OBESITY – A KEY DRIVER IN OSTEOARTHRITIS

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BACKGROUND

Obesity is a contributing factor to many comorbidities, including osteoarthritis (OA). Patients with OA experience poor quality of life due to reduced functionality of their joints, which is mainly due to the painful symptoms associated with OA. Obesity worsens OA pain symptoms by increasing mechanical load and stress in addition to the elevated general inflammatory state. Moreover, this inflammatory drive is the prime suspect in the observed increased OA in non-weight-bearing joints of patients with obesity, such as the hands, suggesting systemic mechanisms are involved. Inflammatory mediators released by adipose tissue, including leptin, interleukin-6 (IL-6), and C-reactive protein (CRP), may contribute to heightened pain sensitivity and reduced pain thresholds in individuals with obesity.

There has been a recent surge in research focusing on the role of obesity in OA and how weight loss drugs can provide a valuable tool in improving patients' OA pain.

We aimed to investigate here the association between the painful experience and the body mass indices of patients at baseline in a previous phase III clinical trial. Furthermore, we evaluated the change in painful experience resulting from weight loss or gain after 2 years, as measured in the last follow-up of the clinical trial.

METHODS

A post-hoc analysis of a randomized, double-blind, 2-year multi-center OA trial (NCT00486434), using factorial ANCOVA. 1175 patients met the OA diagnostic criteria set by ACR at baseline with 674 patients having complete pain data for the follow up analysis of weight loss or gain after 2 years. In the follow up the effect of 5% weight loss/gain on change in WOMAC scores after 2 years.

RESULTS

Association between BMI and WOMAC scores

	All participants	<25 kg/m²	25 - 30 kg/m²	30 - 35 kg/m²	>35 kg/m²
Target knees	1175	226	526	302	121
Nontarget knees	1156	226	517	299	114
Age, years	64. (59.6, 69.1)	64.9 (59.9, 68.7)	64.7 (59.7, 69.2)	64.8 (59.6, 69.6)	63.2 (58.5, 67.4)
Sex, female	804 (68.4%)	172 (75.8%)	320 (60.8%)	215 (71.2%)	97 (80.2%)
Race					
Asian	104 (8.8%)	49 (21.6%)	47 (8.9%)	8 (2.6%)	0
White	1071 (91.1%)	178 (78.4%)	478 (90.9%)	294 (97.4%)	121 (100%)
Other	1 (0.09%)	0	1 (0.2%)	0	0
BMI, kg/m²	28.4 (25.7, 31.6)	23.4 (22.5, 24.3)	27.5 (26.2, 28.8)	32 (30.9, 33.4)	37.5 (35.9, 39.5)
Kellgren-Lawrence grade					
Target					
2	1032 (87.8%)	208 (91.6%)	464 (88.2%)	256 (84.8%)	104 (86%)
3	144 (12.2%)	19 (8.4%)	62 (11.8%)	46 (15.2%)	17 (14%)
Kellgren-Lawrence grade					
Nontarget					
0	36 (3.1%)	6 (2.7%)	20 (3.9%)	6 (2%)	4 (3.4%)
1	229 (20.0%)	56 (24.9%)	110 (21%)	49 (16.6%)	14 (12.7%)
2	633 (55.3%)	133 (59.1%)	281 (54.7%)	170 (57.4%)	49 (44.5%)
3	215 (18.8%)	28 (12.4%)	87 (16.9%)	61 (20.6%)	39 (35.5%)
4	32 (2.8%)	2 (0.9%)	16 (3.1%)	10 (3.4%)	4 (3.6%)
Target knee WOMAC score					
WOMAC total, 2400 points	1097 (851, 1395.8)	1027 (830, 1342)	1070.5 (848, 1392)	1180.5 (866, 1420)**	1201 (928.3, 1491.5)**
WOMAC function, 1700 points	781 (595.3)	735.5 (557, 961)	757 (585, 994)	836 (617, 1021)*	845 (639.5, 1077)**
WOMAC pain, 500 points	228.5 (179, 286.5)	220 (172.3, 274.5)	228.5 (180, 284)	232 (189, 291)	239 (180.8, 287)
WOMAC stiffness, 200 points	100 (65, 131)	93 (57, 129.8)	99 (66, 128)	104 (67, 134)	104 (64.3, 135)
Nontarget knee WOMAC score					
WOMAC total, 2400 points	888 (486.5, 1280)	798 (474, 1165)	880 (432, 1275)	916 (535, 1309)*	1061 (625, 1479)***
WOMAC function, 1700 points	640 (323, 931)	566 (306, 867)	627 (302.8, 922.3)	659 (393.8, 974.8)*	751 (448, 1066)***
WOMAC pain, 500 points	173 (90, 253.3)	159 (80, 239)	173 (83.8, 257.3)	177 (105, 246.8)	199 (110, 286)*
WOMAC stiffness, 200 points	75 (32, 117)	71 (29.5, 105.8)	74 (27.8, 115)	76 (34, 120.8)	94 (46, 135)*

Table 1. Patients in higher BMI ranges show higher WOMAC scores than lower BMI. Data presented as median (Q25, Q75) or number (percentage). Statistical significance *P <0.05 and **P <0.01 vs. <25 kg/m2 and #P <0.05 vs. 25 - 30 kg/m2 using ANCOVA test.

