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Long-term results after weight loss intervention in knee arthroplasty patients with obesity

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ABSTRACT

Introduction. Obesity is a well-known problem in patients undergoing total knee arthroplasty (TKA). We have previously shown that it is feasible and safe to implement an intensive weight loss programme shortly before TKA. Preoperatively, the programme produced an average weight loss of 10.7 kg while also improving body composition and reducing cardiovascular risk factors. One year after TKA, the patients in the weight loss programme managed to maintain their weight loss, whereas no change was observed in the control group. Both groups showed major improvements in health-related quality of life (QoL) and knee function. The aim of this study was to investigate the long-term effect of a weight loss intervention in patients with obesity undergoing TKA.

Methods. This was a seven-year follow-up study from a randomized controlled trial. Body weight, blood pressure and waist circumference were measured. Additionally, data on patient-reported outcome, range of knee motion (ROM), hypertension and diabetes status were collected.

Results. Forty-nine patients were examined at the follow-up. No differences were found between the intervention and the control group on body weight, hypertension, diabetes, waist circumference or knee ROM. The intervention group had increased their mean weight significantly more than the control group (difference = 3.1, 95% confidence interval: 1.3-4.8). 66% had hypertension and 38% had Type 2 diabetes. Pain, function and QoL were improved for both groups.

Conclusion. The patients in the intervention group were unable to maintain their preoperative weight loss when measured seven year after TKA.

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Trial registration. not relevant.

Osteoarthritis (OA) is a joint disease associated with pain and lack of mobility. The knee is the weight-bearing joint most commonly affected by OA [1], and OA is one of the major causes of pain, disability and reduced health-related quality of life (QoL). The risk of developing OA of the knee increases with age and with higher BMI. Furthermore, the susceptibility to OA may also be increased in part by genetic inheritance, occupational activities from jobs that require regular knee bending and lifting or carrying heavy loads. Such activities predispose to OA of the knee. Women have a higher risk of OA after the age of 50 years, much higher than the risk for men, but studies have been inconsistent with respect to the link between gender and the development of

OA [1-4]. Obesity is a well-documented risk factor and predictor for the development of OA due to chronic joint load, altered body composition and subacute inflammation [3, 5, 6]. Globally, obesity is a growing health problem [3]. Obesity is also an increasing problem in patients after total knee arthroplasty (TKA), and studies have shown that obesity is associated with poor knee function and QoL [2, 7, 8]. Weight loss may be beneficial in the treatment of OA of the knee and has been linked to an improved patient-reported outcome (PRO) on knee pain, function, range of motion (ROM) and QoL [5, 7]. Weight loss is a symptomatic treatment of OA, but may be vital in postponing disease progression.

However, evidence of the role of obesity in the outcome after TKA is conflicting. Some studies have shown that obesity seems to have a negative effect on the outcome after TKA compared with people with a BMI < 30 kg/m^2 [2, 7, 8]. Other studies found no differences in pain, function and QoL between patients with or without obesity after TKA [9-11]. Moreover, knowledge is sparse about the long-term outcome of weight loss interventions before TKA. The aim of the present study was to investigate the long-term effect of weight loss intervention in TKA patients with obesity.

