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ORIGINAL ARTICLE

Determinants and outcome of amiodarone-associated thyroid dysfunction

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Summary

Objective Amiodarone is frequently associated with thyroid dysfunction. Identifying predictors for amiodarone-associated thyroid dysfunction and assessing treatment outcome may aid clinicians in daily practice.

Methods We included 303 consecutive patients with amiodarone therapy for cardiac arrhythmias (260 with atrial fibrillation and 43 with ventricular arrhythmias). Thyroid function tests were performed every 6 months.

Results Mean age was 63 ± 12 years and 66% was male. After median follow-up of 3·3 (0·1–24) years, 23 (8%) patients developed amiodarone-associated thyrotoxicosis (incidence rate 1·9 per 100 person years) and 18 (6%) hypothyroidism (incidence rate 1·1 per 100 person years). The only predictor for amiodarone-associated thyrotoxicosis was age <62 years [HR = 2·4 (95% CI 1·0–5·7), $P = 0·05$]. Predictors for amiodarone-associated hypothyroidism were thyroid stimulating hormone >1·4 mU/l at baseline [HR = 5·1 (95% CI 1·1–22·4), $P = 0·03$], left ventricular ejection fraction <45% [HR = 3·8 (95% CI 1·1–13·3), $P = 0·04$] and diabetes mellitus at baseline [HR = 3·3 (95% CI 1·1–10·3), $P = 0·04$]. Gender was not a predictor for amiodarone-associated thyroid dysfunction. Five out of 12 (42%) patients with thyrotoxicosis exhibited spontaneous normalization of thyroid function on continuation of amiodarone therapy. Mean time to normalization in the total group was 6·2 ± 3·3 months, with no difference between continuing or discontinuing amiodarone (6·6 ± 3·8 *vs* 5·8 ± 2·8 months, $P = 0·5$).

Conclusions During median follow-up of 3·3 years, the incidence of amiodarone-associated thyrotoxicosis was higher compared to hypothyroidism. Only general predictors for amiodarone-associated thyroid dysfunction were observed. Discontinuation of amiodarone did not influence treatment outcome.

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Introduction

Amiodarone has been shown to be superior to other drugs in maintaining sinus rhythm in patients with persistent atrial fibrillation (AF), and to be safe in patients with left ventricular dysfunction and post myocardial infarction.[1–5] It is, however, associated with many side effects, the most prevalent being thyroid dysfunction.[6,7] Amiodarone-associated thyroid dysfunction is an important clinical issue as it can cause major adverse cardiovascular events such as recurrence of arrhythmias and heart failure.[8–12] There is conflicting evidence whether amiodarone-associated thyroid dysfunction is associated with exposure time and higher (cumulative) dosages.[7,13,14] The incidence of amiodarone-associated thyrotoxicosis and hypothyroidism differs between different parts of the world, partly due to ambient iodine intake.[15–17] In Europe, iodine intake is low to moderate rendering patients more sensitive to effects of exogenous iodine and resulting in a higher incidence of amiodarone-associated thyrotoxicosis compared to hypothyroidism.[18] Amiodarone-associated thyrotoxicosis is further divided into two sub-types, type I and II. Type I occurs mainly in patients with an underlying thyroid condition, in which excess thyroid hormone is produced. Type II is a form of thyroiditis due to the direct toxic effect of amiodarone, which releases an excess of thyroid hormone.[19] Monitoring patients for thyrotoxicosis is difficult as it often has a sudden and explosive onset.[16] In addition, treatment is based on the different pathogenesis of both types, but in clinical practice mixed forms often exist.[19] No diagnostic tool so far including colour flow Doppler sonography has proven to be able to make an absolute distinction between the two sub-types.[20] Antithyroid drugs are used in the current treatment of type I but with varied success.[17,18] Discontinuation of amiodarone is recommended if possible.[20] Type II is treated with prednisone and amiodarone can often be continued.[21,22] It is not known whether risk factors exist for development of amiodarone-associated thyroid dysfunction.

