Biomarkers and OLGIM Stage for Prospective Preneoplastic Risk Stratification

Dear Editor:

It is generally accepted that serum pepsinogen (PG) tests correlate with the occurrence of gastric atrophy and intestinal metaplasia.[1] However, because of its low sensitivity, Huang et al[2] report that in North America, where *Helicobacter pylori* prevalence is low (8%) and the use of proton pump inhibitors is frequent, the discrimination value for gastric preneoplastic lesions, atrophic gastritis, and intestinal metaplasia of gastropanel biomarkers is too low to obtain good results ($c<0.7$).

The results reported by the authors give an apparent contradictory conclusion concerning other studies performed in countries with a low incidence of gastric cancer (eg, the Netherlands, Norway, and Italy).[3,4] den Hollander et al[3] showed an overall risk of neoplastic progression of 0.3% per year during a follow-up period of 4.7 years of surveillance for preneoplastic gastric lesions of 279 patients. Of note, they indicated that combining histopathology data with PG serologic markers adequately discriminated between low-risk and high-risk patients; none of the patients ($n = 132$) with PGI/PGII >3 and OLGIM 0-II developed dysplasia or invasive neoplasia during the follow-up period. Conversely, 3 patients (3.8%) with a PGI/PGII ratio ≤ 3 ($n = 79$) were considered in the high-risk group, consisting of patients with OLGIM III-IV. These patients showed neoplastic progression during the follow-up period ($P = .02$). These results underlined the importance of serologic tests combined with histopathology as a prospective risk stratification tool.

Serum PGs correlate with the functional status of gastric cells, and in our previous studies, we showed that PGI serum levels decreased with severe OLGIM stage, with a PGI cutoff of ≤ 47.9 ng/mL that was corrected for patient age. This level was the most discriminatory for an OLGIM stage ≥ 2.[4] Moreover, serum PGII (>13 ng/mL) correlates with *H pylori*–positive gastritis[4,5] and higher gastrin G17 levels (>66 pmol/L) with autoimmune atrophic gastritis or neuroendocrine tumors when combined with a reduced PGI/PGII ratio <2.3.[6]

Therefore, our data support serum PGs and G17 as helpful tools to discriminate advanced preneoplastic lesions (OLGIM ≥ 2). In 1 of our studies,[4] we proposed a predictive risk stratification model for advanced OLGIM stages based on a combination of gastrin G17, PGI, and patient age. First, risk stratification was used where patients at high risk had G17 >66 pm/L and PGI ≤ 22 ng/L independent of their age; then, patients were considered at high risk with G17 ≤ 66 pm/L according to the PGI level associated with their age as follows: PGI ≤ 54 ng/mL for patients younger than 40 years old; PGI ≤ 71 ng/mL for patients between 40 and 65 years old; and PG I ≤ 88 ng/mL for patients 65 or older.

Considering that the usefulness of PGs may be different between countries and that PGs are dependent on the physiopathologic status of subjects, these biomarkers should be validated with OLGA/OLGIM results before practically using them for the screening of preneoplastic lesions in the general population.

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