Differentiation Between the Two Types of Amiodarone-Associated Thyrotoxicosis Using Duplex and Amplitude Doppler Sonography

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Differentiation Between the Two Types of Amiodarone-Associated Thyrotoxicosis Using Duplex and Amplitude Doppler Sonography


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Purpose: To evaluate the usefulness of Doppler parameters in the differentiation between the two types of amiodarone-associated thyrotoxicosis (AAT).

Material and Methods: One hundred thirty-seven individuals were selected at our institution. They were divided into four groups: 84 normal subjects (N), 30 euthyroids taking amiodarone (A), 14 AAT type 1 patients (AAT1), and nine AAT type 2 patients (AAT2). Each AAT type was classified according to $^{131}$I uptake and clinical outcome. Blindly, the resistance and pulsatility indexes (RI, PI), systolic peak velocity, and color pixel density (CPD) were calculated.

Results: AAT1 had greater CPD than AAT2 ($P=0.02$). The latter group had similar vascularization to the N and A groups ($P=0.45$). The area under the receiver operating characteristic (ROC) curve showed that systolic peak velocity in the inferior thyroid arteries and CPD were the best parameters in the differentiation between AAT type 1 and AAT type 2 (Az=0.83 and 0.84, respectively). Impedance indexes were useless.

Conclusion: Our results demonstrate that objective tests such as systolic peak velocities in the thyroid arteries and CPD are reliable parameters for differentiating between the two types of AAT.

Key words: Amiodarone; duplex-color Doppler ultrasonography; iodine non-deficient population; thyroid vascularization; thyrotoxicosis

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Amiodarone is an iodine-rich drug useful in the treatment of several cardiac arrhythmias (19). Although this medication is useful for cardiac rhythm control, it may cause some organic disorders (13, 17). The effects of amiodarone on the thyroid are complex and may lead to thyrotoxicosis or hypothyroidism (10).

Amiodarone-associated thyrotoxicosis (AAT) occurs more frequently in geographical areas where iodine intake is low and hypothyroidism is more prevalent in areas with sufficient iodine intake (11). The frequency of thyrotoxicosis in amiodarone users ranges from 1% to 23% (10). AAT may occur from 4 months to 3 years after the start of amiodarone or even after its interruption, and it is not related to the accumulative dosage of the drug (11, 14).

Two distinct types of AAT are generally seen. Type 1 results from a hyperfunction of the gland due to the iodine excess (Jod-Basedow phenomenon) (12). Usually, there is a previous thyroid condition, such as goiter or autonomous nodule, and the remission time is prolonged. Type 2 is secondary to a destructive thyroiditis, as a result of a direct toxic effect caused by amiodarone, which generally develops in individuals with normal glands. In this type, thyrotoxicosis is due to the release of stored hormones in the follicles (10).
The AAT pathophysiology is complex and not yet completely understood (12). The diagnosis of AAT in patients with cardiac conditions is very important, because amiodarone may mask thyrotoxicosis symptoms due to its antiadrenergical action and its inhibitory effect on T4 in T3 peripheral conversion (10).

The differentiation between the two types of thyrotoxicosis is an essential step for management and approach, because each type has a different treatment. AAT type 1 is usually treated with thionamides and perchlorate, whilst AAT type 2 should be treated with corticosteroids (15).

The distinction between the two types of AAT using color Doppler sonography could be very useful, because this method is widely available, inexpensive, quick, and it does not use ionizing radiation. Some studies on AAT differentiation using color Doppler sonography only considered subjective analysis and left the objective parameters unconsidered (4, 5, 8, 22). Therefore, it is important to demonstrate the possibility of distinguishing the two AAT types using objective criteria. The aim of this study was to determine the usefulness of objective duplex-color Doppler thyroid sonography parameters in order to differentiate AAT types 1 and 2.

Material and Methods

Subjects
All individuals taking amiodarone in the present study were selected from an electronic database of the Instituto do Coração (INCOR) do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP), from March 2004 to August 2005. This database contained information about the use of amiodarone and thyroid hormones. It comprised 1037 patient records: 661 euthyroid, 342 hypothyroid, and 34 with thyrotoxicosis.

All euthyroid volunteers (control group) came from a religious community (74 people) and the hospital staff (31 individuals).

