

## **Abstract**

The cluster of obesity, insulin resistance and other associated comorbidities represents a significant health risk for the affected individuals as well as the whole population. Chronic low-grade inflammation of adipose tissue is considered one of the main mechanisms responsible for the progression from simple obesity to a fully developed metabolic syndrome. The aim of our study was to explore two different approaches that could potentially ameliorate adipose tissue inflammation – therapeutic hypothermia and the adipocytokine clusterin.

In the first part, we showed that a period of deep hypothermia associated with the anoxic phase of cardiac surgery significantly delayed the onset of systemic inflammatory response induced by surgery. The relative gene expression of the studied genes was not altered during the hypothermic period, but was significantly increased in five out of ten studied genes (IL-6, MCP-1, TNF- $\alpha$ , HIF1- $\alpha$ , GLUT1) and decreased in two genes (IRS1, GPX1) at the end of surgery. We conclude that deep hypothermia delays the onset of local adipose tissue hypoxia and inflammation. These results could partially explain the positive effects of therapeutic deep hypothermia on postoperative morbidity and mortality in cardiac surgery patients.

In the second part, we examined plasma levels and mRNA expression of the adipocytokine clusterin in subcutaneous adipose tissue and its relation to insulin resistance and obesity. We also evaluated the influence of selected weight reducing interventions including very low-calorie diet (VLCD) and bariatric surgery (sleeve gastrectomy). Plasma clusterin levels did not differ between healthy individuals and obese patients with or without type 2 diabetes mellitus (DM2) and were affected only partially by short-term weight reduction. On the other hand, mRNA expression of clusterin in subcutaneous adipose tissue was higher in obese subjects with and without DM2 compared to healthy lean subjects and it decreased after bariatric surgery, but not after VLCD. Clusterin mRNA expression was positively associated with markers of obesity, serum triglycerides, fasting insulin, HOMA-IR index and concentrations of CRP. Plasma clusterin levels were not influenced by hyperinsulinemic euglycemic clamp (HEC) and did not correlate with insulin sensitivity index. mRNA expression of clusterin was elevated at the end of HEC compared to baseline only in the normoglycemic, but not in the IGT or T2DM patients. In summary, our data suggest a possible local regulatory role for clusterin in the adipose tissue rather than its systemic involvement in the regulation of energy homeostasis.

**Key words:** Adipose tissue, subclinical inflammation, insulin resistance, hypothermia, clusterin.