RESEARCH ARTICLE

Effects of Bariatric Surgery on Knee Articular Cartilage and Osteoarthritis Symptoms—A 12-Month Follow-Up Using T2 Relaxation Time and WOMAC Osteoarthritis Index

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Background: Obesity is a significant risk factor for osteoarthritis (OA). The most effective treatment for morbid obesity is bariatric surgery.
Purpose: To study the effects of potential surgically induced weight loss on knee articular cartilage and OA symptoms of obese patients over a 12-month follow-up.
Study Type: Prospective longitudinal cohort study.
Subjects: 45 obese patients (38 female, BMI $= 42.3 \pm 6.5$ kg/m^2) who underwent gastric bypass (intervention group), and 46 age-matched conservative-care controls (37 female, BMI $= 39.8 \pm 4.6$ kg/m^2).
Field Strength/Sequence: Multiecho spin echo sequence at 3 T.
Assessment: Knee cartilage T2 measurements and WOMAC Indices were measured presurgery and after 12 months. The intervention group was split into successful (≥20% total weight loss (TWL)) and unsuccessful (<20% TWL) weight loss groups. T2 and WOMAC indices were also measured in controls at baseline and after 12 months. Changes among the three groups were analyzed.
Statistical Tests: Analysis of variance (significance level 0.05).
Results: Twenty-six (58%) intervention patients achieved ≥20% TWL. The <20% TWL group demonstrated significantly more T2 reduction in the deep lateral femur over 12 months compared with the ≥20% TWL group (-3.83 ± 8.18 msec vs. 2.47 ± 6.54 msec, respectively), whereas no significant differences were observed on the medial femoral compartment ($P = 0.385$, $P = 0.551$, and $P = 0.511$ for bulk, superficial and deep regions, respectively). Changes in WOMAC indices over 12 months were significantly greater in the ≥20% TWL group compared with controls. In the <20% TWL group, pain significantly improved over 12 months compared with controls, while stiffness and function changes were not statistically significant ($P = 0.063$ and $P = 0.051$, respectively).
Data Conclusion: Cartilage matrix, measured by T2, showed improvement on lateral femoral cartilage with <20% TWL compared with ≥20% TWL. Bariatric surgery provided significant improvements in knee symptoms with ≥20%

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TWL compared with conservative WL. This effect is also seen to some extent with <20% TWL compared with conservative WL.
Level of Evidence: 2
Technical Efficacy: Stage 4

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Obesity is a worldwide problem and has nearly tripled in frequency since 1975; currently, 650 million (13%) of all adults worldwide over the age of 18 are obese.[1] It has been identified as a risk factor for a number of diseases, such as osteoarthritis (OA), which is the most common articular disease worldwide.[2]

Despite its high prevalence and the recognized influence of genetics, the exact mechanism of OA is unclear.[3] It has been demonstrated that OA of the knee is associated with and accelerated by obesity.[4] It has also been shown that chondrocytes are modified by altered mechanical demands in their microenvironment.[5] Therefore, it has been hypothesized that at least a part of the cartilage injury is a result of altered mechanical stress owing to obesity.[6] More recent research has considered OA to be a disease of the entire joint affected by a metabolic component, such as inflammatory cytokines.[7] Some of the adipokines, cytokines secreted by adipose tissue, may play an important role in the development of OA.[8] However, the correlation between weight loss and structural pathology in OA affected joints is unclear.[9]

The most effective treatment for morbid obesity is bariatric surgery.[10] It has been demonstrated that in addition to pure weight loss, bariatric surgery also provides benefits such as reduction in comorbidities, increased quality of life,[10,11] reduced musculoskeletal pain,[12] decreased step width,[13] and reduction of total mortality.[14] Previous studies have shown that bariatric surgery can be cost-effective from 4 years after the surgery[10] with effectiveness further increasing over time.[15]

The Western Ontario and McMaster Universities (WOMAC) OA Index is a questionnaire which has been specifically developed for knee and hip OA and takes account of pain, stiffness, and physical function. WOMAC has been demonstrated to be a reliable tool in evaluating knee OA symptoms.[16]

Quantitative MRI (qMRI) has shown promising potential in cartilage research owing to its noninvasiveness and quantitative nature.[17] T2 relaxation time is an established parameter, which can evaluate cartilage ultrastructure and composition and mechanical properties.[17] Changes in T2 relaxation reflect changes in collagen content, fibril network orientation and integrity, and hydration of articular cartilage.[18] T2 relaxation time is increased in degenerated cartilage.[17]

The aim of this study was to investigate the effects of the Roux-en-Y gastric bypass operation[19] on knee articular cartilage and OA symptoms in obese patients over a 12-month follow-up, using T2 relaxation times and WOMAC indices. A further aim was to compare the results with those in a control group under conservative-care. We hypothesized that we would observe lower T2 relaxation times as well as lower WOMAC scores in the intervention group, indicating improved cartilage quality and OA symptoms. We also hypothesized that the changes would be more significant with major weight loss (≥20% total weight loss (TWL)) than with moderate weight loss (<20% TWL).

Materials and Methods

Subjects

This prospective cohort study was approved by The Ethical Committee of Northern Ostrobothnia Hospital District (Diary No. 13/2014). All the patients provided a written informed consent for the study. Patients on the waiting list for bariatric surgery at Oulu University Hospital were offered the opportunity to participate in the study between November 2014 and November 2017. Inclusion criteria were 1) age 20–70 years old; 2) body mass index (BMI) between 35 and 55 kg/m^2 (BMI > 40 kg/m^2 with and without comorbidities of obesity (type II diabetes, sleep apnea, high blood pressure, movement impairing musculoskeletal disease, polycystic ovary syndrome, cardiovascular disease); BMI 35 to 40 kg/m^2 with comorbidities or risk factors of comorbidities), 3) BMI ≥35 kg/m^2 for at least 5 years. Four study participants with BMI <35 (range: 32.2–34.8) kg/m^2 were also deemed eligible for the study. These patients initially had a BMI ≥35 at the time of inclusion but had successfully lost weight before the procedure. They were still considered eligible to benefit from the procedure. Fifty-nine patients were enrolled and all underwent Roux-en-Y gastric bypass operation performed by a gastrointestinal surgeon (V.K., 19 years of experience in bariatric surgery). This intervention group was later split into two groups based on the TWL over a 12-month follow-up period: successful weight loss (≥20% TWL), and unsuccessful weight loss (<20% TWL). TWL ≥20% has been proposed as a measure of weight loss success.[20] An age- and sex-matched control group was also recruited and consisted of 59 individuals who were treated with conservative weight reduction regimens in local health care centers between November 2015 and October 2018.