Exclusion criteria for all groups
The exclusion criteria for all groups were: 1) younger than 20 years of age; 2) pregnancy; 3) delivery occurring in less than 12 months; 4) use of thyroid hormones, interferon-2, interleukin-2, or lithium; 5) thyroidectomy; 6) thyroid biopsy or trauma; and 7) agenesis or hypoplasia of the thyroid gland. All study groups are described below.

Control group subjects (group N, n=84)
Inclusion criteria for this group were normal levels of TSH, T3, T4, fT4, antiperoxidase, and TRAb (see “Laboratory evaluation”). Of all 105 studied volunteers, 84 individuals (54 women and 30 men) fit in the inclusion criteria. Their age ranged from 20 to 69 years (mean 41.6 ± 13.0 years). The remaining 21 did not fit the inclusion criteria because of the presence of autoantibodies (antiperoxidase) and/or high levels of TSH.

Euthyroid subjects taking amiodarone (group A, n=30)
Thirty subjects (17 men, 13 women) with a mean age 64 ± 8.0 years (range 50–80 years) were randomly recruited among the 661 euthyroid individuals in the database. The inclusion criteria in this group were: 1) taking any dosage of amiodarone for at least 30 days; 2) normal TSH, T3, and T4 (see “Laboratory evaluation”) levels. The period on amiodarone ranged from 0.5 to 7 years (3.6 ± 1.9 years), and the accumulated dosage ranged from 3.1 to 170.8 g (29.1 ± 33.6 g). The medication in this group was mainly indicated because of atrial fibrillation (53%) and ventricular extra-systoles (23%).

Amiodarone-associated thyrotoxicosis subjects (groups AAT 1 + AAT 2, n=23)
From 34 thyrotoxic patients obtained from the database, 11 could not be found. The age of the remaining 23 individuals with thyrotoxicosis (nine men and 14 women) ranged from 27 to 88 (mean 61.9 ± 14.9) years. The period on amiodarone ranged from 4 months to 8 years (2.7 ± 1.7 years), and the accumulated dosage ranged from 1.5 to 48.8 g (16.5 ± 10.2 g). The medication in this group was indicated due to several arrhythmias, where atrial fibrillation was most frequent (52%), together with extra-systoles (39%). Seventeen out of the 23 patients had normal TSH levels, and none had clinical thyroid complaints when starting with amiodarone.

After the initial examinations, all AAT patients were prospectively followed and levels of TSH, T3, T4, and fT4 were tested every 2 months until hormonal levels normalized and after 6 and 8 months. The inclusion criteria in this group were: 1) taking any dosage of amiodarone for at least 30 days; 2) TSH levels under 0.3 mU/l; and 3) T3 levels higher than 2.3 nmol/l or T4 higher than 166 nmol/l (see “Laboratory evaluation”).

All AAT patients filled out inclusion and exclusion criteria forms. They were divided into two groups: group I, composed of 14 individuals, three
men and 11 women, aged between 36 and 88 (mean 66.3 ± 12.4) years; group II, composed of nine patients, six men and three women, aged between 27 and 75 (mean 55.0 ± 15.8) years. The inclusion and exclusion criteria for groups I and II were as follows. Group I inclusion criteria: 24-hour radioactive iodine uptake ($^{131}$I) higher than 3%; and/or hyperfunctioning nodule; and/or extended thyrotoxicosis treatment (> 3 months), regardless of thionamides and/or prednisone. Group I exclusion criteria: interleukin-6 levels higher than 250 fmol/l, as used by BARTALENA et al. (2), as long as the 24-hour radioactive iodine uptake ($^{131}$I) was ≤ 3%; and/or persistent hypothyroidism after thyrotoxicosis treatment. Group II inclusion criteria: interleukin-6 levels higher than 250 fmol/l, as long as the 24-hour radioactive iodine uptake ($^{131}$I) was ≤ 3%; and/or persistent hypothyroidism after thyrotoxicosis treatment; and/or recovery time less than 3 months with exclusive prednisone use. Group II exclusion criteria: 24-hour radioactive iodine uptake ($^{131}$I) higher than 3%; and/or extended thyrotoxicosis treatment (> 3 months), regardless of prednisone.

Patients were generally treated with either prednisone or thionamides. The concomitant use of these drugs was reserved to two patients who were hospitalized due to poor clinical condition and severe thyrotoxicosis. These two individuals were included in group II based on the other inclusion criteria.

Ultrasonography examination

Equipment. Exams were performed using a Philips HDI 5000 device (Philips Medical Systems, Bothell, Wash., USA), manufactured in 2000, attached to a broadband linear probe (5–12 MHz) with a 3.8-cm-wide field of view at a 4-cm depth of view.

