

Evaluation of Thyroid Fine Needle Aspiration Cytology by the Bethesda Reporting System: A Retrospective Analysis of Rates and Outcomes from the King Chulalongkorn Memorial Hospital

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Background: Fine-needle aspiration (FNA) cytology is a gold standard for preoperative evaluation of thyroid nodules. Recently introduced the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) has attempted to standardize reporting and cytological criteria in aspiration smears. This reporting format suggested six diagnostic categories, briefly defined as follows: 1) non-diagnostic, 2) benign, 3) atypia of undetermined significance (AUS), 4) follicular neoplasm, 5) suspicious for malignancy, and 6) malignant. Previous experience with thyroid FNA from Thailand was reported in several local publications, and none of these employed TBSRTC.

Objective: To investigate the distribution of thyroid cytological diagnoses according to TBSRTC, to correlate FNA findings with the results of the histopathological examination, and to compare our results with available studies from Thailand.

Material and Method: We reviewed all thyroid FNA reports between 2009 and 2015 performed at the KCMH. The FNA results were classified according to TBSRTC. Histopathology reports for operated cases were used to correlate cytology and final histopathology.

Results: Two thousand seven hundred sixty two FNA of thyroid nodules from 2,004 patients were reviewed. The rate of non-diagnostic, benign, AUS, follicular neoplasm, suspected for malignancy, and malignant cases was 47.6%, 40.8%, 3.9%, 2.6%, 1.9%, and 3.2% respectively. Very high rate of non-diagnostic samples was likely attributed to performer's skills, high prevalence of cystic nodules, and variations in microscopic interpretation. Malignancy rate in 457 operated thyroid nodules was 19.2%, 14%, 37.9%, 20.9%, 81.5%, and 93.6% for categories 1 to 6, respectively.

Conclusion: The Bethesda system is recommended as a uniform system for reporting thyroid cytopathology, facilitating communication between pathologists and clinicians, leading to more consistent management algorithms. Additional efforts are needed to reduce the rate of non-diagnostic thyroid biopsies in the KCMH. There is substantial proportion of undetermined nodules (categories 3 to 5) that needs further stratification with ancillary techniques.

Keywords: Thyroid nodule, Thyroid cancer, Fine-needle aspiration, Cytology, The Bethesda system for reporting thyroid cytopathology, Risk of malignancy

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Thyroid nodules are common, with prevalence depending on the screening approach, e.g. found in 2 to 6% population by palpation, in 19 to 35% by ultrasound, and up to 60% on autopsy⁽¹⁾. Most patients present with asymptomatic neck mass, sometimes with compressive symptoms, and rarely with signs of thyroid dysfunction (hypothyroidism, hyperthyroidism). Widespread diagnostic imaging with a high resolution

is largely responsible for the growing incidence of thyroid nodules worldwide.

Thyroid cancer is a rare, but the most serious clinical condition behind a solitary thyroid nodule. In this regard, malignancy should be excluded during diagnostic workup of all thyroid nodules. The incidence of thyroid carcinoma is growing in the line with a rising trend of thyroid nodules. The most recent statistical estimates rank thyroid carcinoma among the top 10 most common malignancies in Thailand, and the fourth most prevalent in women⁽²⁾. One study predicted that in 2019 thyroid carcinoma will be the third most common cancer in the US female population⁽³⁾. Major authorities in the field agree that such rise mainly reflects

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overdiagnosis of indolent asymptomatic nodules (microcarcinoma), incidentally found on ultrasound (US) examination⁽⁴⁾.

Despite the excellent prognosis of thyroid cancer, it is often a challenge for clinicians to determine whether a nodule is malignant and should be surgically removed, or it is benign, which can be treated conservatively⁽⁵⁾. US and fine-needle aspiration (FNA) cytology, often combined together as US-guided FNA, are the main techniques to render preoperative diagnosis.

