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Original Article

Obesity and High Risk Pathological Features of Papillary Thyroid Carcinoma: A Retrospective Analysis of a University Hospital in Pakistan

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Abstract

Background: Incidence of papillary thyroid carcinoma (PTC) and the frequency of obesity is increasing globally. In literature, relationship between excessive body weight and bad prognostic features of PTC is still debatable. In this study, we aimed to explore the association of obesity with high risk pathological features of PTC in a population treated by total thyroidectomy +/– neck dissection.

Materials and methods: Retrospective analysis of patients at Aga Khan University Hospital from January 2013 to December 2014, who underwent total thyroidectomy +/– neck dissection due to PTC. Patients were grouped according to World Health Organization (WHO) classification of BMI. They were categorized into two groups, i.e. normal (BMI= 18.5 – 24.9 kg/m^2) and obese (BMI ≥ 30 kg/m^2) as none of our patients lie in underweight and overweight category. Pathological features i.e. T–stage, multifocality, bilaterality, extrathyroidal extension, vascular invasion and N–stage were assessed. All tumors were staged according to TNM staging system proposed by 2010 American Joint Committee on Cancer (AJCC). Odds ratio (OR) with 95% confidence interval was used to examine the association between BMI & pathological characteristics of PTC.

Results: A total of 53 patients were treated for PTC in two–years period. There were 38 female and 15 male patients. Twenty–eight patients had BMI in normal while twenty–five in obese category. Patients who were in obese category had a significantly greater risk of having a multifocal tumor (OR=5.55, p–value=0.02) and bilaterality (OR=6.54, p–value=0.01) compared to normal weight patients. No positive associations were identified between BMI and extrathyroidal extension, high T–stage, vascular invasion and N–stage.

Conclusion: Obesity is not associated with high risk pathological features such as extrathyroidal extention, high T–stage, vascular invasion and N–stage in PTC. Although it has been correlated with multifocal and bilateral tumors in this retrospective study, the presence of these factors alone is not adequate to support the association conclusively.

Keywords: Papillary thyroid carcinoma, Body Mass Index, Pathological features, Total thyroidectomy, Obesity

Introduction

The frequency of obesity has increased worldwide,[1] and studies have shown that excess body weight, manifested as a higher Body Mass Index (BMI), is associated with increased risk of thyroid cancer and other cancers in both genders.[2–5]

Papillary thyroid carcinoma (PTC), the most common histologic type of thyroid malignancy, is also increasing globally.[6] Although the reason for this rise in incidence are not clear, enhanced detection of early–stage tumors with the use of neck ultrasound and ultrasound–guided biopsy play a major role.[7]

In literature, relationship between obesity and pathological features of PTC is indistinct. Less aggressive tumor features, such as the absence of nodal metastasis and tumor invasion was reported by Paes et al [8], while Kim et al [9] reported a positive association between obesity and advanced tumor stage.

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In this study, we aimed to explore the association of obesity with high risk pathological features of PTC in a population treated by total thyroidectomy +/– neck dissection.

Materials and Methods

We retrospectively reviewed medical records and pathology reports of 101 consecutive patients with thyroid carcinoma at Aga Khan University Hospital from January 2013 to December 2014. We excluded 48 patients with different histologic type than PTC. Thyroid function tests (serum TSH, free T3, and free T4) of all patients were preoperatively checked. We also collected medical history of diabetes mellitus, hypercholesterolemia, smoking and alcohol intake. A total of 53 cases were included in this study. Height and weight of each patient were recorded from preoperative anesthesia chart and by applying the formula of Body Mass Index (i.e., BMI = weight (kg) / height (m^2)), BMI of each patient was calculated. We divided our cases according to World Health Organization (WHO) classification of BMI, i.e. underweight (<18.5 kg/m^2), normal (18.5 – 24.9 kg/m^2), overweight (25–29.9 kg/m^2) and obese (≥30 kg/m^2). None of our cases lie in underweight and overweight category so there were two groups in our study, i.e. normal and obese.

A standard operative procedure of total thyroidectomy +/– neck dissection was performed in all patients in our setting with pre–operative diagnosis of PTC by fine–needle aspiration cytology(FNAC), even if the case falls in low risk category. Since there is no role of elective neck dissection in PTC, only therapeutic neck dissection in the form of either central, unilateral, bilateral or contra lateral was performed on the basis of positive neck node found pre–operatively through neck examination and/or imaging or intra–operatively through frozen section. All pathology specimens were reviewed by two experienced pathologists to confirm diagnosis, tumor characteristics and the extent of disease. All tumors were staged according to TNM staging system proposed by 2010 American Joint Committee on Cancer (AJCC).[10] As this was a retrospective study of routinely collected clinical data, patient consent was not required.