METHODS

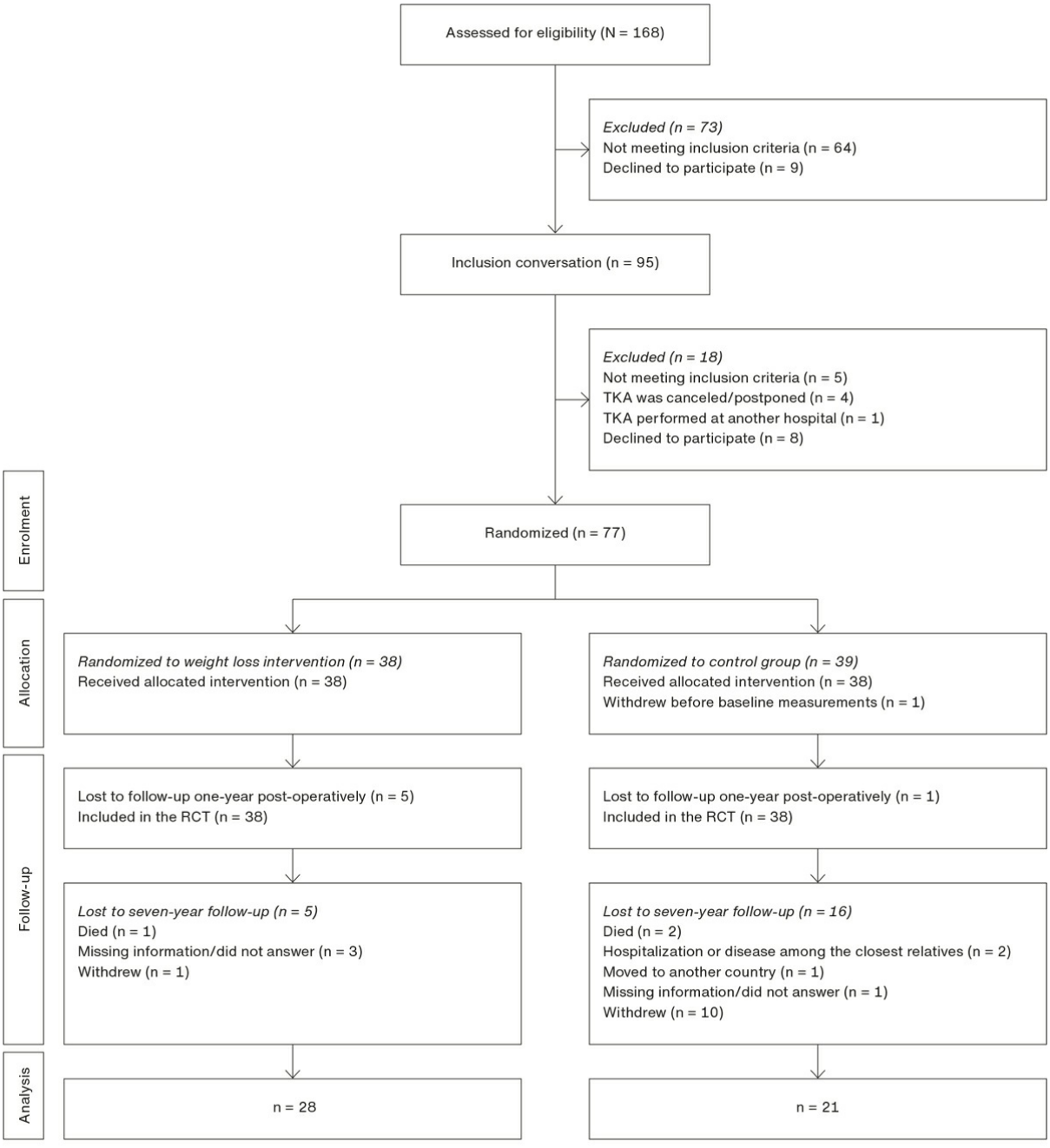
Study design

This was a seven-year observational follow-up study of a randomized controlled trial (RCT) [12]. The RCT investigated whether a weight loss intervention before primary TKA would improve QoL, knee function, mobility and body composition one year after surgery. Patients with obesity scheduled for primary TKA due to OA of the knee were randomized to a control group receiving standard care or to an intervention group receiving an eight-week low-energy diet before TKA. Changes in outcome of QoL, knee function, mobility and body composition from baseline to one year after TKA were compared between groups. The baseline in this study is the time of measurement immediately before TKA, when the patients in the intervention group have successfully finished an eight-week low-energy diet.

Participants

Seventy-six patients with OA who had undergone TKA at the hospital of Southern Jutland in the period from August 2011 to April 2013 participated in the RCT. Patients were recruited from an outpatient clinic and were eligible for inclusion if they had a BMI >30 kg/m^2 and were motivated to participate in a weight loss intervention [12]. At the one-year follow-up, six patients had withdrawn from the study; five in the intervention group and one in the control group (**Figure 1**). In January 2020, data were available on 59 patients. Three patients had died. Thus, 56 patients were contacted by telephone by the primary investigator of this study. Forty-nine patients accepted to participate in the study. Among those, 47 accepted to participate in the clinical control conducted as a home visit by the primary investigator and another two accepted to complete the questionnaires.

