Reader's Comments: Subclinical Hypothyroidism and the Risk of Cardiovascular Disease

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Dear Sir,—We highly appreciated the long-term study by Moon et al on the substantial increased risk of ischemic cerebrovascular and cardiac events in individuals younger than 65 years old with subclinical hypothyroidism.[1] We wish to draw the attention to a curable mechanism driving this association, that is the infection by pathogenic strains of *Helicobacter pylori (H. pylori)*. Such organisms are marked by the production of the cytotoxin-associated gene A protein (CagA) and are endowed with an increased inflammatory potential. The infection by CagA positive *H. pylori* strains has been associated with several autoimmune diseases, including autoimmune thyroiditis, and disorders that recognize in the inflammatory response an important pathogenetic event.[2] *H. pylori* is well known for its ability to mimic human antigens, and to elicit autoantibodies against cells of several organs, including the thyrocyte. Autoimmune thyroid diseases are sustained by elevated proinflammatory cytokine levels, namely interleukin-6 and tumor necrosis factor-alpha, which are strongly elevated by infection with *H. pylori* expressing CagA.[3] These same cytokines can promote premature myocardial infarction and ischemic stroke, pathologies that are likewise associated with infection the pathogenic strains of *H. pylori*.[4] Not last, infection by this pathogen can induce lymphoid accumulation in the stomach, a phenomenon that is strictly similar the lymphoid infiltration in the gland of patients with Hashimoto thyroiditis. The variability with which subclinical hypothyroidism is associated with stroke and premature myocardial infarction in different studies might well depend on the highly variable circulation of pathogenic strains in different areas. These strains are far more prevalent in Asian and South American countries than in the US.

Disclosures

None of the authors has anything to disclose.

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Some Thoughts About the Different Ballooning Patterns in Patients With Recurrent Takotsubo Syndrome from the Ones During Their Index Takotsubo Episode

Perusal of the 4,204 articles, published in PubMed from its inception to February 23, 2019, accessed in response to MeSH term "takotsubo," reveals that Takotsubo syndrome (TTS) occasionally recurs in some patients, and such recurrence emerges within days, weeks or years (sometimes >10), after the index TTS episode.[1–3] A parallel observation deriving from the same source is that the ballooning pattern affecting the left and/or right ventricle(s) displays different "regionality" in the index and the recurrent TTS episodes.[1–3] Thus, while the patient was found for example, to have an apical ballooning during the index illness, as assessed by echocardiography, contrast ventriculography, or cardiac magnetic resonance imaging, the left basal ventricular, or the left mid-ventricular myocardial territory, or any combination of the above, is/are found during the recurrent TTS episode. The identified regional contraction abnormalities in TTS are apical, mid-ventricular, basal (i.e., reverse or inverse TTS), focal, global, and right ventricular, and any combination of the above.[1–3] An associated issue is the TTS-triggering stressful condition, which has been identified to be emotional or physical in nature, (herein one wonders whether it is possible for a patient to suffer a physical stress completely devoid of an emotional overlay), although a sizeable proportion of patients have suffered TTS in the absence of any identifiable inciting stressful patient experience. It has been observed that the recurrent TTS episodes may be triggered by the stressors of the same or different nature, as the index TTS episodes.[1]

Although the pathophysiology of TTS is still elusive, compelling insights attribute the emergence of this illness to an unbridled autonomic sympathetic nervous system seethe and/or blood-borne catecholamines flooding the circulation, from adrenal hypersecretion.[1–3]

The occurrence of the frequent apical ballooning pattern in patients with TTS has been attributed to a higher β-adrenergic receptor density at the apex than at the base, shown in dog experiments,[4] but not demonstrated in humans,[5] resulting in a more intense adrenergic stimulation of the apical than the basal myocardium. What has been shown in humans is an increased sympathetic innervations of the heart's base compared with the apex,[6] functionally compensated by a larger β-adrenergic receptor density in the apex than the base.[4] Additionally the sympathetic innervation is more dense in the anterior than in the inferior left ventricle in humans,[6] which explains the more frequent anterior than inferior regional wall motion abnormalities in patients with TTS. Another postulated pathophysiological mechanism resulting in TTS, which has been explored in a rat model,[7] was shown to precipitate an adrenergic apical stimulation of β_2-adrenoceptors, with a shift from the canonical Gs (stimulating)-, to a Gi (inhibiting)-based signal transduction, leading to cardiodepressant/cardioprotective effects on the myocardium, during the catecholamine assault. Some of the above pathomechanisms, lead to an as yet not completely understood complex autonomic adrenergic neural input to the human heart (cardiomyocytes and/