MRI Acquisition

Each participant underwent imaging of the knee joint on a 3.0 T MRI unit (Skyra, Siemens Healthcare, Erlangen, Germany) using an 18-channel body matrix coil and a 32-channel spine coil. The most symptomatic knee was chosen to be imaged, and if there was no difference in symptoms between the knees, the left knee was selected. Sagittal 2D T2 mapping was acquired using a multiecho spin echo sequence (TR = 1680 msec; TEs = 13.8, 27.6, 41.4, 55.2, 69 msec; field of view = 160 × 160 mm^2; matrix = 256 × 256; resolution = 0.62 × 0.62 × 3.00 mm^3; 18 slices). Each patient was scanned at baseline (prior to the surgery) and 12 months postoperatively. Each control group participant was also scanned at baseline and 12 months later. T2 relaxation time maps were calculated pixel-wise using a monoexponential model fitting and mean T2 values were obtained by segmenting sagittal T2 maps of the knee joint.

Cartilage Segmentation and Slice Selection

Cartilage segmentation was performed by one of the authors (A.K., 3 years of experience) using an in-house developed software, programmed using Matlab (MATLAB, Mathworks Inc., Natick, MA). First, the bone-cartilage interface and the cartilage surface were determined manually by drawing lines for both femoral (F) and tibial (T) cartilage (C) in the sagittal T2-weighted images (Fig. 1). The software then automatically calculated the midline between the two drawn lines, resulting in two cartilage layers: superficial (s) and deep (d). Second, two lines were drawn for both FC and TC to isolate the weight-bearing central (c) cartilage. These lines were determined at anterior and posterior end of the menisci for FC, and at anterior and posterior tip of the menisci for TC. This resulted in four regions of interest (ROI): superficial and deep central femur (scF and dcF, respectively), and superficial and deep central tibia (scT and dcT, respectively). Superficial and deep components were also combined to generate bulk (b) central femur and tibia ROIs (bcF and bcT, respectively).

The three middlemost sagittal slices for lateral (L) and medial (M) femoral condyles were selected to represent the highest weight-bearing regions of the knee joint. We then proceeded to calculate pixel-weighted T2 averages for each ROI using these three slices of the condyles. This resulted in 12 ROIs, 6 for each compartment (lateral compartment: scFL, dcFL, bcFL, scTL, dcTL, bcTL; medial compartment: scFM, dcFM, bcFM, scTM, dcTM, bcTM). The mean values in these ROIs were used in the statistical analysis.

Symptom Questionnaire

A WOMAC questionnaire[16] was administered to all participants by a medical professional. The difference compared with the standard WOMAC questionnaire was that a numeric scale (from 0 to 10) was used for answers, which was more easily comprehensible to the Finnish natives enrolled in this study. The questionnaire consisted of 24 questions, which considered pain ($n = 5$), stiffness ($n = 2$), and physical function ($n = 17$). The scale of 0–10 was then converted to the international five-grade scale as follows: no symptoms (0), mild (1–2), moderate (3–5), severe (6–8), and extreme (9–10).

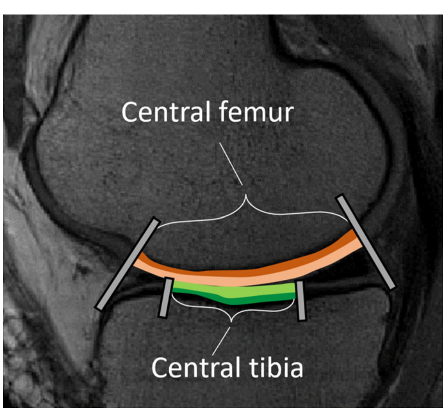

FIGURE 1: Sagittal T2-weighted image of tibiofemoral joint. ROI are color-coded: central femur (brown), central tibia (green). Lighter color indicates superficial (s) and darker color deep (d) cartilage. Bulk (b) cartilage contains both superficial and deep segments.

Kellgren–Lawrence (KL) Grading

Each participant underwent plain radiography of the knee joint. OA of the knee was evaluated from the radiographs by a board-certified radiologist with fellowship training in musculoskeletal radiology (M.N., 8 years of experience) using KL-grading.[21] OA scaling from 0 to 4 is as follows: 0) absence of radiographic OA changes, 1) possible osteophytes, doubtful joint space narrowing, 2) definite osteophytes, possible joint space narrowing, 3) several moderate osteophytes, definite joint space narrowing, mild sclerosis, possible bone deformity, 4) prominent large osteophytes, severe joint space narrowing, major sclerosis, and prominent bone deformity.

Statistical Analysis

Pearson's chi-square test was used to evaluate differences in KL-grades and sex among groups. Repeated measures analysis of variance (ANOVA) was used to evaluate age differences among groups. Subsequent analyses were adjusted for KL-grade, sex or age if these differed significantly among groups. A patient was left out of the statistical analysis if the patient was lost to follow-up ($n = 4$ and $n = 6$ for the intervention and control groups, respectively), or T2 maps were not recorded ($n = 10$ and $n = 7$, respectively). Differences in BMI, T2 relaxation times and WOMAC indices were normally distributed and studied using ANOVA and Tukey's post hoc tests. Linear regression analysis was used to examine the relationship between the change in BMI and the changes in T2 relaxation time and WOMAC indices over the 12-month follow-up. T2 relaxation times, BMI and WOMAC indices are presented as means with standard deviations (SD). A P-value <0.05 was considered statistically significant. The statistical analyses were performed using IBM SPSS for Windows, version 27.

Results

Demographics and KL Grading

The intervention group consisted of 45 patients (37 female and 8 male) aged from 38 to 68 (mean = 50 and SD = 7) years with BMI ranging from 32.2 to 54.9 (mean = 42.3 and SD = 6.5) kg/m^2 (Table 1). The age- and sex-matched control group consisted of 46 patients (38 female and 8 male) aged from 29 to 65 (mean 51 and SD 8) years with BMI ranging between 32.7 and 53.7 (mean 39.8 and SD 4.6) kg/m^2. Successful weight loss (≥20% TWL) was achieved by 26 (58%) patients and unsuccessful weight loss (<20% TWL) was observed in 19 (42%) of the 45 patients (Table 1). In the control group, the mean BMI change over 12 months was -0.2 kg/m^2 (SD = 1.5 kg/m^2). No significant differences were observed in BMI between the three groups at baseline ($P = 0.110$; Table 2).

