

# Thyroidectomy for Graves' Disease Predicts Postoperative Neck Hematoma and Hypocalcemia: A North American cohort study

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Sadaf Mohtashami, MD<sup>1</sup> , Keith Richardson, MD<sup>1</sup>, Veronique-Isabelle Forest, MD, MSc<sup>1</sup>, Alex Mlynarek, MD, MSc<sup>1</sup>, Richard J. Payne, MD, MSc<sup>1</sup>, Michael Tamilia, MD<sup>2</sup>, Marc P. Pusztaszeri, MD<sup>3</sup>, Michael P. Hier, MD<sup>1</sup>, Nader Sadeghi, MD<sup>1,4</sup>, and Marco A. Mascarella, MD, MSc<sup>1,5,6</sup> 

## Abstract

**Objective:** Examine the association of Graves' disease with the development of postoperative neck hematoma.

**Design:** A cohort of patients participating in the Thyroid Procedure-Targeted Database of the National Surgical Quality Improvement Program from January 1, 2016 to December 31, 2018.

**Setting:** A North American surgical cohort study.

**Methods:** 17906 patients who underwent thyroidectomy were included. Propensity score matching was performed to adjust for differences in baseline covariates. Multivariate logistic regression was used to ascertain the association between thyroidectomy for Graves' disease and risk of postoperative adverse events within 30 days of surgery. The primary outcome was postoperative hematoma. Secondary outcomes were postoperative hypocalcemia and recurrent laryngeal nerve injury.

**Results:** One-to-three propensity score matching yielded 1207 patients with mean age (SD) of 42.6 (14.9) years and 1017 (84.3%) female in the group with Graves' disease and 3621 patients with mean age (SD) of 46.7 (15.0) years and 2998 (82.8%) female in the group with indications other than Graves' disease for thyroidectomy. The cumulative 30-day incidence of postoperative hematoma was 3.1% (38/1207) in the Graves' disease group and 1.9% (70/3621) in other patients. The matched cohort showed that Graves' disease was associated with higher odds of postoperative hematoma (OR 1.65, 95% CI 1.10-2.46) and hypocalcemia (OR 2.04, 95% CI 1.66-2.50) compared with other indications for thyroid surgery. There was no difference in recurrent laryngeal nerve injury among the 2 groups.

**Conclusions:** Patients with Graves' disease undergoing thyroidectomy are more likely to suffer from postoperative hematoma and hypocalcemia compared to patients undergoing surgery for other indications.

## Keywords

Graves' disease, thyroidectomy, hematoma, hypocalcemia, recurrent laryngeal nerve injury

## Introduction

Graves' disease is the most common cause of hyperthyroidism and is managed with antithyroid medications, radioactive iodine ablation or thyroidectomy. Oftentimes, surgery is a favored treatment modality with patients preferring outpatient over inpatient thyroidectomy.<sup>1,2</sup> Despite the growing evidence for early discharge, same-day discharge is limited by the risk of postoperative neck hematoma with the majority of patients manifesting symptoms within the first 12 hours after surgery<sup>3-7</sup> as well as hypocalcemia and rarely bilateral vocal cord paralysis. Despite being an infrequent postoperative adverse event, 0% to 6.5% of patients develop a neck hematoma, a potentially life threatening complication that can rapidly result in airway obstruction.<sup>8-11</sup> In spite

<sup>1</sup>Department of Otolaryngology—Head and Neck Surgery, McGill University, Montreal, QC, Canada

<sup>2</sup>Division of Endocrinology, Department of Medicine, McGill University, Montreal, QC, Canada

<sup>3</sup>Department of Pathology, McGill University, Montreal, QC, Canada

<sup>4</sup>Research Institute of the McGill University Health Center, Montreal, QC, Canada

<sup>5</sup>Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, QC, Canada

<sup>6</sup>Department of Biomedical Sciences, Faculty of Medicine, University of Montreal, Montreal, QC, Canada

### Corresponding Author:

Marco A. Mascarella, MD, MSc, Department of Otolaryngology-Head and Neck Surgery, McGill University Health Centre, 1001 boul. DeCarie, Montreal, QC H4 A3J1, Canada.

Email: marco.mascarella@mail.mcgill.ca

of the risk of postoperative hematoma, many studies have shown that outpatient thyroidectomy remains a safe option.<sup>6,12</sup> Recognizing patients at increased risk of this adverse event may prevent unnecessary increases in the hospital admissions of low-risk patients while preventing early discharge of those patients at a higher risk.

Multiple studies have reported rates of postoperative hematoma in patients with Graves' disease, although most are limited by the limited selection of a control group and lack of prospectively collected data.<sup>8,10,13-16</sup> Additionally, post-thyroidectomy neck hematoma in Graves' disease patients is a rare outcome; single institution studies may be underpowered to demonstrate statistically significant associations. Using a large national database may seem to be a solution for studying such a rare outcome; however, these databases collect generalized surgical variables and outcomes and they do not contain thyroid specific variables.<sup>17-20</sup> To address this limitation, in January 2013, a thyroidectomy-specific module was added to the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) which became widely used after.<sup>17</sup> This database represents a randomized sample of patients who underwent thyroid operations in most hospitals in the United States and Canada.

In this study, the Thyroid Procedure-Targeted NSQIP Database was used to ascertain the association between Graves' disease as an indication for thyroidectomy with postoperative neck hematoma. We also evaluated the relationship of thyroidectomy for Graves' disease with postoperative hypocalcemia and RLN injury as secondary outcomes.

## Methods

This study was conducted in accordance with the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (2018). A waiver of consent for this study was granted by the McGill University Health Centre Research Ethics Board (MP-37-2018-3568), Montreal, Canada.