What are the high risk pathological features?

Features including higher T–stage (T3/T4) and N–stage (N1), bilaterality (tumor focus present in both lobes of thyroid), multifocality (more than one tumor focus present in either lobe of thyroid), distant metastasis, extrathyroidal extention and vascular invasion in final histopathology specimen are consider high risk as these factors are poor prognostic correlates[11] and indicator for adjuvant radioactive iodine (RAI) therapy according to National Comprehensive Cancer Network (NCCN) guidelines version 2.2013.[12]

Statistical analysis

Patient data was compiled and analyzed using Statistical Package for Social Sciences (SPSS) Version 21. Frequency and percentage were computed for categorical variables like gender, T–stage, multifocality, bilaterality, extrathyroidal extension, vascular invasion and N–stage. Mean ± SD was calculated for quantitative variables i.e. age, weight, height and Body Mass Index (BMI). Stratification was done on gender, age, T–stage, multifocality, bilaterality, extrathyroidal extension, vascular invasion and N–stage to see the effect of these modifiers on obesity using Chi–square test and Fisher's exact test and p–value ≤0.05 was considered as significant.

Association between obesity and the pathological characteristics of PTC, as expressed in terms of odds ratio (OR) with 95% confidence interval (CI). The pathological factors of PTC were treated as binary variables: extrathyroidal extention (present or absent), multifocality (present or absent), T stage (T1/T2 or T3/T4), bilaterality (present or absent), N–stage (N0 or N1) and vascular invasion (present or absent). All OR were adjusted for age and gender.

Results

Baseline pathological characteristics in patients with PTC

Pathological features of patients with PTC are summarized in Table 1. Among 53 patients, 38 (71.7%) were female and 15 (28.3%) were male. The mean age was 44.6 ± 14.3 years (range, 12 to 80 years). Based on WHO classification, there were 28(52.8%) normal and 25(47.1%) obese patients. Two (3.7%) subjects in normal and three (5.6%) in obese category had known history of diabetes mellitus, hypercholesterolemia and smoking. Similarly, three (5.6%) cases in each group had thyroid dysfunction which was preoperatively corrected. None of our patients had history of alcohol intake. Forty–three percent tumors had higher T–stage i.e. T3 and T4 while more than 10% cases had multifocal and bilateral PTCs along with extrathyroidal extention in final pathology specimens. Vascular invasion was found in 10(18.9%) cases while neck node metastasis was present in more than 40%. Only 2 cases (3.7%) with BMI in obese group had distant metastasis to lungs at the time of initial presentation.

Characteristics		n (%)
Age (years)	≤ 45	27 (50.9)
	>45	26 (49.1)
Gender	Male	15 (28.3)
	Female	38 (71.7)
BMI	Normal	28 (52.8)
	Obese	25 (47.1)
T Stage	T1 and T2	30 (56.6)
	T3 and T4	23 (43.4)
Multifocality	Yes	13 (24.5)
	No	40 (75.5)
Bilaterality	Yes	14 (26.4)
	No	39 (73.6)
Extrathyroidal Extension	Yes	12 (22.6)
	No	41 (77.4)
Vascular Invasion	Yes	10 (18.9)
	No	43 (81.1)
N Stage	N0	29 (54.7)
	N1	24 (45.3)

Table 1: Baseline characteristics of patients with papillary thyroid carcinoma (PTC)

Acronyms: n = number of cases; BMI = body mass index; T stage = tumor stage; N stage = nodal stage

Associations between BMI and pathological features of PTC

Patients who were obese had a significantly greater risk of having a multifocal tumor (OR=5.55, p–value=0.02) and bilaterality (OR=6.54, p–value=0.01) compared to normal. Cases in obese group also had higher frequencies of advanced T–stage and N–stage tumors along with lesions having extrathyroidal extention and vascular invasion, but it was not statistically significant (Table 2).

