Abstract

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**Improved testing for vitamin B\textsubscript{12} deficiency: correcting MMA for eGFR reduces the number of patients classified as vitamin B\textsubscript{12} deficient.**

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**BACKGROUND:** Methylmalonic acid (MMA) can detect functional vitamin B\textsubscript{12} deficiencies as it accumulates early when intracellular deficits arise. However, impaired clearance of MMA from blood due to decreased glomerular filtration rate (eGFR) also results in elevated plasma MMA concentrations. Alternative to clinical trials, a data mining approach was chosen to quantify and compensate for the effect of decreased eGFR on MMA concentration.

**METHODS:** Comprehensive data on patient's vitamin B\textsubscript{12}, eGFR and MMA concentrations were collected (n = 2906). The relationship between vitamin B\textsubscript{12}, renal function (eGFR) and MMA was modelled using weighted multiple linear regression. The obtained model was used to estimate the influence of decreased eGFR on MMA. Clinical impact was examined by comparing the number of patients labelled vitamin B\textsubscript{12} deficient with and without adjustment in MMA.

**RESULTS:** Adjusting measured MMA concentrations for eGFR in the group of patients with low-normal vitamin B\textsubscript{12} concentrations (90-300 pmol/L) showed that the use of unadjusted MMA concentrations overestimates vitamin B\textsubscript{12} deficiency by 40%.

**CONCLUSIONS:** Through a data mining approach, the influence of eGFR on the relation between MMA and vitamin B\textsubscript{12} can be quantified and used to correct the measured MMA concentration for decreased eGFR. Especially in the elderly, eGFR-based correction of MMA may prevent over-diagnosis of vitamin B\textsubscript{12} deficiency and corresponding treatment.

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