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D-galactose induced aging aggravates and accelerates the impairment of bone homeostasis in obesity

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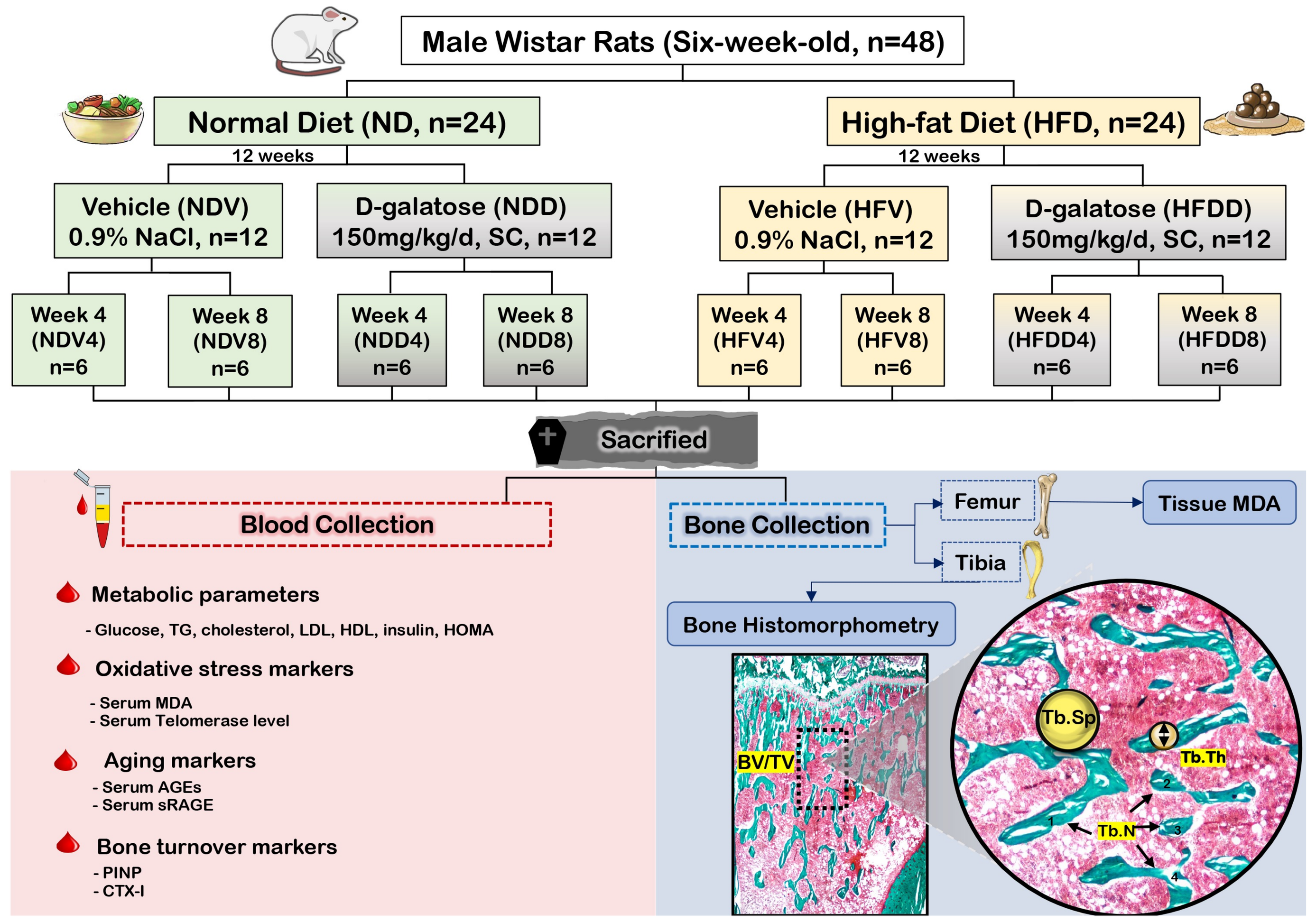
INTRODUCTION

Aging process is one of a critical factors leads to an imbalanced bone homeostasis, potentially resulting in osteoporosis and consequently increased risk of fracture. "Adipaging" is defined as a synergistic reciprocity of a combination of aging and obese conditions [1]. Several pieces of evidence have revealed that obesity exerts the effects consistent with all nine hallmarks of aging [2,3], However, the negative impact of adipaging on bone health has never been compared with either aging or the obese condition alone.