## Data Set

Data from patients participating in the Thyroid Procedure-Targeted Database of the NSQIP from 2016 to 2018 was used. The NSQIP is provided by the American College of Surgeons with the goal of measuring and improving the quality of surgical outcomes and represents patients from more than 680 hospitals.<sup>21</sup> At each hospital, a trained and certified surgical clinical reviewer prospectively collects data on over 150 variables such as preoperative risk factors, intraoperative variables, and 30-day postoperative mortality and morbidity outcomes for patients undergoing surgical

procedures in both the inpatient and outpatient setting.<sup>22</sup> To ensure the data collected is of highest quality, annual audits of selected participating hospitals are performed where both medical charts and operating room logs are evaluated.

## Participants

All patients who underwent thyroidectomy (lobectomy/hemithyroidectomy, total thyroidectomy or completion thyroidectomy) within the Thyroid Procedure-Specific Database of the NSQIP, from January 1, 2016, to December 31, 2018, were included. Only patients who underwent a thyroid operation as a primary procedure were included and those who had thyroid operation as a secondary procedure as part of a laryngectomy or major head and neck surgery were excluded. A full list of *Current Procedural Terminology (CPT)* codes can be found in eTable 1 in the supplement. Patients undergoing thyroid operations for both benign and malignant conditions were included. Patients with either an unknown indication of thyroid surgery or unknown neck hematoma status were excluded.

## Covariates

In this study, the following demographic data and comorbidities were used for propensity score matching: age, sex, body mass index, American Society of Anesthesiologists classification, diabetes, bleeding disorder, dyspnea, history of severe chronic obstructive pulmonary disease, hypertension, congestive heart failure, smoking status, corticosteroid use, weight loss and extent of surgery (hemi, total or completion thyroidectomy). Disseminated cancer was not used as only 1 patient with Graves' disease had disseminated cancer. Also, T4 staging was not used as no patient with Graves' disease had a T4 tumor. Race, ethnicity and laboratory results such as platelet level, prothrombin time, international normalized ratio and partial thromboplastin time were not used as the data were missing for most patients.

Thyroid surgery-specific variables included primary indication for the operation (Graves' disease, any goiter and Graves' disease, goiter, multinodular goiter, severe goiter, goiter with substernal component, differentiated malignancy, poorly/undifferentiated malignancy, other malignancy and solitary nodule or goiter), surgical specialty (otolaryngology, general surgery, and other), clinical toxicity, prior neck surgery, preoperative needle biopsy results, central neck dissection, use of any vessel sealant device for hemostasis, intraoperative electrophysiologic or electromyographic recurrent laryngeal nerve (RLN) monitoring, T staging in case of malignancy, whether the neoplasm was multifocal or unifocal and the extent of the operation (thyroid lobectomy/hemithyroidectomy, total thyroidectomy and completion thyroidectomy).

## Exposure and Outcome

The exposure of interest was Graves' disease as the indication for thyroid operation. Patients were divided in 2 groups based on the primary indication for thyroidectomy: those with Graves' disease and any goiter and those with Graves' disease were classified as Graves' disease. Those with goiter, multinodular goiter, severe goiter, goiter with substernal component, differentiated malignancy, poorly/undifferentiated malignancy, other malignancy and solitary nodule or goiter were classified as non-Graves' disease. The primary outcome was postoperative hematoma within 30 days of the index surgery. This variable was coded as binary including any hematoma requiring additional observation, tracheostomy, other interventions such as opening of the incision to evacuate clot or reoperation (eTable 2 supplement).

The secondary outcomes were postoperative hypocalcemia and RLN injury or dysfunction following surgery as measured by the NSQIP. Patients with hypocalcemia prior to discharge or hypocalcemia within 30 days of discharge were considered to have hypocalcemia. Corrected serum calcium level  $<2.2$  mmol/L or  $<8.5$  mg/dL was considered as hypocalcemia. RLN injury or dysfunction was documented as whether the patient experienced hoarseness and/or laryngoscopy demonstrating vocal cord injury or dysfunction. However, dysphonia on the day of surgery and postoperative day 1 was not included as some patients develop hoarseness immediately after extubation. Of note, no information regarding preoperative RLN function is available in this dataset.

## Statistical Analysis

Descriptive statistics were used to measure covariates in both the Graves' disease and non-Graves' disease groups. Propensity score matching was subsequently performed to ascertain the relationship between thyroidectomy in Graves' disease patients and outcome as many covariates may confound the data.<sup>23</sup> Propensity score matching creates exposure and comparison groups that are balanced on measured confounders.<sup>24-27</sup> Propensity score matching allows for unbiased estimates of average exposure effect and improves the validity of the estimates.<sup>28</sup> Higher matching sets can yield increased precision and smaller confidence intervals.<sup>29,30</sup>

Propensity scores were calculated using logistic regression for both groups: patients with Graves' disease and patients without Graves' disease, with 46 demographic, comorbidity and thyroid specific variables (Table 1). Covariates were selected based on their potential association with the exposure (Graves' disease) and primary outcome (hematoma) according to the literature.<sup>31-33</sup> One-to-three nearest-neighbor matching without replacement were conducted. Standardized mean biases were evaluated

to ensure balancing of covariates after propensity score matching. A sensitivity analysis of the unmatched cases was performed using both stepwise and non-stepwise multivariable logistic regression for the outcome of neck hematoma, hypocalcemia and RLN injury after adjusting for clinically important variables (eTable 3-5 supplement). RStudio software, version 1.3.1073 (PBC Corp.) and SPSS software version 27.0 (IBM Corp.) were used for all statistical analysis and significance was confirmed at a  $P$ -value  $<.05$ .

## Results

### Patients Characteristics

A total of 17906 patients met the inclusion criteria with an average age of 51.7 (range=18-90, SD=15) and 13929 (77.8%) female. Their demographics, comorbidities and thyroid-specific characteristics are presented in Table 1. A total of 1207 (6.74%) patients underwent thyroid surgery for Graves' disease and 16699 (93.3%) underwent thyroid surgery for indications other than Graves' disease (Figure 1). After one-to-three propensity score matching 1207 patients with Graves' disease were matched with 3621 patients with non-Graves' disease (Table 1). Figure 2 shows the standardized mean differences for all covariates. Substantial improvements in standardized mean differences across all covariates were achieved. One-to-three matching showed small standardized mean differences; only age maintained an elevated standardized mean difference of approximately 0.5. This follows from the known pathophysiology of Graves' disease, which develops at a much younger age than the majority of other indications for thyroid surgery.

