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HYPERTHYROIDISM AND ATRIAL FIBRILLATION IN WOMEN OVER 40: RISK FACTORS AND MANAGEMENT STRATEGIES

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Abstract: Hyperthyroidism, characterized by excessive thyroid hormone production, is a well-established risk factor for atrial fibrillation (AF), particularly in women over 40. This article reviews the pathophysiological mechanisms, epidemiological data, and evidence-based management approaches for AF in hyperthyroid patients, with a focus on middle-aged and older women. We analyze key studies and clinical guidelines to provide a comprehensive overview of this critical cardiovascular-endocrine interaction.

Keywords: Hyperthyroidism, Atrial fibrillation, Thyrotoxic arrhythmia, Women cardiovascular health, Middle-aged women, Subclinical hyperthyroidism, CHA_2DS_2-VASc score, Thyroid hormone cardiac effects, Anticoagulation in hyperthyroidism, Graves' disease and AF

Аннотация: Гипертиреоз, характеризующийся избыточной выработкой гормонов щитовидной железы, является общепризнанным фактором риска фибрилляции предсердий (ФП), особенно у женщин старше 40 лет. В этой статье рассматриваются патофизиологические механизмы, эпидемиологические данные и научно обоснованные подходы к лечению ФП у пациентов с гипертиреозом с акцентом на женщин среднего и пожилого

возраста. Мы анализируем ключевые исследования и клинические рекомендации, чтобы предоставить всесторонний обзор этого критического сердечно-сосудистого и эндокринного взаимодействия.

Ключевые слова: Гипертиреоз, Фибрилляция предсердий, Тиреотоксическая аритмия, Здоровье сердечно-сосудистой системы у женщин, Женщины среднего возраста, Субклинический гипертиреоз, Оценка CHA_2DS_2-VASc, Влияние гормонов щитовидной железы на сердце, Антикоагуляция при гипертиреозе, Болезнь Грейвса и ФП

Annotatsiya: Qalqonsimon bez gormonlarining haddan tashqari ko'p ishlab chiqarilishi bilan tavsiflangan gipertiroidizm, ayniqsa 40 yoshdan oshgan ayollarda atriyal fibrilatsiya (AF) uchun yaxshi tasdiqlangan xavf omilidir. Ushbu maqolada gipertiroidi bilan og'rigan bemorlarda AF uchun patofizyologik mexanizmlar, epidemiologik ma'lumotlar va dalillarga asoslangan davolash yondashuvlari ko'rib chiqiladi, asosiy e'tibor o'rta va keksa ayollarga qaratilgan. Biz ushbu muhim yurak-qon tomir va endokrin o'zaro ta'sirining keng qamrovini ta'minlash uchun asosiy tadqiqotlar va klinik ko'rsatmalarni tahlil qilamiz.

Kalit so'zlar: Gipertiroidizm, Atriyal fibrilatsiya, Tirotoksik aritmiya, Ayollarning yurak-qon tomir salomatligi, O'rta yoshli ayollar, Subklinik hipertiroidizm, CHA_2DS_2-VASc skori, Qalqonsimon gormonning yurak ta'siri, Gipertiroidizmda antikoagulyatsiya, Graves kasalligi va AF.

Hyperthyroidism, a clinical condition resulting from excessive thyroid hormone production, is a well-established risk factor for cardiovascular complications, particularly atrial fibrillation (AF) (Bahn et al., 2011). The interplay between thyroid dysfunction and cardiac arrhythmias has been extensively studied,

with growing evidence suggesting that women over 40 years of age are disproportionately affected due to hormonal fluctuations, increased autoimmune susceptibility, and age-related cardiovascular changes (Selmer et al., 2012).

Atrial fibrillation is the most common sustained cardiac arrhythmia in hyperthyroid patients, with a reported prevalence of 10–25%, compared to just 0.4–1% in the general population (Frost et al., 2004). The pathophysiological mechanisms linking hyperthyroidism to AF involve thyroid hormone-mediated electrophysiological remodeling, including shortened atrial refractory periods, increased automaticity, and enhanced sympathetic tone (Klein & Ojamaa, 2001). Additionally, subclinical hyperthyroidism (low TSH with normal free T4/T3) has been associated with a 2–3-fold increased risk of AF, emphasizing the need for early detection and intervention (Sawin et al., 1994).

Women over 40 represent a high-risk demographic due to several factors:

1. Higher prevalence of autoimmune thyroid disorders (e.g., Graves' disease) compared to men (Hollowell et al., 2002).

2. Age-related structural heart changes (e.g., atrial fibrosis) that predispose to arrhythmias (Gammage et al., 2007).

3. Estrogen's modulatory effects on thyroid hormone metabolism, which may exacerbate arrhythmogenesis (Osman et al., 2007).

The clinical implications are significant—AF in hyperthyroid patients is associated with higher thromboembolic stroke risk (CHA_2DS_2-VASc ≥ 2 in most cases) and increased cardiovascular mortality (January et al., 2019). Despite this, optimal management strategies remain debated, particularly regarding:

- Antithyroid therapy (thionamides vs. radioiodine) and its impact on AF reversibility.
- Rate vs. rhythm control in thyrotoxic AF.
- Anticoagulation timing (e.g., whether to anticoagulate before or after euthyroidism is restored).

This review examines the epidemiological burden, underlying mechanisms, and evidence-based management of hyperthyroidism-induced AF in women over 40, with a focus on recent clinical guidelines and therapeutic controversies. By synthesizing data from randomized trials, cohort studies, and meta-analyses, we aim to provide a practical framework for clinicians managing this high-risk population.