TABLE 1. Demographic Characteristics and KL-Grades of the Control Group, Unsuccessful Intervention Group (<20% TWL), and Successful Intervention Group (≥20% TWL)

	Control	<20% TWL	≥20% TWL	*P*-value
N	46	19	26	
KL-grade				**0.001**[a]
0	27 (58.7%)	8 (42.1%)	5 (19.2%)	
1	7 (15.2%)	3 (15.8%)	9 (34.6%)	
2	8 (17.4%)	2 (10.5%)	11 (42.3%)	
3–4	4 (8.7%)	6 (31.6%)	1 (3.8%)	
Sex				0.442[a]
Female	38 (82.6%)	14 (73.7%)	23 (88.5%)	
Male	8 (17.4%)	5 (26.3%)	3 (11.5%)	
Age (years)	51 ± 8 (29–65)	53 ± 8 (40–68)	48 ± 6 (38–60)	0.078[b]

Values for age are presented as means with SD and ranges. The bold values indicates statistical significance *P*-value <0.05.
TWL = total weight loss; *N* = number of participants; KL = Kellgren–Lawrence.
[a]Pearson's Chi-Square test.
[b]Analysis of Variance (ANOVA).

TABLE 2. BMI and WOMAC Indices Presented as Means With SD for the Control Group, Unsuccessful Weight Loss Group (<20% TWL), and Successful Weight Loss Group (≥20% TWL)

		Baseline		Difference	
		Mean (SD)	*P*-value	Mean (SD)	*P*-value
BMI	Control	39.8 (4.6)	0.110	−0.2 (1.5)	**<0.001**[a,b,c]
	<20% TWL	42.1 (7.1)		−6.2 (2.4)	
	≥20% TWL	42.5 (6.1)		−11.1 (2.4)	
Pain	Control	6.7 (4.8)	0.442	1.2 (3.6)	**<0.001**[a,b]
	<20% TWL	7.3 (4.9)		−2.3 (4.6)	
	≥20% TWL	8.2 (4.6)		−4.0 (3.1)	
Stiffness	Control	3.3 (2.2)	0.571	0.5 (2.1)	**0.001**[b]
	<20% TWL	3.2 (1.7)		−0.9 (1.7)	
	≥20% TWL	3.8 (2.1)		−1.4 (2.0)	
Function	Control	17.0 (16.3)	0.656	2.8 (9.0)	**<0.001**[b]
	<20% TWL	18.9 (16.2)		−4.5 (12.5)	
	≥20% TWL	20.6 (14.5)		−10.3 (11.3)	

Difference indicates the change over 12 months. *P*-values are presented for the differences of the baseline values, and for the change over 12 months. The bold values indicates statistical significance $P < 0.05$.
BMI = body mass index; TWL = total weight loss; SD = standard deviation.
[a]Statistical difference between control group and <20% TWL group using Tukey's post hoc test.
[b]Statistical difference between control group and ≥20% TWL group using Tukey's post hoc test.
[c]Statistical difference between <20% TWL group and ≥20% TWL group using Tukey's post hoc test.

KL-grading showed difference among the three groups (control, <20% TWL, and ≥20% TWL), and its effect on the T2 relaxation times and WOMAC indices was studied using univariable ANOVA. However, the KL-grade did not show a significant effect on any of the outcome variables (Table S1 in the Supplemental Material) and, consequently, it was not included in the final analysis.

T2 Relaxation Time Measurements

No significant differences were observed in T2 relaxation time between the groups at baseline ($P = 0.967$ for bcFL, $P = 0.302$ for scFL, $P = 0.726$ for dcFL, $P = 0.101$ for bcTL, $P = 0.738$ for scTL, $P = 0.057$ for dcTL, $P = 0.868$ for bcFM, $P = 0.698$ for scFM, $P = 0.704$ for dcFM, $P = 0.185$ for bcTM, $P = 0.968$ for scTM, $P = 0.066$ for dcTM) (Table 3; Figs. 2 and 3). At 12 months, the T2 in the dcTM region was significantly higher in the <20% TWL group compared with the control group.

The change of T2 relaxation time over the 12-month follow-up was significantly different in bcFL and dcFL regions (Figs. 4 and 5; Table 3), with the <20% TWL group having a higher reduction in T2 compared with the ≥20% TWL group. However, no significant differences were observed in bcFL with Tukey's post hoc test ($P = 0.073$ (95% confidence interval (CI) −0.24 to 6.86 msec) for control vs. <20% TWL, $P = 0.893$ for control vs. ≥20% TWL, $P = 0.051$ (95% CI −7.84 to 0.01 msec) for <20% TWL vs. ≥20% TWL). No significant differences were observed in the change of T2 values over 12 months among the three groups in the lateral tibia or in the medial knee compartment ($P = 0.249$ for bcTL, $P = 0.297$ for scTL, $P = 0.404$ for dcTL, $P = 0.385$ for bcFM, $P = 0.551$ for scFM, $P = 0.511$ for dcFM, $P = 0.899$ for bcTM, $P = 0.928$ for scTM, $P = 0.945$ for dcTM). The results of linear regression analyses examining the relationships between changes in BMI and changes in T2 relaxation times are reported in the Supplemental Material (Figs. S1 and S2). bcTL and scTL were the only regions to show significant correlation (Pearson correlation coefficients 0.208 and 0.222, respectively).

WOMAC Questionnaire

Both the <20% TWL and ≥20% TWL groups had significant pain reduction compared with the control group over 12 months (Table 2). No significant difference was observed between the <20% TWL and ≥20% TWL groups ($P = 0.316$). At baseline, there were no significant differences in experienced pain, stiffness, or physical function between the three groups ($P = 0.442$, $P = 0.571$, and $P = 0.656$, respectively) (Table 2).

