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New evidence about thyroid cancer prevalence: prevalence of thyroid cancer in younger and middle-aged Japanese population

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Abstract. We have made a cross-sectional investigation of men in the Japanese military for the presence of thyroid abnormalities and thyroid cancer to document the prevalence of thyroid disease in these persons. Six thousand, four hundred and twenty-two Japanese military men and women were screened for thyroid disease by history, physical examination and ultrasound examination. Among them, 6,182 were men 50 years of age, 47 were women 50 years of age, and 149 were men 40 years of age and 44 were women 40 years of age. Among the 50 years old men, thyroid nodules were found in 924 men (14.9%); Nineteen individuals (0.31%) had thyroid cancers ranging from 1 mm to 30 mm in diameter (12.5 mm in mean), pathological TNM staging revealed 7 cases of stage I, 2 cases of stage II and 9 cases of stage III. There was a significant increase in thyroid nodules in 50 years old men compared to that in 40 year old men, but there was no significant difference between men and women ($p>0.05$). Our data document that the detection rate of thyroid cancer in 50 years old men was 0.31%, and the rate of thyroid nodules increased with age in men, but the frequency of thyroid nodules were similar in men and women of the same age.

Key words: Prevalence of thyroid cancer, Younger and middle-aged Japanese men, Thyroid screening

SCREENING for thyroid disease in women during breast cancer screening is popular in Japan. Some studies concerning screening for thyroid disease have previously been reported in Japan [1, 3, 4, 16, 17, 23] and other countries [2, 5-15, 18-21, 24]. The prevalence of thyroid nodule is reported to be from 1.2 [3] to 35.3% [9], and the prevalence of thyroid cancer is reported to be from 0.08 [12] to 3.9% [20]. Most of these studies primarily included women. The detection rate of thyroid nodule and thyroid cancer has been reported to be higher in women than that in men [3, 7, 12, 14]. Screening for thyroid cancer in men, especially those nearing military retirement aged over 50 and 40 years old has not, to our knowledge, been previously done. We therefore investigated the frequency of thyroid nodules and thyroid cancers in military men at retirement and compared the data to a small number of

military women who were screened by physical examination and ultrasonography in Japan and in other countries to see whether thyroid nodule and cancer are more common in women than men.

Materials and Methods

Six thousand, four hundred and twenty-two Japanese military men and women were screened with questionnaire, physical examination and ultrasound examination for thyroid disease at the Japanese Self Defense Force Hospital (Central, Hanshin and Kumamoto) from 1990 to 2012. The prevalence of thyroid nodules (excluding pure thyroid cysts) and thyroid cancer was determined. All patients were asymptomatic. Patients with obvious thyroid symptoms were excluded from this database. Among studied patients, 6,182 were men 50 years of age, 47 were women 50 years of age, and 149 were men 40 years of age and 44 were women 40 years of age. No patient had a family history of thyroid cancer or had a past exposure to radiation. We defined “thyroid nodule” as the maximum diameter ≥ 3 mm. We excluded the

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pure cysts, with about 6% of our study, from this study. The maximum diameter of thyroid nodule was also measured. Nodule ≥ 5 mm with suspicious characteristics of malignancy were considered for cytological examination by fine needle aspiration (FNA using TOSHIBA-SSA-250A; the cycle of the probe is 7.5 Mega Hertz until 2002, and TOSHIBA-Aplio XG; 8 Mega Hertz from 2004). In case of inadequate specimen or difficulty for diagnosis, we usually repeated the FNA twice. Diffuse thyroid disease by ultrasonography, which was examined only at Japan Self Defense Force Kumamoto Hospital, was assessed by the definition in Thyroid Salivary Gland Atlas (Vector Core Inc.2004) [22]. Thyroid enlargement was defined as more than 20 mm in width or thickness, and thyroid atrophy as less than 10 mm in width and in thickness in its mid-section.

Statistical analysis

The significant differences between two groups were evaluated with the Chi Square test and Fisher's exact test. A two-sided *p* value of <0.05 was considered statistically significant.

Results

Thyroid screening

50 years old men (Table 1)

Thyroid nodules including multinodular goiters and follicular neoplasms were found in 924 men (14.9%). About 1% of 50 years old men had diffuse thyroid diseases.

