Endokrynologia Polska/Polish Journal of Endocrinology
Tom/Volume 59; Numer/Number 5/2008
ISSN 0423–104X

Fine needle aspiration of thyroid nodules in a general teaching hospital setting performing moderate number of biopsies: outcome of indeterminate cytologic results

Biopsja aspiracyjna cienkoigłowa guzków tarczycy w szpitalu klinicznym, w którym stosunkowo rzadko wykonuje się takie procedury: niejednoznaczne wyniki badań cytologicznych

Hamidreza Bazrafshan[1], ***Ramin Azarhoush***[2], ***Ali Gholamrezanezhad***[3, 4]

[1]*Department of Endocrinology, Golestan Medical University*
[2]*Department of Pathology, Golestan Medical University*
[3]*Research Institute for Nuclear Medicine, Medical Sciences/Tehran University*
[4]*Young Researchers Club. Tehran Medical Unit. Azad University*

Abstract

Introduction: Our aim was to assess the usefulness of fine-needle aspiration cytologic biopsy (FNA) of the thyroid in our general teaching hospital with average health care facility performing moderate number of such procedures and to evaluate the outcome of Indeterminate Cytologic Results.

Material and method: We studied on all consecutive patients referred for FNA of the thyroid nodule. All samplings were performed primarily by one endocrinologist performing moderate number of samplings and interpreted by one pathologist. Cytological findings were classified as malignant, histologic control recommended (suspicious or indeterminate), benign, and unsatisfactory.

Results: Four hundred and seventy six biopsies were performed. Patient acceptance of this procedure was good and no complication was encountered. 64/476 of samples were considered as insufficient (13.4%). Of the remaining samples (355 F, 57 M), 321 specimens (67.4%) were reported to be non-neoplastic lesions, including 251 (52.7%) colloid nodules, 39 (8.2%) hemorrhagic nodules and 31 (6.5%) cases of thyroiditis. A neoplastic nodule was confirmed in 91/476 of cases (19.1%), of which 14 were cytologically malignant (3.0%). Follicular lesions were identified in the remaining 77/476 cases (16.1%). Excluding 21 patients who were lost to follow-up, the remaining 56 patients (72.7%) were surgically followed up. Upon excision, benign lesions were diagnosed in 47/56 (83.8%), of which 32 lesions (57.1%) were follicular adenoma and 15 cases (26.7%) of colloid nodules. Malignancy was confirmed histopathologically in 9 cases (16.2%), including 4 follicular variant papillary carcinomas and 5 follicular carcinomas.

Conclusions: FNA is an inexpensive, safe, practical, well tolerated, and easily applied method, even in not fully-experienced hands and provides useful information. Based on our study findings, suspicious cytologic results (cytologically follicular neoplasms) are inconclusive and are associated with a remarkable chance of malignant involvement; hence surgical treatment is necessary for clarification.

(Pol J Endocrinol 2008; 59 (5): 385–389)

Key words: *fine needle aspiration, thyroid nodule, follicular lesion*

Streszczenie

Wstęp: Celem badania była ocena użyteczności biopsji aspiracyjnej cienkoigłowej tarczycy w szpitalu klinicznym przeciętnie wyposażonym w sprzęt, przeprowadzającym stosunkowo rzadko takie procedury oraz ocena częstości uzyskiwania niejednoznacznych wyników badania cytologicznego.

Materiał i metody: Do badania włączono wszystkich pacjentów zgłaszających się na biopsję cienkoigłową guzków tarczycy. Wszystkie bioptaty zostały pobrane przez jednego endokrynologa, wykonującego stosunkowo niewiele takich procedur, a następnie ocenione przez jednego patomorfologa. Wynik badania cytologicznego klasyfikowano następująco: zmiana złośliwa, zalecana dalsza kontrola histologiczna (zmiana podejrzana lub nieokreślona), zmiana łagodna, niedostateczna ilość materiału biopsyjnego.