Therefore, we assessed patients treated with amiodarone for the incidence of and predictors for amiodarone-associated thyrotoxicosis and hypothyroidism. Thyroid function tests were performed every 6 months according to the American endocrinologists guidelines.[23] In addition, we assessed clinical characteristics and treatment outcome of patients with amiodarone-associated thyroid dysfunction.

Subjects and methods

Patients

We identified 504 consecutive patients from 1984 to 2007 on first time amiodarone treatment for documented cardiac arrhythmias in a prospectively set-up database. Data was retrieved retrospectively. Thyroid function tests at baseline prior to amiodarone initiation were available in 303 patients, 260 (86%) patients with persistent AF and 43 (14%) with ventricular arrhythmias. In the remaining 201 patients thyroid function tests were not performed prior to amiodarone initiation, or had thyroid function tests in the subclinical range and were therefore excluded from the analysis. Free triiodothyronine serum levels were not systematically measured at baseline and throughout follow-up and were available in half of the patients. Thyrotoxicosis and hypothyroidism were defined according to thyroid stimulating hormone (TSH) and free thyroxine (FT_4) values (see Follow-up below). Patient charts in the Department of Cardiology at the University Medical Center Groningen, the Netherlands were screened.

Amiodarone dosage

Before amiodarone treatment was started, a history, physical examination, a chest x-ray and an electrocardiogram were available. Patients with persistent AF were loaded with 600–800 mg oral amiodarone daily for 4 weeks and daily dose was lowered to 200 mg. For ventricular arrhythmias, patients were loaded with 800–1200 mg oral amiodarone for 4 weeks. Maintenance dose was lowered to 200–400 mg. During follow-up, maintenance dose of amiodarone was temporarily increased if inadequate suppression of ventricular arrhythmias occurred. In case of high serum levels and adequate arrhythmia suppression daily amiodarone dose was lowered. It was left up to the treating physician and patient whether cessation of amiodarone was indicated in case of an occurrence of an amiodarone-related adverse event.

Follow-up

During follow-up, patients were seen according to standard clinical practice, at least every 6 months. During follow-up, thyroid function, renal function and liver function tests were evaluated in addition to amiodarone and desethylamiodarone serum levels. Duration of follow-up was computed from the start of amiodarone until death, or to the date when the last follow-up data was obtained. The cumulative amiodarone dosage was calculated as the summation of all daily amiodarone dosages, in grams.

Patients with increased TSH >7·2 mU/l were referred to an endocrinologist. In case of symptoms patients were started on levothyroxine therapy and in case of lack of symptoms patients were monitored for TSH after 6 weeks and 3 months. Patients were also referred to an endocrinologist when TSH was below 0·03 mU/l with increased FT_4 values (thyrotoxicosis) and when repeated TSH values were between 0·03 and 0·4 mU/l (subclinical thyrotoxicosis). Patients were assessed for family history of thyroid disease in addition to clinical and physical symptoms of amiodarone-associated thyroid dysfunction. In addition, thyroglobulin and thyroid peroxidase antibodies were measured and I^{131} uptake scans were performed if sufficient distinction between type I and II could not be made on the basis of history and physical examination. Type II amiodarone-associated thyrotoxicosis was present in case of negative family history of thyroid disease, absence of thyroid antibodies and no iodine uptake on I^{131} uptake scan. Thyroid ultrasounds were not performed routinely. Treatment of type II consisted of prednisone. In case of inadequate treatment response thiamazole was added. Adequate treatment response was defined as normalization of thyroid function tests within 3 months. In severe biochemical and/or clinical thyrotoxicosis or undefined type of thyrotoxicosis both drugs were given. Severe clinical thyrotoxicosis was defined as thyrotoxicosis associated with arrhythmias or weightloss. Potassium perchlorate was further added in case of inadequate treatment response. Type I amiodarone-associated thyrotoxicosis was treated with thiamazole. After treatment evaluation and insufficient effect prednisone or potassium perchlorate was added. Achieving euthyroid state was defined by attaining TSH levels in the normal range. The treating endocrinologist could deviate from the standard treatment protocol if the clinical situation warranted it. An initial wait-and-see approach was often adopted in case of discontinuation of amiodarone and no clinical symptoms. Amiodarone was discontinued at the discretion of the treating cardiologist.

