Journal of BUON **16:** 174-179, 2011

ORIGINAL ARTICLE

Real-time ultrasound-guided fine needle cytology of the thyroid gland by capillary action. A modified technique without aspiration

M.G. Gkeli[1], D. Daskalopoulou[2]

[1]*Department of Radiology, Unit of Sonography;* [2]*Department of Cytology, "Saint Savvas" Anticancer Hospital of Athens, Athens, Greece*

Summary

Purpose: *To present a modified technique of real-time (Rt) ultrasound-guided (Ug) fine-needle (FN) cytology of thyroid nodules without aspiration (RtUg-FNNAC).*

Methods: *We retrospectively studied 958 patients with 1202 thyroid nodules referred to our institution between January 2009-January 2010. The efficacy of RtUg-FNNAC was determined by the number of satisfactory specimens that were obtained. Furthermore, we compared the RtUg-FNNAC results with the surgical histological results.*

Results: *All specimens were adequate for diagnosis. Two hundred and twelve (22.1%) patients with malignant cytological findings and 20 (2.1%) with indeterminate cytological findings were referred for surgery. All nodules with malignant and indeterminate cytological findings were confirmed histologically. From 20 indeterminate cytological findings 17 (85%) were malignant. From 66 patients with initial benign RtUg-FNNAC who were subjected to surgery the results were true negative in 65 and false negative in 1. Finally, RtUg-FNNAC was true positive in 229 cases and false positive in 3. The overall sensitivity, specificity, positive predictive value and negative predictive value of RtUg-FNNAC were 99.6, 95.6, 98.7 and 98.7%, respectively. Accuracy for the detection of malignancy was 98.7%.*

Conclusion: *RtUg-FNNAC is a technique that combines the benefits of real time US-guidance with those of capillary action sampling, maximizing cellular yield and minimizing bloody artefacts in cytologic examination.*

Key words: capillary action, non-aspiration fine needle cytology, thyroid cancer, thyroid nodules, ultrasound guidance

Introduction

Fine needle cytology (FNC) of thyroid nodules may be performed either by palpation or by ultrasound (US) guidance (Ug). US has several advantages over palpation. Ug-FNC of the thyroid is a simple and cost-effective technique that allows a definite cytological diagnosis in patients with benign or malignant nodules, even when they are small and nonpalpable [1]. FNC (palpation-guided or Ug) can be performed with or without aspiration. In the non aspiration cytology the needle is used with no syringe attached. The needle is passed back and forth through the lesion several times without applying suction which is replaced by the principle of capillary suction of fluid or semifluid material into the thin channel of a fine needle (capillary action). The needle is withdrawn when a small amount of material fills its hub and the content of the needle is sprayed onto a slide [2]. Advocates for the non aspiration technique believe that grasping the needle hub directly improves operator sensitivity in placing the needle tip within a small lesion and that less bleeding occurs, which is an advantage in the biopsy of a richly vascular tissue such as the thyroid gland [2-4].

The purpose of this article was to present a modified technique for Ug-FNC of thyroid nodules without aspiration under real time US monitoring (RtUg-FNNAC).

Methods

Patients

A total number of 1202 RtUg-FNNAC specimens of the thyroid gland from 958 outpatients was retro-

Correspondence to: Dr. Myrsini G. Gkeli. "Saint Savvas" Anticancer Hospital, 171 Alexandras Ave, 115 22 Athens, Greece.
Tel: +30 210 6409417, Fax: +30 210 6420146, E-mail: myrgel@gmail.com

Received 30-08-2010; Accepted 17-11-2010

spectively analyzed. The samples were obtained between January 2009-January 2010.

All patients with preoperative malignant or indeterminate cytological findings were referred for surgery, and their surgical histologic results were compared with preoperative RtUg-FNNAC.

Another group of 66 patients with benign RtUg-FNNAC cytological findings underwent surgery, and their surgical histologic results were also compared with preoperative RtUg-FNNAC.

RtUg-FNNAC procedure

Patients were placed in a supine position with the neck slightly extended and superimposed on a pillow. The procedure was performed with a freehand modified technique without aspiration and without a guide system or an attached syringe [5] under real time US monitoring by an expert radiologist.

