



# Outcomes and Predictors of 30-Day Readmissions for Hyperthyroidism: A Nationwide Study

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Hyperthyroidism is associated with an elevated risk of cardiovascular events and worse hospital outcomes. The Nationwide Readmissions Database (NRD) 2018 was used to determine the characteristics of 30-day readmission in patients with hyperthyroidism. The 30-day all-cause readmission rate for hyperthyroidism was 10.3%. About 21.7% had hyperthyroidism as the principal diagnosis on readmission. Readmissions were associated with an increased odds of inpatient mortality (odds ratio, 7.04; 95% confidence interval [CI], 3.97 to 12.49), length of stay (5.2 days vs. 4.0 days; 95% CI, 0.7 to 1.8), total hospital charges, and cost of hospitalizations. Independent predictors of 30-day all-cause readmissions included Charlson Comorbidity Index  $\geq 3$  (adjusted hazard ratio [aHR], 1.76; 95% CI, 1.15 to 2.71), discharge against medical advice (aHR, 2.30; 95% CI, 1.50 to 3.53), protein-energy malnutrition (aHR, 1.54; 95% CI, 1.15 to 2.07), and atrial fibrillation (aHR, 1.41; 95% CI, 1.11 to 1.79). Aggressive but appropriate monitoring is warranted in patients with hyperthyroidism to prevent readmissions.

**Keywords:** Hyperthyroidism; Patient readmission; Hospital mortality

## INTRODUCTION

Several studies have indicated a substantial increase in hospital cost, length of stay, and mortality in patients readmitted under 30 days for a variety of clinical conditions. Some of the risk factors for readmissions are, in fact, preventable and could improve hospital outcomes [1,2]. Hyperthyroidism is associated with an elevated risk of cardiovascular events and worse hospital outcomes [3,4]. Consequently, it is essential to understand more about the impacts of hyperthyroidism and other related factors on readmissions in order to prevent it. This study aims to analyze the impacts of hyperthyroidism on the readmission rate, the clinical outcomes, and predictors for readmissions.

## METHODS

### Ethical considerations

The Nationwide Readmissions Database (NRD) database lacks patient identifiers. The Cook County Health Institutional Review Board deemed the research project exempt from approval since it is a retrospective review of already collected, de-identified data sets.

### Design and data source

This was a retrospective cohort study involving adult hospitalizations for hyperthyroidism in the United States in 2018. The NRD for 2018 was the data source. The NRD is the largest pub-

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licly available all-payer inpatient health care readmission database drawn from the Agency for Healthcare Research and Quality (AHRQ) Healthcare Cost and Utilization Project (HCUP) State Inpatient Databases (SID). The NRD 2018 contains discharge data for 58.7% of all United States hospitalizations. It includes both patient and hospital-level information. Up to 40 discharge diagnoses and 25 procedures are collected for each patient using the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM/PCS). Hospitals are stratified according to ownership control, the number of beds, teaching status, urban/rural location, and geographic region. The NRD allows a weighted analysis to obtain 100% of the United States admissions within a given year.

### Study population and definition

The study involved hospitalizations from the NRD with hyperthyroidism as the principal diagnosis for index admission using ICD-10 codes (E05.X). Principal diagnoses and comorbidities were identified using the appropriate ICD-10 codes. NRD variables were used to identify each patient's age, sex, insurance type, median household income, hospital bed size, teaching status, length of hospital stay (LOS), and total hospital charges (THC). The cost of hospitalization (COH) was obtained from the cost to charge ratio data provided by HCUP.

Hospitalizations with age less than 18 and elective hospitalizations were excluded. December hospitalizations were also excluded as they did not contain complete data to assess 30-day readmissions. Using unique hospitalization identifiers, index hospitalizations were identified, and one subsequent hospitalization within 30 days was tagged as readmission. Elective and traumatic hospitalizations were excluded from readmissions. Comorbidity burden was assessed using Sundararajan's adaptation of the modified Deyo's Charlson Comorbidity Index (CCI) [5].

### Outcome measures

This study compared the groups of patients with index admission and patients with readmission. The primary outcome was the rate and reasons for 30-day readmission in patients with hyperthyroidism. Secondary outcomes included the mortality rate, LOS, THC, COH, and predictors of 30-day all-cause readmissions in patients with hyperthyroidism [6].

