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Parenchymal microcalcifications in the thyroid gland

Clinical significance and management strategy

Younghee Yim, PhD[a], Hye Sun Park, PhD[b], Jung Hwan Baek, PhD[b,*], Hyunju Yoo, MD[c], Jin Yong Sung, MD[d]

Abstract

This study is firstly, to investigate the presence of microcalcification among the patients who underwent thyroid ultrasound and biopsy and to evaluate the incidence of intrathyroid lymphatic spread and cervical lymph node metastasis of thyroid cancer with thyroid microcalcifications. Also, we compared the diagnostic performance between fine needle aspiration (FNA) and core needle biopsy (CNB) for assessing parenchymal microcalcifications in the thyroid gland. We retrospectively assessed total 66 patients with thyroid microcalcifications on ultrasound. The histopathologic characteristics of the surgical specimens considered as the gold standard for diagnosing malignancy. Patients with surgically proven malignancy were evaluated for multifocality, intrathyroid lymphatic spread in the opposite lobe, or cervical lymph node metastasis. Among the 66 confirmed patients, 53 patients had malignant lesions (80.3%) and 13 patients had benign lesions (19.7%). The pathologic results of the 44 patients who underwent total thyroidectomy. Among them, 33 patients (75%) showed multifocality, 30 patients (68.2%) showed intrathyroid lymphatic tumor spread. CNB was performed on 41 patients, and FNA was performed on 54 patients. Both CNB and FNA were performed on 29 patients. There were no statistical differences in terms of diagnostic performance between CNB and FNA. Thyroid microcalcifications demonstrate a high prevalence of malignancy. Both CNB and FNA demonstrate similar diagnostic accuracies.

Abbreviations: AUS = atypia of undetermined significance, CNB = core needle biopsy, FLUS = follicular lesion of undetermined significance, FN = follicular neoplasm, FNA = fine-needle aspiration cytology, LN = lymph node, PTC = papillary thyroid carcinoma, SFN = suspicious for follicular neoplasm, US = ultrasound.

Keywords: CNB, FNA, intrathyroid lymphatic spread, lymphnode metastasis, microcalcification, thyroid gland, thyroid neoplasms, thyroid ultrasound

1. Introduction

Parenchymal microcalcifications in the thyroid gland are defined as multiple echogenic dots measuring <1 mm, with or without acoustic shadow on ultrasound (US).[1–3] The microcalcifications in thyroid are one of the predictors of malignancy in thyroid imaging.[4–8] Especially the diffuse sclerosing variant of papillary thyroid carcinoma (PTC), a rare subtype of PTC, can present as diffuse scattered microcalcifications (i.e., the so-called "snowstorm appearance").[7,9] The diffuse sclerosing subtype of PTC frequently involves both lobes of the thyroid gland and demonstrates higher incidence of cervical lymph node (LN) and lung metastasis compare to conventional PTC, thereby resulting in an unfavorable prognosis.[7,9] Pathologically, thyroid parenchymal microcalcifications correspond to clusters of psammoma bodies and they indicate intrathyroid lymphatic tumor spread.[3,10] To the best of our knowledge, there are few published studies that describe the US characteristics of thyroid cancer with diffuse parenchymal microcalcification.[11,12] Although recent study reported presence of thyroid microcalcifications without a nodule is suspicious for PTC,[13] it is limited with small sample size. In addition, previous studies lack data about the incidence of intrathyroid lymphatic spread or cervical LN metastasis of thyroid cancer that manifests as microcalcifications, both of which are important for determining the optimal surgical plan.

Therefore, we evaluated the incidence of multifocal intrathyroid lymphatic spread and cervical LN metastasis of thyroid

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cancer with parenchymal microcalcifications. We also compared the diagnostic performance between fine needle aspiration (FNA) and core needle biopsy (CNB) for assessing parenchymal microcalcifications in the thyroid gland.