The transducer was used with a sterile cover placed over its head. Before RtUg-FNNAC, the skin was sterilized with chlorhexidine gluconate, a noniodine containing biguanide [6]. Instead of US gel, a local anaesthetic (lidocaine/prilocaine) gel was used, serving as a primary coupling agent [7]. A plane perpendicular to the ultrasonographic probe was chosen for needle insertion, because there is virtually no chance of the needle puncturing the carotid artery or jugular vein [8,9]. Patients were instructed not to swallow or speak during the insertion of the needle. The procedure was performed using a conventional 23-gauge needle [10]. The preferred number of needle passes was one with a maximum of two punctures/nodule.

When the needle reached the target, sampling was made by using the "modified sampling technique without aspiration" (Figure 1). This nonaspirate technique relies on capillary action to draw the sheared cells within the small-caliber needle [2-4,11]. The technique is performed as follows: after the needle has entered into the nodule, it is moved gently in various positions and directions, using a forward and backward movement without aspiration, under real-time US monitoring, for a few seconds only, by movement of the operator's wrist. During the procedure, all needle movements are continuously visualized in real time. When a small amount of material fills the hub of the needle, it is withdrawn and the puncture site is compressed for several minutes.

When the procedure was concluded, US examination of the thyroid and the neck was obtained for the presence of possible complications, most frequently a small hematoma [5,12].

A post-procedure follow up period of at least 30 min was considered to observe progressive swelling and ecchymosis [13]. Restrictions on activity were given individually, depending on each patient's condition.

Figure 1. RtUg-FNNAC. The puncture is performed with a conventional 23-gauge needle without an attached syringe. A freehand non aspiration technique is used, and the needle is placed just above the transducer.

Criteria for cytological diagnosis

A representative slide was stained and assessed for adequacy by the cytopathologist on site [14]. Slides were prepared with Quik-Giemsa stain. If there was adequate material for interpretation, the biopsy was concluded. If the material was inadequate, an additional puncture was performed and then it was rechecked for adequacy by the cytopathologist [10].

The nodules were classified as benign (abundant colloid and typical follicular cells), malignant (atypical follicular cells with malignant nuclear features), indeterminate (follicular and Hürthle cell neoplasms as well as specimens considered suspicious for malignancy), or nondiagnostic (fewer than 6 clusters of follicular cells visualized on at least two smears) (Figure 2). Interpretation of the slides was performed by an experienced cytopathologist.

Results

Patient characteristics

Of the 958 outpatients evaluated with RtUg-FNNAC, 144 were males and 814 females, aged 15 to 85 years. In total, 1202 thyroid nodules underwent RtUg-FNNAC. The nodules' diameter ranged from 0.5 to

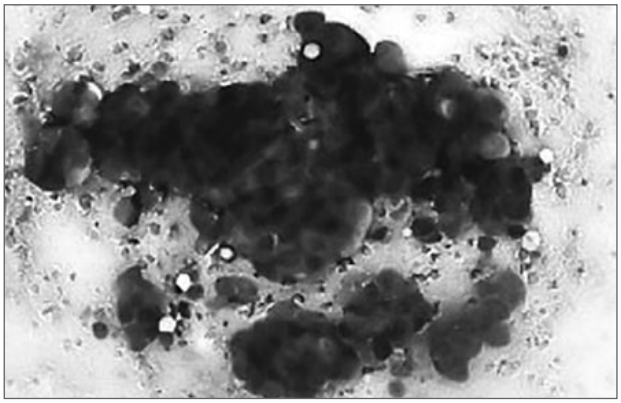

Figure 2. Classic cytological pattern of papillary carcinoma.

4.3 cm (average 1.7±1.1), 85 were <1 cm and 245 >2 cm. They were located at both lobes with the same frequency, 76 nodules at the isthmus and 10 substernally and adjacent to large vessels. Fifty-five percent of the nodules were located deep within the thyroid and the rest were superficial. Eighty-nine percent of the patients were euthyroid at the time of the procedure. The average number of passes for each nodule was 1.5±0.5 (range 1-2). There were a few complications such as pain and small hematomas in 3 patients treated with direct pressure and cold ice packs on the biopsy site. There were no major complications.