Thyroid FNA was introduced for the first time in 1930 by Martin and Ellis who used an 18-gauge-needle aspiration technique⁽⁶⁾. However, it became a mainstream approach much later, after introducing of so-called small-needle aspiration biopsy⁽⁷⁾. Today, thyroid FNA biopsy is considered as a gold standard test for evaluation of thyroid nodules⁽⁸⁾. The sensitivity of thyroid FNA to detect malignancy is higher than that of US, thyroid scan, or frozen sections^(9,10). Furthermore, US-guided FNA approaches almost 100% sensitivity, which makes it method of choice in pre-operative diagnosis of thyroid nodules⁽¹¹⁾.

For many years, cytological terminology for thyroid FNA varied significantly among different laboratories, creating much confusion for pathologists, and also between pathologists and clinicians. To avoid this ambiguity by unifying various classifications, and to make the consensus between cytopathologists, the Bethesda system for reporting thyroid cytopathology (TBSRTC) was introduced in 2007, and appeared in the current edition two years later⁽¹²⁾. The Bethesda system divided all of the cytological diagnoses of thyroid FNA into six categories, which can be briefly entitled as follows: 1) non-diagnostic, 2) benign, 3) atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS), 4) follicular neoplasm (FN) or suspicious for a follicular neoplasm (SFN), 5) suspicious for malignancy (SM), and 6) malignant. Each category has implied risk of malignancy and recommended clinical management^(13,14).

TBSRTC is highly advised by the most of current guidelines on the management of thyroid nodules and thyroid cancer^(8,15,16). However, despite of being widely acclaimed, the Bethesda system is far from perfection. One of the issues extensively debated today refers to the group of indeterminate thyroid nodules, comprised of the lesions from categories 3 to 5 (AUS/FLUS, FN/SFN, and suspicious for malignancy). It seems like cytology alone cannot adequately predict benign or malignant behavior of these nodules⁽¹²⁾.

Advanced molecular techniques have very promising potential in such clinical scenarios⁽¹⁷⁾.

Numerous reports have been published since the introduction of the Bethesda system with an aim to share institutional or nationwide experience, which allowed to perform meta-analysis and to consider further evolution of TBSRTC^(13,14,18). Unfortunately, no studies from Southeast Asia were included in meta-analysis projects, because such reports have not been published. In general, studies of thyroid FNA from ASEAN countries are scarce, and often have drawbacks, e.g. small sample size, poor design and data presentation, limited access due to availability in local language only. As a result, so far, there are no well-designed studies from Southeast Asia, which share local experience with TBSRTC.

The aim of the present paper was to investigate the distribution of thyroid cytological diagnoses in our local settings according to the Bethesda system, to correlate FNA findings with the results of the histopathological study, and to compare our experience with previously published studies from Thailand.

Material and Method

Study settings

This retrospective study was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (Certificate of Approval No. 440/2016). All thyroid FNA biopsies sampled from January 1, 2010 to December 31, 2015 in the King Chulalongkorn Memorial Hospital, Bangkok, Thailand (KCMH) were retrieved from database of the Department of Pathology. Thyroid FNA in the KCMH is performed by various specialists, including surgeons, ENT physicians, radiologists and cytopathologists, with qualification ranged from academic staff to residents. US guidance was not routinely used for each patient, and our database had no information regarding US assistance during biopsy. Cytological smears from cervical lymph nodes, perithyroid lesions with uncertain location, liquid-based preparations and consultation cases were excluded.

Preoperative cytological and final histopathological diagnosis

All thyroid smears during the study period were signed out by six experience pathologists with academic affiliation. The terminology of TBSRTC is not mandatory in the KCMH, and thus was not uniformly used. For the needs of the present study we adjusted

all the cytological diagnoses to the Bethesda system categories⁽¹²⁾. Category 1 (non-diagnostic) in addition to initially unsatisfactory smears, included samples signed out as hemorrhagic content, old hemorrhagic content, air dry, benign fat, lymphoid cells, and no cells. Category 2 (benign) included FNA diagnosed as nodular goiter, multinodular goiter, adenomatous goiter, benign thyroid tissue, Hashimoto's thyroiditis, lymphocytic thyroiditis, and colloid fluid. Categories 3 to 5 were usually signed out with the Bethesda terminology. Category 6 (malignant) referred to various malignancies according to their particular histological type, e.g. papillary carcinoma, anaplastic carcinoma, lymphoma, etc. Relevant demographic (age, sex) and clinical (size of the nodule, repeated FNA) data were collected. Cytological smears with unclear terminology were retrieved from the archive and re-classified as per the Bethesda criteria by the senior pathologist (SK).

