J Multidisciplinary Scientific Journal

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A Very Low-Calorie Ketogenic Diet Approach for Post-Bariatric Weight Regain: A Pilot Study

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Abstract: Weight regain (WR) after bariatric surgery, particularly sleeve gastrectomy, is a significant challenge, often driven by a combination of metabolic, behavioral, and lifestyle factors. Non-surgical interventions to manage WR are critical, given the increased risks and reduced efficacy of revisional surgeries. In this context, very low-calorie ketogenic diets (VLCKDs) have gained attention for their potential to promote weight loss and improve body composition in individuals struggling with WR. This study assessed the safety and efficacy of a VLCKD in 11 patients who experienced WR following sleeve gastrectomy. Over an 8-week period, patients demonstrated a significant average weight loss of 6.3% (p = 0.005), along with improvements in body composition, including reductions in body fat percentage (p = 0.003) and waist circumference (p = 0.003). Metabolic markers, such as insulin resistance (HOMA-IR), also improved significantly (p = 0.041). Although a decrease in the glomerular filtration rate was observed (p = 0.007), this finding is unlikely to be clinically relevant over the short term. Importantly, no major adverse events were reported, with only mild constipation observed. These results suggest that VLCKDs may be a promising non-surgical approach for managing WR post-bariatric surgery, though further studies are needed to assess long-term effects, especially on renal function.

Keywords: sleeve gastrectomy; very low-carbohydrate diet; body composition; insulin resistance; kidney function; weight loss; obesity; complications

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Citation: Ernesti, I.; Watanabe, M.; Genco, A. A Very Low-Calorie Ketogenic Diet Approach for Post-Bariatric Weight Regain: A Pilot Study. *J* **2024**, *7*, 482–488. https://doi.org/10.3390/j7040029

Academic Editor: Omorogieva Ojo

Received: 11 September 2024
Revised: 3 November 2024
Accepted: 8 November 2024
Published: 12 November 2024

1. Introduction

Obesity is a chronic, multifactorial disease that often requires several treatments to be controlled. Among these, bariatric surgery is currently the most effective long-term strategy [1]. However, especially in those lost to surgical and nutritional follow-up, weight regain (WR) is relatively common. Several aspects have been proposed in the literature as contributors to WR after bariatric surgery involving lifestyle, diet, socioeconomic status, genetics, and metabolic imbalances, in addition to surgical and anatomical factors [2]. However, the preoperative factors that predispose patients to significant WR remain unclear [3,4]. In particular, sleeve gastrectomy, representing 60% of all metabolic surgeries worldwide due to its safety, efficacy, and ease of procedure, is burdened by a 30% WR over the long term [5].

Among nutritional strategies, the ketogenic diet is one of the pivotal therapies for the treatment of obesity, with excellent evidence in terms of weight loss and improvement in complications of excess weight [6]. Its application in post-bariatric patients is, however, only scarcely evaluated. Correa and colleagues reported in a retrospective case series the efficacy and safety of a very low-calorie ketogenic diet (VLCKD) in 11 patients with insufficient weight loss or WR after gastric bypass, reporting an excellent safety profile, good tolerability, and an average weight loss of 9 kg in 2 months of therapy [7]. It has also been reported by Lopes Gomes and colleagues that whey protein supplementation in 16 patients undergoing bariatric surgery improved body composition after 16 weeks of treatment, although there was no reduction in caloric intake in the treated group compared to the control group following a low-fat diet [8]. Recently, Vinciguerra et al. showed that a heterogeneous population with previous mini bypass or sleeve gastrectomy and subsequent insufficient weight loss or WR responded well to a VLCKD in terms of efficacy and safety [9]. Although promising, the data in the literature are extremely scarce and no ad hoc study has been conducted in patients having specifically undergone sleeve gastrectomy with satisfactory weight loss and subsequent WR. We herein aimed to test whether the application of a VLCKD is a safe and effective treatment in these individuals, who represent a significant proportion of post-bariatric patients.

