

Gross and histopathologies of thyroid gland in cadavers from the South of Thailand

Pornsawan Duangsuwan* Walaiporn Plirat*

Anupong Nitiruangjaras** Wattana Sinkijcharoenchai***

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Background : *Thyroid gland is highly vascular, a butterfly-shaped endocrine gland, located in the front part of the neck. It plays an important role in releasing hormones that control the metabolism. The thyroid glands in cadavers were well preserved by embalming materials and could be sectioned for histopathological diagnosis.*

Objective : *To investigate abnormalities of thyroid glands of cadavers from the South of Thailand.*

Methods : *Gross and histological assessment of thyroid glands were studied in 102 (42 females and 60 males) cadavers of the Department of Anatomy, Faculty of Science, Prince of Songkla University. Statistical analysis was done using SPSS 16.0 statistical software.*

Results : *Histologically, the thyroid gland specimens from cadaver revealed satisfactory microscopic features of cells and connective tissues under paraffin section with hematoxylin and eosin staining. Five types of histopathology were diagnosed: nodular goiter, multinodular goiter, Hashimoto thyroiditis, mixed nodular goiter/Hashimoto thyroiditis and Grave's disease, with prevalence at 20.6%, 17.7%, 4.9%, 2.0% and 2.9%, respectively. Specimens from the females showed significantly higher prevalence of multinodular goiter than those from the males.*

* Department of Anatomy, Faculty of Science, Prince of Songkla University

** Department of Pathology, Faculty of Science, Prince of Songkla University

***Department of Otolaryngology, Faculty of Medicine, Prince of Songkla University

Conclusion : *The prevalence of the five thyroid conditions diagnosed from cadavers' specimens were much higher than those reported in clinical studies, suggesting a high possibility of subclinical cases of thyroid dysfunctions in normal population.*

Keywords : *Thyroid gland, gross pathology, histopathology, cadaver, nodular goiter, multinodular goiter, Hashimoto thyroiditis, Grave's disease.*

Correspondence to: Duangsuwan P. Department of Anatomy, Faculty of Science, Prince of Songkla University, Kanchanavanij Rd, Hatyai, Songkhla 90112, Thailand.

Email: pornsawan.d@psu.ac.th

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พยาธิกายวิภาคและจุลพยาธิวิทยาของต่อมไทรอยด์ในร่างอาจารย์ใหญ่คนไทยภาคใต้.
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เหตุผลของการทำวิจัย : ต่อมไทรอยด์เป็นต่อมไร้ท่อที่มีหลอดเลือดมาเลี้ยงมากมาย ลักษณะคล้ายปีกผีเสื้อตั้งอยู่บริเวณฐานของคอ มีบทบาทสำคัญในหลังฮอร์โมนควบคุมเมตาโบลิซึมของร่างกาย ต่อมไทรอยด์จากร่างอาจารย์ใหญ่ได้รับการรักษาสภาพเป็นอย่างดีและสามารถนำมาศึกษาเพื่อการวินิจฉัยทางจุลพยาธิวิทยาได้

วัตถุประสงค์ : เพื่อศึกษาความผิดปกติของต่อมไทรอยด์ในร่างอาจารย์ใหญ่

วิธีการทำวิจัย : ศึกษาลักษณะโครงสร้างทางกายวิภาคและจุลกายวิภาคต่อมไทรอยด์ในร่างอาจารย์ใหญ่ 102 ร่าง (เพศหญิง 42 ร่าง และเพศชาย 60 ร่าง) ที่ได้รับบริจาคร่างกายให้แก่ภาควิชากายวิภาคศาสตร์ คณะวิทยาศาสตร์ มหาวิทยาลัยสงขลานครินทร์ นำข้อมูลที่ได้จากการศึกษาไปวิเคราะห์ข้อมูลทางสถิติด้วยโปรแกรม SPSS 16.0

ผลการศึกษา : ลักษณะทางจุลกายวิภาคของต่อมไทรอยด์จากร่างอาจารย์ใหญ่โดยใช้เทคนิคพาราฟิน ย้อมสี hematoxylin และ eosin พบเซลล์และเนื้อเยื่อเกี่ยวพันอยู่ในสภาพดี ผลการศึกษาทางจุลพยาธิวิทยาพบเนื้อเยื่อที่มีพยาธิสภาพ 5 ชนิด: nodular goiter, multinodular goiter, Hashimoto thyroiditis, mixed nodular goiter/Hashimoto thyroiditis และ Grave's disease คิดเป็นร้อยละ 20.6, 17.7, 4.9, 2.0 และ 2.9 ตามลำดับ พยาธิสภาพชนิด multinodular goiter พบในเพศหญิงมากกว่าเพศชายอย่างมีนัยสำคัญทางสถิติ

สรุป : อุบัติการณ์ความผิดปกติของต่อมไทรอยด์ในร่างอาจารย์ใหญ่ มีอัตราสูงกว่าที่ได้มีการรายงานการศึกษาทางคลินิก ซึ่ให้เห็นถึงความเป็นไปได้สูงที่ความผิดปกติไม่แสดงอาการในประชากรปกติ

คำสำคัญ : ต่อมไทรอยด์, พยาธิกายวิภาค, จุลพยาธิวิทยา, อาจารย์ใหญ่, nodular goiter, multinodular goiter, Hashimoto thyroiditis, Grave's disease.

