Outcome of Initial Screening for Lynch Syndrome in Chinese Patients with Colorectal Cancer

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BACKGROUND: Lynch syndrome (LS) is the most common inherited colorectal cancer (CRC) and caused by deleterious germline mutations in one of the mismatch repair (MMR) genes, which usually causes MMR proteins dysfunction. As is known to all, patients with CRC from China has different clinical features compared with western populations. The age of onset is usually 10-12 years earlier and incidence of tumors in the distal colorectum is much higher. However, few data are available regarding clinical and molecular characterization in Chinese patients with LS. According to the recommendation of NCCN guideline, immunohistochemical (IHC) staining to identify the MMR protein deficiency could be the first step for LS screening and *BRAF* gene mutation test subsequently could exclude somatic tumors.

HYPOTHESIS: Chinese patients with LS may have different mutation spectrum and phenotype. The routine method for LS screening is not suitable for them.

METHODS: A total of 1405 consecutive patients, who underwent surgery for CRC at Sun Yat-sen University Cancer Center (Guangzhou, China) from July 2011 to January 2014, were reviewed. Patients with FAP or those have received chemotherapy or radiotherapy before surgery were not included. All patients were analyzed for expression of MMR proteins (MLH1, MSH2, MSH6, and PMS2) by IHC and relevant clinicopathological details were documented. For individuals without expression of MLH1, screening for *BRAF* gene mutation was performed.

RESULTS: There were 180 patients (13%) failed to express MMR proteins staining by IHC, which means deficient MMR (dMMR) status. The mean age of these patients were 55 years old and 116 patients (64%) were male. MMR proteins deficiency is more common in proximal colon and patients with right hemicolon carcinoma showed more dMMR status than tumors in left side (26.5% *vs.* 7.5%). Among these patients, 5 patterns of MMR IHC were identified: MLH1 loss alone or with PMS2 (n =74, 41.2%), MSH2 loss alone or with MSH6 (n =39, 21.7%), isolated PMS2 loss (n=13, 7.2%), isolated MSH6 loss (n=38, 21.1%), and others (ie, loss of unpaired MMR proteins or all four proteins, n = 16, 8.9%).This is inconsistently with the previous reports for western populations. The proportion of dMLH1 was lower, while dMSH6 was significantly higher. Further evaluation of *BRAF* gene for dMLH1 patients demonstrated that only 9% of the cases were mutated type, which is much lower than reports from western country.