Endocrine (2019) 65:365–370
https://doi.org/10.1007/s12020-019-01973-2

ORIGINAL ARTICLE

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Thyroid core needle biopsy: patients' pain and satisfaction compared to fine needle aspiration

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Received: 27 March 2019 / Accepted: 27 May 2019 / Published online: 15 June 2019

Abstract

Purpose The purpose of this study was to compare patients' pain and satisfaction of fine needle aspiration (FNA) and core needle biopsy (CNB) for a thyroid nodule.

Methods We consecutively enrolled patients with thyroid nodules who underwent ultrasound-guided FNA or CNB in our institution. The patients answered a questionnaire about pain scores during the procedure, immediately after the procedure and 20 min after the procedure, and any complication after the biopsy. Through a phone interview which was conducted 2 weeks after the procedure, a researcher asked the patients about residual pain and overall subjective satisfaction score about the procedures. Patients were also asked to report any complication or complaint after the procedures on the phone interview.

Results The 167 patients who had undergone thyroid FNA ($n = 87$) or CNB ($n = 80$) were included. The pain scores were not significantly different between the two groups during the procedure and after the procedure. Overall satisfaction scores after 2 weeks were not different, either. There was no acute or delayed major complication in both groups.

Conclusions Differences regarding patients' pain and satisfaction scores between CNB and FNA were not demonstrated.

Keywords Thyroid nodule · Fine needle aspiration · Core needle biopsy · Pain

Introduction

The detection of thyroid nodules has become increased with the introduction of high-resolution ultrasound (US) devices. Thyroid nodules are detected in 4–8% of the general population via palpation, while in 19–67% of the general population via the US [1–3]. Once detected, determining whether the nodule is cancerous, which is diagnosed in 9–15% of the nodules via fine-needle aspiration (FNA) biopsy, is clinically important [1–4]. Most differentiated thyroid cancers harbor a rather favorable prognosis if identified in the early stages [5]. However, if identified in the advanced stage IV, the 30-year mortality rate may go up to 65% [6].

FNA is a standard initial diagnostic tool for thyroid nodules due to its cost-effectiveness, low complication rate, and rapid preoperative investigation [7, 8]. However, the technique produces indeterminate cytologic results ranging from 15 to 42%, as well as nondiagnostic aspirates, ranging from 10 to 33.6% [9]. Recently, core needle biopsy (CNB) has been suggested as an alternative diagnostic technique for thyroid nodules, especially for those initially showing nondiagnostic specimen or indeterminate cytologic results [10–13]. Several studies have reported that CNB, as opposed to FNA, has lower rates of inconclusive results and a higher diagnostic accuracy [14–17]. However, there are concerns about the risks associated with CNB; in particular, the risk of hemorrhagic complications [18]. Moreover, subjective pain and satisfaction of patients undergoing CNB have not been thoroughly evaluated. Hence, the purpose of this study was to compare pain, satisfaction, and complications between patients with thyroid nodules who underwent FNA and CNB procedures.

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Materials and Methods

Patients

This study was approved by the institutional review board. All participants provided written informed consent. We consecutively enrolled patients with thyroid nodules who underwent US-guided FNA or CNB at our institution between July and December of 2015. The selection of biopsy procedure (FNA or CNB) was based on the operator's preference. Patients who did not answer questionnaires on the day of the procedure or those who did not participate in the phone interview 2 weeks after the procedure were excluded. Finally, 87 patients who underwent FNA and 80 patients with CNB were included in the study.

FNA or CNB procedures

Three board-certified radiologists (with 5–19 years of experience) performed either FNA or CNB, after a thorough review of all relevant imaging studies. Before the procedure, patients taking aspirin were asked to cease medication for 5 days. Subcutaneous lidocaine was injected in all patients. All procedures were conducted using US guidance. IU 22 diagnostic US system, with a 5–12 MHz linear probe (Philips Medical Systems, Netherlands), was used. For FNA, a 26-gauge needle with a syringe was employed. The needle was placed in the nodule and moved finely for several seconds. For CNB, an 18-gauge semiautomated biopsy needle (TSK Acecut; Create Medic, Yokohama, Japan) was utilized. One to three needle passes were made for CNB. The number of CNB specimens was determined by examining the gross core specimen by the operator. After the FNA or CNB, the patient compressed puncture site for 20 min, and US was performed after 20 min to evaluate post-procedural hemorrhage [19].