### Outcome

The cumulative 30-day incidence of neck hematoma in the Graves' disease and non-Graves' disease groups was 3.1% (38/1207) and 1.9% (70/3621) respectively. After one-to-three propensity score matching, Graves' disease was associated with higher odds of postoperative neck hematoma (OR 1.65, 95% CI 1.10-2.46), our primary outcome, compared with other indications for thyroid surgery (Table 2). Out of 38 Graves' disease patients who developed postoperative neck hematoma, 31 required additional observation or extended length of stay, 4 did not require any additional observation, 3 had tracheostomy and none required further incision, drainage or reoperation (Table 3).

Similarly, Graves' disease was associated with higher odds of postoperative hypocalcemia (OR 2.04, 95% CI 1.66-2.50) compared with other indications for thyroid surgery; 167 (13.8%) patients with Graves' disease had hypocalcemia and 264 (7.3%) patients without Graves' disease had hypocalcemia (Table 2).

**Table 1.** Baseline Characteristics of Patients Undergoing Thyroid Surgery.

Characteristics	Full cohort (n = 17906)		Propensity score-matched cohort (n = 4828)		P-value
	GD (n = 1207)	Non-GD (n = 16699)	GD (n = 1207)	Non-GD (n = 3621)	
Age, mean (SD), years	42.6 (14.9)	52.4 (14.9)	42.6 (14.9)	46.7 (15.0)	<.001
Female	1017 (84.3)	12912 (77.3)	1017 (84.3)	2998 (82.8)	.231
BMI					
Underweight (<18.5)	31 (2.6)	138 (0.8)	31 (2.6)	46 (1.27)	.015
Normal (18.5–24.9)	324 (26.8)	3677 (22.0)	324 (26.8)	860 (23.8)	.019
Overweight (25.0–29.9)	373 (30.9)	4838 (29.0)	373 (30.9)	1060 (29.3)	.166
Obese (30.0–34.9)	237 (19.6)	3642 (21.8)	237 (19.6)	780 (21.5)	.324
Morbid obesity (≥35)	221 (18.3)	4034 (24.2)	221 (18.3)	847 (23.4)	<.001
ASA class					
1–2	786 (65.1)	10622 (63.6)	786 (65.1)	2298 (63.5)	.297
≥3	417 (34.5)	5981 (35.8)	417 (34.5)	1310 (36.2)	.304
Diabetes with oral agents					
Insulin-dependent diabetes	38 (3.1)	668 (4.0)	38 (3.1)	152 (4.2)	.082
Non-insulin-dependent diabetes	47 (3.9)	1653 (9.9)	47 (3.9)	214 (5.9)	.003
No diabetes	1122 (93.0)	14378 (86.1)	1122 (93.0)	3255 (89.9)	.001
Current smoker within 1 year	302 (25.0)	2272 (13.6)	302 (25.0)	735 (20.3)	.001
History of bleeding disorder	18 (1.5)	182 (1.1)	18 (1.5)	35 (0.97)	.173
Dyspnea					
No dyspnea	1132 (93.8)	15534 (93.0)	1132 (93.8)	3335 (92.7)	.042
With exertion or at rest	75 (6.2)	1165 (7.0)	75 (6.2)	286 (7.9)	.042
History of severe COPD	30 (2.5)	426 (2.6)	30 (2.5)	114 (3.15)	.215
Hypertension requiring medication	428 (35.5)	6422 (38.5)	428 (35.5)	1382 (38.2)	.090
CHF 30 days before surgery	10 (0.8)	67 (0.4)	10 (0.8)	21 (0.58)	.391
Long-term corticosteroid use	59 (4.9)	447 (2.7)	59 (4.9)	120 (3.31)	.022
> 10% Weight loss in past 6 months	37 (3.1)	75 (0.4)	37 (3.1)	45 (1.24)	.001
Surgical subspecialty					
General surgery	736 (61.0)	8725 (52.2)	0	2059 (56.9)	.012
Otolaryngology	471 (39.0)	7974 (47.8)	0	1557 (43.0)	.013
Clinical thyroid toxicity					
Not clinically toxic	722 (59.8)	13307 (79.7)	722 (59.8)	2705 (74.7)	<.001
Clinically toxic	384 (31.8)	909 (5.4)	384 (31.8)	550 (15.2)	
Prior neck surgery	38 (3.1)	1807 (10.8)	38 (3.1)	163 (4.50)	.027

(continued)