Thyroid gland is a highly vascular, butterfly shaped endocrine gland, located in the base of neck.

⁽¹⁾ It plays an important role in release hormones that control metabolism. Thyroid nodule is referred as a discrete lump within the thyroid gland. The reported incidences varied on the methods used to investigate, 19–35% with ultrasound, and 8–65% in autopsy data.

⁽²⁾ They are usually asymptomatic. Although 95% of thyroid nodules are benign, the major concern is whether it is a malignant nodule to provide the appropriate treatment.

Based on histological characteristics, thyroid nodules are classified into five types: hyperplastic, neoplastic, colloid, cystic and thyroiditic nodules (nodular Hashimoto's thyroiditis). ⁽³⁾ It was also found that the thyroid gland in the cadavers had been well preserved by embalming materials and could be sectioned for histopathological diagnosis. ^(4, 5)

Methods

The study was performed in 102 cadavers kept for gross anatomy dissection in the Department of Anatomy, the Faculty of Science, Prince of Songkla University, Thailand. They were consisted of 42 females and 60 males, with an average age of 72.2 years, ranging from 31 to 105 years old. The cause of death was not revealed. The cadavers were fixed in embalming fluid [formalin (8.7%), phenol (1.2%), methanol (44.7%) and glycerin (23.5%)] by intravascular perfusion and immersion for at least 1 year. The cadavers were dissected to expose the thyroid gland; the shape of the gland was observed and photographed.

A small piece (approximate 0.5 mm x 0.5 mm x 0.5 mm) of tissues from all pyramidal lobe (PL) (13

specimens), the muscle levator glandulae thyroideae (LGT) (11 specimens) and that of main thyroid gland, right or left lobes (102 specimens) from each of the cadavers were dissected out, fixed in 10% formalin and processed for paraffin sectioning at 5 μ m thickness and stained with hematoxylin and eosin (H&E). The sections were observed under light microscopy and, from histopathological features, thyroid diseases were diagnosed.

Statistical analysis was performed using SPSS 16.0 statistical software. All values were presented as means \pm SD. For comparing quantitative data, parameters showing normal distributions were compared using independent sample *t*-test to compare the difference in gender groups. Statistical significance was defined when $P < 0.05$. Comparison between the incidence of thyroid gland variations in the female and the male cadavers were tested by Fisher's exact test.

Results

Grossly, normal thyroid gland from cadavers showed normal features of the gland (Figure 1), which had smooth surface. Histologically, the gland was composed of several follicles formed by cuboidal follicular cells. Few parafollicular cells, or calcitonin-producing cells, with large and clear cytoplasm (Figure 1C) were found situated among the follicular cells. The lumen of the follicle was filled with colloid substance. In the specimen from an old man of 105 years old, the follicular cells became squamous-type epithelium, or flattened cells (Figure 1D). The follicles in that specimen also showed follicles with variable sizes and irregular shape; many follicles contained no colloid.

The thyroid gland with nodular goiter was a slightly enlarged gland with smooth surface, and contained a single nodule inside of which was clear brownish jelly substance (Figure 2). The nodule did not contain fibrous capsule but enlarged follicles of variable sizes. The follicular cells were clearly observed, some had become squamous, while other remained cuboidal. Within the colloid, red blood cells were occasionally observed suggesting hemorrhage within the nodule.

The thyroid glands from cadavers with multinodular goiter revealed an increased size with irregular surface (Figure 3). The cut surface revealed several brownish or reddish and white nodules that varied in sizes. Histologically, the nodules contained follicles for varied sizes, mostly without capsule. The follicular cells were either normal cuboidal or flattened squamous, with red blood cells occasionally observed within the colloid.

