Weight loss lead to significant effects on OA pain and function: Do the benefits outweigh the risks?

Bay-Jensen, A.C.[1], Mohamed, K.[1], Frederiksen, P.[1], Bihlet, A.R.[2], Thudium, C.S.[1], Henriksen, K.[1], Karsdal, M.A.[1]

[1]Nordic Bioscience, Herlev, Denmark,
[2]NBCD, Soeborg, Denmark

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BACKGROUND

Drug development in the osteoarthritis (OA) field has proven extremely difficult, with a discordance between joint structure and pain.

Weight loss has been associated with an effect on pain and function. Several molecular endotypes have been suggested for OA, which could be treatable, such as bone, inflammation, and lately, an overweight endotype.

The aim was to investigate the relationship between obesity, weight loss and patient-reported outcomes (PROs) in patients with persistent pain, and the effect on joint and bone tissue related soluble biomarkers.

METHODS

In this post-hoc exploratory analysis, 806 patients with persistent painful OA from oral salmon calcitonin (SMC) trials were included. From the original trials including 2,206 patients, 1,400 were excluded because of lack of persistent pain between screening and month 1, missing weight data at Year 2, or missing WOMAC records at baseline. All patients included had a Kellgren-Lawrence grade of 2 or 3. Patients were divided into lean, overweight, and obese based on their baseline BMIs and by whether the weight gain or loss was 5% or more over two years. Groups were compared using ANCOVA, adjusting for sex and race at the baseline and the sex, race, and treatment arm at follow-up.

RESULTS

Patients were primarily white females, with a median age and BMI of 64 years and 29 kg/m2.

The WOMAC total, function, and stiffness, but not pain, were significantly higher in obese than in overweight and lean patients.

WOMAC total, function, and pain significantly improved in patients losing weight or with stable weight compared to patients gaining weight (**table 1**).

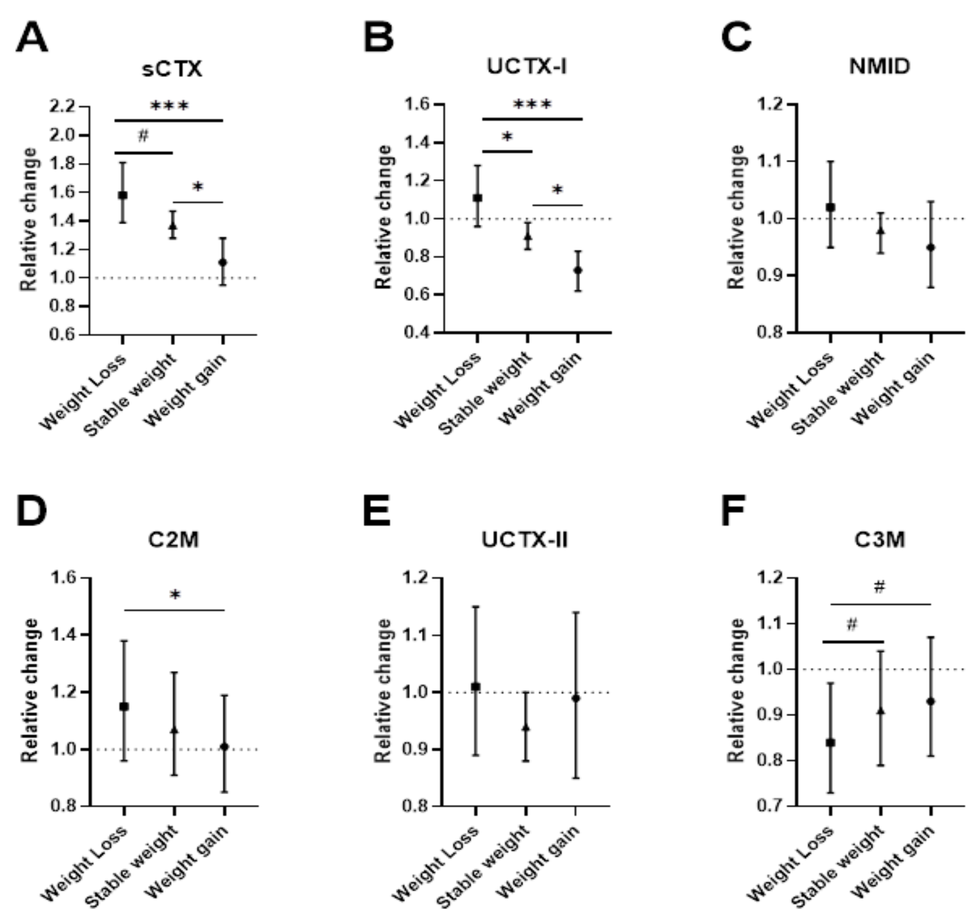
The bone resorption biomarker CTX-I increased 1.58-fold [95% CI 1.39, 1.81], 1.37-fold [1.28, 1.47] and 1.11-fold [0.95, 1.28] in the weight loss, stable and weight gain groups, respectively. The cartilage degradation marker C2M was increased by 1.15-fold [0.95, 1.39], while the interstitial matrix degradation markers C3M was decreased by 0.84-fold [0.73, 0.97] in the weight loss group (**figure 1**).

Table 1. Difference (contrast) in two-year change in WOMAC scores in patients with stable weight, weight loss and gain.

		Weight loss vs. Stable	Weight loss vs. Weight gain	Stable vs. Weight gain
Lean + Overweight	WOMAC total	-110 (-244, 24) 0.32	-18 (-210, 174) 1.0	92 (-60, 243) 0.70
	WOMAC function	-81 (-177, 15) 0.30	-20 (-158, 118) 1.0	61 (-48, 169) 0.81
	WOMAC stiffness	-8 (-21, 5) 0.75	-2 (-20, 17) 1.0	6 (-9, 20) 1.0
	WOMAC pain	-23 (-53, 6) 0.37	3 (-39, 46) 1.0	27 (-7, 60) 0.35
Obese	WOMAC total	-39 (-195, 117) 1.0	-357 (-584, -130) 0.006	-318 (-508, -128) 0.003
	WOMAC function	-31 (-144, 83) 1.0	-270 (-435, -105) 0.004	-239 (-377, -101) 0.002
	WOMAC stiffness	-0 (-14, 14) 1.0	-21 (-42, -0) 0.14	-21 (-39, -4) 0.054
	WOMAC pain	-5 (-39, 30) 1.0	-64 (-114, -14) 0.037	-59 (-101, -17) 0.017

The data are shown as LS-means with 95%CI. adjusted for race, sex, age, treatment arm, and corresponding baseline WOMAC score, the p-values are corrected for multiple comparisons by Bonferroni's method

Figure 1. Relative change from baseline to two years in blood and urine markers in patients that either lost or gained weight in patients with painful radiographic knee OA.



Data are shown as LS- means with 95% confidence intervals adjusted for baseline biomarker level, sex, race, and age. The p values are corrected for multiple comparisons by Bonferroni's method. Significance levels: #, p < 0.1; * p < 0.05; **, p < 0.01; ***, p < 0.001.

CONCLUSION

Changes in PROs were significantly associated with obesity. Weight loss was associated with an increase in bone and cartilage degradation, as well as lowering in the interstitial matrix degradation. These data indicate that weight loss comes with a risk of increased joint tissue loss, but improvement in tissue inflammation.

Contact: Dr. Anne Bay-Jensen MSc, PhD, acbj@nordicbio.com
Disclosures: The authors are employed at Nordic Bioscience and may be shareholders.