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Effect of Cryolipolysis on Insulin Resistance in Type 2 Diabetic Females with Abdominal Obesity

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Abstract

Background: Cryolipolysis is a non-invasive procedure designed to target subcutaneous adipose tissue in obese patients that has emerged as a potential therapeutic approach for modifying insulin resistance(IR) in T2DM individuals.

Aim: to evaluate the efficacy of cryolipolysis in reducing IR among patients diagnosed with T2DM patients exhibiting abdominal obesity.

Research design: Randomized, two-group pre–post-test, controlled design. Patients and Methods: sixty females with T2DM exhibiting abdominal obesity were enrolled. The participants were randomly and equally divided either in Group A (cryolipolysis in combination with aerobic exercise), or in Group B (aerobic exercise therapy alone) for three months. All variables measured Pre- and post-study, including (HbA1c, FBG, fasting insulin level, HOMA testing).

Results: there was statistically significant decrease in all measured parameters of groups A and B post-treatment compared with pre-treatment with a significant increase in water content, muscle mass, and a significant decrease in fat content and visceral fat of groups A and B post-treatment compared with pre treatment. Following the intervention, Group A significantly reduced fat content and visceral fat compared to Group B. However, there were no significant differences in waist-hip ratio, water content, and muscle mass between the two groups post-treatment. Significant improvements in metabolic parameters were observed in Group A compared to Group B. Group A showed a significant decrease in FBG, insulin levels, HbA1c, and HOMA-IR.

Conclusions: Cryoliopolysis is one of the effective strategies for addressing localized fat deposits that enhance glucose absorption and favorable changes in HbA1c and HOMA-IR, that improve insulin sensitivity.

Keywords: Cryolipolysis; Insulin resistance; Type 2 diabetes; Abdominal obesity; HbA1c

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Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from insulin resistance (IR) and insufficient insulin secretion from pancreatic beta cells [1]. Globally, T2DM represents a significant public health challenge, with an estimated 463 million adults aged 20-79 years affected in 2019, and this number is projected to increase to 700 million by 2045 [2]. Obesity,

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particularly abdominal obesity, has been identified as a major predisposing factor for the development of IR and subsequent T2DM [3]. The link between obesity and T2DM is complex and multifactorial, involving a range of metabolic, inflammatory, and hormonal disturbances [4].

Despite advancements in pharmacological therapies for T2DM management, achieving and maintaining optimal glycemic control remains a formidable task, with a substantial proportion of patients failing to attain target glycated hemoglobin (HbA1c) levels [5]. Furthermore, conventional interventions, such as lifestyle modifications and pharmacotherapy, may have limitations in effectively addressing the underlying pathophysiological mechanisms driving IR in T2DM [6]. In recent years, there has been growing interest in exploring novel therapeutic modalities that target adipose tissue dysfunction and metabolic derangements associated with obesity and T2DM [7]. Cryolipolysis, a non-invasive procedure that selectively targets and induces apoptosis of subcutaneous adipocytes through controlled cooling, has emerged as a promising approach for body contouring and fat reduction [8]. Beyond its aesthetic applications, cryolipolysis has been hypothesized to exert metabolic benefits, including improvements in insulin sensitivity and glucose metabolism [9].

Several preclinical and clinical studies have provided preliminary evidence supporting the potential metabolic effects of cryolipolysis. For instance, experimental studies in animal models have demonstrated reductions in adipose tissue inflammation and improvements in insulin signaling following cryolipolysis treatment [10]. Moreover, clinical investigations in non-diabetic individuals have reported favorable changes in metabolic parameters, such as insulin sensitivity and lipid profiles, following cryolipolysis-induced fat reduction [11]. However, the specific effects of cryolipolysis on IR in individuals with T2DM, especially those with abdominal obesity, remain incompletely understood. Given the close interplay between adipose tissue dysfunction, IR, and T2DM pathogenesis, elucidating the potential therapeutic role of cryolipolysis in improving insulin sensitivity represents a compelling area of investigation.

Therefore, the primary objective of this study is to evaluate the impact of cryolipolysis on IR in a cohort of T2DM patients with abdominal obesity. By assessing changes in insulin sensitivity, as measured by indices such as Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), glycemic control, and body composition parameters, this research aims to provide insights into the potential metabolic benefits of cryolipolysis in the management of T2DM.

