Exposure to dental x-rays, particularly multiple exposures, may be associated with an increased risk for thyroid cancer

Memon A, Godward S, Williams D, Siddique I, Al-Saleh K. Dental x-rays and the risk of thyroid cancer: a case–control study. Acta Oncol 2010;49:447-53.

SUMMARY

BACKGROUND

Exposure of the thyroid gland to high-dose ionizing radiation is the only widely accepted environmental cause of thyroid cancer, which may occur from a number of sources, such as diagnostic radioiodine scans and computed tomography, radiation fallout, as occurred in Chernobyl, or stratospheric environmental contamination, as occurred during the 1950s from the testing of nuclear weapons in Nevada. One of the not-so-obvious sources of exposure, however, is dental radiography—a common source of low-dose diagnostic radiation that is not commonly thought to be a cause of thyroid cancer. This source has not been fully studied and thus might be associated with thyroid cancer more often than is generally appreciated. Still, an increased risk for thyroid cancer has been reported in dentists and dental assistants and x-ray workers, and dental radiation has been associated with an increased risk for meningiomas, brain tumors, and salivary tumors. The aim of this study was to examine whether exposure to dental x-rays is associated with a risk for thyroid cancer. This is a population-based case–control interview study of 313 patients with thyroid cancer and a similar number of individually matched control subjects in Kuwait. The study was designed to assess the hypothesis that dental radiography is associated with thyroid cancer.

SUBJECTS AND METHODS

Kuwait has a population of approximately 2.8 million; it has a government-funded national health service for all residents, including dental services. There are a number of specialty hospitals, including the Kuwait Cancer Control Center (KCCC), which provides cancer treatment and follow-up services for the entire population. Every week, a special follow-up clinic is held at the center for patients with thyroid cancer. A population-based cancer registry (the Kuwait Cancer Registry) has been available at the center since 1979; it regularly contributes data to the Cancer Incidence in Five Continents database compiled by the International Agency for Research on Cancer.

For this study, residents of Kuwait who were living and ≤70 years of age and had primary thyroid cancer were identified from the records of the Kuwait Cancer Registry using the International Classification of Diseases for Oncology topography codes. In addition to selecting patients with thyroid cancer, control subjects were selected from local primary health care clinics, in which a wide range of services is offered; all of these subjects had equal opportunity to visit their local clinic. A control subject was matched with each patient with thyroid cancer, based on year of birth (±3 years), sex, nationality, and district of residence in Kuwait. Individuals were eligible to serve as controls if they were visiting the primary care clinic for minor symptoms or were visiting the clinic for other purposes, such as vaccinations.

Study Subjects and Controls

The study subjects comprised 313 patients and 313 matched controls. A bilingual interviewer proficient in Arabic and English who was unaware of the diagnosis of thyroid cancer obtained information from all the participants. The data were recorded in a structured questionnaire that integrated a broad group of information, including sociodemographic characteristics, gynecologic and reproductive history, medical history, and exposure to diagnostic and other x-rays of the head, neck, and chest, radiotherapy, and exposure to and the number of dental x-rays. Also elicited were a family history of thyroid disease and cancer and other clinical and histopathologic information from KCCC.

Validity of Self-Reported Dental X-Rays

The consistency of self-reported dental x-ray exposure was assessed in a validation study using telephone interviews that included a random sample of 49 cases and 42 controls. The participants in the validation study were also questioned about their age (<20 years or ≥20 years) and first exposure to dental x-rays.

For each control, a "pseudo-diagnosis" date—the date on which the subject was the same age as his or her matching subject was at the time of diagnosis—was determined. The analysis of data on exposure to radiation was confined to events before the diagnosis of thyroid cancer (cases) or matching study case date (controls).

