was not able to detect the all cases of occult papillary thyroid carcinoma. Occult carcinoma is difficult pathological entity to be diagnosed by cytologic methods and some recommend ultrasound-guided FNAB [14, 15]. Although the technique of FNA and the intent of the procedure were not specifically evaluated in this study; false negatives may occur as a result of missed sampling or cytological error. On the other hand, identifying an incidental micro carcinoma during FNAB may lead to a resection that has no effect on clinical course.

Indeterminate and nondiagnostic FNAB results remain a significant problem in the evaluation of thyroid nodules. In the present study there were 8 (5.22%) cases of indeterminate (follicular/hurthle cell neoplasm) by FNAB, 4 (50%) of which were diagnosed to be malignant on PP. One of these cases were follicular while the others were papillary carcinoma. This is consistent with the percentages reported by other investigators [8, 16, 17]. Contribution of FS for surgical management in this group was not satisfactory. The percentages of nondiagnostic FNABs in this study (27.45% and) is not excessively high when compared with the literature which has been reported up to 30% [18]. Nondiagnostic FNAB specimens may be a result of characteristics of the thyroid nodule or inadequate sampling. Additionally we must consider the differences between experienced centers and small centers. Referral centers have a large, selected patient population and experienced cytopathologists. They can develop a higher level of experience in interpreting a FNAB. It may not always possible to find an experienced cytopathologist in rural centers such as ours. Alexander and et al reported that repeated ultrasound guided FNAB is often successful and should be the standard approach to thyroid nodules which have initial nondiagnostic cytology. We agree this suggestion. According to our experience, we believe that a negative FNA should not be considered as a reassurance in circumstances of other clinical factors suggesting malignancy.

In this study, the sensitivity, specificity, accuracy, PPV, and NPV for malignancy by FS were determined to be 27.27%, 99.43%, 95.21%, 75%, and 95.65% respectively. When occult papillary carcinomas were excluded, sensitivity, accuracy, and NPV rates for FS reached 42.85%, 97.28%, and 97.77% respectively. FS was practised in 24 of 42 nondiagnostic FNABs, all of which were defined as benign. However, 2 (8.3%) of them were found to have occult papillary carcinoma in PP. Our sensitivity is lower than the reported in literature (53–93%) [10, 19, 20], mainly because of our high false negative results. The probable underlying reasons for this difference might be aligned as follows. Firstly, the number of slices to evaluate a lesion varies

between different centers. The more slices that are taken, the higher is the chance of finding carcinomas, especially in cases of occult carcinomas. In our institute, the lower sensitivity of FS may be attributed to the number of slices that are used which ranges between 2–3. Secondly, in a similar manner, we only perform FS to a dominant nodule in multinodular goiter. However, the possibility of malignancy in a separate nodule that could be detected in PP should be taken in to consideration. DeMay RM reported that FS diagnosis of thyroid lesions is restricted by orientation problems with fresh tissue, suboptimal nuclear detail, freezing artefacts, time and limited sampling and reluctance to commit to a malignant diagnosis [21–23]. In our experience, we can not recommend the alone use of frozen section for thyroid surgery especially in centers where extensive sub-sampling of the specimen is not possible.

The diagnosis of thyroid carcinoma was virtually established when FNAB and FS were concomitantly positive for malignancy, however concordant benign FNAB and FS diagnosis were associated with 2.94% false negative results. The false negatives in this group may be attributed to the small size of tumours. All of the false negatives were occult carcinomas. When FNAB and FS diagnosis were concordant (Benign/Benign and Malignant/Malignant) and occult carcinomas were excluded; sensitivity, specificity, accuracy, PPV, and NPV for malignancy were reached 100%.

In summary, our data support the use of FNAB in the confirmation of malignancy and selecting appropriate candidates for surgery. However, a negative FNAB should never exclude malignancy if there is clinical suspicion. As routine use of FS is not warranted, selective use of FS when FNAB is nondiagnostic or indeterminate may provide some additional information in course of surgical management. Neither FNABs nor FS biopsies achieve the specialty to detect occult carcinomas of thyroid. Each institution should evaluate its own ability to use these modalities, being aware of the fact that both techniques are clinician and pathologist dependent.

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