Turk J Endocrinol Metab 2018;22:57-63

Hemithyroidectomy Seems to be a Reasonable Initial Surgical Approach in Patients with Cytological Bethesda Category III Thyroid Nodules: An Institutional Experience

Önemi Belirsiz Atipi/Önemi Belirsiz Foliküler Lezyon Tiroid Nodüllerinde İlk Cerrahi Yaklaşım Olarak Hemitiroidektomi Mantıklı Gibi Görünmektedir

Bekir Çakır, Muhammet Cüneyt Bilginer, Didem Özdemir, Oya Topaloğlu, Cevdet Aydın, Gürkan Dumlu*, Hayriye Tatlı Doğan**, Reyhan Ersoy

Ankara Yıldırım Beyazıt University Faculty of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey
* Ankara Yıldırım Beyazıt University Faculty of Medicine, Department of General Surgery, Ankara, Turkey
**Atatürk Education and Research Hospital, Department of Pathology, Ankara, Turkey

Abstract

Objective: The atypia of undetermined significance or follicular lesion of undetermined significance is a heterogeneous category of Bethesda system. This study aimed to evaluate the malignancy rates in the initial operation and contralateral thyroid lobe after completion thyroidectomy in patients with atypia of undetermined significance/FLUS thyroid nodules who underwent hemithyroidectomy.

Material and Methods: We reviewed the medical records of 47 (7 male, 40 female; mean age 40.3±13.3 years) patients with cytological atypia of undetermined significance/follicular lesion of undetermined significance nodules (total 48 nodules).

Results: The preoperative cytology was evaluated as atypia of undetermined significance in 32 (66.7%) nodules and follicular lesion of undetermined significance in 16 (33.3%) nodules. The histopathology was reported as benign in 34 (72.3%) patients and malignant in 13 (27.7%) patients. Out of these 13 patients, complementary thyroidectomy was performed in 11 (23.4%) patients, of which 9 (81.8%) patients had benign histopathology and 2 (18.2%) had malignant histopathology.

Conclusion: Lobectomy seems to be a reasonable initial surgical approach in patients with atypia of undetermined significance/follicular lesion of undetermined significance thyroid nodules in cytology.

Keywords: Bethesda category III; atypia or follicular lesion of undetermined significance; malignancy; hemithyroidectomy; completion thyroidectomy

Özet

Amaç: Önemi belirsiz atipi/önemi belirsiz foliküler lezyon Bethesda sisteminin heterojen bir kategorisidir. Bu çalışmada, sitolojide önemi belirsiz atipi/önemi belirsiz foliküler lezyon nodülü olduğu için hemitiroidektomi yapılan hastalardaki başlangıç malignite oranının, tamamlayıcı tiroidektomi ihtiyacının, karşı lobdaki malignite oranının belirlenmeye çalışılması amaçlanmıştır.

Gereç ve Yöntemler: Merkezimizde hemitiroidektomi operasyonu geçiren tiroid nodül sitolojileri (n=48) ÖBA/ÖBFL olan 47 (yedi erkek, 40 kadın; ortalama yaş 40,3±13,3 yıl) hasta çalışmaya dâhil edildi.

Bulgular: Preoperatif sitolojide önemi belirsiz atipi nodül sayısı 32 (%66,7), önemi belirsiz foliküler lezyon nodül sayısı 16 (%33,3) idi. Histopatoloji sonuçları incelendiğinde 34 (%72,3) hasta benign, 13 (%27,7) hasta malign olarak rapor edildi. Malignite saptanan 13 hastadan 11 (%23,4)'ine tamamlayıcı tiroidektomi yapılmıştı. Tamamlayıcı tiroidektomi yapılan hastaların karşı lob histopatolojileri incelendiğinde 9 (%81,8)'unun benign, 2 (%18,2)'sinin malign olduğu saptandı.

Sonuç: Hemitiroidektomi önemi belirsiz atipi/önemi belirsiz foliküler lezyon sitolojili tiroid nodüllerinde başlangıç için makul bir cerrahi yaklaşım gibi görünmektedir.