Questionnaire and phone interview

A questionnaire was designed specifically for this study. The questionnaire included questions regarding the followings: 1) Procedure-related pain at three time points—during the procedure, immediately after the procedure, and 20 min after the procedure and 2) any inconvenience or complication after the biopsy. The pain was scored with a visual pain scale of 0 to 10 (0, no pain at all; 10, the most severe pain). A researcher who was blind to the patients' procedure asked the questions when the patient finished the 20-minute manual compression of the puncture site. When discharged after the biopsy, patients were informed of a phone interview, which was scheduled 2 weeks after the procedure. In the phone interview, a researcher asked about residual pain and overall satisfaction score for the experience of biopsy procedure (evaluated as a scale of 0 to 10; 10, the most satisfied). Patients also had a chance to report any delayed procedure-related complications during the phone interview, if they had experienced any. Major complications were defined as complications that needed hospitalization, medical or surgical intervention. The results were compared between the FNA and CNB groups.

Cytopathologic results

Cytopathologic results were categorized following the Bethesda system; category 1, nondiagnostic or unsatisfactory; category 2, benign; category 3, atypia of undetermined significance [AUS] or follicular lesions of undetermined significance [FLUS]; category 4, follicular neoplasm or suspicious for a follicular neoplasm; category 5, suspicious for malignancy; category 6, malignant. The Bethesda system for CNB has not been standardized for thyroid nodules. For this study, reporting system by the Korean Endocrine Pathology Thyroid Core Needle Biopsy Study Group was employed [20]; CNB histology diagnoses were categorized into six categories; category 1, nondiagnostic or unsatisfactory; category 2, benign lesion; category 3, indeterminate lesion; category 4, follicular neoplasm or suspicious for a follicular neoplasm; category 5, suspicious for malignancy; category 6, malignant.

Imaging characteristics of thyroid nodules

One radiologist who was blind to the biosy procedure of patients or cytopathologic results reviewed the US images. The image characteristics of the nodules were described based on the guidelines set forth by Korean Society of Thyroid Radiology [21]; accordingly, internal content was classified as follows: Solid, predominantly solid, predominantly cystic, and cystic; shape as follows: Ovoid-round, taller than wide, and irregular; margin as follows: Smooth, spiculated or microlobulated, and ill-defined; echogenicity as follows: Markedly hypoechogenicity, hypoechogenicity, isoechogenicity, hyperechogenicity, and anechogenicity (pure cyst); and calcification as follows: Microcalcification, macrocalcification, micro and macrocalcification, rim calcification, and no calcification. Based on these characteristics, the nodules were categorized into either (1) suspicious malignant nodules (if the nodule satisfied at least one of the following; taller than wide, spiculated, markedly hypoechoic, micro or macrocalcified), (2) probably benign nodules (if the nodule did not have a suspicious malignant feature and satisfied one of the follows; spongiform, cystic or predominantly cystic), and (3) indeterminate nodules (if the nodules were not classified into suspicious malignant nodules or probably benign nodules).

Statistics

Statistical procedures were performed using a commercially available software package (SPSS 19.0. IBM Corp., Armonk, NY). The comparison between the CNB and FNA groups was made utilizing independence sample's T-test, and Chi-square test. Chi-square test was also conducted within each group when needed to determine whether there is a significant association between the characteristics of thyroid nodules and inconclusive cytopathologic results.

Results

Patients

A total of 167 patients who had undergone thyroid FNA ($n = 87$, 11 males, age 52.51 ± 13.38) or CNB ($n = 80$, 19 males, age 51.55 ± 11.24) were included. Table 1 demonstrates the US findings for examined thyroid nodules. There were no differences in the distribution of shape, margin, and echogenicity of the nodules between the two groups. In the FNA group, nodules with cystic internal content or predominantly cystic internal content ($p = 0.031$) and nodules without calcification ($p = 0.043$) were more frequent. In the CNB group, solid nodules were more frequent ($p = 0.039$). In the US-based category for malignancy risk, nodules with suspicious malignant features were more frequently observed in the CNB group (37 in FNA and 54 in CNB, $p = 0.002$), and nodules in the probably benign category were more common in the FNA group (14 in FNA and 2 in CNB, $p = 0.007$).

