Gastric corpus atrophy in gastric cancer screenings: Benefits and drawbacks

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Gastric cancer (GC) is one the major health burden in the world. In Iran GC is the most common malignancy among men and second to breast cancer among women and the first cause of cancer mortality.¹ Age-standardized rate of GC follows a particular geographic pattern and it tends to be higher in Northern provinces (Ardabil:49., Golestan: 26.8 among males) than Southern ones (Fars:3.8 among males).²-⁴ The overall 5-year survival of 14-24% among operable patients shows poor prognosis of this malignancy.⁵ This pattern of prognosis highlights the importance of early GC detection. In this editorial our main focus is on the most prevalent type of gastric cancer which is non-cardia GC.

Among a few established risk factors for GC, Infection with Helicobacter pylori (H.pylori) infection happens long time before GC occurrence which results a prolonged latency period for 4-5 decades. This arrangement of exposure and outcome raises opportunity for H.pylori-based preventive programs to be appeared promising.

H.pylori has been suggested as a necessary cause for development of GC. The magnitude of association between H.pylori and GC is sensitive to the design of study. While a prospective study reported that strength of H.pylori association with GC exceeded 40 times more than non-infected individual⁶, retrospective studies or cohorts with recruitment age of more than 40 years old were not able to detect this strength. Meanwhile this prolonged latency period has a drawback for diagnosis. In other words, serologic methods for H.pylori diagnosis are prone to immunologic amnesia therefore old infections could be always falsely ignored. Detection of durable cagA antigen was one of the advances in this field to overcome the problem of false negative serology results. Recently developed multiplex serology method with ability of detecting multiple antigens confirmed the cagA association with GC risk and additionally suggested new antigens such as GroEL to be as potent as cagA.⁷ Yet, the epidemiologic design of study plays a major role in detection of magnitude between H.pylori and GC.

Gastric corpus atrophy as a consequence of long-lasting H.pylori infection attracted the attention of screening programmers because of two main reasons; firstly it was assumed for

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long time that pepsinogens are reliable markers for estimating the function or health of gastric mucosa and methods for their detection were developed since pepsinogen discovery in 18th century. Secondly, according to the model suggested by Correa in 1975, gastric corpus atrophy is an intermediate event between \textit{H. pylori} infection and GC outcome. Given that 50\% of world population is infected with \textit{H. pylori}, detection of corpus atrophy would let health professionals to focus on high risk group in every population with more efficiency.

Serologic detection of corpus atrophy has many advantages for population-based studies and screening purposes meanwhile, the major difficulty is lack of reliable gold standard to compare and validate serologic measurement with actual biologic event. Validation studies reported several cutpoint values of pepsinogen for corpus atrophy diagnosis including PGI < 70 \text{ ug/l} & PGI/II < 3 in Japanese studies, PGI < 28-30 \text{ ug/l} or PGI/II < 3 in Scandinavian studies, PGI < 50-55 \text{ ug/l} and ratio < 3-5 in Chinese studies. These variations in cutpoint values affect the estimate of serologic prevalence of severe corpus atrophy in different populations which ranges from 29\% in to 4\% among older than 50 y/o population. Imperfect sensitivity of pepsinogen is another limitation of this protein as a screening marker.

Despite of well-known role of gastrin in regulation of acid secretion in stomach, some studies have failed to show its additional role in atrophy detection comparing to pepsinogens and some studies showed that when two cutpoint values for gastrin were applied the predictive value of pepsinogens improved. Available gastrin measurement methods are not feasible for population-based studies due to requirement of collecting serum samples after an overnight fasting.

In this issue of MEJD, Shamsdin S.A and colleagues presented a cross sectional study with random sampling among low risk population for GC in Southern Iran and surveyed the prevalence of gastric corpus atrophy among them. Population-based design instead of clinical-based study, gives a true picture of gastric atrophy and provides reliable information for health policy makers. Shamsdin S.A reported 4.3\% atrophy prevalence based on a cutpoint value of PGI/II < 3. As the authors mentioned in the discussion part, PGI has been shown as the more reliable marker for gastric atrophy in most of studies. Reporting the range of prevalence based of different cutpoints is one strategy for reporting gastric atrophy in the absence of validated cutpoint.

In this article, authors reported a negative association between BMI and serum level of PGII, which is a new finding, however the effect is marginal. Proton pump inhibitors (PPI) which are commonly prescribed are the main medications affect the level of serum pepsinogen and gastrin, therefore collection of information on these medications is necessary for evaluation of serologic atrophy. In addition \textit{H. pylori} eradication alters the PGI/II ratio and lack of information on eradication confounds the estimated prevalence in this study.

There is a low possibility to detect strong association between \textit{H. pylori}/cagA and gastric atrophy in a cross sectional studies and particularly in the high endemic areas for \textit{H. pylori}/cagA infection. Therefore as this study shows additional information to cagA serology alone is needed to study the effect of \textit{H. pylori}.

One important aspect of studies with random sampling is reporting the nonparticipation rate of the contacted individual to help readers evaluate to what extent, researchers broke the first random frame. In this study, this figure has not been mentioned however the Female/male ratio of 1.8 gives a figure that probably the participation rate for men was lower. Eradication of \textit{H. pylori} in countries with high prevalence of \textit{H. pylori} infection, high percentage of antibiotic resistance and probably low compli-
ance to treatment among younger age group either in high risk or low risk areas for GC is not feasible. Increasing esophageal adenocarcinoma and reflux should be added to the disadvantages of population H. pylori eradication. Improving methods for screening GC based on H. pylori mediated process i.e gastric corpus atrophy is more practical for early detection of gastric cancer.

CONFLICT OF INTEREST
The author declares no conflict of interest related to this work.

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