Cytological analysis

The efficacy of RtUg-FNNAC was demonstrated by the fact that all specimens were adequate for diagnosis. In 1202 nodules of the 958 patients, there was an adequate number of cells for cytological diagnosis, yielding a diagnostic rate of 100%. The cytologic results were 212 malignant nodules, 20 nodules with indeterminate findings and 970 benign nodules (nodular hyperplasia or hyperplastic nodule ± colloid or cystic degeneration ± Hashimoto thyroiditis).

Comparison of surgical histological results and RtUg-FNNAC results (Table 1)

212 (22.1%) patients with malignant nodules and 20 (2.1%) patients with indeterminate nodules were referred for surgery. All nodules with malignant cytologic findings were confirmed histologically (no false positive results). Of the 20 nodules with indeterminate cytological findings, biopsy showed 7 follicular and Hürthle cell carcinomas, 10 papillary carcinomas and 3 follicular and Hürthle cell adenomas (3 false positive results).

The available patient data with initially benign RtUg-FNNAC and histologic examination after thyroidectomy included 66 (6.9%) patients who had undergone surgery for enlarged multinodular goiter, nodule size > 4 cm, no response to medication (e.g. mildly suppressive doses of thyroxine) and strong risk factors. The histologic findings confirmed the initial benign RtUg-FNNAC diagnosis in 65 (98.5%) patients. In one case a papillary carcinoma of 6 mm was found within a multinodular goiter. In this case, this malignant nodule was not diagnosed as suspicious for malignancy with the pre-procedural US examination and the RtUg-FNNAC was performed only in the dominant nodule which was benign histologically. The total number of patients who were subjected to surgery was 298 (Table 1).

Considering indeterminate lesions as suspicious for malignancy (because these patients were referred for surgery), RtUg-FNNAC was true positive in 229 cases (212 cases with malignant RtUg-FNNAC and 17 cases with indeterminate RtUg-FNNAC) and false pos-

Table 1. Comparison of results from RtUg-FNNAC and surgical histological examination

RtUg-FNNAC	*Patients, n*	*Surgical biopsy*	*Patients, n*
Papillary cancer	203	Papillary cancer	203
Medullary cancer	6	Medullary cancer	6
Anaplastic cancer	1	Anaplastic cancer	1
Lymphoma	1	Lymphoma	1
Metastases	1	Metastases	1
Follicular/Hürthle cell neoplasm	20	Follicular/Hürthle cell carcinoma	7
		Follicular/Hürthle cell adenoma	3
		Papillary cancer	10
Nodular hyperplasia or hyperplastic nodule ± colloid or cystic degeneration ± Hashimoto thyroiditis	66	Nodular hyperplasia or hyperplastic nodule ± colloid or cystic degeneration ± Hashimoto thyroiditis+multinodular goiter	65
		Papillary cancer	1
Total	298		298

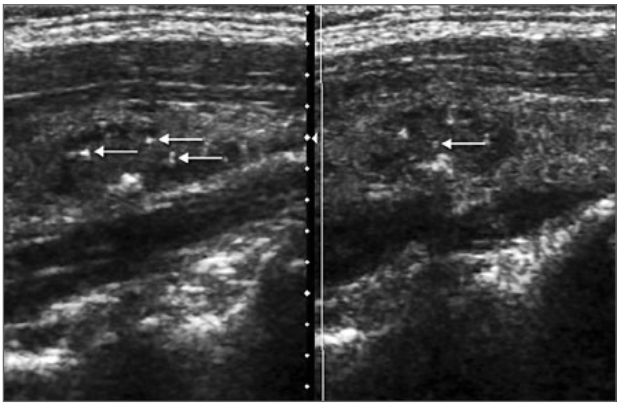

Figure 3. Nonpalpable thyroid nodules with sonographically suspicious characteristics of malignancy. Longitudinal US images show an incidentally detected thyroid lesion with microcalcifications (arrows).

