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ORIGINAL ARTICLE

The Diagnostic Accuracy of Ultrasound Guided Fine-Needle Aspiration Biopsy and Intraoperative Frozen Section Examination in Nodular Thyroid Disease

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Abstract

Objectives. To determine the diagnostic accuracy of combined ultrasound-guided fine needle aspiration biopsy (USG-FNAB) and intraoperative frozen section examinationin (FSE) in diagnosing malignant thyroid nodules.

Methodology. Retrospective review of patients undergoing thyroidectomy with intraoperative frozen section examination following ultrasound guided fine-needle aspiration biopsy. Sensitivity, specificity, positive and negative predictive values and accuracy were calculated with respect to final histology.

Results. A total of 2,239 nodules were subjected to USG-FNAB at the Diabetes, Thyroid and Endocrine Center, St. Luke's Medical Center between January 2007 and December 2009. Two hundred fifty-one nodules were surgically excised following USG-FNAB. Frozen section examinations were taken from 90 of 251 nodules. The USG-FNAB yielded 90.3% (n=1,721) adequate specimens and 9.7% (n=185) inadequate specimens. The histologic examination of the 251 surgically excised nodules revealed 182 (73%) benign and 69 (27%) malignant nodules. The sensitivity, specificity, positive and negative predictive values and accuracy rate of USG-FNAB cytology are 70.3%, 92.8%, 76.5%, 90.4% and 87.2%, respectively. The diagnosis by frozen section was benign in 56 cases (62%), malignant in 10 cases (11%) and deferred in 24 cases (27%). By FSE, the sensitivity, specificity, positive and negative predictive values and accuracy rate are 83.3%, 100%, 100%, 96.4% and 96.7%, respectively. A diagnostic accuracy of up to 97.2% was achieved when USG-FNAB and FSE were combined and when their findings were concordant. When USG-FNAB and FSE diagnoses were discordant, the FSE showed superior accuracy (83.3%) than cytology (16.7%). In the group of nodules with indeterminate or inadequate cytology, the diagnostic accuracy of frozen section is 100%.

Conclusion. Ultrasound guided fine-needle aspiration biopsy is an accurate preoperative test for the evaluation of nodular thyroid disease. It helps to distinguish malignant from benign lesions. The intraoperative frozen section is a valuable test for confirming the cytologic diagnosis. It is especially important in identifying malignant thyroid nodule in cases with indeterminate cytology. The combination of USG-FNAB and FSE greatly improves the accuracy rate in thyroid cancer detection.

Keywords: fine-needle aspiration biopsy; frozen section; diagnostic accuracy, thyroid nodules; thyroid neoplasm

Introduction

Thyroid nodules are commonly encountered problems in endocrine practice. In the past, its reported prevalence range from 3.2% to 4.2% in the Framingham and Wickham studies. [1] At present, the prevalence of clinically apparent thyroid nodules range from 4% to 7%[2] and it escalated to 49.5% based on autopsy series[1-3] and 10-55% with the use of ultrasonography.[3] The clinical presentation of these lesions may range from small, asymptomatic, solitary nodules to large, symptomatic nodules. Benign thyroid disease is extremely common compared to a small proportion of malignant neoplasms. [3-4] It is, therefore, important to identify this malignant thyroid nodule, which occurs in 4-5% of the thyroid nodules,[4-5] so that immediate surgical intervention can be instituted.

Thyroid cancer is the most common endocrine malignancy and accounts for majority of endocrine related deaths each year. In the Philippines, thyroid cancer is the 9th most common cancer for both sexes and it is the 6th leading cancer site among females and 15th among males.[6] Worldwide, the incidence of thyroid cancer is estimated between 5 and 8 cases per 10,000 inhabitants per year and its incidence increases faster than any other known malignancies having a rate of 3.8% per year.[7]

