

The Effect of Combination between Cryolipolysis and Aerobic Exercise in Reducing Abdominal Adiposity Inobese Subject

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ABSTRACT

Background: Cryolipolysis is a treatment option for subjects looking for noninvasive body contouring. Combination between cryolipolysis and aerobic exercise has a significance effect on the reduction of localized fat.

Purpose: To examine the impact of combining cryolipolysis with aerobic activity and a calorie-restricted diet on the waist-to-hip ratio and the skin fold of subcutaneous abdominal fat in obese people.

Subjects and Methods: This was a pretest-posttest randomized controlled clinical study. Forty overweight patients were split evenly into two groups. Patients in group A (control) were instructed to follow a low-calorie diet and engage in aerobic exercise, while participants in group B of the trial were given cryolipolysis sessions in combination to the control group's diet. Assessment of patients was done before and after treatment to measure waist-to-hip ratio (W/H) as well as abdominal skin fold.

Results: Mixed MANOVA was performed to examine the effect of treatment on skin fold and (W/H) ratio. The skin fold and waist to hip (W/H) ratio data collected from both groups before and after treatment were compared statistically. There was a substantial effect of reduction in skin fold and waist-hip ratio of group B as compared to group A post treatment ($P < 0.01$).

Conclusion: Patients who underwent cryolipolysis and aerobic exercise with low caloric diet program exhibited considerable improvement in skin fold of abdominal subcutaneous fat also waist-hip ratio improved the systemic effects of cryolipolysis contrasted to those who were kept on a diet as well as aerobic exercise.

Keywords: Aerobic exercise, Cryolipolysis, Low caloric diet.

INTRODUCTION

Obesity is a serious disease marked by a weight gain of at least 20% beyond one's optimal weight due to fat accumulation ⁽¹⁾.

Obesity has reached pandemic proportions during the previous few decades, and numerous obesity-related disorders, such as heart issues, specific types of cancer, as well as diabetes, have increased at the same time. The foundation of therapeutic intervention for treating or preventing chronic disorders as weight loss through lifestyle adjustment, like a low-calorie diet and working out more, and behavioural strategies to promote these changes. Lifestyle changes typically result in a reduction in body weight. Therefore these approaches are unlikely to help an obese person achieve a healthy weight ⁽²⁾. According to the World Health Organization, several devices, including as cavitation, radiofrequency, cryolipolysis, as well as others, have been utilised in recent studies to address this problem ⁽³⁾.

The cryolipolysis device has been cleared by the FDA for cutaneous cooling and other applications. Cryolipolysis is an innovative, minimally invasive approach. Cryolipolysis is a novel, non-invasive method of selective adipocytes reduction with the use of controlled, localised chilling ⁽⁴⁾.

The waist hip ratio as well as the waist circumference are used by clinicians to determine abdominal obesity. Atherosclerosis and the chance of developing acute coronary syndromes are just two of the many vascular disorders that are linked to these

behaviors ⁽⁵⁾. Energy-restricted diets (deficit of 2100-4200 kJ/d: minimum of 4200-5040 kJ/d for female as well as 5040-5880 kJ/d for male) are often low in fat (30 % of overall daily energy consumption), rich in carbs (55-60% of total daily energy consumption), but also low in protein (10% of total daily energy consumption) ⁽⁶⁾.

Due to the acutely high energy cost and ability to increase fat utilization, aerobic exercise is frequently recommended in conjunction with calorie restriction ⁽⁷⁾. Numerous studies studied the impact of modest caloric restriction either separately or in addition to aerobic activity. According to studies, a walk/jog programme enhanced body fat reduction compared to a group that only followed a diet ⁽⁸⁾.

There is a gap in the literature regarding combining cryolipolysis and aerobic exercise for losing weight, particularly abdominal adiposity, in spite of the fact that several studies have supported the efficacy of each on weight loss. Consequently, this study aimed to ascertain whether losing abdominal adiposity would be more successful when cryolipolysis and aerobic exercise were combined.