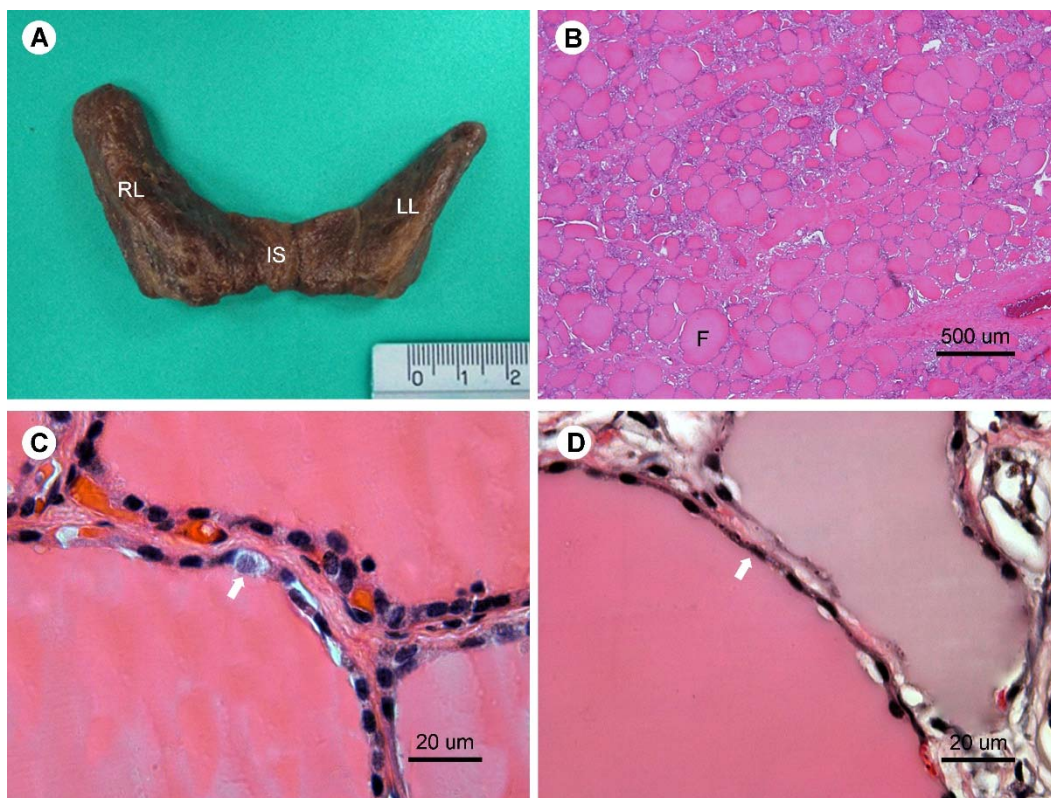


Figure 1. Gross structure of normal thyroid gland from the cadaver specimen, showing smooth surface, the right and left lobes and isthmus (A). Its histology reveals several follicles containing eosinophilic colloid (B), with cuboidal follicular cells and occasional parafollicular cells with larger cell size and clear cytoplasm (C, arrow). The follicular cells of a thyroid specimen of a 105 years old man are found flattened, or squamous (D, arrow). F, follicle; IS, isthmus; LL, left lobe; RL, right lobe