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Patients and Methods

Study Design

This study is a randomized, two-group pre–post-test, controlled study.

Participants

Sixty participants with T2DM and abdominal obesity randomly enrolled from the Department of Physiotherapy at Al-Khanka Hospital and divided into two equal groups for the study. Group (a) who received cryolipolysis with aerobic exercise therapy. Group (b) who were only involved in aerobic exercise therapy (**Figure 1**). Both groups were allocated in parallel, and outcome assessors were masked.

Patients with abdominal obesity, diabetes mellitus (DM) predating five years, a fasting blood glucose (FBG) level exceeding 140 mg/dL, an age range of 35 to 45 years, a body mass index between 25 and 30, and medical control met the inclusion criteria. Patients who required insulin for support, suffered from renal failure, cardiovascular issues, myocardial infarction, neurological disorders, orthopedic complications, abdominal hernias, skin diseases, or were medically unstable were all excluded from the research.

Randomization

Randomization was completed for the 60 participants utilizing 60 closed envelopes prepared by the researcher, and each envelope had a card labeled as either Group A or B. Each patient was requested to choose a closed envelope through 1:1 simple randomization to be randomly allocated to one of either group (n = 30/group).

Ethical Consideration

The Faculty of Physical Therapy's Cairo Medical Ethics Research Committee reviewed and authorized the study protocol (NO: P.T.REC/012/002496), and the study was registered on Clinical trials.gov ID: NCT06223490. All the participants were given a full explanation of the study and were informed about the consent form and assigned it.

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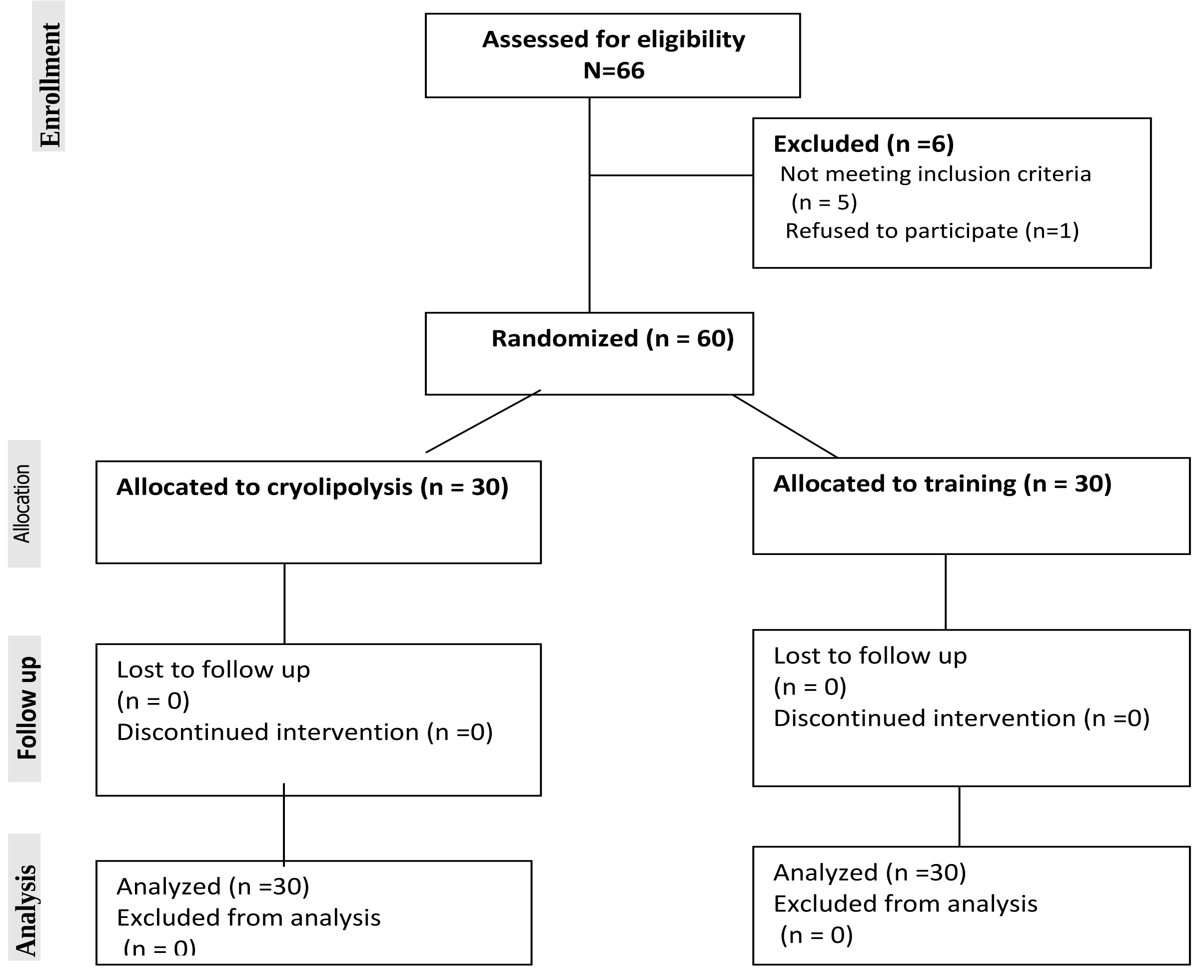