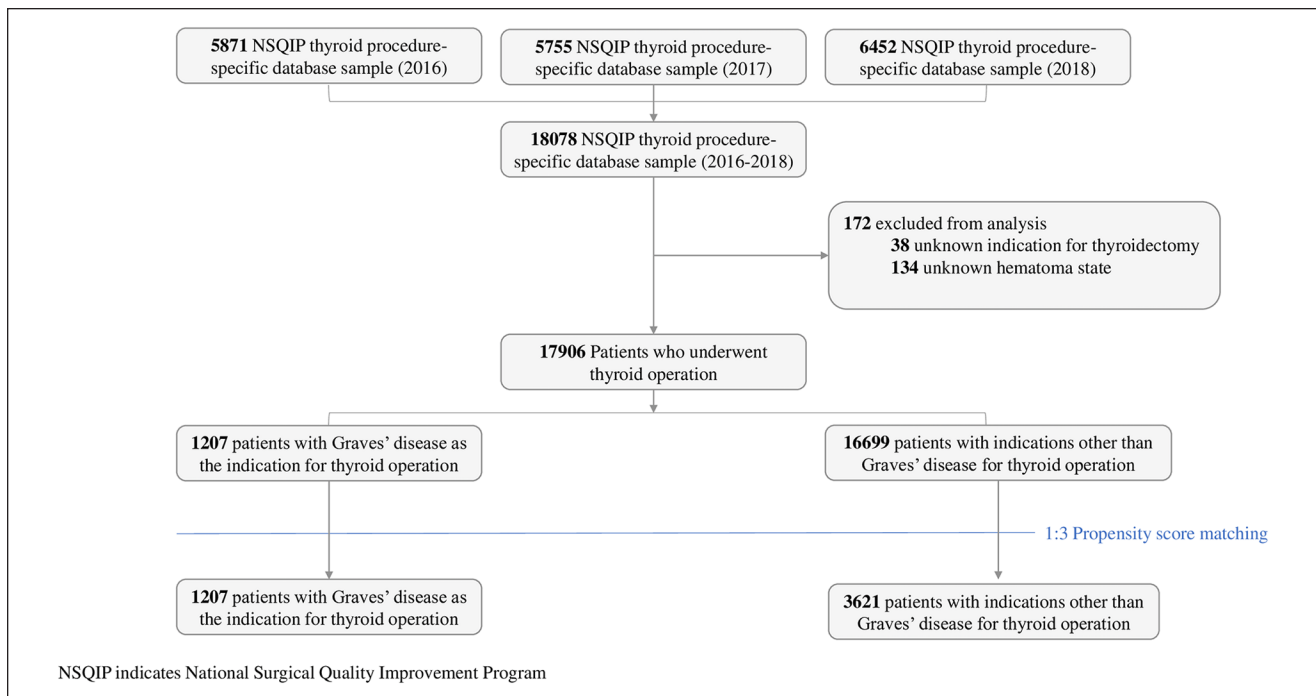
**Table 1. (continued)**

Characteristics	Full cohort (n = 17906)		Propensity score-matched cohort (n = 4828)		P-value
	GD (n = 1207)	Non-GD (n = 16699)	GD (n = 1207)	Non-GD (n = 3621)	
Preoperative needle biopsy result					
Follicular neoplasm	31 (2.6)	2335 (14.0)	31 (2.6)	118 (3.3)	.203
Hürthle cell neoplasm	6 (0.5)	666 (4.0)	6 (0.5)	21 (0.6)	.728
Indeterminate result	39 (3.2)	2356 (14.1)	39 (3.2)	152 (4.2)	.112
Suspicious for papillary thyroid cancer	36 (3.0)	4011 (24.0)	36 (3.0)	143 (3.9)	.001
Other result not described above	118 (9.8)	3330 (19.9)	118 (9.8)	552 (15.2)	<.001
Central neck dissection	139 (11.5)	4194 (25.1)	139 (11.5)	498 (13.8)	.039
No central neck dissection	1052 (87.2)		1052 (87.2)	3071 (84.8)	.038
Use of vessel sealant device	883 (73.2)	10578 (63.3)	883 (73.2)	2543 (70.2)	.049
Conventional hemostasis	302 (25.0)		302 (25.0)	1014 (28.0)	.040
Intraoperative RLN monitoring					
Yes	808 (66.9)	10508 (62.9)	808 (66.9)	2280 (63.0)	.012
No	390 (32.3)	6006 (36.0)	390 (32.3)	1302 (36.0)	.020
T stage					
T0	8 (0.7)	78 (0.5)	8 (0.7)	25 (0.69)	.919
T1	146 (12.1)	3939 (23.6)	146 (12.1)	523 (14.4)	.034
T2	8 (0.7)	1361 (8.2)	8 (0.7)	49 (1.4)	.023
T3	12 (1.0)	1548 (9.3)	12 (1.0)	63 (1.7)	.038
Multifocal or unifocal cancer					
Multifocal	56 (4.6)	3219 (19.3)	56 (4.6)	238 (6.6)	.008
Unifocal	120 (9.9)	4033 (24.2)	120 (9.9)	451 (12.5)	.014
Extent of thyroidectomy					
Lobectomy/hemithyroidectomy	7 (0.6)	1166 (7.0)	7 (0.6)	34 (0.9)	.186
Total thyroidectomy	1191 (98.7)	14638 (87.7)	1191 (98.7)	3557 (98.2)	.264
Completion thyroidectomy	9 (0.7)	895 (5.3)	9 (0.7)	30 (0.8)	.775
Admission status					
Inpatient	434 (36.0)	5961 (35.70)	434 (36.0)	1228 (33.9)	.199
Outpatient	773 (64.0)	10738 (64.30)	773 (64.0)	2393 (66.1)	

Note. Data are presented as number (percentage) of patients unless otherwise indicated.

Abbreviations: GD, Graves' disease; BMI, body mass index (calculated as [703 × weight (lbs)]/[height (in)]<sup>2</sup>); ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure.





**Figure 1.** Study flow diagram.

However, the odds of postoperative RLN injury (OR 1.05, 95% CI 0.79-1.40) was not different between patients who underwent thyroidectomy for Graves' disease and those who underwent thyroidectomy for reasons other than Graves' disease (Table 2).

### Admission Status

Of all 1207 Graves' disease patients, 434 patients were admitted as inpatient and 773 were observed for up to 23 hours which were classified as outpatient. Of all postoperative neck hematomas in the Graves' disease group, 25 were admitted as inpatient versus 13 that were treated as outpatient. The odds of inpatient admission for Graves' disease patients with hematoma was 3.42 (95% CI 1.77-6.26).

