"A Comprehensive Preclinical Model of Postmenopausal Cardiometabolic Dysfunction: Combining Estrogen Depletion, Obesity, and Diabetes in Female Wistar Rats"

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Abstract:

Background: Cardiovascular diseases represent the primary cause of mortality in postmenopausal women, largely attributable to metabolic conditions such as obesity and diabetes mellitus. The absence of a robust preclinical model that incorporates these risk factors impedes progress in cardiovascular research. This study sought to establish and validate a multifactorial preclinical cardiometabolic disease model in 12 female Wistar rats, integrating ovariectomy-induced estrogen depletion, high-fat diet-induced obesity, and streptozotocin-nicotinamide-induced diabetes mellitus to simulate the cardiometabolic risk profile observed in postmenopausal women.

Methods: The model was established in three phases over 25 weeks: (i) Ovariectomy to mimic estrogen deficiency, (ii) High-fat diet administration to induce obesity, and (iii) Diabetes mellitus induction using streptozotocin (50 mg/kg) and nicotinamide (110 mg/kg). Metabolic, cardiovascular, and inflammatory markers were assessed, including fasting blood glucose, lipid profile, electrocardiogram abnormalities, cardiac injury biomarkers (Troponin T, CK-MB), insulin resistance (HOMA-IR), and inflammatory cytokines (IL-6, IL-1β, TNF-α).