AIM

To compare the effects of obesity, aging induced by D-galactose (D-gal), and adipaging on bone homeostasis as indicated by the alterations of oxidative stress in bone, bone turnover, and bone architecture at the 2-time points of D-gal-induced aging.

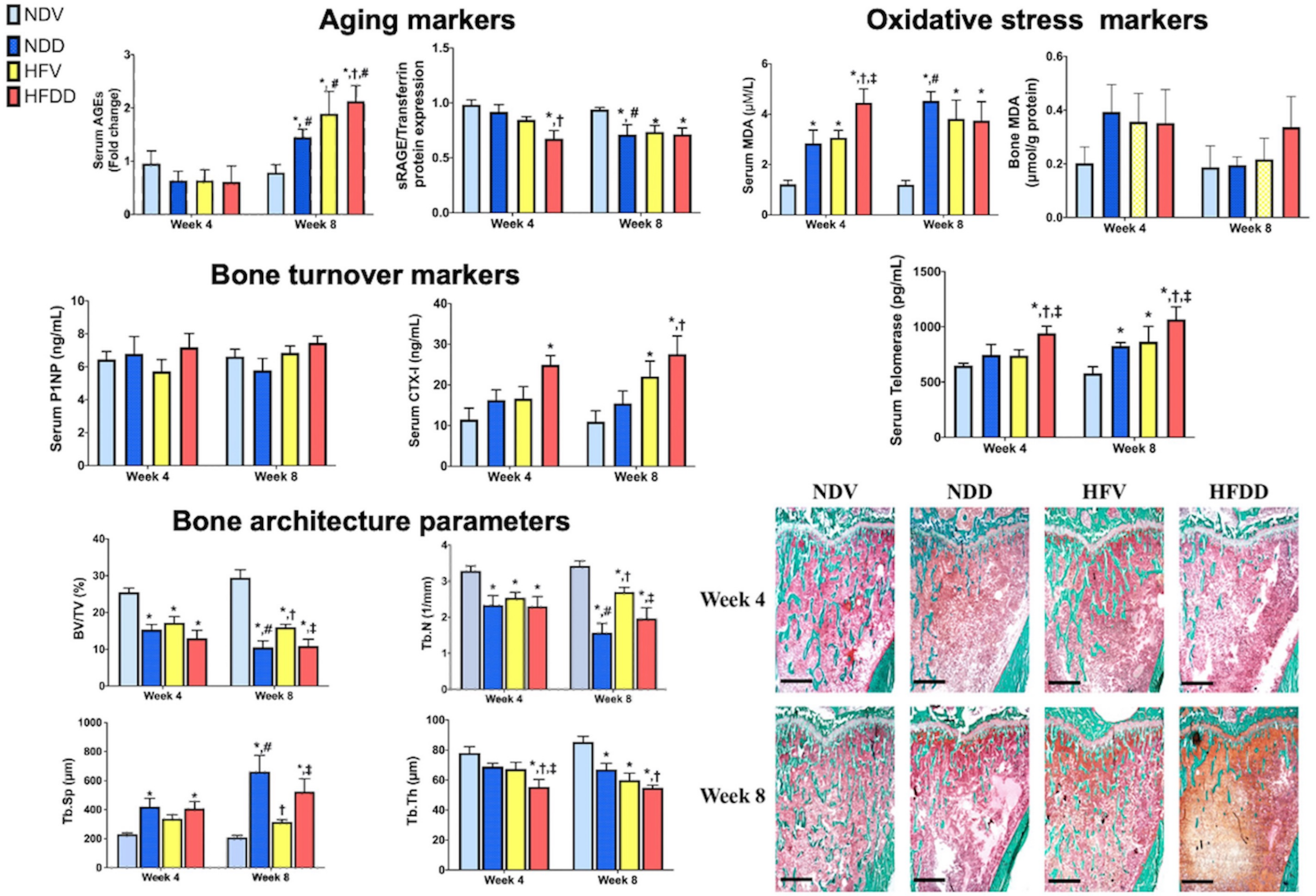
METHOD



RESULTS

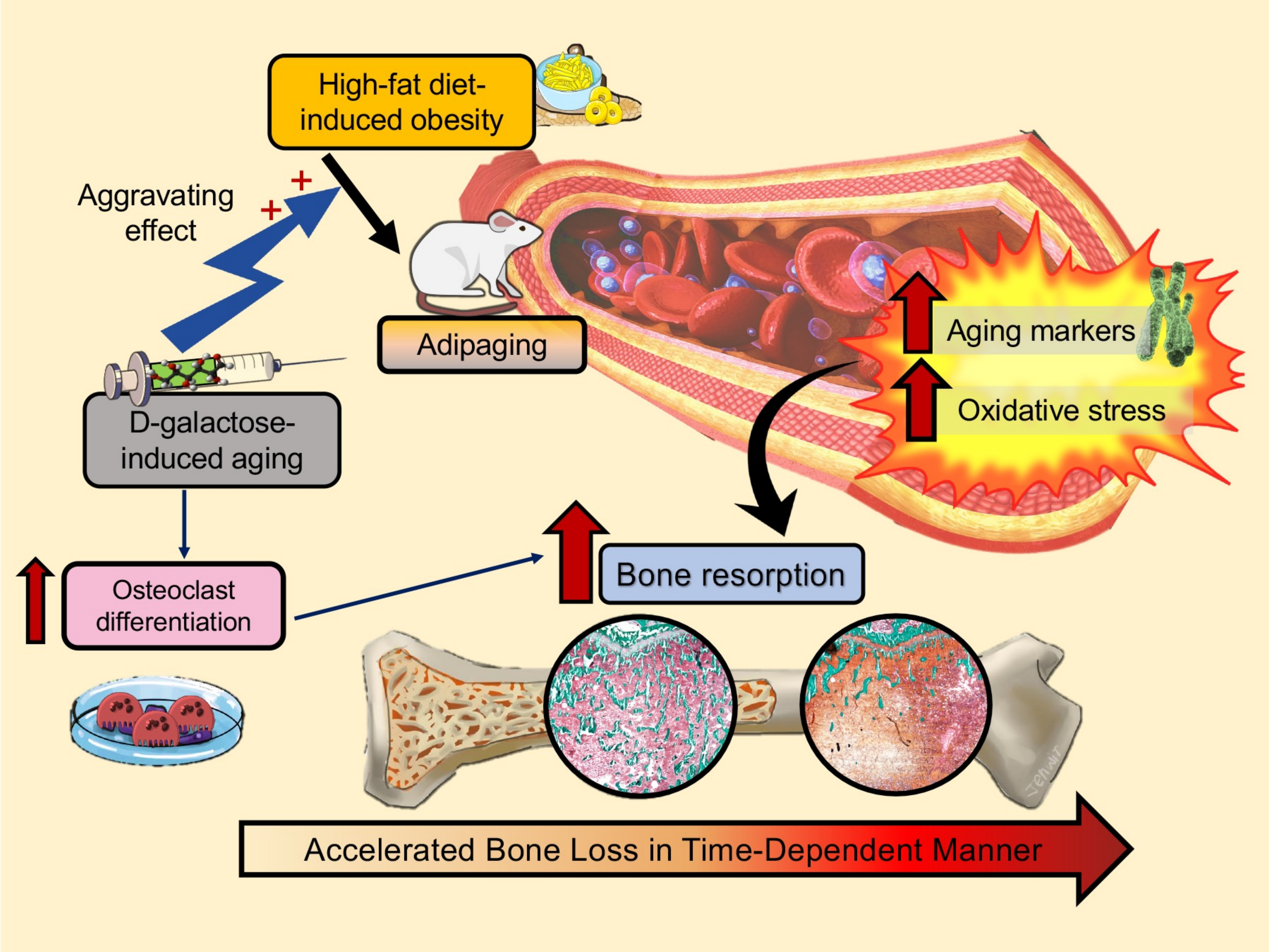
Table 1: Food intake, anthropometry, and metabolic parameters from an *in vivo* study.

