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Association between Body Mass Index and Severity According of Classification of Thyroid Cancer

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1. Abstract

1.1. Purpose: Obesity is associated with aggressive pathological features and poor clinical outcomes in breast and prostate cancers. However, the associations between excess weight and prognostic factors for thyroid cancer are uncertain. This study aimed to evaluate the associations between body mass index (BMI) and severity according of classification of thyroid cancer.

1.2. Methods: Retrospective analysis of 4485 patients with thyroid cancer was performed. Patients were grouped according to BMI (underweight, normal weight, overweight and obesity)-based World Health Organization standardized categories. Clinicopathological factors were analyzed and compared between normal and other groups.

1.3. Results: According to the results, 3789 patients were women (84.5%) and mean age was 47.1 years. 4338 patients (96.7%) were diagnosed with PTC. FTC were 115(2.6%), MTA ware 24(0.5%), ATC were 5(0.1%). There were no significant associations between BMI quartiles and Multifocality, cervical lymph node metastasis, or distant metastasis. Higher BMI were significantly associated with extrathyroidal extension of PTC ($P < 0.001$). And higher BMI were significantly associated with advanced TNM stage ($P=0.005$).

1.4. Conclusion: Increased BMI might elevate the risks of aggressive clinicopathological features of PTC, such as extrathyroidal invasion and advanced TNM stage. However, there were few cases except for PTC, which made it difficult to find statistically significant results. To confirm this result, further studies with long-term follow-up and more patients are required.

2. Introduction

Recently, the incidence of thyroid cancer has been growing worldwide [1]. Higher prevalence of thyroid cancer can be explained in part by the fact that development and use of neck ultrasonography and ultrasound-guided fine-needle aspiration have led to increased diagnostic rate for asymptomatic thyroid cancer [2]. Additional aspects, such as changes in exposure to environmental factors, may also play a role in explaining such increase in prevalence.

However, considering that increase in prevalence of thyroid cancer coincided with increased number of early cancer with small tumor size, as well as various tumor sizes and stages, it is suspected that there are other unidentified factors besides advances in diagnostic tools [3]. The main risk factors for thyroid cancer are exposure to ionizing radiation, a history of benign thyroid disease, and a family history of thyroid cancer [4, 5, 6]. Overweight and obesity, expressed as a high BMI, are possible risk factors for thyroid cancer

Obesity is associated with onset and progression of many cancers, including those of esophagus, colon, kidney, breast, skin, rectum, and gallbladder [7]. Obesity is the second most common, preventable, and modifiable cause of carcinogenesis, after smoking, there is worldwide variation that is dependent on the different incidences of obesity [8]. Although obesity is a known risk factor for carcinogenesis it does not seem to equally impact on all types of cancer. However, there are few reports on the relationship between obesity and thyroid cancer and the underlying mechanism is largely unknown [9 -12].

A review of studies on the association between thyroid cancer and BMI showed that recent studies are reporting that obesity is one of the factors considered to cause increase in thyroid cancer [13, 14]. In addition, some retrospective studies have reported that increase in BMI is associated with aggressive clinicopathological features in patients with papillary thyroid carcinoma [15]. However, the relationship between obesity and poor prognosis associated with thyroid cancer is still controversial [16], and while the basis for the correlation between excessive weight and malignant thyroid tumor has not yet been completely identified, the traditional risk factors of thyroid cancer still remain radiation exposure, high iodine intake, and family history of thyroid cancer [17]. For future evident on the potential negative effect of obesity on thyroid cancer, it is determined that clinical intervention including weight loss programs for overweight and obese people and thyroid cancer screening guidelines would play an important role. Accordingly, the present study aimed to investigate the correlation between clinicopathological parameters and being overweight in relation to thyroid cancer to use the findings to identify the correlation between BMI and cancer aggressiveness in relation to thyroid cancer.

