

The value of the mean peak systolic velocity of the superior thyroidal artery in the differential diagnosis of thyrotoxicosis

ULTRASONOGRAPHY

Tae Kyoon Kim, Eun Ju Lee

Department of Internal Medicine, Inje University College of Medicine, Busan, Korea

ORIGINAL ARTICLE

<http://dx.doi.org/10.14366/usg.14059>
pISSN: 2288-5919 • eISSN: 2288-5943
Ultrasonography 2015;34:292-296

Purpose: The aim of this study was to validate the superior thyroidal artery mean peak systolic velocity (STA-mPSV) as an alternative to other diagnostic parameters in the differentiation of the causes of thyrotoxicosis in Korean patients.

Methods: This study was conducted with newly diagnosed and untreated thyrotoxic patients. Forty patients were diagnosed with Graves disease (GD) and 20 patients with destructive thyroiditis (DT). Another 60 healthy subjects without thyroid disease participated as the control group. Blood samples were taken to evaluate the thyroid function and thyroid autoantibodies (TRAb). Twenty-four hour radioactive iodine uptake (RAIU) scanning was performed to confirm GD or DT. The STA-mPSV was measured using color Doppler ultrasonography.

Results: The STA-mPSV was significantly higher in the untreated GD group than in the DT group (GD, 78.96 ± 29.04 cm/sec; DT, 29.97 ± 14.67 cm/sec; control, 17.55 ± 4.99 cm/sec; $P < 0.001$). The area under the curve (AUC) of the STA-mPSV for the differential diagnosis of untreated GD and DT was 0.9506 (optimal cutoff value, 41.3 cm/sec; sensitivity, 95%, 38/40; specificity, 85%, 17/20) in the receiver operating characteristic analysis. The AUC values of the STA-mPSV, RAIU, and TRAb were 0.9506, 1, and 0.9988, respectively ($P = 0.159$).

Conclusion: In clinical practice, the STA-mPSV has a diagnostic value similar to that of the TRAb and 24-hour RAIU in the differential diagnosis of newly diagnosed Korean thyrotoxic patients.

Keywords: Graves disease; Thyroiditis; Thyrotoxicosis; Ultrasonography, Doppler

Received: December 3, 2014

Revised: March 23, 2015

Accepted: March 24, 2015

Correspondence to:

Tae Kyoon Kim, MD, Department of Internal Medicine, Inje University College of Medicine, 75 Bokji-ro, Busanjin-gu, Busan 614-735, Korea

Tel. +82-51-890-6270

Fax. +82-51-892-0273

E-mail: doctor73kr@gmail.com

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Thyrotoxicosis can be classified into Graves disease (GD) or destructive thyroiditis (DT) according to the pathophysiology. GD can be treated by antithyroid drugs, radioiodine therapy, or subtotal thyroidectomy, whereas DT is usually managed using only conservative therapy. Making a correct and rapid differential diagnosis of GD and DT is extremely important because the treatments and the prognosis of these two conditions are very different from each other.

In general, 24-hour radioactive iodine uptake (RAIU) scans and serum thyroid stimulating hormone receptor antibodies (TRAb) are used to distinguish GD from DT. However, the time required for obtaining the results of these tests depends on the medical facilities. Further, 24-hour RAIU scans may not be useful in certain clinical conditions such as a recent intake of iodine-rich food or injection

Copyright © 2015 Korean Society of Ultrasound in Medicine (KSUM)



How to cite this article:

Kim TK, Lee EJ. The value of the mean peak systolic velocity of the superior thyroidal artery in the differential diagnosis of thyrotoxicosis. Ultrasonography. 2015 Oct;34(4):292-296.

of iodine-based contrast media (coronary angiography, computed tomography, etc.) for certain medical purposes. Color Doppler ultrasonography (US) can be a noninvasive and cost-effective diagnostic alternative for rapidly obtaining useful information in these cases.

It is now generally accepted that color Doppler US for diffuse autoimmune thyroiditis shows a high intra-parenchymal blood flow at onset and at the peak of the disease [1–3]. Thus, the measurement of superior thyroidal artery mean peak systolic velocity (STA-mPSV) might be easier and more convenient to clinicians in discriminating thyrotoxicosis than the pre-established methods. Recent studies tend to emphasize more the justification of the STA-mPSV as a diagnostic alternative and more worldwide validated data are needed [4,5]. The aim of this study was to evaluate the diagnostic value of STA-mPSV and diagnostic coincidence with TRAb and 24-hour RAIU scans in differentiating newly diagnosed and untreated thyrotoxicosis in Korean patients.