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Recent consensus guidelines recommend that thyroid nodules greater than 1 cm and subcentimetric nodules with suspicious sonographic features should undergo fine needle aspiration biopsy. [8-9] Ultrasound guided fine-needle aspiration biopsy (FNAB) is a clinical technique used to obtain cells, tissue, and/or fluid through a thin needle for the purpose of diagnosis and management of thyroid masses.[10-11] The procedure is done under sonographic guidance. It is currently the least invasive, most accurate and safe method to identify high-risk or malignant lesion within the thyroid gland. [10-12] The routine use of FNAB has decreased the number of patients treated surgically for benign thyroid nodules while it increased the diagnosis of malignancy in resected nodules. Before the advent of FNAB, intraoperative frozen section (FS) had a definite role in selecting appropriate surgical therapy by accurately differentiating papillary carcinoma from nodular hyperplasia. While FNAB is an effective triage tool in selecting patients requiring surgical intervention, FS is useful in determining the extent of thyroidectomy. Moreover, FS is valuable in reducing the need for completion thyroidectomy in patients with negative or non-diagnostic FNAB cytology whose clinical factors suggest malignant thyroid disease.[13] In our institution, patients are selected for surgery on the basis of three cytologic diagnoses: follicular neoplasm, suspicious for papillary carcinoma and positive for malignancy (papillary carcinoma, medullary thyroid carcinoma and anaplastic carcinoma). Patients positive for papillary carcinoma are subjected to total thyroidectomy while those with diagnosis of follicular neoplasm or suspicious for carcinoma undergo a lobectomy and depending on the frozen section and other intra-operative findings, a completion thyroidectomy is done within the same procedure. The routine use of FS for confirmation or clarification of preoperative FNAB cytology is still debatable and its use is justified when the diagnosis will alter the course of further surgery.

Objectives

The main objective of this study is to determine the diagnostic accuracy of combined ultrasound-guided fine needle aspiration biopsy (USG-FNAB) and intraoperative frozen section examination in (FSE) in diagnosing malignant thyroid nodules. We also aimed to determine the accuracy of USG-FNAB and intraoperative FSE when used alone in detecting nodular thyroid neoplasm, compare which diagnostic test (USG-FNAB versus FSE) detects nodular thyroid malignancy in discordant findings, and determine the accuracy of FSE in detecting nodular thyroid malignancy in indeterminate USG-FNAB cytology.

Materials and Methods

We retrospectively analyzed the medical charts of 1,737 consecutive patients who underwent USG-FNAB at the Diabetes, Thyroid and Endocrine Center, St. Luke's Medical Center. A total of 2,239 nodules were biopsied during the period of January 2007 to December 2009. All patients who underwent biopsy signed an informed consent. All USG-FNAB were performed in the same room, with the same USG equipment (Sonosite Micromaxx) and the same biopsy tray setup. There were no biopsy related complications in our study cohort. Specimens were submitted for analysis at the Institute of Pathology of St. Luke's Medical Center.

Each thyroid nodule is considered a case. Thyroid nodules that underwent USG-FNAB and were removed by thyroidectomy with intraoperative frozen section examination were included in the data analysis. Information on demographic data of the study population, ultrasound findings and the cytologic, FSE and histologic reports were abstracted after a review of patient's medical record and pathology report.

Each USG-FNAB cytology result was retrospectively classified for study purposes into one of the four categories: **benign cytology** is one in which the result indicates a non-malignant condition and includes nodular goiter, thyroiditis, colloid nodule and other benign conditions. **Malignant cytology** is one in which the result indicates the presence of cancer and may include papillary, anaplastic and medullary thyroid carcinoma. **Indeterminate cytology** is one in which specimens show hypercellularity and a pattern suggestive of follicular- or Hurthle-cell neoplasm or atypical features suggestive of, but not diagnostic for, malignancy. **Inadequate specimen** is one in which cytologic diagnosis is not possible due to paucity of thyrocytes.

Each intraoperative FSE result was also retrospectively classified into one of the three categories: **benign FSE** is one in which the pathology result indicate a non-malignant condition. **Malignant FSE** is one in which the pathology report indicated the presence of carcinoma. **Deferred FSE** is one in which follicular neoplasm or "Hurthle cell tumor" was reported. The foregoing diagnosis may either be benign or malignant lesion and histology demonstrating vascular and/or capsular invasion are required to confirm the presence of malignant conditions.