2. Materials and Methods

2.1. Study Design and Population

This was a single-center, prospective pilot study investigating the safety and efficacy of a VLCKD in the treatment of post-bariatric obesity. The study lasted 8 weeks, and patients were evaluated at baseline and at 4 and 8 weeks in terms of safety, efficacy, and dietary compliance. Patients enrolled were among those accessing the high specialization center for the treatment of obesity (CASCO), Sapienza University of Rome, with the following inclusion criteria: age over 18 years old; a BMI $\geq$ 30 Kg/m^2, previous sleeve gastrectomy, and clinically relevant WR after satisfactory weight loss. Exclusion criteria were the presence of one of the following conditions: type 1 diabetes, chronic kidney disease with a filtration rate of less than 60 mL/min, decompensated cirrhosis, congenital metabolic diseases, pregnancy or lactation, major psychiatric disorders, alcoholism and drug addiction, and patients who were not self-sufficient and without adequate family and social support. Data about demographic characteristics were collected through a structured interview. The study was approved by the local Ethics Committee (rif. 5475), conducted in accordance with the Declaration of Helsinki and the Good Clinical Practice. Written informed consent was obtained from all study participants before enrollment. The primary outcome was weight loss. Secondary outcomes were safety and improvement in metabolic profile and body composition.

2.2. Dietary Treatment

All patients underwent a VLCKD, with a carbohydrate intake of less than 50 g/daily and a protein intake 1.2–1.5 g/kg ideal body weight, and fat made up for the rest of the caloric intake. The energy requirement was calculated adjusting for physical activity level. The first 4 weeks, the patients consumed whey protein supplements kindly provided by Chiru-Med (Pescara, Italy) and one very low-carbohydrate meal per day (i.e., meat, fish, eggs, or cheese). Patients were prescribed a calorie deficit of ~600 kcal in the first 4 weeks, and then one very low-carbohydrate meal per day was added in place of the whey protein supplement, with a deficit of ~300 kcal/daily for the subsequent 4 weeks. Participants were counselled to drink at least 2 L of water/day and choose vegetarian and healthy sources of fat; protein was to come from fish, eggs, fresh dairy products, and lean meat, beyond provided supplements. Patients were counselled by a trained dietician every 4 weeks, and compliance was assessed through a 3-day dietary recall at each visit and beta hydroxybutyrate (BHB) assessment.

2.3. Biochemical Measures

Routine biochemical tests were handled according to standard operating practices, from fasting blood samples (electrolytes, glucose, insulin, lipid profile [triglycerides and total high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol], creatinine, alanine transferase (ALT), aspartate transaminase (AST), uric acid, and estimated glomerular filtration rate (GFR). BHB was measured in duplicate using enzyme colorimetric assays (StanBio, Boerne, TX, USA).

2.4. Anthropometric and Body Composition Assessments

Body weight was measured using a balance beam scale (Seca GmbH & Co., Hamburg, Germany). Height was rounded to the closest 0.5 cm. Waist circumference was measured midway between the lower rib and the iliac crest and hip circumference at the level of the widest circumference over the great trochanters to the closest 1.0 cm. Systolic and diastolic blood pressures (BPs) were measured using an automated digital device. As this dietary intervention is known to reduce BP, those on antihypertensives were advised to contact the study team in case of BP reduction.

2.5. Adverse Events

Adverse events were recorded though a structured questionnaire. The timing, duration, type, and entity of adverse event were recorded at each follow-up visit.

2.6. Statistical Analysis

Descriptive statistics for continuous variables were presented as number, mean, standard deviation, while categorical variables were presented as frequencies and percentages. The paired Wilcoxon signed-rank test was used to assess differences over time. Differences, associations, and interactions were considered significant if $p < 0.05$. The estimated mean weight of the study population based on our data is 115 ± 10. Expecting an 8% weight loss as clinically relevant, we estimated that a total of 10 patients was needed to detect this reduction, with an α of 0.05 and a $(1 - \beta)$ of 80%. Taking into account possible dropouts, 13 patients were enrolled. Statistical analysis was performed using SPSS Armonk, NY, USA, IBM corp. ver. 27.0 for Mac.

