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## Comment “Asymptomatic small intestinal ulcerative lesions: Obesity and *Helicobacter pylori* are likely to be risk factors”

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### Abstract

There are many causes of anemia. It is unreasonable to simply associate anemia with asymptomatic ulcers in the small intestine.

**Key Words:** Intrinsic factor; Iron deficiency anemia; Megaloblastic anemia; Nonsteroidal anti-inflammatory drugs; Statistical bias

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**Core Tip:** Asymptomatic small intestinal ulcers may cause anemia due to vitamin B12 absorption or iron utilization, but anemia can also be caused by other digestive diseases such as gastric ulcer or gastrectomy or other chronic wasting diseases. Establishing a link between anemia symptoms and asymptomatic ulcers in the small intestine requires more extensive data support and other auxiliary examinations. Case reports and small sample investigations are not enough to support this link.

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## TO THE EDITOR

We are glad to read the original article by Fujimori[1] on asymptomatic ulcers in the small intestine. The authors found that small intestinal ulcers were usually not accompanied by obvious symptoms, and the patients' various examinations, such as physical examination and blood routine, were usually normal. However, they found in the limited pathological report of small intestinal ulcers that small intestinal ulcers were usually accompanied by the detection of *Helicobacter pylori* (*H. pylori*) and high body mass index (BMI), and the detection rate of small intestinal ulcers in men was higher than in women. This article provided more detailed data and research background and obtained reasonable results with the author's research and analysis. However, in our opinion, this article has problems worthy of further discussion. We are willing to contribute to the debate and want the author to reply.

In the Abstract section, we noticed that 10% of the healthy subjects mentioned by the author had a ruptured small intestinal mucosa, and the number of ruptures was 1-3. However, in the following, "What should I do if the small intestinal mucosa ruptures?" is written as 1-2. Is this the author's clerical error or is the concept not clearly defined? In the Introduction part, the author cited a recent research report to illustrate the relationship between Crohn's disease and ileal ulcers. However, the number of samples in this report is too small, and there is no rigorous statistical verification and analysis to directly infer the ileal ulcer. The connection with Crohn's disease is considered less rigorously.

Nonsteroidal anti-inflammatory drugs (NSAIDs)[2] and aspirin were used simultaneously to compare the utility of this combination, as mentioned in the analysis of drug administration studies. I think aspirin and NSAIDs should not be a paratactic relation because aspirin is included in NSAIDs. Maybe it is a good idea to modify NSAIDs to other types of NSAIDs.

The author repeatedly mentioned in the article that anemia was an important reminder for further examination. However, there are many reasons for anemia. For example, insufficient intake of folic acid and vitamin B12 can lead to megaloblastic anemia. Although daily diet can meet the needs of folic acid and vitamin B12 for erythropoiesis, the absorption of vitamin B12 requires the participation of intrinsic factors[3,4]. Intrinsic factors are produced by parietal cells in the stomach. After the intrinsic factor is combined with vitamin B12, it promotes the reabsorption of vitamin B12 in the distal ileum through specific receptors on the ileal mucosa. Although the terminal ileum plays an irreplaceable role in maintaining vitamin B12 Levels, disruption of any of these processes can lead to anemia. For example, gastrectomy can affect the secretion of internal factors and cause vitamin B12 reabsorption disorder[5]. In addition, iron is another important factor in the synthesis of red blood cells[6]. Iron deficiency anemia may be caused by insufficient iron intake or excessive iron loss due to chronic blood loss. Therefore, we believe that simply linking anemia with asymptomatic ulcers in the small intestine is unreasonable.

In the analysis, we found some data that were not suitable, in our opinion. For example, in Table 1 (<https://www.wjgnet.com/1007-9327/full/v28/i3/332-T1.htm>), in addition to the increased cases reported in the United States in 2005 and 2007 and Japan in 2016, the number of sample cases provided in other years and regions is too small. Because statistical analyses in cases of too few samples may lead to bias or bias in the results, the results obtained in this case are not representative. In addition, the data provided by the author has a single source and cannot represent the small intestinal ulcer situation of the global population. Therefore, the representativeness of the results of this experiment needs further study. In addition, we can see in Table 2 (<https://www.wjgnet.com/1007-9327/full/v28/i3/332-T2.htm>) that the data provided by Fujimori[1] in 2011 did not include female samples. The author bluntly pointed out in the results that small intestinal ulcers were more common in men. We consider whether such results are a deviation or error due to statistical reasons. Besides, mucosal breaks were strongly correlated with BMI and were significantly more common in *H. pylori*-infected subjects mentioned in the analysis section. I do not understand how this conclusion was drawn. Table 3 (<https://www.wjgnet.com/1007-9327/full/v28/i3/332-T3.htm>) shows the *P*-value for sex, age, and smoking. Among them, the *P*-values for sex, BMI, and *H. pylori* infection were statistically significant. The *P*-value for BMI was the smallest. However, it does not mean that BMI had a strong correlation with mucosal breaks. A *P*-value less than 0.05 only indicate statistical significance. Similarly, the study does not provide convincing evidence to confirm mucosal breaks were significantly more common in *H. pylori*-infected subjects.

## FOOTNOTES

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