The Association between Serum Uric Acid, Bone Mineral Density, Hip Bone Geometry and Fracture Risk: the role of Age and Vitamin C.

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Objectives

We aimed to investigate:

1. the cross-sectional and longitudinal association between uric acid (UA), bone mineral density at femoral neck (FN-BMD), hip bone geometry (HBG) parameters.
2. the association between UA and incident fracture risk.
3. whether these associations were modified by age and dietary vitamin C intake.

Background

Uric acid (UA) is suggested to exert a protective effect in bone metabolism due to its role as an antioxidant and cytoprotectant. Nevertheless, how UA relates longitudinally with bone mineral density, hip bone geometry parameters (HBG) and incident of any type or subtypes of fractures, remains unclear. Furthermore, UA increases with advancing age and vitamin C intake increases UA excretion and therefore lowering the plasmatic levels of UA. Yet, little is known about the role of UA on musculoskeletal outcomes, accounting for these factors.

Methods

Data of 5,074 participants of The Rotterdam Study, a prospective population based cohort, were available (median follow-up, 10.9 years).

» Serum UA was determined from baseline non-fasting samples with a Kone Diagnostica reagent kit and a Kone autoanalyzer.

» FN- BMD was measured at baseline, 2nd, 3rd and 4th visit of the Rotterdam Study.

» HBG parameters were measured at baseline, 2nd and 3rd visit.

» Regression coefficients and 95% Confidence Intervals (β, 95%CI) were calculated using linear regression models fitted into generalized estimated equations.

» Cox proportional hazard models were used to study the association of serum UA with fracture risk.

All associations were corrected for age, gender, height, weight, eGFR, index time, smoking status, Dutch Healthy Diet-index, physical activity, prevalent diabetes mellitus, prevalent cardiovascular disease, history of hip or knee surgery, diuretic drug use, hormone replacement therapy, corticosteroid drug use, thyroid therapy, antigout drugs, serum phosphate, serum total calcium and intake of vitamin C.

Results

The association between UA with FN-BMD and hip bone geometry parameters.

» Serum UA levels (per SD increase) were positively associated with FN-BMD (β=0.007 g/cm^2, 95%CI=0.002; 0.01).

» UA levels were associated with thicker cortices (β=0.002 cm, 95%CI=0.0003; 0.002) lower bone width (β=-0.013 cm, 95%CI=-0.23; -0.003) and lower cortical buckling ratio (β=-0.19, 95%CI=-0.33; -0.06).

» The effects of UA on FN-BMD and cortical buckling ratio tended to become stronger over time (per SD increase in UA, there was an annual increase of 0.0003 (95%CI: 0.000; 0.001, *P*=0.03) and an annual decrease of 0.05 (95%CI: -0.05; -0.002, *P*=0.048) in FN-BMD and cortical buckling ratio respectively).

