FINE NEEDLE ASPIRATION CYTOLOGY VERSUS FROZEN SECTION BIOPSY IN MANAGEMENT OF THYROID NODULES *By*

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ABSTRACT

Background: Thyroid nodules are common clinical finding with a reported prevelalence of 4% to 7% of adult population. Fine needle aspiration cytology (FNAC) is important for initial evaluation but has many falsies. The use of intraoperative frozen section (FS) has been advised. **Objectives:** This study was conducted to evaluate the contribution of both techniques (FNAC and FS) in management of thyroid nodules. **Patients and methods:** 40 patients with clinically palpable thyroid nodule (s) (37 women and 3 men; mean age, 42years) were included in this study. Preoperative (FNAC) and intraoperative (FS) diagnosis were performed and compared with the final pathology report using standard statistical formulas. **Results:** For FNAC, sensitivity was 58.3%, specificity was 100% and accuracy was 87.5%. FS sensitivity, specificity and accuracy were 75%, 100%, 92.5% respectively. **Conclusion:** FNAC is highly accurate and specific in initial evaluation of nodular thyroid diseases but FS has a significant role during thyroid surgery especially in non diagnostic cases by FNAC and proved to have high specificity and accuracy

Keywords: FNAC, FS, thyroid nodule

INTRODUCTION

The thyroid gland is affected by different pathological lesions which either show a diffuse pattern or produce nodules. Nodular lesions comprise the disorders which either consist of non-neoplastic hyperplasia or of benign or malignant tumors. Thus, the problem of appropriate management of thyroid nodules arises because about 5 percent of clinically evident thyroid nodules are malignant⁽¹⁾. So management of patients with thyroid nodule is based on accurate diagnosis.⁽²⁾

The ability to distinguish benign from malignant nodules is vital to avoid unnecessary operation. Fine needle aspiration diagnosis aids the selection of patients for surgery and has become an important examination technique for the initial evaluation of thyroid nodules⁽³⁾.

Nevertheless, like any other test, FNAC has its limitations. The reported pitfalls are those related to specimen adequacy, sampling techniques, the skill of the physician performing the aspiration, the experience of the pathologist interpreting the aspirate and overlapping cytological features between benign and malignant follicular neoplasm⁽⁴⁾.

Many surgeons use intraoperative frozen section biopsies to confirm the diagnosis of FNA cytology and guide the extent of thyroidectomy⁽⁵⁾.

This study was conducted to evaluate the contribution of both techniques to the diagnosis and management of benign and malignant thyroid nodules.

SUBJECTS AND METHODS Patients:

This prospective study was performed at Zagazig University Hospitals over 3 from December vears 2007 to December 2010. Ethical approval was obtained. The study included 40 clinically palpable patients with thyroid nodule. Thyroid function tests and thyroid ultrasound were performed for all patients. All patients (37 women and 3 men; age range, 24-63 years) had (FNAC) preoperative and intraoperative Frozen Section (FS) and final pathological diagnosis using Permanent Section (PS). All FNAC, FS diagnoses were compared with the





final pathology report. From these results, the accuracy, sensitivity, specificity, positive predictive value and negative predictive value were calculated using standard statistical formulas.

Preoperative FNAC:

FNAC was performed by pathologist with a 20-gauge needle attached to a 10 ml disposable syringe. The procedure was done with the patient in the semisitting position; the patient's extended neck was backwards; allowing maximal exposure of the thyroid lesion. After careful thyroid palpation, the nodule or nodules to undergo biopsy were identified. The skin was cleaned with alcohol, no local anesthesia was necessary. With one hand holding the pistol-grip holder and the other hand palpating and fixing the nodule, the aspirator placed the needle into the nodule, applied suction, and moved the needle back and forth within the nodule. As soon as blood tinged fluid appeared in the hub of the needle, the suction was released before the needle was then detached from the syringe and three to four ml of air were taken into the syringe and forced out through the reattached needle to express the specimen on the glass slides. Slides were immediately wet fixed in 95% ethyl alcohol and sent to our laboratory for staining and evaluation. FNAC results were classified into three categories:

1) Benign: including nodular hyperplasia, colloid cyst, and thyroiditis.

2) Malignant when the aspirates had unequivocal cytological findings of malignancy.

3) Suspicious (intermediate) group, including follicular neoplasm and aspirates that showed some features of papillary carcinoma e.g. a few cells with intranuclear inclusions or nuclear grooves but without sufficient criteria for a definitive diagnosis of malignancy, or with non diagnostic criteria.

