

conference abstract

observational

people

Vitamin D levels in the blood can predict future health risks & death

Free, circulating vitamin D levels in the blood may be a better predictor of future health risks in aging men, according to a study being presented at e-ECE 2020. These data suggest the free, precursor form of vitamin D found circulating in the bloodstream is a more accurate predictor of future health and disease risk, than the often measured total vitamin D. Since vitamin D deficiency is associated with multiple serious health conditions as we get older, this study suggests that further investigation into vitamin D levels and their link to poor health may be a promising area for further research.

Vitamin D deficiency is common in Europe, especially in elderly people. It has been associated with a higher risk for developing many aging-related diseases, such as cardiovascular disease, cancer and osteoporosis. However, there are several forms, or metabolites, of vitamin D in the body but it is the total amount of these metabolites that is most often used to assess the vitamin D status of people. The prohormone, 25-dihydroxyvitamin D is converted to 1,25-dihydroxyvitamin D, which is considered the active form of vitamin D in our body. More than 99% of all vitamin D metabolites in our blood are bound to proteins, so only a very small fraction is free to be biologically active. Therefore the free, active forms may be a better predictor of current and future health.

Dr Leen Antonio from University Hospitals Leuven in Belgium and a team of colleagues investigated whether the free metabolites of vitamin D were better health predictors, using data from the European Male Ageing Study, which was collected from 1,970 community-dwelling men, aged 40-79, between 2003 and 2005. The levels of total and free metabolites of vitamin D were compared with their current health status, adjusting for potentially confounding factors, including age, body mass index, smoking and self-reported health. The total levels of both free and bound vitamin D metabolites were associated with a higher risk of death. However, only free 25-hydroxyvitamin D was predictive of future health problems and not free 1,25-dihydroxyvitamin D.

Dr Antonio explains, "These data further confirm that vitamin D deficiency is associated with a negative impact on general health and can be predictive of a higher risk of death."

As this is an observational study, the causal relationships and underlying mechanisms remain undetermined. It was also not possible to obtain specific information about the causes of death of the men in the study, which may be a confounding factor.

"Most studies focus on the association between total 25-hydroxyvitamin D levels and age-related disease and mortality. As 1,25-dihydroxyvitamin D is the active form of vitamin D in our body, it was possible it could have been a stronger predictor for disease and mortality. It has also been debated if the total or free vitamin D levels should be measured. Our data now suggest that both total and free 25-hydroxyvitamin D levels are the better measure of future health risk in men," says Dr Antonio

Dr Antonio and her team are currently finalising the statistical analysis and writing a manuscript on these findings.

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Abstract
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Free 25-hydroxyvitamin D, but not free 1.25-dihydroxyvitamin D, predicts all-cause mortality in ageing men

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Background: Total 25 hydroxyvitamin D (25(OH)D) and total 1.25 dihydroxyvitamin D (1.25(OH)2D) are associated with all-cause mortality. The free hormone hypothesis postulates that only the free vitamin D fraction can exert its biological function. Recently some studies suggested that free 25(OH)D levels might be a better predictor for clinical outcomes, including mortality.

Objective: To study the association between total and free 25(OH)D and 1.25(OH)2D with all-cause mortality in a prospective cohort of community-dwelling European men.

Methods: 1970 community-dwelling men, aged 40-79, participated in the European Male Ageing Study (EMAS) between 2003-2005. In 5 of 8 EMAS centres, survival status was available until 1 April 2018. Total 25(OH)D levels were measured by radioimmunoassay and recalibrated to NIST standard reference material. Total 1.25(OH)2D was measured by mass spectrometry and vitamin D binding protein (DBP) by immunodiffusion. Free 25(OH)D and free 1.25(OH)2D were calculated from the total hormone and DBP concentration. Vitamin D measurements and DBP were divided into quintiles. Cox proportional hazard models were used to study the association between vitamin D status and all-cause mortality. Because of the wide age range at inclusion, age was used as time scale instead of years since inclusion adjusting for age. Results were expressed as hazard ratios (HR) with 95% confidence intervals, adjusted for centre, BMI, smoking and self-reported health.

Results: 524 (26.6%) men died during a mean follow-up of 12.3±3.4 years. Men who died had a higher BMI ($p=0.002$) and lower physical activity level ($p<0.001$), but there was no difference in smoking status. Men in the lowest total 25(OH)D and the lowest total 1.25(OH)2D quintile (cutoff $<9.3 \mu\text{g/L}$ and $<46 \text{ ng/L}$ respectively) had increased mortality risk (HR compared to men in the highest quintile (HR 1.83 (95%CI 1.34-2.50); $p<0.001$ and 1.41 (1.04-1.90); $p<0.05$ respectively). Likewise, men in the lowest three free 25(OH)D quintiles (levels $<4.43 \text{ ng/L}$) had a higher mortality risk compared to men in the highest quintile (HR 1.91 (1.34-2.73); $p<0.001$ for the lowest quintile). However, mortality risk was similar for across all free 1.25(OH)2D and DBP quintiles.

Conclusions: Low total 25(OH)D levels and low total 1.25(OH)2D levels in community-dwelling middle-aged and elderly men have an increased future mortality risk. However, only low free 25(OH)D but not free 1.25(OH)2D levels predict all-cause mortality. Vitamin D deficiency is associated with a negative impact on general health and is predictive of a higher mortality risk.

Notes for Editors

1. The poster "[*Free 25-hydroxyvitamin D, but not free 1.25-dihydroxyvitamin D, predicts all-cause mortality in ageing men*](#)" was presented on Monday 7 September 2020, online during e-ECE 2020.
2. e-ECE 2020 was held online on the 5-9 September. Catch up on [ESE On-Demand](#).
3. The [European Society of Endocrinology](#) was created to promote research, education and clinical practice in endocrinology by the organisation of conferences, training courses and publications, by raising public awareness, liaison with national and international legislators, and by any other appropriate means.