40 years old men (Table 1)

Thyroid nodules were present in 12 men (8.1%) and thyroid cancer was present in one man (0.67%).

50 years old women (Table 1)

Thyroid nodules were present in 5 women (10.6%).

40 years old women (Table 1)

Thyroid nodules were present in 5 women (11.3%).

Thyroid cancer of 50 years old men (Table 2A, B)

Sixty-three percent of thyroid cancers were papil-

lary carcinomas, diagnosed preoperatively by fine needle aspiration. Twenty-six percent were occult cancers concomitant benign thyroid nodules detected postoperatively by pathological examination. Ten percent were minimally invasive follicular carcinomas detected postoperatively by pathological examination.

Nineteen individuals (0.31%) were confirmed to have thyroid cancers ranging from 1 mm to 30 mm in maximum diameter 12.5mm in mean. Clinical TNM staging revealed 8 cases of stage I, 4 cases of stage II and 6 cases of stage III. Pathological TNM staging revealed 7 cases of stage I, 2 cases of stage II and 9 cases of stage III. One patient diagnosed cytologically as papillary carcinoma denied the surgical treatment.

Comparison the rate of thyroid nodule between age, and gender (Table 3A, B, C)

Fifty year old men had more thyroid nodules than 40 year old men. Men and women had a similar number of thyroid nodules.

Discussion

Our thyroid screening data of Japanese military 50 years old men revealed that 14.9% had thyroid nodules and 0.3% had histologically confirmed thyroid cancers (Table 1). Comparing our data of 50 years old men with those in 50 years old women, and 40 years old men and women, the detection rate of thyroid nodules in men had increased with age but that there was no significant difference between sexes. However, the detection rate of thyroid cancer in men had not increased with age. This will suggest that some small thyroid cancers will not always appear to be advanced cancers.

Prevalence of thyroid nodules and cancers reported in references was shown in Table 4. Our detection rate of thyroid cancer was similar [8, 12, 16, 17], or lower than that previously reported [10, 20]. Chung [10] did thyroid screening, including for the patients with breast cancers, and Lin [20] reported screening for patients with thyroid nodules.

Table 1 Thyroid screening 1990~2012 (palpation+ultrasonography)

Age	Gender	Case	Normal	Abnormal	Nodule	Cancer
50 years old	male	6182	4983	—	924 (14.9%)	19 (0.31%)
	female	47	34	8 (17.0%)	5 (10.6%)	0
40 years old	male	149	87	34 (22.8%)	12 (8.1%)	1 (0.67%)
	female	44	25	16 (36.3%)	5 (11.3%)	0

—, Unknown or not decided

Table 2A Thyroid cancer 19 cases: 50 year old men

Thyroid cancer	Cases	Case/all patients	Case/thyroid cancer	remarks
Occult cancer	5	0.08%	26.3%	Concomitant benign thyroid tumor
Preoperatively diagnosed papillary carcinoma	12	0.2%	63.2%	
Follicular carcinoma	2	0.03%	10.5%	2 cases: Minimally invasive
Total	19	0.31%		

Table 2B Thyroid cancer 19 cases

No	Surgery	Histology	pTNM	Stage	T(mm)	B
1	Rt lobectomy+D1	PTC, LN(-)	T1N0M0	I	15	
2	Rt lobectomy+D1	PTC, LN(+)	T1N1M0	III	15	
3	Lt lobectomy+D1	PTC(oc)	T1N0M0	I	1	AN
4	Rt lobectomy+D1	PTC, LN(+)	T1N1M0	III	18	
5	Rt lobectomy+D1	PTC, LN(+)	T2N1M0	III	20	
6	ST+D2	PTC, LN(+)	T1N1M0	III	4	
7	Rt lobectomy+D1	PTC(oc)	T1N0M0	I	1	AN
8	Rt lobectomy+D1	PTC, LN(-)	T1N0M0	I	8	
9	Lt lobectomy+D1	PTC, LN(+)	T2N1M0	III	20	
10	ST+D2	PTC, LN(+)	T2N1M0	III	20	
11	ST+D2	PTC(oc)	T1N0M0	I	1	AN
12	Rt lobectomy+D1	FTC	T2N0M0	II	20	
13	Lt lobectomy+D1	PTC, LN(+)	T1N1M0	III	8	
14	ST+D2	PTC(oc)	T1N0M0	I	1	AN
15	Rt lobectomy+D1	PTC(oc)	T1N0M0	I	1	AN
16	Rt lobectomy+D2	PTC, LN(+)	T1N1M0	III	17	
17	Rt lobectomy+D1	PTC, LN(+)	T1N1M0	III	18	
18	Rt lobectomy+D1	FTC	T2N0M0	II	30	
19	—	PTC	—	—	20*	