In order to identify the nodules with histopathological follow-up, all the patients who underwent thyroid FNA were matched with thyroid surgical pathology database. Histopathological reports were analyzed with a special emphasis on malignancy. The pathological diagnosis of thyroid tumors was based on the WHO classification⁽¹⁹⁾. Thyroid microcarcinomas (10 mm or less) were categorized as incidental and non-incidental, where available⁽²⁰⁾. Only non-incidental microcarcinomas located at the FNA site were considered as true malignant lesions⁽²¹⁾. Surgical samples with equivocal diagnosis were resolved by two pathologists with thyroid expertise (SK,AB).

Statistics

The number of nodules corresponded to each Bethesda category was determined. Final histopathology was compared with initial FNA results to provide a risk of malignancy (ROM) for each Bethesda category. In case of repeated preoperative FNA, only the latest cytological diagnosis was considered. The comparison of continuous variables was performed using Mann-Whitney U test. A *p*-value of less than 0.05 was considered to be statistically significant.

Results

Thyroid samples constitute 11.5% of all cytopathology specimens submitted to our department. The mean number of the thyroid FNAs is 454 cases per year.

A total of 2,762 thyroid nodules from 2,004 patients underwent FNA during the study period. The

age of the patients ranged from 4 to 95 years (mean age = 50.1±15.2), and female-to-male ratio was 6: 1. There was statistically significant difference between mean age of male and female population (56.5 vs. 49.0, *p*<0.01 by Mann-Whitney U test). Substantial proportion of patients (n = 587; 29.3%) were subjected to repeated FNA, with a number of repeats from 1 to 6.

The incidence of each Bethesda category was presented in Table 1. To summarize, the majority of nodules were signed out as non-diagnostic (47.6%) and benign (40.8%). The remaining FNAs were distributed among AUS/FLUS (3.9%), malignant (3.2%), FN/SFN (2.6%), and SM (1.9%) categories.

Four hundred fifty seven patients (22.8%) underwent surgical resection with available histopathology. More than 70% of patients with cytological diagnosis corresponding to the Bethesda categories 1 to 4 were treated by lobectomy. A method of choice for cases with malignant FNA was total thyroidectomy. Finally, for the nodules suspicious for malignancy by FNA, lobectomy or total thyroidectomy was equally performed.

The cytological-histological correlations with ROM as a major outcome were shown in Table 2. Approximately every third surgically operated nodule was malignant (29.5%). There was a high rate of concordance regarding malignancy prediction in the Bethesda categories 5 (81.5%) and 6 (93.6%). The most common malignancy was papillary thyroid carcinoma (71%), followed by follicular thyroid carcinoma (16%), and other cancers (13%).

Table 1. Distribution of preoperative thyroid FNA results as per the Bethesda diagnostic category

TBSRTC category	Number of nodules	Frequency
1) Non-diagnostic	1,314	47.6%
2) Benign	1,127	40.8%
3) AUS/FLUS	108	3.9%
4) FN/SFN	72	2.6%
5) SM	53	1.9%
6) Malignant	88	3.2%
Total	2,762	100%

TBSRTC = The Bethesda System for Reporting Thyroid Cytopathology; AUS/FLUS = Atypia of undetermined significance/Follicular lesion of undetermined significance; FN/SFN = Follicular neoplasm/Suspicious for a follicular neoplasm; SM = Suspicious for malignancy

Table 2. Rate of malignancy in each Bethesda category

Bethesda category	Number of operated cases	Malignancy in surgical specimens	Risk of malignancy
1) Non-diagnostic	104	20	19.2%
2) Benign	207	29	14.0%
3) AUS/FLUS	29	11	37.9%
4) FN/SFN	43	9	20.9%
5) SM	27	22	81.5%
6) Malignant	47	44	93.6%
Total	457	135	

Discussion

FNA biopsy is an accurate technique to distinguish benign and malignant thyroid nodules. It guides clinicians towards management of the patient, and reduces the number of unnecessary thyroid surgeries. Before the Bethesda system was introduced, it was difficult to summarize and compare incidence or malignancy rates from different cytopathology reports due to high variation in terminology used. The TBSRTC helps to analyze data from different studies and to develop evidence-based guidelines for the management of thyroid nodules^(8,13).