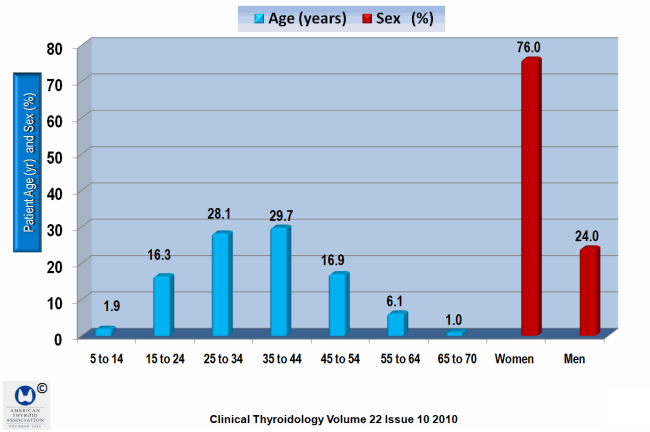

Figure 1. This figure shows the distribution of 313 patients with thyroid cancer by age at the time of diagnosis and by sex. The peak age at which thyroid cancer occurred from dental x-rays was 35 through 44 years, with a low range of 5 to 14 years to a high range of 64 to 70 years. The data for this figure and Figures 2 and 3 are derived from Table 1 of Memon et al.

A conditional logistic-regression analysis was used to assess the association between exposure to dental x-rays and the risk for thyroid cancer (odds ratio with 95% confidence intervals adjusted for confounding variables as necessary). Also examined was the dose-response pattern according to the number of exposures to dental x-rays. Subgroup analyses were performed to determine the risk of thyroid cancer according to age at the time of diagnosis, sex, nationality, level of education, parity, and histology.

RESULTS

The Demographic Features of the Patient Cohort (Figures 1 and 2)

Of the 313 patients with thyroid cancer, 238 (76%) were women, and 75 (24%) were men *(Figure 1)*. A total of 172 (55%) were Kuwaiti nationals and the remainder were non-Kuwaitis, among which the majority (70%) were from Arab countries, 26% were from Southeast Asia, and 4% were other nationalities *(Figure 2)*. Most of the thyroid cancers (74%) were diagnosed at a young age (range, 15 to 24 years). The average age (±SD) at the time of diagnosis in women was 34.7±11.0 years, (range, 10 to 65), and in men was 39.0±13.4 years (range, 6 to 69). The median age at diagnosis was 35 and 38 years in women and men, respectively; however, there was no difference in mean age at diagnosis between Kuwaiti and non-Kuwaiti patients.

The Incidence of Thyroid Cancer (Figures 3 to 6)

Papillary carcinoma was the most common histopathologic tumor, comprising 83% of all cases of thyroid cancer *(Figure 3)*. There was approximately a twofold increased risk for thyroid cancer among individuals who were exposed to dental x-rays (odds ratio, 2.1, 95% confidence interval, 1.4 to 3.1, P = 0.001) *(Figure 4)*. There also was a statistically significant dose-response pattern, which revealed an increasing trend in risk with the increasing number of dental x-rays (P for trend <0.0001) *(Figure 5)*. The association between dental x-rays and the risk for thyroid cancer was observed across all investigated subgroups, including age at the time of diagnosis, sex, nationality, level of education, parity, and histology *(Figure 6)*. The histologic subtypes were essentially papillary thyroid cancers, including cases classified as mixed papillary/follicular variant thyroid cancer.

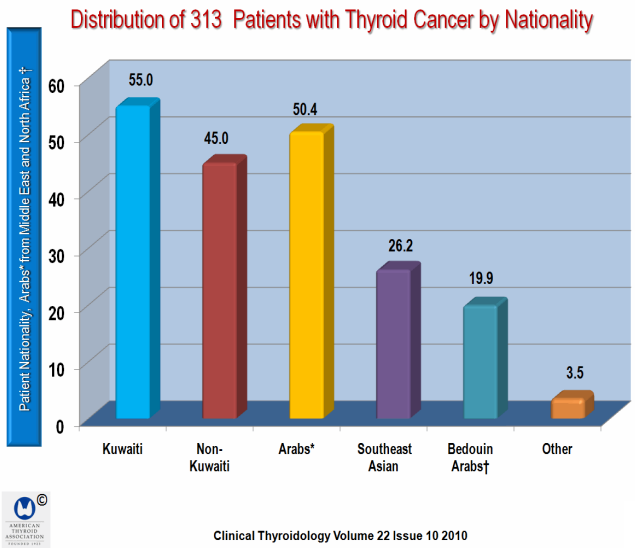

Figure 2. This figure shows the distribution of 313 patients by nationality, the majority of whom were from Kuwaiti. Arabs* = Arabs from Middle East and North Africa; Bedouin Arabs† = "stateless" Arabs resident in Kuwait.

