

Biomarkers may help predict outcomes in gastric cancer patients who abuse alcohol

January 10 2018



Immunohistochemical staining of transcription factor IIB-related factor 1 (BRF1) in gastric cancer (GC). A and B: High BRF1 expression in GC tissue. C: Positive BRF1 expression in GC para-tumor tissue. D and E: Low BRF1 expression in GC tissue. F: Negative BRF1 expression in GC para-tumor tissue. Original magnification: x100 (A and D); x400 (B, C, E, and F). Credit: *The American Journal of Pathology*

Alcohol consumption has been identified as a modifiable risk factor for



cancers such as gastric cancer. A new report in the *The American Journal of Pathology* sheds light on how specific proteins interact with alcohol, and how that interplay impacts survival and response to platinum-based adjuvant chemotherapy in patients with gastric cancer who may or may not still be drinking. It is the first time that a correlation between a key microRNA-processing modulator, transcription factor IIBrelated factor 1 (BRF1), and prognosis of gastric cancer patients has been demonstrated. Investigators also determined that breast cancer susceptibility gene BRCA1/2, and myeloperoxidase (MPO) are more frequent in gastric cancer patients who engage in hazardous or harmful alcohol consumption.

"Alcohol consumption is a known risk factor for gastric cancer, which carries high morbidity and mortality in China. We found that DNA repair-related markers—BRF1, BRCA1/2, and MPO—have good prognostic value in gastric cancer <u>patients</u> with or without harmful <u>alcohol</u> consumption habits. Moreover, these proteins are also associated with how effective platinum-based adjuvant chemotherapy will be for gastric cancer patients," explained Hua Wang, MD, PhD, and co-senior author Kangsheng Gu, MD, PhD, both of the Department of Oncology at First Affiliated Hospital of Anhui Medical University, Hefei, Anhui (China).

Researchers analyzed tumor tissue from 77 patients who had undergone surgery for primary gastric adenocarcinoma and 69 tissue samples taken from outside the tumor area. Among them, 66 patients received radical surgery and 57 patients received platinum-based adjuvant chemotherapy. All 77 patients were followed for an average of 18 months, during which time 94% (62/66) experienced disease recurrence. Patients remained free of disease for an average of 14 months (disease free survival, DFS) whereas the median overall survival (OS) was 20 months.

BRF1, BRCA1/2, and MPO were also helpful in predicting which



patients would benefit more from platinum-based adjuvant chemotherapy. For example, DFS was extended two-fold or more in patients who underwent chemotherapy and showed negative or low BRCA1/2 expression. For those with negative or low BRCA1, the average disease-free interval was 18 months compared to nine months in the high-expression group. Patients with negative MPO also had a better outcome trend, although it was not statistically significant.

Importantly, investigators found that alcohol continued to have a detrimental effect in patients. High BRF1 expression and MPO-positive inflammatory cell infiltration were more frequent in gastric cancer patients with hazardous or harmful alcohol consumption habits. Abnormal changes in BRCA1 in tissues outside the tumors were more frequent in alcohol abusers. In previous studies, these investigators found similar correlations between BRF1 and alcohol consumption in breast and liver <u>cancer</u> patients.

Understanding the mechanisms of how these proteins interact with alcohol and contribute to carcinogenesis is still being investigated. It is thought that RNA Pol III transcribes genes play a crucial role in alcoholmediated tumorigenesis. BRF1 regulates RNA Pol III gene transcription, and its overexpression acts though BRCA1 to alleviate inhibition of RNA Pol III transcription. Measurement of MPO is interpreted as a measure of the gastric inflammation and oxidative damage induced by alcohol. BRCA1/2 and MPO also play key roles in DNA damage repair.

"Until now, there have been no good markers to indicate <u>alcohol</u> <u>consumption</u> in <u>gastric cancer</u> tissue," noted Dr. Wang. "Future larger clinical trials are planned to explore the prognostic utility of these biomarkers in gastric and other cancers in patients who consume hazardous quantities of alcohol."

More information: Yiyin Zhang et al, Prognostic Value of the



Expression of DNA Repair–Related Biomarkers Mediated by Alcohol in Gastric Cancer Patients, *The American Journal of Pathology* (2018). DOI: 10.1016/j.ajpath.2017.10.010

Provided by Elsevier

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