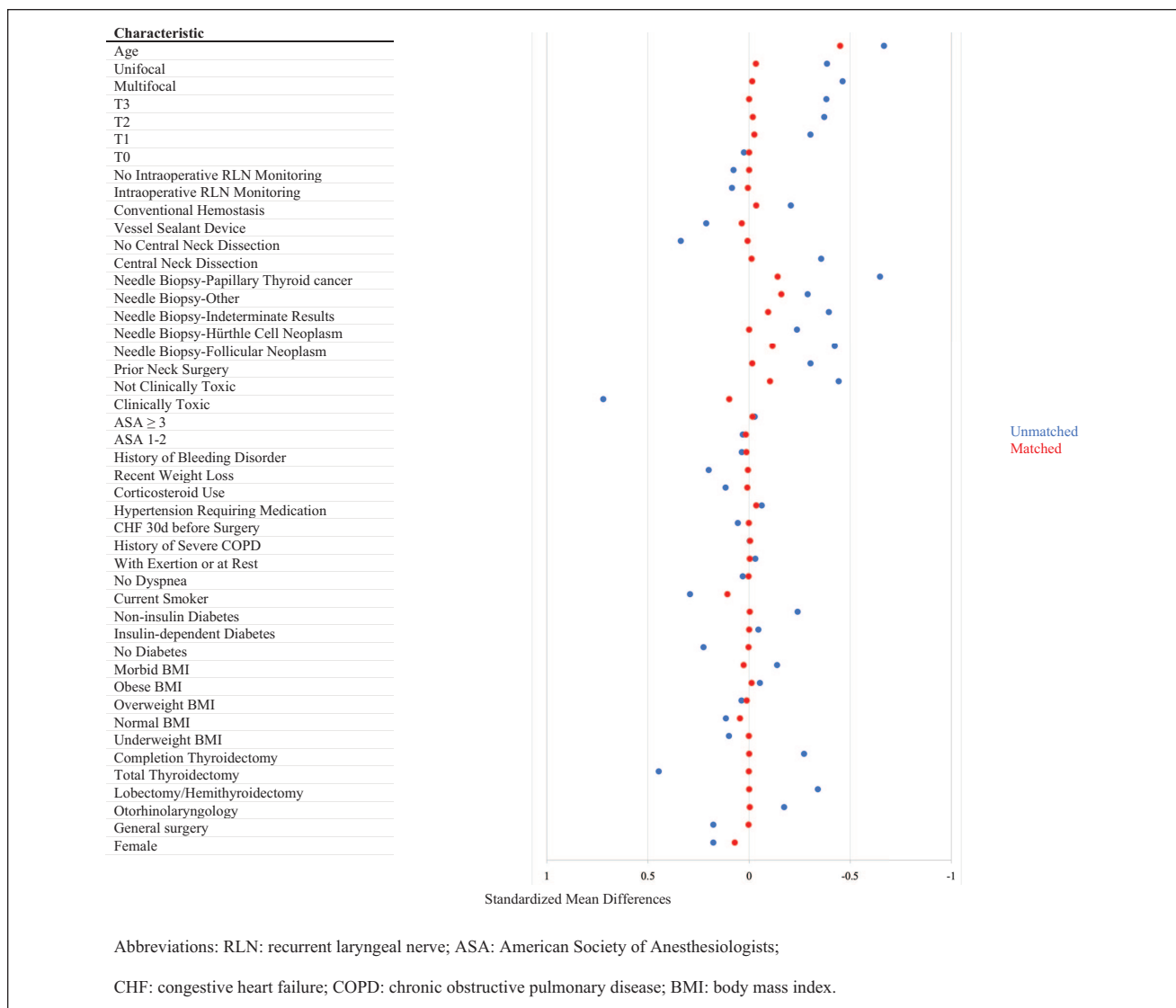
### Sensitivity Analysis

For sensitivity analysis, patients with unknown hypocalcemia status and unknown intraoperative nerve injury were excluded. A multivariable logistic regression model of the full unmatched cohort showed that Graves' disease was associated with higher odds of postoperative neck hematoma (OR 2.22, 95% CI 1.51-3.25) and postoperative hypocalcemia (OR 2.05, 95% CI 1.68-2.50) compared with other indications for thyroid surgery; however Graves' disease was not found to be associated with RLN injury (OR 1.05,

95% CI 0.80-1.37) (eTable 3a-5a supplement). Stepwise multivariable logistic regression model showed that history of bleeding disorder, hypertension requiring medication, dyspnea with exertion or at rest, ASA class  $\geq 3$ , conventional hemostasis and male sex were also significantly associated with higher odds of postoperative hematoma.

In regard to hypocalcemia, this analysis showed that central neck dissection, multifocal cancer, female sex, clinically toxic thyroid, prior neck surgery, dyspnea with exertion or at rest, ASA class  $\geq 3$  and hypertension requiring medication were associated with higher odds of postoperative hypocalcemia. Younger age, intraoperative RLN monitoring, use of any vessel sealant device for homeostasis, operations performed by otolaryngologist surgeons and diabetes were associated with lower odds of postoperative hypocalcemia (eTable 3b and 4b supplement).

One-to-one and one-to-two propensity score matching with 1207 patients with Graves' disease and 1207 (1:1) and 2414 (1:2) patients with indications other than Graves' disease for thyroidectomy showed similar associations between the primary and secondary outcomes and Graves' disease. For RLN injury, sensitivity analysis showed that history of bleeding disorder, dyspnea with exertion or at rest, multifocal cancer, central neck dissection, surgeries performed by non-otolaryngologist surgeons, no use of intraoperative monitoring and older age were associated with nerve injury (eTable 5b supplement).



**Figure 2.** Standardized mean differences comparing the full unmatched cohort with the propensity score-matched cohort.