Materials and Methods

Subjects

The Institutional Review Board of our institution approved this study. Sixty patients (age, >18 years; 19 males and 41 females) who presented at our endocrinology department with newly diagnosed and drug-naïve thyrotoxicosis between February 2010 and July 2011 were enrolled in this prospective study in the order of their visit to the department. Thyrotoxicosis was defined as elevated serum-free thyroxine (FT4, >1.71 ng/dL) and suppressed thyroid-stimulating hormone (TSH, <0.27 mIU/L) concentrations. Patients with thyrotoxicosis, elevated TRAb concentrations ($\geq 15\%$), elevated 24-hour RAIU ($\geq 40\%$), and/or typical features such as diffuse goiter and exophthalmos were defined as having GD. The remaining patients with thyrotoxicosis, decreased TRAb concentrations (<15%), and suppressed 24-hour RAIU (<40%) were diagnosed as having DT. Among these patients, 40 patients were confirmed to have GD and classified into the GD group; the remaining 20 patients were confirmed to have DT and classified into the DT group. An additional 60 healthy subjects without thyroid disease were also enrolled to create a control group. The control group consisted of patients who visited the endocrinology internal medicine department for thyroid screening. The exclusion criteria were as follows: (1) recent or previous antithyroidal treatment history (antithyroid drugs, radioiodine therapy, or subtotal thyroidectomy); (2) nodule, cyst, or thyroid cancer on the measured site; (3) multinodular goiter; (4) toxic nodular goiter; (5) drug-induced or trauma-induced thyroiditis; (6) pregnancy or lactation; and (7) hashitoxicosis, subacute granulomatous thyroiditis, or postpartum thyroiditis.

Data Analysis

The differential diagnosis of thyrotoxicosis was made by measuring FT4, TSH, TRAb, and 24-hour RAIU. In general, assays to estimate FT4 are more widely validated and recognized as useful diagnostic tools than those to estimate FT3 in clinical practice. Therefore, we decided to use only FT4 in this study. Serum FT4 and TSH were measured by a commercial electrochemiluminescence immunoassay (Roche Diagnostics GmbH, Mannheim, Germany; FT4 measurement range, 0.023 to 7.77 ng/dL [normal range, 0.93 to 1.71 ng/dL]; TSH measurement range, 0.005 to 100 mIU/L [normal range, 0.27 to 4.2 mIU/L]). Serum TRAb was measured by a two-step radioreceptor assay (RSR Ltd., Cardiff, UK; TRAb normal range, <15%). The RAIU was measured at 24 hours after ingestion of iodine-131 (normal range, 15% to 40%). After the patients rested in the supine position for 10 minutes, their thyroid glands were scanned longitudinally and transversally by using color Doppler US (HD 11 XE, Phillips, Bothell, WA, USA) with a 5–12 MHz linear transducer in both the B-mode and the color-flow mode. STA-mPSV was measured 3 times in all groups on the right superior thyroidal artery at the point where it runs parallel to the common carotid artery (Figs. 1, 2). The STA-mPSV was measured 3 times at the same site, and we calculated the average of these measured values. The average value was considered the STA-mPSV of each patient. One examiner (T.K.K.) examined all the patients in order to avoid interobserver variations.

Statistical Analysis

This study was designed as a pilot study to ascertain the diagnostic value and clinical usefulness of STA-mPSV in the differential diagnosis of thyrotoxicosis. The data were presented as the mean value \pm standard deviation for continuous variables and frequencies for nominal variables. An analysis of variance (ANOVA) or Kruskal-Wallis test and a t-test or Wilcoxon's rank-sum test were performed after the normality test in order to compare the results of the blood tests among the groups. To assess the efficacy of STA-mPSV in predicting the GD, the sensitivity, specificity, area under the curve (AUC), and cutoff values were calculated by using receiver operating characteristic (ROC) curves. An ROC curve was computed to assess the diagnostic value of STA-mPSV as an alternative to other diagnostic parameters. A P-value of <0.05 was considered statistically significant. All statistical analyses were conducted using SAS ver. 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