Assays

Prior to July 1999 normal values for thyroid stimulating hormone (TSH), free thyroxine (FT_4) and free triiodothyronine (FT_3) were 0·3–5·0 IU/l, 9·0–26·0 and 3·0–8·4 pmol/l. (Amersham Amerlite® enhanced luminescent immunometry assay (Amersham International, Amersham, Bucks, UK). Between July 1999 and March 2006 normal values for TSH, FT_4 and FT_3 were 0·4–7·2 mU/l, 6·3–18·2 and 2·4–6·7 pmol/l respectively. (Delfia® system (PerkinElmer Life and Analytical Sciences, Boston, MA, USA). After March 2006 normal values were 0·5–4·0 mU/l, 11·0–19·5 and 4·4–6·7 pmol/l, using immunochemiluminometric E-module assay (Roche Diagnostics, Indianapolis, IN, USA). The thyroid function tests values were converted using a validated method to the values used after March 2006. The following formulas were used for TSH: E-module = 1·145 × Delfia + 0·0018 and Delfia = 1·33 × Amerlite + 0·05. Free thyroxine values were converted using the following formulas: E-module = 1·223 × Delfia−0·7983 and Delfia = 0·72 × Amerlite + 1·58. Free triiodothyronine values were converted using the following formulas: E-module = 0·762 × Delfia−0·4793 and Delfia = 0·95 × Amerlite−0·91.

Amiodarone-associated thyrotoxicosis was defined as TSH <0·25 mU/l and elevated FT_4 or FT_3 and amiodarone-associated hypothyroidism as TSH >10 mU/l and decreased FT_4 or FT_3, while on amiodarone therapy or ≤3 months discontinuation.

Statistical analysis

Baseline descriptive statistics are presented as the mean ± standard deviation (SD) or median (range) for continuous variables and numbers with percentages for categorical variables. Differences between variables in patients who encountered amiodarone-associated thyroid dysfunction (i.e. thyrotoxicosis and/or hypothyroidism) *vs* those who did not were evaluated by Students *t*-test or Mann–Whitney *U*-test, depending on normality of the data, for continuous data and by Fisher exact test or Chi-square test for categorical data.

Incidence rate per 100 person years were calculated for all amiodarone-associated thyrotoxicosis and hypothyroidism. Multivariate stepwise Cox regression analysis was performed to determine predictors for the occurrence of amiodarone-associated thyrotoxicosis and hypothyroidism compared to patients without any thyroid dysfunction. Cut off points of continuous variables were chosen as the median value. Variables identified as significant univariate predictors ($P \leq 0{\cdot}1$) were tested in a multivariate model. Interaction was investigated. Event-free survival curves were constructed. A *P*-value <0·05 was considered statistically significant in all analyses. The statistical analyses were carried out using the statistical program SPSS, version 16.0 (SPSS Inc., Chicago, IL, USA).

Results

Patient characteristics

Between May 2006 and March 2008, data was retrospectively retrieved regarding 303 cardiac arrhythmia patients. The patients consisted of 260 (86%) with AF and 43 (14%) with ventricular arrhythmias. The excluded patients had comparable baseline characteristics to patients with available normal thyroid function tests at baseline (data not shown). The baseline characteristics of the included patients are shown in Table 1. Median total follow-up was 3·3 (0·1–24) years with a median total duration of amiodarone use of 1·4 (0·1–24) years. A total of 41 (14%) patients encountered thyroid dysfunction 23 (8%) cases of amiodarone-associated thyrotoxicosis and 18 (6%) cases of amiodarone-associated hypothyroidism.

