Colorectal cancer and surgery - insights into insulin resistance and inflammatory markers

av

Bayar Baban

Akademisk avhandling

Avhandling för Medicine doktorsexamen i medicinsk vetenskap med inriktning mot kirurgi, som kommer att försvaras offentligt fredag den 15 mars 2024 kl. 13.00, Campus USÖ X4425, Örebro universitet

Opponent: Professor Ismail Gögenur
Department of Surgery
Center for Surgical Science
Zealand University Hospital
Department of Clinical Medicine
University of Copenhagen

Örebro universitet
Institutionen för medicinska vetenskaper
701 82 ÖREBRO
Abstract
The art of surgery has progressively extended from the realm of anatomy to encompass physiology and beyond, in search of further refinement and optimal recovery. Integral to this is a deeper understanding of the body's essential metabolic and inflammatory responses to surgical trauma.

This thesis aims to provide insights into the intricate interplay between insulin resistance, inflammation and surgical interventions in colorectal cancer patients, as each has an influence on postoperative recovery. Particular emphasis is placed on the role of inflammasomes - central mediators of the innate immune response, adapt at detecting and responding to a diverse range of triggers, yet insufficiently explored in these specific contexts.

Study I is a comparative analysis of the hyperinsulinemic euglycemic clamp and Homeostatic Model Assessment (HOMA) in determining postoperative insulin resistance in 113 patients undergoing various elective surgeries. The findings establish the clamp as the accurate method, detecting key physiological distinctions missed by the Homeostatic Model Assessment.

Study II, an exploratory case-control study, assesses insulin sensitivity and inflammatory markers in 20 colorectal cancer patients compared to 10 matched healthy controls. Results indicate insulin resistance, reduced inflammasome activity in circulating immune cells, and elevated systemic IL-1β and IL-6 levels in patients.

Study III, a pilot exploratory study of 17 patients from Study II, assesses the impact of surgical technique, open versus minimally invasive surgery, on postoperative insulin resistance and inflammation in colorectal cancer resections. It indicates a differential inflammatory response with higher levels in open surgeries, yet a consistent degree of insulin resistance across both surgical techniques.

Study IV explores the perioperative temporal sequencing of inflammation and inflammasome action in 18 patients from Study II undergoing elective colorectal cancer resections. It points to a more immediate and pronounced inflammatory response in open surgery compared to minimally invasive surgery, though both techniques show reduced intraoperative caspase-1 activity.

In conclusion, the hyperinsulinemic euglycemic clamp is the accurate method in determinations of postoperative insulin resistance. Patients with colorectal cancer, in comparison to matched healthy controls, exhibit insulin resistance and higher levels of inflammation, but decreased inflammasome (caspase-1) activity in circulating immune cells. Finally, colorectal cancer resections induce both insulin resistance and inflammation, however the surgical technique utilized only significantly affects the latter, with generally higher inflammatory / inflammasome responses in open.