3. Methods

The study population included 4,485 patients who received surgical treatment at Kosin University Gospel Hospital between January 2005 and December 2015 and were subsequently diagnosed with thyroid cancer. All medical records of these patients, including histopathological results, were retrospectively analyzed. BMI of each patient was calculated using the height and weight measured at the time of admission for the surgery. Using the standard BMI categories from the World Health Organization (WHO), the patients were divided into four groups: underweight (18.5), normal (18.5~24.9), overweight (25.0~29.9), and obese (≥30.0). [18]. The clinicopathological factors of the normal group were compared to those of other groups, while tumor size, multifocality, lymph node (LN) metastasis, advanced TNM staging, and recurrence were compared as factors suggesting aggressiveness of the tumor. Advanced TNM staging was divided according to the classification system given by the American Joint Committee on Cancer (AJCC; 8th edition) [19], and stages 1 and 2 were compared and analyzed against stages 3 and 4, representing advanced cancer. Recurrence was defined as new pathologically confirmed lesion in a patient who had been determined to be in remission during the follow-up observation period. Univariate analyses including chi-square test and one-way analysis of variance (ANOVA) were performed to determine the significance between BMI and the variables, while multivariate analysis was performed on the factors suggesting cancer aggressiveness. A logistic regression model was used to estimate the odds ratio (OR) and 95% confidence interval (CI), while adjusted OR was calculated by adjusting for age, gender, and TSH value. All statistical analyses were performed using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA) with statistical significance set to P-value <0.05.

4. Results

Among a total of 4,485 patients, there were 3,789 females (84.5%) and 696 males (15.5%). The mean age was 47.1 years (14~82 years) and mean BMI was 24.0 ± 3.3 (15.0~41.2). Based on BMI categories, the patients were divided into the underweight (n=112, 2.5%), normal (n=2,824, 63.0%), overweight (n=1,341, 29.9%), and obese (n=208, 4.6%) groups.

Based on Pathology, There were 4,338 (96.7%) patients with papillary thyroid cancer, 115(2.6%) patients with Follicular thyroid carcinoma, 24 (0.5%) patients with Medullary thyroid carcinoma, 5 (0.1%) patients with Anaplastic thyroid carcinoma.

The mean tumor size was 12.1 mm (2~72mm), there were 2,602 cases (58.0%) with tumor size ≤1cm and 1,470 cases (32.8%) had multifocality. Extrathyroid invasion and LN metastasis was found in 2,100 cases (46.8%) and 1,824 cases (40.7%), respectively, where LN metastasis involved the central neck LN in 1,430 cases (31.9%) and lateral neck LN in 394 cases (8.8%). In advanced TNM staging, the number of cases classified as stage 1, 2, 3, and 4 was 2,768 (61.7%), 84 (1.9%), 1,435 (32.0%), and 197 (4.4%), respectively, while in adjusted TNM staging for statistical analysis, there were 2,853 cases (63.6%) of stages 1 and 2 and 1,632 cases (36.4%) of stages 3 and 4. The mean follow-up period was 1,721±464.2 days, and during the follow-up period, there were 88 cases (2.0%) of recurrences. Of those cases, recurrence found in the central neck LN, lateral neck LN, and contralateral thyroid in 3 cases (3.4%), 62 cases (70.5%), and 23 cases (26.1%), respectively (Table 1).

There were few cases except for PTC, which made it difficult to find statistically significant results (Table 2).

1) Normal group versus underweight group

The mean BMI in the normal and underweight group was 22.3 ± 1.6 and 17.7 ± 0.7, respectively (Table 2), while there were no significant differences between the two groups with respect to tumor size, multifocality, extrathyroid invasion, LN metastasis, recurrence, and thyroiditis. However, in the univariate analysis, the normal and underweight groups showed differences based on TNM staging (P=0.000), but such differences were not found in the multivariate analysis (OR 0.255 [0.062~1.049], P=0.058) (Tables 3, 4).

2) Normal group versus overweight group

The mean BMI in the overweight group was 26.8 ± 1.3 (Table 2), while there were no significant differences between the two groups with respect to LN metastasis, TNM staging, recurrence, and thyroiditis. However, as compared to the normal group, the overweight group showed differences in tumor size (12.0mm± 8.7, p=0.024), multifocality (30.5% vs 36.7%, p=0.000), extrathyroid invasion (44.3% vs 51.6%, p=0.000), and TNM stage (p=0.000) in the univariate analysis and statistically significant differences in multifocality (OR 1.300 [1.127~1.499], P=0.000) and extrathyroid invasion (OR 1.322 [1.152~1.517], P=0.000) in the multivariate analysis (Tables 3, 4).