Anahtar kelimeler: Bethesda kategori III; önemi belirsiz atipi/önemi belirsiz foliküler lezyon; malignite; hemitiroidektomi; tamamlayıcı tiroidektomi

Address for Correspondence: Muhammet Cüneyt Bilginer, Endotem District Policlinic, Ankara, Turkey
Phone: 0312 291 25 25 **E-mail:** cuneytbilginer@hotmail.com **Received:** 23.10.2017 **Accepted:** 13.03.2018

DOI: 10.25179/tjem.2017-58459

Introduction

The fine-needle aspiration biopsy (FNAB) is the gold standard method for differentiation of malignancy in thyroid nodules. National Cancer Institute developed "Bethesda system for reporting thyroid cytopathology" to create a common language for and ensure standardization in the assessment of thyroid nodule cytology (1). There are six groups in the Bethesda system: nondiagnostic or unsatisfactory; benign; atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS); follicular neoplasm or suspicious for a follicular neoplasm; suspicious for malignancy (typically papillary cancer); and malignant. The AUS/FLUS constitutes 15% to 30% of all cytology samples and these nodules carry a malignancy risk of 5% to 15% (2). Although it has a low predictive value, male patients and those with advanced age and nodule size of greater than 4 cm have an increased risk of malignancy (3-5). Cytologically, if limited surgery is preferred in patients with an undetermined solitary nodule, lobectomy is recommended as the initial surgical method. This decision can be changed depending on the clinical and ultrasonographic features, patient's preference, and molecular tests (6). Total thyroidectomy is recommended if the undetermined nodule is large (>4 cm), sonographically suspicious, and carcinoma-specific mutation positive and if the patient has a family history of thyroid cancer and/or self-history of head and neck radiotherapy. Completion thyroidectomy is not always necessary in patients with intrathyroidal papillary thyroid cancer and low-risk follicular thyroid cancer (6). The surgical risk of completion thyroidectomy performed following lobectomy is close or similar to that of total thyroidectomy (7). This study aimed to determine thef adequacy of hemithyroidectomy as an initial surgical method in patients diagnosed with AUS/FLUS and identify the malignancy risk in the initial operation and contralateral malignancy rate after completion thyroidectomy.

Materials and Methods

The medical records of 474 patients who underwent either total thyroidectomy or hemithyroidectomy because of AUS/FLUS cytological results from January 2009 to November 2015 were retrospectively reviewed. Furthermore, 47 patients whose cytology results showed AUS/FLUS and who underwent hemithyroidectomy were enrolled in the study. The demographic characteristics of the patients include age and gender. In laboratory evaluations, thyroid stimulating hormone (normal range: 0.4-4.0 uIU/mL), free thyroxine (normal range: 0.61-1.12 ng/dL), free triiodothyronine (normal range: 1.57-4.71 pg/mL), anti-thyroid peroxidase (anti-TPO) antibody (normal range: <10 IU/mL), and anti-thyroglobulin (anti-TG) antibody (normal range: <30 IU/mL) levels were evaluated. The presence of euthyroidism, hyperthyroidism, and hypothyroidism was evaluated according to the relevant laboratory tests and drug usage information such as levothyroxine, propylthiouracil, and methimazole. The histopathology of these patients was reviewed. The initial malignancy rate was estimated after hemithyroidectomy, and furthermore, the indications of completion thyroidectomy and contralateral malignancy rate were identified. In the light of these data, the selection of hemithyroidectomy was questioned for patients whose histopathology results were benign or showed microcarcinoma and who were in the low-risk group.

Ultrasound

Esaote color Doppler US (model 796FDII; MAG Technology Co. Ltd., Yung-Ho City, Taipei, Taiwan) and superficial probe (model LA523 13-4, 5.5-7.8 MHz) were used for ultrasonographic evaluation. The ultrasonographic characteristics examined were nodule count, nodule diameter (mm), nodule localization (right lobe or left lobe), nodule component (cystic, solid, and mixed), echogenicity (isoechoic, hypoechoic, iso-hypoechoic, heterogeneous, anechoic, and hyperechoic), margin (regular or irregular), calcifications (microcalcification, macrocalcification, and peripheral macrocalcification), presence of halo, and shape (anteroposterior (AP)/transverse (T) ratio). The suspicious ultrasound findings were hypoechogenicity, presence of microcalcification, irregular margin, absence of halo, and appearance of taller than wide (increased AP/T ratio) shape (6).