Examination technique. The ultrasonography study was performed with the patient in the supine position with a cushion under the shoulders and the neck hyperextended. In order not to underestimate the vascularization intensity, the probe was lightly positioned on the skin without any compression (Fig. 1). The images were obtained on amplitude and pulsed Doppler.

Amplitude Doppler. A breath hold was requested from the patients during the duplex-color Doppler recordings. The equipment was set up to "thyroid," configured as follows: PRF 700 Hz, Map 1, WF Med, Flow Opt: Med V.

In order to quantify the vascularity of the parenchyma, the color pixel density (CPD) was calculated as follows. 1) The digital images containing the longitudinal middle third of the thyroid lobes were stored on optical disks in the "Data Exchange File Format – DEFF" (.CRI) format. The color Doppler images were stored when the vessels were more prominent (i.e., maximum filling of the systolic phase). 2) These files were uploaded to an external workstation equipped with software that easily calculates the CPD (SysArea version 1.1). This software was set up as follows: filter 15, amplitude color mode, and black background. CPD was defined as the percentage of the area of interest occupied by color velocity signals, calculated as the color pixel area divided by the total area of the region of interest (ROI) × 100 (dimensionless). 3) Later, a polygonal ROI was drawn around the thyroid surface by the researcher (T.A.A.M.). If necessary, the ROI was altered point by point to exactly conform to the shape of the lobe.
cross-section (Fig. 2). The maximum area of the ROI (≈5.6 cm²) was limited by the color Doppler area box and the probe’s field of view. 4) After the selection, the computer promptly displayed the CPD value. The gland CPD value was equal to the average between the two lobes.

**Pulsed Doppler.** The sampling gate was set to 2 mm. The PRF was set according to the speed of the flow and to obtain the best graphic representation. The evaluation of the superior thyroid artery was accomplished with the probe positioned in the oblique sagittal plane, close to the superior thyroid pole, as demonstrated in Fig. 3.

The inferior thyroid artery was examined in the oblique axial plane, close to the transition between the middle and the inferior third of the thyroid (Fig. 4). For the evaluation of the inferior thyroid artery, the cursor was set close to the trachea in order to avoid artifacts coming from the common carotid artery and the internal jugular vein.

The systolic peak velocity, and resistance and pulsatility index (RI and PI) values in the superior and inferior thyroid arteries were obtained. The Doppler angle was corrected to values under or equal to 60°. The mean of the values found in the right and left lobes was used as a representative parameter.

**Laboratory evaluation and radioactive iodine uptake.** All patients were submitted to serological analysis of T₃, T₄, fT₄, antiperoxidase (AutoDELFIA kits; PerkinElmer Wallac Oy, Turku, Finland), and TRAb (TR-AB; CIS Bio International, Gif-Sur-Yvette Cedex, France). The normal value ranges for these tests at our laboratory are TSH 0.3–4.2 mU/l, T₃ 1.3–2.5 nmol/l, T₄ 69–141 nmol/l, fT₄ 10.2–17.0 pmol/l, antiperoxidase <30 mU/l, and TRAb <12%. Twenty-four-hour ¹³¹I uptake was
performed in all thyrotoxic patients, and was considered low when <3%.

**Statistical analysis**

One-way ANOVA, Kruskal-Wallis, and Tukey-Kramer tests were used to compare the differences between the groups' continuous variables. The chi-squared test was used to compare nodule frequencies. Receiver operating characteristic (ROC) curve analysis was obtained in order to identify the best diagnostic parameters to distinguish AAT types 1 and 2. The Youden index ([sensibility + specificity] − 1) was calculated to suggest the best cut-off continuous variable values. The minimum sample sizes for groups N, A, I, and II were 56, 21, 14, and seven, respectively, using a high-power statistical model (>90%). All these analyses were done using the NCSS statistical package (August 4, 2005 release; Kaysville, Utah, USA). It was considered significant when \( P < 0.05 \).

**Ethics**

This study and the terms of consent were approved by our institution's Committee of Ethics in Research. All subjects signed the terms of consent with no restriction.

**Results**

It was possible to obtain values from all individuals. Except for the resistance index (RI), all other continuous variables were non-Gaussian. The
Examinations lasted for approximately 23 min, and the time spent for the color pixel density (CPD) analysis was 2 min for each subject. All patients had excellent outcome.