3. Results

Thirteen patients were enrolled. Of these, two dropped out during the second week of dietary treatment and were therefore excluded from the analysis. The reasons for dropping out were gastrointestinal intolerance (nausea) and scarce compliance to the diet (excess hunger). The mean time since bariatric surgery was 5 years; more specifically, most patients reported WR 3 years after reaching nadir weight. Baseline characteristics are summarized in Table 1.

Patients lost an average of 6.3% of their body weight over the eight-week period, with a statistically significant reduction from 112.92 ± 25.12 kg to 105.78 ± 22.52 kg ($p = 0.005$). Although the decrease in BMI from 41.78 ± 6.91 kg/m^2 to 40.03 ± 6.66 kg/m^2 did not reach statistical significance ($p = 0.074$), there were significant improvements in body composition. Waist circumference was reduced from 121.55 ± 19.98 cm to 112.00 ± 16.03 cm ($p = 0.003$), and hip circumference decreased from 129.91 ± 10.36 cm to 124.73 ± 9.62 cm ($p = 0.045$). Body fat percentage also showed a significant reduction from 42.22 ± 5.48% to 39.66 ± 6.38% ($p = 0.003$), while lean mass percentage increased from 57.78 ± 5.48% to 60.34 ± 6.38% ($p = 0.003$). Correspondingly, the fat/lean mass ratio improved from 0.77 ± 0.17 to 0.70 ± 0.19 ($p = 0.003$) and the waist-to-hip ratio (WHR) decreased from 0.93 ± 0.12 to 0.90 ± 0.10 ($p = 0.013$) (Table 1).

In terms of metabolic parameters, insulin resistance, as measured by HOMA-IR, significantly improved, with a reduction from 3.11 ± 1.67 to 2.18 ± 1.47 ($p = 0.041$). There was also a notable decrease in total cholesterol from 176.82 ± 40.84 mg/dL to 159.36 ± 38.31 mg/dL ($p = 0.041$), while HDL cholesterol showed a modest reduction from 58.55 ± 14.91 mg/dL to 53.27 ± 12.83 mg/dL ($p = 0.046$). Triglycerides and LDL cholesterol both trended lower, though these changes were not statistically significant. Uric acid levels remained stable, as did the electrolyte balance. A significant reduction in the glomerular filtration rate (GFR) was also recorded after the intervention, from 89.32 ± 18.09 mL/min/1.73 m^2 to 82.27 ± 16.75 mL/min/1.73 m^2 ($p = 0.007$), while blood urea nitrogen (BUN) showed a significant increase ($p = 0.003$) (Table 1). There were no significant changes in blood pressure, and no major adverse events were reported, with mild constipation being the only side effect noted.

Table 1. Baseline and post-intervention characteristics of the study population.