Fine-Needle Aspiration Biopsy

Ultrasound-guided biopsy (Logic Pro 200 GE and 7.5 MHz probe; Kyunggigo, Korea) was performed for all solid thyroid nodules equal to or larger than 10 mm and smaller than 10 mm but had highly suspicious ultrasound findings using a 27-gauge needle and 20-mL syringe by an experienced endocrinologist. All smears were air-dried.

Cytology

Smears were stained using May-Grunwald Giemsa stain and evaluated by experienced pathologists. The Bethesda system was used for

cytological classification. The patients diagnosed with Bethesda category III (AUS/FLUS) were included in the study (2).

Histopathology

The histopathology of carcinoma, carcinoma variant, carcinoma foci count, and carcinoma diameter (mm) was given in the histopathological data. The patients with a tumor size of <10 mm (microcarcinoma) and papillary carcinoma of follicular, oncocytic, and clear cell variants were considered the low-risk group (6). In this study, the low-risk group refers to patients who do not need completion thyroidectomy following hemithyroidectomy as per the recommendations. The patients with tumor size of ≥10 mm, papillary carcinoma with the tall cell, columnar cell, insular, solid, diffuse sclerosing variants of papillary cancer, and invasive follicular cancer were considered the high-risk group (6).

Statistical Analysis

All statistical analyses were performed using SPSS 15.0 software package (SPSS Inc., Chicago, IL, USA). Descriptive analyses were presented using mean ±standard deviation (SD) for normally distributed variables, median and range (min-max) for non-normally distributed variables, and the number of cases (%) for nominal variables. The approval of the local ethics committee was obtained for this study.

Results

A total of 47 patients whose cytopathology results were AUS/FLUS and who underwent hemithyroidectomy were examined in this study. Out of these patients, 7 (14.9%) were male and 40 (85.1%) were female. The mean age was found to be 40.3±13.3 SD (range: 17-72 years; Table 1).

According to the preoperative thyroid function tests, 38 (80.8) patients had euthyroidism, 1 (2.1%) had hyperthyroidism, and 8 (17%) had hypothyroidism. The number of anti-TPO or anti-TG positive patients was 19 (40.4%), whereas the number of anti-TPO and anti-TG negative patients was 28 (59.6%). The mean nodule count was 1.6±1.2 SD (range: 1-8). A total of 28 (59.6%) patients had a solitary nodule and 19 (40.4%) had multinodular thyroid disease. Among these 19 patients, 3 (6.3%) had bilateral multinodular thyroid disease and 16 (34.1%) had unilateral multinodular thyroid disease.

A total of 48 AUS/FLUS nodules were obtained from 47 patients. The AUS nodules were observed in 32 (66.7%) patients, and the FLUS nodules were present in 16 (33.3%) patients (Table 2). The mean diameter of these nodules was 20.7±11.3 mm (range: 6.6-51.2 mm). In terms of ultrasonographic characteristics, 23 (47.9%) AUS/FLUS nodules were located in the right lobe and 25 (52.1%) were located in the left lobe. The nodule margin was regular in 31 (64.6%) and irregular in 17 (35.4%) nodules. Halo was present in 24 (50%) and absent in remaining 24 (50%) nodules. Peripheral macrocalcification was present in 5 (10.4%) and absent in 43 (89.6%) nodules. Microcalcification was present in 12 (25%) and absent in 36 (75%) nodules. Regarding the nodule component, 45 (93.8%) nodules were solid, 1 (2.1%) was mixed, and 2 (4.2%) were cystic. In terms of nodule echogenicity, 19 (39.6%) nodules were isoechoic, 6 (12.5%) were hypoechoic, 21 (43.8%) were iso-hypoechoic, and 2 (4.2%) were anechoic.

According to the histopathology results of 47 patients diagnosed with AUS /FLUS who underwent hemithyroidectomy, 34 patients (72.3%) were reported to have benign nodules and 13 (27.7%) were reported to have malignant nodules. Out of the 13 patients diagnosed with the malignant

Table 1. Demographics and baseline characteristics of patients.