Patients with thyroid dysfunction had both a longer median follow-up as well as a longer median duration of amiodarone use compared to patients who encountered no thyroid dysfunction [4·6 (1·0–24) *vs* 3·2 (0·1–20) years, $P = 0{\cdot}003$ and 3·2 (0·2–24) *vs* 1·4 (0·1–14) years, $P < 0{\cdot}001$]. As a result, median cumulative amiodarone dose in the thyroid dysfunction group was also significantly higher compared to the no thyroid dysfunction group [212 (23–1311) *vs* 90 (2–943) grams, $P = 0{\cdot}001$]. Patients with amiodarone-associated thyrotoxicosis were younger compared to patients with amiodarone-associated hypothyroidism (58 ± 13 years *vs* 65 ± 11 years, $P = 0{\cdot}07$) and had significantly lower median baseline TSH value [1·5 (0·55–9·0) *vs* 3·7 (1·1–6·87) mU/l, $P < 0{\cdot}001$]. During follow-up 47 patients died.

Amiodarone-associated thyrotoxicosis

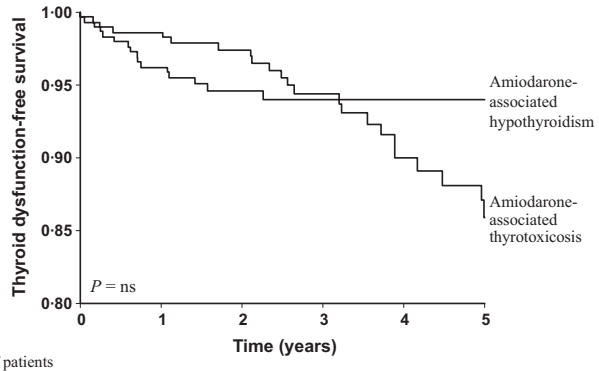
The incidence rate per 100 person years was 1·9 for amiodarone-associated thyrotoxicosis and it occurred throughout follow-up (Fig. 1). The median serum levels of both amiodarone and desethylamiodarone at the time of event were in the normal range [0·8 (0·1–2·2) and 0·6 (0·1–1·3) mg/l respectively].

Table 2a and b summarize complaints, diagnostic and treatment data of the patients with amiodarone-associated thyrotoxicosis in whom amiodarone therapy was either continued or discontinued. Twelve out of the total 23 (52%) patients had complaints, mostly palpitations. In five out of 12 (42%) patients thyroid function normalized without therapy and continuation of amiodarone therapy

Table 1. Baseline characteristics

	Total group (n = 303)	Amiodarone-associated thyrotoxicosis (n = 23)	Amiodarone-associated hypothyroidism (n = 18)	No-thyroid dysfunction (n = 262)
Age (years)	63 ± 12	58 ± 13	65 ± 11	63 ± 12
Male	200 (66%)	15 (65%)	10 (56%)	175 (67%)
Atrial fibrillation/ventricular arrhythmia	260/43 (86/14%)	20/3 (87/13%)	14/4 (78/22%)	226/36 (86/14%)
Total follow-up (years)	3·3 (0·1–24)	5·0 (1·6–13·7)	3·9 (1·2–24)	3·2 (0·1–20)**
Total amiodarone duration (years)	1·5 (0·1–24)	3·9 (0·2–8·2)	2·9 (0·2–24)	1·4 (0·1–14)**
Total cumulative amiodarone dose (g)	109 (2–1311)	296 (24–616)	214 (23–1311)	95 (2–999)**
Body mass index (kg/m^2)	29 ± 5	27 ± 3	28 ± 5	29 ± 5
Thyroid stimulating hormone (mU/l)	1·4 (0·4–9·2)	1·5 (0·55–9·0)*	3·7 (1·1–6·87)*	1·7 (0·49–9·2)
Free thyroxine (pmol/l)	14·6 (9·3–18·7)	14·5 (10·7–17·0)	13·7 (10·0–17·0)	14·8 (9·3–18·7)
Free triiodothyronine (pmol/l)	3·8 (0·28–6·4)	3·75 (2·34–5·41)	3·83 (2·1–4·55)	3·82 (0·28–6·38)
Beta blocker, n (%)	187 (62%)	16 (70%)	10 (56%)	161 (61%)

*Significant difference between amiodarone-associated thyrotoxicosis and hypothyroidism.
**Significant difference between no-thyroid dysfunction and amiodarone-associated thyrotocicosis and hypothyroidism.



