# Impact of Hypothyroidism on Occurrence and Outcome of Acute Coronary Syndrome from the National Inpatient Sample

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Thyroid hormones have a profound effect on cardiovascular physiology. We utilized a large national inpatient database in the United States (National Inpatient Sample) to study hypothyroidism in relation to the prevalence of coronary heart disease (CHD) and its impact on outcomes (mortality, the length of stay, and hospitalization cost) in the acute coronary syndrome (ACS) subgroup of CHD patients. We found that although hypothyroidism has an increased association with CHD (odds ratio [OR] 1.11, 95% confidence interval [CI] 1.09 to 1.12, p <0.001), the odds of developing ACS in these CHD patients is lower in the hypothyroid group (OR 0.71, 95% CI 0.70 to 0.72, p <0.001) after adjusting for multiple risk factors. Additionally, patients with hypothyroid ACS have a reduced odds of in-hospital mortality (OR 0.86, 95% CI 0.83 to 0.88, p <0.001), shorter length of stay by 0.45 days (p <0.001), and lower hospitalization cost by $1,531.45 (p <0.001) compared with the euthyroid group. Our findings suggest that hypothyroidism has an increased CHD risk but a lower risk of development of ACS in hospitalized CHD patients, as well as a better short-term prognosis including ACS-associated mortality.    © 2017 Elsevier Inc. All rights reserved. (Am J Cardiol 2017;120:2160–2163)

Coronary heart disease (CHD) is the commonest heart disease in the United States[1] with ≈1 of every 7 deaths attributed to it.[2] Similarly, thyroid disorder is quite common with a prevalence of ≈ 9.5% for elevated TSH and 2.2% for decreased TSH levels.[3] The cardiovascular system is very sensitive to the effect of thyroid hormones, and sometimes a change in cardiac hemodynamics may be the only manifestation of thyroid disease.[4] The association of hypothyroidism with atherosclerosis was first observed over a century ago,[5] and hypothyroidism, even subclinical, has been linked to an increased CHD risk and severity.[6–12] Thyroid hormones, in relation to CHD, have been studied with conflicting results.[8–10,13–15] The aim of our study was to estimate the association of hypothyroidism with CHD and the outcome in the acute coronary syndrome (ACS) subgroup of hospitalized CHD patients.

## Methods

We used the National Inpatient Sample, which is the largest publicly available all-payer inpatient database in the United States that contains ~20% sample of all US hospitalizations (>7 million hospital stays each year) and is sponsored by the Agency for Healthcare Research and Quality as a part of the Healthcare Cost and Utilization Project. The weighted estimates of this sample using the discharge weights represent >95% of the hospitalized US population.

We used data from the years 2009 to 2011 to identify adults (≥18 years) with CHD using Clinical Classifications Software codes 100 and 101. The Clinical Classifications Software is a categorization scheme developed as a part of the Healthcare Cost and Utilization Project, where several International Classification of Diseases, Clinical Modification, Ninth Revision (ICD-9-CM) codes are collapsed into clinically meaningful categories. Among CHD, we selected a subgroup of ACS using the ICD-9-CM codes for MI and unstable angina (410.x and 411.1). The codes for CHD have been reported to have a positive predictive value of 0.95, and the positive predictive value of the codes 410 and 411 for ACS were found to be 0.96 and 0.86, respectively.[16,17] We identified patients with hyperthyroidism, hypothyroidism, and euthyroid sick syndrome using the ICD-9-CMI codes 242.x, 244.x, and 790.94, respectively. We labeled patients with no hyperthyroidism, hypothyroidism, and euthyroid sick syndrome as euthyroid. We included only hypothyroid and euthyroid patients in our final analysis (Figure 1).

We performed univariate and multivariate analyses (controlling for conventional risk factors for CHD including age, gender, diabetes, hyperlipidemia, hypertension, obesity, smoking, status of previous revascularization) to estimate the association of hypothyroidism with CHD and ACS. Furthermore, the association of hypothyroidism with ACS outcomes (in-hospital mortality, the length of stay, and hospitalization cost) were analyzed. We chose only the ACS subgroup because other CHD subtypes do not usually lead to hospitalization. Two-tailed p <0.05 was considered significant. We used STATA version 13.0 (College Station, TX) for analysis.