3) Normal group versus obese group

The mean BMI in the obese group was 32.2 ± 2.2 (Table 2), while there were no significant differences between the two groups with respect to tumor size, LN metastasis, TNM staging, and recurrence. However, as compared to the normal group, the obese group showed differences in multifocality (OR 1.671 [1.241~2.251], P=0.001), extrathyroid invasion (OR 1.630 [1.206~2.202], P=0.001), and thyroiditis (OR 0.642 [0.449~0.919], P=0.016) in both univariate and multivariate analyses (Tables 3, 4).

Table 1: Baseline clinicopathological characteristics of patients diagnosed with thyroid carcinoma

Characteristic	Total **(N=4485)**
Gender	
Female	3789 (84.5%)
Male	696 (15.5%)
Mean Age (years)	47.1 ± 11.5
<55	1888 (42.1%)
≥55	2597 (57.9%)
BMI (kg/m2)	24.0 ± 3.3
Pathology	
Papillary thyroid carcinoma	4338 (96.7%)
Follicular thyroid carcinoma	115(2.6%)
Medullary thyroid carcinoma	24 (0.5%)
Anaplastic thyroid carcinoma	5 (0.1%)
Etc.	3 (0.1%)
Tumor size (mm)	12.1 ± 9.0
≤10	2602 (58.0%)
> 10	1883 (42.0%)
Multifocality	1470 (32.8%)
Extrathyroidal invasion	2100 (46.8%)
LN metastasis	1824 (40.7%)
Central LN	1430 (31.9%)
Lateral LN	394 (8.8%)
TNMstage	
1	2768 (61.7%)
2	85 (1.9%)
3	1435 (32.0%)
4	197 (4.4%)
Recurrence	88(2.0%)
central LN	3 (3.4%)
lateral LN	62 (70.5%)
opposite gland	23 (26.1%)
Thyroditis	1174 (26.2%)

Table 2: Clinicopathological characteristics of patients diagnosed with thyroid carcinoma

	Underweight (N=112)	**Normal (N=2824)**	**Overweight (N=1341)**	**Obese (N=208)**	**p**
Gender					0
Female	109 (97.3%)	2457 (87.0%)	1052 (78.4%)	171 (82.2%)	
Male	3 (2.7%)	367 (13.0%)	289 (21.6%)	37 (17.8%)	
Mean age (years)	40.1 ± 13.0	46.3 ± 11.3	49.7 ± 11.2	46.2 ± 11.9	0
< 55	78 (69.6%)	1264 (44.8%)	446 (33.3%)	100 (48.1%)	
≥55	34 (30.4%)	1560 (55.2%)	895 (66.7%)	108 (51.9%)	
BMI(kg/m2)	17.7 ± 0.7	22.3 ± 1.6	26.8 ± 1.3	32.2 ± 2.2	0
Pathology					0.564
PTC	109 (97.3%)	2741 (97.1%)	1288 (96.0%)	200 (96.2%)	
FTC	3 (2.7%)	64 (2.3%)	42 (3.1%)	6 (2.9%)	
MTC	0 (0.0%)	14 (0.5%)	9 (0.7%)	1 (0.5%)	
ATC	0 (0.0%)	4 (0.1%)	1 (0.1%)	0 (0.0%)	
Etc.	0 (0.0%)	1 (0.1%)	1 (0.1%)	1 (0.1%)	
Tumor size (mm)	12.4 ± 9.2	11.8 ± 8.7	12.5 ± 9.5	13.0 ± 10.0	0.036
≤10	65 (58.0%)	1653 (58.5%)	772 (57.6%)	112 (53.8%)	0.592
> 10	47 (42.0%)	1171 (41.5%)	529 (41.1%)	96 (46.2%)	
Multifocality	32 (28.6%)	859 (30.4%)	491 (36.6%)	88 (42.3%)	0
Extrathyroidal invasion	46 (41.1%)	1248 (44.2%)	687 (51.2%)	119 (57.2%)	0
Lymph node Mets	46 (41.1%)	46 (41.1%)	543 (40.5%)	87 (41.8%)	0.987

