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Research Article

# Early Diagnosis and Optimization of the Management of Amiodarone-Induced Thyroid Dysfunction in the Aral Sea Region

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## Abstract

Amiodarone-induced thyroid dysfunction (AITD) is a clinically significant complication, particularly in environmentally high-risk regions such as the Aral Sea area, where iodine deficiency and environmental pollution prevail. This study aimed to develop and validate an algorithm for early diagnosis and optimized management of AITD. A total of 98 patients receiving amiodarone therapy for cardiac arrhythmias were prospectively observed from 2022 to 2024. Thyroid dysfunction was classified as overt or subclinical hypothyroidism, overt or subclinical thyrotoxicosis, or euthyroid hyperthyroxinemia. Hormonal (TSH, free T4, free T3, TRAb, anti-TPO, anti-TG), biochemical, electrocardiographic, Holter, and echocardiographic parameters were assessed. Individualized therapy for hypothyroidism (L-thyroxine) and thyrotoxicosis (antithyroid drugs or glucocorticoids) was applied. The proposed algorithm enables early detection of AITD, optimization of therapy, prevention of complications, and improvement of patient outcomes in iodine-deficient regions.

## Keywords

Amiodarone-induced Thyroid Dysfunction, Thyrotoxicosis, Hypothyroidism, Early Diagnosis, Aral Sea Region, Arrhythmias, Patient Management

## 1. Introduction

Amiodarone is a widely used antiarrhythmic drug prescribed for various tachyarrhythmias [4, 9]. This iodine-containing benzofuran derivative demonstrates high clinical efficacy and, at a standard dose of 200 mg/day, is primarily administered for supraventricular arrhythmias [2, 8]. However, despite proven effectiveness, amiodarone is associated with the risk of thyroid dysfunction, particularly hypothyroidism. Literature reports indicate that 15–25% of

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patients receiving amiodarone develop thyroid-related complications [3, 14]. Despite national iodine deficiency prevention programs, thyroid dysfunction remains prevalent in endemic areas, including the Aral Sea region, especially among patients with increased thyroid sensitivity to sudden high doses of iodine [1]. Excess iodine in amiodarone can trigger thyrotoxicosis, particularly in individuals with unstable compensatory thyroid mechanisms [5]. Considering the cardiovascular impact of thyrotoxicosis, especially in patients with chronic cardiac pathology, studying clinical, hormonal, and functional features of AITD is highly relevant. The complexity of amiodarone-induced hypothyroidism (AIH) pathogenesis and the high prevalence of cardiovascular diseases underscore the need for clear diagnostic and management algorithms. Timely detection and appropriate therapeutic strategies improve treatment effectiveness, reduce complications, and enhance patients' quality of life. Development and implementation of methodological guidelines for optimized diagnosis and management of AITD are thus an important objective of modern clinical practice.

## 2. Objective

To develop and scientifically substantiate an algorithm for early diagnosis and optimized management of amiodarone-induced thyroid dysfunction in patients with cardiovascular diseases in the Aral Sea region.

## 3. Materials and Methods

### 3.1. Study Design and Population

A prospective cohort study was conducted from January 2022 to December 2024 at the Republican Specialized Cardiology Center of Karakalpakstan. All patients were followed prospectively for 12 months. Historical data were analyzed retrospectively to establish baseline characteristics and prior thyroid status. Ninety-eight patients meeting inclusion criteria were enrolled. Inclusion criteria were age 18–75 years, cardiac arrhythmias requiring amiodarone therapy (ischemic heart disease, hypertension, dilated cardiomyopathy, valvular disease), ≥3 months of therapy, and informed consent. Exclusion criteria included pre-existing thyroid disorders, severe somatic pathology (decompensated liver/kidney failure, terminal heart failure), pregnancy or lactation, and inability or refusal to participate in follow-up.

### 3.2. Assessments

Clinical assessments included history, physical examination, and SF-36 quality-of-life evaluation. Laboratory assessments included TSH, free T4, total T3, anti-TPO, anti-TG, and TRAb, as well as creatinine, glucose, lipids, and electrolytes. Instrumental assessments included ECG, Holter monitoring, echocardiography, and thyroid ultrasound.