**Ultrasonography findings**

Thyroid volume was significantly higher in group I (40.01 ± 33.80 cm³) compared to the other groups (P < 0.001) (Table 1). Ten group I patients (71.43%), 12 (40%) group A, and none from group II had nodules (Table 2). Nodules were statistically more frequent in group I (P < 0.005).

The color pixel densities (CPD) in groups A, I, and II were 3.67 ± 5.63%, 3.21 ± 3.36%, 17.22 ± 20.00%, and 2.38 ± 2.09%, respectively. The CPD was significantly higher in group I (P < 0.001) than in the others (II and A) (Table 1). Furthermore, systolic peak velocities in the superior and inferior thyroid arteries were higher in group I than in the other groups (P < 0.01) (Table 1). There was no difference between impedance indexes (RI and PI) in groups I and II (P = 0.684). Fig. 5 illustrates the systolic peak velocities and impedance indexes in the inferior thyroid artery in groups I and II.

**Laboratory analyses**

The presence of TRAb was significantly higher in group I than in the other groups (P < 0.001). In spite of a specificity of 75% (6/8), TRAb had a sensitivity of 42.8% (6/14) in diagnosing AAT type 1.

T₄ and fT₄ levels were higher in the groups taking amiodarone (euthyroid and thyrotoxic individuals) than in group N (P < 0.001) (Table 3).

Three patients (21.4%) from group I presented with positive anti-TPO results, while two individuals (22.2%) from group II presented with low anti-TPO test results (anti-TPO 45 and 40 mU/l).

Only one patient, included in group II, presented IL-6 levels higher than 250 fmol/l. Therefore, there was no statistical difference in the interleukin-6 levels between the studied groups (P = 0.61).

The hormone evolution curves in groups I and II, after the start of treatment for thyrotoxicosis, are illustrated in Fig. 6.

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**Table 1.** Means and standard deviations of thyroid volume, systolic peak velocity (SPV), and resistance (RI) and pulsatility indexes (PI) of the superior and inferior thyroid arteries and color pixel density in all studied groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>N (n=84)</th>
<th>A (n=30)</th>
<th>I (n=14)</th>
<th>II (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B-mode</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume, cm³</td>
<td>13.05 ± 5.67</td>
<td>20.89 ± 7.56</td>
<td>40.01 ± 33.80</td>
<td>13.93 ± 3.88</td>
</tr>
<tr>
<td><strong>Doppler</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPVS, cm/s</td>
<td>25.84 ± 8.76</td>
<td>22.84 ± 6.18</td>
<td>38.54 ± 18.62</td>
<td>24.54 ± 6.86</td>
</tr>
<tr>
<td>SPVI, cm/s</td>
<td>21.50 ± 7.72</td>
<td>20.49 ± 7.74</td>
<td>35.35 ± 18.08</td>
<td>18.21 ± 6.37</td>
</tr>
<tr>
<td>PIST</td>
<td>1.04 ± 0.24</td>
<td>1.09 ± 0.31</td>
<td>1.21 ± 0.38</td>
<td>1.33 ± 0.61</td>
</tr>
<tr>
<td>PIHT</td>
<td>0.88 ± 0.18</td>
<td>0.96 ± 0.28</td>
<td>1.10 ± 0.29</td>
<td>1.12 ± 0.36</td>
</tr>
<tr>
<td>RIST</td>
<td>0.62 ± 0.07</td>
<td>0.64 ± 0.07</td>
<td>0.69 ± 0.16</td>
<td>0.67 ± 0.11</td>
</tr>
<tr>
<td>RIHT</td>
<td>0.57 ± 0.07</td>
<td>0.59 ± 0.08</td>
<td>0.65 ± 0.10</td>
<td>0.64 ± 0.08</td>
</tr>
<tr>
<td>CPD, %</td>
<td>3.67 ± 5.63</td>
<td>3.21 ± 3.36</td>
<td>17.22 ± 20.81</td>
<td>2.38 ± 2.09</td>
</tr>
</tbody>
</table>

N: control group; A: amiodarone euthyroid group; I: amiodarone-associated thyrotoxicosis type 1; II: amiodarone-associated thyrotoxicosis type 2; SPVS: systolic peak velocity in the superior thyroid artery; SPVI: systolic peak velocity in the inferior thyroid artery; PIST: pulsatility index in the superior thyroid artery; PIHT: pulsatility index in the inferior thyroid artery; RIST: resistance index in the superior thyroid artery; RIHT: resistance index in the inferior thyroid artery; CPD: color pixel density of the thyroid parenchyma.