FIGURE 1 Flow chart of patients and patients lost to follow-up from baseline to seven-year follow-up.



RCT = randomized controlled trial.

Intervention

Patients in the intervention group received a low-energy diet (810 kcal/day) with commercially available formula foods and received nutritional education by an experienced dietitian for eight-weeks preoperatively. The second phase of the intervention started immediately after TKA and ended one year post-operatively. The intervention is described in detail in Liljensøe et al. [12] .

Clinical controls performed as home visits

Forty-seven clinical controls performed as home visits and one phone interview were conducted in the course of

five days in late January and early February 2020. The visits lasted 20-60 minutes. One patient participated in the clinical control by telephone. Thus, clinical data were available for 47 patients who had participated the clinical controls.

Measurement and procedures

Clinical measures

At the clinical controls, the primary investigator measured the patients' body weight (Sandstroem, Denmark); blood pressure, using a digital sphygmomanometer (UA-852) on the patient's right arm; and abdominal waist circumference in centimetres, using a measuring tape (150 cm). The recommended upper limit for waist circumference in men is less than 94 cm and in women less than 80 cm. A waist circumference in men exceeding than 94 cm indicates a health risk and if larger than 102 cm an even greater risk. The same applies to women with a waist circumference exceeding 80 cm and 88 cm [13]. The patients' height was measured in the RCT [12].

Patient-reported outcome measures

The Knee Injury and Osteoarthritis Outcome Score (KOOS) [14] consists of 42 questions distributed on five subscales: pain, other symptoms, function in daily living, function in sport and recreation and knee-related QoL. Zero represents extreme problems and 100 represents no knee problems [14]. The Copenhagen Knee Range of Motion Scale (CKRS) is a method to measure and evaluate passive knee ROM [15]. Previously, the evaluation of passive knee ROM was a procedure performed by health professionals with a goniometer, but the development and validation of the CKRS has enabled patients to self-report their passive knee ROM [15].

At the clinical controls, patients were asked if they had diabetes (No/Type 1 diabetes/Type 2 diabetes), used any medicine due to diabetes (No/Yes) or had hypertension (No/Yes). Data were stored in a project management database (Procordo, Denmark).

Statistics

Demographics and baseline characteristics were presented with frequencies (%) for categorical variables and with mean (range/95% confidence interval (CI)) for continuous variables.

Differences in weight, BMI, blood pressure and PRO measured at baseline and at the seven-year follow-up between groups were analysed using Student's t-test and presented as means with 95% CI and p-values. The assumptions of the t-test were met.

The prevalence of hypertension and diabetes were presented descriptively with frequencies (%) and compared with baseline values. Waist circumference and CKRS were measured only at the seven-year follow-up and were presented descriptively.

Trial registration: not relevant.

RESULTS

Loss to follow-up

Patient characteristics of the 49 patients in this study and the 27 patients who were lost to follow-up are presented in **Table 1**. Patients lost to follow-up were more likely to be women with a higher BMI, more likely to have diabetes, be unskilled and living alone than patients who participated in the seven-year follow-up.

TABLE 1 Patient characteristics measured before intervention for the study population and for the patients lost to follow-up.

	Lost to follow-up (N_l = 27)	Study population (N_s = 49)	Intervention (N_i = 28)	Control (N_c = 21)
Female, n (%)	21 (78)	33 (67)	18 (64)	15 (71)
Age, mean (range), yrs	63.7 (47-83)	64.7 (46-85)	65.2 (46-81)	64.0 (46-85)
Height, mean (95% CI), m	1.65 (1.62-1.69)	1.68 (1.65-1.70)	1.68 (1.63-1.72)	1.68 (1.64-1.71)
BMI, mean (95% CI), kg/m²	37.4 (35.2-39.5)	34.9 (33.7-36.2)	33.6 (32.0-35.2)	36.8 (34.8-38.9)
Hypertension, n (%)	17 (63)	28 (57)	16 (57)	12 (57)
Diabetes, n (%)				
Type I	2 (18)	2 (17)	1 (14)	1 (20)
Type II	9 (82)	10 (83)	6 (86)	4 (80)
Subtotal	11 (41)	12 (24)	7 (25)	5 (24)
Education, n (%)				
Unskilled worker	13 (48)	18 (37)	11 (39)	7 (33)
Skilled worker	11 (41)	25 (51)	13 (46)	12 (57)
Bachelor's/master's degree	3 (11)	6 (12)	4 (14)	2 (10)
Residence, n (%)				
Farm/house	16 (59)	36 (72)	21 (75)	15 (71)
Apartment	11 (41)	13 (28)	7 (25)	6 (29)
Living alone, n (%)	13 (48)	9 (19)	4 (15)	5 (25)
Smoking, n (%)	1 (4)	7 (15)[a]	5 (18)	2 (10)[b]

