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The Risk of Papillary Thyroid Cancer Is Increased Among First- to Third-Degree Relatives

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Oakley GM, Curtin K, Pimentel R, Buchmann L, Hunt J. Establishing a familial basis for papillary thyroid carcinoma using the Utah population database. JAMA Otolaryngol Head Neck Surg. October 3, 2013 [Epub ahead of print].

SUMMARY

Background

The incidence of thyroid cancer—the most common endocrine cancer, mainly composed of papillary thyroid cancer (PTC; ~80%)—has increased worldwide over the past several decades. Known risk factors for thyroid cancer include a history of head and neck radiation, iodine deficiency or excess, and other thyroid disease. Although most cases of PTC are sporadic, a small proportion may be genetically linked. The objective of this study was to assess the familial risks of PTC using a large population database.

Methods

This retrospective case–control study assessed familial patterns of PTC using the Utah Population Database from 1966 through 2011. The database contained 6.5 million patient records linked to the state's cancer records obtained from the Surveillance, Epidemiology, and End Results (SEER) database. Cases of PTC identified by International Classification of Diseases (ICD) codes were matched with controls by sex, year of birth, and place of birth in a ratio of 5:1, and assessed for the incidence of PTC diagnosed among first- through fifth-degree relatives.

Results

There were 4460 patients (78% women; mean [±SD] age at diagnosis, 44±15.9 years) with PTC during the study period. The odds ratios of PTC were increased among relatives of the index cases: 5.35 (95% CI, 4.4 to 6.5) in first-degree relatives, 2.24 (95% CI, 1.8 to 2.8) in second-degree relatives, and 1.76 (95% CI, 1.5 to 2.1) in third-degree relatives. The risks of PTC were not increased among fourth- to fifth-degree relatives or in the spouses of the probands.

Conclusions

In this large U.S.-based population research database, there was a fivefold increased risk of PTÇ among first-degree relatives of index cases; smaller but still significant risks were also observed among second- and third-degree relatives.

ANALYSIS AND COMMENTARY

The genetic susceptibility of a small proportion of nonmedullary thyroid cancer (NMTC) cases, excluding syndromic causes, is well known. Several studies have shown that familial NMTC, which accounts for 3% to 10% of all NMTC cases (1), is associated with increased risks of up to approximately eightfold among first-degree relatives. The major limitation among these previous studies was their inclusion of multiple subtypes of thyroid cancer. In the current study assessing only PTC, similarly increased risks, up to fivefold, were observed among first- to third-degree relatives.

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The strengths of this study include its large size, long duration of follow-up, and confirmation of thyroid cancer diagnoses using a comprehensive population research database and statewide cancer registry records. Although these data suggest a hereditable basis for a minority of PTC cases, these data were assessed using the population of one state, in which the incidence of thyroid cancer is relatively low, although the incidence in Utah was comparable and even slightly higher than national SEER data from 2006 to 2010 (2). In addition, the controls were matched using the general population, rather than individuals with known thyroid nodules, who would have represented a more comparable group with a similar risk of malignancy. Finally, although the findings suggest a familial basis for a proportion of PTC, further research is needed to elucidate whether these risks are truly based on genetic predisposition, perhaps through use of molecular markers and multi-institutional collaborations linking familial data, rather than a clustering of sporadic PTC cases.

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