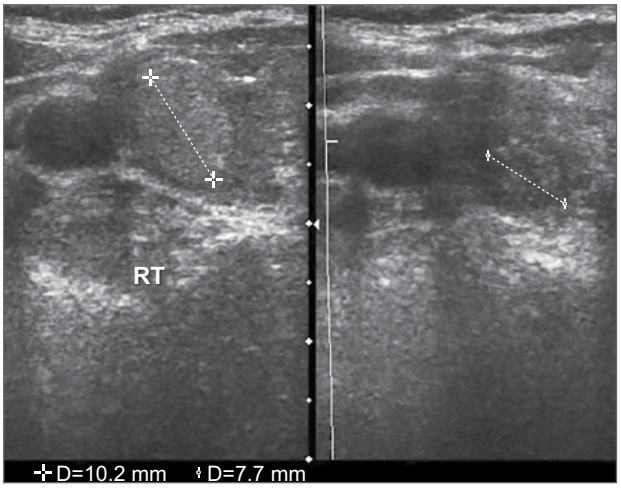

Figure 4. Transverse US images obtained in a 53-year-old woman with multiple nonpalpable thyroid nodules show a 10.2 mm dominant, well-circumscribed hyperechoic lesion in the right thyroid lobe (left image); a 7.7 mm hypoechoic nodule with blurred margins and microcalcifications is visible (right image). The diagnosis of RtUg-FNNAC was adenomatous hyperplasia in the dominant nodule and papillary carcinoma in the smaller nodule with the suspicious US findings.

itive in 3 (3 cases with indeterminate RtUg-FNNAC). From 66 patients with an initial benign RtUg-FNNAC who underwent surgery, the results were true negative in 65 and false negative in 1. The overall sensitivity, specificity, positive predictive value and negative predictive value of RtUg-FNNAB were 99.6, 95.6, 98.7 and 98.7%, respectively. Accuracy for the detection of malignancy was 98.7%.

Discussion

In this study we have demonstrated that RtUg-FNNAC is a highly effective method for the evaluation of thyroid nodules with a high yield of satisfactory aspirates (100%) with just 1-2 needle passes, reducing patient discomfort and short-term complications.. The false positive results were attributed to the nature of the nodule and were associated with follicular and Hürthle cell neoplasms. The false negative results that were attributed to the size and US features of the nodule were mainly associated with multinodular goiter.

The use of the needle without an attached syringe increases the accuracy for targeting small nonpalpable nodules or specific areas in a nodule, decreases the number of required needle passes, and enables sampling in several different areas of the target nodule at once. This technique maximizes cellular yield and minimizes bloody artefacts in cytologic examination, producing specimens of better quality [2].

Court-Payen et al. [15] and Accurso et al. [16] demonstrated that inadequate specimens with Ug-FNA were 16% and 22% respectively, and Cesur et al. [17] demonstrated that inadequate specimens with Ug-FNA were 21% but inadequate specimens with palpation were 32.3% (p=0.004). All patients underwent both Ug-FNA and palpation-guided FNA (p-FNA). The rate of inadequate material with p-FNA was significantly higher only for smaller nodules 10-15 mm (37.6 vs. 24.2%; p=0.009).

Several authors have compared Ug-FNA, p-FNA, palpation-guided FNNAC (p-FNNAC) and Ug-FNNAC for diagnosis of thyroid lesions.

Carmeci et al. [18], Danese et al. [19], and Hatada et al. [20] demonstrated that inadequate specimens with Ug-FNA were 7, 4, and 17%, but inadequate specimens with p-FNA were 16, 9, and 30%, respectively. Cesur et al. [17], Danese et al. [19], and Hatada et al. [20] have reported that the sensitivity of p-FNA was 57, 92 and 45%, and the sensitivity of Ug-FNA was 86, 97 and 62%, respectively.

Pothier and Narula [21] reported that FNA and FNNAC are equal; however, taking into consideration all evidence available, it seems that FNNAC may be easier to perform and may produce better samples.