CI = confidence interval.
a) N_s = 48.
b) N_c = 20.

Clinical measures

The differences between the intervention group and the control group at baseline due to the preoperative weight loss intervention had disappeared at the seven-year follow-up; and body weight, BMI and blood pressure were similar in the two groups (**Table 2**).

TABLE 2 Presentation of clinical outcomes: weight, BMI and blood pressure, and patient-reported outcomes: KOOS in the intervention group and the control group preoperatively and at seven-year follow-up (N_{total} = 49).

	Before TKA		7-yr follow-up		Did not remember		Difference in change between groups at 7-yr follow-up	p-value[a]
	intervention (N_i = 28)	control (N_c = 21)	intervention (N_i = 28)	control (N_c = 21)	intervention (N_i = 28)	control (N_c = 21)		
Primary outcomes								
Weight, mean (95% CI), kg	93.6 (88.8-98.3) (n = 27)	102.6 (96.5-108.6) (n = 20)	104.1 (97.8-110.4) (n = 27)	104.8 (96.8-112.8) (n = 20)	10.5 (6.8-14.1) SD: ± 9.1 (n = 27)	2.2 (–0.7-5.2) SD: ± 6.4 (n = 20)	–8.2 (–13.0–-3.4) SD: ± 9.0 (n = 47)	0.001 (n = 47)
BMI, mean (95% CI), kg/m²	33.5 (31.9-35.2) (n = 27)	36.3 (34.5-38.2) (n = 20)	37.3 (34.9-39.8) (n = 27)	37.1 (34.6-39.6) (n = 20)	3.8 (2.4-5.2) (n = 27)	0.8 (–0.3-1.8) (n = 20)	–3.1 (–4.8–-1.3) (n = 47)	0.001 (n = 47)
Systolic blood pressure, mean (95% CI), mmHg	134.4 (128.1-140.8) (n = 27)	146.5 (136.7-156.4) (n = 20)	147.4 (137.9-157.0) (n = 20)	140.9 (132.0-149.8) (n = 20)	13 (1.1-24.9) (n = 27)	–5.6 (–15.7-4.5) (n = 20)	–18.6 (–34.–-2.7) (n = 47)	0.022 (n = 57)
Diastolic blood pressure, mean (95% CI), mmHg	80.6 (76.8-84.4) (n = 27)	83.8 (78.7-88.9) (n = 20)	82.1 (77.8-86.5) (n = 27)	79.9 (75.0-84.7) (n = 20)	1.6 (–3.8-6.9) (n = 27)	–4.0 (–8.2-0.3) (n = 20)	5.5 (–1.5-12.5) (n = 47)	0.122 (n = 47)
Secondary outcomes, mean (95% CI)								
KOOS ADL	52.4 (46.3-58.5) (n = 28)	54.0 (45.3-62.7) (n = 21)	70.1 (60.2-80.0) (n = 28)	77.1 (66.9-87.3) (n = 21)	17.7 (7.1-28.3) (n = 28)	23.1 (13.1-33.2) (n = 21)	5.4 (–9.3-20.1) (n = 49)	0.449 (n = 49)
KOOS QOL	29.5 (22.8-36.1) (n = 28)	33.0 (27.4-38.7) (n = 21)	59.2 (48.6-69.7) (n = 28)	67.3 (56.0-78.5) (n = 21)	29.7 (17.7-41.6) (n = 28)	34.2 (21.1-47.3) (n = 21)	4.5 (–12.9-22.0) (n = 49)	0.599 (n = 49)
KOOS SYMP	52.2 (45.9-58.4) (n = 28)	55.8 (46.9-64.7) (n = 21)	74.6 (66.8-82.4) (n = 28)	79.6 (73.5-85.7) (n = 21)	22.4 (14.4-30.5) (n = 28)	23.8 (14.1-33.5) (n = 21)	1.4 (–10.9-13.6) (n = 49)	0.824 (n = 49)
KOOS PAIN	43.6 (38.1-49.1) (n = 27)	50 (42.5-57.5) (n = 21)	75.2 (65.4-85.0) (n = 27)	81.4 (72.3-90.4) (n = 21)	31.6 (20.6-42.6) (n = 27)	31.4 (21.3-41.5) (n = 21)	–0.2 (–14.8-14.4) (n = 48)	0.977 (n = 48)
KOOS SPORT	16.6 (10.0-23.4) (n = 27)	11.5 (6.8-17.9) (n = 21)	26.5 (16.4-.7) (n = 21)	39.9 (26.1-53.7) (n = 20)	9.9 (–2.1-21.9) (n = 27)	28.4 (15.2-41.6) (n = 20)	18.5 (1.2-35.9) (n = 47)	0.037 (n = 47)

