Vitamin D and lung function

Afzal *et al*[1] recently reported that low plasma 25-hydroxyvitamin D is associated with a decline in lung function and chronic obstructive pulmonary disease (COPD). While this finding persisted after adjustment for possible confounding variables, and concurs with the findings of others,[2] we believe it might still be spurious.

First, we suggest the association between plasma vitamin D and lung function is subject to a threshold effect, evident in both the cross-sectional data (figures 1 and 3, reference 1) and prospective data (figure 2 and table 2—see our figure 1 below), and primarily limited to the lowest two quintiles (ie, only for the 1st–2nd quintiles can a relationship be consistently identified). By contrast, for the 3rd–5th quintiles, which roughly correspond to normal vitamin D levels (>50 nmol/L), the relationship between vitamin D levels and lung function is no longer apparent (ie, flattens in figures 1, S1 and S2 or fails to significantly diverge in figures 2, 3, 4, S3 and S4, with overlapping CIs, reference 1). The presence of a threshold effect is critically important as 'adjustment' for relevant confounding variables (eg, smoking dose, age and height) assumes a linear relationship, not a threshold effect where stratification to match for potential confounding variables better identifies confounding or mediating effects. Interestingly, the relationship evident for lung function decline in the 1st–2nd vitamin D quintiles (figure 2) is all but lost in the sensitivity analysis (after adjustment for height and gender, figure S3).[1] Second, we are also concerned that the vitamin D association with FEV_1%predicted is consistently mirrored for FVC%predicted (see published figures and our figure below), but has no effect on the FEV_1/FVC ratio (ie, cornerstone of the COPD definition).[1 2] This global reduction in lung function could be explained by the mediating/confounding effects of one or a combination of reduced physical performance (frailty)[3] or increased systemic inflammation,[4] both of which correlate with low vitamin D levels (<50 nmol/

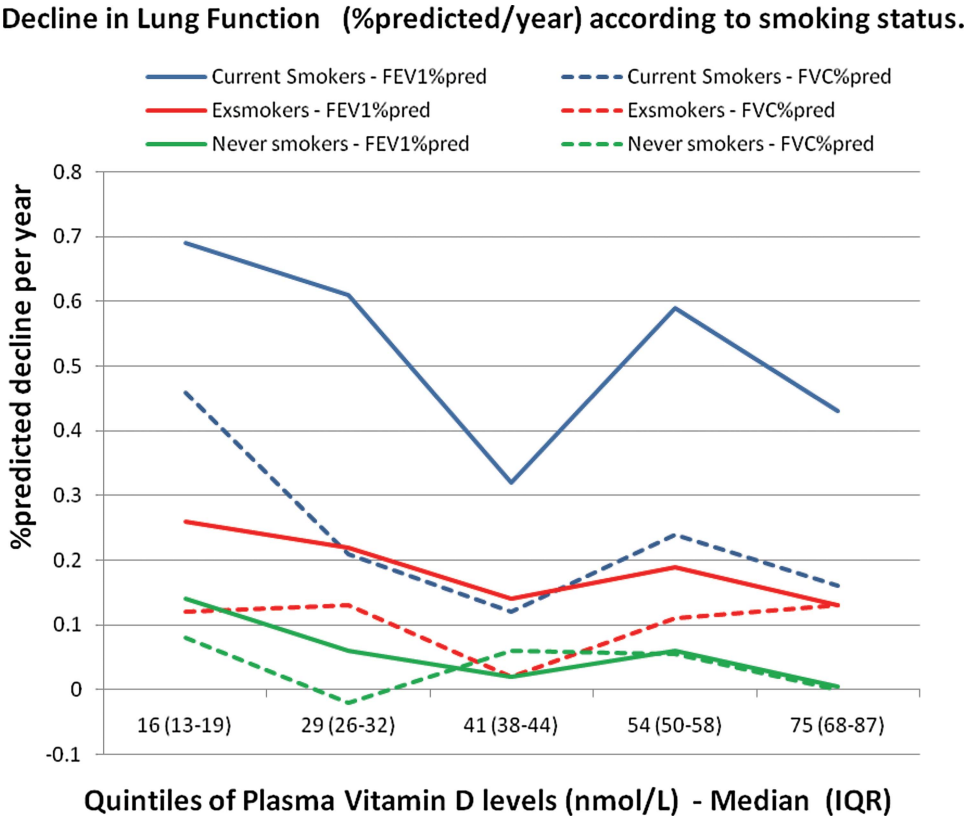

Figure 1 Decline in lung function according to smoking status and quintile of vitamin D level in a prospective cohort.

L) in older adults.[3 4] In a recently reported prospective population study, increased systemic inflammation was associated with greater declines in lung function.[5] Given the effect of low vitamin D on lung function decline is sensitive to smoking status (see our figure 1 below), it is difficult to simply link vitamin D level with COPD.

These observations suggest to us that despite the excellent study design of the Danish study[1] (large sample size, comparable validating cohort, prospective data and statistically significant differences), further analysis (including c-reactive protein (CRP) levels) is required to better understand the role of vitamin D status in COPD.

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