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Title of project: Colonic resection as diabetogenic risk factor: A Translational Research Study Exploring the Pathophysiological Effects of Colon Resection on Glucose homeostasis, Gastrointestinal Hormones, Microbiota, Visceral Fat Accumulation and Low-grade Inflammation in patients with colon cancer

ABSTRACT

Colon cancer (CC) survivors have an increased risk of developing type 2 diabetes (T2D). A recent study revealed that the surgical procedures per se may be causally involved. Hence, resection of the left part of the colon increased the risk of developing T2D. In addition, treatment with chemotherapy may play a role in the pathogenesis. Given the steadily improving survival rate after a CC diagnosis, prevention of secondary diseases such as T2D is important to improve quality of life in these patients and to reduce socioeconomic expenses. This study aims to elucidate the effects of tumor resection on the left part of the colon on pathophysiological intermediates, which may lead to T2D 12 months post-surgery or later. The physiological mechanism might be a changed postprandial secretion of gut hormones including glucagon-like peptide 1 (GLP-1) secreted from L-cells in the left part of the colon maybe stimulated by colonic contents. We will investigate changes in primarily glucose homeostasis as well as in gastrointestinal hormones, microbiota, visceral fat accumulation, markers of low-grade inflammation and appetite in CC survivors who underwent a left hemicolectomy or sigmoidectomy and compare the findings with those obtained after right hemicolectomy.

Material and Methods: 60 patients will be included in this explorative clinical study. Patients will be divided into 4 groups depending on surgical procedure and treatment with chemotherapy. In the group of patients undergoing left hemicolectomy or sigmoidectomy \pm treatment with chemotherapy 30 patients will be included, and in the group of patients scheduled to undergo right hemicolectomy \pm treatment with chemotherapy 30 patients will be included. During the 3 study visits (before surgery, 2-4 weeks post-surgery and 12 months post-surgery) the following test will be performed: An oral glucose tolerance test, blood and fecal sampling, a DXA scan and an ad libitum meal test.

Implications: With this study we expect to obtain an insight in the pathogenesis behind the possible development of T2D in CC survivors who underwent a resection of the left part of the colon \pm treatment with chemotherapy. This insight may also help scientists develop new ways of treating or preventing T2D in general.