The ≥20% TWL group had significantly improved function and significantly reduced stiffness compared with the control group over 12 months (Table 2). Differences between the <20% TWL and control group were not significant ($P = 0.063$ (95% CI −2.76 to 0.06) for stiffness, $P = 0.051$ (95% CI −14.69 to 0.02) for function). No significant differences were observed between the <20% TWL and ≥ 20% TWL groups ($P = 0.705$ for stiffness, $P = 0.200$ for function). The results of the linear regression analyses examining the change in BMI and the change in WOMAC indices are reported in the Supplemental Material (Fig. S3). All three WOMAC indices had significant correlation with the change in BMI (Pearson correlation coefficients 0.518, 0.394, and 0.514 for pain, stiffness, and function, respectively).

Discussion

This study describes the status of articular cartilage of the knee in several regions of the tibiofemoral joint using T2 relaxation time in a 12-month follow-up after Roux-en-Y gastric bypass operation. BMI was measured to determine the success of weight loss,[20] and the WOMAC OA index to determine the effectiveness of the surgery on the symptoms and function of the knee joint.

We hypothesized that we would observe lower T2 relaxation times with greater weight loss. Surprisingly, the decrease in T2 relaxation time over 12 months was significantly greater in the <20% TWL group than in the ≥20% TWL group in bcFL and dcFL regions, suggesting improved cartilage quality of the lesser weight loss group.[17] This was not observed in scFL, and did not achieve significance in bcFL after post hoc analysis. We speculate that the difference in dcFL could be owing to changes in lower limb biomechanics, as bariatric surgery has been shown to affect patient walking patterns by reducing step width.[13] An average of 17% TWL has also been shown to alter knee biomechanics and slow down cartilage degradation in some patients but the effect is highly dependent on the changes of gait loading.[22] Therefore, we speculate that ≥20% TWL increases biomechanical pressure on the lateral knee compartment owing to reduced step width and decreases pressure on the medial compartment compared with <20% TWL. Moreover, the results may be affected by the amount of water in cartilage: higher loss of BMI reduces overall mechanical compression of the cartilage, enabling more interstitial water to accumulate in the matrix.[23] This, in turn, would increase the T2 relaxation time of cartilage,[24] possibly explaining the observed differences on lateral femoral cartilage.

It could also be suggested that higher weight loss (of the ≥20% TWL group) and improvement of OA symptoms may have increased the amount of exercise taken by patients in this group, potentially resulting in altered mechanical stimulus and biochemical activity of the chondrocytes,[23] which could increase cartilage degeneration of the larger weight loss group. It should also be noted that questions related to physical performance, such as those in the WOMAC questionnaire, may subconsciously encourage an increase in exercise. However, a review by Xu et al. reported contradicting data

TABLE 3. Mean T2 Relaxation Times With SD for the Control Group, Unsuccessful Weight Loss Group (<20% TWL), and Successful Weight Loss Group (≥20% TWL) in Each Region of Interest

	Baseline		Follow-up		Difference	
	Mean (SD)	*P*-value	Mean (SD)	*P*-value	Mean (SD)	*P*-value
Lateral						
Femur						
bcFL						
Control	55.4 (5.9)	0.967	56.4 (5.7)	0.088	0.96 (6.03)	**0.044**[a]
<20% TWL	55.8 (5.3)		53.4 (5.8)		−2.35 (5.65)	
≥20% TWL	55.8 (6.4)		57.3 (6.4)		1.57 (4.05)	
scFL						
Control	57.2 (5.1)	0.302	58.2 (5.7)	0.147	1.01 (5.55)	0.328
<20% TWL	57.2 (5.0)		56.2 (6.1)		−1.06 (4.77)	
≥20% TWL	59.1 (5.3)		59.7 (6.2)		0.64 (4.44)	
dcFL						
Control	53.7 (8.8)	0.726	54.7 (7.8)	0.131	1.00 (7.93)	**0.021**[b]
<20% TWL	54.5 (8.6)		50.6 (7.2)		−3.83 (8.18)	
≥20% TWL	52.4 (8.4)		54.9 (8.3)		2.47 (6.54)	
Tibia						
bcTL						
Control	36.1 (4.6)	0.101	36.6 (5.1)	0.706	0.53 (4.39)	0.249
<20% TWL	39.3 (7.1)		37.9 (7.1)		−1.45 (5.33)	
≥20% TWL	37.2 (5.8)		36.9 (5.5)		−0.35 (3.60)	
scTL						
Control	44.4 (5.1)	0.738	45.1 (5.4)	0.914	0.69 (4.66)	0.297
<20% TWL	45.7 (6.6)		44.6 (7.2)		−1.17 (5.84)	
≥20% TWL	45.0 (7.4)		44.6 (7.3)		−0.42 (3.43)	
dcTL						
Control	27.1 (6.5)	0.057	27.7 (7.1)	0.245	0.57 (6.41)	0.404
<20% TWL	32.5 (8.8)		30.9 (8.3)		−1.59 (6.15)	
≥20% TWL	29.1 (5.7)		28.6 (5.5)		−0.49 (4.99)	
Medial						
Femur						
bcFM						
Control	51.4 (4.8)	0.868	52.0 (4.7)	0.411	0.61 (4.01)	0.385
<20% TWL	52.0 (6.4)		53.3 (4.8)		1.34 (5.20)	
≥20% TWL	52.0 (5.3)		51.5 (4.8)		−0.48 (4.74)	

TABLE 3. Continued

	Baseline		Follow-up		Difference	
	Mean (SD)	*P*-value	Mean (SD)	*P*-value	Mean (SD)	*P*-value
scFM						
Control	55.3 (5.5)	0.698	56.4 (5.1)	0.985	1.03 (3.92)	0.551
<20% TWL	55.3 (9.2)		56.6 (7.6)		1.27 (5.08)	
≥20% TWL	56.6 (5.5)		56.6 (6.6)		0.00 (4.63)	
dcFM						
Control	47.3 (6.9)	0.704	47.6 (7.8)	0.188	0.23 (6.36)	0.511
<20% TWL	49.1 (10.1)		50.3 (7.6)		1.23 (7.28)	
≥20% TWL	47.4 (7.9)		46.3 (5.9)		−1.05 (6.59)	
Tibia						
bcTM						
Control	35.0 (4.4)	0.185	34.4 (4.8)	0.226	−0.51 (4.15)	0.899
<20% TWL	37.6 (6.7)		36.9 (5.4)		−0.69 (3.39)	
≥20% TWL	35.9 (5.5)		35.7 (6.4)		−0.17 (3.93)	
scTM						
Control	45.8 (5.1)	0.968	45.6 (6.4)	0.856	−0.12 (5.28)	0.928
<20% TWL	45.7 (6.3)		45.2 (5.6)		−0.50 (4.48)	
≥20% TWL	46.1 (6.1)		46.2 (5.0)		0.10 (5.31)	
dcTM						
Control	23.4 (5.3)	0.066	22.7 (5.7)	**0.042**[c]	−0.70 (4.68)	0.945
<20% TWL	29.1 (11.9)		28.0 (9.4)		−1.04 (5.61)	
≥20% TWL	25.5 (8.2)		24.9 (9.5)		−0.57 (4.17)	

