S9 - Detection of Methylated Septin 9 DNA in Blood for Diagnosis, Prognosis and Surveillance of Patients with Colorectal Cancer

LEUNG Wai-keung
Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Background: With the increasing incidence and mortality of colorectal cancer (CRC), early and accurate diagnosis is of paramount priority to combat this cancer. Epigenetic alterations such as DNA methylation are innovative biomarkers for CRC, due to their stability, frequency, and accessibility in bodily fluids. In particular, detection of methylated septin 9 (mSPET9) DNA in blood was recently approved by the Food and Drug Administration of the United States for the screening of CRC.

Aim: To evaluate the role of detecting methylated SEPT9 in blood for diagnosis, prognosis and surveillance of patients with CRC.

Method: Blood samples were prospectively collected from patients scheduled for colonoscopy in our hospital or newly diagnosed to have CRC. For cancer patients, blood was taken immediately before and serially after resection of the primary tumor. Blood samples were processed for the determination of mSEPT9 and carcinoembryonic antigen (CEA) in a blinded manner. mSEPT9 DNA was determined by a commercially available assay (Epi proColon 2.0, Epigenomics, Germany).

Results: A total of 282 patients (117 CRC, 45 with advanced colorectal adenoma, 50 with non-advanced adenoma and 70 normal control) were included. The overall sensitivity of using mSEPT9 methylation status for diagnosing CRC was significantly higher than using elevated CEA levels (73.2% vs 48.2%; p value < 0.001). The sensitivities of both tests increased with more advanced tumor staging (mSEPT9: $P = 0.004$ and CEA: $P = 0.04$). Combined mSEPT9 and CEA had higher accuracy than single CEA or mSEPT9 ($P = 0.009$ and 0.532 separately). An increase in the methylation level of mSEPT9 detected in the post-operative samples was associated with a higher mortality rate (15.2% vs 1.8%; $P = 0.024$) and the presence of metastasis (27.3% vs 7.0%; $P = 0.013$).

Conclusions: mSEPT9 was more sensitive than CEA for diagnosing CRC, and combined mSEPT9 and CEA was even more sensitive for CRC. After curative resection, detection of increased mSEPT9 methylation level may indicate adverse outcomes.

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