Pain and satisfaction scores

The pain scores were not significantly different between the two groups during the procedure and immediately after the procedure (mean score ± standard deviation, FNA vs. CNB; during the procedure, 2.91 ± 1.48 vs. 2.53 ± 1.79; immediate after the procedure, 1.44 ± 1.56 vs. 1.46 ± 1.79; 20 min after the procedure, 0.86 ± 0.84 vs. 0.89 ± 1.14, all $p > 0.05$), (Table 2). The pain scores at 2 weeks after the procedure were also not significantly different between the two groups (mean score ± standard deviation, FNA vs. CNB; 0.64 ± 1.00 vs. 0.54 ± 0.95, $p = 0.52$). The overall satisfaction scores after 2 weeks were not different between the two groups (mean score ± standard deviation, FNA vs. CNB; 7.95 ± 1.93 vs. 8.28 ± 1.71, $p = 0.39$), either.

Complications

In both groups, there was no case of major complication. In the FNA group, four patients had minor complications—nausea ($n = 1$), vomiting ($n = 1$), headache ($n = 1$), and sore throat ($n = 1$)—on the day of the procedure. One patient reported a minor complication—bruise that persisted for 3 days after the procedure—during the phone interview. In the CNB group, four patients had minor complications—dizziness ($n = 2$), bruising ($n = 1$), and sore throat ($n = 1$)—on the day of the procedure. One minor complication—bruise that lasted for 7 days after the procedure—was reported in the phone interview. On the post-procedural US, capsular hematoma was found in 3 cases with FNA and 2 cases with CNB. There was no case of parenchymal hemorrhage.

Cytopathologic results

The rate of the nondiagnostic or unsatisfactory specimen was significantly higher in the FNA group (14 in FNA and 0 in CNB, $p = 0.001$) on cytopathologic results (Table 3). Benign result was more prevalent in the FNA group ($p = 0.011$) and malignancy was more prevalent in the CNB group ($p = 0.002$).

Discussion

In this study, patients' pain, overall satisfaction, and complication rate were comparable between thyroid CNB and FNA. There has been a paucity of studies that investigated the difference of subjective experience of patients between FNA and CNB procedures in thyroid nodules. Nasrollah et al. reported that there was no significant difference in patients' tolerability between CNB and FNA when patients' subjective tolerability was measured 2 weeks after each procedure [22]. Stangierski et al. reported that most patients who underwent CNB experienced moderate pain based on the visual analog scale [23]. Our results are in line with the two previous reports. Regarding the evolution of pain, more patients experienced pain during CNB than FNA for the first minutes, and the pain subsided at later time points [22, 23]. In our study, the temporal change of pain was also noted. The pain was most severe during the biopsy and gradually subsided at immediate after the procedure and 20 min after the procedure. The remaining pain after 20 min scored less than 1 point.

CNB has emerged as a useful complementary tool to acquire pathologic results of thyroid nodules, reducing nondiagnostic or indeterminate results. Several reports have suggested the efficacy of CNB after inconclusive FNA [10–13]. Samir et al. reported that CNB compared with repeated FNA, showed a significantly higher diagnostic yield in subjects with prior nondiagnostic FNA result [11]. Na et al. reported subsequent CNB had significantly lower AUS/FLUS result compared with repeat FNA in patients with

