

Brief Review: Atrial Fibrillation in Hyperthyroidism Increases Propensity to Stroke

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Abstract

Context: Deregulations of the bodily systems increase the predisposition to cerebrovascular diseases (CVDs). Thyroid hormone deregulations lead to an observed increase in predisposing such patients to stroke.

Evidence Acquisition: Online literature search was conducted using PubMed, Google Scholar, and Cochrane as databases.

Results: Increase in thyroid hormone level affects the cardiovascular system by increasing the density of beta-adrenergic receptors on cardiomyocytes. The highest post diagnosis risk in hyperthyroidism has been reported for atrial fibrillation and arterial embolism, which increases the risk of ischemic and nonischemic stroke. Atrial fibrillation has thromboembolic stroke as one of the feared outcomes.

Conclusions: Preexisting literature has considerable evidence of increased risk of CVDs in patients with hyperthyroidism and atrial fibrillation together, compared with patients who have either of these diseases.

Keywords: Atrial Fibrillation, Hyperthyroidism, Stroke, Cerebrovascular

1. Context

Cerebrovascular diseases (CVDs) are caused by multiple factors and deregulations of bodily systems. Deregulation of endocrine system such as thyroid hormones abnormality has also been observed to predispose to stroke. Thyroid hormones disorders most commonly manifest in the form of hypo- or hyperthyroidism along with subclinical stages as detected by screening tests (1, 2). New hyperthyroid cases have been reported at a rate of 23 - 93/100,000 per year in different countries across the globe (3). Thyroid hormones have substantial effects on the cardiovascular system, particularly by increasing the density of beta-adrenergic receptors on the cardiomyocytes (4), which in turn can lead to atrial fibrillation (AF) occurring at a rate of 5% to 15% in hyperthyroidism (5).

The highest post diagnosis risk in hyperthyroidism has been reported for atrial fibrillation and arterial embolism, which increases the risk of ischemic and nonischemic stroke by 2 to 3 folds (6). AF itself, in the absence of hyperthyroidism, is a strong indicator of future CVDs in patients if not monitored and managed properly.

In previous studies, stroke with determined etiology has been associated with syndromes such as moyamoya syndrome (7), antiphospholipid (8), dissection (9), systemic lupus erythematosus (10), coagulopathy, and migraine (11). Primary purpose of this short review is to find whether the existing literature has evidence of risk multi-

plication for stroke among patients who have both hyperthyroidism and AF simultaneously.

2. Evidence Acquisition

We conducted literature search using PubMed, Google Scholar, and Cochrane as databases. A total of 28 articles were identified by the initial search, out of which 9 were selected for the review as found most relevant by abstract screening.

3. Results

Atrial fibrillation has thromboembolic stroke as one of the feared outcomes. Atrial fibrillation has been reported to lead to 25% of ischemic cardiovascular and 50% of cardioembolic incidences (12). Ischemic strokes are reported at 5-fold increased risk with 1.5-fold increased risk of fatal stroke in atrial fibrillation (13).

In 1981, the reported rate of thromboembolic events in hyperthyroidism was 40% (14). The same study showed 53% of the thromboembolic phenomena as cerebral emboli, which led to ischemic events. Suggestion of anticoagulation was made in such patients with atrial fibrillation. In Framingham study, stroke rate for idiopathic AF was 41.8/1000 person-years, which is 5.6 times that of nonatrial fibrillation strokes (15). In a prospective study, Siu et

al. looked at newly diagnosed ischemic stroke patients in China. They observed ischemic stroke in 9.4% of hyperthyroid patients with AF compared to 3.1% nonthyroid AF ($P = .02$) and 0.6% in hyperthyroid without AF ($P < .001$). The occurrence of ischemic stroke was predicted by hyperthyroidism (HR: 3.5, $P = .03$) and persistent AF (HR: 13.0, 95% CI: 2.88 to 58.80, $P < .01$), when analyzed by Cox regression (16).

Hyperthyroidism has been associated with blood hypercoagulability. Blood hypercoagulability increases the risk for ischemic events. Hwang et al identified the occurrence of thrombotic events in brain vasculature in patients with hyperthyroidism. They specifically reported cases on superior sagittal sinus thrombosis (17). In November 2014, Chaker et al. conducted a meta-analysis of multiple studies from 1984 - 1998, and they found that subclinical hyperthyroidism increased the risk of stroke. One of the reviewed studies revealed a statistically significant adjusted hazard ratio (HR) of 3.39, while the overall pooled estimated HR of 1.17 (95% CI 0.54 - 2.56) showed no association of subclinical hyperthyroidism (18).

In January 2014, Chen et al. looked into the level of D-dimer and ischemic events in 3 study groups: (1) Hyperthyroid AF, $n = 62$; (2) Nonthyroid AF, $n = 107$, and (3) Hyperthyroid without AF, $n = 100$. The D-dimer levels were significantly higher in hyperthyroid with AF than in the other 2 groups. Over a period of 3 years, the follow-up showed higher incidence of ischemic stroke, when compared with nonthyroid AF (hazard ratio, HR: 3.2, 95% confidence interval, CI: 1.01 - 5.59, $P = 0.04$) (19). Dekker et al. looked at all-cause mortality in hyperthyroidism, which they found it to be the highest in the first 3 months postdiagnosis (HR: 4.62, 95% CI: 4.40 - 4.85), moreover, they reported an elevated mortality in the 3-year (long-term) follow-up (HR: 1.35, 95% CI: 1.33 - 1.37). The risk for all examined ischemic and nonischemic stroke was increased by 2 - 3 folds in these patients (6).

Yang et al. used national health insurance research database of Taiwan to look for stroke in thyroid disorders. The results showed 38% increased hazard of developing cerebrovascular insults in hyperthyroidism with HR of 1.38; hypothyroidism showed even a higher risk with HR of 1.89 (20).

4. Conclusions

Preexisting literature has considerable evidence of increased risk of CVDs in patients with hyperthyroidism and atrial fibrillation together, compared with patients who have either of these diseases. Therefore, we encourage researchers to devise strategies to confirm this observation with more extensive and robust studies. This will not only help to make guidelines but it will also enable physicians

and patients to apply timely preventative measures to minimize the augmented risk of stroke.

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