MATERIAL AND METHODS

The current research was a pretest-posttest randomized controlled trial, which was conducted in a non-public

medical facility and Quesna Central Hospital in the period between November 2022 and April 2023.

Inclusion criteria: Patients from both sexes, between the ages of 35 and 50 with a BMI of 30 and 40 kg/m² who had been categorized as having abdominal obesity also referred to physiotherapist by an internal medicine specialist or a family physician were participated in this research.

Exclusion criteria:

Patients taking any medication to control their weight or fat mass, pregnant or nursing, diagnosed with chronic illness (e.g. diabetes mellitus or hypertension),

subjects sensitive to cold, subjects dehydrated for any reason, subjects with bleeding problem and subjects with peptic ulcer.

Sample Size and Randomization:

G*power test software was used to calculate the sample size (version3.0.10). Sample size calculation was done with 80% power at $\alpha=0.05$ level, number of measurements 2, The minimal sample size suggested for a study with two groups was 40. d effect size =0.46 using F-test MANOVA within as well as between interaction effects. The minimum suggested sample size was 40 individuals (Figure 1).

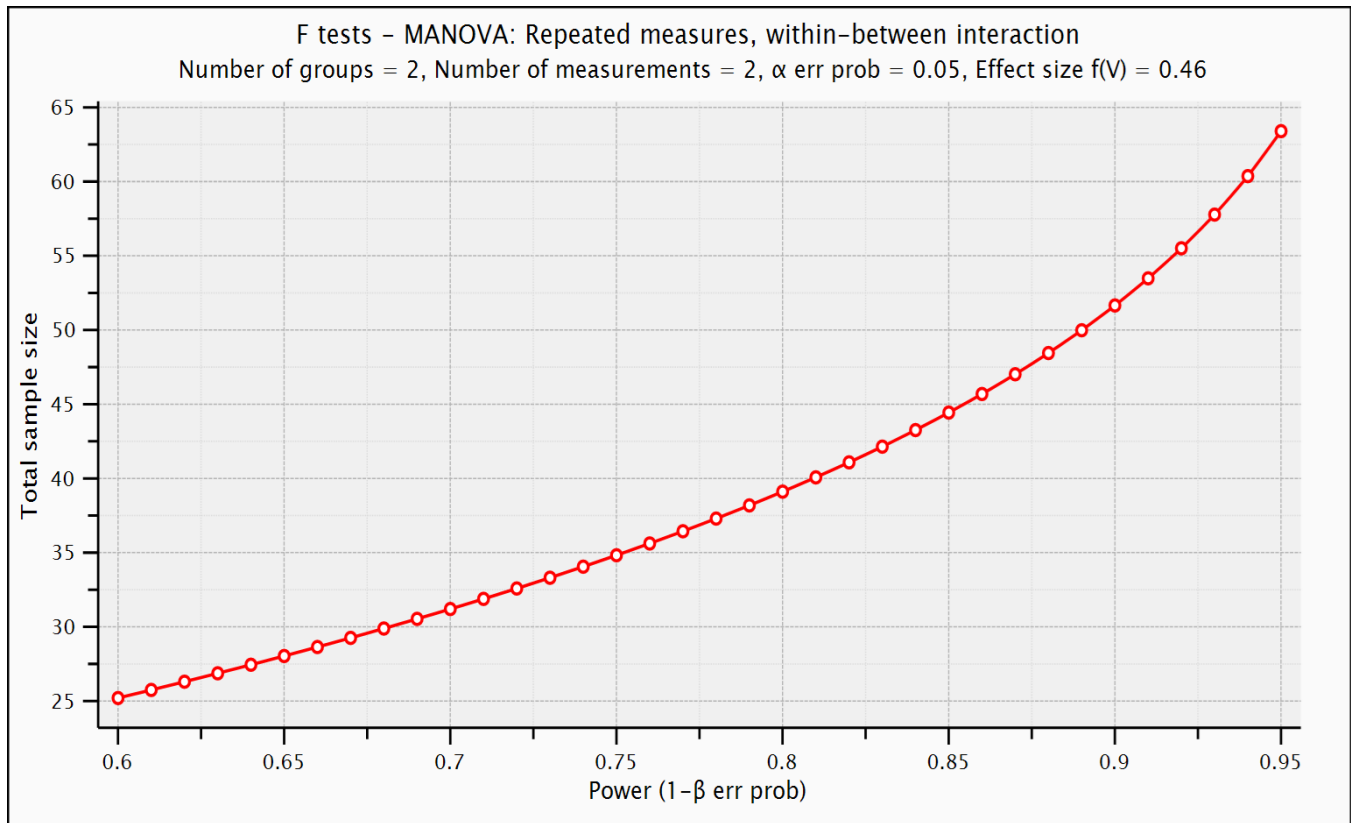


Figure (1): F test.

Outcome measures: After the initial cryolipolysis therapy, patients were followed up for three months later to assess any changes in their outcome measures.

Evaluation of the waist-to-hip ratio: Measurements included both the waist circumference as well as WHR in accordance with the Stepwise (STEPS) procedure of the World Health Organization ⁽⁹⁾.

Fat caliper skinfolds:

They were observed consistently at the same time, at the same temperature, using the same tools, and by the same researcher each time ⁽¹⁰⁾. Subjects were asked to stand while their right thighs, bellies, chests, triceps, and backs were measured at certain locations. The marking made sure that the USG as well as caliper measurements were taken at the 25+ exact similar places According to **Eston and Reilly** ⁽¹¹⁾.

The amount of your subcutaneous fat, or fat that lies beneath the skin, is measured by skinfold calipers at specific body sites. There are either three or seven points on the body where measurements are taken. Different sites are used by men and women. Measuring points of skinfold measurements: Abdominal Fold, horizontal fold elevated 3 cm lateral & 1 cm inferior to the ⁽¹¹⁾.

The food frequency questionnaire (FFQ): to evaluate each group's devotion to their respective low-calorie diets at the conclusion of the trial's two months. The FFQs were developed to assess dietary patterns by asking about the types and amounts of food eaten on a regular basis during a given period of time ⁽¹²⁾. It is appropriate for adults to collect data on a large number of food options, fruit, vegetables, carbohydrate, milk, meat, as well as fat are all examples of