Central LN	35 (31.2%)	904 (32.0%)	423 (31.5%)	68 (32.7%)	0.998
Lateral LN	11 (9.8%)	244 (8.6%)	120 (8.9%)	19 (9.1%)	
TNMstage					0
1	93 (83.0%)	1814 (64.2%)	724 (54.0%)	137 (65.9%)	
2	2 (1.8%)	55 (1.9%)	27 (2.0%)	1 (0.5%)	
3	13 (11.6%)	847 (30.0%)	513 (38.3%)	62 (29.8%)	
4	4 (3.6%)	108 (3.8%)	77 (5.7%)	5 (2.4%))	
Recurrence	3 (2.7%)	50 (1.8%)	30 (2.2%)	3 (1.5%)	0.665
central LN	0 (0.0%)	2 (4.0%)	0 (0.0%)	1 (20.0%)	0.282
lateral LN	3 (100.0%)	35 (70.0%)	22 (73.3%)	2 (40.0%)	
opposite gland	0 (0.0%)	13 (26.0%)	8 (26.7%)	2 (40.0%)	
Thyroditis	35 (31.2%)	770 (27.3%)	327 (24.4%)	42 (20.2%)	0.025

Table 3: Univariate analysis of parameters according to body mass index

	Underweight (N=109, 2.5%)	**Normal (N=2741,** 63.2%)	**Overweight (N=1288,** 29.7%)	**Obese (N=200,** 4.6%)
Tumor size (mm)	11.9 ± 8.5	11.3 ± 8.0	12.0 ± 8.7	12.1 ± 8.3
P value	0.46	Reference	0.024	0.19
Multifocality	30 (27.5%)	837 (30.5%)	473 (36.7%)	86 (43.0%)
P value	0.572	Reference	0	0
Extrathyroid invasion	44 (40.4%)	1214 (44.3%)	664 (51.6%)	115 (57.5%)
P value	0.477	Reference	0	0
LN metastasis	46 (42.2%)	1132 (41.3%)	535 (41.5%)	87 (43.5%)
P value	0.929	Reference	0.913	0.592
TNM staging				
1	91 (83.5%)	1764 (64.4%)	697 (54.1%)	132 (66.0%)
2	2 (1.8%)	50 (1.8%)	22 (1.7%)	0 (0.0%)
3	12 (11.0%)	826 (30.1%)	496 (38.5%)	60 (30.0%)
4	4 (3.7%)	101 (3.7%)	73 (5.7%)	8 (4.0%)
P value	0	Reference	0	0.287
Recurrence	3 (2.8%)	45 (1.6%)	27 (2.1%)	3 (1.5%)
P value	0.614	Reference	0.374	1
Thyroditis	34 (31.2%)	757 (27.6%)	321 (24.9%)	40 (20.0%)
P value	0.479	Reference	0.078	0.024

Table 4: Multivariate analysis with odds ratio (OR) and 95% confidence interval (CI)

	Underweight (N=109, 2.5%)	**Normal (N=2741,** 63.2%)	**Overweight (N=1288,** 29.7%)	**Obese (N=200,** 4.6%)
Tumor size (mm)				
OR (95% CI)	1.01 (0.985~1.035)	1	1.007 (0.998~1.017)	1.012 (0.994~1.031)
P value	0.455	Reference	0.113	1.198
Multifocality				
OR (95% CI)	0.862 (0.558~1.331)	1	1.3 (1.127~1.499)	1.671 (1.241~2.251)
P value	0.502	Reference	0	0.001
Extrathyroid invasion				
OR (95% CI)	0.846 (0.565~1.267)	1	1.322 (1.152~1.517)	1.63 (1.206~2.202)
P value	0.417	Reference	0	0.001
LN metastasis				
OR (95% CI)	1.098 (0.733~1.644)	1	0.898 (0.780~1.034)	0.885 (0.653~1.198)
P value	0.651	Reference	0.135	0.428
Advanced TNM staging				
OR (95% CI)	0.255 (0.062~1.049)	1	0.775 (0.476~1.261)	0.763 (0.277~2.097)
P value	0.058	Reference	0.304	0.599
Recurrence				
OR (95% CI)	1.727 (0.525~5.675)	1	1.239 (0.762~2.012)	0.835 (0.256~2.727)
P value	0.368	Reference	0.387	0.765
Thyroditis				
OR (95% CI)	1.197 (0.790~1.813)	1	0.863 (0.741~1.005)	0.642 (0.449~0.919)
P value	0.396	Reference	0.058	0.016

5. Discussion

Increased BMI has been associated with a higher cancer incidence for several malignancies, including thyroid cancer [9]. In addition, obesity has been reported to be associated with poor pathological prognostic correlates and the development of recurrence and metastases for several cancer types, including breast, prostate, and colon cancers [7]. Obesity can cause impairment in the metabolic process within the body and also cause a broad range of endocrine abnormalities involving the pituitary, pancreas, gonad, adrenal glands, and thyroid glands [20].

