Impact of Hypothyroidism on Outcomes of Percutaneous Coronary Intervention with Coronary Atherectomy for Calcified Coronary Lesions: A Propensity-matched Analysis

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Abstract

Overt and subclinical hypothyroid states have been depicted as risk factors for a more prominent level of coronary calcification. The utilization of coronary atherectomy with percutaneous coronary intervention (PCI) is on the ascent over the past few years as lesions that are more complex are now attempted with a percutaneous approach. However, the real-world data on hypothyroid status influencing PCI with coronary atherectomy outcomes is very limited. Therefore, we proposed to investigate the outcomes of percutaneous coronary intervention with coronary atherectomy in hypothyroid patients using the largest inpatient database in the United States (US), the National Inpatient Sample (NIS). To minimize the selection bias, we surveyed and compared the outcomes in both the unmatched and propensity-score matched euthyroid and hypothyroid cohorts. Concisely, this propensity-matched analysis, using the largest population-based sample in the US, has established higher cardiovascular comorbidities and worse clinical outcomes of PCI with coronary atherectomy owing to clinical hypothyroidism.

Introduction

Overt and subclinical hypothyroidism have recently been recognized as the risk factors for a greater degree of coronary artery calcification [1, 2]. However, the real-world data on the clinical and subclinical hypothyroid status influencing the cardiovascular hemodynamics are limited. The impact of the hypothyroid state on the outcomes of percutaneous coronary interventions (PCI) specifically for the calcified coronary lesions subset have not been studied. There is a rise in the utilization of PCI with coronary atherectomy (CA) for complex lesions. Therefore, we decided to explore the outcomes of PCI with CA in hypothyroid patients using an inpatient database, the Nationwide Inpatient Sample (NIS).
Materials And Methods

The NIS is the largest publicly accessible all-payer inpatient database in the United States (US) and is sponsored by the Agency for Healthcare Research and Quality as a part of the Healthcare Cost and Utilization Project [3]. The discharge weights were applied to attain the national estimates, which minimizes the margin of error representing over 95% of the US population. After excluding patients <18 years of age, we identified patients in the years 2012-2014 who underwent PCI (00.66, 36.06, 36.07) with coronary atherectomy (CA) (17.55) using ICD-9 procedure codes. Patients with a diagnosis of hyperthyroidism (ICD-9 CM 242.x) and sick euthyroid syndrome (ICD-9 CM 790.94) were excluded. Study subjects were divided into two cohorts: hypothyroid (ICD-9 CM code, 244.x) and a control cohort with remaining patients being considered as euthyroid. Chi-square test and independent sample t-test were performed to compare the baseline characteristics, outcomes (in-hospital mortality, length of stay (LOS), and hospitalization charges), and complications in unmatched and propensity-matched cohorts (1:1) adjusted for age, sex, race, median income, payer status, hospital characteristics, and relevant comorbidities. The primary outcomes were in-hospital mortality and postoperative complications, and secondary outcomes were the LOS and total hospital charges. Two-tailed p<0.05 was considered a threshold for clinical significance. IBM Statistical Package for the Social Sciences (SPSS) Statistics 22.0 (IBM Corp., Armonk, NY) was utilized to perform the analyses.

Results

A total of 9,205 (weighted N=46,025) patients underwent PCI with CA of which 931 (weighted, N=4,655) were found to have hyperthyroidism as a listed comorbidity and remaining 8,274 (weighted N=41,370) patients were considered as euthyroid. In unmatched comparison, hypothyroid patients were more frequently older (mean age 72±12 vs. 65±13, p<0.001), White (82.5% vs. 74.8%, p<0.001), females (54.6% vs. 27.3%, p<0.001) as compared to euthyroid patients. Interestingly, patients with hyperthyroidism appeared to have higher rates of comorbidities such as hypertension (79.3% vs. 72.2%, p<0.001), diabetes with chronic complications (12.0% vs. 6.3%, p<0.001), dyslipidemia (73.4% vs. 70.4%, p<0.001), obesity (18.7% vs. 14.9%, p<0.001), peripheral vascular disorders (PVD) (17.9% vs. 13.4%, p<0.001), and chronic obstructive pulmonary disease (COPD) (22.8% vs. 16.8%, p<0.001) as compared to euthyroid patients in unmatched comparison (Table 1).