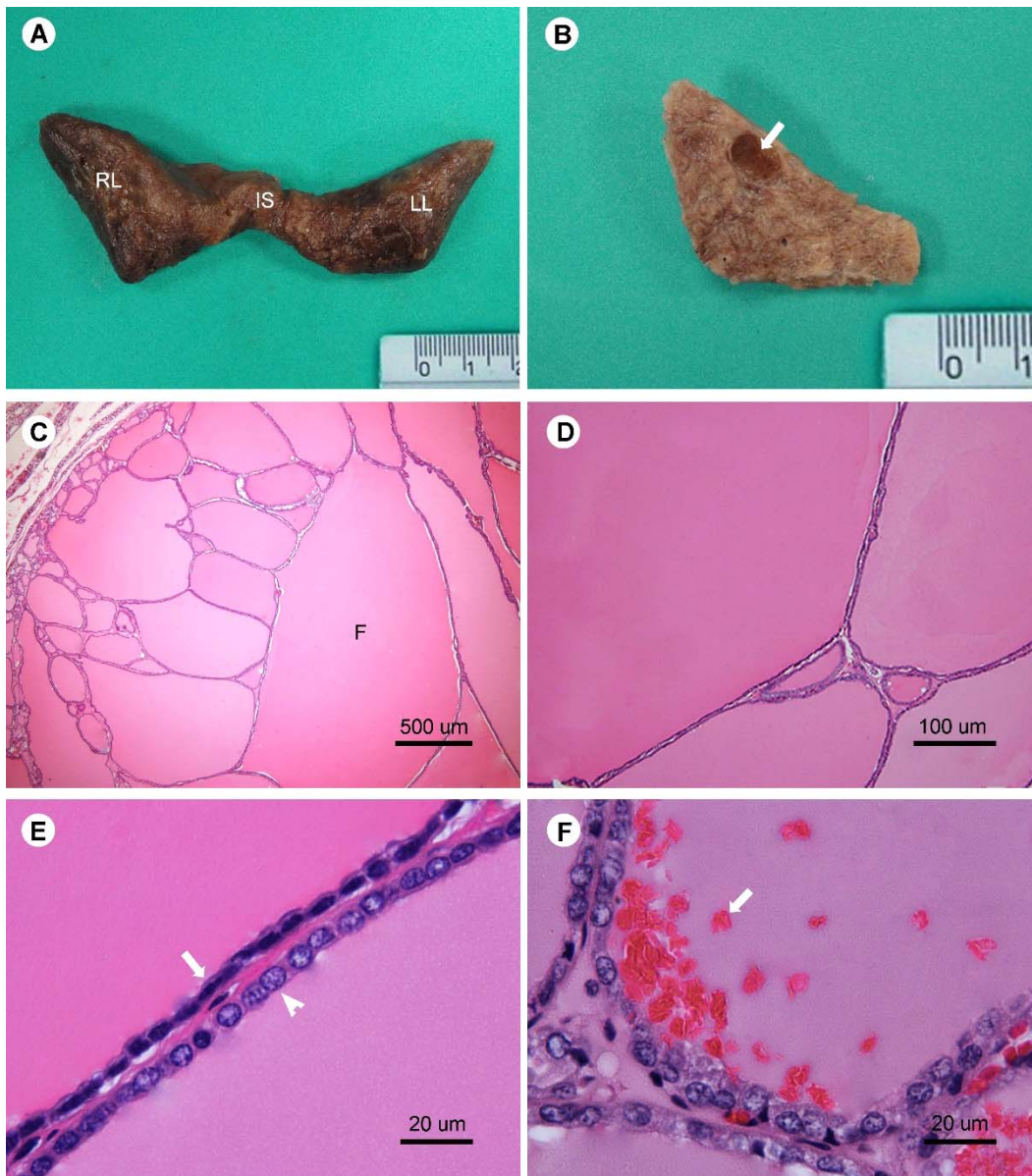


Figure 2. Gross structure of the thyroid gland from the cadaver specimen with nodular goiter showing smooth surface (A) and a single nodule with clear brownish jelly substance inside on the cut surface (B, arrow). Histological structure of the nodule reveals enlarged follicles of variable sizes (C and D). The follicular cells are clearly observed, some were squamous (E, arrow), while others cuboidal (E, arrowhead). Within the colloid, red blood cells are occasionally observed (F, arrow) suggesting hemorrhage within the nodule. F, follicle; IS, isthmus; LL, left lobe; RL, right lobe.