Figure 1. Consort chart of the study.

Procedures

Evaluation Procedures

Anthropometric measurements were taken of every participant. Anthropometric measurements are a non-intrusive method of evaluating nutritional status, identifying at-risk individuals, monitoring the effectiveness of nutrition interventions, and obtaining data on fat and muscle stores [12]. Body mass and height were measured using a floor-type model ZT-120 manufactured in China. The body mass index (BMI) is frequently employed for estimating body fat due to its affordability and ease of use. A non-elastic measuring tape was used to determine the waist and pelvic circumferences. A waist circumference exceeding 102 cm was utilized to quantify visceral adiposity. As a surrogate for assessing body fat distribution between the lower and upper body, the waist-hip ratio (WHR) determines the location of body fat storage. WHR is determined through the division of the waist circumference by the hip circumference; for men, the corresponding risk indicators are ≥1.0, and for women, they are ≥0.85 [13]. A fat caliper is a personal assessment tool utilized to determine the thickness of subcutaneous adipose tissue by measuring skinfold thickness. Additionally, a body composition analyzer approximates an individual's body fat percentage. Using this data, it is possible to estimate body fat, fat-free body

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mass, and total body water. Laboratory assessments were performed on all participants, comprising the following: HbA1c, FBG, and insulin levels, and model HOMA.

Treatment Procedure

Cryolipolysis

Group A underwent cryolipolysis with aerobic exercise therapy; cryolipolysis involves using a vacuum probe connected to the cryolipolysis device (Model FG660L; ADSS) through a cable. The device operated at AC110V/220V 50–60Hz voltage, with a power consumption < 400 W, and maintained a temperature of –10–4 °C with a pressure output of 0–900 Kpa. The device had two handles, one measuring 5.5*14 cm and the other measuring 6*17 cm. A protective membrane is placed over the patient's lower abdomen to prevent freezing, and the process specifically targets the abdominal region. Patients were positioned in a state of relaxation, and the designated region underwent suctioning for 45–60 min, maintaining a consistent output power, working strength, and suction level. The output power was set at 600 W, the working strength was adjustable, and the suction level had five different settings, depending on the patient's tolerance. Cryolipolysis was conducted in a trilogy of three sessions, with a frequency of once per month over three months. To enhance suction, the patient's skin was shaved [14].