Romitelli et al. [3] demonstrated that inadequate specimens with Ug-FNA were 16.3 vs. 5.8% with Ug-FNNAC (p=0.015). From these literature results there seems to be some evidence favoring US guidance and FNNAC The authors have demonstrated that with RtUg-FNNAC there were not inadequate specimens with just 1-2 needle passes for each nodule.

Critical factors for the high accuracy and the sufficiency of RtUg-FNNAC of the thyroid by capillary action without aspiration are the pre-procedural planning, the procedure of RtUg-FNNAC and the post-procedural care, with special emphasis on the factors that

may limit material adequacy and lead to complications or false negative results.

Before performing RtUg-FNNAC in a patient with one or more thyroid nodules, a complete history is obtained searching for risk factors for thyroid cancer [1]. A history of any other previous malignancy is sought, because there is a possibility of metastatic thyroid disease [22].

Even though a screening test for coagulation is not routinely needed, bleeding diathesis is contraindication for RtUg-FNNAC. So the patient is carefully questioned about recent or current anticoagulant therapy and a pre-procedure prothrombin time is obtained [23].

A meticulous US examination of the thyroid and the neck can reveal suspicious features such as microcalcifications (Figure 3), marked hypoechogenicity or hypoechoic solid nodules, an irregular or microlobulated margin, shape which is taller than wide, intranodular vascularity, presence of central calcifications (coarse calcifications), direct tumor invasion of adjacent soft tissue or signs of extracapsular spread and metastasis to one or more lymph nodes [24,25].

Comparison with previous US is made in case of a rapidly growing nodule. Any nodule with suspicious US features is considered for RtUg-FNNAC even in cases of multiple nodules, because if only the dominant or largest nodule is biopsied, a thyroid cancer could be missed (Figure 4) [24].

If there is a discrepancy between the US findings and those of cytologic analysis, a repeat RtUg-FNNAC is considered at least 3 months after the initial biopsy [26].

Conclusion

RtUg-FNNAC is a modified technique that combines the benefits of US guidance with those of capillary action sampling. Grasping the needle hub directly without an attached syringe improves the sensitivity of the operator in placing the needle tip within a small nodule or within a specific area in a nodule. The accuracy for targeting small nonpalpable nodules increases, the number of required needle passes decreases, enabling sampling in several different areas of the target nodule at once. Furthermore, the RtUg-FNNAC maximizes cellular yield, minimizes bloody artefacts in cytologic examination and less bleeding occurs, which is an advantage in the cytology of a richly vascular tissue such as the thyroid gland. In this way, RtUg-FNNAC reduces patient discomfort and short-term complications. Finally, the technical ease of this method may make RtUg-FNNAC widely accepted in hospitals with a high volume of patients.