The accuracy of USG-FNAB and FSE was assessed by comparing the initial cytology and pathology reports with the final histopathology report. This comparison was used to calculate the values of the test. Histopathology examination is the gold standard in the diagnosis of thyroid cancer. The histologic result was classified into one of the two categories, namely, **malignant** when histology indicates the presence of cancer (papillary, anaplastic, medullary, follicular thyroid carcinoma) and **benign** when histology indicates a benign condition (follicular adenoma, Hurthle cell adenoma, thyroiditis and other benign findings).

Statistical Analysis

To assess the accuracy of USG-FNAB and intraoperative FSE the following were analyzed: (1) sensitivity (Sen), the proportion of patients with malignant thyroid disease and positive cytologic findings; (2) specificity (Sp), the proportion of patients without malignant thyroid disease and negative cytologic findings; (3) positive predictive value (PPV), proportion of patients with malignant thyroid disease and positive cytologic findings; (4) negative predictive value (NPV), proportion of patients not having malignant thyroid disease and with a negative cytologic finding; (5) false positive rate (FPR), proportion of patients with malignant FNAB or FSE who are found to have benign histology findings; (6) false negative rate, proportion of patients with benign FNAB or FSE who were confirmed to have malignant histology findings; and (7) accuracy rate (AR), proportion of correct results (true positive and true negative) in relation to all cases studied.

Results

Majority of our population consisted of females with a ratio of 7:1 and the median age is 46 yrs old (range 14-88 yrs old). The average number of FNAB was 1.3 per nodule (range 1-3). Among the 2,239 nodules, 1,721 (90.3%) yielded adequate specimens that include benign cytology in 64.4 %(765 with nodular goiter, 662 with colloid goiter, 83 with thyroiditis) and malignant cytology in 3% (65 with papillary thyroid carcinoma and 3 with malignant neoplasm). In the group with inadequate specimen, 64% (n=333) were cystic nodules. The rate of inadequate specimen was 9.7% after excluding cystic nodules.

Accuracy of USG-FNAB in the diagnosis of malignancy

In 2,239 biopsied cases, 251 nodules (11%) were surgically excised. Primary thyroid surgery consisted of either total thyroidectomy, unilateral thyroid lobectomy, isthmusectomy or subtotal thyroidectomy. The final histologic diagnosis was obtained from the paraffin embedded specimens.

Histologic examination of excised nodules showed 182 benign (72%) and 69 malignant (28%) lesions. Table 1 shows the correlation of USG-FNAB with definitive histologic diagnosis.

The FNA cytology indicated a benign diagnosis in 114 cases and was correct in 103 of the cases (90.4%). Among the nodules with benign cytology, 11 were found to have carcinoma on histology giving a 9.6% false negative rate. Five of the false negative cases were papillary microcarcinoma. The preoperative FNA cytology also indicated a malignant diagnosis in 34 cases, however, a malignant histology finding was noted in only 26 of the cases (76.5%). Of these nodules, 8 were found to have a benign lesion on histology resulting in a 23.5% false positive rate. The sensitivity, specificity, positive predictive value and negative predictive value are 70.3%, 92.8%, 76.5%, 90.4%, respectively. The overall accuracy rate of USG-FNAB is 87.2% for diagnosing malignant thyroid nodules.

In 74 cases, an indeterminate diagnosis was made and only 36.5% were correctly diagnosed as malignant nodules on histology. Twenty-two cases of the malignant nodules were papillary thyroid carcinoma, and of these 6 were follicular variant of papillary thyroid carcinoma. FNA cytology was inadequate for diagnosis in 29 nodules and the final histology was benign in 83%. The yield of carcinoma when USG-FNAB is applied preoperatively is 28% and the test identified malignancies in 26 nodules preoperatively (37.7%).

Accuracy of Intraoperative Frozen-Section Examination in the diagnosis of thyroid malignancy

Among the 251 nodules that were excised, 36% had intraoperative frozen section examination (n=90). Histologic examination showed 72 benign lesions (78%) and 18 malignant lesions (22%). Table 2 shows the correlation of FSE with definitive histologic diagnosis.