2. Materials and methods

2.1. Study population and enrollment criteria

This retrospective study was approved by our institutional review board, which waived the need for informed consent. Since the information included in the study was retrospectively collected and only imaging data were analyzed anonymously, the consent was not obtained. We reviewed 3512 patients who underwent thyroid US and biopsy between March 2005 and November 2010 in a tertiary referral center for pathologically evaluating abnormality detected on prior thyroid imaging. Among them, we reviewed 75 patients who had thyroid parenchymal calcifications with or without definite nodule on US. We excluded 9 patients without final diagnosis. Finally, 66 patients were enrolled (M:F ratio = 7:59; mean age = 39.6 years; range = 25–83 years) (Fig. 1). A malignant lesion was diagnosed if 1 of 3 characteristics was noted: (1) histopathologically confirmed as malignant lesion on surgery; (2) histopathologically confirmed as malignant lesion on both FNA and CNB; or (3) cervical LN metastasis confirmed using FNA. A benign lesion was diagnosed if 1 of 3 characteristics was noted: (1) histopathologically confirmed as benign lesion on surgery; (2) histopathologically confirmed as benign lesion on FNA or CNB, and demonstrated no change on follow-up examinations lasting > 1 year; or (3) histopathologically confirmed as a benign lesion on ≥2 FNA and/or CNB procedures.

All patients underwent FNA (n = 54), CNB (n = 41), or both (n = 29). Subsequent thyroidectomy or follow-up US was performed according to the biopsy results. The incidence of multifocal tumor, intrathyroid lymphatic spread, and cervical LN metastasis were evaluated in patients with confirmed as malignancy on surgery. The diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of both FNA and CNB were evaluated.

2.2. Procedures and assessments

US examinations and US-guided procedures were performed using a 10-MHz linear probe and real-time US system (Aplio SSA-770A; Toshiba Medical Systems, Otawara-shi, Japan) by an experienced thyroid radiologist (18 years of thyroid US experience). In all cases, a comprehensive US evaluation of the thyroid gland was performed.[14] The extent of any microcalcifications and nodule around the microcalcifications were also evaluated. FNA was performed using 21–23-gauge needles. Direct smears were made in all cases, and fixation with alcohol was done immediately. Cellblocks were also made for all aspirates. The operator determined the number of needle passes during the FNA procedure. CNB was performed using a disposable, 18-gauge, double-action, spring-activated needle (1.1- or 1.6-cm excursion) (TSK Ace-cut; Create Medic, Yokohama, Japan). Using the freehand technique, the tip of the biopsy needle was advanced into the edge or within the lesion, and the stylet and cutting cannula of the needle were sequentially fired. A second or third CNB procedure was performed if the lesion was inaccurately targeted or an adequate tissue core could not be determined on visual inspection. Tissue cores were immediately placed in 10% buffered formalin after biopsy and conventionally processed. After biopsy, each patient was observed while applying firm compression to the biopsy site for 20–30 minutes to prevent possible immediate post-procedural complication such as pseudoaneurysm or hematoma.[15–17]

The type of procedure (FNA or CNB) to be performed was determined by the operator based on the location and size of the nodule.

2.3. Cytological and histological analysis

A histopathologist with >10 years of experience evaluated multifocality, the presence of intrathyroid lymphatic spread, and cervical LN metastasis in all surgical thyroid cancer specimens. FNA cytology and CNB histology were also reviewed. Cytological diagnoses were categorized into 6 according to the Bethesda System for Reporting Thyroid Cytopathology: nondiagnostic, benign, AUS (atypia of undetermined significance)/