	Pre Mean ± st.dev.			Post Mean ± st.dev.			p
Age (years)	52.64	±	10.18	52.64	±	10.18	
Gender (%F)		69.00			69.00		
Body weight (kg)	112.92	±	25.12	105.78	±	22.52	**0.005**
BMI (kg/m^2)	41.78	±	6.91	40.03	±	6.66	0.074
Waist circumference (cm)	121.55	±	19.98	112.00	±	16.03	**0.003**
Hip circumference (cm)	129.91	±	10.36	124.73	±	9.62	**0.045**
Body fat (%)	42.22	±	5.48	39.66	±	6.38	**0.003**
Lean mass (%)	57.78	±	5.48	60.34	±	6.38	**0.003**
Fat mass (kg)	47.60	±	12.00	41.40	±	10.00	**0.003**
Lean mass (kg)	62.90	±	15.90	61.50	±	16.40	0.11
Fat/lean ratio	0.77	±	0.17	0.70	±	0.19	**0.003**
WHR	0.93	±	0.12	0.90	±	0.10	**0.013**
HOMA-IR	3.11	±	1.67	2.18	±	1.47	**0.041**
GFR (mL/min/1.73 m^2)	89.32	±	18.09	82.27	±	16.75	**0.007**
Blood urea nitrogen	35.38	±	10.82	44.91	±	14.63	**0.003**
AST	18.36	±	3.17	21.45	±	6.70	0.073
ALT	17.45	±	4.74	19.36	±	6.28	0.219
K	4.49	±	0.47	4.39	±	0.33	0.606
Na	142.75	±	4.10	140.55	±	2.50	0.16
Hba1c (%)	5.40	±	0.48	5.30	±	0.48	0.476
Uric acid mg/dL	6.01	±	1.72	5.90	±	1.55	0.248
Total cholesterol (mg/dL)	176.82	±	40.84	159.36	±	38.31	**0.041**
HDL cholesterol (mg/dL)	58.55	±	14.91	53.27	±	12.83	**0.046**
Triglycerides (mg/dL)	92.09	±	39.43	72.91	±	15.47	0.075
LDL cholesterol (mg/dL)	99.85	±	33.22	91.51	±	32.72	0.131

Baseline and post-intervention characteristics of the study population, including body composition, metabolic parameters, and safety markers. Results are presented as mean ± standard deviation. The *p*-values indicate the statistical significance of changes observed between baseline (Pre) and post-intervention (Post) values using a Wilcoxon signed-rank test. Significant differences are highlighted in bold. Abbreviations: BMI, Body Mass Index; WHR, Waist-to-Hip Ratio; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase; K, Potassium; Na, Sodium; HbA1c, Hemoglobin A1c; HDL, High-Density Lipoprotein; and LDL, Low-Density Lipoprotein.

4. Discussion

The present study provides important insights into the potential of a VLCKD as a therapeutic approach for WR in patients following sleeve gastrectomy, one of the most common bariatric procedures globally. Sleeve gastrectomy is known for its safety and effectiveness, yet it is burdened by significant long-term WR. This study aligns with and expands on the limited existing data that suggest VLCKDs may offer a non-surgical alternative to manage WR, a particularly relevant finding given the limitations of revisional surgeries, which are often less effective and come with an increased risk of complications compared to primary bariatric procedures [10].

The efficacy of the ketogenic diet in general obesity management is well established, with evidence supporting its role in inducing substantial weight loss and improving metabolic complications of excess weight. However, its application in the post-bariatric population, particularly following sleeve gastrectomy, remains underexplored. Previous studies have reported the efficacy and safety of VLCKDs in patients with insufficient weight loss or WR after bariatric procedures such as gastric bypass, mini-bypass, or sleeve gastrectomy [7,9]. Our study builds on these foundations by specifically targeting patients with WR following sleeve gastrectomy, a population that has not been adequately studied in the context of ketogenic diet interventions. The results of our study demonstrate significant weight loss and improvements in body composition, similar to those reported in earlier studies of post-bariatric populations. These findings are particularly encouraging given that WR after bariatric surgery is a multifactorial issue, often associated with poor long-term adherence to dietary and lifestyle changes, making non-surgical interventions critical for patient management [11,12]. The significant reduction in body fat percentage, waist circumference, and fat/lean ratio observed in our study further supports the use of VLCKDs as a means of not only promoting weight loss but also improving overall body composition in post-sleeve gastrectomy patients.

The absence of significant adverse events in our study population is particularly noteworthy, as safety concerns are a key consideration in managing patients after bariatric surgery. The mild constipation reported by a few patients was the only side effect, aligning with previous studies that have highlighted the good tolerability of ketogenic diets in both the general and bariatric populations [6,7,9]. Importantly, the intervention did not adversely affect key clinical markers such as blood pressure, electrolytes, or liver function, suggesting that VLCKDs can be implemented safely in this population.