Among the 56 nodules with a benign diagnosis, the FSE was correct in 96.4% of the cases (n=54). Two nodules were found to have carcinoma on final histology giving a 3.6% false negative rate. In 10 nodules, the FSE and final histopathology both showed malignancy. The sensitivity,

Table 1. Distribution of Cases According to the Results of the Fine Needle Aspiration Biopsy Cytology and Final (Definitive) Histopathology Diagnosis

Fine needle aspiration biopsy	Histology (n= 251)										
	Benign lesion					Malignant lesion					
	NG (n=152)	FA (n=17)	HA (n=5)	LT (n=8)	subtotal	PTC (n=60)	FTC (n=5)	HC (n=3)	MTC (n=1)	subtotal	Total
Benign (n=114)	90	7	1	5	103	9	1	1	0	11	114
Malignant (n= 34)	8	0	0	0	8	25	0	0	1	26	34
Indeterminate (n=74)	32	8	4	3	47	22	3	2	0	27	74
Inadequate (n= 29)	22	2	0	0	24	4	1	0	0	5	29
Totals					182					69	251

NG, nodular goiter; FA, follicular adenoma; Hurthle cell adenoma; LT, lymphocytic thyroiditis; PTC, papillary thyroid carcinoma; FTC, follicular thyroid carcinoma; HC, Hurthle cell carcinoma; MTC, medullary thyroid carcinoma

SENSITIVITY 70.3% SPECIFICITY 92.8% PPV 76.5% NPV 90.4%

Table 2. Distribution of Cases According to the Results of the FSE Cytology and the Final Histopathology Diagnosis

Frozen section examination	Histology (n= 90)										
	Benign lesion					Malignant lesion					
	NG (n=57)	FA (n= 10)	HA (n=3)	LT (n=2)	subtotal	PTC (n=16)	FTC (n=1)	HC (n=1)	MTC (n=0)	subtotal	totals
Benign	51	0	1	2	54	2	0	0	0	2	56
Malignant	0	0	0	0	0	10	0	0	0	10	10
Deferred (n=24)	6	10	2	0	18	4	1	1	0	6	6
totals					72					18	90

NG, nodular goiter; FA, follicular adenoma; Hurthle cell adenoma; LT, lymphocytic thyroiditis; PTC, papillary thyroid carcinoma; FTC, follicular thyroid carcinoma; HC, Hurthle cell carcinoma; MTC, medullary thyroid carcinoma

SENSITIVITY 83.3% SPECIFICITY 100% PPV 100% NPV 96.4%

specificity, positive and negative predictive values and accuracy rate of FSE in diagnosing malignant thyroid nodules are 83.3%, 100%, 100%, 96.4% and 96.7%, respectively. In 24 cases, a deferred intraoperative FSE diagnosis was made and the definitive histology was benign in 75% of the nodules (n=18). The yield of carcinoma when FSE is applied intraoperatively is 22% and the test identified malignancies in 100% of the cases.

Accuracy of combined USG-FNAB and FSE in the diagnosis of thyroid malignancy

The correlation of combined USG-FNAB and FSE with final histology is shown in Table 3. The accuracy of combined USG-FNAB and FSE is shown in Table 4.

In the group with concordant USG-FNAB and intraoperative FSE findings (B/B and M/M), there were 5 nodules diagnosed as malignant by FNAB/FSE and in the final histology. Twenty-nine nodules initially diagnosed as benign by FNAB/FSE, had the same final histology. One nodule diagnosed as benign on FNAB/FSE was malignant on histology causing a 5% false negative rate. There was no false positive in the result. The sensitivity, specificity and accuracy rate in diagnosing thyroid malignancy are 83.3%, 100% and 97.1%.

In the group with discordant USG-FNAB and intraoperative FSE findings (B/M, M/B), there were 3 nodules with benign preoperative cytology were diagnosed as malignant on FSE and histology. Two nodules with malignant preoperative cytology were diagnosed as benign on FSE and histology. When the USG-FNAB and FSE were discordant, diagnostic accuracy of FSE was significantly better than the USG-FNAB: 83.3% versus 16.7%, respectively.