*Thyroid Dysfunction Definitions*

Overt hypothyroidism: TSH >4.5 mIU/L with free T4 <0.8 ng/dL

Subclinical hypothyroidism: TSH 4.5–10 mIU/L with normal free T4

Overt thyrotoxicosis: TSH <0.4 mIU/L with free T4 >1.8 ng/dL

Subclinical thyrotoxicosis: TSH <0.4 mIU/L with normal free T4

Euthyroid hyperthyroxinemia: elevated T4 or T3 with normal TSH

*Study Population*

Inclusion criteria:

1) Age 18–75 years;
2) Cardiac arrhythmias requiring amiodarone therapy (ischemic heart disease, hypertension, dilated cardiomyopathy, valve disease);
3) Amiodarone therapy ≥3 months;
4) Signed informed consent.
5) Exclusion criteria:
6) Pre-existing thyroid disorders;
7) Severe somatic pathology (decompensated liver/kidney failure, terminal heart failure);
8) Pregnancy/lactation;
9) Refusal or inability to undergo follow-up.

### 3.3. Statistical Analysis

Data were expressed as mean ± SD. Differences between groups were evaluated using Student's t-test or the Mann–Whitney U-test for nonparametric variables. A p-value below 0.05 was considered statistically significant. Effect sizes were additionally calculated to complement the p-values and reduce dependence on statistical significance alone.

## 4. Results

A total of 98 patients receiving amiodarone therapy were included. Thyroid dysfunction developed in 50 patients (51.0%), including 8 cases of thyrotoxicosis (8.2%) and 42 cases of hypothyroidism (42.9%), while 48 patients (49.0%) remained euthyroid. Baseline characteristics (age, sex, BMI, cardiovascular diagnoses) were comparable between groups ($p > 0.05$). (Table 1).

*Table 1. Dynamics of Parameters in Patients with Thyrotoxicosis After 6 Months of Thiamazole Therapy (n = 8).*

| Parameter | Baseline (M ± SD) | After 6 months (M ± SD) | p-value |
|---|---|---|---|
| Body weight, kg | 84.38 ± 21.02 | 85.88 ± 19.36 | 0.156 |
| TSH, mIU/L | 0.15 ± 0.07 | 1.31 ± 0.89 | 0.007 |
| Free T4, ng/dL | 3.55 ± 0.41 | 1.83 ± 0.56 | <0.001 |
| Free T3, ng/dL | 3.19 ± 0.66 | 1.89 ± 0.32 | <0.001 |
| TRAb, IU/L | 153.63 ± 22.60 | 94.25 ± 7.09 | <0.001 |
| HR max, bpm | 162.9 ± 40.9 | 141.3 ± 18.8 | 0.039 |

Patients with thyrotoxicosis demonstrated significantly reduced TSH and elevated free T4/free T3 levels at baseline, along with increased TRAb titers. After 6 months of thiamazole therapy significant improvements in thyroid hormone profile and heart rate parameters were observed ($p < 0.05$), although heart rate variability (SDNN) decreased, indicating reduced autonomic reserve.

Among patients with hypothyroidism, L-thyroxine therapy led to significant reductions in TSH and increases in free T4/free T3. Ventricular extrasystoles markedly decreased ($p = 0.033$), confirming improved myocardial electrical stability. Mild structural cardiac changes (increased posterior wall thickness) were noted, requiring further monitoring.

*Table 2. Dynamics of Parameters in Patients with Hypothyroidism after 6 Months of L-Thyroxine Therapy (n = 42).*

| Parameter | Baseline (M ± SD) | After 6 months (M ± SD) | p-value |
|---|---|---|---|
| TSH, mIU/L | 6.40 ± 1.63 | 4.95 ± 2.11 | <0.001 |
| Free T4, ng/dL | 0.42 ± 0.34 | 0.90 ± 0.85 | <0.001 |
| Free T3, ng/dL | 0.70 ± 0.29 | 0.89 ± 0.32 | <0.001 |
| Average HR, bpm | 74.6 ± 19.4 | 81.7 ± 15.1 | 0.013 |
| Ventricular extrasystoles (single), units | 1255.4 ± 3366.7 | 166.7 ± 290.8 | 0.033 |

Euthyroid patients showed minor hormonal shifts and reductions in supraventricular extrasystoles under ongoing amiodarone therapy, reflecting its antiarrhythmic effects. Small echocardiographic changes were observed without major functional impairment.

*Table 3. Dynamics of Parameters in Euthyroid Patients After 6 Months of Follow-Up (n = 48).*

| Parameter | Baseline (M ± SD) | After 6 months (M ± SD) | p-value |
|---|---|---|---|
| TSH, mIU/L | 2.85 ± 1.01 | 3.30 ± 1.42 | 0.004 |
| Free T3, ng/dL | 0.95 ± 0.33 | 1.16 ± 0.52 | 0.009 |
| Maximum HR, bpm | 123.9 ± 23.4 | 117.2 ± 17.9 | <0.001 |
| Supraventricular extrasystoles (single), units | 14.0 ± 35.0 | 5.0 ± 9.2 | 0.034 |

Note: HR variations may be influenced by multiple factors; they were interpreted in the context of thyroid function and arrhythmic control.

