

Evaluating the accuracy of fine needle aspiration and frozen section based on permanent histology in patients with follicular lesions

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Abstract

Background: Fine needle aspiration (FNA) has led to a decrease in unnecessary surgeries for thyroid nodules. This study was designed to compare diagnostic value of FNA and frozen section methods in the follicular lesions.

Methods: This is a cross-sectional study based on the medical records of 42 patients who were referred to surgery clinic of Rasool-e-Akram hospital in Tehran with complaint of thyroid nodules. All FNAs were diagnosed as follicular lesions in pathologic evaluation. All the patients underwent thyroid surgery and their frozen section results were also assessed. Finally, diagnostic value of the two tests was compared based on final permanent histologic report.

Results: Forty two patients with follicular thyroid nodules diagnosed with FNA were included. During the operation, using frozen sections, diagnosis of papillary carcinoma, non-papillary malignancies, benign lesion and intermediate cytology was made in 13 (31%), 3 (7%), 25 (59.5%), 1 (2.5%) patients, respectively. Results of permanent histology showed that follicular adenoma is the most prevalent lesion which appeared in 25 (59.5%) cases. Papillary and follicular carcinomas were detected in 10 (23.8%) and 4 (9.5%) cases, respectively.

Conclusion: Results of the study demonstrate a 73% reduction in second surgery in patients with follicular thyroid lesions based on intraoperative frozen section results.

Keywords: Thyroid nodule, Follicular lesion, Frozen section, FNA.

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Introduction

Thyroid nodules are relatively widespread involving 4-7% of general population (1-3). These nodules are more common in female gender and their prevalence increases with aging, history of radiotherapy and also goiterogenic regimen intake (3). The majority of the nodules consist of benign ones. However, it is impossible to distinguish them from malignant nodules in clinical

settings.

Many diagnostic tests such as radionuclide scan, high resolution ultrasound and also biopsy by FNA (fine-needle aspiration) have been introduced for patients in need for surgical interventions. Previous studies have demonstrated that FNA biopsy is an exact, cheap and also the simplest diagnostic test for rapid definition of thyroid nodules (4-6).

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It has been even shown that FNA is associated with higher sensitivity and specificity than frozen section method (7-9). As a result, FNA is making the surgical decision making easier leading to a decrease in unnecessary surgeries for thyroid nodules as well as significant benefits in searching for malignancies of the gland (4, 5, 10).

Due to cheapness, easiness, accessibility and absence of significant adverse effects, use of FNA is increasing resulting in early detection of malignancies in early stages. However the procedure is also associated with some imperfections besides its gains. The defects mostly relates to lack of sample competence, sampling techniques, the pathologist's expertise and the overlap in cellular characteristics for benignity or malignancy (11-13).

Based on some studies, accuracy and sensitivity of this method in determination of thyroid nodules situation has been questioned. Having that in mind, we designed this study to assess the patients which were reported as follicular lesions in their pre-operative FNA and their frozen section evaluation were of other pathologic diagnosis. The conclusions of the study not only can be a basis for future studies, but also may be used in decision making for therapeutic strategies.

Methods

In this cross-sectional study, records of adult (above 18 years old) patients with thyroid nodule referred to surgery or internal medicine clinics of Rasoul-e-Akram hospital were reviewed, from year 2013 to 2014. Patients' data including age, gender, duration of nodule appearance, family history of the condition and the primary FNA results were gathered. For patients underwent thyroid surgery, frozen section and permanent pathologic results were recorded too. Among the cases, the prevalence of follicular adenoma, papillary and follicular carcinoma, Hurtle cell adenoma and carcinoma in frozen sections and permanent pathology were obtained. Final pathologic findings were compared with frozen sec-

tions. The descriptive statistics such as mean \pm SD and frequencies were reported.

Results

In this study, 42 patients with thyroid nodule were included whose FNA results were reported as a follicular lesion. Frozen section was performed for all patients intraoperatively. Mean \pm SD age of patients was 39.3 \pm 16.51 years (range: 9-80 years). About 67% (n= 28) and 32% (n= 14) of patients were male and female, respectively. Location of the lesions in the gland in 20(47.6%) cases was in the right side; however left-sided (35.7%) and bilateral (16.7%) lesions were also observed.

Diagnosis of papillary carcinoma was made for 13 (31%) patients in frozen section. The procedure also defined 25 (59.5%) cases as benign, 3 cases as non-papillary malignancies.

Results of permanent histology showed that follicular adenoma is the most prevalent lesion which appeared in 25 (59.5%) cases with follicular lesions. After that, papillary and follicular carcinoma were seen in 10 (23.8%) and 4 (9.5%) cases, respectively. Hurtle cell pathologies were the least common findings, including adenoma (4.8%) and carcinoma (2.4%).

