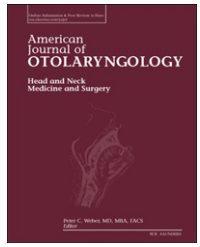
Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/amjoto



Relationship between obesity, diabetes and the risk of thyroid cancer☆,☆☆

Benjamin Oberman, MD[a], *Aliasgher Khaku, BS*[a], *Fabian Camacho, MS, MA*[b], *David Goldenberg, MD*[a,*]

[a] *Department of Surgery, Division of Otolaryngology–Head and Neck Surgery, The Pennsylvania State University, College of Medicine, Hershey, PA, USA*
[b] *Department of Public Health Sciences, Division of Health Services and Behavioral Research, The Pennsylvania State University, College of Medicine, Hershey, PA, USA*

ARTICLE INFO

Article history:
Received 5 January 2015

ABSTRACT

Purpose: Analyze the relationship between obesity and type-2 diabetes mellitus (DM) and the development of differentiated thyroid cancer (DTC).

Materials and methods: A randomized case-controlled retrospective chart review of outpatient clinic patients at an academic medical center between January 2005 and December 2012. DTC patients were compared to two control groups: primary hyperparathyroidism (PHPTH) patients with euthyroid state and Internal Medicine (IM) patients. Exposure variables included historical body-mass-index (BMI), most recent BMI within 6 months and DM. Multivariate logistic regressions adjusting for gender, age, and year of BMI assessed the adjusted Odds Ratio (OR) of DTC with both BMI and DM.

Results: Comparison of means showed a statistically significant higher BMI in DTC (BMI = 37.83) than PHPTH, IM, and pooled controls, BMI = 30.36 p = <0.0001, BMI = 28.96 p = <0.0001, BMI = 29.53 p = <0.0001, respectively. When compared to PHPTH, DM was more frequent in DTC (29% vs. 16%) and prevalence trended towards significance (p = 0.0829, 95% CI = 0.902–5.407). BMI adjusted OR was significant when compared to PHPTH, IM and pooled controls: 1.125 (p = 0.0001), 1.154 (p = <0.0001), and 1.113 (p = <0.0001), respectively. DM adjusted OR was significant when compared to PHPTH and pooled controls at 3.178 (95% 1.202,8.404, p = 0.0198) and 2.237 (95% 1.033,4.844, p = 0.0410), respectively.

Conclusion: Our results show that obesity and, to a lesser degree, DM are significantly associated with DTC. BMI in particular was a strong predictive variable for DTC (C = 0.82 bivariate, C = 0.84 multivariate).

☆ This paper was presented at the AAO-HNSF 2014 Annual Meeting and OTO Expo, Orlando, FL, September 23, 2014.

☆☆ Funding: Wells Fargo Jane Barsumian and Mary Lyons Trust Grant.

* *Corresponding author at:* The Pennsylvania State University, College of Medicine, Department of Surgery, Division of Otolaryngology–Head and Neck Surgery, 500 University Drive, MC H091, Hershey, PA 17033-0850. Tel.: +1 717 531 8946; fax: +1 717 531 6160.
E-mail address: dgoldenberg@hmc.psu.edu (D. Goldenberg).

http://dx.doi.org/10.1016/j.amjoto.2015.02.015
0196-0709/

1. Introduction

In recent decades there has been a notable trend in the increase of thyroid cancer, although the specific reasons for this increase have not yet been well defined. Recent reports show that the incidence of thyroid cancer in 2009 increased to 14.3 cases per 100,000 persons in the United States, nearly triple the 1975 rate of 4.9 cases per 100,000 individuals. More than fifty percent of that increased rate has occurred since 2007. The increase has primarily been secondary to a rise in papillary thyroid cancer, which has increased by 9.1 per 100,000 persons in the past 30 years. When considering gender as a factor, the increase has also been more prevalent in women than men [1].

National data compiled in 2010 shows that Pennsylvania has the highest incidence of thyroid cancer amongst all states [2]. Ongoing research suggests that the rising incidence of thyroid cancer in Pennsylvania is statistically more significant than the national correlate [3]. When considering the overall increases in thyroid cancer, much of the rise in incidence may be due to improved detection methods, however this does not sufficiently explain the increased incidence in larger tumors, in all size categories [4]. It has been hypothesized that factors such as diabetes mellitus (DM) and obesity may be factors playing a role in the increase of thyroid cancer.

