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Vitamin D and the risk of selected neoplasms – Evidence from prospective cohort studies

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Vitamin D inadequacy constitutes a largely unrecognized epidemic in many populations worldwide. Many lines of research support the concept that inadequate vitamin D supply may be involved in the pathogenesis and/ or progression of several disorders, including cancer, hypertension, cardiovascular disease, neuromuscular diseases, osteoarthritis, diabetes, and other autoimmune diseases. In recent years, several studies have addressed the association of cancer risk and serum 25(OH)D levels representing an integrated measure for vitamin D from diet, dietary supplements, and skin production, but results from single studies have remained inconclusive and study results have been reported in a very heterogeneous manner. Systematic reviews and meta-analyses of longitudinal epidemiological studies evaluating the association between serum 25(OH)D levels and risk of various forms of cancers by using methods for comprehensive trend estimation from summarized dose-response data have been lacking so far. It has been long hypothesized that VDR and CASR polymorphisms may play a role for the risk of various cancers. A number of studies have estimated the association of one or several VDR and CASR polymorphisms with selected forms of cancers. However, results have remained inconclusive.

The aim of this dissertation was to critically review, summarize and extend evidence on the association between vitamin D and the risk of several selected neoplasms.

First, systematic reviews and meta-analyses of longitudinal epidemiological studies evaluating the association between serum 25(OH)D levels and risk of selected neoplasms, such as colorectal cancer, prostate cancer, breast cancer, ovarian cancer, and colorectal adenoma were conducted using methods for comprehensive trend estimation from summarized dose-response data. This way confirm that serum 25(OH)D levels were shown to be inversely related to CRC and CRA risk. For breast cancer a decreased risk associated with higher serum 25(OH)D was seen in case-control studies only, but not in longitudinal studies. Observational studies have provided little evidence of an association of serum 25(OH)D with incidence of prostate cancer and ovarian cancer. The evidence available for the association with other cancers and mortality of all cancers was too sparse for meaningful meta-analyses.

Second, I used data from the population-based ESTHER I cohort study to estimate the association between baseline serum 25(OH)D levels and detection of colorectal neoplasms at colonoscopies conducted during follow-up. ESTHER is a cohort study of almost 10,000 older adults conducted in Saarland, Germany. The analyses are based on baseline and 5-year follow-up data. Multiple imputation was employed to account for missing values in covariates in multivariable analyses. Because the prevalence of cancer at colonoscopies was very low, cancers and adenomas were combined to form a common endpoint termed colorectal neoplasm. In these analyses, an inverse association between serum 25(OH)D levels and risk of colorectal neoplasm could not be confirmed.

Third, polymorphisms of the VDR (BsmI: rs1544410; FokI: rs2228570; Cdx2: rs11568820; TaqI: rs731236; VDR-5132: rs1989969) were determined in participants of three cohort studies (ESTHER I, ESTHER II and the VERDI) using Taqman methodology. No associations were observed for VDR BsmI (rs1544410), VDR FokI (rs2228570), VDR Cdx2 (rs11568820), VDR TaqI (rs731236), and VDR-5132 (rs1989969) with colorectal cancer risk.

Fourth, polymorphisms of the VDR (BsmI: rs1544410; FokI: rs2228570) and CASR (rs1801725) were determined among participants of screening colonoscopy in the BliTz study by Taqman methodology. No associations were observed for VDR BsmI and VDR FokI with colorectal adenoma risk, but a significant positive association between GT genotype of the CASR polymorphism and colorectal adenoma risk was found, compared with the GG genotype.

In conclusion, there are indications that low levels of serum vitamin D are associated with an increased risk of colorectal neoplasms even though this association could not be confirmed in own analyses from a population-based study from Germany. For breast cancer, an inverse association of serum vitamin D levels was seen in case-control studies only, and evidence is shown more sparse for other forms of cancers. Further longitudinal studies, ideally taken both additional genetic and environmental factors into account, are needed to further elucidate the role of vitamin D on cancer risk and potential prevention.