Recent studies are also reporting that obesity is associated with increased incidence of thyroid cancer [21]. Kim et al. [21]. Performed a case–control study in which the authors hypothesized that overweight and obesity would be associated with higher risk of PTC in an adolescent Korean population (BMI≥25 at age 18 years). They included 1549 cases and selected 15 490 controls matched 1: 10 for age (±5 years) and sex who were all more than 20 years age. After adjustment for potential confounders, a BMI at least 25 at the age of 18 was associated with a higher risk of developing PTC compared with those with BMI less than 23 [hazard ratios 4.31 (3.57–5.22)], both in men [hazard ratios 6.65 (4.76–9.27)] and women [hazard ratios 3.49 (2.74–4.43)] [22]. In an analysis conducted in the US, increase in the incidence of thyroid cancer according to increase in BMI was observed in both males and females, while a study conducted in the French Polynesian region with relatively high prevalence of thyroid cancer also confirmed such correlation. Especially in the study from French Polynesian region, BMI ≥25 in those aged 18 years or older, the period when they are entering adulthood, showed high probability of thyroid cancer (OR 6.2, $P < 0.01$) [23].

Other reports have also indicated that higher BMI manifests more aggressive forms of cancer, including breast cancer. [21] According to Harari et al. [21], in terms of thyroid cancer, obese patients showed higher stage and more aggressive form of PTC. In their study, the percentage of those in stage 3 or 4 among normal, overweight, obese, and morbidly obese groups was 13.2%, 22.7%, 24.3%, and 35.7%, respectively, while the relative risk in overweight, obese, and morbidly obese groups was 1.94, 2.11, and 3.67, respectively (P=0.04) [24].

According to a report by Feng et al. [24] of 417 papillary thyroid cancer patients, 31.6% were overweight and 6% were obese. After adjusting for clinicopathological features, overweight was associated with vascular invasion [hazard ratios 3.9 (1.06–14.31)], while obesity was associated with ETE [hazard ratios 6.14 (1.81–0.89)] and vascular invasion [hazard ratios 9.19 (1.73–51.71)], when compared with those who were normal weight. No statistically significant differences were reported in PTC recurrence among the BMI groups [25]. In an analysis by Kim et al. [25] BMI at least 25 at age 18 years was positively associated with ETE [hazard ratios 1.5 (1.06–2.12)] and tumor stage at least 2 [hazard ratios 1.94 (1.03–3.65)], but not with lymph node stage at least 1 or BRAF V600E mutation positivity compared with those with BMI less than 23. [22]. Similar results were reported by Grani et al. [22], who investigated the association between overweight or obesity and aggressive features of DTC among 432 patients in Italy [n=154 (35.6%) overweight and n=86 (19.9%) obese]. Obese patients were significantly more frequently male and old age. Most PTCs were at low-risk (67.8%) and the majority had never been treated with 131I (69.2%). In their analysis, BMI as a categorical variable was not associated with aggressive DTC features, while patients with ETE had a significantly higher BMI when evaluated as a continuous variable [26].

In this study, the results demonstrated that BMI was closely associated with aggressive oncologic features of PTC, such as tumor multiplicity and extrathyroid invasion. Tumor multiplicity is not a strong prognosticator of PTC, but based on this, it was determined that obesity can affect the aggressive tendency of PTC (invasive metastasis) and cancer susceptibility of patients, such as multifocality. Moreover, the univariate and multivariate analyses results in the present study confirmed that the obese group had higher rate of multifocality and extrathyroid invasion than the normal group, while the rate of thyroiditis was actually lower. In the comparison between the overweight and normal groups, the univariate analysis results also confirmed higher rate of multifocality, extrathyroid invasion, and advanced TNM staging, while the multivariate analysis results confirmed higher rate of only multifocality and extrathyroid invasion. In the comparison between the underweight and normal groups, there were no factors that showed significant differences.