Discussion

In literature many studies on the correlations between thyroid cancer, specifically papillary thyroid carcinoma and obesity have been published.[13–16] However there were variations that exists in majority of studies due to which there is no definite conclusion on the association between obesity and thyroid malignancy. According to Renehan et al. [4], higher incidence of thyroid malignancy has been associated with increased BMI. Other works also suggested positive link between excessive body weight and risk of developing thyroid and other types of cancer.[2–5] In a study done by Sung et al. [16], greater the height, higher the chances of developing thyroid cancer in both genders. Previous studies exploring the associations between obesity and pathological features of PTC reported inconsistent results. Study from South Korea[9] showed a favorable relation between obesity and tumor stage, even though the association was not statistically significant. On the other hand, research from Ohio State University Medical Center[8] reported lower risk of tumor invasiveness & nodal metastasis with excessive BMI. Our study also showed no association between obesity & poor pathological features namely extrathyroidal extension, vascular invasion, tumor size and cervical metastasis. Unlike Kim et al.[11], which described strong relationship of higher BMI with large tumor size, microscopic extrathyroidal invasion and advanced tumor–node–metastasis stage, our study showed positive link with only multifocal and bilateral tumors. There have been number of prior studies about the origin of multifocal and bilateral PTC foci with evidence supporting two opinions, i.e., de novo carcinogenesis or intrathyroidal metastasis. But why multifocal and bilateral tumor foci had favorable association with obesity, we unable to explain. Similarly, the negative connection between elevated weight, pathological features of tumor and clinical course is unknown. One explanation for this when compared to breast cancer in which obesity has strong relationship with poor clinical behavior of tumor is that the amount of adipose tissue in the thyroid is significantly lesser than breast tissue. This cancer–adipocyte interaction may be the cause of difference in behavior in these two types of malignancy. Furthermore, certain cytokines such as leptin released from fat cells are also involved on thyroid cancer progression.[17] Prior researches reported high blood levels of leptin along–with expression of its receptor in patients with PTC. Akinci et al.[18] and Cheng et al. [19] also described this leptin–tumor aggressiveness correlation in their published papers. Conversely, adiponectin levels were shown to be negatively associated with body fat and BMI [17] and circulating adiponectin was inversely linked with the risk of thyroid cancer.[20] Additional researches required to find out the potential mechanisms underlying the interaction between obesity and high risk features in papillary thyroid cancer.

In the future, we are planning to follow these cases for longer duration to detect whether this positive or negative association of obesity with high risk pathological features has impact on tumor recurrence or not.

The limitations of our study was its retrospective nature, small sample size and lack of information regarding physical activity. We only selected patients

		Obese BMI n=25(%)	Normal BMI n=28(%)	Total n=53(%)	p-value	OR (95% CI)
T Stage	T1 & T2	11(44)	19(67.9)	30(56.6)	0.10	0.37 (0.12 - 1.14)
	T3 & T4	14(56)	9(32.1)	23(43.4)		
Multifocality	Yes	10(40)	3(10.7)	13(24.5)	0.02	5.55 (1.31 - 23.45)
	No	15(60)	25(89.3)	40(75.5)		
Bilaterality	Yes	11(44)	3(10.7)	14(26.4)	0.01	6.54 (1.56 - 27.48)
	No	14(56)	25(89.3)	39(73.6)		
Extrathyroidal Extension	Yes	7(28)	5(17.9)	12(22.6)	0.51	1.78 (0.48 - 6.58)
	No	18(72)	23(82.1)	41(77.4)		
Vascular invasion	Yes	7(28)	3(10.7)	10(18.9)	0.16	3.24 (0.73 - 14.26)
	No	18(72)	25(89.3)	43(81.1)		
N stage	N0	12(48)	17(60.7)	29(54.7)	0.41	0.59 (0.20 - 1.77)
	N1	13(52)	11(39.3)	24(45.3)		

Table 2. Association of BMI and pathological features in patients with PTC

Acronyms: n = number of cases; BMI = body mass index; OR = odds ratio; CI = confidence interval; T stage = tumor stage; N stage = nodal stage

who underwent total thyroidectomy and not included those in which lobectomy was performed. Although BMI determinations have been the most commonly used assessment scale for obesity in the medical practice, but measurements such as waist circumference, neck circumference and skin–fold thickness may be better tools for this type of study.

Conclusion

In the end, we conclude that obesity is not associated with high risk pathological features such as extrathyroidal extention, high T–stage, vascular invasion and N–stage in PTC. Although it has been correlated with multifocal and bilateral tumors in this retrospective study, the presence of these factors alone is not adequate to support the association conclusively. Further corroborative studies to confirm these findings are essential.

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