Aerobic Exercise Program

Both Groups A and B received moderate aerobic therapy [15, 16], but Group B did not undergo Cryolipolysis treatment. The protocol involved a three-month aerobic exercise program, three sessions weekly involving cycling (the Stamina Intone Folding Recumbent Exercise bicycle model), intervention time was 40 min, and the program was as follows: (1) the first 5 min dedicated to warming up and stretching exercises to prepare for the more intense activity in the second phase, (2) followed by 30 min of cycling on the Stamina Intone Folding Recumbent Exercise bicycle. The initial session started with a duration of 15 minutes, and each subsequent session increased the time by 2 min [17, 18]. Throughout the sessions, participants were involved in continuous cycling training until they reached 65%–80% of their target heart rate for that particular session, where they started at a minimum intensity of 65%, which was gradually increased to a maximum intensity of 80%. The training heart rate intensity was calculated using the Karvonen formula: HR= [(A-B) × target intensity]+B, where A and B represent maximum (220–age) and resting heart rate (average from three readings), respectively [19]. (3) The last 5 min for cooling down was similar to the warming up phase, serving as a means of recuperation after the more demanding activities of the primary exercise period. The physiotherapist monitored the patient while they exercised on the bicycle in every session, and the exercise program was stopped once the patient requested or at the first sign of dizziness, confusion, cyanosis, pallor, and nausea [20, 21].

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Statistical Analysis

Sample Size

The sample size was calculated using the G*POWER statistical software (version 3.1.9.2; Franz Faul, Universitat Kiel, Germany) with BMI data from [22]. The analysis determined that 26 patients per group were needed for this study. The number of ladies considering the dropout was augmented by 15% to reach 30. The calculation was performed using a significance level (α) of 0.05, a statistical power of 80%, and an effect size of 0.8 (**Figure 2**).

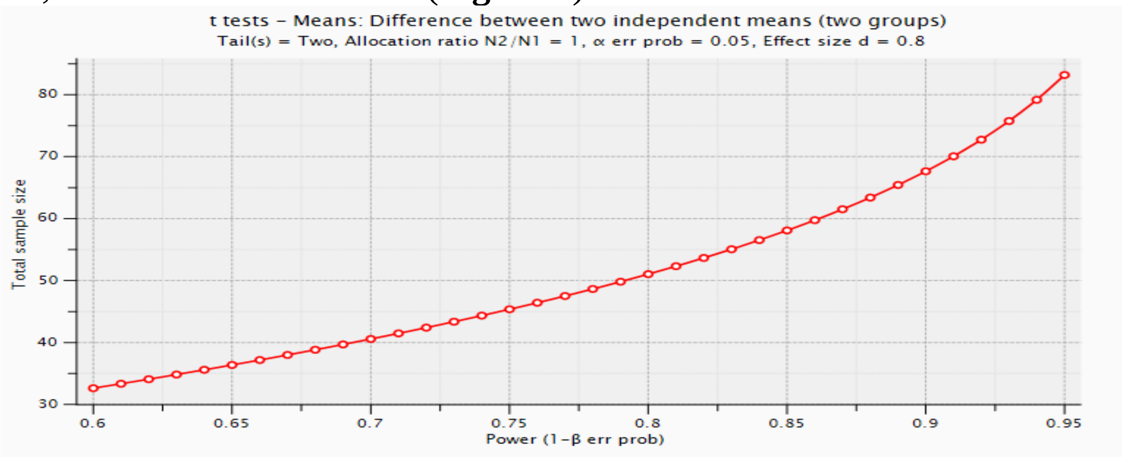

Figure 2. Chart for sample size calculation.

An unpaired t-test was employed to compare the subject characteristics between the groups. A MANOVA with mixed effects was conducted to assess the impact of time (pre- versus post-treatment), treatment (between groups), and the interaction between time and treatment on various variables, including weight, BMI, waist and hip circumference, W/H ratio, umbilical fold, water and visceral fat content, muscle mass, FBG, insulin levels, HbA1c, and HOMA-IR. Post-hoc tests were conducted to make multiple comparisons using the Bonferroni correction. The statistical tests were conducted with a significance threshold set at $p < 0.05$. The statistical analysis was conducted using the SPSS software version 25 for Windows.

Results

Baseline Characteristics

Sixty female participants diagnosed with T2DM and abdominal obesity were included in the study and randomly assigned to Group A (n=30) and Group B (n=30). Baseline characteristics, including age, duration of DM, BMI, and FBG levels, were comparable between the two groups **(Table 1)**.

Table 1. Comparison of age, gender, and height between studied groups.

