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Original Article

The use of fine needle aspiration and trends in incidence of thyroid cancer in Taiwan

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Abstract

Background: Thyroid cancer is the most prevalent endocrine malignancy, and the incidence of thyroid cancer has increased worldwide. Fine needle aspiration (FNA) for cytology of thyroid tissue is used for differentiating thyroid cancers from benign thyroid nodules. Overuse of FNA may detect subclinical thyroid cancer and play a role in the increased incidence of thyroid cancer. The aim of this study was to evaluate trends in incidence of thyroid cancer and the use of palpation-guided FNA thyroid and ultrasound-guided FNA thyroid in Taiwan.

Methods: By retrospectively analyzing a cohort dataset of one million people randomly sample to represent as NHI beneficiaries of Taiwan National Health Insurance Research Database from 2004 to 2010, patients who received palpation-guided and ultrasound-guided thyroid FNA were identified. Individuals who were diagnosed as having thyroid cancer were determined. Age-standardized, yearly rates of palpation-guided thyroid FNA and ultrasound-guided FNA, and age-standardized, yearly incidence rates of thyroid cancer were calculated.

Results: In the study period, a total of 541 patients were newly diagnosed with thyroid cancer, 14,240 individuals received palpation-guided thyroid FNA, and 3823 individuals underwent ultrasound-guided thyroid FNA. There was a 94.8% increase in the age-standardized annual incidence rate of thyroid cancer. The age-standardized rates of palpation-guided thyroid FNA and ultrasound-guided thyroid FNA increased by 10.9% and 349.3%, respectively.

Conclusion: FNA for cytology of thyroid tissue, especially ultrasound-guided FNA, was conducted by physicians more frequently in Taiwan. Increased use of FNA, especially ultrasound-guided FNA for cytology of thyroid tissue, may attribute to the increased incidence of thyroid cancer in Taiwan.

Keywords: Fine needle aspiration of the thyroid; Thyroid cancer; Ultrasound

1. Introduction

Thyroid cancer is the most common endocrine system malignancy, and the incidence of thyroid cancer has increased dramatically worldwide.[1−3] The rising incidence of thyroid cancer, especially papillary thyroid cancer, may represent an

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actual increase in the number of cases[4–6] or an increase in the detection of clinically occult thyroid "incidentalomas" with increased use of ultrasonography and fine needle aspiration (FNA).[7–9] Some experts argued that these incidentalomas would not have caused symptoms or death if left undetected,[10–12] and that the screening and diagnostic tools for thyroid cancer was overused, causing overdiagnosis of thyroid cancer and even "thyroid cancer epidemic".[2–4,7,13,14]

FNA for cytology of thyroid tissue is recommended for clinically suspicious nodules because ultrasound features cannot differentiate malignant thyroid cancers from benign thyroid nodules accurately.[15] In an era with widespread use of medical ultrasound, ultrasound-guided FNA for cytological study of thyroid nodules has been conducted by physicians more and more frequently.[2–4,13,14] With the assistance of ultrasonography, physicians can aspirate thyroid nodules more accurately, even though the nodules are not palpable physically or measuring less than one cm in diameter, which may lead to the detection of a reservoir of occult disease.[4,7]

Data regarding the use and trend of FNA and the incidence of thyroid cancer is scarce in Asia. The single-payer National Health Insurance (NHI) program in Taiwan was launched in 1995 and covers more than 99.5% of the nation's inhabitants.[16] The data from Taiwan's National Health Insurance Research Database (NHIRD, http://nhird.nhri.org.tw/) have provided trustworthy information for population-based research for more than ten years.[17] Hence, it is worthwhile to evaluate the use of palpation-guided thyroid FNA, ultrasound-guided FNA and incidence of thyroid cancer by analyzing the NHIRD. We hypothesized there was a correlation between the increased use of thyroid FNA, ultrasound guided FNA and the increased incidence of thyroid cancer in Taiwan.

2. Methods

2.1. Databases

The NHI has provided comprehensive health insurance coverage in Taiwan since March 1995. From that time, the NHRI has released the NHIRD, comprised of health claim data of the NHI. In this study, we used a cohort dataset of one million people randomly sampled to represent NHI beneficiaries (Longitudinal Health Insurance Database 2005: LHID2005). Both hospitalization and ambulatory records, including encrypted personal identification number, date of birth, gender, diagnosis using the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM)[18] and procedure coded in the fee schedule and reference list for medical services of NHI[19] were analyzed in this study. In addition, the registry of contracted medical facilities (HOSB) was used to know the category of hospitals. The registry for catastrophic illness patients (HV) was utilized in order to accurately identify patients who had the diagnosis of malignant thyroid cancer. The study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional review board of Taipei Veterans General Hospital according to Republic of China law (VGHIRB No.: 2013-04-005E).

