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Vitamin D insufficiency is common in patients with nonmetastatic prostate cancer

Christopher S. Choo[a], Alexandre Mamedov[a], Matthew Chung[a], Richard Choo[b], Alex Kiss[c], Cyril Danjoux[a,*]

[a]*Department of Radiation Oncology, Odette Cancer Centre, University of Toronto, Toronto, Ontario, Canada*
[b]*Department of Radiation Oncology, Mayo Clinic, Rochester, MN, USA*
[c]*Department of Health Policy, Sunnybrook Health Sciences Center, Management, and Evaluation, University of Toronto, Ontario, Canada*

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Abstract

Because an inverse relationship between serum 25-hydroxyvitamin D (25[OH]D) levels and the risk of prostate cancer has been suggested, it was hypothesized that vitamin D insufficiency would be common in patients with prostate cancer. To test the hypothesis, an exploratory study was conducted to examine serum 25(OH)D levels in a cohort of patients with nonmetastatic prostate cancer. The study aim was to assess the prevalence of vitamin D insufficiency in these patients. *Vitamin D insufficiency* was defined as serum 25(OH)D less than 75 nmol/L. Serum 25(OH)D levels measured prospectively at baseline and, then, yearly during a 5-year follow-up were analyzed. Various parameters were examined to assess their possible association with vitamin D insufficiency at baseline, using both a univariate analysis and a logistic regression model. Analyses including descriptive statistics for all variables were carried out with SAS version 9.1 (SAS Institute, Cary, NC). A total of 106 patients were available for analysis. The median age was 66.3 years. At baseline, mean and median vitamin D level was 72.4 and 70.0 nmol/L, respectively. Sixty-four patients (60.4%) met the definition of vitamin D insufficiency with serum 25(OH)D less than 75 nmol/L. Forty (37.7%), 20 (18.9%), and 2 patients (1.9%) had serum 25(OH)D less than 62.5, less than 50, and less than 25 nmol/L, respectively. On a logistic regression model, season was the only significant variable associated with vitamin D insufficiency. Of a total 477 serum 25(OH)D measurements from the baseline and yearly follow-ups, 187 (39.2%) met the definition of vitamin D insufficiency. In conclusion, vitamin D insufficiency was prevalent among patients with nonmetastatic prostate cancer.

Keywords: Prostate; Neoplasm; Vitamin D; Insufficiency; Prevalence
Abbreviations: BMI, body mass index; PTH, parathyroid hormone; 25(OH)D, 25-hydroxyvitamin D.

1. Introduction

Vitamin D has been reported in recent years to have antitumor activity, in addition to its well-known pivotal role in calcium and phosphorus homeostasis and mineralization of the bone. In both epidemiological and laboratory studies, there have been increasing evidence supporting the anti-tumor activity of vitamin D. On an epidemiological level, many studies have suggested an inverse relationship between serum 25-hydroxyvitamin D (25[OH]D) levels (calcidiol, a metabolite of nutrient vitamin D) and the risk of various cancers including prostate cancer. Garland et al [1] reported, in reviewing 63 observational studies, that vitamin D insufficiency was associated with an increased risk of

* Corresponding author. Tel.: +1 416 480 4998.
E-mail address: cyril.danjoux@sunnybrook.ca (C. Danjoux).

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colon, breast, ovarian, and prostate cancers. On a laboratory level, vitamin D is known to be involved with cell proliferation, differentiation, and apoptosis. For prostate cancer, in vitro studies have shown that 1,25-dihydroxy-vitamin D (calcitriol, the active form of vitamin D) increases cell differentiation and apoptosis, while it decreases proliferation, invasiveness, and metastasis of prostate cancer cells [2].