Parameters	Week 4				Week 8			
	NDV	NDD	HFV	HFDD	NDV	NDD	HFV	HFDD
Food intake (g/day)	23.55 ± 1.1	22.98 ± 1.3	24.38 ± 0.8	23.42 ± 0.9	24.46 ± 1.1	23.74 ± 1.2	23.88 ± 0.8	24.53 ± 1.0
Body weight (g)	460 ± 11.5	472.7 ± 13.3	635.8 ± 6.5*†	638.9 ± 9.6*†	473.6 ± 8.4	479.7 ± 7.6	645.3 ± 8.7*†	655.7 ±15.2*†
Visceral fat weight (g)	19.75 ± 1.5	23.58 ± 1.1	47.26 ± 4.9*†	54.84 ± 4.2*†	22.86 ± 1.1	23.91 ± 1.2	54.98 ± 1.8*†	60.87 ± 2.5*†
Plasma glucose (mg/dL)	130.4 ± 4.7	128.9 ± 6.1	127.9 ± 5.08	129.7 ± 4.6	144.2 ± 9.1	141.9 ± 10.8	147.5 ± 12.4	145.8 ± 9.8
Plasma insulin (ng/ml)	4.26 ± 0.6	9.856 ± 1.9*	8.956 ± 0.9*	12.01 ± 1.4*	4.459 ± 0.9	11.34 ± 3.05*	10.57 ± 2.2*	12.84 ± 2.2*
AUC of glucose (mg/dl × min × 10^4)	2.34 ± 0.1	3.16 ± 0.1*	3.06 ± 0.3*	2.98 ± 0.8*	2.11 ± 0.2	3.07 ± 0.2*	3.09 ± 0.3*	2.77 ± 0.1*
HOMA-IR	19.28 ± 2.0	56.98 ± 4.2*	71.93 ± 4.1*	74.84 ± 9.2*	20.49 ± 2.2	97.17 ± 11.4*	93.20 ± 9.9*	79.13 ± 14.2*
Triglyceride (mg/dL)	89.87 ± 5.4	89.59 ± 2.9	87.04 ± 7.2	99.58 ± 1.6	86.82 ± 5.6	89.06 ± 3.1	84.42 ± 4.8	84.11 ± 3.8
Total cholesterol (mg/dL)	81.19 ± 4.0	84.11 ± 2.7	109.5 ± 14.9*†	105.7 ± 5.2*†	78.77 ± 5.7	80.35 ± 2.6	122.8 ± 4.9*†	112.1 ± 3.9*†
HDL cholesterol (mg/dL)	34.45 ± 1.3	32.7 ± 1.0	24.33 ± 1.0*†	24.72 ± 1.6*†	35.31 ± 0.9	33.32 ± 1.5	25.27 ± 2.5*†	24.0 ± 3.5*†
LDL cholesterol (mg/dL)	23.69 ± 3.5	25.77 ± 3.1	44.11 ± 5.0*†	42.32 ± 4.0*†	25.73 ± 2.1	26.59 ± 2.2	44.90 ± 4.4*†	48.13 ± 1.6*†



*Bar graphs presented as means ± SEM (n = 5-6/ group). * p<0.05 vs NDV at the same time point, † p<0.05 vs NDD at the same time point, ‡ p<0.05 vs HFV at the same time point, # p<0.05 vs same group at the different time point. AGEs, advanced glycation end products; CTX-I, C-terminal telopeptide of type I collagen; HFD, high-fat diet; HFDD, high-fat diet with D-galactose; HFV, high-fat diet with vehicle; MDA, Malondialdehyde; NDD, normal diet with D-galactose ; NDV, normal diet with vehicle; P1NP, procollagen type I N-terminal propeptide; sRAGE, soluble receptor for advanced glycation end products.*

CONCLUSIONS



Our results highlighted sequential metabolic and skeletal alterations in D-galactose-induced aging, obesity, and D-galactose plus HFD-induced adipaging. We clearly elucidated that obesity aggravated systemic aging, systemic oxidative stress, and bone dyshomeostasis in D-galactose-induced aging in a time-dependent manner. Therefore, early interventions, such as caloric restriction and exercise is considered highly beneficial to reduce adipaging-induced bone pathology.

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