Sex	
Male	40 (85.1%)
Female	7 (14.9%)
Age	
Mean±SD	40.3±13.3
Range	17-72
Thyroid function test	
Euthyroidism	38 (80.8%)
Hypothyroidism	8 (17%)
Hyperthyroidism	1 (2.1%)
Antibody positivity	
Anti-TPO and/or anti-TG positive	19 (40.4%)
Anti-TPO and anti-TG negative	28 (59.6%)
Size according to nodule number	
Solitary nodule	28 (59.6%)
Multinodular	19 (40.4%)
Bilateral	3
Unilateral	16
Mean nodule number	
Mean±SD	1.6±1.2
Median	1
Range	1-8

nodule, 11 patients (23.4%) underwent completion thyroidectomy and 1 underwent hemithyroidectomy. Furthermore, one patient dropped out of postoperative follow-up (Table 3).

Furthermore, the histopathology results revealed that 12 patients (92.3%) with malignant nodule had papillary carcinoma and 1 (7.7%) had Hurthle cell carcinoma. In terms of papillary cancer variants, seven patients (53.8%) were in the classical papillary variant group, 3 (23.1%) in the follicular variant group, 1 (7.7%) in the solid variant group, and 1 (7.7%) in the encapsulated follicular variant group. Out of 13 patients with the malignant nodule, 9 (19.2%) showed high-risk characteristics and 4 (8.5%) showed low-risk characteristics. However, all patients in the high-risk and low-risk groups underwent completion thyroidectomy, as patients in the low-risk group desire to be comfortable in the follow-up period. According to the histopathology of the contralateral lobe, nine nodules (81.8%) were benign and two (18.2%) were malignant. The mean carcinoma foci count was 1.6±1.5 (1-6), and ten patients (76.9%) had a single focus, 1 (7.7%) had two foci, one (7.7%) had four foci, and one (7.7%) had six foci. Evaluating the patients with multiple foci separately, the patient diagnosed with six foci was found to have a solitary nodule in the preoperative ultrasonographic evaluation and the long axis of the nodule was 37 mm. The patient's pathology was papillary carcinoma follicular variant, and the primary tumor diameter was 30 mm. The remaining cancer foci were millimetric. This patient underwent completion thyroidectomy, and no malignancy was detected in the contralateral lobe. The patient diagnosed with four foci was found to have four nodules (one in the right lobe and three in the left lobe) in the preoperative ultrasonographic evaluation. The histopathology of the single AUS nodule was benign. The tumor was identified as incidental and showed bilaterality, i.e., the histopathology of contralateral lobe was malignant. The tumor histopathology was papillary carcinoma classical variant, and the tumor diameter was 1 to 5 mm in the left lobe and 3 to 6 mm in the right lobe. The patient diagnosed with two foci was found to have a single nodule in the preoperative ultrasonographic evaluation, and the long axis of the nodule was 6.6 mm. The carcinoma diameter was 3 mm and the histopathology was papillary carcinoma classical variant. This patient underwent completion thyroidectomy, and malignancy was detected in the contralateral lobe (papillary cancer, 1 mm). Among the patients diagnosed with one focus and no contralateral malignancy, seven patients were found to have a single nodule and three were found to have two nodules in the preoperative ultrasonographic evaluation. The nodules of these patients were in the same lobe. After hemithyroidectomy and completion thyroidectomy, the mean diameter of dominant carcinoma (n=15) was 13.8±11.5 mm (1-40 mm).

Table 2. Ultrasonographic features of nodules in AUS/FLUS patients.

Cytology (n=48)	
FLUS	16 (33.3%)
AUS	32 (66.7%)
Nodule localization (n=48)	
Right lobe	23 (47.9%)
Left lobe	25 (52.1%)
Nodule diameter (n=48)	
Mean±SD	20.7±11.3 mm
Range	6.6-51.2 mm
Component (n=48)	
Cystic	2 (4.2%)
Solid	45 (93.8%)
Mixed	1 (2.1%)
Echogenicity (n=48)	
Isoechoic	19 (39.6%)
Hypoechoic	6 (12.5%)
Iso-hypoechoic	21 (43.8%)
Anechoic	2 (4.2%)
Border regularity (n=48)	
Regular	31 (64.6%)
Irregular	17 (35.4%)
Peripheral macrocalcification (n=48)	
Present	5 (10.4%)
Absent	43 (89.6%)
Microcalcification (n=48)	
Present	12 (25%)
Absent	36 (75%)
Halo (n=48)	
Present	24 (50%)
Absent	24 (50%)

AUS: Atypia of undetermined significance; FLUS: Follicular lesion of undetermined significance.