Difference indicates the change of T2 relaxation time after 12 months. *P*-values are presented for the differences of the baseline values, follow-up values, and the change over 12 months. The bold values indicates statistical significance $P < 0.05$.
TWL = total weight loss; SD = standard deviation; b = bulk; s = superficial; d = deep; c = central; F = femur; T = tibia; M = medial; L = lateral.
[a]Tukey's post hoc test did not display differences between individual groups.
[b]Statistical difference between <20% TWL group and ≥20% TWL group using Tukey's post hoc test.
[c]Statistical difference between control group and <20% TWL group using Tukey's post hoc test.

regarding the correlation between physical activity and OA progression in MR images. Individual studies examined in the review revealed both protective and damaging properties of physical activity.[25] We also know that the nutrition of patients with successful or unsuccessful weight loss can be very different,[26] which could also affect metabolism, including that of cartilage.

Changes in bone mineral density (BMD) may also play an important role. Previous research has suggested an association between reduced BMD and increased cartilage damage.[27] Bariatric surgery is known to significantly reduce BMD, and a recent study has shown that bone resorption begins shortly after bariatric surgery and reaches a peak 1–2 years after the operation.[28] A TWL ≥20% could result in higher loss of BMD and expose the knee joint to further cartilage damage. On the contrary, a TWL <20% could potentially yield beneficial effects on cartilage by not compromising BMD in the joint area. This could also explain why the observed changes are in the deep cartilage segment, which is located closer to the bone.

In this study, we did not detect significant differences in T2 relaxation times at baseline between groups. At 12 months, the dcTM region had significantly higher T2 in the <20% TWL group compared with the control group.

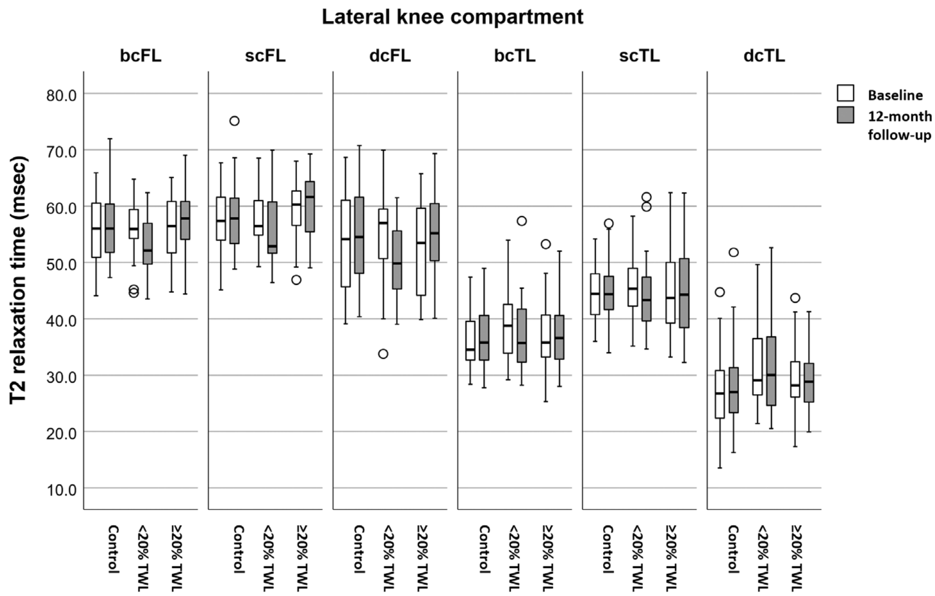

FIGURE 2: Boxplots of T2 relaxation times for each region of interest in control and intervention (<20% TWL and ≥20% TWL) groups on lateral knee compartment. No significant differences could be observed between baseline and 12-month follow-up values in any of the three groups. b = bulk; s = superficial; d = deep; c = central; F = femoral; T = tibial; L = lateral; TWL = total weight loss.

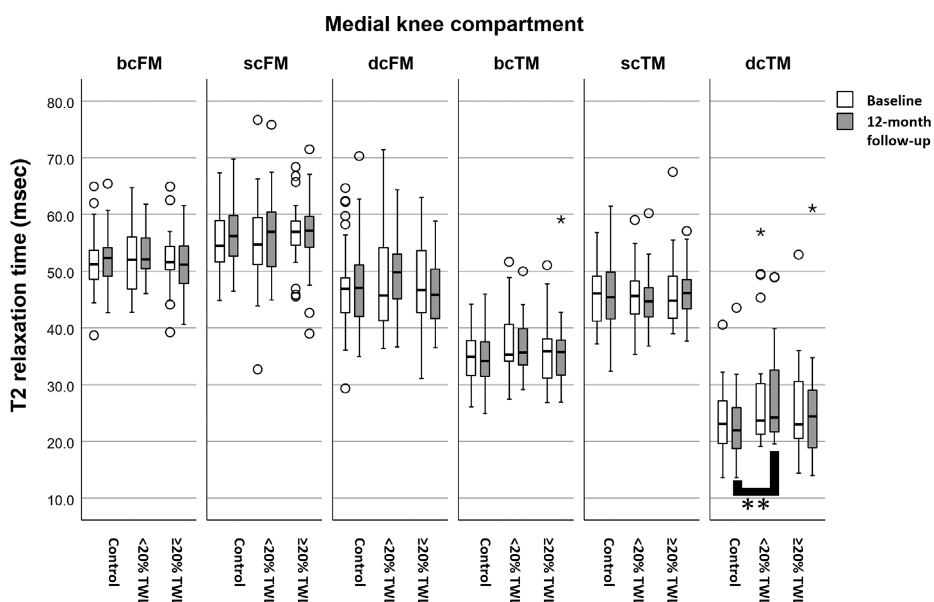

FIGURE 3: Boxplots of T2 relaxation times for each region of interest in control and intervention (<20% TWL and ≥20% TWL) groups on medial knee compartment. Significant differences ($P < 0.05$) are indicated by double asterisk (**). b = bulk; s = superficial; d = deep; c = central; F = femoral; T = tibial; M = medial; TWL = total weight loss.