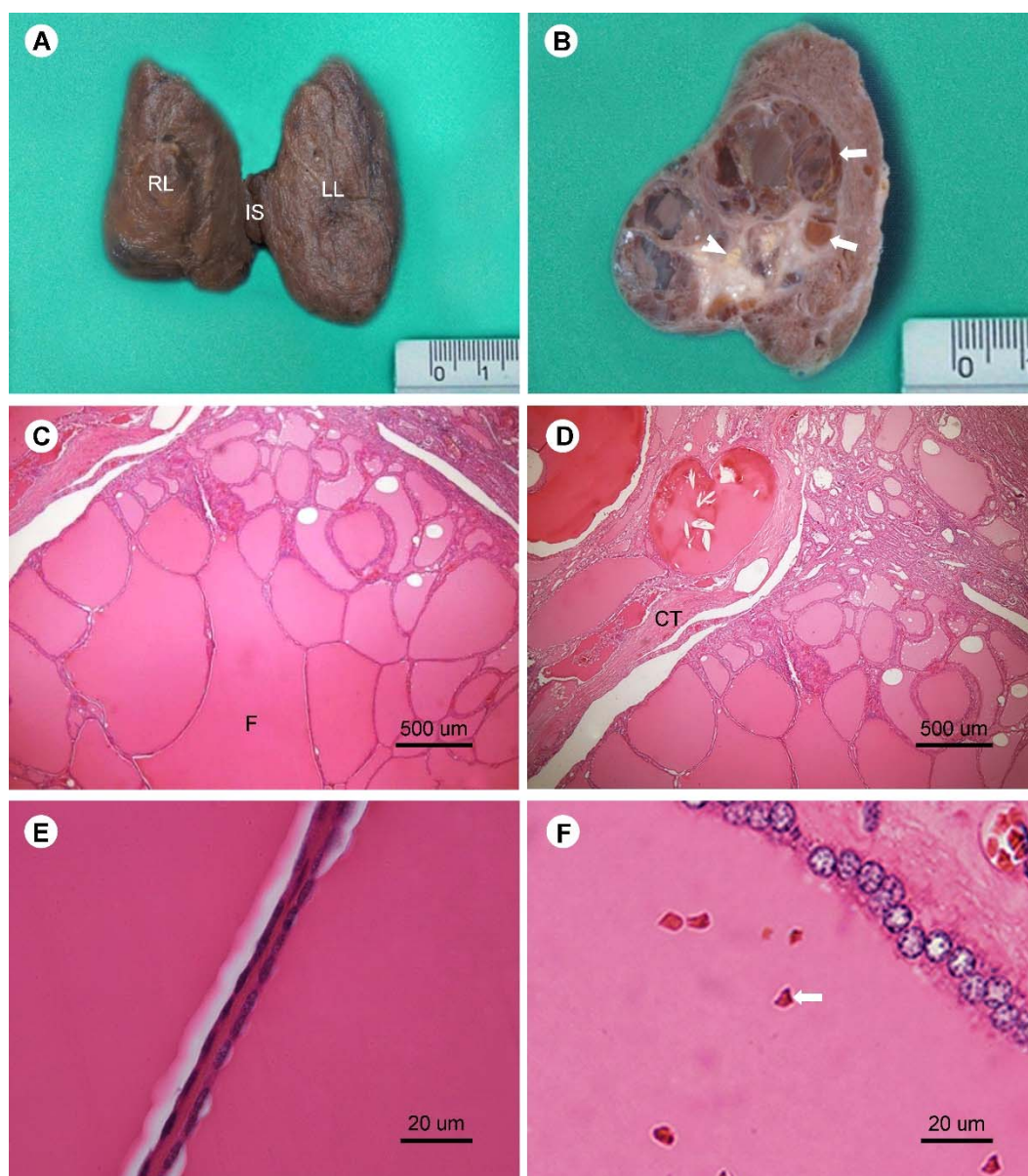


Figure 3. The thyroid gland from cadavers with multinodular goiter reveal an increased size of the gland with irregular surface (A). The cut surface shows several brownish or reddish (arrows) and white nodules (arrowhead), with variable sizes (B). Histologically, the nodules contained variable sizes of follicles (C), and each individual nodules are surrounded by dense connective tissue (D). The follicular cells are either squamous (E) or normal cuboidal (F), with red blood cells occasionally observed within the colloid (F, arrow). CT, connective tissue; F, follicle; IS, isthmus; LL, left lobe; RL, right lobe.

The thyroid glands from cadavers with Hashimoto thyroiditis revealed an increased size and the cut surface showed several brownish patches (Figure 4). Histologically, the glands contained numerous bands of dense collagenous connective tissue and patches of lymphocyte aggregations. The aggregation of lymphocytes was observed in

the interstitial tissue as well as in invading thyroid follicles. Germination center of the lymphocytes were occasionally observed (Figure 4E). Several follicular cells were enlarged with spherical nuclei and abundant eosinophilic cytoplasm, namely "Hurthle cells" (Figure 4F).⁽⁶⁾

