Prognostic Significance of CpG Island Methylator Phenotype in Colorectal Cancer

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CIMP-high CRCs present with distinct clinicopathological and molecular features such as older age, female gender, proximal tumor location, poor differentiation, and high rate of MSI, KRAS and BRAF mutation, compared to CIMP-low/negative CRCs. However, the association between CIMP status and CRC prognosis are inconsistent in previous published reports. In this issue of Gut and Liver, Kang et al., investigated the MSI and CIMP status in Korean colon cancer patients except many rectal cancer patients, and examined their correlation with clinicopathological features including survival. The authors showed that regardless of the MSI status, CIMP-high colon cancer was associated with a poor survival outcome, and colon cancer with CIMP-high/MSI-negative in subgroup analysis showed a poor survival outcome compared to CIMP-low and negative/MSI-negative colon cancers. However, as the authors described, this study population was relatively small and had low incidence of MSI-high or CIMP-high cancers, which might influence some results, especially the association of CIMP status for CRC prognosis.

Other Korean studies also showed that CIMP-high CRCs were significantly associated with female gender, proximal tumor location, poor differentiation, nodal metastasis, more advanced cancer, BRAF mutations, MSI, and poor prognosis. According to the combination of CIMP and MSI status, the CIMP-high/MSI-negative subtype showed the worst clinical outcome due to BRAF mutation. The clinicopathological and molecular features of CIMP-high CRCs in Korean studies were similar with those of previous published reports. However, although
CIMP-high CRC patients were related to poor prognosis in many studies including Korean studies, other studies reported no association between CIMP-high CRC patient and prognosis or even noted a better survival benefit from adjuvant chemotherapy.5–7 There are several explanations for this discrepancy. First, results are inconsistent, perhaps due to variable factors including MSI, KRAS and BRAF mutations, variations in use of adjuvant chemotherapy, the ambiguous pathophysiology of CIMP, methodologic differences such as differences in the selected methylation markers and definitions of CIMP.5,6 Actually, specific methylated loci using for definition of CIMP and prevalence of CIMP status are different among studies. It is the major concern in studying CIMP status in variable cancers. Second, CIMP is an event that predominantly occurs in early stage of carcinogenesis and may less involve to cancer progression. Therefore, although much effort has been made to identify the impact of CIMP status as prognostic biomarkers in clinical practice, it still cannot be concluded whether association between CIMP status and CRC prognosis exist.

In future, large-scale well-designed studies should be considered in order to clarify the impact of CIMP on the prognostic significance in CRC patients.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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