AB074. Why 'Skinny-Fat' is bad for colorectal cancer: an analysis of body composition, the perioperative human metabolome and five-year colon cancer outcomes

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Background: High visceral adiposity (VA) and low skeletal muscle area (SMA) are poor prognostic factors in many cancers. In this study we aimed to characterise the perioperative human metabolome (combined end-product of cellular metabolism) in differential body compositions and correlate preferential metabolic pathways to five-year cancer outcomes.

Methods: Patients undergoing elective resection for non-metastatic colon cancer were prospectively enrolled. Serum samples were phlebotomised at three time points: (I) pre-operatively (PreOp); (II) 24 hours post-op (24 hrs); (III) post-operative day five (POD5). Body composition was defined radiologically on pre-operative computerized tomography (CT) using Horos (Horos Project 2015) and gender-specific validated cut-off points used. The metabolome was extracted from serum samples using a modified Bligh-Dyer technique followed by online derivatisation using GC-mass spectrometry for targeted analysis. Data processing was performed using WiPP (Workflow for Improved Peak Picking) followed by standard post-processing statistical analysis.

Results: Twenty four patients were analysed. Among these, 75% (n=18) were male, 25% (n=6) were female, median age was 62 years. Median follow-up was 72 months (IQR, 62). Four patients (16.7%) developed recurrence by five years and there were three (12.5%) disease-specific mortalities. The perioperative metabolome in high VA showed a significant preference for anaerobic metabolism compared to normal VA levels PreOp (P=0.04), at 24 hrs (P<0.001) and on POD5 (P=0.002). Similar trends were observed in low SMA. Furthermore, pre-operatively this was significantly associated with disease recurrence [HR 1.4 (09.0–1.9), P=0.002] and disease-specific mortality [HR 1.6 (0.8–2.2), P<0.001].

Conclusions: Patients with high visceral adiposity and low muscle mass metabolise through altered anaerobic metabolic pathways compared to preferred balanced central carbon metabolism in the perioperative period from pre-op to POD5 and this is associated with worse five-year cancer outcomes.

Keywords: Peri-operative; colorectal cancer; metabolomics; cancer outcomes