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Original Article

Ultrasound-Guided Core Needle Biopsy versus Fine-Needle Aspiration Biopsy for Thyroid Nodules

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Abstract

Objective: The use of core needle biopsy (CNB) may help overcome limitations of fine needle aspiration biopsy (FNAB) for thyroid nodules. The aim of the present study was to compare ultrasound-guided (US-G) CNB with US-G FNAB in terms of diagnostic adequacy based on the 2017 Bethesda System for Reporting Thyroid Cytopathology (the 2017 Bethesda System).

Patients and Methods: A retrospective cohort study of two groups of patients with thyroid nodules who underwent US-G FNAB and CNB at Pakkred Community Hospital between January 1, 2017 to December 31, 2020 was performed. The two groups were compared in terms of diagnostic adequacy.

Results: There were 31 patients in each group. In the CNB group, adequate results in terms of the 2017 Bethesda System were obtained in 77% of patients, while FNAB yielded only 26% adequacy, a statistically significant difference ($p < 0.001$). Size of the thyroid nodule greater than 2 cm was significantly related to increased adequacy. Cystic or solid or mixed composition of nodules did not significantly impact adequacy.

Conclusion: Ultrasound-guided CNB performed better than FNAB in terms of adequate biopsy results based on the 2017 Bethesda System.

Keywords: Core needle biopsy, Fine needle aspiration biopsy, Thyroid nodule

Introduction

Thyroid nodules are a common clinical problem. The prevalence of thyroid nodules is 4% to 7% of the population.[1,2] The incidence of thyroid nodules is 0.8% annually, commonly found in women.[1,2] The probability of thyroid cancer in thyroid nodules is 7% to 15% depending on age, gender, previous radiation exposure, family history, and other factors.[3] Thyroid ultrasound (US) plays a key role in determining characteristics of thyroid nodules in terms of size, solid or cystic composition, as well as to help guide biopsy.

US-guided biopsy can help diagnose whether a thyroid nodule is benign or malignant.[3] The more tissue sample is obtained, the more accurate the diagnosis. The diagnosis of thyroid nodule is usually based on the 2017 Bethesda System for Reporting Thyroid Cytopathology (the 2017 Bethesda System). There are six categories of diagnosis: B1: nondiagnostic (ND) or unsatisfactory (UNS); B2: benign; B3: atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS); B4: follicular neoplasm (FN) or suspicious for follicular neoplasm (SFN); B5: suspicious for malignancy (SUS); and B6: malignancy.[4,5]

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In terms of adequacy, benign, FN/SFN, SUS, and malignant categories (B2, B4-6) are considered adequate biopsy results, representing enough tissue to make a definitive diagnosis. Inadequate results consist of ND/UNS and AUS/FLUS categories (B1, B3), which may require re-biopsy or excision.

Fine needle aspiration biopsy (FNAB) is a biopsy method using an 18-gauge needle under negative pressure to collect cellular tissue from different parts of the thyroid nodule, usually done under US guidance. It is a simple procedure with few complications and is recommended as a first-line biopsy method when a thyroid nodule is suspected of being cancerous. However, results of FNA are often inadequate.[1,6] When a finding is inadequate or indeterminate, FNA can be repeated until a determinate result is obtained.[4-5] In some cases, surgeons may need to perform excisions because of persistent inadequate FNA results.

Core needle biopsy (CNB) is an alternative biopsy method using a biopsy gun, and an 18 gauge needle, to enable more tissue to be removed, also usually done under US guidance. It is commonly used for solid tumors, providing higher diagnostic accuracy than FNAB. CNB can often obtain adequate tissue to determine whether the nodule is benign or malignant. It is expected to be more accurate than FNAB.[8-19]

The aim of the present study was to compare the diagnostic effectiveness between CNB and an FNAB, under US guidance, in terms of adequate biopsy results for thyroid nodules, based on the 2017 Bethesda System. A secondary aim is to identify factors related to obtaining adequate biopsy results.

Patients and Methods

The present study is a retrospective cohort study of patients with thyroid nodules seen at the surgical clinic of Pakkred Community Hospital, Nonthaburi, Thailand. The data is collected from medical records of patients who underwent an ultrasound-guided FNA and/or CNB from January 1st, 2017 to December 31st, 2020, obtaining diagnosis based on the 2017 Bethesda System. Under a type I error of 5% and type II error of 20%, and the assumed proportion of adequate biopsy for of 67% and 33% for CNB and FNAB respectively, the sample size is at least 29 patients per group. Thus, a sample size of 31 patients per group or 62 patients overall is sufficient.