Discussion

The American Association of Clinical Endocrinologists, the American Thyroid Association, and the European Thyroid Association recommend surgical treatment for patients with recurrent AUS/FLUS

Table 3. Pathologic characteristics of patients at first surgery and completion thyroidectomy.

Histopathology (n=47)	
Benign	34 (72.3%)
Malignant	13 (27.7%)
Low risk	4 (8.5%)
High risk	9 (19.2%)
Histopathology at completion thyroidectomy (n=11)	
Benign	9 (81.8%)
Malignant	2 (18.2%)
Benign + low risk	38 (80.8%)
Histopathology of carcinoma after hemithyroidectomy and completion thyroidectomy (n=15)	
Papillary cancer	14 (93.3%)
Hurthle cell carcinoma	1 (6.7%)
Carcinoma focus number	
Mean±SD	1.6±1.5
Median	1
Range	1-6
Carcinoma focus distribution	
1	10
2	1
3	0
>4	2
Carcinoma diameter (n=15)	
Mean±SD	13.8±11.5 mm
Range	1-40

results (6,8). The malignancy rate of 5% to15% in these patients leads to different approaches in determining the operation size (2). In addition, a biopsy is performed again and some patients do not undergo surgery because of the benign nodule, which leads to a relative increase in the malignancy rate in operated patients (9). In previous studies, the malignancy rate was between 14.4% and 45.7% for patients with AUS/FLUS nodules (10-14). The differences between the rates are assumed to be caused by ultrasonographic and clinical findings. In this study, the malignancy rate was 27.7%. In a recent study, we reported the malignancy rate as 23.4% (of the 449 operated nodules, 105 were malignant (13). This rate is similar to that found in the study conducted by Kuru et al. (22.8% (14). The malignancy rate was reported to be 28.3% by Layfield et al. (10), 25% by Renshaw et al. (11), 45.7% by PE Vanderlaan et al. (9), and 14.4% by Bongiovanni M (12).

In fact, another factor to be considered in this subject is the application of hemithyroidectomy in patients with a low expectation of malignancy or patients with malignancy but with a satisfactory expectation of prognosis. As this study only included patients who underwent hemithyroidectomy, the malignancy rate was compared only within this group. Ryu et al. conducted a study with 51 patients who underwent hemithyroidectomy because of AUS. In addition, 36 patients had benign nodules and 15 had malignant nodules, which indicate a malignancy rate (29%) similar to that found in this study (15). However, studies including a large patient population are required on this subject. Despite the time period of five years, the number of patients in this study was low, which is because of the fact that total thyroidectomy is the preferred surgical method in our institution, Endocrinology and Metabolism Department of Ankara Yildirim Beyazit University Total thyroidectomy is preferred because of patient and surgeon desire to avoid a possible second surgery because of malignancy risk, ultrasonographic tumor size, and multinodular thyroid presence. Therefore, the majority of patients who underwent hemithyroidectomy in our clinic (57.4%) had a solitary thyroid nodule.

In this study, 23.4% of the patients underwent completion thyroidectomy. In fact, when the need for completion thyroidectomy is considered rela-

tive to the risk groups, the high-risk group constitutes 19.2% of all patients. The difference came from the microcarcinomas with 5 to 9 mm tumour diameter. The completion thyroidectomy is preferred in these patients, considering there may be difficulties related to malignancy follow-up (inability to effectively use laboratory and imaging techniques such as whole-body iodine scan, thyroglobulin, and anti-thyroglobulin), risk of recurrence, or possibility of incidental tumor. The rate of completion thyroidectomy was approximately 11.7% in a study by Ryu et al. (15). In the study with a similar number of patients conducted by Dobrinja et al., the completion thyroidectomy rate was reported to be 10.5% (16). When considered relative to 11 patients who underwent completion thyroidectomy, the contralateral malignancy rate was 18%. Badr Ibrahim et al. found the contralateral malignancy rate to be 48% in patients who underwent hemithyroidectomy (17). In addition, the contralateral malignancy rate was reported to be 44% by Pacini et al. and 36% by Kim et al. (18,19).

