

## Lower folate levels in gastric cancer: Is it a cause or a result?

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### Abstract

Folate deficiency and its association with cancer have been studied in the literature, but its clinical impact is still unknown. Folate deficiency and its result on gastric cancer is a mysterious part of oncology, with ongoing studies hopefully clarifying its impact on gastric cancer management. Lee *et al* studied folate deficiency and its impact on staging and clinical results. Here we try to contribute to the field by expressing our own thoughts about the paper.

**Key words:** Gastric cancer; Folate deficiency; Vitamin B12 deficiency

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**Core tip:** The analysis by Lee *et al* in the paper has some limitations that must be pointed out. The severity of folate deficiency, replacement strategies, and probable vitamin B12 deficiencies should have been discussed. The paper does not do enough to accurately conclude a relationship between folate deficiency and gastric cancer severity.

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### TO THE EDITOR

We have read the case control study by Lee *et al*<sup>[1]</sup> with great interest. Well designed and with good control group selection, the study provided appropriate evaluation of the effects of folate deficiency on gastric cancer. Although the study by Vollset *et al*<sup>[2]</sup> could not demonstrate folate deficiency as a risk factor for gastric cancer, this paper reminded us of the necessity for further workup.

Folate deficiency as a cause of cancer has been studied before. Its functions in purine metabolism and S-adenosyl methionine production made it an important part of DNA repair and methylation, as well as being necessary for DNA structure stabilization. The importance of low and high levels of folate, which has been demonstrated *via* animal studies, shows the necessity for further clinical studies. However,

folate levels are difficult to interpret in a clinical study. Gastric cancer cases are usually related to *Helicobacter pylori*, pernicious anemia, and atrophic gastritis. These pathologies coexist with vitamin B12 deficiency, which is normally present with folate deficiency; when evaluating folate levels, vitamin B12 must be evaluated as well. Besides gastric premalignant pathologies, gastric cancer patients usually present with dyspepsia and have a history of a few months of decreased oral intake. Irritant vegetables are the most problematic foods for these patients, and so it is not surprising that patients may present with folate deficiency at initial diagnosis. With the increased stage of the disease, more symptomatic patients may present with less oral intake, and as a result, lower folate levels may ensue. So, is folate deficiency a result or a cause of gastric cancer? Unfortunately, it is currently a difficult subject to analyze and, therefore, to form a conclusion on.

Other information not mentioned in the paper was the folate replacement strategy and that medications used during therapies can interfere with folate absorption and metabolism. As concluded in other studies, higher levels of folate can further induce a malignant transformation<sup>[3]</sup>. Folate replacement strategies and the efficacy of replacement should have been included in the analysis. Drugs that interfere with folate pharmacokinetics are not usually used in gastric cancer therapy, but antiepileptics for platinum-induced

neuropathy can decrease absorption of folate. Folate supplementation strategy during therapy may be an important determinant of survival.

Folate and colon cancer association has been widely studied in the literature. Further clinical studies are needed to answer the current questions on the effects of folate metabolism on gastric cancer.

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