Wyniki: Wykonano łącznie 476 biopsji. Akceptacja badania wśród pacjentów była dobra, nie odnotowano żadnych powikłań związanych z tą procedurą. Sześćdziesiąt cztery sposród 476 próbek zawierało zbyt mało materiału, aby przeprowadzić badanie (13,4%). Pozostałe bioptaty (355 kobiet, 57 mężczyzn) oceniono następująco: w 321 próbkach (67,4%) stwierdzono zmiany nienowotworowe, w tym 251 (52,7%) guzków koloidowych, 39 (8,2%) guzków krwotocznych i 31 (6,5%) przypadków zapalenia tarczycy. Nowotworowy charakter zmian stwierdzono u 91/476 badanych (19,1%), z czego 14 miało cytologiczne cechy złośliwości (3,0%). Zmiany pęcherzykowe wykryto u 77/476 badanych (16,1%). Po wykluczeniu 21 osób niedostępnych do dalszej obserwacji, pozostało 56 pacjentów (72,7%), których poddano leczeniu chirurgicznemu. Badanie histopatologiczne wyciętych tkanek wykazało łagodny charakter zmian u 47/56 osób (83,8%), w tym

Ali Gholamrezanezhad, M.D., Shariati Hospital, Medical Sciences, Tehran University, North Karegar St. 14114. Tehran, Iran, tel.: 009 891 221 070 37, e-mail: gholamrezanejhad@razi.tums.ac.ir

32 przypadki (57,1%) gruczolaka pęcherzykowego i 15 przypadków (26,7%) guzków koloidowych. Zmiany złośliwe potwierdzono u 9 (16,2%) chorych, w tym 4 przypadki raka brodawczakowego i 5 raka pęcherzykowego.
Wnioski: Biopsja aspiracyjna cienkoigłowa jest niedrogą, bezpieczną, praktyczną, dobrze tolerowaną przez pacjentów i łatwą do przeprowadzenia procedurą (nawet przez lekarza nie mającego dużego doświadczenia w przeprowadzaniu tego typu procedur), a przy tym dostarczającą przydatnych informacji. Badanie autorów wskazuje, że wyniki badania cytologicznego określone jako zmiana podejrzana (zmiany pęcherzykowate) są niekonkluzywne i wiążą sie ze znacznym ryzykiem procesu złośliwego; dlatego w celu wyjaśnienia wątpliwości diagnostycznych konieczna jest interwencja chirurgiczna. **(Endokrynol Pol 2008; 59 (5): 385–389)**

Słowa kluczowe: *biopsja aspiracyjna cienkoigłowa, guzki tarczycy, zmiany pęcherzykowe*

Introduction

Thyroid nodules are a common occurrence in the general population, but only a small number of them are eventually diagnosed to be malignant [1]. Thyroid fine-needle aspiration (FNA), in experienced hands, is the standard procedure for the clinical triage of thyroid nodules [2] and has been considered as a safe, reliable, and effective method for differentiating benign from malignant nodules [3]. Also it has been claimed that FNA biopsy has a substantial cost-saving effect on thyroid practice [4]. Moreover it has been confirmed that the diagnostic value of clinical data alone is inferior to that of FNA alone [5]. In spite of these advantages, there are different conclusions about the accuracy of the procedure, with its sensitivity ranging from 65% to 98% [6] and its specificity ranging from 55% [7] to 100% [6] in different settings.

The adequate FNA specimen is usually categorized as benign, malignant, or indeterminate, cytopathologically. The latter group usually includes follicular neoplasm (follicular adenoma and follicular carcinoma), follicular variant of papillary carcinoma (FVPC) and sometimes a more specific diagnosis such as Hurthle cell neoplasm or follicular lesion/neoplasm with Hurthle cell change [8]. The main limitations of cytologic examination have been considered to be the difficulty in distinguishing some benign cellular adenomas from their malignant counterparts, arising as indeterminate, non-diagnostic results or cellular follicular neoplasms in cytologic reports [9–11], which in fact need not negate continued use of FNA biopsy [11]. In fact, the cytologic differentiation of cellular colloid nodules from follicular neoplasms has not been possible because of the scanty amount of tissue obtained by this technique and because of the infrequent preparation of cell blocks, which precludes appreciation of the tissue architecture [12]. The prevalence of such problem is significantly different among studies and populations and there is no data about it in regions with history of iodine deficiency, which has been corrected using supplemental iodine (such as north of Iran). These debates remain until recently [13, 14].

Our aim was to assess the use and usefulness of fine-needle aspiration cytologic biopsy of the thyroid in our general teaching hospital setting with average health care facility performing moderate number of such procedures and to evaluate the outcome of Indeterminate Cytologic Results.

Material and methods

Between 1997 and 2004, we conducted a study on all consecutive patients referred to our endocrinology department for FNA of the thyroid. All the patients had been selected based on the detection of a palpable solitary thyroid nodule or a dominant nodule in the context of a multinodular goiter. All the patients gave informed consent to participate in the study.

