Vitamin D as a prognostic marker in rheumatoid arthritis (RA): Disease activity, treatment response and cardiopulmonary co-morbidity in early DMARD-naïve patients, and chronic RA patients followed up for 10 years

Mette Herly, MD, junior registrar in rheumatology and internal medicine. PhD student at Institute of Clinical Research, University of Southern Denmark.

Main supervisor: Torkell Ellingsen, clinical professor/head of research and chief consultant, Department of Rheumatology at Odense University Hospital / University of Southern Denmark.

Co-supervisors:
Peter Vestergaard, professor, Department of Endocrinology, Aalborg University Hospital.
Trine Bay Laurberg, MD, PhD, senior registrar, Diagnostic Center, Region Hospital Silkeborg.
Kristian Stengaard-Pedersen, clinical professor department of Rheumatology, Aarhus University Hospital.
Robin Christensen, adj professor in clinical epidemiology, editor of Cochrane´s musculoskeletal group, biostatistician at the Parker Institute at Copenhagen University.

Background: Several studies indicate a connection between low vitamin D metabolite levels and RA, studies finding Vitamin D receptor and alfa-1-hydroxylase activity in immune cells as well as in the rheumatoid lesion (1, 2, 3). There are diverging results concerning the influence of 25OHD in disease activity and prognosis in RA (4, 5, 6) and none of these investigate the association between 25OHD and 1,25(OH)2D in early, treatment-naïve RA.

RA patients have high cardiovascular risk profile, the risk of CVD on the level of that in patients with diabetes. (7, 8, 9, 10) In our study we investigate cardiovascular risk-profile in a newly diagnosed RA cohort with extensive cardiovascular evaluation, as well as in a cohort with established RA, to see if Vitamin D and metabolites at baseline are associated to cardiovascular risk.

Hypothesis 1: Baseline vitamin D metabolite levels correlate with disease activity in early DMARD- and steroid-naïve RA patients and cardiovascular events during a 10-year follow-up (CIMESTRA cohort). Our data in 160 DMARD- and steroid-naïve patients, show a statistically significant inverse association between baseline vitamin D metabolites and markers of disease activity. This association is important since tender joints are part of the new criteria for the diagnosis of RA in the diagnostic criteria for RA (11). In collaboration with the CIMESTRA group.

Hypothesis 2: Baseline vitamin D metabolite levels are prognostic for treatment response in early DMARD- and steroid-naïve RA patients (CIMETRA cohort). We found no association between vitamin D metabolites and the remission criteria (ACR/EULAR40 remission, DAS28<2.6 and DAS28<3.2) in a multivariate regression analysis. Interestingly, the multivariate logistic regression analysis with backwards selection showed a significant association between several baseline parameters (VASglobal, NTJ, NSJ, DAS28 (P<0.01) and their ability to predict the disease course at 3, 6 or 12 months of follow-up. In collaboration with the CIMESTRA group.

Hypothesis 3: Baseline vitamin D metabolite levels correlate with progression of cardiovascular and pulmonic co-morbidity in newly diagnosed RA patients over a 2 year period (INCEPTION cohort at Regional Hospital Silkeborg). The project will quantify co-morbidity at the time of diagnosis, with the possibility of long-term follow-up, to create a baseline algorithm for predicting later serious development of co-morbidity after 2 and 5 years. The cohort will be extensively evaluated at baseline and after 2 years (CT and MRI of the heart, speckle tracking echocardiography, extended lung function, central vessel wall stiffness, insulin resistance, whole body DXA scanning for body composition, co-morbidity clinically scored (Charlson index) and scoring of heart/lung function (NYHA and MRC score).

Moreover, baseline vitamin D metabolite levels will be associated to progression of the cardiovascular and pulmonary co-morbidity after 2 years of follow-up. In collaboration with colleagues from Diagnostic centre Silkeborg.

Hypothesis 4: Vitamin D metabolite levels correlate with cardiovascular co-morbidity in RA patients with long disease duration (SARA cohort, disease duration of 10 years).

The SARA cohort consists of 750 Danish RA patients from outpatient clinics at Vejle, Gråsten and Odense departments of rheumatology. We will investigate the association between vitamin D at baseline and the risk of cardiovascular disease in patients with long disease duration. In collaboration with the SARA group.
Reference List