Biopsies were obtained under local anesthesia using a portable US machine, an 18-gauge needle, and a 10-mL syringe for FNAB (Figure 1), or a biopsy gun with an 18-gauge biopsy gun needle for CNB (Figure 2). All patients were placed in a supine position with hyperextended neck and a pillow under the shoulders. Lidocaine was used for local anesthesia. For FNAB, an 18-gauge needle under manual negative pressure was placed in the thyroid nodules for tissue sampling. If a cystic nodule is found, all fluid in the cyst was removed. When a solid nodule is found, samples were drawn from 2 to 3 different directions. Tissue samples from FNAB were smeared onto glass slides and fixed in 95% alcohol to be examined under the microscope. For CNB, a biopsy gun and an 18-gauge biopsy gun needle were used for obtaining tissue samples. Tissue obtained from CNB were fixed in formalin for microscopic examination.

Data collected included age, gender, thyroid function test, size of thyroid nodules, and solid/cystic composition of thyroid nodules as seen on US.

Figure 1 An 18-gauge needle and a 10 mL syringe

Figure 2 A biopsy gun and an 18-gauge biopsy gun needle

The outcome was categorized as adequate or inadequate biopsy result, as previously defined. Data were compared between the two biopsy methods. Summary statistics were in terms of frequency and percentage or mean and standard deviation (SD) as appropriate. Chi-squared test or Fisher's exact test was used for categorical data and unpaired *t*-test for quantitative data. Statistical significance was defined as a *p*-value less than 0.05.

Results

Sixty-five patients underwent US-guided biopsy of the thyroid nodule during the period under study. Three were excluded due to loss to follow-up and lack of US results. A total of 62 patients were included in the study, with 31 patients in each of the CNB and FNAB groups. Clinical characteristics of 62 patients are shown in Table 1. The majority of patients were women (84%). The average age was 50.4 ± 16.4 years (range, 12 to 78 years). The average thyroid stimulating hormone (TSH) level was 1.43 ± 1.04 uIU/mL and the average free thyroxine (FT4) level was 1.16 ± 0.28 ng/dL. There were no significant differences between the CNB and FNAB groups in terms of age, gender, TSH and FT4 levels.

Characteristics of all 62 thyroid nodules are also shown in Table 1. The average size of thyroid nodules was 2.9 ± 1.2 cm (range, 1 to 7 cm). The composition of thyroid nodules on US examination included pure solid component in 29 (47%), mixed solid and cystic components in 17 (27%), and pure cystic lesion in 16 patients (26%). None of these characteristics were significantly different between the two groups.

Overall, B1, B2, B3, B4, B5 and B6 categories were seen in 29 (47%), 28 (45%), 1 (2%), 1 (2%), 2 (3%), and 1 (2%) patients, respectively. The major differences between CNB and FNAB in terms of these outcomes were that for CNB, 6 (19%) and 20 (65%) patients were in categories B1 and B2, respectively, while for FNAB 23 (74%) and 8 (26%) were in categories B1 and B2. Thus, there was a significantly higher proportion of adequate biopsy results in the CNB group (28/31 or 77%) than in the CNB group, (7/31 or 23%) ($p < 0.001$; see Table 2).

Table 1 Clinical characteristics of patients

Characteristic	Overall (N = 62)	CNB (N = 31)	FNA (N = 31)	*p*-value
Women: number (%)	52 (84)	27 (87)	25 (81)	0.490
Age (years): mean ± SD	50.4 ± 16.4	50.4 ± 17.9	50.5 ± 15.0	0.981
TSH (uIU/mL): mean ± SD	1.43 ± 1.04	1.51 ± 1.11	1.35 ± 0.99	0.552
FT4 (ng/dL): mean ± SD	1.16 ± 0.28	1.16 ± 0.32	1.16 ± 0.24	0.999
Size (cm): mean ± SD	2.9 ± 1.2	3.0 ± 1.2	2.7 ± 1.2	0.329
Composition of thyroid nodule:				
Solid: number (%)	29 (47)	18 (58)	11 (36)	0.135
Solid-cystic: number (%)	17 (27)	8 (26)	9 (29)	
Cystic: number (%)	16 (26)	5 (16)	11 (36)	

SD: standard deviation; TSH: thyroid stimulating hormone; FT4: free thyroxine; CNB: core needle biopsy; FNA: fine needle aspiration

Table 2 Diagnosis of thyroid nodules according to the 2017 Bethesda System

Diagnosis: number (%)	Overall (N = 62)	CNB (N = 31)	FNA (N = 31)	*p*-value
B1: ND/UNS	29 (45)	6 (19)	23 (74)	< 0.001*
B2: Benign	28 (45)	20 (65)	8 (26)	
B3: AUS/FLUS	1 (2)	1 (3)	0	
B4: FN/SFN	1 (2)	1 (3)	0	
B5: SUS	2 (3)	2 (7)	0	
B6: Malignant	1 (2)	1 (3)	0	
Adequate results (B2 & B4-6)	32 (52)	24 (77)	8 (26)	< 0.001

