Visceral obesity alters expression of inflammatory mediators in patients undergoing gastrointestinal resection

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Visceral adipose tissue fuels a state of chronic inflammation\(^1\) and has been identified as a risk factor for post-op complications\(^2\). In this study we first aimed to retrospectively investigate the association between visceral obesity and post-op inflammation using the markers CRP and CRP:albumin ratio. Secondly, we aimed to identify additional inflammatory mediators that are differentially regulated in viscerally obese patients post-op using prospectively recruited patients.

Retrospectively, visceral fat area (VFA) was calculated from diagnostic CT scans of gastrointestinal cancer patients undergoing resection \((n = 324)\). Visceral obesity was classified as a VFA \(> 130 \text{ cm}^2\)\(^3\). CRP and albumin levels pre-op and at days 1, 3, 7 and 14 post-op were obtained from the laboratory database. As part of ongoing prospective studies, peripheral blood mononuclear cells (PBMC), serum and plasma samples are collected on oesophageal adenocarcinoma patients pre-op and on days 1, 3, 7 and 14 post-op. In a test cohort of 3 non-obese and 3 obese patients, PBMC collected pre-op and on days 1 and 7 post-op were analysed for expression of 370 genes involved in acute inflammatory response using a PCR based array. Circulating levels of TNF-\(\alpha\), IL-6, IL-8 and IFN-\(\gamma\) were measured by ELISA in 12 non-obese and 16 obese patients at all time points. In all cases \(p < 0.05\) was considered statistically significant.

Following resection, visceral obesity was significantly associated with higher CRP on days 1, 3, 7 and 14 post-op and higher CRP:albumin ratio on day 3 post-op \((p < 0.05)\). Higher circulating levels of TNF-\(\alpha\), IL-6, IL-8 and IFN-\(\gamma\) were observed in obese compared to non-obese patients on day 1 post-op but these differences were not significant. The inflammatory array revealed an up-regulation on post-op day 1 in IL-6 expression \((> 7\text{-fold})\) in PBMC from obese compared to non-obese patients. In addition, members of the TNF super family, TNFSF14 and lymphotoxin-\(\gamma\), which induce inflammatory cytokine production and NFkB activation, were up-regulated in obese \((> 5\text{-fold and} > 2\text{-fold respectively})\) compared to non-obese patients.

Excess visceral adiposity significantly alters the acute inflammatory response post-op. Inflammatory mediators such as IL-6, TNFSF14 and lymphotoxin-\(\beta\) may prove important targets for pharmacotherapy and immunonutrition to improve post-op outcomes in obese patients.