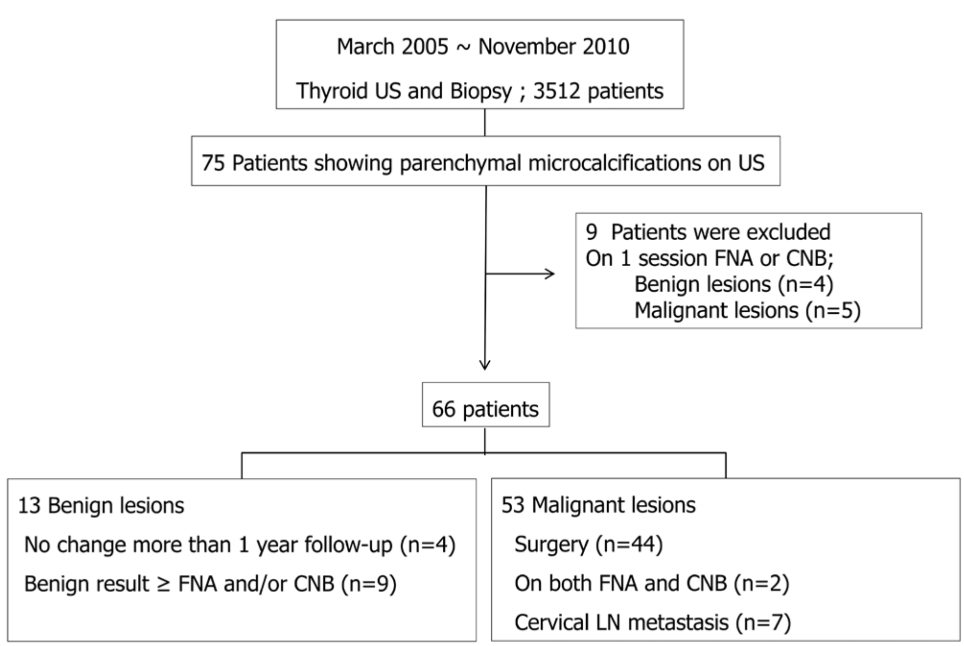

Figure 1. Flowchart for assessing patients with thyroid microcalcifications. CNB = core needle biopsy; FNA = fine-needle aspiration cytology; LN = lymph node; US = ultrasound.

FLUS (follicular lesion of undetermined significance), FN (follicular neoplasm)/ suspicious for follicular neoplasm, malignancy suspected, or malignant.[18]

2.4. Statistical analyses

Differences in the patient characteristics were statistically evaluated using the Fisher exact test for categorical variables or Mann–Whitney test for quantitative variables. We calculated the diagnostic accuracies, sensitivities, specificities, positive predictive values, and negative predictive values of FNA and CNB for the diagnosis of thyroid cancer and compared both groups using the chi-square test. The statistical analyses were performed using SPSS software (version 19.0 for Windows; SPSS, Chicago, IL).

3. Results

Thyroid microcalcifications were detected in 2.1% of patients (75 of 3512 patients). Among 66 finally confirmed patients, 13 patients showed diffuse microcalcification without nodule while 46 patients showed nodule (size range 4–39 mm) with calcifications both inside and outside of the nodule and 7 patients showed nodule (size range 4–14 mm) with microcalcification outside of the nodule. Total 44 patients underwent thyroidectomy (total thyroidectomy 39 patients, partial thyroidectomy 5 patients), and 53 patients had malignant lesions (80.3%) and the last 13 patients had benign lesions (19.7%). All 13 patients with benign results on biopsy were diagnosed as chronic thyroiditis (13 of 13 patients; 100%). 51 patients (96.3%) were confirmed as conventional PTC and 2 patients (3.7%) were confirmed as sclerosing variant (Figs. 2 and 3).

Among 53 patients with thyroid cancer, 8 patients (15.1%) were initially considered as having only microcalcifications without definite nodule on US, but they all have actual nodule in the surgical specimen. When we retrospectively reevaluated, it turns out that aggregated or clustered microcalcifications with focal or parenchymal low-echoic changes in background of the diffuse microcalcifications on US is possible primary focus of cancer.

The total and subgroup baseline characteristics of the FNA and CNB groups are summarized in Table 1. FNA was performed on 54 patients, and CNB was performed on 41 patients. Both FNA and CNB were performed on 29 patients. There were no statistically significant differences in baseline characteristics between the FNA and CNB groups. No immediate or delayed complication was reported after all FNA and CNB procedures.

The pathologic results of the 44 patients who underwent total thyroidectomy are summarized in Table 2. Among 44 patients, 33 patients (75.0%) had multifocal cancer, 30 patients (68.2%) had intrathyroid lymphatic tumor spread, and 34 patients (77.3%) had central or lateral cervical LN metastases. Accordingly, 40 patients (90.9%) had 1 of the 3 following characteristics: multifocal tumors in the contralateral lobe; intrathyroid lymphatic spread to the contralateral lobe; or cervical LN metastases (Figs. 2 and 3).