Discussion

Despite constituting only 1% of human malignancies, thyroidal cancer is the most common endocrine malignancy. The condition is also responsible for the highest mortality in endocrine cancers (14). The incidence increases with aging. As a matter of fact, the peak incidence of papillary, follicular and medullary types is in fourth and fifth decades of life and also in seventh and eighths for anaplastic carcinoma (15). The exact etiology has not been recognized yet (16). Papillary carcinoma is the most common type of thyroid cancer which typically involves individuals with age between 30 to 40; women are more involved than men (17). It shows a strong lymphotropic nature having a great tendency to metastasize to lymph nodes and progressing to a multifo-

cal pattern in thyroid gland. The prognosis is excellent with appropriate treatment extending 10 year survival up to 90% (18, 39, 40). The present study was designed to compare frequency of papillary cancers in patients with thyroid nodules that were initially detected as follicular lesions by FNA. Forty two patients with thyroid nodules in which FNA showed follicular lesions participated. Mean age of patients was 39.33 and women were twice as men.

In a study conducted by Herrera et al, clinical presentations and prognostic factors were assessed in 229 Mexican patients with PTC (papillary thyroid carcinoma). The mean age was 42 ± 16 that is very close to the result of our study. In addition, proportion of women to men was 205 to 24 which is greater than the relation in our patients (18).

In our study based on final histology results, 15 out of 42 patients needed repeated surgery for total thyroidectomy among which 11 patients underwent the surgery based on their frozen section performed during the first surgery. In fact in 73.3% of patients, repeated surgery was avoided. Based on the results of frozen section, in 5 patients whom underwent total thyroidectomy, final pathology did not confirm existence of malignancy. Regarding diagnosis of PTC in patients with follicular lesions reported in frozen sections, 13 cases were diagnosed as papillary carcinoma. However, 5 cases were reported as benign lesions eventually.

According to our data, diagnostic sensitivity of frozen section for detecting papillary carcinoma was 84.4% with a specificity of 80%. Positive and negative predictive values were 61.5% and 93%, respectively. We can conclude that negative reports reported by frozen section for papillary diagnosis is valuable and lobectomy can be performed with certainty based on negative results.

Callcut et al, in 2004 assessed 102 patients undergoing surgical resection due to follicular neoplasm. Mean age was 47 years and 76% of cases were female. Mean age in

our study was lower but higher frequency of female patients was a common point. In mentioned study, 41 (32%) patients had benign lesions as reported by frozen section. 5 (4%) and 3 (2%) also were reported as malignant and intermediate. All patients with malignant frozen section result, had malignancy in their final pathologic report. In the study, sensitivity, specificity, positive and negative predictive values were 67%, 100%, 100% and 96%, respectively.

In another study published by Chen et al, 125 patients with the follicular lesions undergoing exploratory surgery were included. In 104 patients frozen section was performed. Frozen section changed type of surgery only in 4 cases. Besides, wrong results of frozen section were observed by histology in 6 patients (22). In our study, frozen section changed the type of surgery in 16 (38%) cases. According to the, a second surgery was avoided in 11 out of 15 cases (73.3%).

In a study by Udelsman et al, evaluation of frozen section results in patients with follicular lesions, among 61 patients who had surgery, frozen section was obtained for 29 ones. In the group without frozen section, one patient had undergone the method due to the nodule's appearance which turned out to be follicular carcinoma. Malignancy was reported in 1 (3.4%) patient's frozen section for which total thyroidectomy was performed. Histology reported well-differentiated thyroid cancer in 6 (21%) patients in frozen section group and 3 (10%) patients in non-frozen section group. In our study, diagnostic accuracy of frozen section was lower than Udelsman's study.

In another study performed in 2009 regarding FNA cytology and frozen section results in patients with follicular lesions, 210 patients with thyroid nodule and also follicular thyroid neoplasm's that frozen section was obtained for them at the time surgery were included. Mean age was 43 years (from 18 to 76 years) and 77.6% of participants were female. For all patients, sonography-guided FNA was performed.

Final histology reported follicular carcinoma in 23 (10.95) cases. Follicular adenoma and hyperplasia were observed in 181 (86.2%) and 6 (2.9%) cases. In the present study follicular adenoma was the most repeated diagnosis too (60%). Sensitivity, specificity, positive and negative predictive values and accuracy of FNA was 13%, 97.3%, 37.5%, 90% and 88.1%, respectively. These were 17.4%, 100%, 100%, 90.8% and 91% for frozen section respectively (23).

Conclusion

Results of the study demonstrated a 73% reduction in second surgery in patients with follicular thyroid lesions. This percentage is differed in different studies and is mostly affected by pathologists and case selection criteria. Due to the reduction in reoperation and consequently, adverse effects and costs, obtaining a frozen section at the time of surgery in patients with follicular thyroid lesions is recommended.

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Conflict of interests

The authors declare that they have no competing interests.