	,	**Group B N=30**	***P***
Female; N (%)	16 (53.3%)	14 (46.7%)	0.606
Male; N (%)	14 (46.7%)	16 (53.3%)	
Age (years); mean±SD	39.07 ± 3.06	40 ± 2.97	0.236
Height (cm); mean±SD	171.6 ± 5.12	169.43 ± 4.22	0.079

Within-Group Comparison

Group A participants receiving combined aerobic exercise therapy and cryolipolysis demonstrated significant improvements in anthropometric and metabolic parameters compared to those in Group B, who underwent aerobic exercise therapy alone.

A significant decrease in weight, BMI, waist circumference, hip circumference, and umbilical fold was observed in Group A compared to Group B (p < 0.001) **(Table 2)**. Moreover, Group A exhibited a significant increase in water content and muscle mass, along with a significant decrease in fat content and visceral fat, when compared to Group B (p < 0.001) **(Table 3)**.

Table 2. Comparison of anthropometric measures between studied groups.

		Group A N=30	Group B N=30	P^1
Weight (kg)	**Before**	88.07±4.3	85.94±4.33	0.061
	After	79.83±3.43	79.16±3.49	0.457
	Improvement (%)	9.36%	7.89%	0.064
	P^2	<0.001	<0.001	
BMI (kg/m²)	**Before**	29.92±1.24	29.93±0.89	0.979
	After	27.13±1.12	27.59±1.16	0.122
	Improvement (%)	9.32%	7.82%	0.070
	P^2	<0.001	<0.001	
Waist circumference (cm)	**Before**	115.3±5.97	114.63±4.94	0.639
	After	103.77±5.35	107.53±5.06	0.007
	Improvement (%)	10%	6.19%	<0.001
	P^2	<0.001	<0.001	
Hip circumference (cm)	**Before**	121.47±3.92	121.92±3.27	0.631
	After	114.33±3.58	118.97±3.26	<0.001
	Improvement (%)	5.88%	2.42%	<0.001
	P^2	<0.001	<0.001	
W/H Ratio	**Before**	94.88±2.63	94.01±2.7	0.211
	After	90.75±3.53	90.38±3.11	0.665
	Improvement (%)	4.35%	3.86%	0.418
	P^2	<0.001	<0.001	
Umbilical-Fold (cm)	**Before**	46.93±4.35	46.03±4.02	0.409
	After	33.7±3.54	40.7±3.47	<0.001
	Improvement (%)	28.19%	11.58%	<0.001
	P^2	<0.001	<0.001	

P1, a comparison between groups A and B, p2, a comparison across time.

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Table 3. Comparison of body composition between studied groups.

		Group A N=30	Group B N=30	P^1
Water (%)	**Before**	30.97±2.5	31.4±2.01	0.462
	After	38.43±3.3	38.33±2.32	0.892
	Improvement (%)	24.09%	22.07%	0.489
	P^2	<0.001	<0.001	
Fat (%)	**Before**	43.94±2.65	42.8±1.69	0.052
	After	35.9±1.71	38.63±1.73	<0.001
	Improvement (%)	18.3%	9.74%	<0.001
	P^2	<0.001	<0.001	
Visceral fat (%)	**Before**	18.5±1.8	18.43±1.45	0.875
	After	12.23±1.19	15.27±1.44	<0.001
	Improvement (%)	33.89%	17.15%	<0.001
	P^2	<0.001	<0.001	
Mass (%)	**Before**	22.63±4.44	22.8±2.47	0.858
	After	29.3±3.8	28.87±3.82	0.661
	Improvement (%)	29.47%	26.62%	0.281
	P^2	<0.001	<0.001	

P1, a comparison between groups A and B, p2, a comparison across time.

Metabolic Parameters

Significant improvements in metabolic parameters were observed in Group A compared to Group B. Group A showed a significant decrease in FBG, insulin levels, HbA1c, and HOMA-IR ($p < 0.001$) **(Table 4).**

Table 4. Comparison of laboratory parameters between studied groups.