Fine needle aspiration

All thyroid aspirations were performed by an endocrinologist performing moderate number of such procedures (about 100 FNA/year). After localizing the nodule by palpation, the FNA was performed using a 25-gauge needle attached to a 20-ml syringe. On average, 4 passes were made in each nodule, resulting in six alchohol-fixed smears. Subsequently all smears were stained by modified Papanicolaou technique and were analyzed and interpreted by a blinded pathologist. The results of the cytopathologic analysis were reported based on the following categories: benign, malignant, histologic control recommended (indeterminate or suspicious) and insufficient. The adequate FNA specimen was defined as containing at least 8–10 cell groups on 2 slides, with 8–10 follicular cells in each group [15].

All patients with follicular lesion were advised to undergo lobectomy to accurately determine the nature of the neoplasm and the post-operative pathology results were recorded.

Statistical analysis

A descriptive analysis was done on all variables to obtain a frequency distribution. The quantitative variables were expressed as the mean ± SD and range. Statistical analysis was performed using SPSS software package version 15.0.

Results

Four hundred and seventy six patients entered in the study and underwent FNA of the dominant (or the

solitary) thyroid nodule. The mean age ± SD of the participants was 38.37 ± 9.81yrs (age range: 14–75 yr). No complication was found among the studied patients and patient acceptance has been high.

Out of 476 samples, 64 cases were considered as insufficient for cytopathological analysis (13.4%). These were excluded from the series, leaving 412 cases. Of the remaining samples (355 F, 57 M), 321 specimens (67.4%) were reported to be non-neoplastic lesions, including 251 (52.7%) colloid nodules, 39 (8.2%) hemorrhagic nodules and 31 (6.5%) cases of thyroiditis. A neoplastic nodule was confirmed in 91/476 of cases (19.1%), of which 14 were cytologically malignant (3.0%, including both papillary lesions and FVPC). Follicular lesions were identified in the remaining 77/476 cases (16.1%).

In spite of the fact that all patients with follicular lesion were advised to undergo lobectomy to accurately determine the nature of the neoplasm, only 56 patients (72.7%) received surgical treatment. Upon excision in this subgroup of patients, benign lesions were diagnosed in 47/56 patients (83.8%), of which 32 lesions (57.1%) were follicular adenoma and 15 cases (26.7%) of colloid nodules. Thyroid malignancy was confirmed histopathologically in 9 cases (16.2%), including 4 FVPC and 5 follicular carcinomas. Finally, based on the FNA analysis (both cytologically malignant and indeterminate reports with subsequent surgical resection), 23/391 (5.9%) of adequate samples were malignant (excluding those patients who did not undergo surgical resection).

Discussion

There are some confirmed facts that prove the utility of FNA in the routine practice and management of thyroid nodules:

1. The cancer removal rate is higher with FNA and surgery than with surgery alone [16].
2. The percentage of patients operated on decreases from 95% to 60% [17].
3. FNA is of great value since it enables greater cancer detection in a cost-effective manner [16, 17].
4. It can be performed even without the guidance of ultrasonography, successfully [18]; however, ultrasonographically-guided FNA is superior to palpation-guided FNA for obtaining adequate material especially for small-sized nodules, as well as providing more accurate cytologic evaluation [19]. Indeed, the difference between the costs of two procedures might be acceptable [19].
5. As it was confirmed in our study, there is no remarkable side effect or complications in this procedure.

In our study, 13.4% of the samples were diagnostically insufficient. This rate compares very favorably with major referral centers [20–22], especially highly developed countries [23, 24] and even lower than their failure rates [25–27]. Although it has been stated that the frequency of inadequate smears, in turn, is strongly related to the type of physician performing the aspiration [27] and the frequency was highest among community-based clinicians (32.4%) [27], based on our findings it seems that FNA of thyroid nodules even in the hands of not fully expert endocrinologists performing moderate numbers of such procedure and also without the guidance of ultrasonography (in developing countries and in general hospital settings) can be as efficacious as highly developed and equipped situations. Previously similar conclusions were drawn: It has been stated that FNA is a well tolerated, and easily applied procedure without its highly desirable features being compromised, even when a moderate number of such procedures are performed [28]. Although Haas et al [29] and other groups [30, 31] have shown that the incidence of inadequate specimens decreases inversely from 18% to 6% with the increase in the experience of operator and hence, it can be concluded that our experience in blind aspiration of nodules is borderline (with 13.4% failure rate), however, our failure rate is lower than many developing countries with full experience on this procedure [31]. Fitz-Patrick et al stated that when an experienced endocrinologist and cytopathologist are available, aspiration biopsy is the diagnostic procedure of choice [32]; however, in our opinion FNA can be the procedure of choice even in the hands of inexperienced physicians. In fact, we are in agreement with Silverman et al conclusion in that special referral centers are not needed to interpret the cytologic material and well trained surgical pathologists can become proficient in interpreting the FNA biopsies without significant loss in accuracy, thereby render a definite diagnosis in the vast majority of the cases [33]. These conclusions are against the statement of Friedman [34] and also Willems and Löwhagen [35] that interpretation requires an experienced cytologist and endocrinologist.