Patient Characteristics

Table 1 shows the demographic and clinical characteristics for

Korean participants with GD or DT and the control group with a normal thyroid function. Serum FT4 values were significantly higher in the GD group than in the other groups (GD, 4.76 ± 1.90 ng/dL; DT, 3.57 ± 2.04 ng/dL). TSH values were fully suppressed in the GD and DT groups, showing significant differences between the groups. The TRAb values were significantly higher in the GD group than in the DT group (GD, $55.13 \pm 22.36\%$; DT, $8.50 \pm 5.28\%$). Twenty-four hour RAIUs in the GD group were significantly higher than those in the DT group. STA-mPSV in the GD group was significantly higher than in the DT and control groups (78.96 ± 29.04 cm/sec vs. 29.97 ± 14.67 and 17.55 ± 4.99 cm/sec, respectively; $P < 0.001$) (Table 1, Figs. 1–3). There were statistically significant differences in

the parameters of all groups except for sex and age. The diagnostic accuracy of GD with an STA-mPSV value of more than 67.4 cm/sec was the highest (sensitivity, 100%) and that of DT with an STA-mPSV value of less than 29 cm/sec was also the highest (sensitivity, 100%).

Table 1. Demographic and clinical characteristics for Korean participants with Graves disease (GD) or destructive thyroiditis (DT) and the control group with a normal thyroid (NT) function

Variable	GD (n=40)	DT (n=20)	NT (n=60)	P-value
Sex (M:F)	12:28	7:13	25:35	0.488
Age (yr)	43.23 ± 14.56	41.70 ± 13.97	47.33 ± 15.59	0.273
FT4	4.76 ± 1.90	3.57 ± 2.04	1.31 ± 0.11	< 0.001
TSH	0.006 ± 0.001	0.32 ± 1.34	2.83 ± 0.62	< 0.001
TRAb	55.13 ± 22.36	8.50 ± 5.28	N/A	< 0.001
24-hr RAIU	60.97 ± 12.36	0.71 ± 0.51	N/A	< 0.001
STA-mPSV	78.96 ± 29.04	29.97 ± 14.67	17.55 ± 4.99	< 0.001

N/A, not available; STA-mPSV, superior thyroidal artery–mean peak systolic velocity. Serum-free thyroxine (FT4) normal range: 0.93–1.71 ng/dL; thyroid-stimulating hormone (TSH) normal range: 0.27–4.2 mIU/L; thyroid autoantibodies (TRAb) normal range: <15%; 24-hour radioactive iodine uptake (RAIU) normal range: 15%–40%.

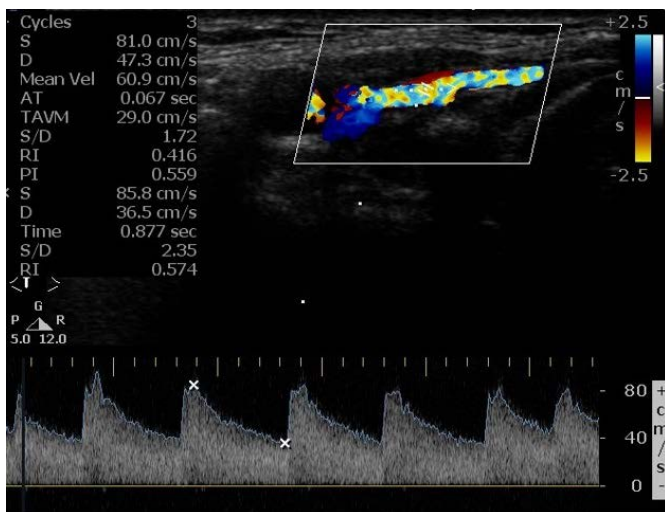


Fig. 1. Color Doppler sonogram of a 55-year-old woman diagnosed with Graves disease. The superior thyroidal artery–mean peak systolic velocity is measured to be 81.0 cm/sec.