Thyroiditis being lower in the obese group has not been mentioned in existing reports, and thus, additional studies on this topic are needed. The present study had the limitations of being a retrospective study with relatively short follow-up period. Moreover, the study did not fully account for confounding factors, such as smoking, drinking, activity level, and diabetes. However, a major significance of the study can be found in the fact that it analyzed the correlation between obesity and aggressiveness of PTC, including recurrence, using a high number of cases and confirmed that BMI is closely associated with aggressive oncologic features, such as multifocality and extrathyroid invasion.

6. Conclusions

Retrospective analysis of the association between BMI and cancer aggressiveness in patients with PTC showed that the obese group showed higher rate of multifocality and extrathyroid invasion than the normal group. Although various cause may play a role in the onset of PTC, maintaining BMI at an appropriate level may be a method for preventing the onset of PTC with more aggressive tendencies, such as multifocality and extrathyroid invasion. However, there were few cases except for PTC, which made it difficult to find statistically significant results. To confirm this result, further studies with long-term follow-up and more patients are required.

References

1. Davies L, Morris L, Hankey B. Increases in thyroid cancer incidence and mortality. JAMA 2017; 318: 389-390.
2. Oh CM, Won YJ, Jung KW, Kong HJ, Cho H, Lee JK, et al. Cancer Statistics in Korea: Incidence, Mortality, Survival, and Prevalence in 2013. Cancer research and treatment : official journal of Korean Cancer Association. 2016; 48(2): 436-50. Epub 2016/03/19. doi: 10.4143/crt.2016.089. PubMed PMID: 26987395; PubMed Central PMCID: PMC4843732.
3. Chen AY, Jemal A, Ward EM. Increasing incidence of differentiated thyroid cancer in the United States, 1988-2005. Cancer. 2009;115(16):3801-7. Epub 2009/07/15. doi: 10.1002/cncr.24416. PubMed PMID: 19598221.
4. Imaizumi M, Usa T, Tominaga T, Neriishi K, Akahoshi M, Nakashima E, Ashizawa K, Hida A, Soda M, Fujiwara S, et al. Radiation dose–response relationships for thyroid nodules and autoimmune thyroid diseases in Hiroshima and Nagasaki atomic bomb survivors 55–58 years after radiation exposure. Journal of the American Medical Association 2006 295 1011-1022. (doi:10.1001/jama.295.9.1011).
5. Preston-Martin S, Franceschi S, Ron E & Negri E. Thyroid cancer pooled analysis from 14 case–control studies: what have we learned? Cancer Causes & Control 2003 14 787-789. (doi:10.1023/A:1026312203045)
6. Iribarren C, Haselkorn T, Tekawa IS & Friedman GD. Cohort study of thyroid cancer in a San Francisco Bay area population. International Journal of Cancer 2001 93 745-750. (doi:10.1002/ijc.1377).
7. Wolin KY, Carson K, Colditz GA. Obesity and cancer. The oncologist. 2010;15(6):556-65. Epub 2010/05/29. doi: 10.1634/theoncologist.2009-0285. PubMed PMID: 20507889; PubMed Central PMCID: PMC3227989.
8. Budny A, Grochowski C, Kozlowski P, et al. Obesity as a tumour development triggering factor. Ann Agric Environ Med 2019; 26: 13-23.
9. Renehan AG, Tyson M, Egger M, Heller RF & Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008 371 569–578. (doi:10.1016/S0140-6736(08)60269-X).
10. Dal Maso L, La Vecchia C, Franceschi S, Preston-Martin S, Ron E, Levi F, Mack W, Mark SD, McTiernan A, Kolonel L et al. A pooled analysis of thyroid cancer studies. V. Anthropometric factors. Cancer Causes & Control 2000 11 137–144. (doi:10.1023/A:1008938520101)
11. Rinaldi S, Lise M, Clavel-Chapelon F, Boutron-Ruault M-C, Guillas G, Overvad K, Tjønneland A, Halkjær J, Lukanova A, Kaaks R et al. Body size and risk of differentiated thyroid carcinomas: findings from the EPIC study. International Journal of Cancer 2012 131 E1004–E1014. (doi:10.1002/ijc.27601).