In our study the frequencies of all three subgroups of benign, suspicious and malignant FNA cytologic results are in the range of those reported in the literature [6, 36]. For example, based on the comprehensive review of Gharib and Goellner, rates for four main cytologic categories, based on data pooled from seven large series, were as follows: benign, 69%; suspicious, 10%; malignant, 4%; and nondiagnostic, 17% [6]. However, in the study of Kumar et al on patients from an iodine deficient region, FNA cytology was positive for malignancy in 6.2% of patients [37], which is higher than our results. The etiologic significance of this difference and its relationship to iodine deficiency and measures performed in our country to overcome iodine deficiency needs to be further evaluated.

On the other hand, in our population the frequency of malignancy among those who has been cytologically categorized as follicular neoplasm (16.2%) was lower than that of few other populations [8, 38], while higher than others [39]. For example, in the study of McHenry et al pathologic evaluation of these cases revealed cancer in 9%, adenoma in 43%, colloid nodule in 45%, epithelial cyst in 2%, and thyroiditis in 1% of cases [39]. As another example, Piromalli et al stated that in their study on 795 Italian cases, all patients with cytological diagnosis of follicular tumor had a benign lesion at histology [40]. Moreover, McHenry et al stated the "nondiagnostic" cytology is a significant limitation of FNAB associated with a 52% neoplasia rate and a 9% incidence of malignancy [39]. Based on these differences, it seems that the prevalence of malignancy in cytologically follicular lesions depends on geographic, nutritional, ethnicity, and other factors. According to these facts and also based on the conclusion of Layfield et al [41] that stated once an aspiration diagnosis of "follicular neoplasm" had been made, no clinical, radiologic, or laboratory test aided in the distinction of follicular adenoma from follicular carcinoma, it seems necessary to perform histologic evaluation on all patients with non-diagnostic cytology. Similarly, in previous studies it has been advised that in order to avoid a missed carcinoma, surgical treatment of persistent "non-diagnostic" FNA in a dominant hypofunctioning nodule is indicated [39]. Similar to our study, Tamez-Pérez et al evaluated the definitive histological results of a group of 41 patients with FNA of thyroid nodule catalogued as "indeterminate/non diagnostic" sent for surgical treatment. Finally they found that the majority of patients with a diagnosis of "indeterminated/non diagnostic" had benign lesions (60.9%). The usual predictive factors for malignity such as age, sex, size of nodule, did not present a significant support in the differential diagnosis [42] and hence surgical intervention seems to be necessary.

Study limitations

1. In our study, for inadequate samples and also those with cytologic diagnosis of follicular lesion, repeated aspiration did not performed, as numerous papers in this field failed to reveal any advantage [21, 43].
2. In our study only 72.7% of those patients who required surgical intervention underwent thyroid surgery. Although this rate seems to be low, it is even considerably higher than the same rate in even developed countries [44]. In the study of Maxwell et al [44], in 21 patients the FNA gave indication for thyroid surgery, yet surgery was done in only 12 (57.1%). Fortunately, this finding emphasizes on the fact that the patient's motivation and also medical follow-ups in the developing regions are effective enough.
3. In our study, FNA samplings were not done using ultrasonography (US)-guided method, as there were limitations in US facilities. Although Yokozawa et al reported that this limitation would increase the probability of palpable cancers with insufficient cell material for analysis or cancers with calcified lesions [36], some other previous reports concluded that in palpable nodules sensitivity, specificity, accuracy, and positive and negative predictive values of US-guided FNA for malignancy were not significantly different from those of palpation-guided FNA [18].

Conclusion

From the results of this study and other studies in the literature, it can be concluded that FNA is an inexpensive, safe, practical, well tolerated, and easily applied method, even in not fully-experienced hands and provides useful information for further clinical decision about thyroid nodules (although in some cases surgical exploration is required for diagnosis). Based on our study findings, suspicious cytologic results (cytologically follicular neoplasms) are inconclusive and are associated with a remarkable chance of malignant involvement; hence surgical treatment is necessary for clarification.