2.2. Study population

We obtained the medical records from 2004 to 2010 for the current study. Patients who received palpation-guided thyroid FNA were identified by having an NHI procedure code in their medical records with 29011C and without 19007B at the same time. Those who received ultrasound-guided thyroid FNA were identified by having an NHI procedure code in their medical records with both 29011C and 19007B at the same time. Individuals who were diagnosed as having malignant thyroid cancer were determined by using the ICD-9-CM code 193 in the HV dataset. Age-standardized yearly rates of palpation-guided thyroid FNA and ultrasound-guided FNA were calculated as the number of individuals who received these procedures per 100,000 individuals. In similar, age-standardized yearly incidence rate of thyroid cancer was calculated as the number of individuals who were newly diagnosed with thyroid cancer per 100,000 individuals. The age-standardized rate was adjusted based on the 2000 WHO world standard population.

Table 1
Demographic characteristics of patients diagnosed with thyroid cancer documented in the registry for catastrophic illness patients: 2004 to 2010.

Characteristics	Number of patients	%
Age, years old		
<18	5	0.9
19–40	170	31.4
41–65	307	56.7
>65	59	10.9
Gender		
Male	118	21.8
Female	423	78.2

Table 2
Demographic characteristics of patients who underwent thyroid fine needle aspiration and ultrasound guided thyroid fine needle aspiration: 2004 to 2010.

	Palpation-guided FNA, N = 14,240		Ultrasound Guided thyroid FNA, N = 3823	
	N	%	N	%
Age, years old				
<18	203	1.4	58	1.5
19–40	3772	26.5	948	24.8
41–65	8646	60.7	2363	61.8
>65	1619	11.4	454	11.9
Gender				
Male	2181	15.3	690	18.0
Female	12,059	84.7	3133	82.0
Hospital category				
Medical center	7969	56.0	1248	32.6
Regional hospital	4191	29.4	2387	62.4
District hospital	1559	10.9	188	4.9
Clinics	521	3.7		
Physician specialty				
Internist	12,092	84.9	2922	76.4
Surgeon	1151	8.1	483	12.6
Otorhinolaryngologist	599	4.2	293	7.7
Family physician	318	2.2	90	2.4
Neurologist	17	0.1	6	0.2
Radiologist	3	<0.1	12	0.3
Others	60	0.4	17	0.4

2.3. Data analysis

PostgreSQL version 9.34 (The PostgreSQL Global Development Group, http://www.postgresql.org), the database management software, and Python version 2.7.10 (Python Software Foundation, Delaware, US) were used for data processing. Microsoft Excel version 2013 (Microsoft, Washington, US) was used for statistical analysis.

3. Results

From 2004 to 2010, a total of 541 patients were newly diagnosed with thyroid cancer, with a female-to-male ratio (F:M) of 3.6:1. Among patients who were newly diagnosed with thyroid cancer, 307 (56.7%) were between 41 and 65 years old (Table 1).

In total, 14,240 (F:M = 5.7:1) individuals received palpation-guided thyroid FNA, and a total of 3823 (F:M = 4.5:1) individuals underwent ultrasound-guided thyroid FNA. The majority of individuals receiving thyroid FNA were between 41 and 65 years old (palpation-guided thyroid FNA: n = 8646, 60.7%; ultrasound-guided thyroid FNA: n = 2363, 61.8%). Most of the procedures were ordered by physicians with the specialty of internal medicine (palpation-guided thyroid FNA: n = 12,092, 84.9%; ultrasound guided thyroid FNA: n = 2922, 76.4%) (Table 2).

