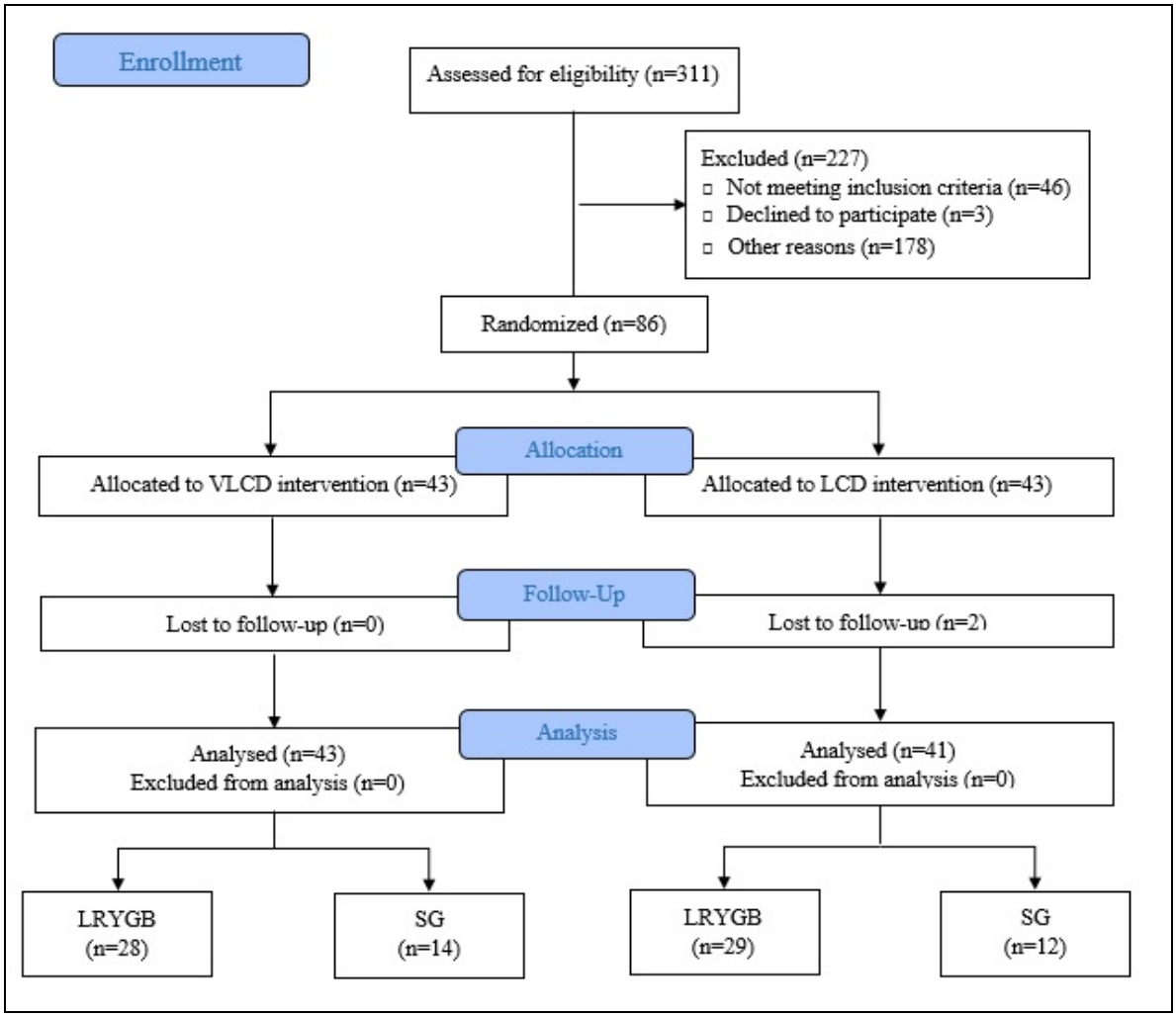
Participant Flow



Abbreviations: VLCD, very low calorie diet; LCD, low calorie diet; LRYGB, laparoscopic Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy.