Diagnostic accuracy of FSE in diagnosing thyroid malignancy in FNAB with Indeterminate and Inadequate cytology

In the group of nodules with indeterminate and inadequate preoperative cytology but with diagnostic FSE result (InD/B, InD/M,InAd/B, InAd/M), the sensitivity, specificity and diagnostic accuracy of FSE diagnosing thyroid malignancy are 100%. Of the 39 nodules with indeterminate cytology, there were 20 benign nodules (51%) and 2 malignant nodules (5%) on histology that were correctly diagnosed by FSE. Among the nodules labeled as inadequate cytologic specimen, 90% (9 out of 10) were benign on FSE and final histology.

Discussion

Since the introduction of FNAB of thyroid nodules, there has been a reduction in the number of patients undergoing surgery for benign thyroid nodules and an increase in the prevalence of malignancy in pathologic thyroid specimens. While FNAB is useful as a diagnostic tool in selecting patients for thyroidectomy, the application of intraoperative frozen section has been a useful guide to formulate the optimal surgical plan. We have presented the results of an in-depth analysis of the utility of ultrasound guided fine-needle aspiration biopsy and frozen section examination in the management of nodular thyroid disease at St. Luke's Medical Center.

We evaluated the adequacy of our USG-FNAB in a large series of 2,239 consecutive cases and compared the results of USG-FNAB and FSE with the post-operative findings in thyroidectomy cases. In our study, the adequacy rate of USG-FNAB is 90.3%. Worldwide, the adequacy rate of FNAB ranges from 70-100% and our result is comparable to published studies.[14-22] The rate of malignant, indeterminate and benign cytodiagnosis are 3.3%, 11% and 76%. In most institutions, the range of malignant, indeterminate and benign cytodiagnosis are 5-38%, 11-42% and 22-65%, respectively.[13-22] The rate of inadequate FNAB specimen after excluding cystic thyroid nodules is 9.7% comparing to 5-29%[14-22] from the previous series. The inadequacy rate in our series may be due to the significant number of aspirated complex thyroid nodules wherein there is usually a paucity of thyrocyte numbers in the biopsied sample.

Table 3. Accuracy of Ultrasound Guided-Fine Needle Aspiration Biopsy and Frozen Section Examination Compared with Final Histology Diagnoses.

UTZ GUIDED FINE NEEDLE ASPIRATION DIAGNOSIS / FROZEN SECTION DIAGNOSIS	FINAL HISTOLOGIC DIAGNOSIS	
	BENIGN	MALIGNANT
B / B	29	1
B /M	0	3
M / B	2	1
M / M	0	5
IND / B	20	0
IND / M	0	2
IND / DEF	12	5
INAD/B	9	0
INAD / M	0	1
INAD / DEF	0	0
TOTALS	72	18

B, benign; M, malignant; InD, indeterminate; Def, deferred; InAd, inadequate

Table 4. Accuracy of Combined USG-FNAB and FSE in the Diagnoses of Nodular Thyroid Malignancy. –

Index	Concordant findings (combined FNAB and FSE) N=35	USG-FNAB findings discordant with FSE N=6	FSE findings discordant with USG-FNAB N=6
% Sensitivity	83.3	25	75
% Specificity	100	0	66.7
% PPV	100	33.3	100
% NPV	96.7	0	66.7
Accuracy rate	97.1	16.7	83.3

FNAB, fine-needle aspiration biopsy; FSE, frozen section examination; PPV, positive predictive value; NPV, negative predictive value