*Fisher's exact test; ND: nondiagnostic; UNS: unsatisfactory; AUS: atypia of undetermined significance; FLUS: follicular lesion of undetermined significance; FN: follicular neoplasm; SFN: suspicious for follicular neoplasm; SUS: suspicious for malignancy; CNB: core needle biopsy; FNA: fine needle aspiration

Overall, the only factor significantly associated with adequate biopsy result was size of thyroid nodule larger than 2 cm. US findings of cystic and/or solid component did not significantly relate to adequacy (Table 3). In the CNB group, the nodule size (larger than 2 cm) was also significantly related to adequate biopsy results, but cystic/solid components were of borderline significance (Table 4). In the FNAB group, neither nodule size nor cystic/solid components were significantly related to adequate biopsy results. While solid nodules were more likely to yield adequate biopsy in the FNAB group, as might be expected, this seemed not to be the case in the CNB group.

Table 3 Factors related to adequate biopsy results: all patients

Factor	Overall (N = 62)	Inadequate results (N = 30)	Adequate results (N = 32)	*p*-value
Size > 2 cm: number (%)	**44 (71)**	**17 (57)**	**27 (84)**	**0.016**
Composition: number (%)				0.395
Solid	29 (47)	12 (40)	17 (53)	
Solid-cystic	17 (27)	8 (27)	9 (28)	
Cystic	16 (26)	10 (33)	6 (19)	

Table 4 Factors related to adequate biopsy results: core needle biopsy (CNB)

Factor	CNB (N = 31)	Inadequate results (N = 7)	Adequate results (N = 24)	*p*-value
Size > 2 cm: number (%)	22 (71)	2 (29)	20 (83)	0.012*
Composition: number (%)				0.043*
Solid	18 (58)	7 (100)	11 (46)	
Solid-cystic	8 (26)	0	8 (33)	
Cystic	5 (16)	0	5 (21)	

*Fisher's exact test

Table 5 Factors related to adequate biopsy results: fine needle aspiration (FNA)

Factor	FNA (N = 31)	Inadequate results (N = 23)	Adequate results (N = 8)	*p*-value
Size > 2 cm: number (%)	22 (71)	15 (65)	7 (88)	0.379*
Composition: number (%)				0.052*
Solid	11 (31)	5 (21)	6 (75)	
Solid-cystic	9 (29)	8 (35)	1(13)	
Cystic	11 (31)	10 (44)	1 (13)	

*Fisher's exact test

Discussion

The aim of the present study was to compare the rate (proportion) of adequate biopsy results between CNB and FNAB under US guidance for thyroid nodules, based on the 2017 Bethesda System. There were no significant differences between the CNB and FNAB groups in terms of baseline characteristics, which included gender, age, and TSH and FT4 levels. There were more women than men in both CNB and FNAB groups, which was related to the generally higher prevalence of thyroid nodules in women.[1,2]

There were also no significant differences between CNB and an FNAB groups in terms of size and solid/cystic components of the thyroid nodules. CNB was able to obtain more thyroid tissue for more adequate diagnosis as compared to FNAB. This result is similar to those of other studies.[9,13,14,16-18] CNB can reduce false negative results, or prevent unnecessary excision after FNAB.[9,13,14,16-18]

CNB can be safely performed in the outpatients department, with few complications.[13,14] Pain during the procedure, tolerability, and complications were similar between the two biopsy methods.[20,21] Some studies recommend using CNB instead of a repeat FNAB after a prior inadequate FNAB result.[13-16] Other studies recommend using CNB as a first-line biopsy method for high risk solid thyroid nodules.[18] The present study seemed to affirm the use of CNB as a first-line biopsy method.

Overall, without regards to biopsy methods, patients with thyroid nodules larger than 2 cm were more likely to have adequate biopsy. On the other hand, presence of cystic/solid components did not significantly affect biopsy adequacy. In the CNB group, both larger nodule size and cystic/solid components were related to adequate biopsy. But, for CNB, solid nodules were less likely to obtain adequate biopsy, a counterintuitive result. This could be explained by the small size of the nodule. That is, for the 7 patients with inadequate CNB result, 5 had nodules smaller than 2 cm (Table 4). In the FNAB group, while both size and components of the nodules were not strictly significantly related to adequate biopsy, the cystic/solid component were of borderline significance. For FNAB, solid nodules were more likely to obtain adequate biopsy. This was as expected, since solid nodules should yield more cells. Also, size of the nodule might be important: it can be seen that in the 8 patients with adequate FNAB, 7 had nodules larger than 2 cm (Table 5).

