

Comparative Effects of Different Immobilization Conditions on Cartilage Biomarkers

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INTRODUCTION: Immobilization occurring during hospitalization, postoperative recovery, or in elderly and critically ill individuals is associated with a range of physiological consequences, including muscle atrophy, bone demineralization, cardiovascular deconditioning, and metabolic alterations [1]. Moreover, immobilization is recognized as a significant risk factor for the development of osteoarthritis, primarily through the induction of catabolic processes within the joint that may lead to cartilage degradation [2]. Dry immersion (DI) is a validated and standardized ground-based model used to investigate the effects of mechanical unloading on musculoskeletal and joint integrity. As an alternative to the well-established head-down tilt bed rest (HDT) model, DI is increasingly employed in space medicine and musculoskeletal research to simulate the physiological effects of microgravity and disuse. Both DI and HDT models offer valuable insights into how immobilization influences cartilage metabolism. Cartilage oligomeric matrix protein (COMP) is a mechanosensitive serum biomarker that reflects early alterations in cartilage homeostasis and loading conditions [3]. Matrix metalloproteinase-3 (MMP-3), also known as stromelysin-1, is an enzyme that plays a key role in the breakdown of the cartilage extracellular matrix [4]. The aim of the present study was to examine how serum COMP and MMP-3 concentrations change following 5 days of immobilization induced by DI, compared to 5 days of HDT, in healthy male individuals.

METHODS: The DI study (Vivaldi 2 study) was conducted at the MEDES in Toulouse, France and the HDT study (Short-Term Bed Rest Artificial Gravity 2 (STBR-AG2)) was carried out at the DLR in Cologne, Germany. Only healthy men (DI: N=19, 28±4 years, 177±4 cm, 72±7 kg; HDT: N=10, 29±6 years, 179±4 cm, 78±4 kg) were involved in both studies due to a combination of physiological, methodological, and logistical factors. Both studies are composed of the following phases: a baseline data collection (BDC), 5 days of unloading (UL) using DI or HDT, and a recovery phase (R). Fasting venous blood samples were collected at BDC-26h, UL46h, UL118h, and during recovery (R+22h for HDT; R+46h for DI). Serum COMP and MMP-3 were measured using commercially available ELISA kits (COMP: BioVendor for DI, AnaMar for HDT; MMP-3: Quantikine), and values were normalized to BDC-26h (due to differing assay units for COMP). Independent two-tailed t-tests were used to compare groups at UL46h and UL118h.

RESULTS: In both unloading models, serum concentrations of COMP and MMP-3 decreased during the UL phase (Table 1). The reduction in COMP levels was more pronounced in the DI model compared to HDT. Following remobilization, serum levels of both COMP and MMP-3 increased in both the DI and HDT conditions and exceeded BDC levels.

DISCUSSION: DI and HDT induce similar changes in both serum COMP and MMP-3 concentrations, with a more marked response observed in the DI condition for serum COMP changes. The more pronounced reduction observed under DI conditions may be attributed to the presumably greater degree of immobilization compared to the HDT model [5]. A limitation of this analysis is that the original studies were not designed for direct comparison.

SIGNIFICANCE/CLINICAL RELEVANCE: Even brief periods of immobilization induce changes in biomarkers of cartilage metabolism indicating the induction of degenerative processes. This finding is supported by two studies utilizing distinct forms of immobilization.

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Table 1: Mean and 95% CI of serum biomarker concentrations at the different time points (separated for biomarkers and immobilization models).

Biomarker	Studies	BDC _{-26h}	UL _{46h}	UL _{118h}	R _{+46h} (DI) and R ₊₂₂ (HDT)
COMP [%]	DI	100	65.2 (58.9-72.6)	59.0 (53.4-64.6)	114.7 (104.8-124.7)
	HDT	100	77.4 (72.5-82.3)	84.9 (79.8-89.9)	110.2 (98.0-122.4)
p-value			p=0.01	p<0.001	
MMP-3 [%]	DI	100	80.1 (70.0-90.2)	81.7 (72.6-90.8)	124.3 (107.6-141.0)
	HDT	100	76.5 (69.7-83.3)	81.0 (75.9-86.1)	91.0 (81.4-100.6)
p-value			p=0.079	p=0.270	