The propensity-matched (1:1) cohorts consisted of 827 (weighted N=4135) patients in both the groups. The proportions of age, sex, race, type of admission, location/teaching status of the hospital were comparable in both unmatched and propensity-matched cohorts. Similar to unmatched cohorts, hypertension, dyslipidemia, PVD, and COPD were more prevalent in the hypothyroid group after propensity matching (Table 1). However, the significant difference in the prevalence of diabetes with chronic complications between the two groups disappeared. In addition, the comorbidities uncomplicated diabetes (31.0% vs 27.8%, p=0.002) and coagulopathy (3.3% vs. 4.5%, p=0.004) were found to be more prevalent in the hypothyroid group after propensity score matching.
## Age in years (Mean±SD)

| Age Group | Mean±SD | p Value
|-----------|---------|----------
| 65±13     |         | <0.001   |
| 72±12     |         | 0.001    |
| 46±9      |         | <0.001   |
| 72±12     |         | <0.001   |

## Indicator of Sex

| Gender   | Male   | Female |
|----------|--------|--------|
|          | 72.7%  | 27.3%  |
|          | 45.4%  | 54.6%  |
|          | 51.9%  | 48.1%  |
|          | 44.6%  | 55.4%  |

## Race

| Race                  | White | African American | Hispanic | Asian and Pacific Islander | Native American | Others |
|-----------------------|-------|------------------|----------|----------------------------|-----------------|--------|
|                       | 74.8% | 8.7%             | 8.2%     | 3.2%                       | 0.6%            | 4.6%   |
|                       | 82.5% | 4.9%             | 6.8%     | 2.3%                       | 0.6%            | 3.1%   |
|                       | 74.2% | 10.9%            | 9.1%     | 2.7%                       | 0.7%            | 2.4%   |
|                       | 83.8% | 4.4%             | 6.5%     | 1.7%                       | 0.5%            | 3.1%   |

## Type of Admission

| Type of Admission | Non-elective | Elective |
|-------------------|--------------|----------|
|                   | 81.5%        | 18.5%    |
|                   | 79.5%        | 20.5%    |
|                   | 91.2%        | 8.8%     |
|                   | 81.0%        | 19.0%    |

## Location/Teaching Status of Hospital

| Status                        | Rural | Urban - non teaching | Urban - teaching |
|-------------------------------|-------|----------------------|------------------|
|                               | 3.6%  | 32.8%                | 63.5%            |
|                               | 3.5%  | 34.4%                | 62.1%            |
|                               | 3.7%  | 38.8%                | 57.4%            |
|                               | 3.1%  | 36.2%                | 60.7%            |

## Comorbidities

| Comorbidity                         | 65±13 | 72±12 | p Value |
|-------------------------------------|-------|-------|---------|
| Hypertension                        | 72.2% | 79.3% | <0.001  |
| Diabetes, uncomplicated             | 30.6% | 30.1% | 0.429   |
| Diabetes with chronic complications | 6.3%  | 12.0% | <0.001  |
| Dyslipidemia                        | 70.4% | 73.4% | <0.001  |
| Obesity                             | 14.9% | 18.7% | <0.001  |
| Congestive heart failure            | 1.4%  | 1.5%  | 0.531   |
| Coagulopathy                        | 4.3%  | 4.5%  | 0.558   |
| Peripheral vascular disorders       | 13.4% | 17.9% | <0.001  |
| Smoking                             | 43.4% | 33.8% | <0.001  |
| Chronic obstructive pulmonary disease | 16.8% | 22.8% | <0.001  |