References

1. Hayashi N, Kitaoka M. Fine-needle aspiration biopsy of the thyroid nodule: uses and limitations. Nippon Rinsho 2007; 65: 2003–2007.
2. Jeffrey PB, Miller TR. Fine-needle aspiration cytology of the thyroid. Pathology (Phila) 1996; 4: 319–35.
3. Lopez LH, Canto JA, Herrera MF et al. Efficacy of fine-needle aspiration biopsy of thyroid nodules: experience of a Mexican institution. World J Surg. 1997; 21: 408–411.
4. Hadi M, Gharib H, Goellner JR et al. Has fine-needle aspiration biopsy changed thyroid practice? Endocr Pract 1997; 3: 9–13.
5. Ongphiphadhanakul B, Rajatanavin R, Chiemchanya S et al. Systematic inclusion of clinical and laboratory data improves diagnostic accuracy of fine-needle aspiration biopsy in solitary thyroid nodules. Acta Endocrinol (Copenh) 1992; 126: 233–237.
6. Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. Ann Intern Med 1993; 118: 282–9.
7. Klemi PJ, Joensuu H, Nylamo E. Fine needle aspiration biopsy in the diagnosis of thyroid nodules. Acta Cytol 1991; 35: 434–438.
8. Pu RT, Yang J, Wasserman PG et al. Does Hurthle cell lesion/neoplasm predict malignancy more than follicular lesion/neoplasm on thyroid fine-needle aspiration? Diagn Cytopathol 2006; 34: 330–334.
9. Furlan JC, Bedard YC, Rosen IB. Single versus sequential fine-needle aspiration biopsy in the management of thyroid nodular disease. Can J Surg 2005; 48: 12–18.
10. Castro MR, Gharib H. Thyroid fine-needle aspiration biopsy: progress, practice, and pitfalls. Endocr Pract 2003; 9: 128–136.
11. Gharib H. Fine-needle aspiration biopsy of thyroid nodules: advantages, limitations, and effect. Mayo Clin Proc 1994; 69: 44–49.
12. Kung IT, Yuen RW. Fine needle aspiration of the thyroid. Distinction between colloid nodules and follicular neoplasms using cell blocks and 21-gauge needles. Acta Cytol 1989; 33: 53–60.
13. Solymosi T, Tóth GL, Gál I et al. Influence of iodine intake on the diagnostic power of fine-needle aspiration cytology of the thyroid gland. Thyroid 2002; 12: 719–723.
14. Słowińska-Klencka D, Klencki M, Sporny S et al. Fine-needle aspiration biopsy of the thyroid in an area of endemic goitre: influence of restored sufficient iodine supplementation on the clinical significance of cytological results. Eur J Endocrinol 2002; 146: 19–26.