Smears showing a minimum of six clusters of epithelial cells with more than 20 cells in each cluster were considered adequate⁽⁶⁾.

Patients with a malignant or suspicious cytological result were recommended to undergo surgery, whereas those with a benign cytological diagnosis underwent thyroid surgery in cases of a rapid growing nodule, local compression symptoms or for cosmetic reasons⁽⁷⁾

Frozen sections:

The resected specimens were submitted for frozen sections. The tissue slices were cut in a cryostat (- 21° C) at 6 µm and stained with haematoxylin and eosin.

RESULTS

Forty patients who were included in this study underwent a type of thyroidectomy (for a thyroid nodule). The 37 women (92.5%) and 3 men (7.5%) had a mean age of 42 years (range, 24 to 63 years) and SD of \pm 13.5 years. The mean size of thyroid nodule was 2.7 cm (SD, \pm 1.6 cm).

Thyroid FNA cytology results versus section diagnoses frozen were compared to the results of final histological study in order to calculate the values of the tests. The cytology results of (FNA) were benign in 50% (20 of 40 cases), the most common benign diagnosis was colloid goiter (Figure 1) (17 of 20 cases; 42.5%). The second was Hashimoto's thyroiditis in three cases (7.5%) (Figure 2). Malignant results were identified in 7 cases (17.5%). Papillary carcinoma was the most common malignancy (Figure 3) in six cases (15%), aspirates were characterized by increased cellularity, tumor cells arranged in sheets, papillary cell groups and typical nuclear abnormalities, which include intranuclear hopes and grooves cytoplasmic (intranuclear pseudo-





inclusions). The other malignant lesion was follicular carcinoma in one case (2.5%), in which small clusters of malignant follicular cells with hyperchromatic nuclei and frequent mitotic figures were shown (Figure 4). 13 cases were suspicious or indeterminate (32.5%) for which a clear cytological diagnosis cannot be made because no clear-cut cytology criteria were available to help the clinician with the diagnosis. Follicular neoplasm, hurthle cell neoplasm, papillary atypical thyroid cancer, lymphoma, and even hyperplastic nodules of goiters had generally been considered (table 1).

Table (1):Fine needle aspirationcytology results

FNAC	No	%
Benign	20	50
Malignant	7	17.5
Indeterminate	13	32.5

Frozen section examination affected intraoperative decision making regarding the extent of thyroidectomy in only 2 patients (5%); one of whom had papillary thyroid cancer (Figure 3') and the other one interpreted as follicular neoplasm (Figure 4'). Definitive diagnosis of the last case as follicular carcinoma was confirmed in permanent pathologic examination on the basis of capsular or vascular invasion.

All the 7 cases, that give malignant picture on FNAC, give malignant result on frozen section. These cases also proved to be malignant by permanent section.

Of the 20 cases that appeared to be benign on FNAC, FS showed 14 benign cases, which proved also to be benign by permanent section. The remaining 6 cases were suspicious. These 6 suspicious (intermediate) results were detected by PS to be benign, except one case was reported to be malignant (table 2).

The last group of FNAC results was suspicious (non diagnostic) cases (13/40) 32.5%. Frozen section revealed 2 malignancies which proved also to be malignant by PS. While FS interpreted as benign in 5 cases. Those proved to be benign but one of these cases was found to be malignant by PS. The remaining 6 suspected cases by FNAC was also classified by FS as suspicious. 4 cases were proved to be benign and the other 2 cases were found to be malignant by PS (table 3).

Statistical analysis was done getting the following results (table 4, 5 and 6).

FNAC	Benign lesions (20 cases)				FNAC	
FS	Benign 14	Malignant 0	Sus	picious 6		
PS	14	0	Benign 5	Malignant 1		

Table (2): Fine needle aspiration cytology (FNAC) benign cases; results of their (FS) and permanent section (PS).

Table (3): Fine needle aspiration cytology (FNAC) suspicious (intermediate) cases; results of their (FS) and permanent section (PS).