Our study is based on the data from the KCMH, one of the largest hospitals in Thailand and a tertiary referral center for thyroid patients from both urban and rural areas. We believe that a large cohort of patients from the KCMH represents the entire population of Central Thailand, and may be considered as a valid reference dataset. Below, we discuss the most practically relevant findings addressed not only to cytopathologists, but also to clinicians dealing with thyroid nodules.

High non-diagnostic rate in the KCMH

Non-diagnostic, false negative and false positive results are the major drawbacks of any medical test, including thyroid FNA. In our study we found very high rate of non-diagnostic biopsy approaching almost 50% over the study period. After comprehensive literature analysis we could not find reports with comparable results. In order to investigate the issue, we performed additional search in our database, dating back to 2004. It was found that rate of non-diagnostic thyroid cytology with a mean of 46.3% is typical for the KCMH, being consistently high in the last 12 years (Fig. 1).

According to TBSRTC, non-diagnostic category applies to specimens that are unsatisfactory

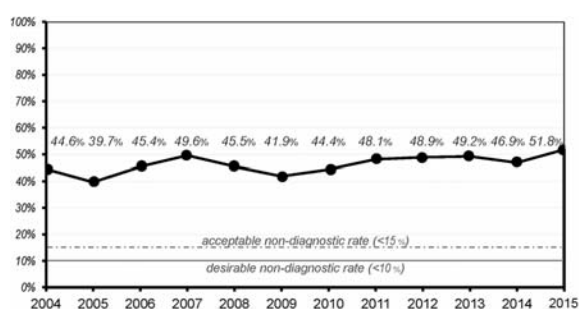


Fig. 1 Rate of non-diagnostic thyroid FNA in the King Chulalongkorn Memorial Hospital.

owing to obscuring blood, overly thick smears and air drying, or contains inadequate number of follicular cells, e.g. less than 6 groups of benign follicles composed of at least 10 cells⁽¹²⁾. In our set most of non-diagnostic smears were represented by hemorrhagic (45%) or old hemorrhagic content (42%), as per original reports.

It is recommended that number of non-diagnostic/unsatisfactory samples ideally should be limited to no more than 10% of thyroid FNAs⁽¹²⁾. Recent survey of almost 700 practicing thyroid specialists from all over the world found that frequency of non-diagnostic FNA less than 10% was reported by 66% of respondents, including 35% with non-diagnostic rate less than 5%⁽²²⁾. We suppose that a threshold of 15% is still acceptable, because it is not uncommon to see this rate in the recent international publications. However, non-diagnostic rate exceeding 20% of all thyroid FNAs should alert a hospital that the service needs audit and improvement. Potential underlying causes should be considered from both clinical (sampling technique, operator experience) and pathological (sample processing, microscopic interpretation) sides.

For palpable lesions, the importance of the experience and skills of the FNA operator is critical.

Numerous reports found the association between sample adequacy and operator's experience⁽²³⁻²⁵⁾. The Bethesda conference emphasized the importance of special training, credentialing and re-credentialing for the performance of thyroid FNA⁽²⁶⁾. It was suggested that at least 200 procedures are needed to develop basic skills of the procedure⁽²⁷⁾. There is no relevant information about operator in our database, nevertheless during personal communication we learned that substantial amount of thyroid FNA in the KCMH was performed by the inexperienced residents. US guidance is an important tool in the hands of operator, which significantly reduces non-diagnostic rate^(11,28). As far as we know, US-guided FNA is not routinely performed in the KCMH at the first visit.

One of the possible reasons behind the excessive non-diagnostic rate is a high prevalence of cystic nodules in local population. This was suggested independently by senior cytopathologist (Department of Pathology, KCMH) and senior endocrinologist (Division of Endocrinology, KCMH) during personal communication. Furthermore, we found that 40.6% of all surgical thyroid samples in our database were represented by non-neoplastic nodules, which were signed out as nodular, multinodular and adenomatous goiter (AB, unpublished data). However, a search of literature from Thailand and Southeast Asia could not yield any supportive evidence, because the issue of prevalence of cystic thyroid nodules has not been addressed so far.

