IS OBESITY DIRECTLY INVOLVED IN CAUSING THYROID CANCER?

Kitahara CM, Platz EA, Freeman LE, Hsing AW, Linet MS, Park Y, Schairer C, Schatzkin A, Shikany J, Berrington de González A. **Obesity and thyroid cancer risk among U.S. men and women: a pooled analysis of five prospective studies.** Cancer Epidemiol Biomarkers Prev 2011;20:464-72. Epub January 25, 2011.

SUMMARY

BACKGROUND

Both thyroid cancer and obesity are increasing in the general population, but are the two connected?

METHODS

The statistical connection between body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) and thyroid cancer was analyzed using the data from five prospective U.S. National Cancer Institute studies that were performed over various periods between 1979 and 2009 (mean follow-up, 10 years). Baseline questionnaires from approximately 414,000 women and 435,000 men provided data on demographics, lifestyle, and medical history. Participants' height and weight were measured in one study, whereas this information was self-reported in four. Cancer information was obtained from self-reports (three studies), cancer registry linkage (four), death certificates (three) and/or the National Death Index (four). The type of thyroid cancer was established from clinical and pathology records, and cancer registry linkage. Of 1156 participants diagnosed with a malignant first primary thyroid neoplasm, histologic data were available on 1024 (80% were papillary, 15% follicular, 3% medullary, and 2% anaplastic). The mean age at study entry was 58 years, and 20% of participants were obese. Data were adjusted for education, race, marital status, cigarette smoking, alcohol intake, physical activity, and sex. There was no significant heterogeneity between the studies. Participant data were collected up to the first diagnosis of any cancer (other than nonmelanoma skin cancer), death, or the last questionnaire completed.

RESULTS

When BMI was modeled as a continuous variable, and data from men and women were combined, the relationship between BMI and thyroid cancer was log-linear. The hazard ratio (HR) was 1.17 and the 95% confidence interval (CI) was 1.10 to 1.24. When participants' BMIs were segregated into normal (18.5 to 24.9), overweight (25.0 to 29.9) or obese (>30), the HR was 1.20 for overweight (95% CI, 1.04 to 1.38) and 1.53 for obesity (95% CI, 1.31 to 1.79) (approximately 3000 individuals were excluded from analysis because of a BMI <15 or >50). There was no significant difference between histologic types, and no modification by other factors.

When the data were examined for each sex separately, thyroid cancer was associated with a high BMI in two of four studies for men (not significant) and four of five studies for women (HR, 1.16). However, if the first 2 years of follow-up were excluded to eliminate bias from participants who might have had preclinical disease at baseline—and thus whose weight might have changed as a result of the disease—the hazard ratio became significant for men as well as women.

CONCLUSIONS

This pooled analysis supports previous findings that obesity is a significant independent risk factor for thyroid cancer in both sexes.

COMMENTARY

There could be a specific detection bias if obese patients had more frequent or more thorough examination of their thyroids, along with assessment of their thyroid function. Contrariwise, self-reported weight is often underestimated while height is overestimated, factors that might have biased the study against what was actually found. Various mechanisms have been suggested as possible connections between obesity and carcinogenesis. From an endocrine viewpoint, obesity is associated with increased production of estrogen, insulin, insulin-like growth factor 1, adipokines, and inflammatory mediators. Many xenobiotics accumulate in adipose tissue and then are released over the long term; some can act directly as carcinogens by forming bulky DNA adducts that resist normal repair pathways, others activate pro-carcinogens via CYP- and aryl-hydrocarbon receptor-mediated pathways, and some alter the production of free radicals or have epigenetic effects.

If we were to begin a giant prospective epidemiologic study over 20 or 30 years, would it actually identify some of the factors related to obesity-related thyroid cancer? Maybe not, but if the incidence of thyroid cancer in the general public continues increasing at the rate observed over the past decade, even skinny people may wish there were such a study. Nonetheless, telling ourselves that obesity increases the risk of thyroid cancer developing by 50% probably will not motivate us to lose weight or to increase our awareness of the spectrum of xenobiotics that can be present in the American diet.

— Stephen W. Spaulding, MD