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**Table 2.** Nodule frequencies, and TRAb (anti-TSH receptor antibodies) and antiperoxidase (anti-TPO) serological presence in the studied groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>N (n=84)</th>
<th>A (n=30)</th>
<th>I (n=14)</th>
<th>II (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodule</td>
<td>30</td>
<td>35.71</td>
<td>12</td>
<td>40.00</td>
</tr>
<tr>
<td>TRAb (+)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Anti-TPO (+)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

N: control group; A: amiodarone euthyroid group; I: amiodarone-associated thyrotoxicosis type 1; II: amiodarone-associated thyrotoxicosis type 2.
Nuclear medicine

Only five of 14 patients in group I had a 24-hour radioactive iodine uptake > 3.0% and/or hyperfunctioning nodules.

**ROC analysis and cut-off values**

The areas under the curve are expressed in Table 4 and illustrated in Fig. 7. There were no statistically significant differences between the ROC curves ($P > 0.277$). According to the highest Youden index, the best cut-off values for distinguishing the two types of AAT were 6.75% for CPD, 18.36 cm$^3$ for thyroid volume, 24.78 cm/s for SPVI, and 30.88 cm/s for SPVS (Table 4).

**Discussion**

Color Doppler-based thyroid vascularization evaluation has been used for the differential diagnosis of diffuse and neoplastic diseases. This method is widely available, fast, relatively cheap, and non-invasive, does not involve ionizing radiation, and is able to measure blood flow and calculate impedance indexes.

Systolic peak velocities in the superior and inferior thyroid arteries were useful in differentiating between the two types of AAT. These results may be correlated to those found in patients with Graves’ disease, which is similar to AAT type 1.

Impedance indexes were not useful in differentiating the two types of AAT, probably because the resistance versus the compliance vessel product in each group was unchanged (6).

Color pixel density (CPD) is a good parameter for distinguishing the two types of AAT and should be performed as much as possible. However, in spite of its capacity to quantify thyroid gland vascularization, the CPD calculation has some disadvantages, such as: 1) it is more

![Fig. 5. Duplex-color Doppler of the inferior thyroid artery in patients with AAT types 1 (A) and 2 (B). Note that the systolic peak velocity in the group I patient (53.4 cm/s) was higher than in the group 2 patient (12.5 cm/s). In both examples, however, the impedance indexes were very similar.](image)

Table 3. Means and standard deviations of laboratory analyses and 24-hour radioactive iodine uptake (RAIU) in the studied groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>N (n=84)</th>
<th>A (n=30)</th>
<th>I (n=14)</th>
<th>II (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td><strong>Laboratory</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>TSH, mU/l</td>
<td>2.03 ± 0.92</td>
<td>1.76 ± 0.99</td>
<td>0.04 ± 0.02</td>
<td>0.03 ± 0.02</td>
</tr>
<tr>
<td>T3, nmol/l</td>
<td>2.12 ± 0.28</td>
<td>1.62 ± 0.36</td>
<td>3.01 ± 1.40</td>
<td>3.39 ± 1.73</td>
</tr>
<tr>
<td>T4, nmol/l</td>
<td>108.17 ± 25.01</td>
<td>139.64 ± 20.59</td>
<td>185.70 ± 22.56</td>
<td>216.5 ± 54.26</td>
</tr>
<tr>
<td>fT4, nmol/l</td>
<td>13.79 ± 2.56</td>
<td>18.19 ± 3.65</td>
<td>32.9 ± 11.75</td>
<td>43.19 ± 23.86</td>
</tr>
<tr>
<td>T3/T4 ratio, %</td>
<td>2.01 ± 0.19</td>
<td>1.20 ± 0.41</td>
<td>1.65 ± 0.62</td>
<td>1.51 ± 0.41</td>
</tr>
<tr>
<td>IL-6</td>
<td>96.77 ± 63.79*</td>
<td>92.50 ± 34.52†</td>
<td>125.7 ± 99.67</td>
<td>312.1 ± 655.4</td>
</tr>
<tr>
<td><strong>Nuclear medicine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAIU, %</td>
<td>–</td>
<td>–</td>
<td>5.21 ± 3.24</td>
<td>2.56 ± 0.88</td>
</tr>
</tbody>
</table>

* Thirteen individuals; † eight individuals. N: control group; A: amiodarone euthyroid group; I: amiodarone-associated thyrotoxicosis type 1; II: amiodarone-associated thyrotoxicosis type 2; IL-6: interleukin-6.
laborious and has to be performed after the examination; 2) a workstation is needed to import the digital images from the ultrasound equipment; 3) it depends on compatible colored pixel-analysis quantification software; and 4) it can be rather dependent on machine settings. In order to minimize the disadvantages in obtaining CPD, the producers of ultrasound devices should include such an application package in their machines. Because of its simplicity, the costs of this inclusion would certainly be minimal.