It is known that predominantly cystic nodule is a strong independent predictor of non-diagnostic cytology^(26,29). US-guided FNA is recommended in such a case, however it has limited effectiveness in large dominant nodules⁽³⁰⁾. On the other hand, thyroid nodules less than 10 mm were also reported as common sources of unsatisfactory biopsy⁽²⁶⁾. We compared mean size of diagnostic (30.2±18.3 mm) vs. non-diagnostic samples (31.3±23.7 mm) with surgical follow-up, and could not find a statistically significant difference between the two groups ($p = 0.76$ by Mann-Whitney U test). Also there was no difference in size between diagnostic and non-diagnostic samples within subgroups of solid and cystic nodules. Interestingly, we found that number of slides submitted per one case could impact an accuracy of the diagnosis (mean 4.3±2.1 slides in diagnostic vs. 3.7±1.4 in non-diagnostic categories, $p = 0.02$ by Mann-Whitney U test). This finding did not advocate extensive sampling with loads of needle passes, but rather suggested that in challenging situation even one additional smear might

be helpful.

The main issue concerning pathological interpretation of non-diagnostic samples was that the cases cytologically appearing as cyst fluid only should be considered unsatisfactory, as per TBSRTC. If the nodule was purely cystic, with no worrisome US features, an endocrinologist might proceed as if the cyst fluid only result was a benign instead of non-diagnostic⁽¹²⁾. It is in the line with our previous notion regarding possible high prevalence of cystic nodules in the local population. We reviewed random 100 non-diagnostic smears from our set, and found that up to 10% of them could be reclassified as cyst fluid only, and thus, potentially, be treated as benign according to the management algorithms. However, all these cases by definition could not be eliminated from the Bethesda non-diagnostic category.

Non-diagnostic results bring harms to both patient and hospital. Approximately 10% of cases with non-diagnostic FNAs from our cohort were submitted for lobectomy and thyroidectomy, which disclosed malignancy in only 19.2%. Thus, every 4 operative interventions out of 5 could be considered diagnostic. These surgeries pose a risk of hypothyroidism and hypoparathyroidism, for example 12% of surgical samples from non-diagnostic cases contained unintentionally removed parathyroid glands. Needless to say that physical harm is added by frustration and anxiety upon receiving of non-diagnostic conclusion after biopsy. On the other hand, the hospital is facing with added costs for repeat testing (more than 200 patients every year), strain on radiology facility, waste of reagents and consumables by pathology laboratory. Additional efforts are needed to eliminate high rate of non-diagnostic FNA in the KCMH, which can be achieved through coordinated actions of clinical and pathological units. However, it is supposed to be challenging since there is no actual centralized care of thyroid patients in our settings.

Predictive value of the Bethesda system

Diagnostic categories of the Bethesda system consider a thyroid lesion placed into a specific category would show histological evidence of malignancy with a chance predicted by the ROM. Each of the categories has implied cancer risk (the higher category, the higher risk) that translates into a recommendation for clinical management⁽¹³⁾. For instance, benign nodules require clinical follow-up, FN/SFN and malignant nodules are submitted for lobectomy and thyroidectomy, respectively⁽¹²⁾. Non-diagnostic and indeterminate

FNAs should be repeated, preferably with ultrasound guidance.

ROM in our study was basically within the reference range, published in the original TBSRTC and more recent meta-analysis papers⁽¹²⁻¹⁴⁾. We found quite high malignancy rate in benign and SM diagnostic categories, whereas a ROM in malignant category was lower than expected. There may be several reasons contributed to these deviations, e.g. sampling technique, co-existence of dominant benign nodule and cancer, tertiary center bias, etc. But more likely these unusual rates were caused by interpretation errors by readers. For instance, some true malignant smears were interpreted as SM by pathologist resulting in higher ROM in SM category, and, subsequently lower ROM in malignant category.