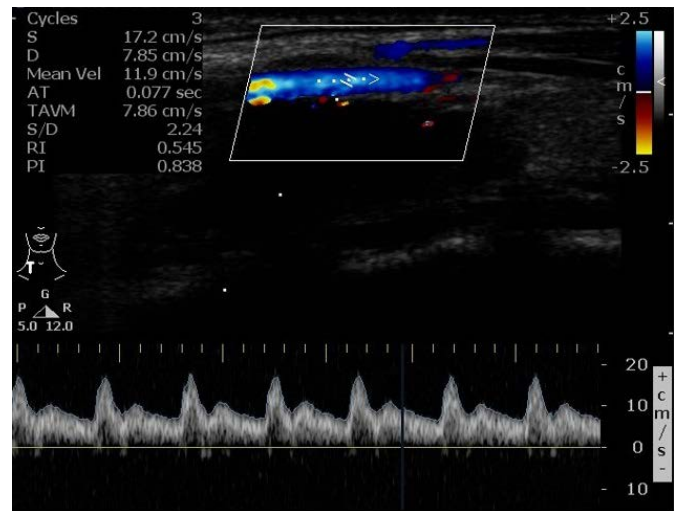


Fig. 2. Color Doppler sonogram of a 31-year-old man diagnosed with destructive thyroiditis. Superior thyroidal artery–mean peak systolic velocity is measured to be 17.2 cm/sec.

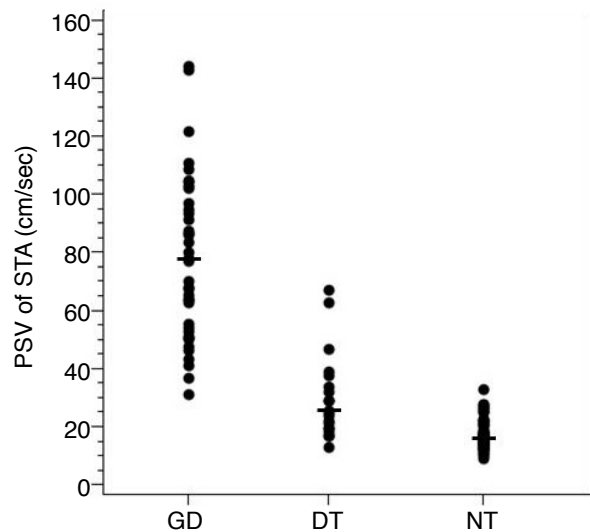


Fig. 3. The distribution of superior thyroidal artery–mean peak systolic velocity (STA-mPSV) among groups with Graves disease (GD), destructive thyroiditis (DT), and euthyroidism. Each dot represents an individual value of STA-mPSV among groups. The STA-mPSV value was the highest in the untreated GD group, followed by DT and then, the control group. The horizontal lines represent the mean values of STA-mPSV, $P < 0.001$, among groups. NT, normal thyroid.

Table 2. Diagnostic value of STA-mPSV for the differential diagnosis of thyrotoxicosis

Variable	Cutoff value	Sensitivity	Specificity	Odds ratio	95% Confidence interval	P-value
GD vs. DT	41.3 cm/sec	95%	85%	107.67	16.46–704.44	<0.001

STA-mPSV, superior thyroidal artery–mean peak systolic velocity; GD, Graves disease; DT, destructive thyroiditis.

ROC Curve of STA-mPSV for the Differential Diagnosis of Thyrotoxicosis

We computed and analyzed the ROC curve of STA-mPSV in order to discriminate the cause of newly diagnosed thyrotoxicosis. Most STA-mPSV values in untreated GD patients were greater than 41.3 cm/sec. In contrast, those in DT patients were less than 41.3 cm/sec. The optimal sensitivity and specificity to differentiate untreated GD from DT were 95% (38/40) and 85% (17/20), respectively, when the cutoff value was set to 41.3 cm/sec (odds ratio, 107.67; 95% confidence interval [CI], 16.46 to 704.44) (Table 2). The AUC of STA-mPSV to distinguish the cause of thyrotoxicosis was 0.9506 (95% CI, 0.8966 to 1.0000).

Diagnostic Concurrence of STA-mPSV Compared with TRAb and 24-hour RAIU

In patients with thyrotoxicosis (n=40), the ROC curves of the AUC of the TRAb and 24-hour RAIU were 0.9988 and 1, respectively, and the ROC curve of the STA-mPSV was 0.9506. Although the areas under the ROC curves of the TRAb and 24-hour RAIU were higher than that of the STA-mPSV, there were no statistically significant differences (P=0.159) (Fig. 4).