Among the patients who underwent hemithyroidectomy, the patients with benign pathology (72.3%) should be considered separately. Hospitalization duration and comorbidities (hypoparathyroidism, vocal cord paralysis, permanent hypothyroidism, and high-dose levothyroxine needs) of these patients may be lower than that of patients who underwent total thyroidectomy (20,21). The frozen section procedure and transition to total thyroidectomy as a result of an intraoperative decision are recommended for patients in the benign group, constituting the majority of patients. A second surgery may be avoided for patients diagnosed with malignant nodules in the frozen section procedure. The frozen section procedure was used for 58 patients with AUS/FLUS in a study conducted by SPosillico et al. and resulted in a definitive benign or malignant diagnosis in 37 (64%) patients. In the latter study, however 32 patients had a benign nodule and the operation was limited to hemithyroidectomy, four patients underwent total thyroidectomy because of malignancy. Furthermore they reported that the frozen section procedure did not produce any results for 36% of the patients, which is a limitation of the procedure (22).

This study has some limitations. The number of patients who underwent hemithyroidectomy is relatively low in our clinic because total thyroidectomy is preferred, which is the major limitation of this study.

Conclusions

In patients with AUS/FLUS, lobectomy is appropriate initially, as 80.8% of the patients are in the benign and low-risk cancer group after surgery. It should be considered that the frozen section procedure may produce more positive results in terms of long-term morbidity in patients with malignant nodules when applied by experienced pathologists. In addition, long-term retrospective studies that evaluate the results of hemithyroidectomy and total thyroidectomy in these patients are necessary. Recurrence and contralateral malignancy rates in patients who underwent hemithyroidectomy should be evaluated using larger patient populations.

Source of Finance: During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest: No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Bekir Çakır, Cevdet Aydın; Design: Muhammet Cüneyt Bilginer, Reyhan Ersoy; Control/Supervision: Oya Topaloğlu, Didem Özdemir, Cevdet Aydın; Data Collection and/or Processing: Cevdet Aydın, Reyhan Ersoy, Bekir Çakır; Analysis and/or Interpretation: Muhammet Cüneyt Bilginer, Gürkan Dumlu, Hayriye Dogan; Literature Review: Bekir Çakır, Reyhan Ersoy; Writing the Article: Didem Özdemir, Muhammet Cüneyt Bilginer; Critical Review: Didem Özdemir, Oya Topaloğlu; References and Fundings: Cevdet Aydın, Bekir Çakır; Materials: Muhammet Cüneyt Bilginer, Gürkan Dumlu, Hayriye Dogan.

References

1. Baloch ZW, Cibas ES, Clark DP, Layfield LJ, Ljung BM, Pitman MB, Abati A. The National Cancer Institute Thyroid fine needle aspiration state of the science conference: a summation. Cytojournal. 2008;5:6.
2. Cibas ES, Ali SZ; NCI Thyroid FNA State of the Science Conference. The Bethesda System for Reporting Thyroid Cytopathology. Am J Clin Pathol. 2009;132:658-665.