foods that are high in different nutrients, and the diet can be adjusted such that it is shorter and focuses on these ⁽¹³⁾. The subject's adherence for each group was evaluated with the FFQ, which consisted the six different food categories in precise amounts that were to be quantified in grams. This was done so that each subject's compliance could be evaluated in each group. Next, we determined each group's level of adherence, and the relationship between the groups also the level of adherence was figured out by using χ^2 .

Intervention: A low-calorie diet (1200–1500 cal) was followed by both control also study groups as well as aerobic exercise.

Low-caloric diet: For three months, individuals from both groups were ordered to precede a flexible low-caloric diet plan created by the nutritionist. In accordance with the Recommended Dietary Intake (RDI), the calorie-restricted diet with three precisely measured meals contained an appropriate amount of

carbohydrate & protein, with low in fat, but rich in vegetables, fruits plus fibers ⁽¹⁴⁾.

Cryolipolysis: Through the use of integrated sensors within the applicator's cooling plates, cryolipolysis keeps the temperature below the predetermined threshold of 0°C throughout the application. The cold induces the programmed death of fat cells, which leads to a progressive reduction in fat. Cryolipolysis does not have an instant effect ⁽¹⁵⁾.

Three Max Chill Shaping Cryolipolysis Equipment (ESM-8100MO; EunSung global, Korea) was utilised. Heads that can be cooled to temperatures between -10 and 5 degrees Celsius with a vacuum controller were modified following a thorough assessment of the patient's sensations and vital signs during each session to ensure a comfortable experience. Two Cryolipolysis treatments totaling 45 minutes each were administered to each patient in the experimental group at the hypogastrium region, 5 cm below the navel, by means of an anti-freezing membrane to prevent cold burn. A gentian violet ink marker was first used to mark the area on the infraumbilical region, 5 cm below the navel towards to the pubic symphysis & 10 cm to the side, towards the waist, in order to conduct the treatment. The overall surface was 30 cm by 10 cm, with 10 cm x 10 cm in each area. A control region with markings of the same size was placed on the left and right sides. A single application was used to send the participant. A control region with markings of the same size was placed on the left and right sides. A single application was submitted to the participant. The patient was placed in the dorsal decubitus posture as well as the stretcher was tilted at a 45-degree angle during the application session ⁽¹⁶⁾. The patient was told that if any aberrant sensation becomes intolerable, they should immediately turn off the device by removing the key. If hyperemia or similar abnormal skin state was seen, stroking massage was performed for two minutes at the end of each session ⁽¹⁷⁾.