References

1. Can AS. Cost-effectiveness comparison between palpation and ultrasound-guided thyroid fine-needle aspiration biopsies. BMC Endocr Disord 2009; 9: 14.
2. Santos JE, Leiman G. Nonaspiration fine needle cytology. Application of a new technique to nodular thyroid disease. Acta Cytol 1988; 32: 353-356.
3. Romitelli F, Di Stasio E, Santoro C, Iozzino M, Orsini A, Cesareo R. A comparative study of fine needle aspiration and fine needle non-aspiration biopsy on suspected thyroid nodules. Endocr Pathol 2009; 20: 108-113.
4. Tublin ME, Martin JA, Rollin LJ, Pealer K, Kurs-Lasky M, Ohori NP. Ultrasound-guided fine-needle aspiration versus fine-needle capillary sampling biopsy of thyroid nodules: does technique matter? J Ultrasound Med 2007; 26: 1697-1701.
5. The American Thyroid Association Guidelines Task Force. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2006; 16: 1-33.
6. Tomoda C, Kitano H, Uruno T et al. Transcutaneous iodine absorption in adult patients with thyroid cancer disinfected with povidone-iodine at operation. Thyroid 2005; 15: 600-603.
7. Gursoy A, Ertugrul DT, Sahin M, Tutuncu NB, Demirer AN, Demirag NG. The analgesic efficacy of lidocaine/prilocaine (EMLA) cream during fine-needle aspiration biopsy of thyroid nodules. Clin Endocrinol (Oxf) 2007; 66: 691-694.
8. Rausch P, Nowels K, Jeffrey RB Jr. Ultrasonographically guided thyroid biopsy: a review with emphasis on technique. J Ultrasound Med 2001; 20: 79-85.
9. Kim MJ, Kim EK, Park SI et al. US-guided fine-needle aspiration of thyroid nodules: indications, techniques, results. RadioGraphics 2008; 28: 1869-1889.
10. Oertel YC. Fine-needle aspiration of the thyroid: technique and terminology. Endocrinol Metab Clin North Am 2007; 36: 737-751, vi-vii.
11. Degirmenci B, Haktanir A, Albayrak R et al. Sonographically guided fine-needle biopsy of thyroid nodules: the effects of nodule characteristics, sampling technique, and needle size on the adequacy of cytological material. Clin Radiol 2007; 62: 798-803.
12. Hegedus L. Clinical practice. The thyroid nodule. N Engl J Med 2004; 351: 1764-1771.
13. Noordzij JP, Goto MM. Airway compromise caused by hematoma after thyroid fine-needle aspiration. Am J Otolaryngol 2005; 26: 398-399.
14. Zhu W, Michael CW. How important is on-site adequacy assessment for thyroid FNA? An evaluation of 883 cases. Diagn Cytopathol 2007; 35: 183-186.
15. Court-Payen M, Nygaard B, Horn T et al. US-guided fine-needle aspiration biopsy of thyroid nodules. Acta Radiol 2002; 43: 131-140.
16. Accurso A, Rocco N, Palumbo A et al. Usefulness of ultrasound-guided fine needle aspiration cytology in the diagnosis of non-palpable small thyroid nodules. Tumori 2005; 91: 355-357.
17. Cesur M, Corapcioglu D, Bulut S et al. Comparison of palpation-guided fine needle aspiration biopsy to ultrasound-guided fine-needle aspiration biopsy in the evaluation of thyroid nodules. Thyroid 2006; 16: 555-561.
18. Carmeci C, Jeffrey RB, McDougall IR, Nowels KW, Weigel RJ. Ultrasound guided fine-needle aspiration biopsy of thyroid masses. Thyroid 1998; 8: 283-289.
19. Danese D, Sciacchitano S, Farsetti A, Andreoli M, Pontecorvi A. Diagnostic accuracy of conventional versus sonography-

guided fine-needle aspiration biopsy of thyroid nodules. Thyroid 1998; 8: 15-21.
20. Hatada T, Okada K, Ishii H et al. Evaluation of ultrasound-guided fine-needle aspiration biopsy for thyroid nodules. Am J Surg 1998; 175: 133-136.
21. Pothier DD, Narula AA. Should we apply suction during fine needle cytology of thyroid lesions? A systematic review and metaanalyses. Ann R Coll Surg Engl 2006; 88: 643-645.
22. Titton RL, Gervais DA, Boland GW, Maher MM, Mueller PR. Sonography and sonographically guided fine-needle aspiration biopsy of the thyroid gland: indications and techniques, pearls and pitfalls. Am J Roentgenol 2003; 181: 267-271.
23. Kien-Fong Vu C, Chang F, Doig L, Meenan J. A prospective control study of the safety and cellular yield of EUS-guided FNA or Trucut biopsy in patients taking aspirin, nonsteroidal anti-inflammatory drugs, or prophylactic low molecular weight heparin. Gastrointest Endosc 2006; 63: 808-813.
24. Tollin SR, Mery GM, Jelveh N et al. The use of fine-needle aspiration biopsy under ultrasound guidance to assess the risk of malignancy in patients with a multinodular goiter. Thyroid 2000; 10: 235-241.
25. Kim EK, Park CS, Chung WY et al. New sonographic criteria for recommending fine-needle aspiration biopsy of nonpalpable solid nodules of the thyroid. Am J Roentgenol 2002; 178: 687-691.
26. Kim MJ, Kim EK, Park SI et al. US-guided fine-needle aspiration of thyroid nodules: indications, techniques, results. RadioGraphics 2008; 28: 1869-1889.