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Plasma Extracellular Vesicles Reflect Immune Alterations in Morbid Obesity and Are Modified by Bariatric Surgery

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INTRODUCTION & AIM

Obesity is a major public health challenge of the 21st century and a growing global epidemic, projected to affect 51% of the world's population within the next decade. Morbid obesity, defined as a body mass index (BMI) of 40 kg/m² or higher, is the most prevalent chronic metabolic disease in developed countries and is associated with numerous comorbidities. Its management involves lifestyle modifications, including dietary changes, increased physical activity, and behavioral adjustments. When these measures prove insufficient, bariatric surgery becomes the most effective treatment for significant and sustained weight loss.

The rising prevalence of obesity is driven by complex genetic, environmental, and behavioral factors. In addition to its systemic effects, obesity triggers chronic low-grade inflammation, leading to cellular and molecular alterations that impact overall health. In this context, extracellular vesicles (EVs) have gained significant attention due to their role in intercellular and interorgan communication, as well as in the regulation of metabolic processes. These nanostructures, released by all cell types, carry bioactive cargo such as proteins, which can modulate the function of recipient cells. EVs also act as mediators of inflammation, and their composition is influenced by the originating cell type and its physiological state.

This study aimed to characterize EVs isolated from plasma and assess the presence of immune cell markers in plasma-derived EVs from patients with morbid obesity before and after bariatric surgery, as well as in healthy controls.

METHOD

Patients with morbid obesity (BMI > 40, aged 30–60) from the surgical obesity treatment program at Hospital Clínico de Valencia, along with healthy controls, were recruited. EVs were isolated from frozen plasma using size-exclusion chromatography (qEV2 70 nm, IZON) and characterized by electron microscopy, nanosight, and western blot. Immune cell markers were also analyzed by western blot.

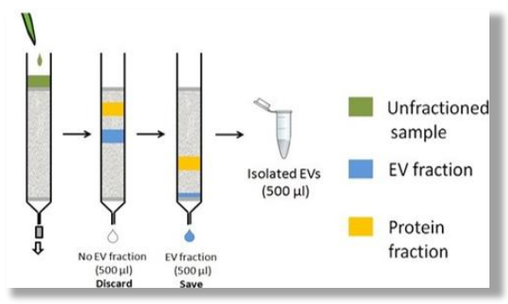

Figure 1. Plasma-derived extracellular vesicles (EVs) were isolated by size-exclusion chromatography using IZON columns with a 70 nm cutoff.

CONCLUSION

Our findings show that plasma EVs from patients with morbid obesity express both general EV markers and specific markers related to their cellular origin. EV numbers significantly decreased after bariatric surgery. Immune-related EVs showed altered profiles in obesity, with most markers reduced and normalized post-surgery—except for proinflammatory monocytes and APCs, which were elevated in obesity and returned to baseline after surgery. Adiponectin was decreased and perilipin increased in obesity; both tended to normalize six months post-surgery. These findings suggest that plasma EVs may serve as potential biomarkers for tracking metabolic alterations and immune changes in obesity and after bariatric surgery. Further research is warranted to better understand their functional role

