

Metabolic surgery reduces CRC disease progression mediated by circulating bile acid diversion

Obesity is a global epidemic characterized by energy disequilibrium, metabolic disorders, and fat mass development that greatly affect the health status of individuals. There is evidence that the intake of a high-fat diet and overweight are associated with the incidence of colorectal cancer (CRC). Metabolic surgery has been associated with improvements in obesity-related comorbidities and a reduction in the overall cancer risk. However, the underlying mechanism by which metabolic surgery reduces the risk of CRC remains unknown. To understand the anti-tumoral mechanism of bariatric surgery, we analyzed the development of CRC after Roux-en-Y gastric bypass surgery (RYGB) in a RYGB-CRC mouse model. Here, we showed that RYGB surgery substantially reduced primary tumorigenesis and prevented metastasis. This protective effect was mediated by bile acid (BA) exclusion from the proximal small intestine, leading to BA diversion in the preceding parts of the gastrointestinal tract and in circulation. The diverted BA profile in RYGB mice showed anti-tumoral and anti-metastatic effects that were verified by BA exclusion of the proximal small bowel without the systemic metabolic installations of RYGB surgery by a cholecysto-intestinal shunt (CIS) surgery. RYGB surgery thus leads to reduced primary BAs and elevated secondary BAs in circulation. In a translational study involving patients with CRC with metachronous liver metastases (CRLM), we confirmed that reduced primary bile acid concentrations in the serum were associated with prolonged time to metastasis, underscoring the critical role of bile acids in CRC progression and metastatic development.

Preferred type of presentation

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