		Group A N=30	Group B N=30	P^1
FBG (mg/dL)	**Before**	201.57±12.78	204.67±12.71	0.350
	After	117.23±5.97	138.13±7.75	<0.001
	Improvement (%)	41.84%	32.51%	<0.001
	P^2	<0.001	<0.001	
insulin	**Before**	8.63±0.55	8.4±0.41	0.074
	After	5.48±0.81	7.04±0.34	<0.001
	Improvement (%)	36.5%	16.19%	<0.001
	P^2	<0.001	<0.001	
HbA1C (%)	**Before**	8.69±0.74	8.9±0.33	0.160
	After	6.52±0.52	7.33±0.37	<0.001
	Improvement (%)	24.97%	17.64%	<0.001
	P^2	<0.001	<0.001	
HOMA	**Before**	4.23±0.48	4.25±0.44	0.854
	After	1.59±0.27	2.4±0.19	<0.001
	Improvement (%)	62.41%	43.53%	<0.001
	P^2	<0.001	<0.001	

P1, a comparison between groups A and B, p2, a comparison across time.

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Post-Treatment Comparison

Following the intervention, Group A significantly reduced fat content and visceral fat compared to Group B ($p < 0.001$). However, there were no significant differences in waist-hip ratio, water content, and muscle mass between the two groups post-treatment ($p > 0.05$**) (Tables 2–4)**.

Discussion

The purpose of the study was to investigate the effect of cryolipolysis on IR in T2DM females with abdominal obesity. The current study was conducted on 60 women selected from the physical therapy department of Al Khanka Hospitals with T2DM and abdominal fat who were controlled on medical treatment (FBG > 140 mg/dl) with abdominal obesity.

Their age range was 35-45 years old, with 25-30 kg/m2, who were randomly allocated into two equal groups. Group A of 30 women with an age average of 39.07 ± 3.06 years who received cryolipolysis (45-60 minutes; 3 sessions, once per month for 3 consecutive months), plus an aerobic exercise program, and Group B of 30 women with age average 40 ± 2.97 years who received moderate aerobic exercise therapy program (3 sessions per week for 3 consecutive months, for 60 min per session) only.

Participants were assessed to determine their weight, BMI, waist and hip circumference, waist/ hip ratio, as well umbilical fold, water and fat content, also visceral fat and muscle mass, FBG, insulin level, HbA1c and HOMA-IR.

Outcomes of comparison demonstrated a statistically significant decrease in all measured parameters of groups A and B post-treatment compared with pre-treatment. There was a significant increase in water content muscle mass and a significant decrease in fat content and visceral fat of groups A and B post-treatment compared with pre-treatment.

Following the intervention, Group A significantly reduced fat content and visceral fat compared to Group B. However, there were no significant differences in waist-hip ratio, water content, and muscle mass between the two groups post-treatment.

Significant improvements in metabolic parameters were observed in Group A compared to Group B. Group A showed a significant decrease in FBG, insulin levels, HbA1c, and HOMA-IR.

The majority of traditional T2DM treatment approaches involving the use of medications to control blood glucose, such as glucose-lowering and insulin-sensitizing drugs, might not be sufficient to prevent the progression of the disease and may not adequately address the underlying IR [23]. As a result, alternative

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therapeutic modalities that directly target IR are gaining increasing attention to reduce cardiovascular risk and enhance metabolic health in individuals with T2DM [24].

So, Our research aimed to assess the effectiveness of cryolipolysis, a non-invasive technique specifically developed to target and diminish subcutaneous adipose tissue, altering IR in female patients diagnosed with T2DM and abdominal obesity.

Our result showed that Cryolipolysis exhibited a significant reduction in post-weight, waist circumference, BMI, and central adiposity compared to pre-evaluation. These results agreed with De Marco et al. [25], who studied cryolipolysis sessions on flanks and abdomen in 175 individuals for four sessions and concluded that the effects of cryolipolysis may be attributed to its selective targeting of subcutaneous fat cells through controlled cooling. This process, also known as "fat freezing," is thought to induce apoptosis (programmed cell death) in adipocytes while sparing surrounding tissues. As a result, the treated fat cells are gradually eliminated from the body through natural metabolic processes. This mechanism may contribute to the reduction in post-weight, BMI, and waist circumference observed after cryolipolysis treatment. Additionally, cryolipolysis could potentially stimulate local inflammation and tissue remodeling, further aiding in fat reduction and body contouring [26]

Our results are also consistent with the findings of Abdel-Aal et al. [27], who had studied the adding effect of Cryolipolysis to a low-calorie diet program on lipid profile, liver enzymes, body mass index, waist-to-hip ratio, and volume reduction of subcutaneous fat tissue in sixty central obese women. The result showed that there was a better improvement in components of lipid profile and liver enzymes in women following cryolipolysis than in women who were maintained over the diet program alone.