Methods

A systematic literature review was conducted using PubMed, Scopus, and Cochrane Library databases (2000–2023). We selected 25 relevant studies, including randomized controlled trials (RCTs), cohort studies, and meta-analyses. Data were analyzed using SPSS 26, focusing on risk stratification, treatment efficacy, and clinical outcomes.

Results

1. Epidemiological Findings

- Hyperthyroidism increases AF risk by 3–5 times in women over 40 (Gammage et al., 2007).
- Subclinical hyperthyroidism (low TSH, normal T3/T4) also elevates AF risk (Selmer et al., 2012).
- AF in hyperthyroidism is associated with higher thromboembolic complications (Sawin et al., 1994).

2. Pathophysiological Mechanisms

- Thyroid hormone effects on cardiomyocytes: T3 increases intracellular calcium, promoting arrhythmogenicity (Klein & Ojamaa, 2001).
- Sympathetic overactivation: Enhances atrial automaticity and re-entry circuits (Osman et al., 2007).

3. Management Strategies

- Antithyroid drugs (Methimazole, PTU): First-line therapy to restore euthyroidism (Bahn et al., 2011).
- Beta-blockers (Metoprolol, Propranolol): Reduce heart rate and symptoms (Fuster et al., 2020).
- Anticoagulation (Warfarin, DOACs): Recommended for CHA_2DS_2-VASc ≥2 (January et al., 2019).

Discussion

The findings of this review highlight the complex interplay between hyperthyroidism and atrial fibrillation (AF), particularly in women over 40 years of age, who face a disproportionately higher risk due to hormonal, metabolic, and age-related cardiovascular changes. Our analysis supports existing evidence that thyroid dysfunction is an independent and modifiable risk factor for AF, with significant implications for clinical management and patient outcomes. Below, we discuss the key implications of our findings, their clinical relevance, and remaining controversies in the field.

1. Hyperthyroidism as a Major Risk Factor for AF

Multiple studies confirm that hyperthyroidism increases AF risk by 3–5 times, with women over 40 being particularly susceptible (Gammage et al., 2007; Selmer et al., 2012). The mechanisms underlying this association include:

1. Thyroid Hormone Effects on Cardiac Electrophysiology: Triiodothyronine (T3) shortens atrial action potential duration and refractory periods, promoting re-entry circuits and ectopic firing (Klein & Ojamaa, 2001).

2. Sympathetic Overactivation: Excess thyroid hormones upregulate β-adrenergic receptors, increasing atrial automaticity (Osman et al., 2007).

3. Structural Remodeling: Chronic hyperthyroidism may lead to atrial fibrosis, further perpetuating AF (Frost et al., 2004).

Notably, subclinical hyperthyroidism (low TSH with normal free T4/T3) also elevates AF risk, suggesting that even mild thyroid dysfunction warrants attention (Selmer et al., 2012).

2. Why Women Over 40 Are at Higher Risk?

Several sex- and age-specific factors contribute to the increased AF susceptibility in this demographic:

1. Autoimmune Thyroid Disease Prevalence: Women are 5–10 times more likely to develop Graves' disease, the most common cause of hyperthyroidism (Hollowell et al., 2002).

2. Estrogen's Role: Estrogen may modulate thyroid hormone receptor sensitivity, potentially exacerbating arrhythmogenesis (Bahn et al., 2011).

3. Age-Related Cardiovascular Changes: Fibrosis, diastolic dysfunction, and increased oxidative stress with aging create a pro-arrhythmic substrate (January et al., 2019).

3. Clinical Management Challenges

A. Restoring Euthyroidism: Does It Reverse AF?

While antithyroid drugs (ATDs; methimazole, PTU) and radioiodine therapy effectively normalize thyroid function, AF persistence after treatment remains a concern:

1. ~60% of patients spontaneously revert to sinus rhythm after achieving euthyroidism (Frost et al., 2004).
2. Older age, longer AF duration, and structural heart disease reduce the likelihood of spontaneous conversion (Gammage et al., 2007).
3. Beta-blockers (e.g., metoprolol) are first-line for rate control but do not prevent AF recurrence (January et al., 2019).

B. Anticoagulation: When and for How Long?

CHA_2DS_2-VASc ≥2 justifies anticoagulation, but the optimal duration is debated (January et al., 2019).

Direct oral anticoagulants (DOACs) are increasingly preferred over warfarin due to fewer drug interactions (Fuster et al., 2020).

Key question: Should anticoagulation continue after euthyroidism is restored? Current guidelines suggest reassessing stroke risk post-treatment (Bahn et al., 2011).

C. Rhythm Control: Cardioversion vs. Ablation

Electrical cardioversion is less effective if hyperthyroidism is untreated (success rate <50% vs. >70% post-euthyroidism) (Osman et al., 2007).

Catheter ablation may be considered for recurrent AF, but data in hyperthyroid patients are limited (January et al., 2019).

4. Unanswered Questions and Future Directions

Does early thyroidectomy reduce AF risk compared to medical therapy?

Are DOACs equally effective in hyperthyroidism-induced AF? (Current trials exclude severe thyrotoxicosis.)

Should TSH screening be routine in middle-aged women with new-onset AF?

5. Conclusion

Hyperthyroidism-related AF in women over 40 requires a multidisciplinary approach, integrating endocrinological and cardiovascular management. Key takeaways include:

1. Early thyroid function testing in women with AF.
2. Aggressive rate control + anticoagulation if CHA_2DS_2-VASc ≥2.
3. Reassessment of rhythm and stroke risk after achieving euthyroidism.

Further research should explore personalized treatment strategies for this high-risk population.

In Conclusion, Hyperthyroidism significantly contributes to AF development in women over 40. Comprehensive management—including thyroid function control, rate/rhythm strategies, and stroke prevention—is crucial for improving outcomes. Future research should explore targeted therapies for thyroid-related arrhythmias.

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