ADL = function in daily living; CI = confidence interval; KOOS = Knee Injury and Osteoarthritis Outcome Score; PAIN = pain; QOL = knee-related quality of life; SD = standard deviation; SPORT = function in sport and recreation; SYMP = other symptoms; TKA = total knee arthroplasty.
a) For the differences between the intervention and control group.

At the seven-year follow-up, patients in the intervention group had gained 10.5 kg (95% CI: 6.8-14.1 kg), whereas the patients in the control group had gained 2.2 kg (CI: –0.7-5.2 kg). The mean waist circumference was 123 cm for men (standard deviation (SD): ± 9.2 cm) and 115.8 cm for women (SD: ± 12.3 cm).

Patient-reported outcome

For both groups, all KOOS sub-scores increased from baseline to the seven-year follow-up and no differences were observed in the KOOS sub-scores between the two groups, except from KOOS SPORT where the difference between the intervention group and control group was statistically significant (Table 2). Distribution of the patients' knee ROM in their operated knee calculated by CKRS is presented in **Table 3.**

TABLE 3 The distribution of the patients' knee range of motion in their operated knee seven years after total knee arthroplasty. The results are calculated by Copenhagen Knee Range of Motion Scale with frequency (%) (N_{total} = 45). Three patients could not remember, which leg they were operated in during this study (two in the intervention group and one in the control group).

	Surgery in right knee		Surgery in left knee		Did not remember	
	intervention (N_i = 18)	control (N_c = 11)	intervention (N_i = 7)	control (N_c = 9)	intervention (N_i = 2)	control (N_c = 1)
Flexion, °						
60	0	0	0	0	0	0
75	1 (6)	0	0	0	0	0
90	3 (17)	0	1 (14)	1 (11)	0	0
105	3 (17)	2 (18)	2 (29)	2 (22)	1 (50)	0
120	4 (22)	2 (18)	3 (43)	1 (11)	1 (50)	0
135	7 (39)	7 (64)	1 (14)	5 (55)	0	1 (100)
Extension, °						
0	0	0	0	0	0	0
15	1 (6)	0	0	1 (11)	0	0
30	5 (28)	2 (18)	1 (14)	3 (33)	1 (50)	0
45	6 (33)	4 (36)	6 (86)	2 (22)	0	0
Hyperextension	6 (33)	5 (45)	0	3 (33)	1 (50)	1 (100)