Aerobic Exercise:

Due to its acutely high energy cost and capacity to increase fat utilization, aerobic exercise is frequently recommended in conjunction with energy restriction. There are many different kinds of aerobic exercise that we can engage in, or we can combine two types, like walking and jogging ⁽¹⁸⁾.

The patients in this research walked for 30 to 60 minutes at various local Asheville locations, including a university trail and a nearby park, all of which have reasonably flat terrain. The main author conducted one-on-one walks of 1 to 1.5 miles with each subject. Subjects were encouraged to talk about any subjects that concerned them. However, there is room for improvement in the intervention's implementation, particularly in terms of patient recruitment and encouragement to engage fully. The pilot had very few tools at his disposal.

Ethical Approval: The study was approved by the Ethics Board of Cairo University (Reference number P.T. REC/012/004466) and the patients were given all the information they need about the trial. An informed written consent was taken from each participant in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. Clinical Trials Registry, registration number: NCT05852652.

Statistical analysis:

To compare subject characteristics across groups, an unpaired t-test was performed. The Shapiro-Wilk test was used to ensure that the data followed a normal distribution. The homogeneity of the groups was tested using Levene's test for homogeneity of variances. Mixed MANOVA was performed to investigate the impact of treatment on skin fold and (W/H) ratio. Multiple comparisons were handled with post hoc testing using the Bonferroni method of adjustment. All statistical tests were performed at the $P \leq 0.05$ level of significance. The Windows version of the SPSS statistical software (version 25) was used for all analyses (IBM SPSS, Chicago, IL, USA).

RESULTS

Table (1) presented the subject characteristics of group A & B. There was no substantial difference between groups in age, weight, height as well as BMI ($p > 0.05$).

Table 1: Comparison of subject characteristics between group A and B

	Group A		Group B		MD	t-value	p-value
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD			
Age (years)	40.50 ± 3.83	39.30 ± 4.85			1.2	..0.86	0.39
Weight (kg)	94.23 ± 10.97	94.82 ± 11.22	-		0.59	-0.16	0.86
Height (cm)	163.70 ± 7.81	165.30 ± 7.73	-2.6		-1.05		0.29
BMI (kg/m²)	35.16 ± 3.18	34.44 ± 2.96	0.72		0.74		0.46

SD, Standard deviation; MD, mean difference; p value, Probability value.

Mixed MANOVA showed a substantial interaction effect of treatment also time ($F = 22.99$, $p = 0.001$, partial eta squared = 0.55). There was a substantial main effect of treatment ($F = 3.26$, $p = 0.04$, partial eta squared = 0.15). There was a substantial main effect time ($F = 61.46$, $p = 0.001$, partial eta squared = 0.76). There was a substantial decline in skin fold as well as W/H ratio in group A ($p < 0.05$) also in group B ($p < 0.001$) in contrast to that pretreatment. In group A, the skin fold and W/H ratio changed by 4.96 and 3.12 %

respectively, while they changed by 23.38 and 7.37 % in group B (Table 2).

There was no substantial difference between groups pretreatment ($p > 0.05$). There was a substantial decline in skin fold ($p < 0.01$) also W/H ratio ($p < 0.001$) of group B compared to the group A results after treatment (Table 2).