Baseline Characteristics of Patients Before Weight Change

	All participants	>5% Weight Loss	≤5% Weight Loss or Gain	>5% Weight Gain
Target knees	674	100	518	56
Nontarget knees	671	99	516	56
Age, years	64.3 (59.6, 69.1)	64 (60, 69.8)	64.6 (59.8, 69.1)	62.5 (58.1, 67.4)
Sex, female	433 (64.2%)	71 (71%)	325 (62.7%)	37 (66.1%)
Race				
Asian	42 (6.2%)	6 (6%)	36 (6.9%)	0
White	631 (93.6%)	94 (94%)	481 (92.9%)	56 (100%)
Other	1 (0.1%)	0	1 (0.2%)	0
BMI, kg/m²	29.5 (27.3, 32.6)	30.3 (27.8, 34.1)	29.3 (27.3, 32)	30 (27.4, 33.7)
Treatment				
Placebo	350 (51.9%)	44 (44%)	279 (53.9%)	27 (48.2%)
sCT	324 (48.1%)	56 (56%)	239 (46.1%)	29 (51.8%)
Kellgren-Lawrence grade				
Target				
Target				
2	580 (86.1%)	81 (81%)	448 (86.5%)	51 (91.1%)
3	94 (13.9%)	19 (19%)	70 (13.5%)	5 (8.9%)
Kellgren-Lawrence grade				
Nontarget				
0	19 (2.8%)	2 (2.1%)	14 (2.7%)	3 (5.5%)
1	117 (17.5%)	12 (12.4%)	95 (18.4%)	10 (18.2%)
2	376 (56.4%)	56 (57.7%)	297 (57.7%)	23 (41.8%)
3	133 (19.9%)	22 (22.7%)	97 (18.8%)	14 (25.5%)
4	22 (3.3%)	5 (5.2%)	12 (2.3%)	5 (9.1%)
Target knee WOMAC score				
WOMAC total, 2400 points	1125.5 (871, 1395)	1084 (849.5, 1373.5)	1121.5 (871, 1394)	1247.5 (961.5, 1418)
WOMAC function, 1700 points	799.5 (611, 1007)	779.5 (917, 1000.5)	789 (605, 1010)	882 (675, 1006)
WOMAC pain, 500 points	230.5 (184, 285)	217.5 (175.5, 284)	232.5 (184, 284)	246.5 (194, 304)
WOMAC stiffness, 200 points	103 (70, 132)	100 (57, 135)	103 (71, 132)	110 (82, 132.5)
Nontarget knee WOMAC score				
WOMAC total, 2400 points	875 (463, 1283)	890.5 (570, 1366)	862.5 (424, 1248)	1057.5 (532, 1382)
WOMAC function, 1700 points	628 (308, 940)	697.5 (413, 982)	614.5 (294, 916)	745.5 (298, 1000)
WOMAC pain, 500 points	172 (83, 251)	179 (110, 265)	168.5 (80, 245)	194.5 (112, 261)
WOMAC stiffness, 200 points	76 (30, 117)	76 (32, 115)	74 (30, 116)	92.5 (26, 123)

Table 2. Baseline characteristics of patients included in the post-hoc analysis. Data presented as median (Q25, Q75) or number (percentage).

Weight Loss is Associated with Lower Pain Scores

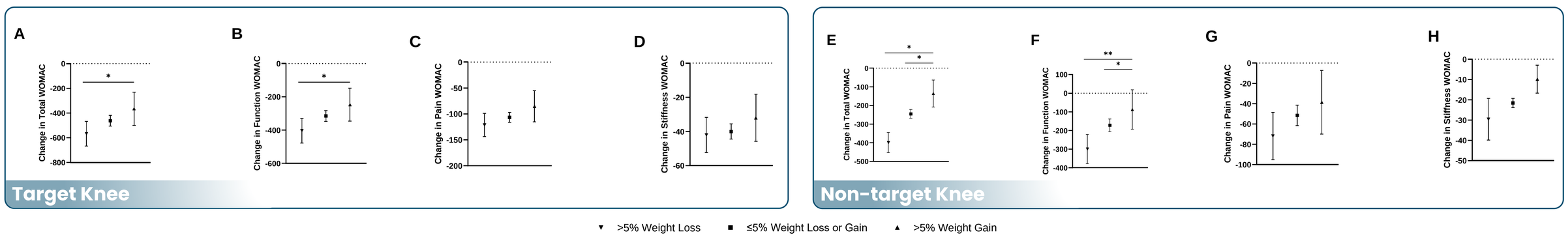

Figure 1. Changes in WOMAC scores in patients who lost or gained weight over two years. For target knee, A) Total, B) Functional, C) Pain, and D) Stiffness WOMAC scores. For non-target knee, E) Total, F) Functional, G) Pain, and H) Stiffness WOMAC scores. ANCOVA was used for analysis. Data presented as mean and error bars indicate 95% Confidence intervals. Statistical significance is indicated by *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, and **** $P < 0.0001$.

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Funding: Marie Skłodowska-Curie grant agreement No. 814244.

CONCLUSION

These studies indicate that increased body weight is associated with increased OA pain which is further confirmed by reduce patient-reported obesity-related OA pain upon undergoing weight loss.

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