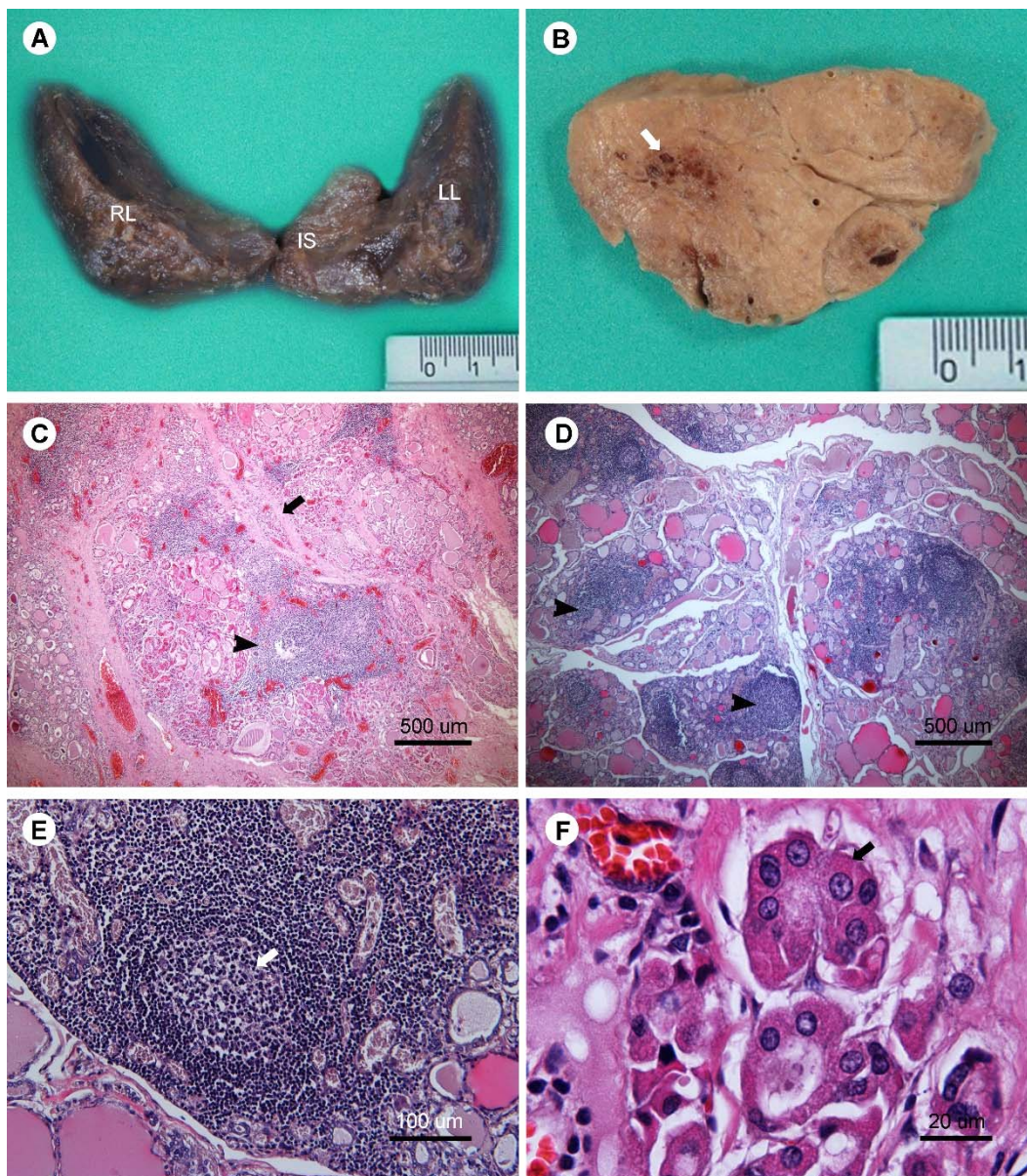


Figure 4. The thyroid gland from cadavers with Hashimoto thyroiditis revealed an increasing size of the gland (A) and the cut surface showed several brownish patches (B, arrow). Histologically, the gland contained numerous bands of dense collagenous connective tissue (C, arrow) and lymphocytic aggregations (C and D, arrowheads). Under high magnification, aggregations of lymphocytes with germinal center replaced normal thyroid follicles (E, arrow) and several follicular cells enlarged with spherical nuclei and abundant eosinophilic cytoplasm, namely "Hurthle cells" (F, arrow). IS, isthmus; LL, left lobe; RL, right lobe

The thyroid glands from cadavers with Grave's disease revealed an increased size and brownish cut surface (Figure 5). Histologically, the gland contained numerous small follicles with decreased amount of

colloid, accompanied by peripheral scalloping appearance typical of thyroid histopathology of Grave's disease. ⁽⁷⁾ Several lymphocytes were found penetrating the interstitial space between follicles.