Table 2: Mean skin fold and W/H ratio pre and post treatment of group A and B

	Pre treatment	Post treatment	M D	% of change	p value
	Mean ±SD	Mean ±SD			
Skin fold (cm)					
Group A	3.83 ± 0.69	3.64 ± 0.67	0.19	4.96	0.03
Group B	3.85 ± 0.84	2.95 ± 0.44	0.9	23.38	0.001
MD	-0.02	0.69			
	p = 0.91	p = 0.003			
W/H ratio					
Group A	0.96 ± 0.05	0.93 ± 0.03	0.03	3.12	0.03
Group B	0.95 ± 0.04	0.88 ± 0.05	0.07	7.37	0.001
MD	0.01	0.05			
	p = 0.77	p = 0.001			

p value	% of change	MD	Post treatment		Pre treatment	
			Mean ±SD	Mean ±SD		
0.03	4.96	0.19	3.64 ± 0.67	3.83 ± 0.69		Skin fold (cm)
0.01	23.38	0.9	2.95 ± 0.44	3.85 ± 0.84		Group A
			0.69	-0.02		Group B
			p = 0.003	p = 0.91		MD
						W/H ratio
0.03	3.12	0.03	0.93 ± 0.03	0.96 ± 0.05		Group A
0.001	7.37	0.07	0.88 ± 0.05	0.95 ± 0.04		Group B
			0.05	0.01		MD
			p = 0.001	p = 0.77		

SD, Standard deviation; MD, Mean difference; p value, Probability value.

DISCUSSION

Noninvasive body contouring may be achievable with the use of cryolipolysis technology, which is a form of energy-based fat reshaping and reshaping that also

involves tissue volume reduction. The aim of this research was to examine the impact of cryolipolysis and aerobic exercise on the skin fold of abdominal adipose tissue as well as the WHR in obese patients on a low-calorie diet program. Pretreatment skin fold measurements showed a mean difference of -0.02 cm between group A also group B. Pretreated groups A and B did not differ substantially in skin fold thickness ($p = 0.91$). Following treatment, there was a 0.69 cm average difference in skin-fold thickness between the two groups. There was a substantial decline in skin fold of group B in contrast to group A ($p=0.91$)

There was no substantial difference in W/H ratio between group A & B pretreatment ($p = 0.77$). The treatment resulted in a mean W/H ratio difference of 0.05 between the groups. There was a substantial decline in W/H ratio of group B in contrast to group A's outcomes after treatment ($p < 0.001$).

After three months of intervention, the outcomes of the current study found that compared to group A, group B had a significantly decreased waist-hip ratio and also abdominal skin fold ($P < 0.001$). This is supported by other studies, which found that a low-calorie diet, either on its own or in addition to regular physical activity had a substantial impact on weight loss and also enhanced lipid metabolism⁽¹⁹⁾. Additionally, the present study found that after three months of intervention, the WHR and abdominal skin fold were substantially lesser in the cryolipolysis group contrasted to those on the low-calorie diet ($P < 0.001$). This loss of abdominal adiposity may be primarily attributed to the combined effects of cryolipolysis, aerobic activity, and low-calorie diet. Additionally, there were statistically substantial differences in the effects of cryolipolysis as well as aerobic exercise on WHR ($P < 0.001$) favoring those involved in cryolipolysis. Despite the fact that the WHR as well as the waist circumference's ability to accurately represent the amount of fat loss varied with the experience of the evaluator, they were still easy to use, reliable, and accurate in determining fat layer thickness⁽²⁰⁾.

Cryolipolysis is a method of selectively eliminating fat cells by exposing them to extremely low temperatures. Cell death via the apoptotic pathway is triggered by low temperatures that are above freezing but below normal⁽²¹⁾. There is little collateral tissue damage because adipocytes are particularly vulnerable to cold temperatures⁽²²⁾. The removal of damaged adipocytes occurs as a result of an inflammatory reaction that begins on day three also reaches its peak on day fourteen⁽²³⁾. By three months following treatment, it is believed that inflammation and lipid metabolism have completely resolved⁽²⁴⁾. The authors of earlier investigations in humans and swine models have shown that this mechanism reduces the fat layer in the treated area⁽²⁰⁾. Without anaesthetics or analgesics, the surgery can be carried out quickly in a clinical

setting. Following the application of coupling gel, to remove the localized fat deposit, a vacuum is used to draw the surrounding tissue into an applicator. After then, the temperature is gradually lowered over the next 45 to 60 minutes by cooling panels on both sides.