Table 1 US findings of the examined thyroid nodules

Variables	FNA ($n = 87$)	CNB ($n = 80$)	p value
Age, years	52.5 ± 13.4	51.5 ± 11.2	0.063
Male, *n*	11	19	0.096
US findings			
Shape			
Ovoid-round, *n* (%)	74 (85.0)	61 (76.2)	0.212
Taller than wide, *n* (%)	11 (12.6)	18 (22.5)	0.140
Irregular, *n* (%)	2 (2.3)	1 (1.2)	1.000
Margin			
Smooth, *n* (%)	34 (39.1)	22 (27.5)	0.156
Spiculated or microlobulated, *n* (%)	12 (13.7)	20 (25.0)	0.101
Ill-defined, *n* (%)	41 (16.1)	38 (47.5)	1.000
Echogenecity			
Markedly hypoechoic, *n* (%)	9 (10.3)	4 (5.0)	0.318
Hypoechoic, *n* (%)	41 (47.1)	45 (56.2)	0.306
Isoechoic, *n* (%)	34 (39.1)	28 (35.0)	0.700
Hyperechoic, *n* (%)	0 (0)	3 (3.7)	0.215
Anechoic (pure cystic), *n* (%)	3 (3.4)	0 (0)	0.274
Calcification			
Microcalcification, *n* (%)	16 (18.4)	25 (31.3)	0.080
Macrocalcification, *n* (%)	6 (6.9)	12 (15.0)	0.151
Micro and macrocalcification, *n* (%)	5 (5.7)	1 (1.3)	0.253
Rim calcification, *n* (%)	1 (1.1)	1 (1.3)	1.000
None, *n* (%)	59 (67.8)	41 (51.2)	0.043
Internal content			
Solid, *n* (%)	64 (73.5)	70 (87.5)	0.039
Predominantly solid, *n* (%)	12 (13.8)	8 (10.0)	0.606
Predominantly cystic, *n* (%)	9 (10.3)	2 (2.5)	0.084
Cystic, *n* (%)	2 (2.3)	0 (0)	0.514
US category			
Suspicious malignant, *n* (%)	37 (42.5)	54 (67.5)	0.002
Indeterminate, *n* (%)	36 (41.4)	24 (30.0)	0.171
Probably benign, *n* (%)	14 (16.1)	2 (2.50)	0.007

US ultrasonographic, *FNA* fine needle aspiration, *CNB* core needle biopsy

Table 2 Pain and overall satisfaction scores

Outcomes	FNA ($n = 87$)	CNB ($n = 80$)	p value
Pain score			
During the procedure	2.90 ± 1.48	2.53 ± 1.79	0.177
Immediate after the procedure	1.44 ± 1.56	1.46 ± 1.79	0.284
20 minutes after the procedure	0.86 ± 0.84	0.89 ± 1.14	0.265
2 weeks after the procedure	0.64 ± 1.00	0.54 ± 0.95	0.517
Overall satisfaction score	7.95 ± 1.93	8.25 ± 1.71	0.391

FNA fine needle aspiration, *CNB* core needle biopsy

prior AUS/FLUS FNA result [10]. Several studies have reported that CNB is useful even as a first-line diagnostic technique. CNB has proven to be comparable to FNA concerning complication rate, the rate of inconclusive results, and diagnostic accuracy [16, 24].

There have been concerns about safety of CNB using large bore needle. Early literatures reported serious complications including post-biopsy hematomas, bleeding from the incision site, pain, infections, transient hemoptysis, and nerve injuries [9]. However, in the recent literatures with large case series, complication rates associated with CNB are low, ranging from 0.5% to 1.0%, similar to those of FNA [9, 14–17, 19, 25–28]. According to recent meta-analysis, the pooled proportion of major complications was 0.06% whereas that of minor complications was 1.08% [28]. From the 14,818 patients, six major complications were reported including two cases of permanent voice change, three cases of hematoma requiring hospitalization, and a case of pseudoaneurysm, Various minor

Table 3 Complications after the procedure

Complications	FNA ($n = 87$)	CNB ($n = 80$)
Major complication requires intervention	0	0
Minor complications reported on the day of procedures	4	4
Nausea, vomiting	2	0
Headache, dizziness	1	2
Sore throat	1	1
Bruise	0	1
Minor complications reported on the 2 weeks interview		
Bruise	1	1
Subcapsular hematoma on the post-procedural ultrasound	3	2

FNA fine needle aspiration, *CNB* core needle biopsy

complications were reported including hematomas, transient voice changes, bleeding from the carotid injury, tracheal punctures, dysphagia, biopsy site infections, hemoptysis and edema [28]. In contrast to older literature regarding the safety of CNB procedures for thyroid nodules, the improved safety of the CNB procedure is probably attributable to the technical enhancements, such as the improvements in biopsy needles and US technology [19, 24].

There are several limitations in our study. First, the number of patients was small. Second, the selection of biopsy procedure was made by the operator's preference, and it was the source of selection bias. On analysis of US features, nodules with probably benign US features were assigned more frequently to FNA group and nodules with suspicious malignant US features were assigned more frequently to CNB group, therefore the pathologic results were different between the two groups. Third, we did not compare the economic burden on patients between FNA and CNB. The economic burden may pose to be an important factor for patients' decision on satisfaction. Therefore, future studies considering these limitations are necessary.

In conclusion, differences regarding patients' pain and satisfaction scores and complications between CNB and FNA were not demonstrated.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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