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**Postoperative Outcomes**

|                         | Euthyroid | Hypothyroid | p-value | Euthyroid | Hypothyroid | p-value | Euthyroid | Hypothyroid | p-value |
|-------------------------|-----------|-------------|---------|-----------|-------------|---------|-----------|-------------|---------|
| All-cause in-hospital mortality | 3.2%      | 4.1%        | <0.001  | 1.0%      | 4.1%        | <0.001  |           |             |         |
| Postoperative myocardial infarction | 8.7%      | 9.7%        | 0.037   | 8.7%      | 9.8%        | 0.088   |           |             |         |
| Any cardiac complications | 12.4%     | 12.4%       | 0.887   | 10.5%     | 12.2%       | 0.015   |           |             |         |
| Postoperative respiratory failure | 0.9%      | 1.6%        | <0.001  | 0.5%      | 1.7%        | <0.001  |           |             |         |
| Postoperative stroke | 0.2%      | 0.3%        | 0.105   | 0.2%      | 0.4%        | 0.317   |           |             |         |
| Acute kidney injury requiring dialysis | 0.8%      | 1.3%        | <0.001  | 0.6%      | 1.2%        | 0.004   |           |             |         |
| Postoperative infection | 1.8%      | 2.1%        | 0.154   | 1.3%      | 2.4%        | <0.001  |           |             |         |
| Length of stay (days) (Mean±SD) | 4.2±5.9   | 4.8±5.3     | <0.001  | 3.9±4.5   | 5.0±5.4     | <0.001  |           |             |         |
| Total hospital charges (USD) (Mean±SD) | 107,711±103,242 | 116,379±97,690 | <0.001  | 95,589±78,745 | 118,072±97,653 | <0.001  |           |             |         |

P-value <0.05 indicates clinical significance.

**TABLE 1: Impact of Hypothyroidism on Outcomes of Percutaneous Coronary Intervention with Coronary Atherectomy for Calcified Coronary Lesions: Before vs. After Propensity-score Matched Analysis**

In unmatched comparison, primary outcomes including all-cause in-hospital mortality (4.1% vs. 3.2%, p<0.01) and postoperative myocardial infarction rate (9.7% vs. 8.8%, p<0.05) were higher in the hypothyroid group as compared to the euthyroid group. However, there was no statistically significant difference in the incidence of any cardiac complications and postoperative stroke between the two groups. In addition, the hypothyroid group appeared to have a higher rate of other complications such as postoperative respiratory failure (1.6% vs. 0.9%, p<0.001) and acute kidney injury (AKI) requiring dialysis (1.3% vs. 0.8%, p<0.001) as compared to the euthyroid group. Secondary outcomes including LOS (days) (4.8±5.3 vs. 4.2±5.9, p<0.001) and total hospital charges (mean $116,379 vs. $107,711, p<0.001) were also higher in the hypothyroid group (Table 1).

Similar to unmatched analysis, propensity-matched analysis demonstrated significantly higher in-hospital mortality (4.1% vs. 1.0%, p<0.001), postoperative respiratory failure (1.7% vs. 0.5%, p<0.001), AKI requiring dialysis (1.2%, 0.6%, p<0.001), postoperative infection (2.5% vs. 1.3%, p<0.001), LOS (5.0±5.4 vs. 3.9±4.5, p<0.001), and total hospital charges (118,072±97,653 vs. 95,589±78,745, p<0.001) in the hypothyroid group. Although numerically higher in the hypothyroid group, there was no statistically significant difference in postoperative myocardial infarction incidence (9.8% vs. 8.7%, p=0.088) between the propensity-matched cohorts. Contrary to unmatched assessment, matched analysis revealed a higher incidence of any cardiac complications (12.2% vs. 10.5%, p=0.015) and postoperative infection (2.4% vs. 1.3%, p<0.001) in hypothyroid patients.

**Discussion**

Propensity-matched analysis demonstrated that the hypothyroid state is associated with higher risk of cardiovascular comorbidities, any cardiac complications, and all-cause in-hospital mortality.
mortality, which is consistent with the previously published studies showing the negative impact of subclinical and clinical hypothyroidism on PCI outcomes [4,5]. With a major strength of being performed on the largest inpatient sample in the US, our study also has a few potential limitations. As with any large database, there is a scope of administrative coding errors. Since the database does not provide the exact number of thyroid hormone levels, it is not possible to assess the strength of association for causality and establish the association between subclinical hypothyroidism and the worse outcomes.

**Conclusions**

In conclusion, by using propensity-matched analysis in the largest US database, we discovered that hypothyroidism was significantly associated to higher cardiovascular comorbidities, LOS, total hospital charges, cardiovascular complications, postoperative respiratory failure, AKI requiring dialysis, postoperative infection, and all-cause in-hospital mortality in the patients undergoing PCI with CA. Therefore, it is recommended that health care professionals be extra vigilant for the development of these complications in patients with hypothyroidism undergoing PCI with CA. Categorization of these patients as "high-risk" may help in the early recognition and management of these complications and curb higher cardiovascular morbidity and mortality in this population.

**Additional Information**

**Disclosures**

Human subjects: Consent was obtained by all participants in this study. Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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