Baseline Characteristics

Table 1. Descriptive characteristics of the participants at baseline

Parameters	**Group** ***n=84***	**VLCD** ***n=43***	**LCD** ***n=41***
Gender, female (*n*/%)	63 (75%)	29 (67.5%)	34 (82.9%)
Age (years)	45.3±10.1	45.2±10.5	45.5±9.7
Weight (kg)	129.1±20.2	131.9±22.6	126.2±17.1
Height (cm)	165.1±8.4	166.7±9.4	163.4±6.8
Body mass index (kg/m^2)	47.3±5.2	47.3±5.3	47.2±5.0
Waist (cm)	135.8±15.1	137.3±16.5	134.2±13.5
SBP (mmHg)	147.8±24.3	145.8±30.0	149.7±17.6
DBP (mmHg)	91.8±12.5	91.4±13.2	92.2±12.1
Comorbidities			
Type 2 diabetes (*n*/%)	15 (17.9%)	11 (25.6%)	4 (9.8%)
Dyslipidemia (*n*/%)	35 (41.7%)	20 (46.5%)	15 (36.6%)
Hypertension (*n*/%)	41 (48.8%)	24 (55.8%)	17 (41.5%)
OSAS (*n*/%)	19 (22.6%)	11 (25.6%)	8 (19.5%)

Abbreviations: VLCD, very low calorie diet; LCD, low calorie diet; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; OSAS, obstructive sleep apnea syndrome; Results are expressed as mean ± standard deviation or number and percentage of individuals.

Outcome Measures

Primary outcome measures

Table 2. Changes in hepatic volume before and after a VLCD or LCD.

Parameters	Baseline (cc)	Final	Change (cc)	Change (%)	Intra groups	
Total participants					**P-value**	**Adjusted P-value†**
VLCD (*N*=34)	2653±654	2208±458	-445±432	-15,6±11,2	<0.001	0.045
LCD (*N*=38)	2600±833	2268±775	-332±340	-12,3±10,6	<0.001	0.045
P-value*	0.768	0.873	0.222	0.212		
Adjusted P-value†	0.923	0.923	0.409	0.409		
Participants with a hepatic volume < 3L						
VLCD (*N*=25)	2355±320	2010±303	-345±226	-14.4±9.1	<0.001	0.045
LCD (*N*=32)	2342±401	2071±360	-271±222	-11.3±8.5	<0.001	0.045
P-value	0.898	0.503	0.227	0.190		
Adjusted P-value	0.923	0.696	0.409	0.409		
Participants with a hepatic volume > 3 L						
VLCD (*N*=9)	3480±643	2757.2±360.3	-723±707	-18.8±15.9	0.015	0.054
LCD (*N*=6)	3975±1203	3317±1439	-657±632	-18.0±18.3	0.052	0.156
P-value	0.316	0.390	0.857	0.923		
Adjusted P-value	0.0517	0.585	0.923	0.923		

Abbreviations: VLCD, very low calorie diet; LCD, low calorie diet; cc: cubic centimeters; NS, not significant.

Results are expressed as mean ± standard deviation. To determine differences between groups a U was applied.

*: P value for between-group differences.

†The Benjamin-Hockberg procedure for multiple-testing was used to calculate adjusted P-values, considering an FDR <0.05 as significant.

Secondary outcomes

Table 3. Changes in weight, body composition and blood pressure after 21 days of VLCD or LCD interventions.