Considerable attention has been recently given to a potential association between vitamin D insufficiency and the risk of several types of malignancy including prostate cancer. Although the anticancer activity of vitamin D is not fully understood, it is thought that these effects are mediated through vitamin D receptors expressed in cancer cells [2]. Given a suggestion that vitamin D insufficiency is linked to a higher risk of prostate cancer, we hypothesized that vitamin D insufficiency would be common in patients with nonmetastasized prostate cancer. To test the hypothesis, we conducted an exploratory study, which examined serum 25 (OH)D levels of a cohort of patients with nonmetastatic prostate cancer. The aims of this study are to assess the prevalence of vitamin D insufficiency in patients with nonmetastatic prostate cancer and to explore various factors that may be associated with vitamin D insufficiency. There has been very limited information in the literature addressing this subject.

2. Methods and materials

2.1. Subjects

Study subjects were a cohort of patients with prostate cancer who participated in a prospective clinical study evaluating the effect of androgen ablation therapy on bone mass density at the Toronto Sunnybrook Regional Cancer Center. The clinical study was approved by the local Research Ethics Committee of Sunnybrook Health Sciences Center. It was open between 2001 and 2002 and accrued a total of 107 patients. All patients had nonmetastatic prostate cancer and were treated with a curative intent with either radiotherapy alone or radiotherapy plus 2 to 3 years of androgen suppression. As part of the study evaluation, patients had serum 25(OH)D level measured prospectively at baseline and, then, yearly during follow-up. This prospectively collected serum 25(OH)D data are the basis of this report examining the prevalence of vitamin D insufficiency in patients with nonmetastatic prostate cancer.

2.2. Evaluations

At study enrollment, patients had the following evaluations: (1) complete medical history; (2) physical examination including height and weight; (3) laboratory tests including serum 25(OH)D, calcium, and parathyroid hormone (PTH); and (4) imaging studies including a standard dual energy x-ray absorptiometry for bone mass density. After the completion of planned radiotherapy, patients were followed annually up to 5 years. At each annual visit, the aforementioned evaluations were repeated.

As part of the evaluation, nutritional information pertinent to the clinical study was obtained. Among them were the amount of dairy product consumption; alcohol and smoking history; and the intake of calcium, vitamin D, and multivitamin supplement. In addition, the history of medical illness such as thyroid dysfunction, kidney stones, and chronic diarrhea that might be related to or affect nutritional status was obtained. This information was surveyed and recorded at baseline and follow-up visits. During the follow-up period, patients did not receive any specific instruction with regard to nutritional supplements including vitamin D. Any subsequent nutritional supplement that patients took beyond the baseline was left to the discretion of individual patient.

Serum 25(OH)D level was prospectively measured at baseline and, then, annually during follow-up. It was measured using a competitive immunochemiluminescent assay configured for Liaison platform (DisSorin, Stillwater, MN). The range of normal serum 25(OH)D was 75 to 225 nmol/L (30-90 ng/mL) in our laboratory. Serum PTH and calcium were measured by second-generation immunoassay and colorimetry, respectively, on the automated Roche Modular Analytics Platform (Roche, Basel, Switzerland).

Vitamin D insufficiency was defined as serum 25(OH)D level less than 75 nmol/L. Prevalence of vitamin D insufficiency was assessed at baseline and subsequent follow-up years.

2.3. Statistical analyses

Descriptive statistics were calculated for all variables of interest. Continuous measures were summarized using means ± SD, whereas categorical measures were summarized using counts and percentages. Various parameters are examined to assess their possible association with vitamin D insufficiency. Age; race; body mass index (BMI); season at the time of serum 25(OH)D measurement; smoking; alcohol; milk consumption; other dairy consumption; vitamin D supplement; intake of multivitamin containing vitamin D; calcium supplement; PTH level; and the medical history of hyperthyroidism, kidney stones, or chronic diarrhea were included in the analysis. Univariate analyses were carried out to examine the relationship between the aforementioned variables and vitamin D insufficiency (defined as <75 nmol/L), using χ^2 analyses for categorical variables or 2-sample t tests for continuous variables. A logistic regression analysis was carried out to assess the impact of several variables simultaneously on the outcome of vitamin D insufficiency. The logistic regression model provides odds ratios and their associated 95% confidence intervals for each variable. $P < .05$ was considered statistically significant for all tests. All analyses were carried out using SAS version 9.1 (SAS Institute, Cary, NC).