A comparison of the diagnostic values for thyroid malignancy is included in Table 3. Both FNA and CNB demonstrated acceptable diagnostic accuracies (85.2% vs 97.6%, respectively; P = .086). In addition, there were no false-positive diagnoses of malignancy by either FNA or CNB, and all patients who underwent surgery received a final diagnosis of malignancy. The sensitivity (81.4% vs 96.9%; P = .044) and negative predictive value (57.9% vs 90.0%; P = .001) of CNB were significantly higher than FNA. Eight patients among the FNA group showed AUS or FLUS, while no patient showed AUS findings among the CNB group. Among the 8 patients with AUS or FLUS results on FNA, 7 patients were finally diagnosed with PTC on follow-up CNB (5 of 7 patients) or cervical LN biopsy (2 of 7 patients). The remaining patient was finally diagnosed with a benign lesion (chronic thyroiditis) on follow-up CNB, and the thyroid lesion showed no interval changes at the 1-year follow-up examination.

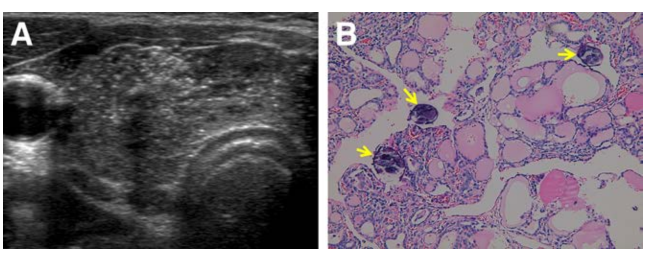

Figure 2. A 37-year-old patient with thyroid cancer. (A) US image showing diffuse scattered thyroid microcalcifications in the right thyroid gland and isthmus. (B) Clusters of psammomma bodies (arrows) were present in the lymphatics, which indicate intrathyroid lymphatic tumor spread. This was diagnosed as the sclerosing variant of PTC.

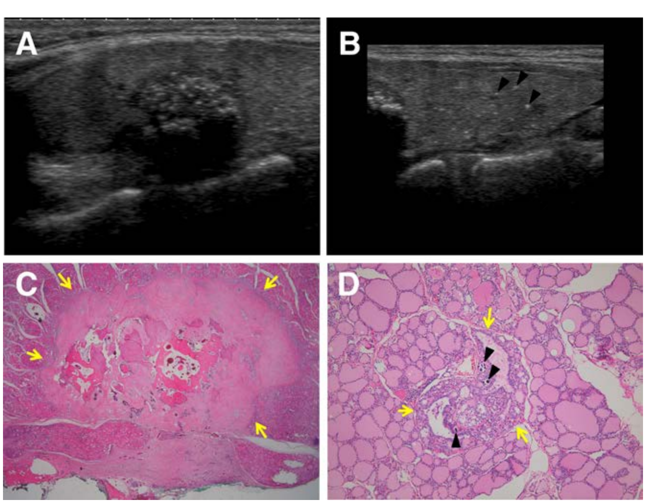

Figure 3. US images showing a hypoechoic nodule with macro- and microcalcifications in the right thyroid gland (A). Scattered thyroid microcalcifications were noted throughout right thyroid gland (arrowheads) (B). On microscopy, osseous metaplasia and dysplastic calcification were noted in the main nodule (C). Tumor emboli (arrows) with psammoma bodies (arrowheads) were noted in the lymphatics (D).

4. Discussion

In our study, the prevalence of thyroid microcalcifications were in 2.1% and the malignancy rate was 80.3% (53 of 66 patients). Both FNA and CNB demonstrated acceptable diagnostic accuracies for detecting malignant thyroid microcalcifications (85.2% vs 97.6%, respectively; P = .086). However, CNB demonstrated higher sensitivity and negative predictive values. PTC with thyroid microcalcifications demonstrated frequent multifocality, intrathyroid lymphatic spread, and cervical LN metastasis on surgical pathology. Even though US might have limitation in documenting the exact extent of microcalcifications and intraglandular tumor spread when compared with final surgical specimen, careful evaluation of US is necessary to have glimpse of the surgical extent decision.