Parameters	Diet	Baseline	Final	Change	Intra groups	
					P-value	Adjusted P-value†
Weight (kg)	VLCD (*n*=42) LCD (*n*=41) P-value* Adjusted P-value†	131.2±22.4 126.2±17.1 0.257 0.402	123.6±21.0 120.8±16.0 0.511 0.608	-7.65±2.66 -5.36±2.21 <0.001 0.002	<0.001 <0.001	0.002 0.002
TWL (%)	VLCD (*n*=42) LCD (*n*=41) P-value* Adjusted P-value†	131.2±22.4 126.2±17.1 0.257 0.402	123.6±21.0 120.8±16.0 0.511 0.608	-5.81±1.71 -4.19±1.55 <0.001 0.002	<0.001 <0.001	0.002 0.002
BMI (kg/m^2)	VLCD (*n*=42) LCD (*n*=41) P-value* Adjusted P-value†	47.2±5.4 47.2±5.0 0.984 0.984	44.5±5.6 45.2±4.8 0.504 0.068	-2.73±0.82 -2.01±0.81 <0.001 0.002	<0.001 <0.001	0.002 0.002
Waist circumference (cm)	VLCD (*n*=42) LCD (*n*=41) P-value* Adjusted P-value†	137.2±16.7 134.2±13.5 0.388 0.530	131.2±15.3 129.5±11.0 0.576 0.670	-5.95±7.13 -4.77±7.01 0.453 0.581	<0.001 <0.001	0.002 0.002
Fat (kg)	VLCD (*n*=42) LCD (*n*=40) P-value* Adjusted P-value†	66.2±16.6 63.7±14.4 0.605 0.681	62.0±15.6 61.1±11.0 0.752 0.800	-4.11±4.43 -2.67±3.14 0.094 0.188	<0.001 <0.001	0.002 0.002
Lean mass (Kg)	VLCD (*n*=42) LCD (*n*=40) P-value* Adjusted P-value†	65.0±15.2 61.6±7.1 0.207 0.379	61.5±13.0 58.9±6.9 0.247 0.402	-3.52±4.59 -2.78±3.32 0.408 0.537	<0.001 <0.001	0.002 0.002
Muscle mass (Kg)	VLCD (*n*=42) LCD (*n*=40) P-value* Adjusted P-value†	61.8±14.5 58.5±6.8 0.202 0.379	58.4±12.4 55.9±6.5 0.247 0.402	-3.38±4.44 -2.65±3.17 0.392 0.530	<0.001 <0.001	0.002 0.002
Water (Kg)	VLCD (*n*=33) LCD (*n*=36) P-value* Adjusted P-value†	48.3±11.4 45.5±6.1 0.212 0.380	45.3±9.9 43.4±5.8 0.360 0.514	-3.08±1.90 -2.08±2.21 0.050 0.104	<0.001 <0.001	0.002 0.002
SBP (mmHg)	VLCD (*n*=38) LCD (*n*=40) P-value* Adjusted P-value†	149.1±21.9 149.7±17.8 0.902 0.940	139.4±14.4 141.5±17.0 0.286 0.433	-9.71±21.85 -8.23±17.05 0.738 0.800	0.009 <0.001	0.020 0.002

DBP (mmHg)	VLCD (*n*=38) LCD (*n*=40) P-value* Adjusted P-value†	91.2±13.3 92.4±12.1 0.731 0.800	84.7±10.4 86.06±11.5 0.342 0.503	-6.50±13.00 -6.36±10.83 0.960 0.980	0.004 <0.001	0.010 0.002

Abbreviations: VLCD, very low calorie diet; LCD, low calorie diet; BMI, body mass index; TWL, total weight loss; SBP, systolic blood pressure; DBP, diastolic blood pressure; NS, not significant.

Results are expressed as mean ± standard deviation. To determine differences between groups a t-student test was applied.

*: P value for between-group differences.

†The Benjamin-Hockberg procedure for multiple-testing was used to calculate adjusted P-values, considering an FDR <0.05 as significant.

Table 4. Changes in glycemic and lipid profiles after 21 days of VLCD or LCD interventions.