3. Tuttle RM, Lemar H, Burch HB. Clinical features associated with an increased risk of thyroid malignancy in patients with follicular neoplasia by fine-needle aspiration. Thyroid. 1998;8:377-383.
4. Tyler DS, Winchester DJ, Caraway NP, Hickey RC, Evans DB. Indeterminate fine-needle aspiration biopsy of the thyroid: identification of subgroups at high risk for invasive carcinoma. Surgery. 1994;116:1054-1060.
5. Kelman AS, Rathan A, Leibowitz J, Burstein DE, Haber RS. Thyroid cytology and the risk of malignancy in thyroid nodules: importance of nuclear atypia in indeterminate specimens. Thyroid. 2001;11:271-277.
6. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG, Sherman SI, Sosa JA, Steward DL, Tuttle RM, Wartofsky L. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2016;26:1-133.
7. Erdem E, Gülçelik MA, Kuru B, Alagöl H. Comparison of completion thyroidectomy and primary surgery for differentiated thyroid carcinoma. Eur J Surg Oncol. 2003;29:747-749.
8. Gharib H, Papini E, Paschke R, Duick DS, Valcavi R, Hegedüs L. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association Medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: executive summary of recommendations. Endocr Pract. 2010;16:468-475.
9. VanderLaan PA, Marqusee E, Krane JF. Clinical outcome for atypia of undetermined significance in thyroid fine-needle aspirations: should repeated fna be the preferred initial approach? Am J Clin Pathol. 2011;135:770-775.
10. Layfield LJ, Morton MJ, Cramer HM, Hirschowitz S. Implications of the proposed thyroid fine-needle aspiration category of "follicular lesion of undetermined significance": a five-year multi-institutional analysis. Diagn Cytopathol. 2009;37:710-714.
11. Renshaw AA. Should "atypical follicular cells" in thyroid fine-needle aspirates be subclassified? Cancer Cytopathol. 2010;118:186-189.
12. Bongiovanni M, Crippa S, Baloch Z, Piana S, Spitale A, Pagni F, Mazzucchelli L, Di Bella C, Faquin W. Comparison of 5-tiered and 6-tiered diagnostic systems for the reporting of thyroid cytopathology: a multi-institutional study. Cancer Cytopathol. 2012;120:117-125.
13. Topaloglu O, Baser H, Cuhaci FN, Sungu N, Yalcin A, Ersoy R, Cakir B. Malignancy is associated with microcalcification and higher AP/T ratio in ultrasonography, but not with Hashimoto's thyroiditis in histopathology in patients with thyroid nodules evaluated as Bethesda Category III (AUS/FLUS) in cytology. Endocrine. 2016;54:156-168.
14. Kuru B, Atmaca A, Tarim IA, Kefeli M, Topgul K, Yoruker S, Elmali M, Danaci M. Risk factors associated with malignancy and with triage to surgery in thyroid nodules classified as Bethesda category III (AUS/FLUS). Eur J Surg Oncol. 2016;42:87-93.
15. Ryu YJ, Jung YS, Yoon HC, Hwang MJ, Shin SH, Cho JS, Lee JS, Kim HK, Kang HC, Lim HS, Yoon JH, Park MH. Atypia of undetermined significance on thyroid fine needle aspiration: surgical outcome and risk factors for malignancy. Ann Surg Treat Res. 2014;86:109-114.
16. Dobrinja C, Trevisan G, Piscopello L, Fava M, Liguori G. Comparison between thyroidectomy and hemithyroidectomy in treatment of single thyroid nodules identified as indeterminate follicular lesions by fine-needle aspiration cytology. Ann Ital Chir. 2010;81:403-410.
17. Ibrahim B, Forest VI, Hier M, Mlynarek AM, Caglar D, Payne RJ. Completion thyroidectomy: predicting bilateral disease. J Otolaryngol Head Neck Surg. 2015;44:23.
18. Pacini F, Elisei R, Capezzone M, Miccoli P, Molinaro E, Basolo F, Agate L, Bottici V, Raffaelli M, Pinchera A. Contralateral papillary thyroid cancer is frequent at completion thyroidectomy with no difference in low- and high-risk patients. Thyroid. 2001;11:877-881.
19. Kim ES, Kim TY, Koh JM, Kim YI, Hong SJ, Kim WB, Shong YK. Completion thyroidectomy in patients with thyroid cancer who initially underwent unilateral operation. Clin Endocrinol (Oxf). 2004;61:145-148.
20. Donatini G, Castagnet M, Desurmont T, Rudolph N, Othman D, Kraimps JL. Partial thyroidectomy for papillary thyroid microcarcinoma: is completion total thyroidectomy indicated? World J Surg. 2016;40:510-515.
21. Osmólski A, Frenkiel Z, Osmólski R. Complications in surgical treatment of thyroid diseases. Otolaryngol Pol. 2006;60:165-170.
22. Posillico SE, Wilhelm SM, McHenry CR. The utility of frozen section examination for determining the extent of thyroidectomy in patients with a thyroid nodule and "atypia/follicular lesion of undetermined significance." Am J Surg. 2015;209:552-556.