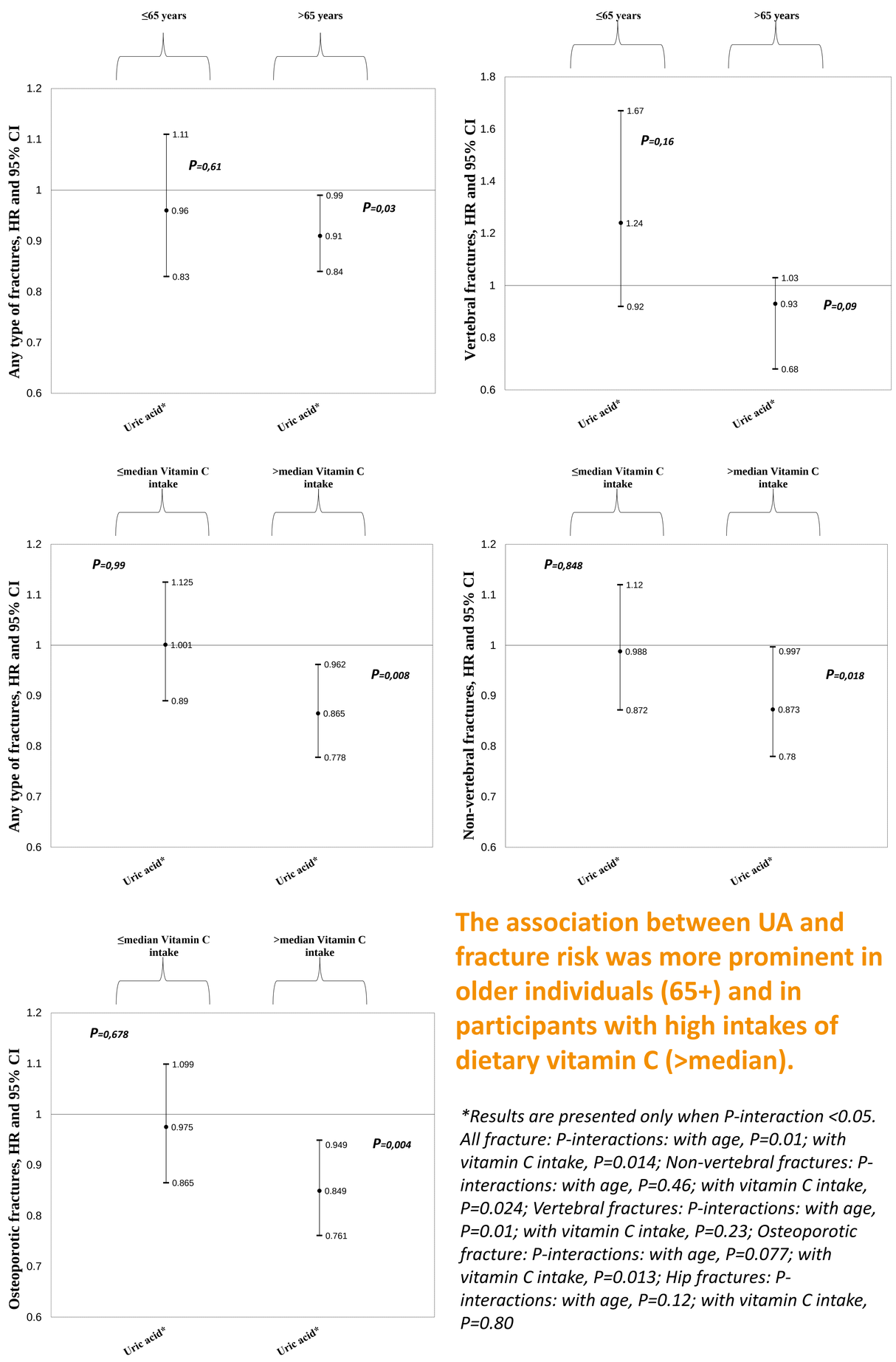
The association between UA and incident fracture risk.

» Hazard Ratios and 95% confidence intervals per SD increase of baseline UA levels for the development of any type of incident fractures, non-vertebral fractures and osteoporotic fractures were 0.92 (*0.86-0.995*), 0.92 (*0.86-0.998)*) and 0.91 (*0.84-0.98*), respectively.

Conclusions

1. Serum UA levels were shown to have protective effect on FN-BMD and favorable configuration of hip bone geometry parameters.
2. Serum UA levels were associated with lower fracture risk.
3. Age and levels of dietary vitamin C intake may modify these relationships.
4. Additional studies are warranted to establish causality, the precise mechanisms of action, and to give more insight into the interplay of UA with age and intake of vitamin C as determinants of bone health and disease.

Figure 1 The association between serum uric acid and fracture risk by age and dietary intakes of vitamin C*.



The association between UA and fracture risk was more prominent in older individuals (65+) and in participants with high intakes of dietary vitamin C (>median).

**Results are presented only when P-interaction <0.05. All fracture: P-interactions: with age, P=0.01; with vitamin C intake, P=0.014; Non-vertebral fractures: P-interactions: with age, P=0.46; with vitamin C intake, P=0.024; Vertebral fractures: P-interactions: with age, P=0.01; with vitamin C intake, P=0.23; Osteoporotic fracture: P-interactions: with age, P=0.077; with vitamin C intake, P=0.013; Hip fractures: P-interactions: with age, P=0.12; with vitamin C intake, P=0.80*

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