FNAC	Suspicious lesions (13 cases)			
FS	Benign 5	Malignant 2	Sus	picious 6
PS	Benign Malignant 4 1	2	Benign 4	Malignant 2

Table (4): FNAC statistics

FNAC	Malignant	Others*	Total
Malignant	7	0	7
Others*	5	28	33
Total	12	28	40

*benign and intermediate results Sensitivity = 58.3%Specificity = 100%Positive predictive value (PVP) = 100%Negative predictive value (PVN) = 84.8%Diagnostic accuracy = 87.5%Kappa = 0.66 (significant)

Table (5): FS statistics

FS	Malignant	Others	Total
Malignant	9	0	9
Others	3	28	31
Total	12	28	40

Sensitivity = 75%Specificity = 100%(PVP) = 100%(PVN) = 90.3%Diagnostic accuracy = 92.5%Kappa = 0.8 (significant)

Table (6): FNAC and FS statistics

FNA	FS	Other	Total
Malignant	7	0	7
Others	2	31	33
Total	9	31	40

Sensitivity = 77.8%. Specificity = 100%

PVP = 100%

PVN = 93.9%

Diagnostic accuracy = 95%

Kappa = 0.84 (significant)

There was a significant agreement between the FNAC and FS.





Figure (1): FNAC of a case of multinodular goiter showing groups of benign follicular cells with uniform appearance in a background of red blood cells (H&E, x 400).



Figure (2): FNAC of a case of Hashimoto's thyroditis showing diffuse infiltrate of small lymphocytes and few benign follicular cells (H&E, x 400)





Figure (3): FNAC of thyroid papillary carcinoma showing clusters of malignant thyroid cells with tendency toward papillae formation surrounded by red blood cells (H&E, x 200)



Figure (3'): Frozen section of the previous case showing numerous papillary structures formed of connective tissue are covered by the malignant cells with ground glass appearance of their nuclei (frozen section x 400)





Figure (4): FNAC of thyroid follicular carcinoma showing small clusters of malignant follicular cells with hyperchromatic nuclei and frequent mitotic figures in a background of red blood cells (H&E, x 200)



Figure (4'): Frozen section of the previous case showing variable sized thyroid follicles lived by malignant cells and filled with small amount of colloid material (frozen section, x 200)



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DISCUSSION

Thyroid nodules are common clinical finding with a prevalence of 4% to 7% of adult population⁽²⁾. Thyroid cancer is the most common endocrine malignancy and accounts for 1% of all cancers⁽⁸⁾.

For single thyroid nodule, FNAC is considered to be the most important diagnostic test, helping selection of appropriate surgery, reducing the number of thyroid operations for benign disease and increasing percentage of operation for malignancy (9).

FNAC contributes significantly to the preoperative investigations in patients with solitary or dominant thyroid nodule ⁽²⁾. Despite its wellrecognized value, there are limitations to the technique used as non diagnostic results usually occur from, limited cellularity (cyst content), absence of follicular cells, or poor fixation and preservation ⁽²⁾. Inadequate (non diagnostic) aspirate results reach 20% ⁽¹⁰⁾ and up to 25% in certain study ⁽¹¹⁾.

Up to 40% of cancer thyroid is often multifocal and easily missed by cytology ⁽¹²⁾. Differentiating benign from malignant lesion preoperatively is not always possible using current cytopathological techniques ^(2,11). This forced many studies to use other methods to help more accurate diagnosis.

The determination of the sensitivity and diagnostic accuracy are affected by how to define and classify suspicious **FNAC** results. The suspicious inclusion of **FNAC** diagnoses with clearly malignant FNAC cases tends to increase the sensitivity of FNAC for detecting thyroid cancer, while decreasing the specificity and overall accuracy of the (11,13,14) test But in this study, suspicious or non diagnostic FNAC results were classified as one group of diagnosis separate from malignant and

benign groups so this increase the specificity and overall accuracy and decrease the sensitivity.

Non diagnostic FNAC results were found to be 13/40 (32.5%), this near to previous studies rates that were between 16% to 54% ^(11,12,13,14,15), but were higher than rates reported by other studies ^(16,17,18,19). This higher non diagnostic cases may be attributed to that no repeating of FNAC or US guided aspiration were performed, also the categorization of suspected and inadequate samples as one intermediate group.

In FNAC the sensitivity was 58,3%, the specificity was 100% and accuracy was 87.5% .. Previous studies showed variable results as sensitivity ranged from 55% to 93% ^(20,21), specificity reported between 73.5% and 100% ^(21,22,23) and accuracy ranged from 76.2% to 97% ^(21,24,25).

So FNAC is a highly specific and accurate method for diagnosis of thyroid nodule but has limitations that lead to non diagnostic cases.