Parameters	Diet	Baseline	Final	Change	Intra groups	
Glucose profile					**P-value**	**Adjusted P-value†**
Serum glucose (mg/dL)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	122.6±49.8 102.7±33.5 0.032 0.068	97.3±15.4 95.7±19.2 0.670 0.699	-25.3±45.3 -7.0±19.9 0.021 0.052	0.001 0.032	0.001 0.068
HbA_1c (%)	VLCD (*n*=43) LCD (*n*=39) P-value* Adjusted P-value†	6.5±1.7 5.9±1.4 0.597 0.655	6.01±1.2 5.7±1.2 0.270 0.374	-0.5±0.6 -0.2±0.3 0.037 0.072	<0.001 <0.001	<0.001 <0.001
Serum insulin (mcUI/mL)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	23.2±14.1 19.0±10.5 0.123 0.213	15.0±8.4 15.0±9.0 0.922 0.922	-8.2±10.5 -4.0±6.5 0.033 0.068	<0.001 <0.001	<0.001 <0.001
HOMA-IR	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	5.4 (3.4-8.6) 4.5 (2.9-6.7) 0.074 0.133	3.25 (2.1-4.3) 3.0 (1.9-4.4) 0.424 0.545	-2.4(-0.9-(-3.4)) -1.3(+0.01-(-2.2) 0.019 0.050	<0.001 <0.001	<0.001 <0.001
Lipid profile						
Total Cholesterol (mg/dL)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	182.0±30.8 190.9±34.9 0.233 0.338	158.3±30.6 172.7±33.0 0.043 0.081	-23.7±23.8 -18.3±21.1 0.274 0.374	<0.001 <0.001	<0.001 <0.001
HDL-cholesterol (mg/dL)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	47.1±10.1 53.0±12.1 0.013 0.037	39.4±9.5 46.3±9.9 0.002 0.001	-7.7±6.7 -6.8±7.6 0.547 0.630	<0.001 <0.001	<0.001 <0.001
LDL-cholesterol (mg/dL)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	106.6±26.3 110.9±31.6 0.560 0.630	95.2±30.8 104.6±29.5 0.162 0.270	-11.4±17.33 -6.6±17.1 0.198 0.297	<0.001 0.022	<0.001 0.052
Triglycerides (mg/dL)	VLCD (*n*=43) LCD (*n*=41) P-value* Adjusted P-value†	126 (97-184) 119 (91-172) 0.450 0.557	107.0 (86-132) 103 (79.5-132.5) 0.458 0.557	-21(+6-(-55)) -13(+7.5-(-50.5) 0.668 0.699	0.001 0.002	0.001 0.006
Uric acid (mg/dL)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	5.90±1.48 5.49±1.22 0.193 0.297	6.0±1.7 6.9±8.9 0.508 0.602	+0.06±1.23 +1.39±8.79 0.328 0.434	0.179 0.683	0.288 0.699

Abbreviations: VLCD, very low calorie diet; LCD, low calorie diet; HbA1c, glycosylated hemoglobin; HDL, High-density lipoprotein; LDL, low density lipoproteins.

Parameters following a normal distribution are expressed as mean ± standard deviation and median (interquartile range: 25-75). To determine differences between groups a t-student test was applied as well as a Mann Whitney test. The Wilcoxon test was used for nonparametric paired data.

*: P value for between-group differences.

†The Benjamin-Hockberg procedure for multiple-testing was used to calculate adjusted P-values, considering an FDR <0.05 as significant.

Table 5. Changes in biochemical parameters after 21 days of VLCD or LCD interventions.