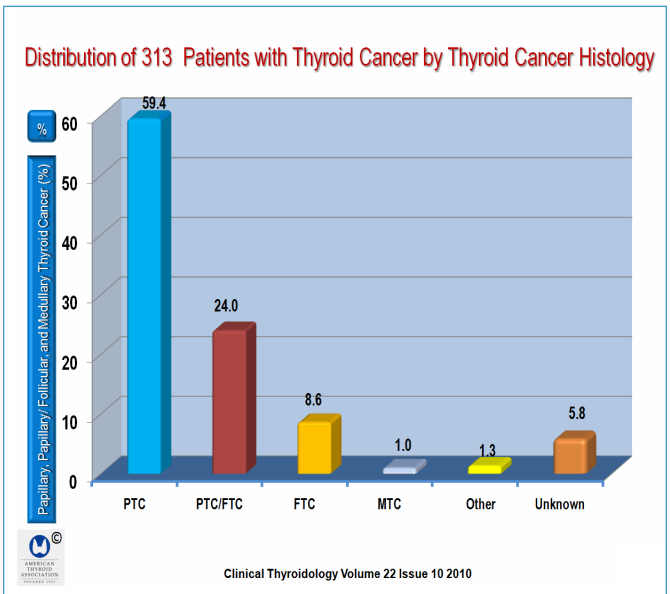

Figure 3. This figure shows the histology of patients in whom cancer was caused by dental x-rays. FTC = follicular thyroid cancer; MTC = medullary thyroid cancer; PTC = papillary thyroid cancer; PTC/FTC = papillary/follicular variant thyroid cancer. PTC comprises the majority (59%) of thyroid cancers.

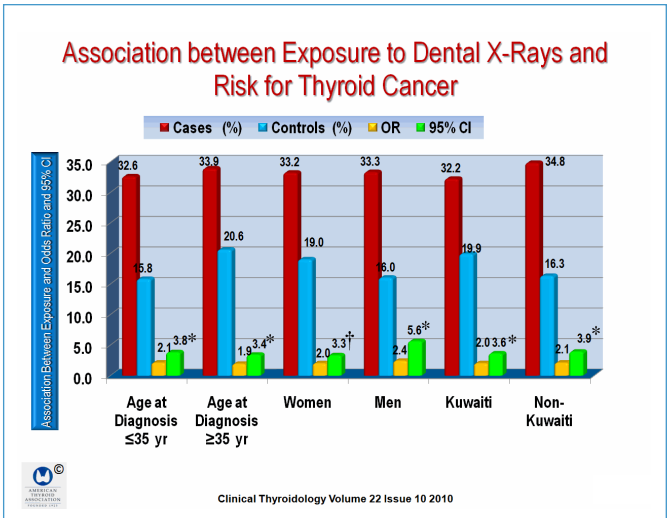

Figure 4. This figure shows the association between exposure to dental x-rays and the risk for thyroid cancer. The figure shows the logistic-regression analysis with results adjusted for upper-body (head, neck, and chest) x-rays.(*P for trend = 0.001, comparing patients with thyroid cancer and controls) Odds ratios [OR} and 95% confidence intervals [CI] for patients with and without thyroid cancer are shown. This figure shows the difference between controls with no dental x-rays and patients with thyroid cancer who received dental x-rays. The data for this figure and Figure 5 are derived from Table 2 of Memon et al.