The prevalence of obesity has increased worldwide in recent decades and studies have shown that an increased body-mass-index (BMI) is a risk for other cancers as well: esophageal, colon, and renal cancers in men as well as endometrial, gallbladder, esophageal and renal cancers in women [5]. In the past 20 years the prevalence of obesity in U.S. adults has doubled, and overweight children and adolescents have tripled [6]. A recent study by Xu et al. showed that the prevalence of obesity increased from 13.4% to 35.7% from 1960–1962 to 2009–2010. This increase was not subject to influence by age, sex, ethnicity, or socioeconomic status [7]. The prevalence of obesity in Pennsylvania in 2010 is reported as 29.2% of the adult population versus 27.6% nationally as recorded by the Behavioral Risk Factor Surveillance System [8]. Various case–control and prospective studies have shown obesity to be an independent risk factor for thyroid cancer in men and women [6,9,10]. Additionally, a positive association between BMI and thyroid cancer risk has been shown in adults of all ages, including particularly young adults aged 18–20 [6].

In concert with the rise in thyroid cancer and obesity, DM has markedly increased in recent decades. Obese people have a 10-fold increased risk of diabetes and over 80% of type 2 diabetics are obese. Moreover, diabetics have a higher prevalence of thyroid disorders than the general population [11–13]. A recent study reported that there are over 250 million people globally with DM which is expected to reach 380 million in the next twenty years [13].

The factors driving the increase in thyroid cancer are not fully understood. In the present study, we sought to distinguish the interplay between obesity, DM, and well-differentiated thyroid cancer. This study took a novel approach by investigating the relationship between obesity, DM, and thyroid cancer by using data from three case-controlled populations, one with evidence of a euthyroid state.

2. Materials and methods

2.1. Study population

A randomized, case–control retrospective chart review was conducted for patients presenting with differentiated thyroid carcinoma (DTC) to the Penn State Hershey Medical Center Otolaryngology outpatient clinic between January 1, 2005 and December 31, 2012. DTC patients were selected by using ICD-9 code 193 "malignant neoplasm of the thyroid gland." Patients were excluded from the study for the following reasons: DTC could not be confirmed pathologically or cytologically, any evidence of undifferentiated thyroid cancer, or if height or weight was not documented. The study included 107 patients diagnosed with DTC from which 48 (9 males, 39 females) cases fit the study criteria. Characteristics of each patient's tumor, the date of diagnosis, age at diagnosis, sex, ethnicity, height, weight, history of diabetes, and other co-morbidities were recorded. The case group was compared to two different control groups for a total of 172 control patients.

The control groups consisted of two independent populations within the study timeline. Group 1 consisted of 70 patients diagnosed primary hyperparathyroidism (PHPTH) who presented to the Otolaryngology outpatient clinic with documented euthyroid state. Group 2 consisted of 102 systematically sampled patients selected from the Internal Medicine (IM) clinic. PHPTH patients were selected using ICD-9 codes 227 and 252 (benign neoplasm of the parathyroid gland and primary hyperparathyroidism, respectively). Parathyroid disease type, patient age and date of PHPTH diagnosis, serum TSH levels, sex, race, height, weight, history of diabetes, and other comorbidities were documented. Patients with history of thyroid dysfunction, thyroid cancer, unconfirmed diagnosis of primary hyperparathyroidism, a history of gastrointestinal bypass or gastrointestinal cancer, or a history of multiple endocrine neoplasia were excluded.

The Internal Medicine control patients were systemically sampled at a rate of 2 controls to 1 DTC case. A randomly selected calendar date was chosen, then every 5th patient presenting to the IM outpatient clinic from that date in each year (2005 through 2012) was selected until the matching quota was reached. A history of diabetes, age, sex, race, height, weight, and other comorbidities were recorded. The only exclusion criterion for this group was any history of thyroid cancer.

This study was approved by the organization's institutional review board.

2.2. Anthropometric analysis

Body Mass Index (BMI) was determined by dividing weight in kilograms by height in meters squared (kg/m^2). BMI data were collected to as far back as 2 years prior to the diagnosis of DTC and as recently as the most recent available BMI data after diagnosis of DTC. The weight data for both control groups were collected to as many as 3 years preceding diagnosis of hyperparathyroidism (PHPTH group) or 3 years preceding year of presentation (IM group). The most recently available weight was recorded as well. BMI was categorized as underweight