Esophageal cancer is a disease in which malignant (cancer) cells form in the tissues of the esophagus. Smoking, heavy alcohol use, and Barrett esophagus can increase the risk of esophageal cancer. Signs and symptoms of esophageal cancer are weight loss and painful or difficult swallowing.

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Obesity is a strong risk factor for esophageal adenocarcinoma (EAC). Nevertheless, not all patients with EAC are obese, and a substantial proportion of obese patients don't suffer from poor prognoses. The mechanisms behind the "obesity paradox" that uncouple obesity from dismal outcomes in EAC are unclear. This study aimed to explore the "obesity-guarding" genes (OGG) profiles and their prognostic values in patients with EAC. Methods: Gene expression data and clinical information of patients with EAC were downloaded from The Cancer Genome Atlas (TCGA) database. Enrichment analysis was used to explore the OGG functions and pathways. Cox regression analysis and nomogram model were performed to investigate the OGG prognostic values for overall survival (OS). In addition, relations between OGG and immune cells were assessed by the "CIBERSORT" algorithm and the Tumor IMmune Estimation Resource (TIMER) tool. Finally, the results were experimentally validated in a real-world study. Results: A total of 69 OGG were retrieved, and 17 significantly differentially expressed genes (SDEG) were identified between normal and EAC tissues. Enrichment analysis showed the OGG were enriched in the mitochondrion-related and various receptor pathways. Univariate Cox regression results showed that the MCM6, ATXN2, and CSK were significantly associated with OS (P=0.036, 0.039, 0.046, respectively). Multivariate Cox regression analysis showed MCM6 and CSK were independent prognostic genes for OS (P=0.025, 0.041, respectively). Nomogram demonstrated that the OGG had good predictive abilities for the 1-, 2-, and 3-year OS. Immunity analysis demonstrated that OGG were significantly associated with immune cells (P <0.05). In addition, clinical correlation analysis revealed that the OGG had significant relations with clinical parameters (P <0.05). The experiment results confirmed that the SDEG were significantly different between normal and EAC tissues (P <0.05). Conclusions: We identified the OGG expression profiles that may uncouple obesity from poor survival in patients with EAC. They have prognostic values in predicting patients' OS, and may be exploited for prognostic biomarkers [1].

[1]

Zhu L, Yang F, Dong L, Wang G, Li Q, Zhong C. Novel evidence of obesity paradox in esophageal adenocarcinoma: perspective on genes that uncouple adiposity from dismal outcomes. J Cancer. 2022 Jan 1;13(2):436-449. doi: 10.7150/jca.65138. PMID: 35069893; PMCID: PMC8771516.

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