However, it should be noted that baseline T2 was higher in the <20% TWL group than in the control group and that the difference was close to significance. Moreover, the <20% TWL group experienced a larger reduction in mean T2 (−1.1 msec) compared with the ≥20% TWL (−0.4 msec) and control (−0.7 msec) groups after 12 months. Despite this, the analysis shows a significant difference, possibly owing to the reduced SD in the <20% TWL group. Therefore, this difference may be a result of chance.

Other groups have also studied the effects of weight loss on knee cartilage T2 relaxation time. Serebrakian et al[29] reported that ≥10% TWL in patients with knee OA risk factors was associated with a slower increase of T2 relaxation times in the medial knee compartment compared with controls who lost <3% BMI over 48 months. Gersing et al[30] have also shown that ≥10% TWL in patients with BMI ≥25 kg/m^2 slowed the increase of T2 in the medial tibia over 48 months. Another study by Gersing et al also reported that

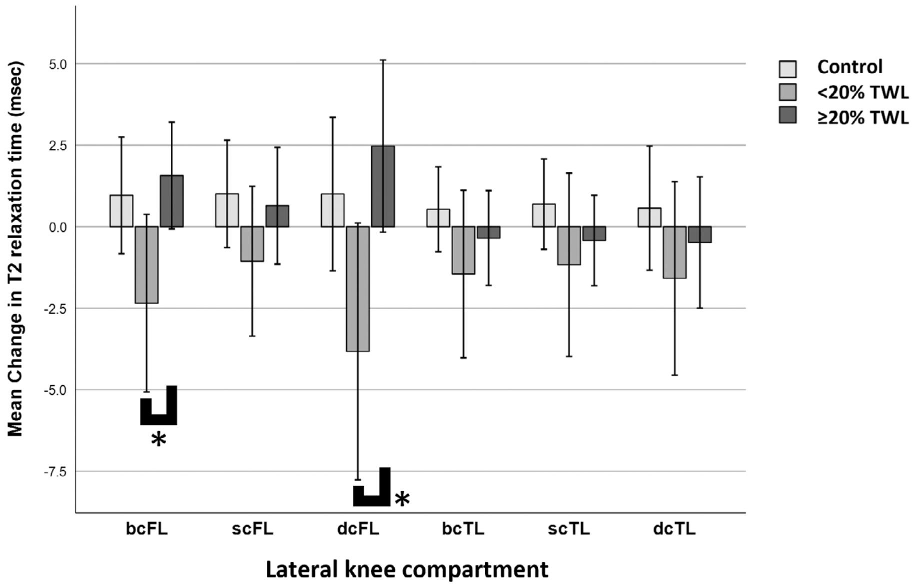

FIGURE 4: Boxplots of change in T2 relaxation time over 12 months for each region of interest in control and intervention (<20% TWL and ≥20% TWL) groups on lateral knee compartment. Error bars show 95% confidence intervals. Significant differences ($P < 0.05$) are indicated by asterisk (*). b = bulk; s = superficial; d = deep; c = central; F = femoral; T = tibial; L = lateral; TWL = total weight loss.

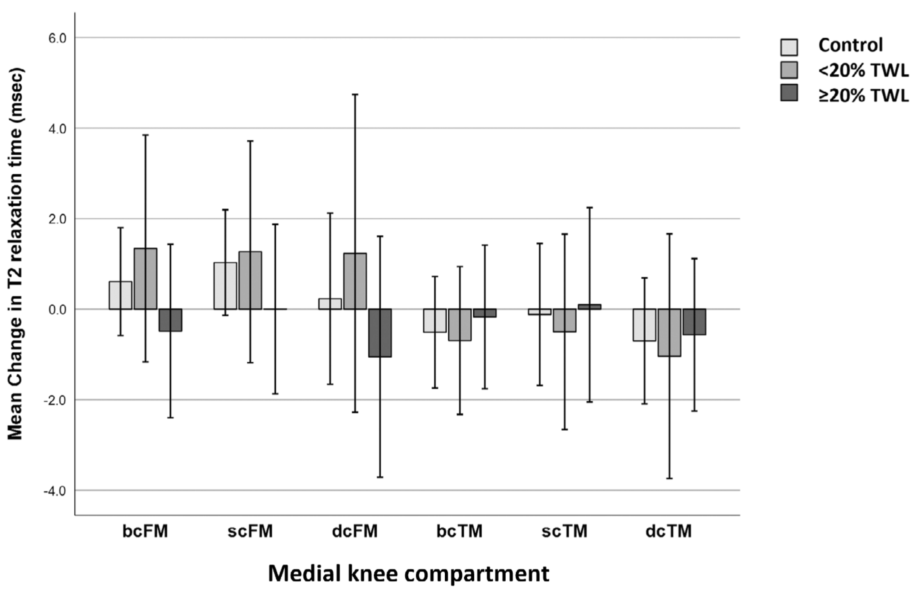

FIGURE 5: Boxplots of change in T2 relaxation time over 12 months for each region of interest in control and intervention (<20% TWL and ≥20% TWL) groups on medial knee compartment. Error bars show 95% confidence intervals. No significant differences could be observed between the three groups. b = bulk; s = superficial; d = deep; c = central; F = femoral; T = tibial; M = medial; TWL = total weight loss.