However, our findings regarding the significant reduction in the glomerular filtration rate (GFR) post-intervention raise important questions about the long-term renal effects of ketogenic diets in bariatric patients. While the reduction in GFR was statistically significant, it is unlikely to be clinically relevant over the short study period, particularly given that no other signs of renal impairment were observed. Nonetheless, this result warrants further investigation in future studies with longer follow-up periods to assess whether the observed decline in GFR persists or worsens over time, particularly in individuals with pre-existing renal risk factors. Noteworthy, bariatric-naïve individuals being treated with a VLCKD even for longer periods are not known to develop any kidney impairment, with even improvements being reported, likely due to the significant weight loss obtained [13]. This aspect of the study highlights the importance of close renal monitoring in patients undergoing VLCKDs, especially as the long-term renal effects of such diets remain unclear.

In a broader context, these results highlight the potential role of VLCKDs as an effective non-surgical intervention for WR following bariatric surgery, particularly sleeve gastrectomy. This is especially relevant considering the limitations of current surgical options, where re-do surgeries often result in suboptimal outcomes and carry increased risks [10]. Given the chronic and multifactorial nature of obesity, non-surgical interventions that provide both efficacy and safety are essential in long-term patient management. Our study highlights the short-term benefits of VLCKDs in achieving significant weight loss and improvements in body composition, but long-term sustainability remains a critical issue. As seen in the broader literature, maintenance of weight loss after ketogenic diets is often challenging without substantial lifestyle modifications or adjunctive pharmacotherapy [14].

Noteworthy, our population was small and with a quite narrow age range, potentially limiting the relevance of our data to other ages. However, the VLCKD has demonstrated efficacy across all age groups, although its effects can vary between younger and older populations. Younger patients generally respond well to VLCKDs with significant reductions in body weight, insulin resistance, and body fat percentage. This population typically shows high metabolic adaptability and fewer adverse events, although adherence remains a challenge due to social and lifestyle factors [6]. In contrast, older adults benefit from VLCKDs in terms of weight loss and improvements in metabolic parameters but face an increased potential risk most importantly due to possible lack of familiar support and higher chances of forgetting essential supplements or water intake [15]. Both age groups show good short-term tolerance to VLCKDs with minimal severe adverse events when monitored by healthcare professionals, although the elderly require more cautious application [13,15].

While the short-term safety and efficacy of ketogenic diets (KDs) are well documented, their long-term effects remain less understood. VLCKDs, such as the one used in this study, are generally intended for short- to mid-term application due to their stringent caloric restriction, whereas isocaloric, high-fat ketogenic diets may be suitable for prolonged use, such as in managing refractory epilepsy. Although most long-term observational studies have not indicated any significant harm [16,17], recent evidence suggests that KDs may contribute to cellular senescence in various organs, including the heart and kidneys, and caution should be therefore used [18].

In conclusion, while our study provides promising evidence supporting the use of VLCKDs for WR following sleeve gastrectomy, further research is needed. Larger studies with longer follow-ups are essential to determine the long-term efficacy and safety of VLCKDs in this patient population. Additionally, future studies should explore whether VLCKDs could benefit patients with insufficient weight loss after sleeve gastrectomy, providing a broader therapeutic application for this dietary approach in bariatric care.

Author Contributions: Conceptualization, A.G., M.W. and I.E.; methodology, I.E. and M.W.; software, M.W.; validation, A.G.; formal analysis, M.W.; investigation, I.E. and M.W.; writing—original draft preparation, M.W.; writing—review and editing, A.G.; funding acquisition, A.G. All authors have read and agreed to the published version of the manuscript.

Funding: Protein supplements were kindly provided by Ketopharma (Chiru-med, Pescara, Italy).

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Policlinico Umberto I (protocol code 5475 24 October 2019). for studies involving humans.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Anonymized data are available upon reasonable request to corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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