PTC, papillary thyroid carcinoma; FTC, follicular thyroid carcinoma; ST, subtotal thyroidectomy; D, lymph node dissection; D1, central node dissection; D2, unilateral neck dissection; LN, lymph node metastasis; T, tumor size; B, concomitant benign thyroid nodule; AN, adenomatous nodule; oc, occult cancer, —, Unknown or not decided; *, scale by ultrasonography

Table 3A Comparison between genders (50 years old)

50 years old	Normal	Non-nodule	Nodule	Total	p value
male	4,983	5,258	924 (14.9%)	6182	0.408
female	34	42	5 (10.6%)	47	

Table 3B Comparison between genders (40 years old)

40 years old	Normal	Non-nodule	Nodule	Total	p value
male	87	137	12 (8.1%)	149	0.496
female	25	39	5 (11.3%)	44	

Table 3C Comparison between age (40 vs. 50 years old in men)

Age	Gender	Case	Normal	Non-nodule	Nodule	p value
50 years old	male	6,182	4,983	5,258	924 (14.9%)	0.019
40 years old	male	149	87	137	12 (8.1%)	

Table 4 Prevalence of thyroid nodules and cancers reported in references

Reporters [ref]	Year	Total N (m:w)	Nodule (%) (m:w)	Cancer (%) (m:w)	Modality
Maruchi [3]	1967	30,359 (14,002:16,357)	1.2 (0.6:1.7)	0.13 (0.08:0.18)	P
Sampson [14]	1974	157 (99:58)	—	5.7 (7.1:3.5)	A
Harach [21]	1985	101(—)	—	35.6 (43.3:27.1)	A
Ishida [16]	1986	152,651 (— :152,651)	—	0.14 (— :0.14)	U
Omata [17]	1986	198,824 (13,538:6,286)	—	0.38 (0.29:0.59)	U
Struve CW [5]	1993	212 (— :212)	21.2 (— :21.2)	—	U
Hsiao YL [7]	1995	1,020 (618:402)	25.0 (19.4:33.6)	0.7 (0.6:0.1)	U
Tomimori E [8]	1995	547 (167:380)	16.5 (16.1:16.5)	0.18 (—)	U
Wiest PW [12]	1998	2,441 (2,416:25)	10.2 (10.1:24.0)	0.08 (—)	U
Furlanetto TW [9]	2000	207 (— :207)	35.3 (— :35.3)	—	U
Chung WY [10]	2001	1,401 (— :1,401)	25.2 (— :25.2)	2.6 (— :2.6)	U
Lin JD [20]	2005	21,748 (3,258:18,490)	—	3.9 (5.7:3.6)	U
Hurtado-Lopez LM [25]	2011	2,401 (423:1,978)	19.6 (—)	0.08 (—)	U

P, palpation; U, ultrasonography with palpation; A, autopsy; ref, reference number; m, men; w, women; —, Unknown or not decided

To our knowledge thyroid screening of 40 and 50 years old military men has not been previously reported, whereas it has been reported in women. One of the reasons is that thyroid disease is thought to be more common in women. Other screening investigations predominantly including women has also been reported in Japan [1, 3, 4, 16, 17] and other countries [2, 5-15, 18-21,24]. According to the literature, the detection rate of thyroid nodules and thyroid cancers is higher in women than that in men. Most of these reports state that thyroid cancer detection rate is higher in women than that in men [24], especially in 30 and 40 years old patients [1-4, 6, 8, 11, 13, 15-18].