DISCUSSION

Results from this follow-up study showed that improvements in the intervention group in body weight, BMI and blood pressure following the RCT weight loss intervention [12] had disappeared seven years later. The results thus indicate that it is difficult for the patients to maintain the weight loss over a longer period after the intervention has concluded. A meta-analysis of clinical trials on weight loss with a minimum one-year follow-up period reported a weight loss by different interventions involving reduced energy diet and/or weight-management medication during the first six months; after six months, weight loss plateaued. Weight loss based on a very-low energy diet resulted in a major mean weight loss of 17.9 kg (16% of body weight) at the six-month follow-up, but this was followed by a rapid weight gain; at the 12-month follow-up, the mean weight loss was 10.9 kg (10% of the patients' body weight) and at 36 months it was 5.6 kg (5% of body weight) [16]. These results support that patients participating in a weight loss intervention slowly regain weight over time. The meta-analysis also showed that patients in studies with a four-year follow-up period had maintained some of the weight loss at that time; a mean 3-6 kg (3-6% of their body weight) [16]. This may indicate a slow weight regain, but it this remains unknown due to the maximum follow-up time of four years.

The lack of a sustained weight loss in our study may be explained by a lack of support after the intervention had concluded and a lack of established new habits on the part of the patients. Understanding the patient's problems maintaining a weight loss may help inform the clinicians in their communication with patients with obesity - who may wish and should be encouraged to lose weight - about the importance of strategies to maintain weight loss over a longer period of time. A study by Christensen et al. [17] showed that it is possible to maintain a weight

loss similar to that achieved in our intervention for three years after patients had lost 10% of their body weight and maintained the weight loss at one-year follow-up. The weight loss scheme comprised a daily meal replacement or intermittent low-energy diet combined with group-based dietary and behavioural interventions lead by a dietitian [17]. In our study, the distribution of formula food in the intervention group concluded one year after surgery. However, it was possible for the patients to buy the formula food themselves.

With weight regain, waist circumference may be expected to expand, and the absence of any change in systolic blood pressure between the groups from preoperatively to the seven-year follow-up may be seen in the context of the regained weight and waist circumference in the intervention group. According to a study by Lean et al. [13], the odds for hypertension will increase with increased waist circumference [13]. Furthermore, it is well known that blood pressure increases with age because the arteries become stiffer and more resilient. Therefore, an increase in blood pressure over time would have been unavoidable. The same study showed an increase in the odds for Type 2 diabetes with an increasing waist circumference; men with a waist circumference equal to or exceeding 102 cm had 4.45 higher odds than men with a waist circumference of less than 94 cm of developing Type 2 diabetes [13]. The prevalence of Type 2 diabetes increases with age; and over the past 20 years, the number of people registered with diabetes has tripled in Denmark. The cause of this increase is probably due to an ageing population that is becoming less physically active and increasingly obese [18, 19]. The results of the aforementioned study [13] may explain why the prevalence of hypertension and Type 2 diabetes had increased from the time before operation to follow-up. In our study, none of the patients had the recommended waist circumference below 94 cm for men and 80 cm for women.

PRO at the seven-year follow-up showed an overall improvement of the KOOS sub-scores within the two groups. This is in agreement with another study with seven-year follow-up after TKA [20] and a meta-analysis of cohort studies with 12-month follow-up [8]. TKA is an effective operation in the treatment of OA of the knee that for many patients entails less pain and increased mobility, and the primary study by Liljensøe et al. [12] verified this.

Limitations

The greatest limitation of this study was the large number of patients lost to follow-up from baseline to the seven-year follow-up; 27 of 76 included patients (35%). The low number of patients in this study reduced its power and increased the risk of type-2 error. A strength of this study was the long follow-up period of seven years after TKA, illuminating how difficult it is to maintain a weight loss after a dietary intervention. This indicates a need for more support to sustain weight losses in this patient group.

CONCLUSIONS

The results at the follow-up seven years after TKA showed that patients were unable to sustain their weight loss without support. The patients in the intervention group gained both the lost and some additional weight, and the majority of the patients had hypertension. At the seven-year follow-up, no differences were observed in hypertension, diabetes, PRO and knee ROM among patients who were randomised to the weight loss intervention and patients who received standard care before TKA.

The results of the present study underpin the importance of support in sustaining weight loss over a longer period in this patient group. The results also show that it is feasible and safe to implement a weight loss intervention before TKA, but the study also demonstrates the need for long-term interventions to support weight maintenance after weight loss interventions in patient with obesity before TKA.