Parameters	Diet	Baseline	Final	Change	Intra groups	
Renal function					**P-value**	**Adjusted P-value†**
Urea (mg/dL)	VLCD (*n*=43) LCD (*n*=39) P-value* Adjusted P-value†	33.4±8.8 35.64±7.3 0.301 0.426	31.3±12.0 36.05 0.038 0.100	-2.1±9.9 +0.4±6.2 0.185 0.308	0.749 0.323	0.832 0.439
Creatinine (mg/dL)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	0.71±0.19 0.74±0.11 0.440 0.522	0.76±0.19 0.77±0.12 0.905 0.933	+0.05±0.11 +0.02±0.06 0.218 0.347	0.005 0.020	0.022 0.067
eGFR (ml/min/1.7)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	106.6±18.1 100.1±13.5 0.067 0.147	101.4±19.6 97.8±14.7 0.354 0.441	-5.2±10.0 -2.0±6.8 0.095 0.200	<0.001 <0.001	0.001 0.001
Hepatic function and liver enzimes						
AST (UI/L)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	22.2±12.4 19.8±5.7 0.251 0.390	29.1±11.2 22.7±7.7 0.003 0.016	+7.0±9.0 +2.9±7.4 0.028 0.078	<0.001 0.017	0.001 0.062
ALT (UI/L)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	27.5±22.6 24.4±11.1 0.396 0.478	39.8±26.4 28.7±15.5 0.023 0.070	+12.3±19.8 +4.2±12.8 0.032 0.086	<0.001 0.043	0.001 0.108
GGT (UI/L)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	40.2±49.7 28.5±18.7 0.153 0.275	28.4±26.5 23.8±16.4 0.339 0.439	-11.7±33.5 -4.7±9.8 0.206 0.335	0.027 0.004	0.078 0.02
Leukocyte count						
Leukocytes (x10^3/ul)	VLCD (*n*=43) LCD (*n*=39) P-value* Adjusted P-value†	7.84±2.05 7.47±1.89 0.349 0.441	6.2±1.5 6.60±1.6 0.296 0.426	-1.60±1.27 -0.87±1.51 0.020 0.067	<0.001 0.001	0.001 0.001
Neutrophils (x10^3/ul)	VLCD (*n*=43) LCD (*n*=39) P-value* Adjusted P-value†	4.72±1.50 4.74±1.60 0.945 0.959	3.6±1.1 4.09±1.27 0.059 0.133	-1.14±0.92 -0.66±1.23 0.045 0.109	<0.001 0.002	0.001 0.012
Lymphocytes (x10^3/ul)	VLCD (*n*=43) LCD (*n*=39) P-value* Adjusted P-value†	2.26±0.66 2.00±0.49 0.051 0.119	1.96±0.5 1.84±0.49 0.277 0.422	-0.30±0.40 -0.15±0.40 0.100 0.200	<0.001 0.022	0.001 0.070

Monocytes (x10^3/ul)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	0.55±0.18 0.51±0.15 0.498 0.571	0.49±0.1 0.49±0.14 0.906 0.932	-0.06±0.12 -0.29±0.10 0.148 0.273	0.001 0.097	0.001 0.200
Protein status and inflammation						
Total proteins (g/dL)	VLCD (*n*=43) LCD (*n*=41) P-value* Adjusted P-value†	7.12±0.35 7.12±0.41 0.964 0.964	7.25±0.37 7.19±0.41 0.514 0.580	+0.13±0.30 +0.05±0.34 0.304 0.426	0.009 0.336	0.037 0.439
Albumin (g/dL)	VLCD (*n*=43) LCD (*n*=41) P-value* Adjusted P-value†	.34±0.23 4.32±0.25 0.882 0.933	4.46±0.24 4.38±0.26 0.135 0.256	+0.13±0.22 +0.05±0.22 0.113 0.220	0.001 0.184	0.001 0.308
Prealbumin (mg/dL)	VLCD (*n*=43) LCD (*n*=40) P-value* Adjusted P-value†	23.75±5.51 23.55±4.04 0.849 0.914	20.74±4.85 21.56±5.27 0.466 0.544	-3.01±3.97 -2.10±4.49 0.327 0.439	<0.001 0.005	0.001 0.022
CRP (mg/dL)	VLCD (*n*=43) LCD (*n*=41) P-value* Adjusted P-value†	0.80 (0.44-1.30) 0.70 (0.50-1.40) 0.805 0.880	0.6 (0.4-1.1) 0.8 (0.5-1.3) 0.160 0.280	-0.10(+0.10-(-0.60) -0.05(0.18-(-0.33)) 0.292 0.423	0.010 0.359	0.039 0.441

Abbreviations: VLCD, very low calorie diet; LCD, low calorie diet; eGFR, estimated glomerular filtration rate; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gammaglutamyltransferase; CRP, C-reactive protein.

