

Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID I

Does Dipeptidyl Peptidase-4 Inhibitor Exacerbate Graves' Disease?

Tomonori Sekizaki, MD¹, Hiraku Kameda, MD, PhD¹,
 Kyu Yong Cho, MD, PhD¹, Nakamura Akinobu, MD, PhD¹,
 Kiyohiko Takahashi, MD, PhD², Norio Wada, MD, PhD²,
 Jun Takeuchi, MD, PhD³, So Nagai, MD, PHD⁴, Hideaki Miyoshi,
 MD, PhD¹, Tatsuya Atsumi, MD, PhD¹.

¹HOKKAIDO UNIV GRAD SCHL OF MED, Sapporo, Japan,

²Sapporo City General Hospital, SAPPORO, Japan, ³Sapporo
 Diabetes and Thyroid Clinic, Sapporo, Japan, ⁴Sapporo Medical
 Center NTT EC, Sapporo, Japan.

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Abstract: [Background] Dipeptidyl peptidase-4 (DPP-4) is expressed as CD26 on the surface of immune cells including T cells, suggesting that inhibition of DPP-4 may affect the immune system (1). Actually, DPP-4 inhibitor (DPP-4i)-induced polyarthritis and bullous pemphigoid have been reported (2, 3). It has also been reported that the prevalence of Hashimoto's thyroiditis was significantly higher in patients on DPP-4i treatment (4). However, relationships between DPP-4i and Graves' disease has been unclear. [Methods] To investigate the impact of DPP-4i administration on the activity of Graves' disease, we conducted a multicenter observational trial that included patients with both Graves' disease and type 2 diabetes mellitus who were administered an oral hypoglycemic agent (OHA) including DPP-4i from December in 2009 to April in 2018. Patients who had systemic diseases affecting thyroid function and those who underwent thyroidectomy or radioiodine treatment within 6 months before or after OHA administration were excluded. Exacerbation of Graves' disease was defined as an increase in antithyroid drug dose within 6 months after OHA administration. The trial was approved by the institutional review board of Hokkaido University Hospital. [Results] Eighty-three patients were enrolled in the study, and they were divided into an exacerbation group ($n = 18$) and a non-exacerbation group ($n = 65$). Comparing baseline characteristics, the percentage of DPP-4i administration was higher in the exacerbation group (83.3%) than in the non-exacerbation group (32.3%) ($p = 0.0001$). Mean age was also significantly higher in the exacerbation group ($p = 0.04$), and the duration of Graves' disease was significantly shorter ($p = 0.01$). Multivariate logistic regression analysis using factors extracted by comparing baseline characteristics demonstrated a significant association between DPP-4i administration and Graves' disease exacerbation (odds ratio 5.62, 95% confidence interval 1.16–27.0, $p = 0.02$). [Conclusion] The current study suggests that DPP-4i administration is associated with exacerbation of Graves' disease.

Reference: (1) Morimoto C et al., *Immunol Rev*. 1998 Feb;161:55–70. (2) Yokota K et al., *Intern Med*. 2012;51(15):2041–4. (3) Yoshiji S et al. *J Diabetes Investig*. 2018 Mar;9(2):445–447. (4) Kridin K et al. *Immunol Res*. 2018 Jun;66(3):425–430.

Thyroid

THYROID NEOPLASIA AND CANCER

Evaluation and Comparison of Ultrasonographic Features According to Histology of Thyroid Nodules

Cátia Ferrinho, MD, Clara Valério Cunha, MD, Eugénia Silva, MD, Catarina Saraiva, MD, Rute Costa Ferreira, MD, Catarina Roque, MD, Martinha Chorão, MD, Manuela Oliveira, MD, João Sequeira Duarte, MD.

Hospital Egas Moniz, Lisboa, Portugal.

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Introduction: The prevalence of thyroid nodules identified by ultrasonography (US) may be up to 70%, with the majority being incidentalomas. Less than 15% of thyroid nodules will be malignant. Ultrasonography plays a key role in the diagnosis and management of thyroid diseases and US features have been described in way to predict the risk of malignancy. **Aim:** Evaluate and correlate US features with histological results, in our hospital, from January 2017 to December 2018. **Materials and methods:** Cross-sectional study. A total of 117 patients were evaluated, 77 had histology of nodular hyperplasia (benign) and 40 had histology of thyroid carcinoma (malign) after partial or total thyroidectomy. We described the size of the nodule (the largest diameter), the US features detailed in the ultrasound report (shape, margins, echogenicity, composition and microcalcifications), the EU-TIRADS score of each nodule and the histology of thyroid. The data were analysed using nonparametric statistical tests. The results are presented as median (interquartile range). The level of significance accepted was $p < 0.05$. **Results:** Of the 117 patients, 82.1% were female, with a median age of 59.7 (25.0) years, nodule size in benign histology group was 35.0 (14.0) mm and in malignant histology group was 20.0 (28.0) mm. Of malignant nodules, 90.0% ($n=36$) were papillary carcinomas. The prevalence of US features: 76.9% were solid, 35.0% had microcalcifications, 25.6% had irregular margins, 17.9% were markedly hypoechoic and 6.8% were taller-than-wide. Three characteristics were significantly related to malignancy: irregular margins ($p=0.001$), markedly hypoechoic ($p=0.001$) and microcalcifications ($p=0.015$). The taller-than-wide feature had the highest specificity of 94.8%; the marked hypoechogenicity with a specificity of 92.2%, had the highest positive likelihood ratio (LHR+: 4.81 (95% CI: 2.02–11.44)) and the highest diagnostic odds ratio (DOR: 7.10 (95% CI: 2.48–20.30)). The EU-TIRADS 5 category had a significant association with malignancy ($p=0.001$) and 80.0% of malignant nodules were classified in this category. The specificity was 62.3%, LHR+ was 2.12 (95% CI: 1.53–2.94) and DOR was 6.62 (95% CI: 2.69–16.31). **Conclusion:** In the evaluation of the US features, marked hypoechogenicity had the highest LHR+ and DOR. It was possible to verify that the EU-TIRADS 5 category was a good predictor of risk to malignancy, which reinforces the importance of categorizing the nodules for selective perform of fine needle aspiration.