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Editorial

Metabolic syndrome and gastrointestinal–hepatobiliary diseases

Metabolic syndrome (MS) is defined as a constellation of clinical biological features closely related to insulin-resistance, and has become a major public health challenge worldwide. In Taiwan, the prevalence rate of MS is about 20%.[1] Primary features of MS include elevated blood pressure, dyslipidemia [increased triglycerides and reduced high-density lipoprotein (HDL) cholesterol], raised fasting glucose, and central obesity, as defined by the International Diabetes Federation.[2]

People with MS have an increased risk of cardiovascular diseases and Type 2 diabetes mellitus, and MS was also found to be associated with several benign and malignant gastrointestinal (GI) and hepatobiliary diseases.

First, erosive esophagitis and Barrett's esophagus were found to be strongly associated with MS in a cross-sectional study.[3] Old age, male, high body mass index (BMI), high waist circumference, and triglyceride and low HDL were all independent risk factors for predicting erosive esophagitis.[4] Additionally, a large nationwide cohort study in Norway showed that increased waist circumference was associated with an increased hazard ratio of esophageal adenocarcinoma.[5] The increased risk in people with obesity partly reflects the role of gastroesophageal reflux disease (GERD) and Barrett's esophagus in carcinogenesis; however, it is likely that other factors such as inflammation, adipokines, and insulin-like growth factor axis are also important.[6]

A systematic review and meta-analysis showed that *Helicobacter pylori* infection is positively associated with MS (higher triglyceride, fasting blood glucose, BMI, homeostatic model assessment of insulin resistance, systemic blood pressure, and lower HDL).[7] One possible mechanism was that the inflammatory conditions induced by chronic exposure to *H. pylori* may influence the cytokine networks, including tumor necrosis factor-α, interleukin-6, angiotensinogen, free fatty acid, leptin, and adiponectin, which subsequently accelerates abnormalities in metabolic parameters and finally leads to the development of MS.[7]

Subjects with hypertension and MS were found to have a significantly higher risk for subsequent adenoma or advanced neoplasms, respectively, during surveillance colonoscopies.[8,9] Colorectal cancer (CRC) risk is associated with high BMI, with an estimated 3% increase in risk with each unit of BMI.[10] A systematic review and meta-analysis showed that MS is associated with an increased risk of CRC incidence and mortality.[11] The plausible biological mechanisms to explain its role in CRC risk include involvement of insulin resistance, as well as acting as an energy depot for cancer cell growth which may be mediated by dysregulation of growth signals, cytokines and cellular crosstalk, and vascular integrity factors. This further enables crosstalk between macrophages, adipocytes, endothelial cells, and epithelial cells, and contributes to cancer-related processes.[11]

A cross-sectional study in Japan found that irritable bowel syndrome is significantly related to MS and elevated triglyceride.[12] There may be a link between visceral adiposity and irritable bowel syndrome, but data about such a connection is still limited.[6] Recent findings also indicate similarities in pathophysiological features between MS and inflammatory bowel disease, including adipose tissue dysregulation, inadequate immune response, and inflammation.[13]

Regarding hepatobiliary pancreatic disease, high BMI, central obesity, and MS increase the risk of gallstones.[6,14] Prospective studies revealed that an increase in BMI and impaired glucose metabolism pose a possible risk for gallbladder cancer and pancreatic cancer.[6,15] Moreover, high BMI, central obesity, MS, and Type 2 diabetes were noted to increase the risk of nonalcoholic fatty liver disease, which can progress to cirrhosis and ultimately hepatocellular carcinoma (HCC).[6,16] Although diabetes may be a surrogate for cirrhosis due to glucose intolerance secondary to the development of cirrhosis, which increases the risk of HCC, a prospective study of 500,000 adults in North Europe showed that high BMI and blood sugar were positively associated with a risk of primary liver cancer.[17]

In conclusion, there are growing evidences suggesting that MS increases the risk of nonmalignant GI disorders such as GERD, nonalcoholic fatty liver disease, and gallstone, premalignant GI disorders such as Barrett's esophagus and colon adenoma, and also increases the risk of GI malignancy including esophageal adenocarcinoma, CRC, and gallbladder cancer. However, further studies are needed to clarify the possible mechanisms and the causal relationship between MS and these GI tract disorders.

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Conflicts of interest

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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