Discussion

We studied the diagnostic value of the STA-mPSV in the differential diagnosis of newly diagnosed and untreated thyrotoxicosis in Korea. The STA-mPSV effectively differentiated the underlying causes of thyrotoxicosis in clinical practice. The sensitivity and the specificity of the STA-mPSV when the cutoff value was set to 41.3 cm/sec were sufficiently high to differentiate GD from DT. Moreover, an STA-mPSV value of more than 67.4 cm/sec shows the highest possibility of GD and that of less than 29 cm/sec shows the highest possibility of DT according to our study.

Several studies have reported that the measurement of the thyroid blood flow and peak systolic velocity (PSV) are clinically useful in differentiating GD from DT [2–7]. Further, increased thyroidal artery blood flow and PSV have been used as good clinical indices in the diagnosis of GD and as a predictor of the disease activity and the recurrence [2,8,9]. Hari Kumar et al. [6] studied the usefulness of inferior thyroidal artery (ITA)-mPSV by color Doppler US in the differential diagnosis of thyrotoxicosis. They reported that the levels

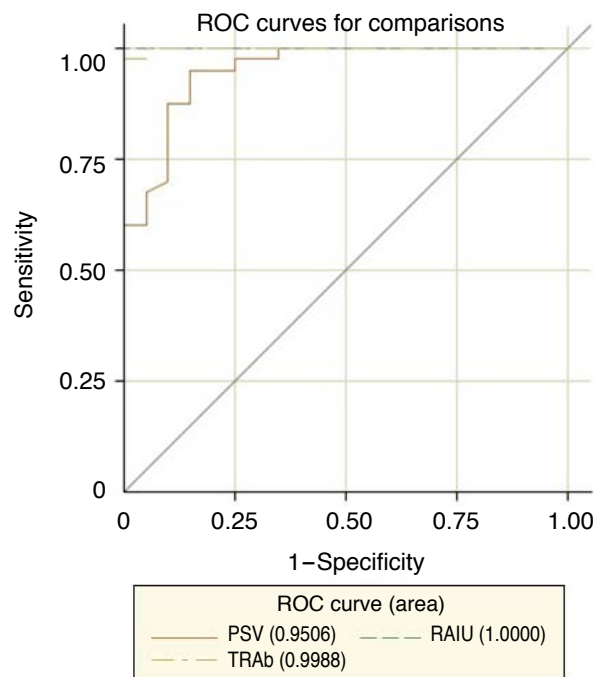


Fig. 4. Diagnostic concurrence of superior thyroidal artery–mean peak systolic velocity (STA-mPSV) compared with that of thyroid function and thyroid autoantibodies (TRAb) and 24-hour radioactive iodine uptake (RAIU). The receiver operating characteristic (ROC) curves of the area under the curve (AUC) were used to assess the diagnostic value of STA-mPSV in comparison with RAIU and TRAb in the differentiation of untreated Graves disease from destructive thyroiditis. The AUC was calculated by multiplying 1-specificity (0–1) with sensitivity (0–1). The AUC values of STA-mPSV, RAIU, and TRAb were 0.9506, 1, and 0.9988, respectively (P=0.159).

of ITA-mPSV were 57.6 ± 13.1 cm/sec in GD patients and 22.4 ± 5.4 cm/sec in DT patients, respectively. Moreover, Caruso et al. [7] reported the color Doppler measurement of the blood flow in ITA could overcome the limitations of a qualitative intraparenchymal analysis in the differential diagnosis of diffuse hyperfunctional thyroid disease.

In clinical practice, the anatomical structure of the superior thyroid artery makes it easier to measure PSV than that of ITA. Recently, Uchida et al. [4] reported that the STA-mPSV values in Japanese patients were 78.48 ± 36.28 cm/sec in the case of untreated GD

and 28 ± 12.84 cm/sec in the case of DT. The optimal sensitivity and the specificity were 83.7% and 92.3%, respectively, when the cutoff value was set to 45 cm/sec in the differentiation. These results showed similar levels of STA-mPSV in GD and DT but a rather high cutoff value as compared to this study. These differences probably resulted from the anatomical and racial differences and different measurement sites. Methods using TRAb and 24-hour RAIU have been used as useful and confirmative diagnostic methods in differentiating thyrotoxicosis. However, they could be time-consuming procedures, and 24-hour RAIU scanning has a clinical limitation due to the use of a radioactive material, which restricts its use in the case of pregnancy.