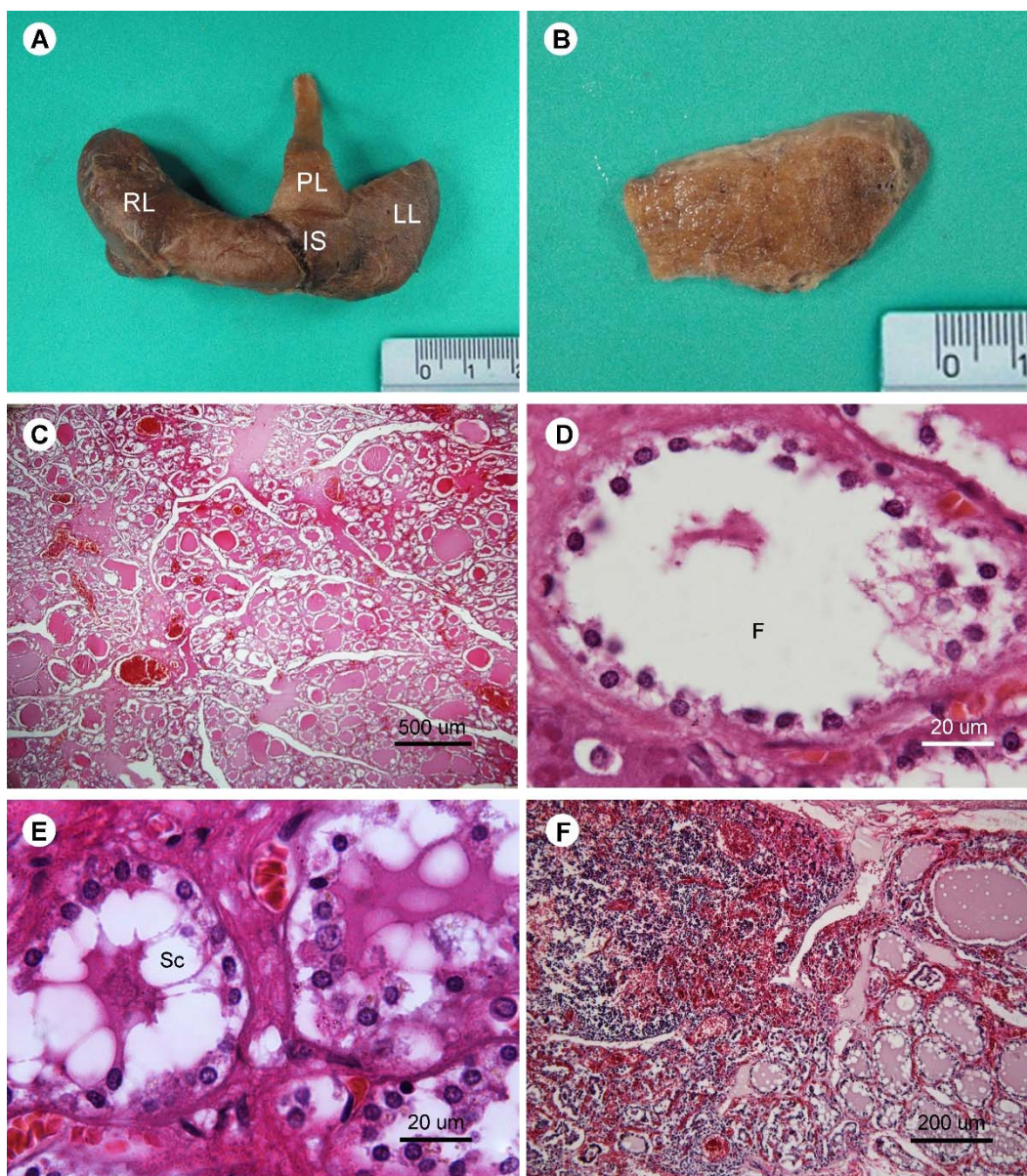


Figure 5. The thyroid gland from cadavers with Grave's disease reveals an increased size of the gland (A) and brownish cut surface (B). Histologically, the gland contains numerous small follicles with clear zone at their periphery (C). Under high magnification, several follicles contained no colloid (D) and some have colloid with peripheral clear zones, or scalloped appearance (E). Several lymphocytes are found penetrating the interstitial space and into the follicles (F). F, follicle; IS, isthmus; LL, left lobe; PL, pyramidal lobe; RL, right lobe; Sc, scalloped appearance.

The thyroid gland diseases mentioned were found in PL, LGT and the main lobes (right and left lobes) of the gland, with the incidence at 46%, 33% and 48%, respectively (Table 1). The incidence observed by histopathology revealed higher prevalence in the female than in the male specimens

(Table 2), with higher incidence of nodular goiter found in male and higher incidence of multinodular goiter found in females. Through Fisher's Exact test, the incidence of multinodular goiter in the female specimens was significantly ($P < 0.01$) higher than those in the male.

Table 1. Histopathological diagnoses of the thyroid tissue in the pyramidal lobe (PL), levator glandulae thyroideae (LGT) and right or left lobes or main thyroid gland (M) from cadavers. The number in parentheses are number of specimens examined.

| Diagnosis | From | | |
|--|----------------|----------------|-----------------|
| | PL (13) | LGT (12) | M (102) |
| Nodular goiter | 4 | 2 | 21 |
| Multi-nodular goiter | | 1 | 18 |
| Hashimoto thyroiditis | 1 | | 5 |
| Nodular goiter + Hashimoto thyroiditis | 1 | | 2 |
| Grave's disease | | 1 | 3 |
| Total | 6 (46%) | 4 (33%) | 49 (48%) |

Table 2. Sex difference in the incidence of thyroid diseases diagnosed from histopathology of the right or left lobe of thyroid glands from 102 cadavers: 42 females and 60 males. Values represent number of cases (% of specimens examined)

| Diagnosis | Female | Male | Total |
|--|-------------------|-------------------|-------------------|
| Nodular goiter | 6 (14.3%) | 15 (25%) | 21 (20.6%) |
| Multinodular goiter | 14 (33.3%) | 4 (6.7%)* | 18 (17.7%) |
| Hashimoto thyroiditis | 1 (2.4%) | 4 (6.7%) | 5 (4.9%) |
| Nodular goiter + Hashimoto thyroiditis | 2 (4.8%) | 0 (0%) | 2 (2.0%) |
| Grave's disease | 1 (2.4%) | 2 (3.3%) | 3 (2.9%) |
| Total | 24 (57.1%) | 25 (41.7%) | 49 (48.0%) |

