Effect of a 3-week multidisciplinary body weight reduction program on the epigenetic age acceleration in obese adults.

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Obesity and aging share common molecular and cellular mechanisms underlying the pathophysiology of cardiovascular diseases (CVD), which occur frequently in both conditions. DNA methylation (DNAm) age, a biomarker of the epigenetic clock, has been proposed as a more accurate predictor of biological aging than chronological age. A positive difference between an individual's chronological age and DNAm age is referred to as epigenetic age acceleration. The objective of the present study was to evaluate the effects of a 3-week in-hospital body weight reduction program (BWRP) on the epigenetic age acceleration, as well as on other cardiometabolic outcomes, in a cohort of 72 obese adults (F/M: 43/29; (chronological) age: 51.5 ± 14.5 yrs; BMI: 46.5 ± 6.3 kg/m^2). At the end of the BWRP, when considering the entire population, BMI decreased, and changes in body composition were observed. The BWRP also produced beneficial metabolic effects as demonstrated by decreases in glucose, insulin, HOMA-IR, total cholesterol, and LDL cholesterol. A post-BWRP improvement in cardiovascular function was also evident (i.e., decreases in systolic and diastolic blood pressures and heart rate). The BWRP reduced some markers of systemic inflammation, particularly C-reactive protein (CRP). Finally, vascular age (VA) and Framingham risk score (FRS) were reduced after the BWRP. When considering the entire population, DNAm age and epigenetic age acceleration did not differ after the BWRP. However, when subdividing the population into two groups based on each subject's epigenetic age acceleration (i.e., ≤0 yrs or >0 yrs), the BWRP reduced the epigenetic age acceleration only in obese subjects with a value > 0 yrs (thus biologically older than expected). Among all the single demographic, lifestyle, biochemical, and clinical characteristics investigated, only some markers of systemic inflammation, such as CRP, were associated with the epigenetic age acceleration. Moreover, chronological age was correlated with DNAm age and VA; finally, there was a correlation between DNAm age and VA. In conclusion, a 3-week BWRP is capable of reducing the epigenetic age acceleration in obese adults, being the BWRP-induced rejuvenation evident in subjects with an epigenetic age acceleration > 0 yrs. Based on the BWRP-induced decrease in CRP levels, chronic systemic inflammation seems to play a role in mediating obesity-related epigenetic remodeling and biological aging. Thus, due to the strong association of CVD risk with the epigenetic clock and morbidity/mortality, any effort should be made to reduce the low-grade chronic inflammatory state in obesity.