No of patients at risk						
hypothyroidism	303	266	220	157	120	92
thyrotoxicosis	303	273	227	158	119	86

Fig. 1 Kaplan–Meier curve: incidence amiodarone-associated thyrotoxicosis and hypothyroidism.

after a mean of 5·7 ± 2·9 months (Table 2a). Another seven (30%) patients showed normalization of thyroid function after cessation of amiodarone therapy without treatment after a mean of 5·2 ± 3·0 months (Table 2b). In the total group, mean time to thyroid function normalization was 6·2 ± 3·3 months, with no significant difference between amiodarone continuation and discontinuation (6·6 ± 3·8 months *vs* 5·8 ± 2·8 months, respectively, $P = 0·5$). Thyroid antibodies were available in half of the patients and were only positive in one patient. I^{131} uptake scans were available in 12 patients showing very low to no uptake.

Amiodarone-associated hypothyroidism

The incidence rate per 100 person years was 1·1 for amiodarone-associated hypothyroidism. Amiodarone-associated hypothyroidism occurred during the first 3 years of treatment (Fig. 1). Median amiodarone and desethylamiodarone serum levels at the time of the event were also in the normal range [1·2 (0·5–2·5) and 0·8 (0·4–0·9) mg/l respectively]. Levothyroxine substitution therapy was started in 16 out of 18 (89%) patients, while still on amiodarone therapy. Euthyroid state was achieved in all patients while on levothyroxine therapy. In two (11%) patients only amiodarone was stopped with return to an euthyroid state.

General predictors for amiodarone-associated thyroid dysfunction and mortality

The only predictor for amiodarone-associated thyrotoxicosis was age <62 years [HR = 2·4 (95% CI 1·0–5·7), $P = 0·05$]. Univariate analysis for predictors for amiodarone-associated hypothyroidism showed TSH >1·4 mU/l at baseline, age ≥62 years, diabetes mellitus at baseline and left ventricular ejection fraction (LVEF) <45% to be correlated. After multivariate analysis TSH >1·4 mU/l at baseline [HR = 5·1 (95% CI 1·1–22·4), $P = 0·03$], LVEF <45%

Table 2. Individual patients with amiodarone-associated thyrotoxicosis who (a) continued and (b) discontinued amiodarone therapy

P	Age (years)	Gender	Treatment	TSH (mU/l)	Max FT_4 (pmol/l)	Time to euthyroid state (months)	Palpitations/ Weight loss/Agitation
(a)							
1	73	Female	P, PCL	<0·005	46	17	−/−/−
2	68	Male	T, PCL	<0·005	70	5·6	−/−/−
3	73	Female	None	0·02	35	6·1	−/−/+
4	22	Female	T, P	<0·005	100	7·6	−/−/−
5	60	Male	T, P, PCL	<0·005	30	5·0	−/−/−
6	52	Male	T, P	<0·005	27	4·2	+/−/−
7	48	Male	None	<0·005	36	4·7	−/+/+
8	67	Male	None	0·09	22	10·2	−/−/−
9	54	Female	None	0·03	28	5·5	−/−/+
10	51	Male	T	<0·005	46	6·1	−/+/−
11	74	Male	None	<0·005	36	2·1	−/−/−
12	60	Male	T	<0·005	24	5·9	−/−/−
(b)							
1	57	Male	T, P	<0·005	100	5·5	−/−/+
2	59	Female	None	0·03	29	10	−/−/−
3	61	Male	T, P	<0·005	84	4·4	+/+/+
4	56	Female	None	0·07	27	5·6	+/−/−
5	50	Male	None	0·01	25	2·6	−/−/−
6	51	Male	None	0·02	21	1·4	+/−/−
7	63	Male	None	<0·005	34	4·9	+/−/−
8	85	Female	None	<0·005	36	8·2	−/−/−
9	67	Female	P	<0·005	55	7·2	+/−/+
10	42	Male	None	<0·005	59	4·0	+/−/−
11	40	Male	T, P	<0·005	75	10	−/−/−

FT_4, free thyroxine; P, prednisone; PCL, perchlorate; T, thiamazole; TSH, thyroid stimulating hormone; complaints yes or no, +/−.

