

GW23-e2146

EFFECT OF FOLIC ACID SUPPLEMENTATION ON THE PROGRESSION OF CAROTID INTIMA-MEDIA THICKNESS: A META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

doi:10.1136/heartjnl-2012-302920w.3

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Objectives We conducted a meta-analysis of relevant randomised trials to assess whether folic acid supplementation reduces the progression of atherosclerosis as measured by carotid intima-media thickness (CIMT)

Methods This analysis included 2052 subjects from 10 folic acid randomised trials with the change in CIMT reported as one of the end points. Summary estimates of weighted mean differences (WMDs) and 95% CIs were obtained by using random-effect models. Meta-regression and subgroup analyses were performed to identify the source of heterogeneity

Results Our analysis showed that folic acid supplementation significantly reduces the progression of CIMT (WMD: -0.04 mm, 95% CI -0.07 to -0.02 , $p < 0.001$), particularly in subjects with chronic kidney disease risk (WMD: -0.05 mm, 95% CI -0.01 , $p = 0.06$) but not in subjects who were generally healthy with only elevated homocysteine concentrations (WMD: 0.00 mm, 95% CI -0.01 to 0.01 , $p = 0.35$). Furthermore, meta-regression analysis of the data showed that the baseline CIMT levels ($p = 0.011$) and the percent reduction of homocysteine ($p < 0.001$) were positively related to the effect size. Consistently, a greater beneficial effect was seen in those trials with baseline CIMT levels > 0.8 mm (WMD: -0.14 mm, 95% CI -0.19 to -0.08 , $p < 0.0001$) and a reduction in the homocysteine concentration $> 30\%$ (WMD: -0.22 mm, 95% CI -0.38 to -0.06 , $p = 0.009$). In the corresponding comparison groups the effect sizes were attenuated and insignificant.

Conclusions Our findings indicated that folic acid supplementation is effective in reducing the progression of CIMT, particularly in subjects with CKD or high CVD risk and among trials with higher baseline CIMT levels or a larger homocysteine reduction.