**Table 2.** Outcomes Before and After Propensity Score Matching.

Outcome	Full cohort (n = 17 906)			Propensity score-matched cohort (n = 4828)		
	Events*	OR (95% CI)	Two-sided P-value	Events*	OR (95% CI)	Two-sided P-value
<b>Hematoma</b>						
GD	38 (3.1)	1.84 (1.30-2.60)	.001	38 (3.1)	1.65 (1.10-2.46)	.01
Non-GD	289 (1.7)	1 (Reference)		70 (1.9)	1 [Reference]	
<b>Hypocalcemia</b>						
GD	167 (13.8)	2.19 (1.84-2.61)	<.001	167 (13.8)	2.04 (1.66-2.50)	<.001
Non-GD	1139 (6.8)	1 (Reference)		264 (7.3)	1 (Reference)	
<b>RLN injury</b>						
GD	67 (5.6)	0.90 (0.70-1.16)	0.48	67 (5.6)	1.05 (0.79-1.40)	.71
Non-GD	101 (6.1)	1 (Reference)		191 (5.3)	1 (Reference)	

Abbreviations: OR, odds ratio; GD, patients with Graves’ disease as the indication for thyroid operation; Non-GD, patients with indication other than Graves’ disease for thyroid operation; RLN, recurrent laryngeal nerve.

\*Number of events (percentage of event in GD and non-GD category) for hematoma, RLN injury or dysfunction, and hypocalcemia.

**Table 3.** Distribution of the Extent of Neck Hematoma Requiring Different Interventions in Full Cohort (n = 17906).

Extent of neck hematoma	GD (n = 38)	Non-GD (n = 289)
Hematoma noted and there is documentation of additional observation or extended length of stay	31	177
Hematoma noted but there is no additional documentation of further observation or other intervention	4	60
Hematoma noted and tracheostomy was performed	3	39
Hematoma noted and there is documentation of additional interventions other than tracheostomy: opening of the incision to evacuate clot, drainage of blood or clot, or reoperation	0	13

## Discussion

This study demonstrates a relationship between thyroidectomy for Graves' disease and postoperative neck hematoma and hypocalcemia within a large cohort of patients. This finding suggests that Graves' disease, along with certain demographic, comorbid and intraoperative techniques, increases the risk of postoperative neck hematoma and are consistent with the literature.<sup>22,33,34</sup> A retrospective study with 147344 patients undergoing thyroid and parathyroid operations, found that Graves' disease, male sex and comorbidity score  $\geq 3$  were associated with higher odds of postoperative hematoma.<sup>34</sup> A recent retrospective cohort study that evaluated 10903 patients in the Thyroid Procedure-Targeted Database of the NSQIP found that vessel sealant devices are associated with lower odds of neck hematoma compared to conventional hemostasis; this is consistent with our findings.<sup>22</sup>

Another important finding in this study is that a larger proportion of Graves' disease patients with a neck hematoma were inpatients. These results are expected as those identified at a higher risk of postoperative adverse events are likely monitored as inpatients following thyroid surgery. More importantly, scheduling of outpatient thyroid surgery for Graves' disease remains possible and safe. Outpatient surgery allows for a higher throughput of operations without overloading inpatient resources. That being said, in Graves' disease patients undergoing total thyroidectomy, these patients are more than 1.5 times more likely to have a hematoma compared to similar patients undergoing thyroidectomy for another indication. Granted that the development of neck hematoma is multifactorial in etiology, the current data suggests that those with multiple risk factors including Graves' disease should be monitored as inpatients.

A limitation of large international databases such as the NSQIP is information bias due to misclassification<sup>35</sup> However, the NSQIP performs annual audits of selected participating hospitals to ensure high quality data with Inter-Rater Reliability disagreement rate of  $\leq 5\%$ . The main

limitation of this study is related to the study design and use of the NSQIP database. Patient population is biased toward those operated at hospitals that participated in NSQIP which are usually large, academic and non-for-profit institutions; however, NSQIP hospitals have the same likelihood as non-NSQIP hospitals for being rural.<sup>36</sup>

Also, variables are limited to those collected by NSQIP which is incomplete and prone to unmeasured confounding. For example, NSQIP does not provide information in regard to a surgeon's level of expertise. It has been shown that surgeons who perform a high volume of thyroidectomy have lower rates of hematoma regardless of the indication for thyroid operation.<sup>37,38</sup> NSQIP does not record medications that patients are on. A retrospective study of 4514 patients who underwent thyroid or parathyroid surgery found that neck hematomas are more likely in patients who were taking anticoagulant or antiplatelet even if held 5 to 7 days prior to surgery.<sup>39</sup>

Other potentially pertinent data points that are unavailable in the database include preoperative free thyroid hormone (T4) level, thyroid stimulating hormone (TSH) level, serum thyroid-stimulating hormone receptor antibody (TRAB) level, the duration of pre-operative euthyroidism and preoperative treatments such as iodine-123 and inorganic iodides. It has been shown that preoperative inorganic iodide such as potassium iodide or potassium iodine (Lugol's solution) reduces both thyroid hormone release, thyroid blood flow, thyroid vascularity and intraoperative blood loss, which may reduce the risk of postoperative hematoma.<sup>40,41</sup> Despite showing the increased risk of hematoma in Graves' disease patients, this study does not explain why these patients are at higher risk of hematoma; expanding the thyroid specific variables collected may help answer this question.

Another limitation in this study is missing data. In our study, a total of 799 patients had unknown hypocalcemia and unknown nerve injury status. However, this only represents 4.4% (799/17906) of the unmatched cohort and it is unlikely that it will affect the results significantly. Propensity score matching eliminated many patients who were not



one-to-three matched and reduced the sample size significantly. Since postoperative neck hematoma is an infrequent outcome of thyroidectomy and it is potentially associated with numerous confounding variables, a parsimonious regression model could result in bias; therefore, propensity score matching was used to balance the exposed and unexposed groups for confounding variables despite eliminating many patients from the study. Lastly, NSQIP data is limited to 30-day outcomes; therefore, long-term outcomes such as permanent nerve injury and permanent hypocalcemia could not be assessed. Long-term follow up is necessary for Graves' disease patients as up to 25% of patients stay symptomatic despite treatment for up to 6 to 10 years after diagnosis, regardless of treatment option.<sup>2</sup>

Future studies on this topic would benefit from prioritizing inclusion of these missing data. Most importantly, being able to control for the surgeon's expertise, intraoperative findings, and biochemical parameters for control of thyroid function and period of euthyroidism would remove a number of potential confounding factors in the current study.