In this study, T₃, T₄, fT₄, and the T₃/T₄ ratio are useless in distinguishing the two types of AAT, as reported previously (8). TRAb presence is not able to exclude AAT type 2 diagnoses (20). However, as also reported previously (18), this study demonstrates that TRAb has a good specificity (75%) in the diagnosis of AAT type 1. Nevertheless, the low sensitivity (42.8%) of TRAb is its greatest limiting factor for diagnosing AAT type 1.

In contrast to the results described by BARTALENA et al. (1), according to our results, interleukin-6 is not useful in distinguishing the two types of AAT. This result has been found by others in regions where iodine intake is sufficient (8).

The best cut-off values for the continuous variables calculated in the present study further help to differentiate the two types of AAT. Values higher than these suggested cut-offs should be considered as AAT type 1.

It is already known that normal or high 24-hour radioactive iodine uptake (RAIU) excludes AAT type 2, but low uptake cannot distinguish the two types of AAT (7). In this study, RAIU was useful in only 36% of AAT type 1 patients, because the high concentration of iodine in the amiodarone molecule inhibits radioactive iodine uptake by the follicular cells. In contrast, BOGAZZI et al. (5) have demonstrated that RAIU is useful at least in non-replete iodine intake populations.

Table 4. Youden index for the main continuous duplex-color Doppler variables to diagnose AAT type 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>Aᵢ (95% CI)</th>
<th>Cut-off value</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Youden index*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPD, %</td>
<td>0.84 (0.60–0.94)</td>
<td>6.75</td>
<td>64.29</td>
<td>100.0</td>
<td>0.64</td>
</tr>
<tr>
<td>SPVI, cm/s</td>
<td>0.83 (0.59–0.94)</td>
<td>24.78</td>
<td>66.29</td>
<td>88.89</td>
<td>0.53</td>
</tr>
<tr>
<td>SPVS, cm/s</td>
<td>0.74 (0.48–0.88)</td>
<td>30.88</td>
<td>64.29</td>
<td>88.89</td>
<td>0.53</td>
</tr>
</tbody>
</table>

* Maximum value for Youden index is 1.00. CPD: color pixel density; SPVS: systolic peak velocity in the superior thyroid artery; SPVI: systolic peak velocity in the inferior thyroid artery; Aᵢ: area under ROC curve.
Some limitations can be proposed in this study. Although CPD is an objective parameter, it is not an absolute measurement and can only semiquantify thyroid vascularization. In addition, CPD can be rather dependent on the type and settings of the ultrasound machine.

In the case of AAT type 2, patients could have thyrotoxicosis not associated with amiodarone, because they could have concomitant diseases such as subacute or autoimmune thyroiditis. However, AAT type 2 cases do not demonstrate the abundant neck and ear pain clinical findings observed in subacute (De Quervain’s) thyroiditis. Furthermore, autoimmune thyroiditis, such as silent lymphocytic thyroiditis, also demonstrates moderate or high levels of autoantibodies, at least in 50% of patients (9, 16). In this study, group II patients did not significantly present with autoantibodies. In addition, lymphocytic thyroiditis has a low prevalence (21) and, in contrast to the findings in group II, has a greater incidence in females (3). Therefore, the AAT type 2 contamination risks with other types of thyroiditis are minimal.

The present study did not evaluate the coexistence of both types of AAT, so-called mixed forms (12). According to the literature, in these cases, the most indicated treatment is the association of thionamides and corticosteroids (7). In spite of the importance of the mixed forms, in our cases more than 90% had excellent outcomes using only one drug. This indicates that the mixed forms were infrequent and/or did not influence AAT outcome in both groups.

In conclusion, our results demonstrate that objective tests such as systolic peak velocities and CPD are reliable parameters for differentiating the two types of AAT.

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**References**