[HR = 3·8 (95% CI 1·1–13·3), $P = 0·04$] and diabetes mellitus at baseline [HR = 3·3 (95% CI 1·1–10·3), $P = 0·04$] were predictors for amiodarone-associated hypothyroidism. Cumulative amiodarone dosage was not a predictor for either amiodarone-associated thyrotoxicosis or hypothyroidism.

Multivariate analysis revealed having diabetes at baseline [HR = 2·0 (95% CI 1·1–3·8), $P = 0·03$] and LVEF <45% [HR=1·8 (95% CI 1·0–3·1), $P = 0·04$] to be predictors for mortality. The occurrence of amiodarone-associated thyroid dysfunction was not a predictor.

Discussion

During a median follow-up of 3 years a higher incidence of amiodarone-associated thyrotoxicosis compared to hypothyroidism was observed in our study. Only general predictors for amiodarone-associated thyroid dysfunction could be identified. The only predictor for amiodarone-associated thyrotoxicosis was age <62 years and for amiodarone-associated hypothyroidism baseline TSH levels >1·4 mU/l, left ventricular function <45% and diabetes mellitus. Treatment for amiodarone-associated hypothyroidism consisted of levothyroxine substitution therapy and continuation of amiodarone in the majority of cases. Treatment of amiodarone-associated thyrotoxicosis was more varied and in approximately 50% of patients amiodarone was continued. Time to achieving euthyroid state was comparable in both groups who continued and discontinued amiodarone. Amiodarone discontinuation was therefore not always required for successful treatment of thyroid dysfunction.

Our study is the first to investigate predictors for amiodarone-associated thyroid dysfunction in a large population. Few smaller studies have investigated predictors for the occurrence of amiodarone-associated thyrotoxicosis and found inconsistent results. Young age and male gender has been shown to be associated with amiodarone-associated thyrotoxicosis.[24,25] Previous observed predictors of amiodarone-associated hypothyroidism have been depressed left ventricular function, organic thyroid pathology, elevated levels of anti-thyroid antibodies and female gender.[16,24] These reports, however, studied only 45 to 62 patients and predominantly males. In patients with congenital heart disease, female gender and cyanotic heart disease also appeared to be risk factors for developing amiodarone-associated thyroid dysfunction.[26] We did not find gender to be a predictor for amiodarone-associated thyroid dysfunction, which may be the result of our study population being larger and relatively well gender-balanced. A considerable drawback of our study, however, is its retrospective nature. We did not have data on thyroid antibodies at baseline, though in the patients measured only one patient was positive. In addition, thyroid antibodies have not shown to develop during amiodarone treatment.[16]

Interestingly, we did find higher TSH levels at baseline to be predictive of amiodarone-associated hypothyroidism in addition to depressed left ventricular function and diabetes mellitus. Patients who have TSH levels in the upper range have increased prevalence of thyroid antibodies and risk of developing hypothyroidism. The Wickham Survey showed that higher TSH levels at baseline (>2 mU/l) were associated with an increased risk of hypothyroidism at 20-year follow-up.[27] Normally, inhibition of iodide oxidation because of excess intrathyroidal iodine (Wolff–Chaikoff effect) is restored by autoregulation. Both patients with underlying thyroid disease and amiodarone-associated hypothyroidism show an increased prevalence of failure to escape the Wolff–Chaikoff effect.[28]