Thyroid nodules with indeterminate cytological diagnosis

Indeterminate thyroid nodules, by definition, often pose difficulties for cytopathologists and clinicians. This cytological group is represented by the lesions from AUS/FLUS, FN/SFN and SM Bethesda categories. It is supposed that approximately 20% of all thyroid aspirates yield an indeterminate or suspicious only result⁽³¹⁾. ROM of indeterminate nodules is not clearly established due to variation of interpretation among the different institutes. It is believed, however, that only 1 out of 3 to 4 uncertain nodules is true malignant⁽¹⁸⁾.

Unfortunately, the vast majority of patients with indeterminate thyroid cytology underwent diagnostic surgery. This aggressive approach is often accompanied by various complications, such as post-operative thyroid hormone imbalance, recurrent laryngeal nerve injury, bleeding or infections. In our cohort, a surgery of categories 3 to 5 could yield only 42% of malignancy.

Ancillary studies employing molecular testing and/or immunocytochemistry showed very promising results for detecting malignancy in indeterminate thyroid FNA. Molecular tests are based on mutation analysis (single gene or panel), gene expression classifiers, and miRNA panels⁽¹⁷⁾. We believe that introducing highly sensitive molecular testing for preoperative thyroid FNA in the KCMH can improve cancer detection and help avoiding unnecessary surgeries.

Studies on thyroid FNA cytopathology from Thailand

We found 10 publications in the local journals

dating back from the early 1990s⁽³²⁻⁴¹⁾. There was a marked variation in the terminology across different authors. None of the recent studies adopted the Bethesda system. As such, we used the same adjustment criteria as in the current study, where possible. Thai experience with thyroid FNA is summarized in Table 3. Only two studies reported about non-diagnostic rate, which was quite high (19.6% and 22.1%), but much lower than in our hospital^(33,38).

Malignancy rate in each category was in the standard range described by TBSRTC, with few exceptions. Sinkijcharoenchai et al reported low rate of true malignancy (73.9%) in malignant category⁽³²⁾. It was likely attributed to reading errors by cytopathologists, the same as in our cohort with high ROM in benign diagnostic category. A recent study from the Ramathibodi Hospital reported unexpectedly high malignancy rate (28.4%) in non-diagnostic category⁽³⁹⁾.

The issue of indeterminate nodules was not addressed well, partially due to diverse terminology. We highly recommend using uniform diagnostic criteria of TBSRTC for the future studies. It will help to avoid misinterpretation while sharing local experience with international audience. It would be also desirable to report distribution of FNA results per the Bethesda diagnostic category.

Concluding remarks

TBSRTC was developed to create a uniform reporting system for thyroid cytopathology that could provide effective communication between pathologists and clinicians, assist cytological-histological correlation of cases, and allow for comparison of data between institutions⁽¹⁴⁾. Meta-analysis studies performed several years after the Bethesda system implementation confirmed effectiveness of this approach. However, many institutions across the world still use morphological terminology out of the Bethesda glossary, which occasionally can create confusion and interfere the sharing of clinically meaningful data among laboratories.

Our study on utility of the Bethesda system is the first from Thailand, and the largest from the Southeast Asia. We found that TBSRTC was feasible regarding uniform terminology and prediction of malignancy in thyroid nodules. Surprisingly, it was a high rate of non-diagnostic thyroid FNAs in the KCMH, most likely attributed to performer's skills, high prevalence of cystic nodules and variations in microscopic interpretation. To eliminate this problem, a