In the present study, the rate of non-diagnostic FNAB results was higher when compared with to other studies. Experience of the US operator, FNA technique, and cytological preparation may also affect the non-diagnostic rates. As our hospital has no cytologist, the slides obtained from FNAB are sent for outside examination. Also, a nodule that is cystic and of size smaller than 2 cm tends to increase the chance of non-diagnostic results.

The present study has several limitations. The retrospective design, the small sample size, and operator-dependent procedures might make the study less valid and less reliable. Pakkred Community Hospital also lacks radiologists and pathologists, and needs to co-ordinate diagnosis and treatment with other provincial hospitals whose services include these specialists. Some patients chose to receive treatment at other hospitals and were lost to follow-up. Finally, with only one US operator who also does the biopsy, the experience of the operator and the technique used may not be generalizable.

Conclusion

CNB under US guide is associated with higher rate of adequate biopsy than FNAB, for thyroid nodules, with adequacy defined by the 2017 Bethesda System. Size of nodules greater than 2 cm was the most consistent predictive factor for adequate biopsy. US-guided CNB is recommended as a first-line biopsy method, in place of FNAB.

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None

Conflict of Interest

None

Ethical Approval

The study was approved by the Institutional Ethics Committee.

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บทคัดย่อ **การเปรียบเทียบการเก็บตัวอย่างส่งตรวจสำหรับก้อนที่ต่อมไทรอยด์ ระหว่างการทำ Fine needle aspiration และการทำ Core needle biopsy ร่วมกับการใช้อัลตร้าซาวด์**

ชลลดา สุวรรณะชฎ, พบ.

กองศัลยกรรม, โรงพยาบาลปากเกร็ด จังหวัดนนทบุรี

วัตถุประสงค์: การทำ Core Needle Biopsy (CNB) ก้อนที่ต่อมไทรอยด์ (thyroid nodule) ถูกนำมาใช้แทนการทำ Fine Needle Aspiration (FNA) ที่มักมีข้อกำจัดคือได้เซลล์ไม่เพียงพอต่อการวินิจฉัยแปลผลตาม Bethesda Classification System (2017) การทำ CNB เป็นการเก็บตัวอย่างที่มักจะได้เซลล์เพียงพอในการแปลผลสามารถแยกวินิจฉัยได้ว่าเป็นก้อนที่ไม่ร้ายแรง (Benign) หรือเป็นก้อนที่มีความเสี่ยงเป็นมะเร็ง (Malignant) วัตถุประสงค์ของการวิจัยนี้คือ การเปรียบเทียบประสิทธิผลของวิธีเก็บตัวอย่างก้อนที่ต่อมไทรอยด์ระหว่าง CNB และ FNA ร่วมกับการใช้อัลตร้าซาวด์ กับการแปลผลตาม Bethesda System

วิธีการศึกษา: การวิจัยนี้เป็นรูปแบบ retrospective cohort study โดยการเก็บข้อมูลจากเวชระเบียนผู้ป่วยที่มีการเก็บตัวอย่างก้อนที่ต่อมไทรอยด์ด้วยวิธีการทำ FNA และ/หรือ CNB ร่วมกับการใช้อัลตร้าซาวด์ที่โรงพยาบาลปากเกร็ด ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2560 ถึงวันที่ 31 ธันวาคม พ.ศ. 2563 ผู้ป่วยถูกแบ่งออกเป็น 2 กลุ่ม คือ กลุ่ม CNB (N = 31) และกลุ่ม FNA (N = 31)

ผลการศึกษา: ผู้ป่วยที่ได้รับการเก็บชิ้นเนื้อตัวอย่างที่เพียงพอในการแปลผลตาม Bethesda System พบในกลุ่ม CNB มากกว่าในกลุ่ม FNA (ร้อยละ 77 และ 26 ตามลำดับ) อย่างมีนัยสำคัญทางสถิติ (p-value < 0.001) ปัจจัยที่มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติ กับความสำเร็จในการเก็บตัวอย่างก้อนที่ต่อมไทรอยด์ได้แก่ขนาดก้อนที่มากกว่า 2 ซม. ส่วนลักษณะของก้อนที่ต่อมไทรอยด์ ไม่มีผลต่อความสำเร็จในการเก็บชิ้นเนื้อตัวอย่างและการแปลผล อย่างมีนัยสำคัญทางสถิติ

สรุปผลการศึกษา: ในการเก็บชิ้นเนื้อตัวอย่างก้อนที่ต่อมไทรอยด์ การทำ CNB มีประสิทธิผลดีกว่า FNA