25-Hydroxyvitamin D levels and Their Relationship to Thyroid Malignancy

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ABSTRACT

Objectives: Vitamin D deficiency is endemic in the USA. Vitamin D deficiency has been observed in many cancer patients and thought to be a possible risk factor. We sought to compare the 25-hydroxyvitamin D level between a cohort of patients undergoing completion and total thyroidectomy for benign and malignant diseases.

Methods: A retrospective IRB approved study with chart review was done at a tertiary referral academic medical center. Data were retrospectively collected on consecutive patients who underwent completion and total thyroidectomy at the University of Arkansas for Medical Sciences between October 2005 and July 2013. Postoperative 25-hydroxyvitamin D [25(OH)D] levels were measured and recorded universally and reported when available. Statistical analysis was performed to determine if 25(OH)D levels varied based on pathology, categorized as either benign or malignant.

Results: A total of 255 total and completion thyroidectomies were performed during the study period. Total thyroidectomy (n=197) was more common than completion (n=58). Of these, 197 had 25(OH)D levels available for analysis: 49 with malignant disease and 148 with benign disease. Median (quartiles) levels of 25(OH)D were 25 (21–37) ng/ml among those with malignant disease versus 27 (19.5–35) ng/ml among those with benign disease; the difference was not statistically significant (P=0.72).

Conclusions: There is no correlation between perioperative 25-hydroxyvitamin D status and pathological findings in patients undergoing completion and total thyroidectomy.

INTRODUCTION

Thyroid cancer is the most common endocrine-related malignancy, accounting for roughly 1% of malignant disease. To date few risk factors have been identified for thyroid cancer and include iodine deficiency and exposure to ionizing radiation. Other established risk factors include genetic mutations and genetically inherited familial syndromes. However, most thyroid malignancies are sporadic with no readily identifiable cause or associated risk factors.

Recent data from the National Health and Nutrition Examination Surveys (NHANES) suggest that about one-third of the US population is at risk for vitamin D inadequacy or deficiency. Deficiencies in Vitamin D have been linked to increased risk of colon, breast, and prostate cancer based in both ecological and population-based cohort studies. Additionally, animal studies have demonstrated increased risk of cancer in models that lack the vitamin D receptor gene which mediates the effect of vitamin D on multiple genes that exert antiproliferative and antimetastatic effects on cells.

With the relatively high prevalence of low Vitamin D—as measured by 25-hydroxyvitamin D [25(OH)D]—in the US population and its suspected contribution to the development of multiple malignancies, we sought to investigate 25(OH)D and its potential relationship to thyroid cancer. This study aimed to examine a cohort of patients undergoing either completion or total thyroidectomy and to compare the 25(OH)D levels between those whose surgical pathology was either benign or malignant.

METHODS AND MATERIALS

A retrospective chart review was performed after approval from the IRB at the University of Arkansas for Medical Sciences. Data were retrospectively collected on consecutive patients who underwent completion and total thyroidectomy at the University of Arkansas for Medical Sciences between October 2005 and August 2013. Postoperative 25(OH)D levels were collected routinely and reported when available. Values reported are in ng/ml.

Pathology reports were also reviewed and either dichotomized as benign or malignant. Additionally, demographic data, which included age, sex, and race, were collected.

Data were summarized by pathology group (benign vs. malignant) using proportions for categorical data, and using medians and quartiles for continuous data. Pathology groups were compared for differences in proportions via Fisher’s exact test, and for differences in means via Kruskal-Wallis test. All comparisons employed an alpha=0.05 significance level, and all analyses utilized SAS v9.3 software (The SAS Institute, Cary, NC).

RESULTS

During the study period, 255 total and completion thyroidectomies were performed. Total (n=197) was more common than completion (n=58) surgery. Benign pathology (n=190) was more common than malignant pathology (n=65). The most common benign pathology was multinodular goiter (69%), followed by Hashimoto’s thyroiditis (14%) and Grave’s disease (14%) (table 1). The most frequent malignant diagnosis was papillary carcinoma, which accounted for 77% of malignant diagnoses (table 1).

The median age of those undergoing thyroidectomy was 50 years for those with benign disease compared to 53 years for those with malignant disease (p=0.12). Females more commonly underwent completion and total thyroidectomy than males for both malignant and benign pathology. In terms of race, whites constituted 83% and blacks constituted 15% of patients undergoing thyroidectomy independent of pathology.

25-hydroxyvitamin D level was analyzed as both a categorical and continuous variable. The overall vitamin D level in the cohort had a median (quartiles) of 26 (20–36) ng/ml. When comparing vitamin D levels as a continuous variable between benign and malignant disease, the medians (quartiles) were 27 (21–37) ng/ml in the malignant group, and were not statistically different (Kruskal-Wallis P=0.72).

Subjects were also categorized as having vitamin D insufficiency if their serum levels were less than 30 ng/ml, following Endocrine Society Guidelines. Using this definition, rates of vitamin D insufficiency were found to be 59% in the malignant group and 57% in the benign group, and were not significantly different (Fisher’s exact P=0.87) (table 2).

DISCUSSION

Vitamin D deficiency has been linked to multiple malignancies including breast, prostate, and colon cancers. However, few studies have examined the relationship between thyroid malignancy and vitamin D status, and the outcomes of these studies have demonstrated somewhat conflicting results.

In a study by Penna-Martinez et al, 172 patients with differentiated thyroid carcinoma (DTC) were compared to 321 healthy controls with respect to expression of vitamin D receptor polymorphisms and serum vitamin D levels as measured by 25(OH)D and 1,25(OH)2D. In this study, patients with DTC had lower circulating levels of 25(OH)D while there was no significant difference in levels of 1,25(OH)2D. This study also demonstrated association of specific alleles and haplotypes of VDR polymorphisms with DTC. A more recent study by the same group, compared 303 healthy controls to 253 patients with DTC and found a higher risk for DTC conferred by haplotypes within the CYP24A1 gene as well as low levels of 1,25(OH)2D in DTC patients.

However, at least one study has demonstrated an increased risk of thyroid malignancy in patients with deficient 25(OH)D. This study found a relative risk of thyroid malignancy of 2.0 in those with vitamin D deficiency, which was defined as a 25(OH)D level below 37.5 nmol/L. Our study demonstrated no relationship between 25(OH)D status and thyroid malignancy. This seems to support the majority of studies in the literature, although the dataset is limited and somewhat inconsistent.

REFERENCES


CONCLUSIONS

Despite the lack of association between 25(OH)D levels and thyroid malignancy in this study, there does still appear to be a potential role for vitamin D metabolism in the development of DTC. Associations with specific genetic polymorphisms involved in vitamin D metabolism, which may impact the circulating level of 1,25(OH)2D and thereby inhibits tumor growth, may be linked to DTC. Therefore, understanding the role of vitamin D in thyroid cancer will involve further investigation into the genetic and molecular aspects of the vitamin D pathway that extend beyond routine laboratory evaluation of 25(OH)D.