## Results

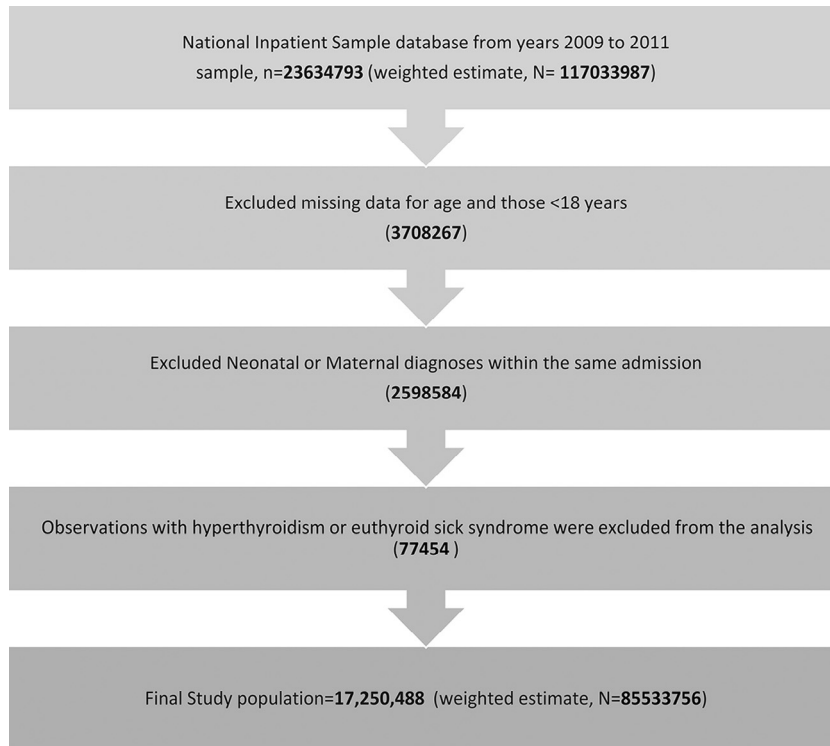Of the 23,634,793 (weighted national estimate, N = 117,033,987) hospitalizations, 17,250,488 (weighted,

Figure 1. Selection process for discharges included in analysis.

Table 1
Baseline characteristics of patients included in the analysis

| Variable* | Euthyroid | Hypothyroid | p value |
|---|---|---|---|
| Total population: | | | |
|   Unweighted | 15,222,226 (88.24%) | 2,028,262 (11.76%) | - |
|   Weighted | 75,510,215 (88.28%) | 10,023,541 (11.72%) | - |
| CHD | 18391315 (24.36%) | 3014954 (30.08%) | <0.001 |
| ACS subgroup of CHD | 3585895 (19.50%) | 436,496 (14.48%) | <0.001 |
| History of prior coronary revascularization | 6964329 (9.22%) | 11299834 (11.27%) | <0.001 |
| Coronary revascularization during current hospitalization (CHD) | 2166310.75 (2.87%) | 206,984.99 (2.06%) | <0.001 |
| Coronary revascularization during current hospitalization (ACS subgroup) | 1425599.27 (39.76%) | 131,448.70 (30.11%) | <0.001 |
| Female | 50.63% | 75.22% | <0.001 |
| Male | 49.37% | 24.78% | |
| Mean age: (years [SE]) | 60.54 [0.14] | 70.11 [0.11] | <0.001 |
| Mean Charlson comorbidity index [SE] | 1.63 [0.009] | 1.86 [0.01] | <0.001 |

CHD = Coronary Heart Disease; ACS = Acute Coronary Syndrome.
* Mentioned numbers are weighted estimates unless otherwise specified.

N = 85,533,756) records were used for analysis after exclusion as described in Figure 1. A total of 25.03% of the total included patients had CHD, of whom 18.79% had ACS. Hypothyroidism was present in 11.72% of patients. Baseline characteristics of the patients included are presented in Table 1.

Hypothyroidism, in comparison with the euthyroid state, was associated with an increased odds of CHD on univariate and multivariate (odds ratio [OR] 1.11, 95% CI 1.09 to 1.12, p <0.001) analyses (Table 2). This association was significant even after stratifying the analysis by gender: females (OR 1.20, 95% CI 1.18 to 1.21, p <0.001) and males (OR 1.34, 95% CI 1.32 to 1.36, p <0.001). Interestingly, these hypothyroid CHD patients had lower odds of developing ACS (OR 0.71, 95% CI 0.70 to 0.72, p <0.001) (Table 2). Also, the rate of coronary revascularization for ACS patients during current hospitalization was lower for the hypothyroid group (30.11% vs 39.76%, p <0.001) (Table 1). Furthermore, hypothyroid ACS patients had lower in-hospital mortality (OR 0.86, CI 0.83 to 0.88, p <0.001), length of stay (linear coefficient = [–0.45], CI –0.51 – (–0.39), p <0.001), and cost of hospitalization (linear coefficient = [–1531.45], CI –1776.80 – (–1286.1), p <0.001) (Table 3).

## Discussion

As per our study results, CHD was more prevalent in hypothyroidism, which is in line with the previous studies that