## Conclusions

Patients with Graves' disease undergoing thyroidectomy were more likely to have a postoperative neck hematoma and hypocalcemia compared to patients undergoing surgery for other indications. The results suggest that the primary indication for thyroid surgery has an impact on postoperative outcome. These findings may guide surgeons to preferentially monitor patients with Graves' disease undergoing thyroidectomy, particularly those with multiple risk factors.

## Authors' Note

This manuscript was not previously presented at any meeting.

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## Authors Contribution

All authors contributed to (1) Analysis and interpretation of data; (2) Revising the article critically for important intellectual content; (3) Approved the final version; and (4) Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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## Ethics Approval

This study was approved by McGill University Health Centre Research Ethics Board (MP-37-2018-3568).

## ORCID iDs

Sadaf Mohtashami  <https://orcid.org/0000-0002-6841-0351>  
Marco A. Mascarella  <https://orcid.org/0000-0002-8880-805X>

## Supplemental Material

Supplemental material for this article is available online.

## Availability of Data and Material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## References

1. Ross DS, Burch HB, Cooper DS, et al. 2016 American Thyroid Association Guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid*. 2016;26(10):1343-1421. doi:10.1089/thy.2016.0229
2. Sjölin G, Holmberg M, Törning O, et al. The long-term outcome of treatment for Graves' hyperthyroidism. *Thyroid*. 2019;29(11):1545-1557. doi:10.1089/thy.2019.0085
3. Inabnet WB, Shifrin A, Ahmed L, Sinha P. Safety of same day discharge in patients undergoing sutureless thyroidectomy: a comparison of local and general anesthesia. *Thyroid*. 2008;18(1):57-61. doi:10.1089/thy.2007.0148
4. Trottier DC, Barron P, Moonje V, Tadros S. Outpatient thyroid surgery: should patients be discharged on the day of their procedures? *Can J Surg*. 2009;52(3):182-186.
5. Lo Gerfo P, Gates R, Gazetas P. Outpatient and short-stay thyroid surgery. *Head Neck*. 1991;13(2):97-101. doi:10.1002/hed.2880130203
6. Snyder SK, Hamid KS, Roberson CR, et al. Outpatient thyroidectomy is safe and reasonable: experience with more than 1,000 planned outpatient procedures. *J Am Coll Surg*. 2010;210(5):575-582. doi:10.1016/j.jamcollsurg.2009.12.037
7. Mowschenson PM, Hodin RA. Outpatient thyroid and parathyroid surgery: a prospective study of feasibility, safety, and costs. *Surgery*. 1995;118(6):1051-1054. doi:10.1016/s0039-6060(05)80113-8
8. Leyre P, Desurmont T, Lacoste L, et al. Does the risk of compressive hematoma after thyroidectomy authorize 1-day surgery? *Langenbecks Arch Surg*. 2008;393(5):733-737. doi:10.1007/s00423-008-0362-y
9. Burkey SH, van Heerden JA, Thompson GB, Grant CS, Schleck CD, Farley DR. Reexploration for symptomatic hematomas after cervical exploration. *Surgery*. 2001;130(6):914-920. doi:10.1067/msy.2001.118384