Table 3. Previously reported studies on thyroid FNA from Thailand

Source	Hospital	Study cohort	Operated nodules	Rate of malignancy in the Bethesda category					
				1	2	3	4	5	6
Himakoun et al, 1991 ⁽³⁸⁾	Srinagarind Hospital, Khon Kaen	1984 to 1990	101	n/a	11.4%	n/a	12.5%	n/a	100%
Issarpan et al, 1991 ⁽³⁷⁾	Ramathibodi Hospital, Bangkok	1988 to 1990	77	n/a	8.6%	31.3%	n/a	n/a	75%
Settakorn et al, 2001 ⁽³³⁾	Chiang Mai University	1996 to 1999	230	n/a	2.5%	n/a	22.6%	n/a	90.2%
Pattarakulchai et al, 2002 ⁽³⁵⁾	Chiang Mai University	1992 to 2000	174	n/a	5.1%	n/a	30.6%	50%	88.2%
Pradittaphonlert et al, 2004 ⁽³⁴⁾	Chonburi Hospital	1999 to 2003	97	17.4%	9.1%	n/a	15.4%	33.3%	100%
Sinkjcharoenchai et al, 2005 ⁽³²⁾	Songklanagarind Hospital, Hat Yai	1999 to 2003	341	n/a	8.5%	n/a	23.2%	68%	73.9%
Nopkumwjai et al, 2005 ⁽³⁶⁾	Ratchaburi Hospital	2001 to 2005	101	n/a	11.4%	n/a	n/a	71.4%	100%
Eamchan et al, 2010 ⁽⁴⁰⁾	Buddhachinaraj Phitsanulok Hospital	2005 to 2009	234	14.3%	6.8%	57.1%	6.1%	92.9%	100%
Himakoun et al, 2012 ⁽³⁹⁾	Ramathibodi Hospital, Bangkok	2005 to 2008	469	28.4%	9.5%	n/a	42.4%	86.7%	100%
Boonyaarunnate et al, 2013 ⁽⁴¹⁾	Siriraj Hospital, Bangkok	2002 to 2004	60	n/a	5.6%	n/a	37.5%	n/a	100%
Current study	KCMH, Bangkok	2010 to 2015	457	19.2%	14%	37.9%	20.9%	81.5%	93.6%
Reference study									
Sheffield et al, 2014 ⁽⁴⁴⁾	TBSRTC meta-analysis	2007 to 2012	8,044	18.7%	6.5%	28.3%	33.1%	65%	98.6%

number of measures should be introduced including improvement of operators' skills, wider use of US-guided FNA, educational support for readers, and closer communication between pathologists and clinicians. The issue of the prevalence of cystic nodules in the local population needs further clarification. In addition, we found a fair amount of indetermined thyroid nodules (categories 3 to 5), which potentially can be resolved by molecular testing instead of diagnostic surgery.

What is already known on this topic?

The Bethesda system is a uniform system for reporting thyroid cytopathology, facilitating communication between pathologists and clinicians, and leading to more consistent management approaches. Numerous studies published since the introduction of the Bethesda system in 2007 showed that TBSRTC is a reliable predictor of malignancy in thyroid FNA. TBSRTC is recommended as a reference reporting system by most of current guidelines on the management of thyroid nodules and thyroid cancer.

What this study adds?

It is the first study on utility of the Bethesda system from Thailand, and the largest from the Southeast Asia. The TBSRTC appeared feasible regarding uniform terminology and prediction of malignancy in thyroid nodules in the local settings. We found a high rate of non-diagnostic thyroid FNAs in the KCMH, which needs further correction. There was meaningful amount of indetermined nodules (categories 3 to 5), which potentially can be resolved by molecular testing.

Authors' contributions

Limlunjakorn P collected and analyzed data, drafted the manuscript.

Keelawat S supervised the project and made critical revisions to the manuscript.

Bychkov A developed research question and designed the study, performed statistical analysis and interpretation of data, participated in drafting and revision of the manuscript.

All authors read and approved the final manuscript.

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Potential conflicts of interest

None.

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การศึกษาทางเซลล์วิทยาของต่อมไทรอยด์ที่ได้จากการเจาะดูดด้วยเข็มเล็กซึ่งรายงานผลตามระบบ Bethesda: ข้อมูลจากการวิเคราะห์ย้อนหลังเพื่อค้นหาสัดส่วนและผลลัพธ์ของการรายงานผลทางเซลล์วิทยาแต่ละกลุ่มในโรงพยาบาลจุฬาลงกรณ์