For FS, this study detected sensitivity, specificity and accuracy of 75%, 100% and 92.5% respectively. The value of FS is a matter of great controversy; some reported accuracy as very low as

19 %⁽²⁶⁾, while other reported accuracy very high to 97% ⁽²⁷⁾, 91% ⁽²⁸⁾ and 88.8%⁽²⁹⁾. The same variation found in sensitivity reports, that was reported to be as very low as 25%⁽³⁰⁾ or as very high as 100%⁽²⁸⁾.

The non diagnostic cases by FS in this study were 12/40 (30%) which are near to previous studies (16%-50%) ^(11,16,18,31,32). the low sensitivity in this study was explained by the fact that management of follicular architecture in the first slide of FS or FNAC of suspected cases was delayed to permanent section to evaluate the capsular and vascular invasion⁽³³⁾.



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FS had changed the intraoperative decision making for extension of surgery in 2 of 13 cases (15.5%). Non diagnostic cases by 32.5%. **FNAC** were Also the difference between FNAC and FS results was found to be significant 0.84%). Some (Kappa studies demonstrated that there was no statistically significant difference in the sensitivity, specificity, or accuracy of FS examination and FNAC⁽³⁴⁾. While in other study, only 1% of cases did correctly modify management FS decision⁽¹⁵⁾. While in Boyel et al study, FS aided their surgical decision in over half of the cases (24 of 46, 52%) when FNAC was unable to further identify the lesion $^{(17)}$.

Although FS was proved by some previous studies to be of little benefits with minimal diagnostic value⁽³²⁾, it was said that the increase cost for the operative time and the pathologist needed to obtain routine FS are not supported with any substantial benefit in patients outcome⁽³⁵⁾. But in this study FS was found to have a significant value especially in non diagnostic cases of FNAC. This is in agreement with some previous studies (17,27,28)

CONCLUSION

FNAC remains the gold standard in the initial evaluation of the patients presenting with nodular thyroid diseases because it is quick ,easy, safe and highly accurate and specific but still the rate of non diagnostic cases is high so FS is significantly helpful especially in these cases and may change the decision during surgery.

ACKNOWLEDGEMENT

Thanks for Prof. Dr. Samia SA El-Gohary, Assistant Professor in Community Medicine Department Faculty of Medicine, Zagazig university for her great help in completing the statistical results of this work.

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سحب الأبرة الرفيعة (الدقيقة) الخلوى بالمقارنة بالمقطع المجمد في تشخيص و علاج عقد الغدة الدرقية

المقدمة : عقد الغدة الدرقية هو عارض مرضى شائع بنسبة تتراوح بين ٤ الى ٧ بالمائة من كل الناس واستخدام سحب الأبرة الرفيعة (الدقيقة) الخلوى مفيد لكن لـه الكثير من القيود. أما استخدام المقطع المجمد فهو أمر قيد الأختلاف.

ا**لهدف من البحث :** يهدف البحث الى تقييم دور سحب الأبرة الدقيقة الخلوى و المقطع المجمد في تشخيص و أختيار طريقة العلاج المثلى لعقد الغدة الدرقية الحميدة او السرطانية.

المرضّى و طرق البحث: أجرى البحث علّى أربعين مريضًا (٣ ذكور و٣٧ إنـاث) متوسط عمر هم ٤٢ عاما يعانون من عقد محسوسة بالغدة الدرقية وتم إجراء سحب الإبرة الدقيقة الخلوي قبل العملية و فحص المقطع المجمد أثناء العملية ثم تم التأكد بالعينة النهائية من التشخيص

النتائج : بمراجعة النتائج مع التحليل النهائي للعينة بعد العملية كانت نسبة الحساسية في سحب الأبرة الرفيعة (الدقيقة) الخلوى ٥٨,٣% ومعامل الفعالية ١٠٠% ومعامل الدقة ٥٨٧، أما في المقطع المجمد كانت نسبة الحساسية ٧٥% ومعامل الفعالية ١٠٠% ومعامل الدقة ٩٢,٥%. وكانت هناك فائدة إحصائية لسحب الإبرة الدقيقة الخلوي و المقطع المجمد.

الأستنتاج : خلص البحّث الى أن استخدام سحب الأبرة الدقيقة الخلوى مفيد ودقيق بدرجة كبيرة فى الفحص المبدئى لأمراض الغدة الدرقية وثبت أن المقطع المجمد أثناء الجراحة قد يفيد فى التشخبص وربما يساهم فى اختيار الجراحة الأمثل أثناء العملية وخاصة فى الحالات التى لم يتم تشخيصها تشخيصا دقيقا بسحب الأبرة الدقيقة الخلوى.