12. Engeland A, Tretli S, Akslen LA & Bjorge T. Body size and thyroid cancer in two million Norwegian men and women. British Journal of Cancer 2006 95 366–370. (doi:10.1038/sj.bjc. 6603249)
13. Dal Maso L, La Vecchia C, Franceschi S, Preston-Martin S, Ron E, Levi F, et al. A pooled analysis of thyroid cancer studies. V. Anthropometric factors. Cancer causes & control : CCC. 2000; (2): 137-44. Epub 2000/03/10. PubMed PMID: 10710197.
14. Han JM, Kim TY, Jeon MJ, Yim JH, Kim WG, Song DE, et al. Obesity is a risk factor for thyroid cancer in a large, ultrasonographically screened population. European journal of endocrinology. 2013;168(6):879-86. Epub 2013/03/21. doi: 10.1530/eje-13-0065. PubMed PMID: 23513231.
15. Kim HJ, Kim NK, Choi JH, Sohn SY, Kim SW, Jin SM, et al. Associations between body mass index and clinico-pathological characteristics of papillary thyroid cancer. Clinical endocrinology. 2013; 78(1): 134-40. Epub 2012/07/21. doi: 10.1111/j.1365-2265.2012.04506.x. PubMed PMID: 22812676.
16. Paes JE, Hua K, Nagy R, Kloos RT, Jarjoura D, Ringel MD. The relationship between body mass index and thyroid cancer pathology features and outcomes: a clinicopathological cohort study. The Journal of clinical endocrinology and metabolism. 2010; 95(9): 4244-50. Epub 2010/06/04. doi: 10.1210/jc.2010-0440. PubMed PMID: 20519347; PubMed Central PMCID: PMC2936072.
17. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid : official journal of the American Thyroid Association. 2009; 19(11): 1167-214. Epub 2009/10/29. doi: 10.1089/thy.2009.0110. PubMed PMID: 19860577.
18. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organization technical report series. 2000; 894:i-xii, 1-253. Epub 2001/03/10. PubMed PMID: 11234459.
19. American Thyroid Association. Thyroid Cancer Staging Calculator (AJCC 8th Edition). Availabrle from: https://www.thyroid.org/professionals/calculators/thyroid-cancer-staging-calculator/.
20. Misra A, Khurana L. Obesity and the metabolic syndrome in developing countries. The Journal of clinical endocrinology and metabolism. 2008; 93(11 Suppl 1): S9-30. Epub 2008/12/04. doi: 10.1210/jc.2008-1595. PubMed PMID: 18987276.
21. De Pergola G, Silvestris F. Obesity as a major risk factor for cancer. Journal of obesity. 2013;2013:291546. Epub 2013/09/28. doi: 10.1155/2013/291546. PubMed PMID: 24073332; PubMed Central PMCID: PMC3773450.
22. Kim KN, Hwang Y, Kim KH, et al. Adolescent overweight and obesity and the risk of papillary thyroid cancer in adulthood: a large-scale case–control study. Sci Rep 2020; 10: 5000.
23. Kitahara CM, Platz EA, Freeman LE, Hsing AW, Linet MS, Park Y, et al. Obesity and thyroid cancer risk among U.S. men and women: a pooled analysis of five prospective studies. Cancer epidemiology, biomarkers & prevention : a publication of the American As-

sociation for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2011;20(3):464-72. Epub 2011/01/27. doi: 10.1158/1055-9965.epi-10-1220. PubMed PMID: 21266520; PubMed Central PMCID: PMC3079276.

24. Harari A, Endo B, Nishimoto S, Ituarte PH, Yeh MW. Risk of advanced papillary thyroid cancer in obese patients. Archives of surgery (Chicago,Ill:1960). 2012; 147(9): 805-11. Epub 2012/08/24. doi: 10.1001/archsurg.2012.713. PubMed PMID: 22914989.

25. Feng JW, Yang XH, Wu BQ, et al. Influence of body mass index on the clinicopathologic features of papillary thyroid carcinoma. Ann Otol Rhinol Laryngol 2019; 128: 625-632.

26. Grani G, Lamartina L, Montesano T, et al. Lack of association between obesity and aggressiveness of differentiated thyroid cancer. J Endocrinol Invest 2019; 42: 85-90.