>5% TWL in patients with BMI > 25 kg/m^2 resulted in significantly reduced T2 relaxation times on both medial and lateral knee compartments over 96 months.[31] In light of previous studies, it is possible that the 12-month time frame may not be long enough for T2 measurements to show an improvement in cartilage quality with ≥20% TWL. However, a study by Jafarzadeh et al has reported opposing T2 results compared with the observations in this study: they found a greater decrease in T2 values in the ≥20% TWL group compared with the <20% TWL group over a 12-month follow-up. The WOMAC indices also showed more reduction with higher weight loss, aligning with our observations.[32]

We hypothesized that we would observe greater improvement of OA symptoms with higher weight loss. The WOMAC questionnaire did not show any differences among the three groups in pain, function, or stiffness of the knees at baseline, suggesting similar burden of disease. However, at 12 months, the ≥20% TWL group showed a significant reduction in pain and stiffness, and improved physical function as compared with the control group. Similarly, the <20% TWL group also showed a significant reduction in pain intensity compared with the control group. Stiffness and physical function also improved more over the 12-month follow-up in the <20% TWL group compared with the control group, but without statistical significance. These findings are in line with our hypothesis and suggest that a greater weight loss is beneficial for the improvement of OA symptoms. Additionally, this suggests that although <20% TWL is classified as an unsuccessful operative treatment result,[20] it still provides some improvement of knee symptoms. No significant differences were observed in the improvement of knee symptoms between the <20% TWL and ≥ 20% TWL groups, highlighting the benefits of bariatric surgery even if the clinically desired weight loss is not achieved.

Other studies have reported similar findings of knee joint symptoms after bariatric surgery using the WOMAC questionnaire. Edwards et al[33] reported significant improvement in pain, stiffness, and function in obese patients with radiographic OA 12 months after bariatric surgery. Similarly, Hooper et al[34] reported significant improvement in WOMAC scores 6–12 months after bariatric surgery. Moreover, a 5-year follow-up study after bariatric surgery by Hacken et al[35] reported that significant improvements in WOMAC scores were maintained throughout the 5-year follow-up. Üstün et al also reported similar findings, as WOMAC scores showed a significant reduction 6 months after bariatric surgery. However, they did not find a significant correlation between BMI change and WOMAC indices, whereas we observed a clear correlation with BMI change in all three indices.[36] A recent meta-analysis by Panunzi et al[37] studied various weight reduction methods and their effect on improvement of OA symptoms in obese individuals, and found that the best methods were bariatric surgery, as well as exercise and low-calorie diet, and exercise and intensive weight loss. However, previous research has shown signs of a reduced benefit of bariatric surgery on symptoms after the first year.[38] The studies discussed above did not separately evaluate the effects of successful and unsuccessful weight loss.

Bariatric surgery has been shown to be the most effective treatment method for morbid obesity,[10] and weight loss has been shown to greatly benefit knee OA symptoms.[37] Therefore, we may speculate that bariatric surgery should be considered as a treatment method for knee OA in patients with morbid obesity, as even an unsuccessful result with <20% TWL demonstrates improvements in knee OA symptoms. In addition, bariatric surgery is already known to be cost-effective in morbidly obese patients.[10,15] However, it is not known whether or not this beneficial effect on OA symptoms is maintained over time in both <20% TWL and ≥20% TWL groups. In a recent study[39] adipose tissue samples from the same patient cohort were analyzed and a significant reduction in the adipose tissue macrophage population was seen after bariatric surgery, regardless of the weight loss. This observation suggests that the overall inflammatory status of obese patients could play a role in OA symptoms, but further data is needed to consolidate such a hypothesis.

Our study has several strengths. First, it was longitudinal, allowing us to observe the study participants over 12 months. Second, our intervention group was split into two subgroups based on the success of the bariatric surgery. Including a control group also enabled us to compare the effects of the bariatric surgery success with conservative weight reduction treatment. Third, the study included a combination of several different types of data: traditional imaging (x-ray images and KL-grading), qMRI data (T2 relaxation time measurements), BMI, and symptoms questionnaire (WOMAC).

Limitations

First, although patients were studied after a 12-month follow-up where we saw significant improvements of knee OA symptoms, we cannot be sure whether the positive effects are maintained over time. Second, although the intervention and control groups had the same sex distribution, both groups had considerably more female participants than male participants. Male participants were harder to recruit for the study and this could possibly have some effect on regional variations of the knee T2 relaxation times, as the hip alignment and, therefore, knee loading may differ between the males and females.[40] However, we do not believe this had effects on experienced joint symptoms measured by the WOMAC questionnaire. It should also be noted that other bariatric surgery studies have had similar gender distributions.[19,20,26,34,38] Third, after splitting the intervention group into successful and unsuccessful weight loss groups, the small size of the two groups may have reduced the statistical power in some analyses. Fourth, no measurements of bone metabolism were available, which could affect the observed T2 findings. Fifth, the knees were too large to fit into conventional knee coils, which required the use of spine and body matrix coils. Nevertheless, it should be noted that no artifacts of any kind were seen.

Conclusion

Cartilage ECM composition, as measured by T2 relaxation time, was improved on lateral femoral cartilage with moderate (<20%) weight loss compared with major (≥20%) weight loss, although the clinical significance of this is not clear. Major weight loss with Roux-en-Y gastric bypass surgery provides significant improvement on knee symptoms and function compared with conservative weight reduction, at 12 months. Moderate weight loss with the surgery also significantly improved knee pain and tended to improve stiffness and function compared with conservative weight reduction.

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Conflict of Interests

All authors state that they have no conflict of interest.