Parameters following a normal distribution are expressed as mean ± standard deviation and median (interquartile range: 25-75). To determine differences between groups a t-student test was applied as well as a Mann Whitney test. The Wilcoxon test was used for nonparametric paired data.

*: P value for between-group differences.

†The Benjamin-Hockberg procedure for multiple-testing was used to calculate adjusted P-values, considering an FDR <0.05 as significant.

Table 6. Surgical complications from the intervention until 6 months

	VLCD *N*=42	LCD *N*=41
Early complications		
Major	Prolonged hospitalization (> 7 days): intra-abdominal collection. (LRYGB)	Prolonged hospitalization (> 7 days): infection of the wound by MARSA that required antibiotic treatment and hospitalization of more than seven days. (LRYGB)
	Surgical site infection (superficial, deep or organ space) requiring debridement or washout in the operating room or percutaneous intervention. (LRYGB)	Prolonged hospitalization (> 7 days): small gastrointestinal anastomosis leak that did not require reoperation. (LRYGB)
	Venous thrombotic event requiring administration of anticoagulant: bilateral pulmonary thromboembolism that required anticoagulant treatment. (LRYGB)	Prolonged hospitalization (> 7 days): prolonged stay in the intensive care unit for pyelonephritis caused by urinary infection. (SG)
		Gastrointestinal hemorrhage requiring transfusion. (LRYGB)
Minor	Urinary tract infection managed with antibiotics. (LRYGB)	Urinary tract infection managed with antibiotics. (LRYGB)
	Symptomatic cholelithiasis. (LRYGB)	
Late complications		
Major	Gastric sleeve stenosis/obstruction requiring revision to a gastric bypass: gastric torsion. (SG)	Gastrointestinal hemorrhage requiring transfusion. (LRYGB)
		Cholecystectomy. (LRYGB)
Minor	No minor or late complications occurred	No minor or late complications occurred

Abbreviations: VLCD, very low calorie diet; LCD, low calorie diet

Table 7. Post operatory hospital stay.

	VLCD ***N*=42**	**LCD** ***N*=41**	**P-value Between groups**
Days of hospital stay	2.8±1.1	3.0±1.7	**NS**

Abbreviations: VLCD, very low calorie diet; LCD, low calorie diet; NS, not significant.

Table 8. Dietary compliance and tolerance

	VLCD ***N*=42**	**LCD** ***N*=41**	**P-value Between groups**
Compliance			
Returned formula sachets	96.7±6.8%	97.0±7.4%	NS
Adherence to the dietary intervention	High adherence: 94% *(≥80% of the sachets consumed)* Low adherence: 6% *(<80% of the sachets consumed).*		NS
Extra food	Very good or good adherence: 95.3% Regular 2.3% Poor: 2.3%	Very good or good adherence: 92.7% Regular 4.9% Poor: 2.4%	NS
Tolerance			
Dizziness *First week*	39.5%	12%	0.008

Asthenia *First week* *Second week*	48.8% 37.2%	17% 21%	<0.05 <0.05
Other recorded tolerance parameters	--	--	NS
Other results			
The percentage of weight lost at 6 months of surgery was 28.8±5.4% in those individuals with high adherence (≥ 80%) and 27.5±12 in those with low adherence (<80%), P= 0.666 between high and low adherence			
No differences in the rate of surgical complications were shown between those individuals with high or lower adherence to the intervention measured by the formula sachets returned P = 0.686.			

Abbreviations: VLCD, very low calorie diet; LCD, low calorie diet; NS, not significant.

Adverse Events

There were no adverse events related to the intervention