* $P < 0.01$, female vs male

Discussion

The appearance of histology of thyroid taken from cadavers in this study was adequate, in terms of quality, to distinguish cell types and histological structures of the gland. Previous reports have also revealed histology and even ultrastructure of the thyroid gland and the parathyroid gland taken directly from the cadavers, but not to the extent of making histopathological diagnosis.^(4, 5) The thyroid follicles of the 105 years old man in this study that had flatten epithelium and variable sizes without colloid were similar to those described elsewhere.⁽⁶⁾

The incidence of thyroid nodules found in cadavers has been reported with wide variation at 8% to 65%, depending on geographical locations.⁽²⁾ However, clinical finding of palpable nodular and multinodular goiter was only 6%, with more prevalence in the females.⁽⁹⁾ The incidence found in normal population by thyroid imaging was much higher, at 40 - 50%.^(10, 11) Obviously, clinical assessment of thyroid goiter, i.e., by palpation, should have accuracy far below than that by thyroid imaging, e.g., ultrasonography, or by post-mortem examinations.

The gross and microscopic pathology of the thyroid glands typical of Hashimoto thyroiditis and Grave's disease from the cadavers were revealed in this study. Again, the prevalence of patients showing clinical manifestations of thyroid diseases is much lower than the post-mortem findings reported herein (Table 3). In the nodular goiter, the ratio of women to men with the disease was about 4:1.⁽⁹⁾ This ratio was quite different from the survey in this study, in which female: male ratio was about 1.5:1, suggesting that a substantial number of men may have subclinical nodular thyroid goiter.

A report of post-mortem cases of autoimmune

thyroiditis were 27% in females and 7% in males,⁽¹²⁾ which was much higher than in this study (Table 3). It is likely that the histological findings in the study by Vanderpump (2011) were all thyroiditis related to autoimmune condition, including Hashimoto thyroiditis. However, clinical manifestation of hypothyroidism was much lower, at the prevalence of 1 - 2%; and this prevalence included that of Hashimoto thyroiditis.^(13, 14) In hyperthyroidism, which most cases are Grave's disease, the prevalence in females was reported at 0.5 - 2.0% for borderline cases and 0.04% for overt cases, and males had about 10x times lower in the prevalence.⁽¹²⁾ The prevalence in the females in their study (0.5 - 2.0%) was slightly lower than that reported in this post-mortem study (2.4%). Surprisingly, the prevalence in the male specimens in this study was at 3.3% (Table 3), which was much higher than the clinical prevalence of the males reported by Vanderpump (2011). Therefore, a possibility of subclinical Grave's disease in males should be considered. Overall, this post-mortem study suggests that the prevalence of subclinical thyroid diseases, i.e., thyroid goiter, Hashimoto thyroiditis and Grave's disease, may be much higher in normal population.

Conclusion

Anatomical and histological features showing normal and abnormalities of thyroid specimens from the southern region of Thailand cadavers. Histological examinations of the cadaveric specimens revealed higher prevalence of nodular goiter, multinodular goiter, Hashimoto thyroiditis, mixed nodular goiter/Hashimoto thyroiditis and Grave's disease, compared to those of clinical reports, suggesting subclinical cases of abnormal thyroid function in normal population.

Table 3. Comparison of thyroid diseases found in this study and those from clinical reports

a. Normal and abnormal thyroid glands discovered by histology of the gland isolated from 60 male and 42 female cadavers. Value = number of cases (%)

| | Female | Male |
|--|------------------|------------------|
| Normal | 18 (42.8%) | 35 (58.3%) |
| Nodular goiter | 6 (14.3%) | 15 (25.0%) |
| Multinodular goiter | 14 (33.3%) | 4 (6.7%) |
| Hashimoto thyroiditis | 1 (2.4%) | 4 (6.7%) |
| Grave's disease | 1 (2.4%) | 2 (3.3%) |
| Nodular goiter + Hashimoto thyroiditis | 2 (4.8%) | 0 (0%) |
| Total | 42 (100%) | 60 (100%) |

b. Prevalence of clinical thyroid diseases

| Thyroid disease | Prevalence | Reference |
|--|---|--|
| Nodular and multinodular goiter | 10% for females; 2% for males 5% by palpation and 50% by ultrasonography | Vanderpump <i>et al.</i> , 1955 Gharib and Papini, 2007 |
| Hypothyroidism, including Hashimoto thyroiditis | 1-2% (10 times lower in males) | Vanderpump and Tunbridge, 2002 |
| Hyperthyroidism, including Grave's disease | 0.5-2.0% (borderline) and 0.04% (overt) for females (10 times lower in males) | Vanderpump, 2011 |

Conflict of interest

All authors, hereby, declare no conflict of interest.

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