Microcalcifications in the thyroid nodules are one of the predictors of malignancy and are found in up to 50% of thyroid cancer.[7,9,10] Parenchymal microcalcifications are defined as microcalcifications in the thyroid parenchyma, which correspond to clusters of psammoma bodies on pathology and

Table 1

Characteristics of the patients in the FNA and CNB groups.

Characteristic	Total (n = 66)	FNA (n = 54)	CNB (n = 41)	*P**
Age	39.6 ± 11.9 (25–83)	41.1 ± 12.3 (25–83)	40.0 ± 10.6 (25–64)	.738
Sex (M:F)	7/ 59	6/ 49	4/ 37	> .99
Extent of microcalcification				.856
Regional	55	44	34	
Diffuse	11	10	7	
Associated thyroid nodule				.351
Absent	13	10	5	
Present	53	44	36	
Thyroiditis				.303
absent	14	14	7	
present	52	40	34	

CNB = core needle biopsy, FNA = fine-needle aspiration cytology.
**P* value compares FNA vs CNB.

Table 2

Pathologic analysis of all thyroidectomy patients.

Pathologic analysis	n = 44
Multifocality	33 (75.0%)
Ipsilateral	28 (63.6%)
Contralateral	16 (36.4%)
Lymphovascular invasion	30 (68.2%)
Ipsilateral	30 (68.2%)
Contralateral	16 (36.4%)
Surgically confirmed neck LN metastasis	34 (77.3%)
Central lymph node	34 (77.3%)
Lateral lymph node	17 (38.6%)
Contralateral spread or lymphatic invasion or lymph node metastasis	40 (90.9%)

Table 3

Comparison of the diagnostic performances of FNA vs CNB.

	FNA (%)	CNB (%)	*P*
Diagnostic accuracy	85.2	97.6	.086
Sensitivity	81.4	96.9	.044
Specificity	100	100	>.99
Positive predictive value	100	100	> .99
Negative predictive value	57.9	90	.001

CNB = core needle biopsy, FNA = fine needle aspiration.

these can be either benign or malignant. Among benign lesions, chronic thyroiditis is the most common cause.[12] In our study, all 13 patients with benign lesions had chronic thyroiditis. In malignant patients, parenchymal microcalcifications indicate intrathyroid lymphatic tumor spread via lymphovascular invasion.[9,10] The diffuse sclerosing variant of PTC is a rare variant of PTC characterized by diffuse scattered microcalcifications which shows more aggressive nature in younger patients than conventional PTC, and demonstrates a higher incidence of cervical LN metastasis.[6,10,18] In our study, we identified 2 patients with the diffuse sclerosing variant of PTC, and both demonstrated diffuse parenchymal calcification throughout the thyroid gland, multiple cancer foci, intrathyroid lymphatic spread, and cervical LN metastasis. Moreover, several previous studies have reported that PTC demonstrates a high frequency of contralateral tumor foci, which ranges between 36–53%.[19–21] However, we identified 40 patients (90.9%) who had multifocal tumor in the contralateral lobe, intrathyroid lymphatic spread to the contralateral lobe, or cervical LN metastases. In addition, lymphatic spread to the contralateral thyroid gland is detected more often on surgical specimens than on US, and surgical specimens demonstrated calcifications more frequently in the contralateral thyroid gland compared to the US. Considering this discrepancy, US may have limited applications for documenting the extent of microcalcifications and intraglandular tumor spread.[22]

Yoon et al[12] reported acceptable diagnostic performance of US-guided FNA in diagnosing parenchymal microcalcifications which is similar to our study. However, several studies have reported that FNA demonstrates inevitable limitations in tissue sampling and cytological interpretation.[23–27] In our study, CNB demonstrated higher sensitivity and negative predictive value than FNA. These results may be related to the advantages of CNB, which include the larger amount of sampled tissue, less operator dependency if the needle successfully penetrates the nodule, and the capability to assess the histological architecture and relationship to the adjacent thyroid tissue.[28]