Previous studies revealed that cryolipolysis is a promising new technique for fat reduction and body reshaping, but these newer studies find the opposite to be true. Cryolipolysis was studied by **Kotlus and Mok**⁽²⁵⁾ who looked at 192 procedures performed on 67 patients. **Stevens and Bachelor**⁽²⁶⁾ conducted a retrospective chart analysis of 528 patients, with the abdomen as a treatment area. An examination of 891 cryolipolysis treatment sites were conducted retroactively on 518 individuals by **Dierickx et al.**⁽²⁷⁾ where caliper measurements and photographic analysis were performed on 49 individuals. After treating 11 patients with cryolipolysis, **Garibyan et al.**⁽²⁸⁾ conducted the first volumetric investigation of its kind utilizing 3D imaging. For 120 minutes, **Stevens and Bachelor**⁽²⁶⁾ used a non-vacuum conformable-surface applicator to apply cryolipolysis to the lateral thighs of 40 women. Cryolipolysis of the inner thighs using a flat-cup applicator (Coolfit, Zeltiq Aesthetics, Pleasanton, CA) was described in a series of 45 patients by **Zelickson et al.**⁽²⁹⁾.

Cryolipolysis with the Micool (Hironic Co., Seongnam, Korea) was first reported by **Kim et al.**⁽³⁰⁾ who used the device on 15 patients. To compare the effectiveness of massage therapy with and without cryolipolysis, **Boey and Wasilenchuk**⁽³¹⁾ treated 17 patients. Aerobic exercise has been shown in numerous trials to effectively reduce abdominal fat (IF), with authors like **Irwin et al.**⁽³²⁾ who reported that an increment in duration (min/week) of physical activity was significantly correlated with a lower body fat percentage⁽³³⁾. IF lowering in response to exercise training may be related to IF levels at baseline (obesity phenotype), as pointed out by **Ross and Janssen**⁽³³⁾.

Contrary to the outcomes of the current investigation, **Friedmann et al.**⁽²⁴⁾ studied 8 patients and discovered no substantial difference between cryolipolysis as well as flank ultrasonic therapy with high-intensity focus. The average flank improvement score after cryolipolysis was 0.56, which is in the middle of the range between no change and noticeable improvement. Another discrepancy was discovered between the current study and a study by **Despres et al.**⁽³⁴⁾, who followed obese participants through 14-months exercise training programme and reported no significant reduction in IF area.

The present study results showed a substantial decline in abdominal skin fold also waist hip ratio combining with aerobic exercise. The findings of the other studies, however, were dependent on either a single session of cryolipolysis or repeated sessions⁽³⁵⁾ without any dietary controls, so the substantial effect of

cryolipolysis and the aerobic exercise group may have been amplified by the effect of a low-calorie diet. It's important to keep in mind some of this study's limitations. First, the study looked at how adding cryolipolysis and aerobic activity to a low-calorie diet and exercise alone could reduce abdominal skin fold and WHR. The findings of the current research should therefore be compared to low-carbohydrate diets or high-protein diet types. After two-months follow-up, this study examined the intermediate effects. Consequently, aerobic exercise and cryolipolysis as part of a calorie-restricted diet need more research to determine their long-term effects. Additionally, cryolipolysis was exclusively used on the abdomen. More study is needed to evaluate its efficacy in relation to other obesity-related sites.

DECLARATIONS

- **Consent for publication:** authors agreed to submit the work.
- **Availability of data and material:** Available
- **Competing interests:** None
Funding: No fund
- **Conflicts of interest:** no conflicts of interest.