Overall, early identification and tailored treatment resulted in significant positive trends in endocrine and cardiological outcomes across all subgroups.

Proposed Algorithm for Early Diagnosis and Management of Amiodarone-Induced Thyroid Dysfunction

Step 1. Baseline evaluation (before initiating amiodarone):

1) TSH, free T4, free T3, anti-TPO, anti-TG, TRAb
2) Thyroid ultrasound
3) Cardiological baseline (ECG, HRV, echocardiography)

Step 2. Monitoring schedule:

1) Every 3 months: TSH, free T4, free T3
2) Every 6 months: thyroid autoantibodies and ultrasound
3) Immediate testing if arrhythmias worsen or symptoms appear

Step 3. Diagnostic criteria:

1) Use established definitions for overt/subclinical hypo- and hyperthyroidism
2) Identify Type 1 vs. Type 2 thyrotoxicosis based on TRAb, vascularity on ultrasound, and T4/T3 ratio

Step 4. Management approach:

Hypothyroidism:

1. Maintain amiodarone
2. Start L-thyroxine (titrate to achieve TSH 2–4 mIU/L)

Type 1 thyrotoxicosis:

1. Thiamazole or propylthiouracil
2. Evaluate autoimmune markers
3. Consider potassium perchlorate (if available)

Type 2 thyrotoxicosis:

1. Oral glucocorticoids (prednisolone 30–40 mg/day with tapering)
2. Continue amiodarone if arrhythmias require it

Mixed / uncertain type:

1. Combination of thiamazole + glucocorticoids
2. Reassess after 4 weeks

Step 5. Cardiological management:

1. Continuous ECG/Holter in severe cases
2. Adjust antiarrhythmic therapy according to endocrine status

Step 6. Follow-up after therapy adjustment:

1. Recheck hormones every 4–6 weeks
2. Evaluate cardiac symptoms, HR, extrasystoles, EF

This algorithm provides a structured, clinically applicable approach for iodine-deficient, environmentally burdened regions such as the Aral Sea area.

## 5. Discussion

The prevalence of amiodarone-induced thyroid dysfunction (51%) in our cohort is consistent with international reports, where the incidence ranges from 15–25% for hypothyroidism and 2–10% for thyrotoxicosis. The higher rate observed in the Aral Sea region likely reflects chronic iodine deficiency, environmental toxic exposure, and increased thyroid vulnerability [1, 6].

Our findings demonstrate that patients with AITD exhibit characteristic hormonal and cardiological patterns that align with previously published studies. Elevated TRAb titers in thyrotoxic patients confirm the autoimmune component described earlier [12]. Structural myocardial changes and arrhythmic instability also correspond to observations reported in previous studies [10, 11], reinforcing the importance of interdisciplinary management.

The effectiveness of thiamazole for Type 1 and glucocorticoids for Type 2 AITD is supported by recent studies [3, 15], and our results confirm substantial hormonal improvement after 6 months of treatment. In hypothyroid patients, L-thyroxine therapy led to significant stabilization of cardiac rhythm, consistent with previous reports [7, 13].

A key advantage of this study is the development of a practical diagnostic and therapeutic algorithm tailored for iodine-deficient regions. The algorithm incorporates endocrine, immunological, and cardiological parameters, enabling earlier detection and reducing the risk of decompensation.

Limitations include a relatively small sample size, single-center design, and incomplete echocardiographic data for all participants. Further multicenter studies are needed to validate and optimize the algorithm.

## 6. Conclusion

Amiodarone-induced thyroid dysfunction is highly prevalent among patients receiving long-term amiodarone therapy in the Aral Sea region. Systematic hormonal monitoring, early identification of thyroid abnormalities, and timely individualized treatment significantly improve both endocrine and cardiac outcomes. The diagnostic and management algorithm proposed in this study provides a practical and effective tool for clinicians working in iodine-deficient and environmentally stressed regions. Further research in larger cohorts is required to validate and refine this clinical framework.

## Abbreviations

| | |
|---|---|
| AITD | Amiodarone-Induced Thyroid Dysfunction |
| TSH | Thyroid-Stimulating Hormone |
| TRAb | Thyrotropin Receptor Antibodies |
| ECG | Electrocardiography |

## Conflicts of Interest

The authors declare no conflicts of interest.

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