On the other hand, Costa et al. [28] revealed that one session of cryolipolysis on more than one body area for 30 days. cryolipolysis did not change body composition, anthropometric measurements, or inflammatory markers when it was applied to twenty-four women aged between 20 and 59 years. This difference between our result and Costa et al. result can be attributed to the short duration of their study since the reduction effects of subcutaneous fat occur more slowly, as it needs up to 90 days.

The findings of our study showed that the cryolipolysis group demonstrated a significant reduction in fat percentage and visceral fat, indicating that cryolipolysis contributes to fat reduction and plays a role in reducing visceral fat content on human body composition analyzer model, and that is in line with Lindhorst et al. [29] who had studied the effects of cryotherapy on body composition measures on twenty-seven mice with the high-fat diet for two months. And found that there was a significant post-treatment reduction in fat percentage and visceral fat observed in the

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cryolipolysis group in the study.

On the other hand, our result is inconsistent with Falster et al. [30], who investigated the effects of a single session of cryolipolysis on the thickness of the lower abdomen adipose layer (visceral fat) of forty-four healthy women after 30,60 and 90 days, found no significant changes were noticed between the groups at any follow-up time points.

The difference between this study and the result of our study may be due to the fact that Falster et al. [30] studied the effect of only a single session of cryolipolysis without any protocol of lifestyle modifications or exercise program.

The results of our study also showed an improvement in glucose, insulin, HbA1C, and HOMA-IR, DM control. This result came in line with the findings of Mazor et al. [31], who revealed that cryolipolysis reduced the volume of mesenteric fat and improved glycemic control in eight obese ossabaw pigs with high-fat diet for 9 months without adverse effects.

A number of studies were analyzed in a meta-analysis by Shah et al. [32] on the therapeutic effects of exercise on glycemic control in 184 patients with T2DM were conducted using electronic databases. Studies with an exercise intervention lasting more than 8 weeks were included and revealed decreases in HbA1c, FBG, BMI, and waist circumference after the exercise intervention [33, 34], which agreed with our results.

Also, several studies agreed with our result that the effect of exercise intervention showed significant improvement in BMI [35, 36].

Although Cox et al. [37] revealed that exercise alone may not lead to substantial weight loss in certain individuals or that the effects might vary depending on the type of exercise undertaken, however, even in studies with conflicting results, exercise often shows benefits such as improved insulin sensitivity, cardiovascular health, and quality of life, suggesting that its role in DM management is still significant**.**

A limitation of the present study was the relatively small sample size, which may limit the generalizability of the findings to a broader population. In addition, the study focused exclusively on women with T2DM and abdominal fat. The study duration of three months may not capture longer-term effects or changes in response over time. Finally, the study did not account for potential confounding factors such as dietary habits or other concurrent interventions that could influence the results.

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Conclusions

Cryolipolysis is a promising, non-invasive, and safe procedure. Application of three sessions for 3 consecutive months has a significant improvement in reducing localized fat that may reduce IR in T2DM adult. This increases insulin sensitivity, allowing cells to take up more glucose and improving HbA1c levels.

Future Perspectives

Future research should focus on resolving the limitations mentioned in our current study and expanding our understanding of the processes that influence the therapeutic effects of cryolipolysis on metabolic parameters and IR. In order to determine factors that can predict the response to therapy and assess how long the treatment benefits last, it is necessary to conduct longitudinal studies with extended durations of follow-up and bigger groups of participants. Moreover, conducting comparative effectiveness studies that evaluate different cryolipolysis procedures, including treatment parameters and combination treatments, has the potential to provide valuable insights into optimizing treatment strategies for maximum therapeutic efficacy.

Data Availability Statement

The data that supports the conclusions of this study can be obtained by contacting the corresponding author.

Conflict of Interest

The authors affirm that they have no conflicts of interest.

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