Color Doppler US is a noninvasive, rapid, and simple method to measure STA-mPSV. To ascertain the diagnostic value of STA-mPSV, we computed and compared the ROC curves of the AUC of STA-mPSV, TRAb, and 24-hour RAIU. The ROC curve of the AUC of STA-mPSV showed as high a diagnostic value as TRAb and 24-hour RAIU. Further, increased STA-mPSV indicated the high possibility of GD and could be used as a reliable and practical diagnostic method to make a more precise differential diagnosis of thyrotoxicosis in clinical practice. This was the first study to show the diagnostic value of STA-mPSV compared with that of 24-hour RAIU and TRAb in Korean thyrotoxic patients.

This study has several limitations. First, we did not enroll patients with current antithyroidal medication and other types of thyrotoxicosis, such as hashitoxicosis, subacute granulomatous thyroiditis, and postpartum thyroiditis. Therefore, we could not determine the characteristics of such cases. Second, the high blood flow might result from a progressive increase in vascular density, which correlates positively with the expression and serum levels of the vascular endothelial growth factor [8,9]. However, the exact pathophysiology of a high STA-mPSV needs to be clarified further. Third, we need to verify whether the STA-mPSV provides additional diagnostic value to the TRAb, 24-hour RAIU, gray-scale US, and color Doppler flow. Finally, our study was based on a pilot study. To secure higher statistical power, multicenter studies with larger samples will be required in the future.

In conclusion, in clinical practice, STA-mPSV has a diagnostic value similar to that of TRAb and 24-hour RAIU in the differential diagnosis of newly diagnosed Korean thyrotoxic patients.

ORCID: Tae Kyoon Kim: <http://orcid.org/0000-0001-6439-9266>; Eun Ju Lee: <http://orcid.org/0000-0003-3700-1640>

Conflict of Interest

No potential conflict of interest relevant to this article has been reported.

Acknowledgments

This study was supported by grants from Inje University in 2011.

References

1. Fobbe F, Finke R, Reichenstein E, Schleusener H, Wolf KJ. Appearance of thyroid diseases using colour-coded duplex sonography. *Eur J Radiol* 1989;9:29-31.
2. Ralls PW, Mayekawa DS, Lee KP, Colletti PM, Radin DR, Boswell WD, et al. Color-flow Doppler sonography in Graves disease: "thyroid inferno". *AJR Am J Roentgenol* 1988;150:781-784.
3. Messina G, Viceconti N, Trinti B. Graves' disease: ultrasonographic, color Doppler and histological aspects. *Recenti Prog Med* 1997;88:513-516.
4. Uchida T, Takeno K, Goto M, Kanno R, Kubo S, Takahashi S, et al. Superior thyroid artery mean peak systolic velocity for the diagnosis of thyrotoxicosis in Japanese patients. *Endocr J* 2010;57:439-443.
5. Chen L, Zhao X, Liu H, Wang Y, Li L, Lu B, et al. Mean peak systolic velocity of the superior thyroid artery is correlated with radioactive iodine uptake in untreated thyrotoxicosis. *J Int Med Res* 2012;40:640-647.
6. Hari Kumar KV, Pasupuleti V, Jayaraman M, Abhyuday V, Rayudu BR, Modi KD. Role of thyroid Doppler in differential diagnosis of thyrotoxicosis. *Endocr Pract* 2009;15:6-9.
7. Caruso G, Attard M, Caronia A, Lagalla R. Color Doppler measurement of blood flow in the inferior thyroid artery in patients with autoimmune thyroid diseases. *Eur J Radiol* 2000;36:5-10.
8. Nagura S, Katoh R, Miyagi E, Shibuya M, Kawaoi A. Expression of vascular endothelial growth factor (VEGF) and VEGF receptor-1 (Flt-1) in Graves disease possibly correlated with increased vascular density. *Hum Pathol* 2001;32:10-17.
9. Iitaka M, Miura S, Yamanaka K, Kawasaki S, Kitahama S, Kawakami Y, et al. Increased serum vascular endothelial growth factor levels and intrathyroidal vascular area in patients with Graves' disease and Hashimoto's thyroiditis. *J Clin Endocrinol Metab* 1998;83:3908-3912.