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Letter to the Editor

Subclinical Hyperthyroidism is One of the Modifiable Risk Factors for Atrial Fibrillation

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The latest European Society Guidelines (ESC) for the diagnosis and management of atrial fibrillation (AF) list thyroid gland disorders as (modifiable) risk factors for AF.[1] Herein, we attempt to explain the great importance of these factors for the treatment of AF.

AF is the most common cardiac complication of hyperthyroidism, occurring in up to 15% of patients with elevated thyroid hormones.[2,3] Higher prevalence of AF is evident in elderly and patients with coexisting risk factors for AF, such as coronary artery disease, congestive heart failure, and valvular heart disease.[4] On the other hand, patients with hyperthyroidism and an enlarged left atrium are associated with AF irrespective of conventional risk factors.[5] Moreover, the relationship between AF and hyperthyroidism seems to be bidirectional.[6] Specifically, a previous study reported a significantly higher incidence of hyperthyroidism in patients with AF compared to the general population without a diagnosis of AF during the 13-year follow-up period.[7]

The effects of thyroid hormones on AF occurrence can be explained by several mechanisms. Thyroid hormones bind to nuclear receptors, which increases the gene transcription of cardiac myocyte proteins and upregulates voltage gated K^+ and Na^+ channels and beta1 adrenergic receptors.[4] This leads to a hyperdynamic cardiovascular state associated with a faster heart rate and enhanced left ventricular systolic and diastolic function, subsequently increasing the prevalence of supraventricular arrhythmias.[2] Furthermore, thyroid hormones indirectly increase cardiac workload by reducing peripheral vascular resistance, which increases tissue oxygen demand.[4]

Subclinical hyperthyroidism, defined as a euthyroid state with lower levels of thyroid stimulating hormones, has also been reported as a risk factor for AF.[2,4,8–10] Actually, the low serum thyroid stimulating hormone is associated with a five-fold higher likelihood for AF with no significant difference between overt or subclinical hyperthyroidism.[2]

AF in thyrotoxicosis is associated with significant mortality and morbidity from cardiovascular and cerebrovascular events. This can be mainly explained by heart failure induction and embolic events, as thyrotoxicosis is complicated by thromboembolism in approximately 15% of cases.[4] The mechanism by which thyrotoxicosis causes thromboembolic complications is complex and multifactorial.[11] Namely, hyperthyroidism increases plasma levels of the von Wilebrand factor and coagulation factors VIII and IX, which may cause a platelet plug formation.[12,13] Furthermore, in overt hyperthyroidism, the fibrinolytic system is disturbed as higher values of thyroid hormones may lead to an increase in antifibrinolytic and decrease in profibrinolytic agents.[14] Both these disorders cause a hypercoagulable state that may trigger thromboembolic complications.[11]

The cornerstone of treatment in patients with AF and hyperthyroidism is the restoration of euthyroid status as the treatment of hyperthyroidism results in conversion to sinus rhythm in up to two-thirds of patients.[8] This is why we should try to restore the euthyroid status before implementing pharmacological or invasive treatment. When euthyroidism is achieved in patients, normal sinus rhythm is spontaneously restored within four months, after which antiarrhythmics should be introduced if conversion to sinus rhythm is planned.

In some countries, AF patients are routinely screened for thyroid diseases. Furthermore, ESC Guidelines advise routine laboratory assessment of thyroid function (alongside kidney function, full blood count and serum electrolytes) in AF patients.[1] However, we believe that all patients with AF should also be screened for thyroid gland disorders.

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Conflict of interest

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References

[1] Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, *et al*. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J 2021;42(5):373–498. doi:10.1093/eurheartj/ehaa612, PMID:32860505.

[2] Bielecka-Dabrowa A, Mikhailidis DP, Rysz J, Banach M. The mechanisms of atrial fibrillation in hyperthyroidism. Thyroid Res 2009; 2(1):4. doi:10.1186/1756-6614-2-4, PMID:19341475.

[3] Osuna PM, Udovcic M, Sharma MD. Hyperthyroidism and the heart. Methodist Debakey Cardiovasc J 2017;13(2):60–63. doi:10.14797/mdcj-13-2-60, PMID:28740583.

[4] N J, Francis J. Atrial fibrillation and hyperthyroidism. Indian Pacing Electrophysiol J 2005;5(4):305–311. PMID:16943880.

[5] Shin DG, Kang MK, Han D, Choi S, Cho JR, Lee N. Enlarged left atrium and decreased left atrial strain are associated with atrial fibrillation in patients with hyperthyroidism irrespective of conventional risk factors. Int J Cardiovasc Imaging 2021;doi:10.1007/s10554-021-02450-6, PMID:34705162.

[6] Mourtzinis G, Adamsson Eryd S, Rosengren A, Björck L, Adiels M, Johannsson G, *et al*. Primary aldosteronism and thyroid disorders in atrial fibrillation: A Swedish nationwide case-control study. Eur J Prev Cardiol 2018;25(7):694–701. doi:10.1177/2047487318759853, PMID:29473461.

[7] Selmer C, Hansen ML, Olesen JB, Mérie C, Lindhardsen J, Olsen AM, *et al*. New-onset atrial fibrillation is a predictor of subsequent hyperthyroidism: a nationwide cohort study. PLoS One 2013;8(2):e57893. doi:10.1371/journal.pone.0057893, PMID:23469097.

[8] Reddy V, Taha W, Kundumadam S, Khan M. Atrial fibrillation and hyperthyroidism: A literature review. Indian Heart J 2017;69(4):545–550. doi:10.1016/j.ihj.2017.07.004, PMID:28822529.

[9] Delitala AP. Subclinical hyperthyroidism and the cardiovascular disease. Horm Metab Res 2017;49(10):723–731. doi:10.1055/s-0043-117893, PMID:28915531.

[10] Smedegaard SB, Riis AL, Christiansen MK, Linde JKS. Subclinical hyperthyroidism and the risk of developing cardiovascular disease - a systematic review. Dan Med J 2020;67(11):A12190701. PMID:33215608.

[11] Kootte RS, Stuijver DJ, Dekkers OM, van Zaane B, Fliers E, Cannegieter SC, *et al*. The incidence of venous thromboembolism in patients with overt hyperthyroidism: a retrospective multicentre cohort study. Thromb Haemost 2012;107(3):417–22. doi:10.1160/TH11-10-0691, PMID:22234657.

[12] Debeij J, Cannegieter SC, VAN Zaane B, Smit JW, Corssmit EP, Rosendaal FR, *et al*. The effect of changes in thyroxine and thyroid-stimulating hormone levels on the coagulation system. J Thromb Haemost 2010;8(12):2823–6. doi:10.1111/j.1538-7836.2010.04054.x, PMID:20840332.

[13] Homoncik M, Gessl A, Ferlitsch A, Jilma B, Vierhapper H. Altered platelet plug formation in hyperthyroidism and hypothyroidism. J Clin Endocrinol Metab 2007;92(8):3006–12. doi:10.1210/jc.2006-2644, PMID:17488803.

[14] Marongiu F, Conti M, Mameli G, Murtas ML, Balzano S, Sorano G, *et al*. Fibrinogen and fibrinolytic activity in hyperthyroidism before and after antithyroid treatment. J Endocrinol Invest 1988;11(10):723–5. doi:10.1007/BF03350928, PMID:2466071.