The number of patients diagnosed with thyroid cancer increased by 125.0%, from 52 in 2004 to 117 in 2010 (Fig. 1A). Furthermore, the total number of individuals who received palpation-guided thyroid FNA increased by 11.0%, from 1810 in 2004 to 2378 in 2010. There was a 440.1% increase in the number of individuals who received ultrasound guided thyroid

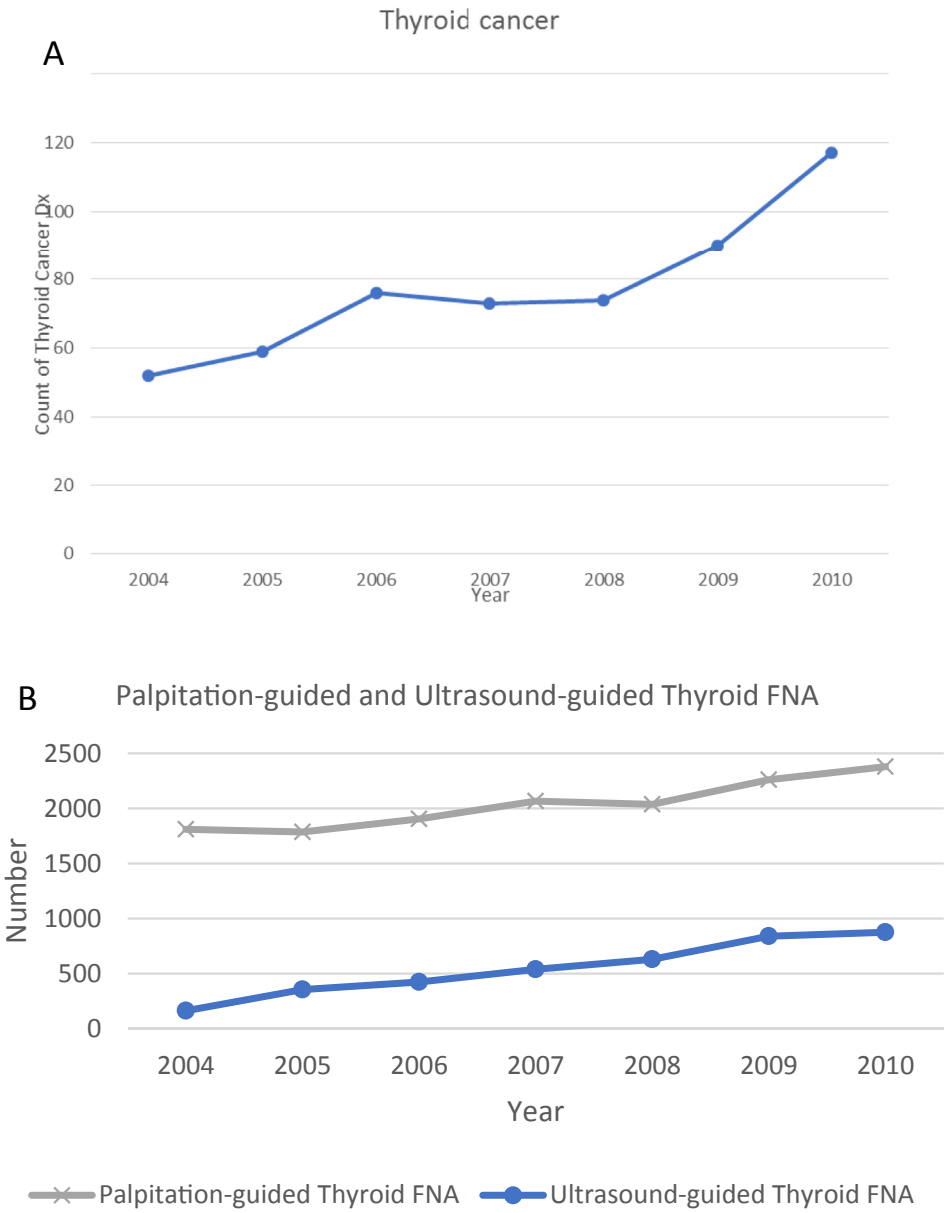

Fig. 1. The changing numbers of (A) diagnosis of thyroid cancer, (B) palpation-guided FNA and ultrasound-guided thyroid FNA from 2004 to 2010.

FNA, from 162 in 2004 to 875 in 2010 (Fig. 1B). Among the patients with thyroid cancer, 55.3% (n = 299) underwent palpation-guided thyroid FNA and 24.4% (n = 132) underwent ultrasound-guided thyroid FNA before diagnosis.