A previous study from one referral center reported that 0.08% of 36,523 patients showed thyroid microcalcifications on US,[12] but showed high malignancy rate (61.5–75.7%).[5,12] In this study, we observed thyroid microcalcifications in 2.1% among 3512 patients and the malignancy rate was 80.3%. In our study, 8 of 52 patients (15.1%) were initially considered not having nodules but only thyroid microcalcifications on US. However, all 8 patients had a nodule on surgical pathology. On surgical specimen, focal aggregated or clustered microcalcifications were primary focus of cancer.[29,30] Therefore, targeting this area could increase diagnostic accuracy.

Our study has several limitations. First, this study was designed retrospectively, which can cause selection bias. In addition, this study contains only small sample size which can hamper the statistic result, but this condition is an inevitable due to the rare thyroid US presentation of thyroid microcalcification. Further, the majority of the benign nodules were not confirmed on surgery.

In conclusion, parenchymal microcalcifications in thyroid gland demonstrate high prevalence of malignancy. Considering that these lesions are more likely to be multifocal, do intrathyroid lymphatic spread, and have cervical LN metastasis, management should be carefully decided. Both CNB and FNA demonstrate acceptable diagnostic accuracies, and CNB demonstrates higher sensitivity and negative predictive value.

Author contributions

Conceptualization: Hye Sun Park, Jung Hwan Baek, Hyunju Yoo, Jin Yong Sung.
Data curation: Younghee Yim, Hye Sun Park, Jung Hwan Baek, Jin Yong Sung.
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Methodology: Jung Hwan Baek.
Software: Jung Hwan Baek.
Supervision: Jung Hwan Baek, Hyunju Yoo.
Writing – original draft: Younghee Yim, Hye Sun Park.
Writing – review & editing: Younghee Yim, Jung Hwan Baek, Hyunju Yoo, Jin Yong Sung.

References

[1] Dugan J, Atkinson B, Avitabile A, et al. Psammoma bodies in fine needle aspirate of the thyroid in lymphocytic thyroiditis. Acta Cytol. 1986;31:330–4.
[2] Cooper DS, Tiamson E, Ladenson PW. Psammoma bodies in fine needle aspiration biopsies of benign thyroid nodules. Thyroidology. 1988;(1):55–9.
[3] Triggiani V, Guastamacchia E, Licchelli B, et al. Microcalcifications and psammoma bodies in thyroid tumors. Thyroid. 2008;18:1017–8.
[4] Takashima S, Fukuda H, Nomura N, et al. Thyroid nodules: re-evaluation with ultrasound. J Clin Ultrasound. 1995;23:179–84.
[5] Khoo ML, Asa SL, Witterick IJ, et al. Thyroid calcification and its association with thyroid carcinoma. Head Neck. 2002;24:651–5.