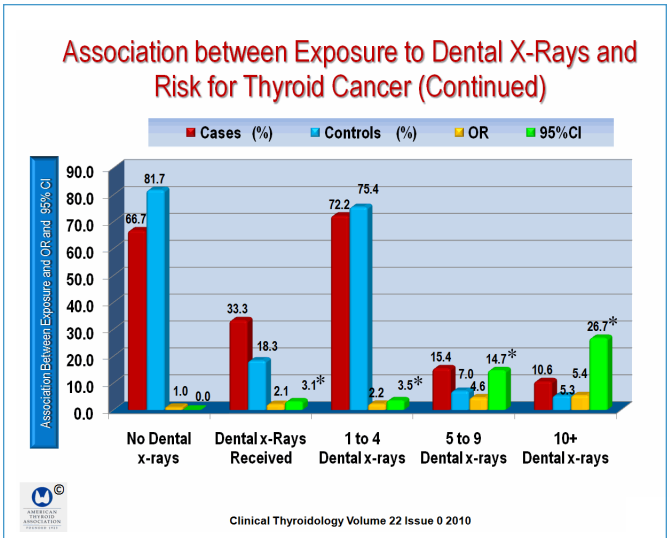

Figure 5. This is a continuation of Figure 4, which shows the risk for thyroid cancer with exposure to dental x-rays as compared with no x-rays. There is a significant difference of (odds ratio [OR], 2.1) for patients with thyroid cancer who were exposed to dental x-rays as compared with an OR of 1 in those who had no dental x-rays. The figure shows that the number of dental x-rays significantly altered the rate of thyroid cancers, ranging from 1 to 4 dental x-rays (OR, 2.2) to ≥10 dental x-rays (OR, 5.4).

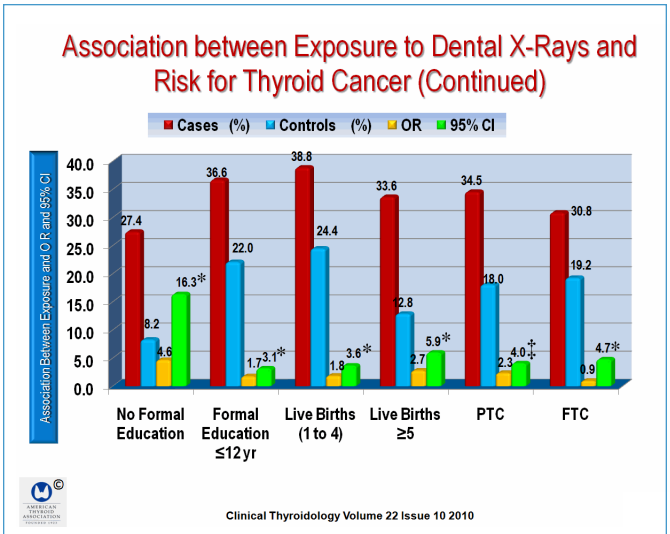

Figure 6. This is a continuation of Figure 5. The figure shows the association between exposure to dental x-rays and the risk for thyroid cancer by age at diagnosis, sex, nationality, level of education, and parity. Patients with no formal education had a lower exposure to dental x-rays as compared with patients with 12 years or more of formal education. Subjects with 1 to 4 live births were at significantly higher risk from those with ≥5 births (*P<0.05). Sex appears to influence the use of dental x-rays (P = 0.002 for papillary thyroid carcinoma [PTC] as compared with follicular thyroid carcinoma [FTC]; P<0.01) for women as compared with men with regard to the age at the time of diagnosis and other forms of thyroid cancer as compared with PTC (P not significant for FTC). †P = 0.002.

CONCLUSION

The authors of this study concluded that self-reported dental x-rays provide support for the hypothesis that exposure to dental x-rays, particularly multiple exposures, may be associated with an increased risk for thyroid cancer, the majority of which are papillary thyroid cancer.

COMMENTARY

The thyroid gland is very sensitive to radiation carcinogenesis, and exposure to high-dose ionizing radiation is especially harmful, particularly during childhood and adolescence. There is a long history of the damaging effects of ionizing radiation in children who were exposed to radiation in the form of x-ray treatment for benign conditions such as enlarged tonsils, ringworm of the scalp (tinea capitis) hemangioma, skin disorders, and spondylosis of the cervical spine (1-3).

The study by Memon et al. shows that the risk for thyroid cancer is associated with exposure to dental x-rays. There was an approximately twofold increased risk for thyroid cancer in individuals exposed to dental x-rays (OR, 2.1; 95% CI, 1.4 to 3.1; P = 0.001). The study also demonstrates a dose-response pattern of an increasing trend in risk for thyroid cancer with an increasing number of dental x-rays (P for trend <0.0001). The association of dental x-rays with thyroid cancer was observed across all the investigated subgroups, including age at the time of diagnosis, sex, nationality, level of education, and parity. The authors of this study point out that the literature on high-dose radiation and thyroid cancer shows a substantial age-related sensitivity, with the patients who are youngest at the time of exposure being the most sensitive; in this study, patients with thyroid cancer were more likely to be exposed to dental x-rays at younger ages as compared with normal controls. Among the patients with thyroid cancer who were <25 years of age at the time of diagnosis, approximately 27% were exposed to dental radiation, as compared with only 18% of the controls; among patients <20 years of age, about 22% were exposed to dental radiation, as compared with none of the controls. Also, the median age for women with thyroid cancer was 35 years; the younger patients at the time of diagnosis had a slightly higher risk for thyroid cancer as compared with older patients. Lastly, a greater proportion of patients exposed to dental radiation (57%) reported that their first dental x-ray exposure occurred before the age of 20 years. Moreover, a similar risk for dental x-rays had a similar association with thyroid cancer across multiple categories such as patient sex, nationality, ethnic background, level of education, type of dental x-ray exposure, and age at diagnosis, suggesting that recall bias or case–