The age-standardized annual incidence rate of thyroid cancer increased by 94.8%, from 4.8 in 2004 to 9.3 in 2010 per 100,000 person-year (Fig. 2A). The age-standardized rate of palpation-guided thyroid FNA increased by 10.9%, from 166.5 in 2004 to 184.7 in 2010 per 100,000 person-year (Fig. 2B). Similarly, there was a 349.3% increase in the age-standardized rate of ultrasound-guided thyroid FNA, from 15.0 in 2004 to 67.4 in 2010 per 100,000 person-year (Fig. 2B). The use of ultrasound-guided FNA grew faster than that of thyroid FNA without ultrasound assistance.

4. Discussion

Whether the increase in the diagnosis of thyroid cancer is a true increase in thyroid cancer incidence or is a result of the overuse of screening and diagnostic tools is controversial.[2–5,13,14] Many authors have argued that the increase in the diagnosis of thyroid cancer is a reflection of the overuse of screening and diagnostic tools such as thyroid ultrasound and FNA.[2–5,13,14] Several studies reported that small papillary thyroid cancers predominantly accounted for the increase in thyroid cancer incidence.[1–3] According to the 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer, thyroid nodules less than one cm in greatest diameter dimension or purely cystic do not require FNA.[15] In the past, without the assistance of appropriate imaging technique, thyroid lesions could only be found when the lesions were palpable and/or the patients were symptomatic.[20] With the advance in image resolution and the availability of ultrasound equipment, physicians now performed thyroid ultrasound and ultrasound-guided thyroid FNA more frequently.[2–5,13,14,20] In our study, while there was only a 31 percent rise in the use of palpation-guided thyroid FNA, the use of ultrasound-guided thyroid FNA grew 4.5-fold

