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# Leukocyte Transcriptome Analysis of Patients with Obesity-Related High Output Heart Failure

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**Abstract :** High output heart failure (HOHF) is characterized a high output state resulting from an underlying disease process and is commonly caused by obesity. As obesity levels increase, more individuals will be at risk for obesity-related HOHF. However, the underlying pathophysiologic mechanisms of obesity-related HOHF are not well understood and need further research. The aim of the study was to describe the differences in leukocyte transcriptomes of morbidly obese patients with HOHF and those with non-HOHF. In this cross-sectional study, the study team collected blood samples, demographics, and clinical data of six patients with morbid obesity and HOHF and six patients with morbid obesity and non-HOHF. The study team isolated the peripheral blood leukocyte RNA and applied stranded total RNA sequencing. Differential gene expression was calculated, and Ingenuity Pathway Analysis software was used to interpret the canonical pathways, functional changes, upstream regulators, and mechanistic and causal networks that were associated with the significantly different leukocyte transcriptomes. The study team identified 116 differentially expressed genes; 114 were upregulated, and 2 were downregulated in the HOHF group (Benjamini-Hochberg adjusted p-value ≤ 0.05 and log2(fold-change) of ±1). The differentially expressed genes were involved with cell proliferation, mitochondrial function, erythropoiesis, erythrocyte stability, and apoptosis. The top upregulated canonical pathways associated with differentially expressed genes were autophagy, adenosine monophosphate-activated protein kinase signaling, and senescence pathways. Upstream regulator GATA Binding Protein 1 (GATA1) and a network associated with nuclear factor kappa-light chain-enhancer of activated B cells (NF-kB) were also identified based on the different leukocyte transcriptomes of morbidly obese patients with HOHF and non-HOHF. To the author's best knowledge, this is the first study that reported the differential gene expression in patients with obesity-related HOHF and demonstrated the unique pathophysiologic mechanisms underlying the disease. Further research is needed to determine the role of cellular function and maintenance, inflammation, and iron homeostasis in obesity-related HOHF.

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