### Statistical analysis

Stata version 16 software (StataCorp., College Station, TX, USA) was used for data analysis. All analyses were conducted using the weighted samples for national estimates in adjunct

with HCUP regulations for using the NRD database. Comorbidities were calculated as proportions of the cohort, and the chi-square test was used to compare these characteristics between the index and readmissions. Univariable regression was used to compare readmission mortality, LOS, THC, and COH. A univariable Cox regression analysis was performed to identify variables with hazard ratios for 30-day readmission  $<0.20$  to obtain confounders for readmission. Subsequently, a multivariable Cox regression analysis was done to identify independent predictors for readmissions with a  $P<0.05$  set as the threshold for statistical significance. Confounder variables included in the final model were grouped age, insurance, and CCI, disposition, dyslipidemia, chronic obstructive pulmonary disease, diabetes mellitus, chronic kidney disease, obesity, protein-energy malnutrition, atrial fibrillation, and history of neoplasm.

## RESULTS

### Baseline characteristics of index admissions and readmissions

The patients in the readmission group were older than those in the index admission group (48.3 years vs. 53.6 years,  $P<0.001$ ). There was no significant difference in sex distribution between both groups. Readmissions were more likely to have a CCI  $\geq 3$  (29.0% vs. 12.9%) and Medicaid as the main insurer (27.3% vs. 40.6%). The readmission group also had higher proportion of patients with comorbid diabetes mellitus (27.2% vs. 17.6%,  $P<0.001$ ), congestive heart failure (23.0% vs. 18.5%,  $P=0.025$ ), chronic kidney disease (10.6% vs. 6.6%,  $P=0.003$ ), and atrial fibrillation (27.0% vs. 32.0%,  $P=0.032$ ) (Supplemental Table S1).

### Rate and etiologies for 30-day readmissions in hospitalizations with hyperthyroidism

There were 6,979 index hospitalizations identified in the current study that met the inclusion criteria. Of these hospitalizations, there were 6,922 (99.2%) patients discharged alive. The 30-day all-cause readmission rate for hyperthyroidism was 10.3%. The highest proportion of readmissions was for hyperthyroidism (21.7%), followed by paroxysmal atrial fibrillation (6.6%), sepsis from unspecified organisms (6.2%), hypertensive heart disease with heart failure (3.7%), and acute renal failure unspecified (2.4%) (Supplemental Table S2).

### Outcomes in the index admissions and readmissions

Readmission following hyperthyroidism was associated with a significantly increased odds of inpatient mortality (5.5% vs.

0.8%; odds ratio [OR], 7.04; 95% confidence interval [CI], 3.97 to 12.49;  $P < 0.001$ ), increased mean LOS (5.2 days vs. 4.0 days; coefficient, 1.3; 95% CI, 0.7 to 1.8;  $P < 0.001$ ), and higher THC and COH (Table 1) when compared to the index admission.

### Predictors of 30-day all-cause readmissions of hyperthyroidism hospitalizations

After adjusting for potential confounders, independent predictors of 30-day all-cause readmissions of hyperthyroidism included index hospitalizations with CCI  $\geq 3$  (adjusted hazard ratio [aHR], 1.76; 95% CI, 1.15 to 2.71;  $P = 0.009$ ), discharge against medical advice (aHR, 2.30; 95% CI, 1.50 to 3.53;  $P < 0.001$ ), protein-energy malnutrition (aHR, 1.54; 95% CI, 1.15 to 2.07;  $P = 0.004$ ), and atrial fibrillation (aHR, 1.41; 95% CI, 1.11 to

1.79;  $P = 0.004$ ) (Table 2).

### DISCUSSION

By analyzing the largest readmission database in the United States, we found that the 30-day all-cause readmission after hospitalization due to hyperthyroidism was 10.3%. Several studies have attempted to identify approaches to decrease these readmissions, especially in patients undergoing thyroidectomy [7,8].

The highest proportion of readmission diagnoses for patients with hyperthyroidism was hyperthyroidism, followed by paroxysmal atrial fibrillation, sepsis from unspecified organisms, and hypertensive heart disease with heart failure. Brito et al. [9] re-

**Table 1.** Clinical Outcomes in Hospitalizations with Hyperthyroidism

Outcome	Index admission, %	30-Day readmission, %	OR (95% CI)	P value <sup>a</sup>
In hospital mortality	0.82	5.49	7.04 (3.97–12.49)	<0.001 <sup>a</sup>
Length of stay, mean	4.0	5.2	1.3 <sup>b</sup> (0.7–1.8)	<0.001 <sup>a</sup>
Total hospital charges, mean US\$	39,565	56,154	16,590 <sup>b</sup> (6,872–26,307)	0.001 <sup>a</sup>
Total hospital cost, mean US\$	9,242	12,351	3,108 <sup>b</sup> (1,448–4,768)	<0.001 <sup>a</sup>

OR, odds ratio; CI, confidence interval.