Dal Masio *et al.* [24] reported that the highest frequency of papillary thyroid carcinoma was observed at 45~49 years old women and at 65~69 years old men. Concerning the gender differences, Kugimoto and Maruchi [1, 3] reported on 30,359 subjects (86.4% of the total inhabitants of the area studied - Nagano, Japan) from 1965 through 1967, and found thyroid cancers in 0.08% in men and 0.18% in women. Ishida *et al.* [16] examined 152,651 women and found 0.14% with small, but detectable, thyroid cancers by mass screening. Omata *et al.* [17] observed an incidence of 0.29% in men and 0.59% in women, totally 0.38% in 19,821 subjects, using ultrasound that is capable of detecting tumors as small as 4mm. On the contrary, Hsiao reported that the rate of thyroid cancer in men is 0.6% which is higher than that in women (0.1%) [7]. Lin reported that the rate of thyroid cancer in men is 5.7% which is higher than that in women (3.6%) [20]. Furthermore, micro-

scopic thyroid cancer is extremely common at postmortem examination [14, 21]. The prevalence rate of 7.1% in men and 3.5% in women was reported by Sampson in 157 consecutive autopsies [14]. The highest prevalence rate of 35.6% with 43.3% in men and 27.1% in women was reported by Harach in 101 consecutive autopsies in patients from Finland [21].

Among, 19 thyroid cancers (0.31%) of 50 years old men, 63.2 % were diagnosed preoperatively by fine needle aspiration biopsy (FNA) using ultrasonography, 26.3 % were occult cancers concomitant benign thyroid nodules that were diagnosed postoperatively by pathological examination, and 10.5 % were minimally invasive follicular carcinomas that were also diagnosed postoperatively by pathological examination. We might have missed more thyroid cancers, because the indication of FNA for thyroid nodules were more than 5 mm, and most patients with benign thyroid nodules would not have surgery. The accurate thyroid cancer prevalence is thought to be more than 0.3%.

Another interesting fact that we reported is that pathological TNM staging revealed 7 cases of stage I, 2 cases of stage II and 9 cases of stage III. About 50% of thyroid cancer screened among asymptomatic 50 years old men had already lymph nodes metastasis. Considering the prognosis of thyroid cancer in elderly men, the thyroid screening using ultrasonography is a more effective and efficient way to identify thyroid cancer at an early stage in middle-aged Japanese population.

However, screening for thyroid cancer has not been recommended in USA. One reason is that most thy-

roid cancers are clinically of little consequence. A second reason is that many thyroid cancers identified by screening will not affect the patient's prognosis. In autopsy studies, the prevalence of occult cancer in adults ranges from 2 to 35.6% [13, 14, 21], in contrast, the annual incidence of clinical thyroid cancer is only 4/100,000 [4, 15]. Microscopic thyroid cancers are found more frequently at autopsy, or when thyroid gland is screened for others pathology, whereas clinically evident thyroid cancer occurs in only about one out of 100 ultrasonographically detectable thyroid nodules. However, a cohort study of mass screening found a significantly higher 7-year cumulative survival rate in patients whose thyroid cancers were detected by screening (98%) when compared with those presenting with symptoms (90%) [16]. This data suggests that patients with small thyroid cancers detected by screening have a favorable course. But to our knowledge, it has not been demonstrated that the detection of patients with thyroid cancer by screening have a better outcome than those having larger tumors and/or clinical symptoms. The American Cancer Society recommends screening for thyroid cancer by palpation every 3 years

in persons aged 21-40 years and annually in those more than 40 years old [19].

We suggest that thyroid screening using ultrasonography is a more effective and efficient way to identify thyroid cancer at an early stage in middle-aged Japanese population.

The limitations of this study are that this is the retrospective study and that the number of 50 years old women, 40 years old men and women was small.

Conclusion

Our data demonstrate that the detection rate of thyroid cancer in retiring Japanese military men (50 years old men) was 0.31%, which is similar to the known rate reported in the literature, and the number of thyroid nodules increased with age in men, but the rate of thyroid nodules is the same between the genders with the same age. Thyroid screening using ultrasonography is currently the most sensitive method for identifying thyroid nodules and cancer at an early stage in younger and middle-aged Japanese men.

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