Ethical approval

Approval for the RCT was obtained from The Regional Committees on Health Ethics for Central Denmark

(Journal number: S-201001309). The study was registered with www.ClinicalTrials.gov (NCT01469403). Furthermore, the study was conducted in accordance with the Helsinki Declaration and good clinical practice guidelines. Finally, the study was approved by the Danish Data Protection Agency (1-16-02-27-20). The patients gave written informed consent prior to their inclusion.

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REFERENCES

1. Felson DT, Anderson JJ, Naimark A et al. Obesity and knee osteoarthritis. The Framingham Study. Ann Intern Med 1988;109:18-24.
2. Järvenpää J, Kettunen J, Soininvaara T et al. Obesity has a negative impact on clinical outcome after total knee arthroplasty. Scand J Surg 2012;101:198-203.
3. Kulkarni K, Karssiens T, Kumar V et al. Obesity and osteoarthritis. Maturitas 2016;89:22-8.
4. Felson DT. An update on the pathogenesis and epidemiology of osteoarthritis. Radiol Clin North Am 2004;42:1-9.
5. Lopez-Gomez JJ, Izaola-Jauregui O, Torres-Torres B et al. Influence of a meal-replacement diet on quality of life in women with obesity and knee osteoarthritis before orthopedic surgery. Nutr Hosp 2018;35:71-7.
6. Hussain SM, Wang Y, Shaw JE et al. Relationship of weight and obesity with the risk of knee and hip arthroplasty for osteoarthritis across different levels of physical performance: a prospective cohort study. Scand J Rheumatol 2019;48:64-71.
7. Liljensøe A, Lauersen JO, Søballe K et al. Overweight preoperatively impairs clinical outcome after knee arthroplasty. Acta Orthop 2013;84:392-7.
8. Pozzobon D, Ferreira PH, Blyth FM et al. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open 2018;8:e017689.
9. Torres-Claramunt R, Hinarejos P, Leal-Blanquet J et al. Does obesity influence on the functional outcomes of a total knee arthroplasty? Obes Surg 2016;26:2989-94.
10. Amin AK, Patton JT, Cook RE et al. Does obesity influence the clinical outcome at five years following total knee replacement for osteoarthritis? J Bone Joint Surg Br 2006;88:335-40.
11. Nunez M, Lozano L, Nunez E et al. Good quality of life in severely obese total knee replacement patients: a case-control study. Obes Surg 2011;21:1203-8.
12. Liljensøe A, Laursen JO, Bliddal H et al. Weight loss intervention before total knee replacement: a 12-month randomized controlled trial. Scand J Surg 2019:1457496919883812.
13. Lean M, Han T, Seidell J. Impairment of health and quality of life in people with large waist circumference. Lancet 1998;351:853-6.
14. Roos EM, Lohmander LS. The Knee Injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. Health Qual Life Outcomes 2003;1:64.
15. Mørup-Petersen A, Holm PM, Holm CE et al. Knee osteoarthritis patients can provide useful estimates of passive knee range of motion: development and validation of the Copenhagen Knee ROM Scale. J Arthroplasty 2018;33:2875-83.e3.
16. Franz MJ, Vanwormer JJ, Crain AL et al. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. J Am Diet Assoc 2007;107:1755-67.
17. Christensen P, Henriksen M, Bartels EM et al. Long-term weight-loss maintenance in obese patients with knee osteoarthritis: a randomized trial. Am J Clin Nutr 2017;106:755-63.

18. Carstensen B, Rønn PF, Jørgensen ME. Prevalence, incidence and mortality of type 1 and type 2 diabetes in Denmark 1996-2016. BMJ Open Diabetes Res Care 2020;8:e001071.
19. Almdal TK, Kolding J, Kjeldsen HC. Type 2-diabetes. https://www.sundhed.dk/sundhedsfaglig/laegehaandbogen/endokrinologi/tilstande-og-sygdomme/diabetes-mellitus/type-2-diabetes/ (2 Aug 2021).
20. Nunez M, Lozano L, Nunez E et al. Total knee replacement and health-related quality of life: factors influencing long-term outcomes. Arthritis Rheum 2009;61:1062-9.