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Vitamin D and microvascular complications in people with type 2 diabetes

Aim: To evaluate the associations of serum 25-hydroxyvitamin D [25(OH)D] and polymorphisms of the vitamin D receptor (VDR) gene sequence with the risk of microvascular complication in a cohort of individuals with type 2 diabetes (T2D).
Methods: The prospective analysis included 14,709 participants with T2D and without diabetic microvascular complications from the UK Biobank. Cox proportional hazard regression models were used to calculate the hazard ratios (HR) and 95% CIs for diabetic microvascular complications, adjusting for several parameters that could influence the levels of vitamin D. The authors included in the analysis a large set of parameters, not only the "classical", such as ethnicity, age, gender or disease duration but also some parameters specific for vitamin D status such as diet, physical activity, time spent outdoors in summer and season of blood drawn.
Results: During a median of 11.2 years of follow-up, 1,370 participants developed at least one diabetic microvascular complication (based on the hospital inpatient records). In comparisons with participants with serum 25(OH)D <25.0 nmol/L, participants with serum 25(OH)D ≥75.0 nmol/L had a multivariate-adjusted HR of 0.65 (95% CI 0.51, 0.84) for composite diabetic microvascular complications (P_{trend}<0.001), 0.62 (0.40, 0.95) for diabetic retinopathy (P_{trend}=0.01), 0.56 (0.40, 0.79) for diabetic nephropathy (P_{trend}<0.001), and 0.48 (0.26, 0.89) for diabetic neuropathy (P_{trend}=0.03). In addition, in comparisons with participants with 25(OH)D <25 nmol/L and minor allele homozygotes of rs1544410 and rs731236, the multivariable-adjusted HRs of composite diabetic microvascular complications were 0.54 (0.38, 0.78) and 0.55 (0.38, 0.80) for participants with serum 25(OH)D ≥50 nmol/L and major allele homozygotes, respectively, although no significant interaction was observed.
Conclusions: Higher serum 25(OH)D was significantly associated with a lower risk of diabetic microvascular complications, including retinopathy, nephropathy, and neuropathy, suggesting a potential beneficial role of maintaining adequate vitamin D status in people with T2D in order to prevent diabetic microvascular complications.

Comments. This prospective study aims to fill the gap in the knowledge about the relationship between vitamin D status and T2D-related microvascular complications, in particular retinopathy, nephropathy and neuropathy. This is the first study, conducted in a large European population, that found a significant association of a lower risk of retinopathy, nephropathy and neuropathy with a higher concentration of serum vitamin D, despite genetic variants in VDR. Interestingly, a linear dose-response relationship was also observed between vitamin D and risks of diabetic complications, although this relationship was not observed for diabetic neuropathy. Albeit, the role of vitamin D on painful diabetic neuropathy was already suggested (Alam U et al *Diabetes Metab Res Rev. 2021;37:e3361*), this study highlights the relevance of vitamin D status in people with T2D, not only for the well-known effects on bone metabolism but also for the impact on microvascular complications. Further studies, designed to assess the effects of vitamin D supplementation on the development of microvascular complications, especially diabetic neuropathy, are needed to clarify the potential clinical use of vitamin D in people with diabetes.

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Reference. Chen X, Wan Z, Geng T, Zhu K, Li R, Lu Q, Lin X, Liu S, Chen L, Guo Y, Shan Z, Liu L, Pan A, Manson JE, Liu G. Vitamin D Status, Vitamin D Receptor Polymorphisms, and Risk of Microvascular Complications Among Individuals With Type 2 Diabetes: A Prospective Study. Diabetes Care. 2023 Feb 1;46(2):270-277. doi: 10.2337/dc22-0513. PMID: 36169213.
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