15. Bakshi NA, Mansoor I, Jones BA. Analysis of inconclusive fine-needle aspiration of thyroid follicular lesions. Endocr Pathol 2003; 14: 167–175.
16. Morayati SJ, Freitas JE. Guiding thyroid nodule management by fine-needle aspiration. Fam Pract Res J 1991; 11: 379–386.
17. Ng EH, Tan SK, Nambiar R. Impact of fine needle aspiration cytology on the management of solitary thyroid nodules. Aust N Z J Surg 1990; 60: 463–466.
18. Takashima S, Fukuda H, Kobayashi T. Thyroid nodules: clinical effect of ultrasound-guided fine-needle aspiration biopsy. J Clin Ultrasound 1994; 22: 535–542.
19. 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.
20. Harsoulis P, Leontsini M, Economou A et al. Fine needle aspiration biopsy cytology in the diagnosis of thyroid cancer: comparative study of 213 operated patients. Br J Surg 1986; 73: 461–464.
21. Blanco Carrera C, García-Díaz JD, Maqueda Villaizán E et al. Diagnostic efficacy of fine needle aspiration biopsy in patients with thyroid nodular disease. Analysis of 510 cases. Rev Clin Esp 2005; 205: 374–378.
22. Brenta G, Schnitman M, Bonnahon L et al. Evaluation of innovative skin-marking technique performed before thyroid ultrasound-guided fine-needle aspiration biopsies. Endocr Pract 2002; 8: 5–9.
23. Ito M, Yamashita S, Ashizawa K et al. Childhood thyroid diseases around Chernobyl evaluated by ultrasound examination and fine needle aspiration cytology. Thyroid 1995; 5: 365–368.
24. Willgerodt H, Keller E, Bennek J et al. Diagnostic value of fine-needle aspiration biopsy of thyroid nodules in children and adolescents. J Pediatr Endocrinol Metab 2006; 19: 507–515.
25. Prinz RA, O'Morchoe PJ, Barbato AL et al. Fine needle aspiration biopsy of thyroid nodules. Ann Surg 1983; 198: 70–73.
26. Tangpricha V, Chen BJ, Swan NC et al. Twenty-one-gauge needles provide more cellular samples than twenty-five-gauge needles in fine-needle aspiration biopsy of the thyroid but may not provide increased diagnostic accuracy. Thyroid 2001; 11: 973–976.
27. Hall TL, Layfield LJ, Philippe A et al. Sources of diagnostic error in fine needle aspiration of the thyroid. Cancer 1989; 63: 718–725.
28. Dwarakanathan AA, Ryan WG, Staren ED et al. Fine-needle aspiration biopsy of the thyroid. Diagnostic accuracy when performing a moderate number of such procedures. Arch Intern Med 1989; 149: 2007–2009.
29. Haas S, Trujillo A, Kunstle J. Fine needle aspiration of thyroid nodules in a rural setting. Am J Med 1993; 94: 357–361.
30. Burch HB, Burman KD, Reed HL et al. Fine needle aspiration of thyroid nodules. Determinants of insufficiency rate and malignancy yield at thyroidectomy. Acta Cytol 1996; 40: 1176–1183.
31. Tambouret R, Szyfelbein WM, Pitman MB. Ultrasound-guided fine-needle aspiration biopsy of the thyroid. Cancer 1999; 87: 299–305.
32. Fitz-Patrick D, Navin JJ, Fukunaga BN. Fine-needle aspiration biopsy of thyroid nodules. A diagnostic method that minimizes the need for surgery. Postgrad Med 1986; 80: 62–65.
33. Silverman JF, West RL, Larkin EW et al. The role of fine-needle aspiration biopsy in the rapid diagnosis and management of thyroid neoplasm. Cancer 1986; 57: 1164–1170.
34. Friedman NM. Fine-needle aspiration biopsy of the thyroid. Superior diagnostic tool. Postgrad Med 1985; 78: 55–57.
35. Willems JS, Löwhagen T. The role of fine-needle aspiration cytology in the management of thyroid disease. Clin Endocrinol Metab 1981; 10: 267–273.
36. Yokozawa T, Fukata S, Kuma K et al. Thyroid cancer detected by ultrasound-guided fine-needle aspiration biopsy. World J Surg 1996; 20: 848–853.
37. Kumar A, Ahuja MM, Chattopadhyay TK et al. Fine needle aspiration cytology, sonography and radionuclide scanning in solitary thyroid nodule. J Assoc Physicians India 1992; 40: 302–306.
38. Tyler DS, Winchester DJ, Caraway NP et al. Indeterminate fine-needle aspiration biopsy of the thyroid: identification of subgroups at high risk for invasive carcinoma. Surgery 1994; 116: 1054–1060.
39. McHenry CR, Walfish PG, Rosen IB. Non-diagnostic fine needle aspiration biopsy: a dilemma in management of nodular thyroid disease. Am Surg 1993; 59: 415–419.
40. Piromalli D, Martelli G, Del Prato I et al. The role of fine needle aspiration in the diagnosis of thyroid nodules: analysis of 795 consecutive cases. J Surg Oncol 1992; 50: 247–250.
41. Layfield LJ, Reichman A, Bottles K et al. Clinical determinants for the management of thyroid nodules by fine-needle aspiration cytology. Arch Otolaryngol Head Neck Surg 1992; 118: 717–721.
42. Tamez-Pérez HE, Gutiérrez-Hermosillo H, Forsbach-Sánchez G et al. Non-diagnostic thyroid fine needle aspiration cytology: outcome in surgical treatment. Rev Invest Clin 2007; 59: 180–183.
43. Orija IB, Hamrahian AH, Reddy SS. Management of nondiagnostic thyroid fine-needle aspiration biopsy: survey of endocrinologists. Endocr Pract 2004; 10: 317–323.
44. Maxwell JG, Scallion RR, White WC et al. Fine-needle aspiration cytology and thyroid surgery in the community hospital. Am J Surg 1996; 172: 529–534.