[6] Jung HK, Hong SW, Kim E-K, et al. Diffuse sclerosing variant of papillary thyroid carcinoma. J Ultrasound Med. 2013;32:347–54.
[7] Kim BK, Choi YS, Kwon HJ, et al. Relationship between patterns of calcification in thyroid nodules and histopathologic findings. Endocr J. 2012;60:155–60.
[8] Kwak JY, Jung I, Baek JH, et al. Image reporting and characterization system for ultrasound features of thyroid nodules: multicentric Korean retrospective study. Korean J Radiol. 2013;14:110–7.
[9] Choi YJ, Baek JH, Ha EJ, et al. Differences in risk of malignancy and management recommendations in subcategories of thyroid nodules with atypia of undetermined significance or follicular lesion of undetermined significance: the role of ultrasound-guided core-needle biopsy. Thyroid. 2014;24:494–501.
[10] Schröder S, Bay V, Dumke K, et al. Diffuse sclerosing variant of papillary thyroid carcinoma. Virchows Archiv A. 1990;416:367–71.
[11] Kwak JY, Kim E-K, Son EJ, et al. Papillary thyroid carcinoma manifested solely as microcalcifications on sonography. Am J Roentgenol. 2007;189:227–31.
[12] Yoon JH, Kim E-K, Son EJ, et al. Diffuse microcalcifications only of the thyroid gland seen on ultrasound: clinical implication and diagnostic approach. Ann Surg Oncol. 2011;18:2899–906.
[13] Whittle C, García M, Horvath E, et al. Thyroid microcalcifications in the absence of identifiable nodules and their association with thyroid cancer. J Ultrasound Med. 2019;38:97–102.
[14] Choi SH, Kim E-K, Kim SJ, et al. Thyroid ultrasonography: pitfalls and techniques. Korean J Radiol. 2014;15:267–76.
[15] Jung CK, Baek JH. Recent advances in core needle biopsy for thyroid nodules. Endocrinol Metab. 2017;32:407–12.
[16] Baek JH. Current status of core needle biopsy of the thyroid. Ultrasonography. 2017;36:83–5.
[17] Na DG, Baek JH, Jung SL, et al. Core needle biopsy of the thyroid: 2016 consensus statement and recommendations from Korean Society of Thyroid Radiology. Korean J Radiol. 2017;18:217–37.
[18] Fujimoto Y, Obara T, Ito Y, et al. Diffuse sclerosing variant of papillary carcinoma of the thyroid: Clinical importance, surgical treatment, and follow-up study. Cancer. 1990;66:2306–12.
[19] Kim ES, Kim TY, Koh JM, et al. Completion thyroidectomy in patients with thyroid cancer who initially underwent unilateral operation. Clin Endocrinol (Oxf). 2004;61:145–8.
[20] Pacini F, Elisei R, Capezzone M, et al. Contralateral papillary thyroid cancer is frequent at completion thyroidectomy with no difference in low-and high-risk patients. Thyroid. 2001;11:877–81.
[21] Pasieka JL, Thompson NW, McLeod MK, et al. The incidence of bilateral well-differentiated thyroid cancer found at completion thyroidectomy. World J Surg. 1992;16:711–6; discussion 716.
[22] Kwak J, Kim EK, Hong S, et al. Value of specimen radiographs in diagnosing multifocality of thyroid cancer. Br J Surg. 2010;97:517–24.
[23] Sung JY, Na DG, Kim KS, et al. Diagnostic accuracy of fine-needle aspiration versus core-needle biopsy for the diagnosis of thyroid malignancy in a clinical cohort. Eur Radiol. 2012;22:1564–72.
[24] Renshaw AA, Pinnar N. Comparison of thyroid fine-needle aspiration and core needle biopsy. Am J Clin Pathol. 2007;128:370–4.
[25] Ha EJ, Baek JH, Lee JH, et al. Core needle biopsy can minimise the non-diagnostic results and need for diagnostic surgery in patients with calcified thyroid nodules. Eur Radiol. 2014;24:1403–9.
[26] Hakala T, Kholová I, Sand J, et al. A core needle biopsy provides more malignancy-specific results than fine-needle aspiration biopsy in thyroid nodules suspicious for malignancy. J Clin Pathol. 2013;66:1046–50.
[27] Trimboli P, Nasrollah N, Guidobaldi L, et al. The use of core needle biopsy as first-line in diagnosis of thyroid nodules reduces false negative and inconclusive data reported by fine-needle aspiration. World J Surg Oncol. 2014;12:61.
[28] Na DG, Kim J-h, Sung JY, et al. Core-needle biopsy is more useful than repeat fine-needle aspiration in thyroid nodules read as nondiagnostic or atypia of undetermined significance by the Bethesda system for reporting thyroid cytopathology. Thyroid. 2012;22:468–75.
[29] Feine U, Lietzenmayer R, Hanke JP, et al. Fluorine-18-FDG and iodine-131-iodide uptake in thyroid cancer. J Nucl Med. 1996;37:1468–72.
[30] Nahas Z, Goldenberg D, Fakhry C, et al. The role of positron emission tomography/computed tomography in the management of recurrent papillary thyroid carcinoma. Laryngoscope. 2005;115:237–43.