10. Promberger R, Ott J, Kober F, et al. Risk factors for postoperative bleeding after thyroid surgery. *Br J Surg*. 2012;99(3):373-379. doi:10.1002/bjs.7824
11. Smith A, Braden L, Wan J, Sebelik M. Association of otolaryngology resident duty hour restrictions with procedure-specific outcomes in head and neck endocrine surgery. *JAMA Otolaryngol Head Neck Surg*. 2017;143(6):549-554. doi:10.1001/jamaoto.2016.4182
12. Seybt MW, Terris DJ. Outpatient thyroidectomy: experience in over 200 patients. *Laryngoscope*. 2010;120(5):959-963. doi:10.1002/lary.20866
13. Calò PG, Pisano G, Piga G, et al. Postoperative hematomas after thyroid surgery. Incidence and risk factors in our experience. *Ann Ital Chir*. 2010;81(5):343-347.
14. Biet A, Zaatar R, Strunski V, Page C. Complications postopératoires dans la thyroïdectomie totale pour maladie de Basedow: comparaison avec la chirurgie des goitres non basedowiens. *Annales d'Otolaryngologie et de Chirurgie Cervicofaciale*. 2009;126(4):190-195. doi:10.1016/j.aorl.2009.06.003
15. Gaujoux S, Leenhardt L, Trésallet C, et al. Extensive thyroidectomy in Graves' disease. *J Am Coll Surg*. 2006;202(6):868-873. doi:10.1016/j.jamcollsurg.2006.02.031
16. Quimby AE, Wells ST, Hearn M, Javidnia H, Johnson-Obaseki S. Is there a group of patients at greater risk for hematoma following thyroidectomy? A systematic review and meta-analysis. *Laryngoscope*. 2017;127(6):1483-1490. doi:10.1002/lary.26195
17. Liu JB, Sosa JA, Grogan RH, et al. Variation of thyroidectomy-specific outcomes among hospitals and their association with risk adjustment and hospital performance. *JAMA Surg*. 2018;153(1):e174593. doi:10.1001/jamasurg.2017.4593
18. Sippel RS, Chen H. Limitations of the ACS NSQIP in thyroid surgery. *Ann Surg Oncol*. 2011;18(13):3529-3530. doi:10.1245/s10434-011-1939-1
19. Goldfarb M, Perry Z, Hodin RA, Parangi S. Medical and surgical risks in thyroid surgery: Lessons from the NSQIP. *Ann Surg Oncol*. 2011;18(13):3551-3558. doi:10.1245/s10434-011-1938-2
20. Caulley L, Johnson-Obaseki S, Luo L, Javidnia H. Risk factors for postoperative complications in total thyroidectomy: a retrospective, risk-adjusted analysis from the National Surgical Quality Improvement Program. *Medicine*. 2017;96(5):e5752. doi:10.1097/md.0000000000005752
21. User Guide for the 2017 ACS NSQIP Participant Use File (PUF). American College of Surgeons National Surgical Quality Improvement Program. Accessed August 27, 2020. [https://www.facs.org/-/media/files/quality-programs/nsqip/nsqip\\_puf\\_userguide\\_2017.ashx](https://www.facs.org/-/media/files/quality-programs/nsqip/nsqip_puf_userguide_2017.ashx)
22. Siu JM, McCarty JC, Gadkaree S, et al. Association of vessel-sealant devices vs conventional hemostasis with postoperative neck hematoma after thyroid operations. *JAMA Surg*. 2019;154(11):e193146. doi:10.1001/jamasurg.2019.3146
23. Braitman LE, Rosenbaum PR. Rare outcomes, common treatments: analytic strategies using propensity scores. *Ann Int Med*. 2002;137(8):693. doi:10.7326/0003-4819-137-8-200210150-00015
24. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika*. 1983;70(1):41-55. doi:10.1093/biomet/70.1.41
25. Rosenbaum PR, Rubin DB. Reducing bias in observational studies using subclassification on the propensity score. *J Am Stat Assoc*. 1984;79(387):516-524. doi:10.1080/01621459.1984.10478078
26. Rosenbaum PR, Rubin DB. Constructing a control group using multivariate matched sampling methods that incorporate the propensity score. *Am Stat*. 1985;39(1):33-38. doi:10.1080/00031305.1985.10479383
27. Austin PC, Mamdani MM. A comparison of propensity score methods: a case-study estimating the effectiveness of post-AMI statin use. *Stat Med*. 2006;25(12):2084-2106. doi:10.1002/sim.2328
28. Sturmer T, Rothman KJ, Avorn J, Glynn RJ. Treatment effects in the presence of unmeasured confounding: dealing with observations in the tails of the propensity score distribution—a simulation study. *Am J Epidemiol*. 2010;172(7):843-854. doi:10.1093/aje/kwq198
29. Rassen JA, Shelat AA, Myers J, Glynn RJ, Rothman KJ, Schneeweiss S. One-to-many propensity score matching in cohort studies. *Pharmacoepidemiol Drug Saf*. 2012;21(Suppl 2):69-80. doi:10.1002/pds.3263
30. Austin PC. Statistical criteria for selecting the optimal number of untreated subjects matched to each treated subject when using many-to-one matching on the propensity score. *Am J Epidemiol*. 2010;172(9):1092-1097. doi:10.1093/aje/kwq224
31. Bergenfelz A, Jansson S, Kristoffersson A, et al. Complications to thyroid surgery: results as reported in a database from a multicenter audit comprising 3,660 patients. *Langenbecks Arch Surg*. 2008;393(5):667-673. doi:10.1007/s00423-008-0366-7
32. Godballe C, Madsen AR, Pedersen HB, et al. Post-thyroidectomy hemorrhage: a national study of patients treated at the Danish departments of ENT Head and Neck Surgery. *Eur Arch Otorhinolaryngol*. 2009;266(12):1945-1952. doi:10.1007/s00405-009-0949-0
33. Beck AC, Sugg SL, Weigel RJ, Belding-Schmitt M, Howe JR, Lal G. Racial disparities in comorbid conditions among patients undergoing thyroidectomy for Graves' disease: an ACS-NSQIP analysis. *Am J Surg*. 2020;221(1):106-110. doi:10.1016/j.amjsurg.2020.05.023
34. Dehal A. Risk factors for neck hematoma after thyroid or parathyroid surgery: ten-year analysis of the nationwide inpatient sample database. *Perm J*. 2015;19(1):22-28. doi:10.7812/tpj/14-085
35. Nørgaard M, Ehrenstein V, Vandenbroucke JP. Confounding in observational studies based on large health care databases: problems and potential solutions – a primer for the clinician. *Clin Epidemiol*. 2017;9:185-193. doi:10.2147/clep.s129879
36. Sheils CR, Dahlke AR, Kreutzer L, Bilimoria KY, Yang AD. Evaluation of hospitals participating in the American College of Surgeons National Surgical Quality Improvement

- Program. *Surgery*. 2016;160(5):1182-1188. doi:10.1016/j.surg.2016.04.034
37. Kandil E, Noureldine SI, Abbas A, Tufano RP. The impact of surgical volume on patient outcomes following thyroid surgery. *Surgery*. 2013;154(6):1346-1352. doi:10.1016/j.surg.2013.04.068
38. Dehal A, Abbas A, Al-Tememi M, Hussain F, Johna S. Impact of surgeon volume on incidence of neck hematoma after thyroid and parathyroid surgery: ten years' analysis of nationwide in-patient sample database. *Am Surg*. 2014;80(10):948-952. doi:10.1177/000313481408001008
39. Oltmann SC, Alhefdhi AY, Rajaei MH, Schneider DF, Sippel RS, Chen H. Antiplatelet and anticoagulant medications significantly increase the risk of postoperative hematoma: review of over 4500 thyroid and parathyroid procedures. *Ann Surg Oncol*. 2016;23(9):2874-2882. doi:10.1245/s10434-016-5241-0
40. Erbil Y, Ozluk Y, Giriş M, et al. Effect of Lugol solution on thyroid gland blood flow and microvessel density in the patients with Graves' disease. *J Clin Endocrinol Metab*. 2007;92(6):2182-2189. doi:10.1210/jc.2007-0229
41. Huang S-M, Liao W-T, Lin C-F, Sun HS, Chow N-H. Effectiveness and mechanism of preoperative Lugol solution for reducing thyroid blood flow in patients with euthyroid Graves' disease. *World J Surg*. 2016;40(3):505-509. doi:10.1007/s00268-015-3298-8