References

1. Khoo ML, Asa SL, Witterick IJ, Freeman JL. Thyroid calcification and its association with thyroid carcinoma. *Head Neck* 2002; 24:651–655.
2. Kim EK, Park CS, Chung WY, Oh KK, Kim DI, Lee JT, et al. New sonographic criteria for recommending fine-needle aspiration biopsy of nonpalpable solid nodules of the thyroid. *AJR Am J Roentgenol* 2002;178:687–691.
3. Papini E, Guglielmi R, Bianchini A, Crescenzi A, Taccogna S, Nardi F, et al. Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color Doppler features. *J Clin Endocrinol Metab* 2002;87:1941–1946.
4. Peccin S, de Castro JA, Furlanetto TW, Furtao AP, Brasil BA, Czepielewski MA. Ultrasonography: is it useful in the diagnosis of cancer in thyroid nodules? *J Endocrinol Invest* 2002;25:39–43.
5. Gupta A, Ly S, Castroneves LA, Frates MC, Benson CB, Feldman HA, et al. A Standardized Assessment of Thyroid Nodules in Children Confirms Higher Cancer Prevalence Than in Adults. *The Journal of Clinical Endocrinology and Metabolism* 2013;98(8):3238–3245. doi:10.1210/jc.2013-1796.
6. Frates MC, Benson CB, Doubilet PM, Cibas ES, Marqusee E. Can color Doppler sonography aid in the prediction of malignancy of thyroid nodules? *J Ultrasound Med* 2003;22:127–131.
7. Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. *Ann Intern Med* 1993;118:282–289.
8. Hamberger B, Gharib H, Melton LJ, Goellner JR, Zinsmeister AR. Fine-needle aspiration biopsy of thyroid nodules: impact on thyroid practice and cost of care. *Am J Med* 1982;73:381–384
9. Mittendorf EA, Tamarkin SW, McHenry CR. The results of ultrasound guided fineneedle aspiration biopsy for evaluation of nodular thyroid disease. *Surgery* 2002;132:648–654.
10. Danese D, Sciacchitano S, Farsetti A, Andreoli M, Pontecorvi A. Diagnostic accuracy of conventional versus sonographyguided fine-needle aspiration biopsy of thyroid nodules. *Thyroid* 1998;8:15–21.
11. Hegedus L. The thyroid nodule. *N Engl J Med* 2004;351:1764–1771
12. Chan BK, Desser TS, McDougall IR, Weigel RJ, Jeffrey RB. Common and uncommon sonographic features of papillary thyroid carcinoma. *J Ultrasound Med* 2003;22:1083–1090.
13. Wienke JR, Chong WK, Fielding JR, Zou KH, Mittelstaedt CA. Sonographic features of benign thyroid nodules: interobserver reliability and overlap with malignancy. *J Ultrasound Med* 2003;22:1027–1031.
14. Lal G, D'Orosio T, McDougall R, Wiegel RJ. Cancer of the endocrine system. In: Abelloff MD, Armitage JO, Niederhuber JE, Kastan MB, McKenna WG, eds. *Abelloff's Clinical Oncology*. 4th ed. Philadelphia, Pa: Elsevier; 2008: 1271–1305.
15. National Cancer Institute. Physician Data Query (PDQ). Thyroid Cancer Treatment. 2012. Accessed at www.cancer.gov/cancertopics/pdq/treatment/thyroid/healthprofessional on August 16, 2012.
16. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Thyroid Carcinoma. V.3.2012. Accessed at
17. Sherman SI, Wirth LJ, Droz JP, Hofmann M, Bastholt L, Martins RG, et al. Motesanib diphosphate in progressive differentiated thyroid cancer. *N Engl J Med* 2008;359:31–42.
18. Udelsman R, Westra WH, Donovan PI, Sohn TA, Cameron JL. Randomized prospective evaluation of frozen-section analysis for follicular neo-

plasms of the thyroid. *Ann Surg* 2001 May; 233(5):716-22.

19. Vaisman A, Orlov S, Yip J, Hu C, Lim T, Dowar M, et al. Application of post-surgical stimulated thyroglobulin for radioiodine remnant ablation selection in low-risk papillary thyroid carcinoma. *Head Neck* 2010; 32:689-698.

20. American Cancer Society. *Cancer Facts & Figures 2012*. Atlanta, Ga: American Cancer Society; 2012.

21. Callcut RA, Selvaggi SM, Mack E, Ozgul O, Warner T, Chen H. The utility of frozen section

evaluation for follicular thyroid lesions. *Ann Surg Oncol*. 2004 Jan;11(1):94-8.

22. Faquin WC. Diagnosis and Reporting of Follicular-Patterned Thyroid Lesions by Fine Needle Aspiration. *Head Neck Pathol* Mar 2009; 3(1): 82-85.

23. Lumachi F, Borsato S, Tregnaghi A, Marino F, Polistina F, Basso SM, et al. FNA cytology and frozen section examination in patients with follicular lesions of the thyroid gland. *Anticancer Res* 2009 Dec;29(12):5255-7.