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ภูมิหลัง: การตรวจทางเซลล์วิทยาโดยวิธีเจาะดูดด้วยเข็มขนาดเล็ก (FNA) เป็นวิธีการตรวจมาตรฐานในการประเมินก่อนการผ่าตัดในเนื้องอกต่อมไทรอยด์ ปัจจุบันมีการนำระบบ Bethesda เพื่อทำการอ่านผลทางเซลล์วิทยาของต่อมไทรอยด์เป็นมาตรฐานเดียวกัน โดยระบบ Bethesda จะแบ่งผลการตรวจเป็น 6 กลุ่มดังต่อไปนี้ 1) non-diagnostic, 2) benign, 3) atypia of undetermined significance (AUS), 4) follicular neoplasm, 5) suspicious for malignancy, และ 6) malignant ที่ผ่านในประเทศไทยพบว่ามีการวิจัยที่อ้างอิงถึงผลการตรวจเซลล์วิทยาในต่อมไทรอยด์จำนวนหนึ่งแต่ไม่มีงานวิจัยเรื่องไหนที่แปลผลตามระบบ Bethesda

วัตถุประสงค์: เพื่อศึกษาสัดส่วนของการวินิจฉัยทางเซลล์วิทยากลุ่มต่างๆ โดยอ้างอิงตามระบบ Bethesda และเชื่อมโยงกับผลทางพยาธิวิทยาของต่อมไทรอยด์รวมทั้งเปรียบเทียบผลการศึกษากับสถาบันอื่นๆ ในประเทศ

วัสดุและวิธีการ: โดยการรวบรวมข้อมูลผลเซลล์วิทยาของต่อมไทรอยด์ทั้งหมดในปี พ.ศ. 2552 ถึง 2558 ในโรงพยาบาลจุฬาลงกรณ์ ซึ่งผลวินิจฉัยของเซลล์วิทยาจะอิงตามระบบ Bethesda และมีการนำผลการอ่านของ FNA ไปเปรียบเทียบกับผลชิ้นเนื้อทางพยาธิวิทยาของต่อมไทรอยด์ที่ได้รับการผ่าตัดตามมาที่หลัง

ผลการศึกษา: มีผลของเซลล์วิทยาของต่อมไทรอยด์ 2,762 รายจากผู้ป่วย 2,004 ราย โดยผลของเซลล์วิทยาแบ่งเป็น non-diagnostic, benign, AUS, follicular neoplasm, suspected for malignancy และ malignancy คิดเป็น 47.6%, 40.8%, 3.9%, 2.6%, 1.9% และ 3.2% ตามลำดับ พบว่าการเกิด non-diagnostic group มากกว่าปกติอาจเนื่องมาจากปัจจัยหลายประการ อาทิเช่น การขาดความชำนาญในการทำหัตถการของแพทย์ อุบัติการณ์ของการเกิด cystic nodule สูง และความหลากหลายในการแปลผลของพยาธิแพทย์แต่ละคน อัตราการเกิดมะเร็งในแต่ละกลุ่มของการวินิจฉัยเซลล์วิทยาคตามระบบ Bethesda จากจำนวนต่อมไทรอยด์ที่ได้รับการผ่าตัดทั้งหมด 457 รายได้ 19.2%, 14%, 37.9%, 20.9%, 81.5% และ 93.6% ตามลำดับ

สรุป: ระบบ Bethesda เป็นระบบ ที่ช่วยในการแปลผลเซลล์วิทยาของต่อมไทรอยด์ให้เป็นมาตรฐานเดียวกันที่ได้รับการยอมรับไปทั่วโลก ระบบนี้ช่วยประสานการทำงานระหว่างพยาธิแพทย์กับแพทย์ผู้รักษาได้ดียิ่งขึ้นและทำให้การรักษาผู้ป่วยมีแนวทางที่ชัดเจนยิ่งขึ้น ส่วนในเรื่องปัญหาของ non-diagnostic ในโรงพยาบาลจุฬาลงกรณ์นั้น จำเป็นต้องมีการเพิ่มมาตรการบางอย่างเพื่อลดจำนวนตัวเลขของกลุ่มนี้ลง นอกจากนี้พบว่าอุบัติการณ์ของกลุ่ม indeterminate nodule (categories 3 ถึง 5) ค่อนข้างมากซึ่งอาจจะต้องอาศัยการตรวจชนิดพิเศษอื่นๆ เพื่อเพิ่มประสิทธิภาพในการวินิจฉัย