control bias are unlikely to account wholly for the significant dose response .

The authors point to two similar studies (4;5), which concluded that interview data alone may be used for case–control comparisons of dental x-ray exposure and would, because of unbiased misclassification, tend to underestimate the relative risks.

Dental radiography has been implicated in the development of other tumors. One group of studies (4-6) found that age <20 years to full-mouth dental x-ray series was related to thyroid cancer (OR, 4.0; P<0.01). Similar studies of glioma (7) and brain cancer (8) also showed similar findings concerning dental x-rays. However, the association of diagnostic x-rays with meningioma was not confirmed in one study (9) of dental x-rays but also have been associated with benign and malignant tumors of the parotid gland. Also, an increased risk for thyroid cancer has been reported in dentists and dental assistants (10;11).

In 2003, The American Dental Association recommended that the National Council on Radiation Protection and Measurements update its recommendations on radiation protection in dentistry. The council concluded that dentists should be aware of, and comply with, applicable federal and state regulations and recommended that dentists should weigh the benefits of dental radiography against the consequences of increasing a patient's exposure to radiation and should implement appropriate radiation control procedures. Recent recommendations by the American Dental Association stress the need for shielding the thyroid (12).

There is little question that this is not a settled problem, but based on the conflicting studies, the recent American Dental Association recommendations are appropriate and should be carefully followed, considering the implications of the study by Memon et al. and other studies of this problem.

— Ernest L. Mazzaferri, MD, MACP

References

1. Ron E, Lubin JH, Shore RE et al. Thyroid cancer after exposure to external radiation: A pooled analysis of seven studies. Radiat Res 1995;141:259-77.

2. Ron E. Cancer risks from medical radiation. Health Phys 2003;85:47-59.

3. Damber L, Johansson L, Johansson R et al. Thyroid cancer after X-ray treatment of benign disorders of the cervical spine in adults. Acta Oncol 2002;41:25-8.

4. Preston-Martin S, Bernstein L, Maldonado AA et al. A dental x-ray validation study. Comparison of information from patient interviews and dental charts. Am J Epidemiol 1985;121:430-9.

5. Preston-Martin S, Henderson BE, Bernstein L. Medical and dental x rays as risk factors for recently diagnosed tumors of the head. Natl Cancer Inst Monogr 1985;69:175-9.

6. Preston-Martin S, Paganini-Hill A, Henderson BE et al. Case-control study of intracranial meningiomas in women in Los Angeles County, California. J Natl Cancer Inst 1980;65:67-73.

7. Longstreth WT, Jr., Phillips LE, Drangsholt M et al. Dental X-rays and the risk of intracranial meningioma: a population-based case-control study. Cancer 2004;100:1026-34.

8. Neuberger JS, Brownson RC, Morantz RA et al. Association of brain cancer with dental X-rays and occupation in Missouri. Cancer Detect Prev 1991;15:31-4.

9. Preston-Martin S, Thomas DC, White SC et al. Prior exposure to medical and dental x-rays related to tumors of the parotid gland. J Natl Cancer Inst 1988;80:943-9.

10. Wingren G, Hallquist A, Degerman A et al. Occupation and female papillary cancer of the thyroid. J Occup Environ Med 1995;37:294-7.

11. Wingren G, Hallquist A, Hardell L. Diagnostic X-ray exposure and female papillary thyroid cancer: a pooled analysis of two Swedish studies. Eur J Cancer Prev 1997;6:550-6.

12. The use of dental radiographs: update and recommendations. J Am Dent Assoc 2006;137:1304-12.