RESULTS

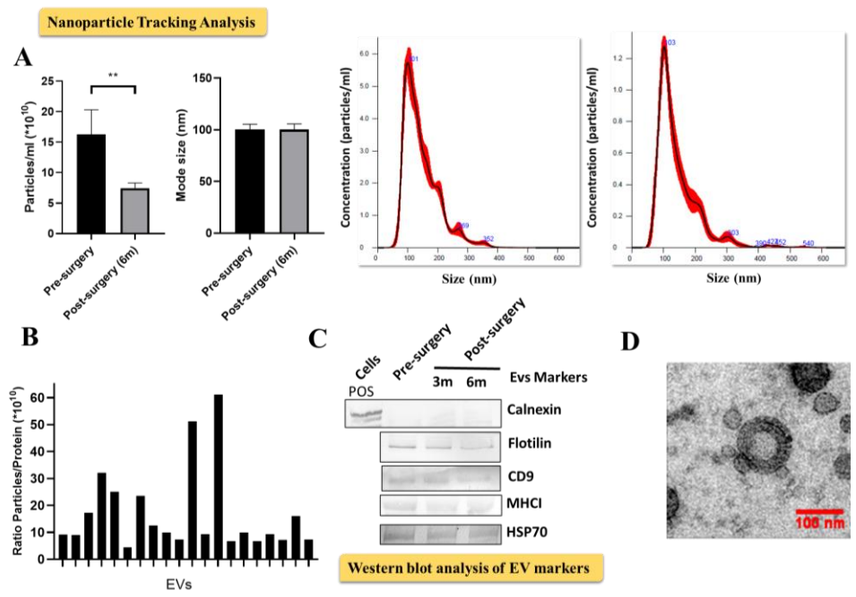

Figure 2. Characterization of extracellular vesicles isolated from the plasma of patients with morbid obesity before and after bariatric surgery. (A) Particle concentration (particles/mL), mode particle size (nm), and representative particle size distribution profiles measured by nanoparticle tracking analysis (NTA) before and after surgery. B) Ratio of total particle number to protein content (particles/mg protein) for each sample. Total particle and protein content were normalized to the initial plasma volume used for EV isolation (2.5 mL), consistent across all samples. (C) Representative Western blot analysis showing the presence of EV markers: calnexin, flotillin-2, CD9, MHCI, and HSP70. (D) Representative transmission electron microscopy (TEM) images of EVs after negative staining. Data are presented as mean ± SEM (n= 10 per group). Statistical analysis was performed using the Wilcoxon signed-rank test. Significant differences from the pre-surgery group are indicated with an asterisk (*); **p < 0.01.

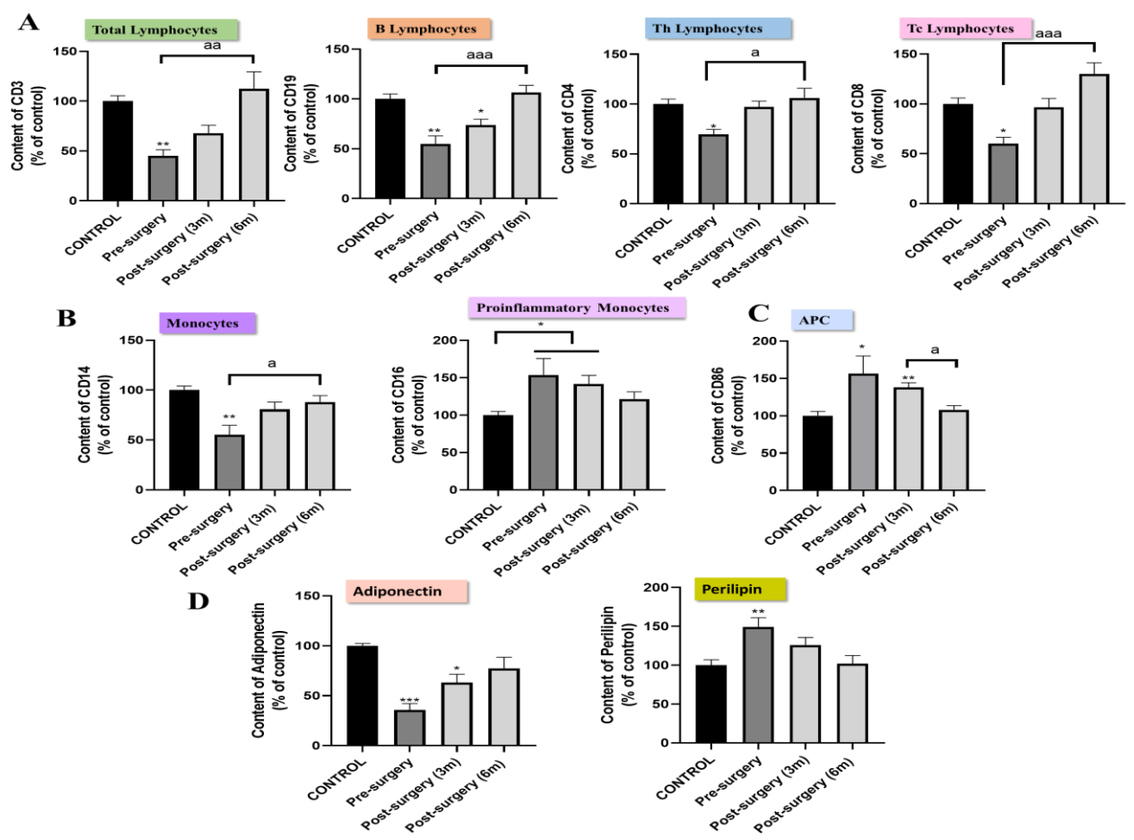

Figure 3. Protein cargo of extracellular vesicles (EVs). (A) Levels of markers related to total lymphocytes (CD3) and specific lymphocyte subtypes: B lymphocytes (CD19), T helper cells (CD4), and cytotoxic T cells (CD8). (B) Levels of monocyte markers: CD14 (total monocytes) and CD16 (proinflammatory monocytes). (C) Levels of the antigen-presenting cell (APC) marker. (D) Levels of adiponectin and perilipin. Markers in panels A–C are associated with immune cells, while those in panel D are related to adipose tissue function and metabolism. Values are expressed as a percentage relative to the control group and represent the mean ± SEM. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test. Significant differences vs. the control group are indicated with an asterisk (*); differences vs. other patient groups are indicated by a (*/a: p < 0.05; **/aa: p < 0.01; ***/aaa: p < 0.001).

ACKNOWLEDGEMENTS

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