<sup>a</sup>Statistically significant; <sup>b</sup>Mean difference.

**Table 2.** Independent Predictors of 30-Day All-Cause Readmissions of Hyperthyroidism Hospitalizations

Variable	aHR	95% CI	P value <sup>a</sup>
Discharge against medical advice	2.3	1.50–3.53	<0.001 <sup>a</sup>
Charlson index of $\geq 3$	1.76	1.15–2.71	0.009 <sup>a</sup>
Protein energy malnutrition	1.54	1.15–2.07	0.004 <sup>a</sup>
Atrial fibrillation	1.41	1.11–1.79	0.004 <sup>a</sup>
Charlson index of 2	1.4	0.92–2.13	0.121
History of neoplasm	1.34	0.87–2.07	0.189
Chronic kidney disease	1.32	0.90–1.94	0.158
Obesity	1.18	0.88–1.57	0.272
Chronic obstructive pulmonary disease	1.16	0.83–1.63	0.383
Diabetes	1.08	0.80–1.45	0.625
Dyslipidemia	1.02	0.77–1.36	0.867
Age, yr <sup>b</sup>			
40–64	0.92	0.67–1.26	0.601
$\geq 65$	0.98	0.64–1.50	0.913
Private insurance <sup>c</sup>	0.56	0.38–0.82	0.003 <sup>a</sup>

aHR, adjusted hazard ratio; CI, confidence interval.

<sup>a</sup>Statistically significant; <sup>b</sup>Relative to patients aged 18–39 years; <sup>c</sup>Relative to Medicaid.

ported that in the United States, hyperthyroidism was mainly treated with antithyroid drug therapy (60%), radioactive iodine (33%), and thyroidectomy (6%). However, the success rates of antithyroid drug therapy were only 50% for antithyroid drug therapy [9]. This might explain the high readmission rates of hyperthyroidism. Additionally, patients with hyperthyroidism treated with radioactive iodine had a higher risk of atrial fibrillation, cardiovascular disease-related hospitalization, and mortality [10,11]. Furthermore, hypothyroidism is a complication from radioactive iodine and thyroidectomy that could increase the risk of sepsis [12].

Readmission following hyperthyroidism was associated with significantly increased odds of inpatient mortality, mean LOS, THC, and COH compared to the index admissions. Hyperthyroidism has been shown to result in increased mortality, with one meta-analysis finding an increase in mortality of about 20% [13]. Being readmitted with hyperthyroidism, as was found to be the case in numerous patients in the readmission cohort, may reflect inadequate control of the condition and thus potentially increased mortality and morbidity [13].

In this study, independent predictors of 30-day all-cause readmissions of hyperthyroidism included index hospitalizations with higher CCI, discharge against medical advice, protein-energy malnutrition, and atrial fibrillation. Patients with these conditions would warrant closer follow-up to avoid readmissions [14,15].

This study has limitations that should be noted. Data from the NRD are subject to biases that are associated with retrospective studies. The database reports information on hospitalizations rather than individual patients; therefore, patients admitted with numerous readmissions are included multiple times in the data set. The database also does not include information about the prescription medications, severity or control of hyperthyroidism, and intensive care unit stay at the time of admission or readmission. Finally, the NRD uses ICD-10 codes to report hospitalizations, making it subject to potential coding errors. Despite the limitations mentioned above, the large sample size, scientific inquiries, long study period, and analysis techniques enabled this study to shed light on hyperthyroidism readmissions while encouraging future large multicenter controlled prospective studies and further discourse on the topic.

In conclusion, patients with hyperthyroidism comorbidities (high CCI, malnutrition, and atrial fibrillation) have increased readmission rates and worsened clinical outcomes of readmissions. Thus, aggressive but appropriate monitoring may be warranted in patients with these conditions and hyperthyroidism.

## CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

## AUTHOR CONTRIBUTIONS

Conception or design: M.S., H.S. Acquisition, analysis, or interpretation of data: M.S., H.S. Drafting the work or revising: M.S., Z.E., A.K., F.W., E.E., H.S. Final approval of the manuscript: M.S., Z.E., A.K., F.W., E.E., H.S.

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