Amiodarone treatment can lead to both thyrotoxicosis and hypothyroidism.[19] In our study population we observed a higher incidence of thyrotoxicosis compared to hypothyroidism. This is consistent with two previous studies conducted in the Netherlands.[7,16] The incidence reported in studies, however, varies greatly. Most data regarding amiodarone-associated thyroid dysfunction comes from the field of cardiology. In recent trials conducted for the prevention of AF a higher incidence of amiodarone-associated hypothyroidism (20%) compared to thyrotoxicosis (3%) was observed after 12–54 months of follow-up.[6] Most of these trials did not, however, define amiodarone-associated thyroid dysfunction explicitly. They also did not always report the type and frequency of thyroid function monitoring. In addition, one of the main factors responsible for the difference in amiodarone-associated thyrotoxicosis and hypothyroidism incidence may be due to differences in ambient iodine intake in different parts of the world.[15,29] Intake of iodine in West Tuscany Italy is low to moderate compared to Worchester USA. This was confirmed using urine excretion of iodine.[15] Higher incidence of amiodarone-associated thyrotoxicosis was seen in Italy compared to higher incidence of hypothyroidism in the USA. Dietary intake in the Netherlands is also relatively low and could account for the higher incidence of amiodarone-associated thyrotoxicosis in the Netherlands.[7,16]

In our study population, 42% of patients who encountered amiodarone-associated thyrotoxicosis reverted to normal thyroid function without any treatment or discontinuation of amiodarone. Most patients were considered to have type II amiodarone-associated thyrotoxicosis. We did not use ultrasound measurements in our study as it is a technique that has only recently emerged. Promising results from colour flow Doppler sonography in distinguishing between the two types of thyrotoxicosis have been shown.[30–33] It may therefore be helpful in an attempt to improve outcome of thyrotoxicosis treatment. Its role, however, in diagnosis and treatment has yet to be established in the guidelines. Our patients who continued and discontinued amiodarone showed similar time to normalization of thyroid function tests. Data on treatment outcome in amiodarone-associated thyrotoxicosis and amiodarone discontinuation is available albeit very limited. Osman *et al.*[21] retrospectively followed treatment outcome in 28 cases of amiodarone-associated thyrotoxicosis type I and II. In total, five patients had spontaneous resolution of thyrotoxicosis and 23 received carbimazole first-line therapy. In addition, they compared amiodarone continuation ($n = 16$) with discontinuation ($n = 12$) and type I ($n = 14$) *vs* type II ($n = 14$) on treatment outcome.[21] Outcome was not influenced by amiodarone discontinuation nor by type of amiodarone-associated thyrotoxicosis. Uzan *et al.*[22] studied 13 patients with type II amiodarone-associated thyrotoxicosis of which 10 continued amiodarone treatment. Eight patients received corticosteroids due to persistent severe symptomatic thyrotoxicosis. All patients recovered with no difference in thyrotoxicosis

duration. Amiodarone-associated thyrotoxicosis can occur suddenly and in a number of patients thyroid function can spontaneously recover. This may reflect the natural history of thyroiditis. It may only be a temporary phenomenon and may not even require treatment. Results of prospective studies on treatment outcome of amiodarone-associated thyrotoxicosis are eagerly awaited.

Patients with amiodarone-associated hypothyroidism were treated with levothyroxine replacement therapy and only a very small number discontinued amiodarone. No data is available on the duration of levothyroxine treatment and whether it can be discontinued over time in these patients.

In conclusion, although the data were analyzed retrospectively, this is the largest group to date in which the incidence of amiodarone-associated thyroid dysfunction was studied. Our study shows a higher incidence of amiodarone-associated thyrotoxicosis compared to hypothyroidism, comparable with previous findings in the Netherlands. Only general predictors for amiodarone-associated thyroid dysfunction could be identified, not applicable in the clinical setting. Amiodarone continuation does not seem to influence outcome of amiodarone-associated thyroid dysfunction, possibly due to the self-limiting nature of the condition. So, amiodarone could be discontinued on the clinical judgment of the treating specialist.

Conflict of interest

Nothing to declare.

Financial disclosure

Nothing to declare.

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