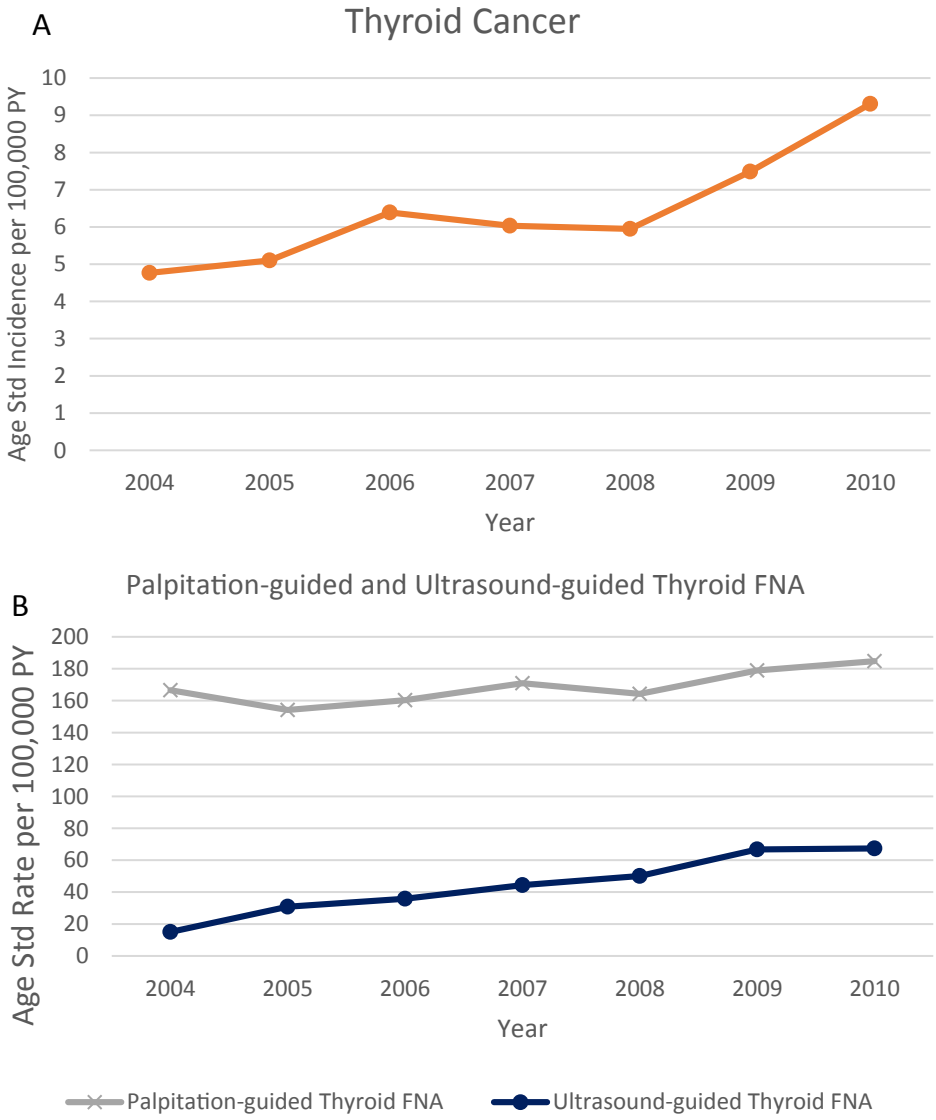

Fig. 2. The changing age standardized incidence per 100,000 person-year of (A) diagnosis of thyroid cancer, (B) palpation-guided FNA and ultrasound-guided thyroid FNA per 100,000 person-year from 2004 to 2010.

between 2004 and 2010. Our results indicate that physicians rely increasingly on ultrasound for diagnosis of thyroid diseases. Additionally, the incidence of thyroid cancer nearly doubled between 2004 and 2010. Our finding confirms that there is an association between the increase use of ultrasound-guided thyroid FNA and the increase detection of thyroid cancer.

In Taiwan, the NHI program covers almost all of the nation's inhabitants.[16] Easy access to healthcare may play an important role in the increased detection of thyroid cancer in Taiwan similar to other countries.[7−9,21] Despite the trend of increase in thyroid cancers, the mortality of thyroid cancer remains almost unchanged.[1,22] The five year-survival rate of thyroid cancer has increased steadily in Taiwan, from 92.69% in 2004 to 95.57% in 2010.[23] Moreover, previous studies reported that, for individuals who died from unrelated illness, 8−35% of autopsies showed papillary thyroid carcinoma.[10,11] "Thyroid cancer epidemic", which denotes the overdiagnosis of thyroid cancer probably owing to widespread use of the screening and diagnostic tools for thyroid cancer, has been proposed by several experts in different countries.[2−5,13,14,20]

Similar to South Korea, many hospitals in Taiwan provide "health checkup" programs including thyroid-cancer screening with ultrasonography.[22] Some experts wrote an open letter to the public about the extraordinary high incidence of thyroid cancer in South Korea and advocated stopping screening thyroid cancer with ultrasonography in March 2014.[22] Subsequently, a marked decrease in thyroid operations was reported in South Korea, since the second quarter of 2014, after the letter attracted media and public attention.[24] The decrease in thyroid operations probably resulted from less screening and fewer diagnosis.[24] Patients who undergo total thyroidectomy often need to receive lifelong thyroid-replacement therapy, and a small number of patients bear the risk of procedure-related complications. Nevertheless, some patients may suffer from disastrous results due to a delayed diagnosis of thyroid cancer. One article indicated that early detection of small thyroid nodules with malignancy would probably improve patients' quality of life.[25] How to strike the balance between the risk and benefit of thyroid-cancer screening and diagnosis requires further future studies.

On the other hand, some researchers noted that increase in the detection and diagnosis of small thyroid tumors is not the sole contributor to the increase in incidence of thyroid cancer.[5,6,26] An alternative explanation would be that there is a true increasing incidence of thyroid cancer, due to certain speculated risk factors, such as diet, hormones, genetic factors or increasing exposure to low-dose ionizing radiation from wider use of radiographic imaging.[27−29] Current diagnostic practices including FNA may enable early diagnosis of thyroid cancer while cancers are small and thereby keep the mortality of thyroid cancer low.[5]

There are some limitations in our study. First, we did not have enough information to analyze the size of the thyroid lesions and their cytology or pathology report. Secondly, the NHI was initiated in 1996; patients who had been diagnosed with thyroid cancer before 1996 and had a diagnosis of thyroid cancer in 2004−2010 in the HV dataset might be misclassified as cases with newly diagnosed thyroid cancer. This scenario might overestimate the overall incidence of thyroid cancer. Therefore, further studies will be necessary to elucidate the points limited by the claims data of Taiwan's NHIRD.

In conclusion, our data demonstrate there has been a trend of increased incidence of thyroid cancer, use of palpation-guided thyroid FNA and use of ultrasound-guided thyroid FNA. The use of ultrasound-guided thyroid FNA grew faster than that of palpation-guided thyroid FNA. Increased use of FNA for cytology of thyroid tissue, especially ultrasound-guided FNA, may contribute to the increased incidence of thyroid cancer.

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