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B-vitamin status and the *MTHFR* 677C→T polymorphism as determinants of bone health in older Irish women from the TUDA ageing cohort study

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Osteoporosis, an increasingly common skeletal disorder characterised by reduced bone mineral density (BMD) and an increased risk of fragility fracture, is associated with increased morbidity and mortality[(1)]. In recent years, B-vitamins involved in 1-carbon metabolism (i.e. folate, vitaminsB12, B6 and riboflavin) have been linked with bone health outcomes. Findings, however, have been somewhat discordant among studies[(2)]. The aim of this investigation was to examine biomarker status of the B-vitamins and the common 677C→T polymorphism in the gene encoding the folate metabolising enzyme methylenetetrahydrofolatereductase (MTHFR), as determinants of low BMD.

Female participants (*n*1, 904) recruited to the Trinity Ulster Department of Agriculture (TUDA) ageing cohort study, and with BMD measured by dual energy X-ray absorptiometry scans, were investigated. Low BMD was defined as a combination of osteopenia (a T-Score between –1 and –2.5 SD) and osteoporosis (a T-Score of -2.5 SD or less).B-vitamin biomarker analysis was performed at Trinity College Dublin and the University of Ulster.

An increased risk of low BMD was significantly associated with age ($\beta = 0.062$, $p < 0.001$), physical inactivity ($\beta = 0.483$, $p = 0.004$), weight ($\beta = -0.056$, $p < 0.001$),and parathyroid hormone ($\beta = 0.011$, $p = 0.004$), but not serum 25-hydroxyvitamin D. Women in the lowest tertile of riboflavin status, or the highest tertile of homocysteine, had a significantly increased risk of low BMD, after adjustment for covariates (Table). The *MTHFR* 677TT genotype was associated with an increased risk of low BMD. This genotype combined with low status of riboflavin was associated with a 1.9 times increased risk of low BMD, compared to those with high vitamin status and the CC/CT genotypes combined (Table).

B-vitamin biomarker(*n* 1,904)	OR	95% CI	P
Plasma homocysteine (μmol/l)	1.3	1.0–1.8	0.028
Red cell folate (nmol/l)	1.2	0.9–1.5	0.154
Serum vitamin B12 (pmol/l)	1.0	0.8–1.2	0.845
Plasma pyridoxal-5-phosphate (nmol/l)	1.1	0.8–1.4	0.521
Riboflavin (EGRac)	1.3	1.0–1.6	0.030
***MTHFR* 677TT genotype**	1.4	1.0–2.1	0.052
Low riboflavin**MTHFR* **677TT genotype**	1.9	1.1–3.2	0.013
Low folate**MTHFR* **677TT genotype**	1.8	1.0–3.4	0.051

Analysis by logistic regression, comparing the lowest tertile of vitamin status (or the highest tertile of homocysteine) to the other tertiles combined, used to determine predictors of low BMD (osteopenia and osteoporosis combined) with adjustment for covariates.

These findings suggest that perturbations of 1-carbon metabolism may have adverse effects on bone health, while optimal B-vitamin status may be protective.

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