The reported sensitivity of FNAB ranges from 54-97% and specificity ranges from 74-98%.[16-25] In this study, the sensitivity for cytologic diagnosis of thyroid malignancy is 70.3%, specificity of 92.8%, positive predictive value of 76.5% and negative predictive value of 90.4%. The sensitivity of our result may be affected by how we chose to define and classify indeterminate FNAB results. Accordingly, the exclusion of indeterminate FNAB diagnoses from the malignant FNAB cases tends to decrease the sensitivity of FNAB for detecting thyroid carcinoma, while increasing its specificity. In our study, indeterminate FNAB diagnoses were separated from the clearly malignant and benign FNAB diagnoses since we intended to calculate the diagnostic accuracy of the USG-FNAB and not to determine its influence on clinical management. Our result translates into a diagnostic accuracy of 87.2% and our data suggest that USG-FNAB is slightly more specific rather than sensitive in detecting thyroid malignancy. Thus, we confirm USG-FNAB a reliable diagnostic test. The reported accuracy rate of FNAB worldwide ranges from 60-98%[14,15,17,18,20-22, 24-25] and our accuracy rate is higher comparing to 67% and 70% accuracy rate reported by Morgan and colleagues of Australia[18] and Leenhardt and colleagues of France,[20] respectively. The false negative rate of our study is 9.6% and this value is in agreement with other studies reporting a false negative rate of 3.6-46%.[16-25] Review of our cases showed that 5 of the 11 false negative cases were papillary microcarcinoma and these lesions may have been missed during the aspiration. Two cases, follicular and Hurthle cell carcinoma diagnosed as nodular and colloid goiter on preoperative cytology, may have resulted from failure to interpret the cytologic specimen. This is due to the fact that FNA is ineffective in recognizing vascular invasion, an obligatory diagnostic criteria for these lesions. Our findings suggest that a negative FNAB should not be used as an assurance of the absence of malignancy. Clinical factors suggestive of malignancy should always be considered in any case. There are several studies delineating the risk factors of malignancy in thyroid nodule and this include history of radiation, local symptoms like recurrent nerve compression or dysphagia, evidence of metastatic disease, tumor size and several sonographic characteristics. These factors may be identified preoperatively, providing an indication for operation. The present study did not specifically analyze these factors.

Indeterminate cytology and inadequate specimen are the two major limitations of FNAB. The indeterminate cytology had been considered the "gray zone" in thyroid FNAB cytology and surgical intervention is generally recommended for these lesions.[26] The rate of malignancy in patients with indeterminate FNAB cytology is reported to be 16-54%.[14,28] Based on the present study, the chance of thyroid malignancy being discovered on histology in indeterminate cytology is 36.5% (27 out of 74 cases) in which 22 (81%) cases were papillary thyroid carcinoma. It is therefore an option to do additional histologic examination like frozen section to confirm the cytology finding and to help the decision making as to the extent of the procedure during thyroidectomy. The accurate diagnosis of malignancy intraoperatively will avoid the need for a completion thyroidectomy in many of these patients.

Frozen section examination has been used by many surgeons to clarify the diagnosis of fine needle aspiration biopsy. The significance of the routine use of this test is still controversial. Some studies suggest the intraoperative FSE of thyroid nodules is not useful and should not be performed routinely.[27,] According to the Johns Hopkins Thyroid Tumor Center[28] and Memorial Sloan-Kettering Cancer Center, [33] the routine use of FS is not warranted because it adds little to the intraoperative decision making. In the contrary, some researchers suggest that FSE is useful to verify FNAB results and that FSE can be expected to influence the choice of surgery in indeterminate FNAB cytology.[26,29,30] This is supported by the Mayo Clinic group which indicated that intraoperative frozen section analysis play an integral role in the management of surgical thyroid patients.[31]

In our series, when frozen section examination was used intraoperatively to determine malignant thyroid nodules, the 83.3% sensitivity, 100% specificity, 100% positive predictive value and 96.4% negative predictive value of our study are comparable with the range reported in other series: sensitivity 19-96%,[13,17,24,30,34-36] specificity 96.5-100%, [13,17,24,30,34-36] positive predictive value 97-100%, [13,17,30,34-36] negative predictive value 81.3-98%. [13,17,30,34-36] This means that intraoperative FSE had a diagnostic accuracy rate of 96.7%, which is higher than FNAB alone. Based on this, we are 100% confident that a benign FSE will have a benign histology. The result also suggests that a malignant FSE finding is useful, despite a benign preoperative cytology, in influencing the intraoperative planning of the extent of surgery. The false negative rate of FSE is 3.6% and this is contributed by occult carcinomas that were missed during the frozen section.