References

1. World Health Organization. *Obesity and overweight*. World Health Organization 2024. Available: https://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight.
2. Arden N, Nevitt MC. Osteoarthritis: Epidemiology. Best Pract Res Clin Rheumatol 2006;20:3-25.
3. Spector TD, MacGregor AJ. Risk factors for osteoarthritis: Genetics. Osteoarthr Cartil 2004;12:39-44.
4. Pottie P, Presle N, Terlain B, Netter P, Mainard D, Berenbaum F. Obesity and osteoarthritis: More complex than predicted! Ann Rheum Dis 2006;65:1403-1405.
5. Urban JPG. The chondrocyte: A cell under pressure. Br J Rheumatol 1994;33:901-908.
6. Vincent HK, Heywood K, Connelly J, Hurley RW. Obesity and weight loss in the treatment and prevention of osteoarthritis. PM R 2012;4(5 Suppl):S59-S67.
7. Fernandes JC, Martel-Pelletier J, Pelletier J-P. The role of cytokines in osteoarthritis pathophysiology. Biorheology 2002;39:237-246.
8. Gegout PP, Francin PJ, Mainard D, Presle N. Adipokines in osteoarthritis: Friends or foes of cartilage homeostasis? Joint Bone Spine 2008;75: 669-671.
9. Daugaard CL, Hangaard S, Bartels EM, et al. The effects of weight loss on imaging outcomes in osteoarthritis of the hip or knee in people who are overweight or obese: A systematic review. Osteoarthr Cartil 2020; 28:10-21.
10. Buchwald H, Owen H, Wangensteen SD, et al. Consensus conference statement bariatric surgery for morbid obesity: Health implications for patients, health professionals, and third-party payers. Surg Obes Relat Dis 2005;1:371-381.
11. Wolfe BM, Kvach E, Eckel RH. Treatment of obesity: Weight loss and bariatric surgery. Circ Res 2016;118:1844-1855.
12. Peltonen M, Lindroos AK, Torgerson JS. Musculoskeletal pain in the obese: A comparison with a general population and long-term changes after conventional and surgical obesity treatment. Pain 2003;104: 549-557.
13. Vartiainen P, Bragge T, Lyytinen T, Hakkarainen M, Karjalainen PA, Arokoski JP. Kinematic and kinetic changes in obese gait in bariatric surgery-induced weight loss. J Biomech 2012;45:1769-1774.
14. Pontiroli AE, Morabito A. Long-term prevention of mortality in morbid obesity through bariatric surgery. A systematic review and meta-analysis of trials performed with gastric banding and gastric bypass. Ann Surg 2011;253:484-487.
15. Picot J, Jones J, Colquitt JL, et al. The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: A systematic review and economic evaluation. Health Technol Assess 2009;13: 1-190.
16. McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster universities osteoarthritis index (WOMAC): A review of its utility and measurement properties. Arthritis Rheum 2001;45:453-461.
17. Nieminen MT, Nissi MJ, Mattila L, Kiviranta I. Evaluation of chondral repair using quantitative MRI. J Magn Reson Imaging 2012;36:1287-1299.
18. Nieminen MT, Rieppo J, Töyräs J, et al. T2 relaxation reveals spatial collagen architecture in articular cartilage: A comparative quantitative MRI and polarized light microscopic study. Magn Reson Med 2001;46: 487-493.
19. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: A systematic review and meta-analysis. JAMA 2004;292:1724-1737.
20. Corcelles R, Boules M, Froylich D, et al. Total weight loss as the outcome measure of choice after roux-en-Y gastric bypass. Obes Surg 2016;26:1794-1798.
21. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957;16:494-502.
22. Liukkonen MK, Mononen ME, Vartiainen P, et al. Evaluation of the effect of bariatric surgery-induced weight loss on knee gait and cartilage degeneration. J Biomech Eng 2018;140. https://doi.org/10.1115/1.4038330
23. Eckstein F, Hudelmaier M, Putz R. The effects of exercise on human articular cartilage. J Anat 2006;208:491-512.
24. Mosher TJ, Dardzinski BJ. Cartilage MRI T2 relaxation time mapping: Overview and applications. Semin Musculoskelet Radiol 2004;8: 355-368.
25. Xu D, Van Middelkoop M, Bierma-Zeinstra SMA, Runhaar J. Physical activity and features of knee osteoarthritis on magnetic resonance imaging in individuals without osteoarthritis: A systematic review. Arthritis Care Res (Hoboken) 2023;75:1908-1913.
26. Ostad AN, Barghchi H, Jangjoo A, et al. Macro- and micro-nutrient intake adequacy in gastric bypass patients after 24 months: A cross-sectional study. Clin Nutr Res 2021;10:341-352.
27. Lee JY, Harvey WF, Price LL, Paulus JK, Dawson-Hughes B, McAlindon TE. Relationship of bone mineral density to progression of knee osteoarthritis. Arthritis Rheum 2013;65:1541-1546.
28. Saad R, Habli D, El Sabbagh R, Chakhtoura M. Bone health following bariatric surgery: An update. J Clin Densitom 2020;23:165-181.
29. Serebrakian AT, Poulos T, Liebl H, et al. Weight loss over 48 months is associated with reduced progression of cartilage T2 relaxation time values: Data from the osteoarthritis initiative. J Magn Reson Imaging 2015;41:1272-1280.
30. Gersing AS, Solka M, Joseph GB, et al. Progression of cartilage degeneration and clinical symptoms in obese and overweight individuals is dependent on the amount of weight loss: 48-month data from the osteoarthritis initiative. Osteoarthr Cartil 2016;24:1126-1134.
31. Gersing AS, Schwaiger BJ, Nevitt MC, et al. Weight loss regimen in obese and overweight individuals is associated with reduced cartilage degeneration: 96-month data from the osteoarthritis initiative. Osteoarthr Cartil 2019;27:863-870.
32. Jafarzadeh S, Tamez J, Totterman S, Clancy M, Felson DT. Longitudinal changes in T mapping of knee cartilage following rapid and substantial weight loss. Osteoarthr Cartil 2018;26:S67-S68.
33. Edwards C, Rogers A, Lynch S, et al. The effects of bariatric surgery weight loss on knee pain in patients with osteoarthritis of the knee. Art Ther 2012;2012:1-7.
34. Hooper MM, Stellato TA, Hallowell PT, Seitz BA, Moskowitz RW. Musculoskeletal findings in obese subjects before and after weight loss following bariatric surgery. Int J Obes (Lond) 2007;31:114-120.
35. Hacken B, Rogers A, Chinchilli V, Silvis M, Mosher T, Black K. Improvement in knee osteoarthritis pain and function following bariatric surgery: 5-year follow-up. Surg Obes Relat Dis 2019;15:979-984.
36. Üstün I, Solmaz A, Gülçiçek OB, Kara S, Albayrak R. Effects of bariatric surgery on knee osteoarthritis, knee pain and quality of life in female patients. J Musculoskelet Neuronal Interact 2019;19:465-471.

37. Panunzi S, Maltese S, De Gaetano A, Capristo E, Bornstein SR, Mingrone G. Comparative efficacy of different weight loss treatments on knee osteoarthritis: A network meta-analysis. Obes Rev 2021;22: e13230.

38. King WC, Chen JY, Belle SH, et al. Change in pain and physical function following bariatric surgery for severe obesity. JAMA 2016;315: 1362-1371.

39. Palomäki VA, Lehenkari P, Meriläinen S, Karttunen TJ, Koivukangas V. Dynamics of adipose tissue macrophage populations after gastric bypass surgery. Obesity (Silver Spring) 2023;31:184-191.

40. Tillman MD, Bauer JA, Cauraugh JH, Trimble MH. Differences in lower extremity alignment between males and females. Potential predisposing factors for knee injury. J Sports Med Phys Fitness 2005; 45:355-359.