Abstract


Homocysteine, cysteine, and risk of incident colorectal cancer in the Women's Health Initiative observational cohort.


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BACKGROUND: Inflammation underlies the etiology of colorectal cancer (CRC). Hyperhomocysteinemia is associated with inflammation and may be a risk marker for CRC. Cysteine is a metabolic product of homocysteine and a precursor of the antioxidant glutathione. It is unknown whether cysteine is associated with CRC.

OBJECTIVE: The objective was to assess the associations between homocysteine and cysteine and CRC incidence in postmenopausal women.

DESIGN: Associations between homocysteine and cysteine and incident CRC in the Women’s Health Initiative observational cohort were assessed by using a nested case-control design. Cases and controls (n = 988/group) were matched for age (mean ± SD age: 67 ± 7 y), ethnicity (85.2% white, 8.9% black, 2.2% Hispanic/Latina, and 3.6% other), hysterectomy status, and date of blood draw. Homocysteine and cysteine were measured by HPLC with postcolumn fluorimetric detection.

RESULTS: Multivariate-adjusted ORs (95% CIs) for CRC were 1.46 (1.05, 2.04) for the highest quartile of homocysteine (>9.85 μmol/L) compared with the lowest quartile (≤6.74 μmol/L) (P = 0.02) and 0.57 (0.40, 0.82) for the highest quartile of cysteine (>309 μmol/L) compared with the lowest quartile (≤260 μmol/L) (P = 0.01). The association with homocysteine was significant for proximal colon tumors (P = 0.008) but not for distal or rectal tumors, whereas the association with cysteine was significant for rectal tumors (P = 0.02), borderline for proximal tumors (P = 0.06), and not significant for distal tumors. The associations with both homocysteine and cysteine were significant for localized tumors (P ≤ 0.01) but not for metastases.

CONCLUSION: High plasma homocysteine is associated with increased risk of CRC, whereas high cysteine is associated with decreased risk. This trial was registered at clinicaltrials.gov as NCT 00000611.

PMID: 23426034