Several series also reported an improved sensitivity and specificity for detection of malignancy when FNAB and FSE are combined and thus recommend both to be used routinely.[17,29-32] When applied to these groups in the present series, the combined test showed an accuracy rate of 97.1% in a concordant FNAB and FSE findings and the result significantly improved the rate of detection of malignancy in nodular thyroid lesions over USG-FNAB alone. Hence, intraoperative FSE complements preoperative FNAB cytology. Although the accuracy rate has improved, the concordant benign cytology and FSE were associated with a 5% false negative rate. The false negative in this series may be contributed by the papillary microcarcinomas which were missed during fine needle aspiration and frozen section.

In the case of discordant USG-FNAB and FSE findings, our result indicate that the frozen section diagnosis is superior than the USG-FNAB, having accuracy rate of 83.3% compared to 16.7%. A similar result reported by Chang et.al.[17] noting that FSE diagnosis is significantly better than FNAB in discordant cases (78.9% vs 21.1%). For that reason, our result suggests that FSE may eliminate FNAB when the findings of both tests are discordant. We identified 3 false negative cases on FNAB that were correctly identified as malignant lesions on FSE. In this case, the reliance on FNAB cytology to determine the extent of surgery would lead to a significant number of completion thyroidectomy. Hence, it is favorable to perform total thyroidectomy when FSE diagnosis is malignant in benign FNA cytology. Another diagnostic dilemma occurs when a malignant FNA cytology meets a benign frozen section diagnosis. In this discordant situation, we identified two false positive cases on cytology that were correctly diagnosed as benign on FSE. In such cases, it is preferable to perform limited surgery following a benign FSE in the face of a malignant cytodiagnosis.

In the case of indeterminate cytology and unsatisfactory FNA result, some studies recommend performing FSE to clarify the preoperative cytology findings. [14, 29] Applying these to the present study, the accuracy (sensitivity, specificity and accuracy rate) of FSE in diagnosing malignant thyroid nodules in cases of indeterminate cytology and FNAB with inadequate specimen is 100%. Our result is better than the 67% sensitivity, 100% specificity and 89% accuracy rate reported by Mandell et.al.[14] Based on our result, we are 100% confident that a malignant FSE will result into a malignant histology in a nodule with indeterminate cytology. This high accuracy rate proved that FSE is a powerful test for intraoperative decision making concerning the extent of thyroidectomy in indeterminate cytologic findings.

The yield of carcinoma for USG-FNAB as diagnostic tool is 28% and that of FSE is 22%. This signifies that both tests increase the yield of malignancy in excised thyroid nodules. The USG-FNAB identified carcinoma in 37.7% (26 out of 34) preoperatively whereas FSE identified 100% of malignancies. This discrepancy is mainly due to the number of indeterminate diagnosis by FNAB cytology which accounted for 29.5% in our series. The diagnosis of follicular carcinoma is defined by vascular or capsular invasion and it is impossible to evaluate these criteria by cytology. These findings suggest that FSE is superior to FNAB in detecting malignant nodular thyroid lesion.

Conclusion

Ultrasound guided FNAB is an accurate preoperative test for the evaluation of nodular thyroid disease. It helps to distinguish malignant from benign lesions for the purpose of selecting patients that need surgical treatment. The intraoperative frozen section is a valuable test for confirming the cytologic diagnosis. It is especially important in identifying malignant thyroid nodule in cases with indeterminate cytology. The combination of USG-FNAB and FSE greatly improves the accuracy rate in thyroid cancer detection.

Our result translates into the following recommendations: (1) USG-FNAB should be the initial diagnostic test to determine malignant nodular thyroid lesions, (2) USG-FNAB should be the triage tool in selecting patients that will undergo thyroidectomy, (3) intraoperative frozen section examination may be use to confirm a malignant or benign FNAB cytology and (3) frozen section examination should be use routinely in cases of indeterminate cytology. The use of FSE in these cases will help the surgeon in decision making during surgery.

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