REFERENCES

1. **Hruby A, Hu F (2015):** The epidemiology of obesity: A big picture. *Pharmacoeconomics*, 33 (7): 673–689.
2. Wadden T, Butryn M, Wilson C (2007): Lifestyle modification for the management of obesity. *Gastroenterology*, 132: 2226–2238.
3. **Mulholland R, Paul M, Chalfoun C (2011):** Noninvasive body contouring with radiofrequency, ultrasound, cryolipolysis, and low-level laser therapy. *Clinics in Plastic Surgery*, 38 (3): 503–520.
4. **Frood S, Johnston L, Matteson C (2013):** obesity, complexity, and the role of the Health System. *Curr Obes Rep.*, 2 (4): 320-326
5. **Lakka H, Laaksonen D, Lakka T et al. (2002):** The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA.*, 288 (21): 2709–2716.
6. **Freedman M, King J, Kennedy E (2001):** Popular diets: a scientific review. *Obes Res.*, 9 (1): 1-40.
7. **Hagan R (1985):** Benefits of aerobic conditioning and diet for overweight adults. *Sports Medicine*, 5: 144-155.
8. **Blumenthal J, Babyak M, Hinderliter A et al. (2010):** Effects of the DASH diet alone and in combination with exercise and weight loss on blood pressure and cardiovascular biomarkers in men and women with high blood pressure: the ENCORE study. *Archives of internal medicine*, 170 (2): 126-135.
9. **World Health Organization (2008):** Waist circumference and waist-hip ratio: report of a WHO expert consultation, Geneva. https://apps.who.int/iris/bitstream/10665/44583/1/9789241501491_e...
10. **Hume P, Marfell-Jones M (2008):** The importance of accurate site location for skinfold measurement *J Sports Sci.*, 26 (12): 1333-1340
11. **Eston R, Reilly T (2009):** Kinanthropometry and exercise physiology - laboratory manual (3rd ed.), Routledge, New York, Pp: 33
12. **Gosadi I, Alatar A, Otayf M et al. (2017):** Development of a Saudi Food Frequency Questionnaire and testing its reliability and validity. *Saudi Med J.*, 38 (6): 636–641.
13. **Cade J, Burley V, Warm D et al. (2004):** Food-frequency questionnaires: A review of their design, validation and utilisation. *Nutr Res Rev.*, 17 (1): 5–22
14. **Muzio F, Mondazzi L, Sommariva D et al. (2005):** Long-term effects of low-calorie diet on the metabolic syndrome in obese nondiabetic patients. *Diabetes Care*, 28 (6): 1485–1486.
15. **Manstein D, Laubach H, Watanabe K et al. (2008):** Selective cryolysis: a novel method of non-invasive fat removal. *Lasers Surg Med.*, 40 (9): 595–604.
16. **Baum T, Cordes C, Dieckmeyer M et al. (2016):** MR-based assessment of body fat distribution and characteristics,” *European Journal of Radiology*, 85 (8): 1512–1518.
17. **Meyer P, Silva R, Oliveira G et al. (2016):** Effects of cryolipolysis on abdominal adiposity. *Case Rep Dermatol Med.*, 2016:1-7.
18. **Hagan R (1985):** Benefits of aerobic conditioning and diet for overweight adults. *Sports Medicine*, 5: 144-155.
19. **Hong K, Li Z, Wang H et al. (2005):** Analysis of weight loss outcomes using VLCD in black and white overweight and obese women with and without metabolic syndrome. *Int J Obes.*, 29 (4): 436–442.
20. **Auh S, Iyengar S, Weil A et al. (2018):** Quantification of noninvasive fat reduction: A systematic review. *Lasers Surg Med.*, 50: 96–110.
21. **Coleman S, Sachdeva K, Egbert B et al. (2009):** Clinical efficacy of non-invasive cryolipolysis and its effects on peripheral nerves. *Aesthetic Plast Surg.*, 33: 482-488.
22. **Bernstein E (2013):** Longitudinal evaluation of cryolipolysis efficacy: twocasesstudies. *JCosmeticDerm.*, 12:149-152
23. **Jewell M, Solish N, Desilets C (2011):** Noninvasive bodysculpting technologies with an emphasis on high-intensity focusedultrasound. *AesthetPlast Surg.*, 35: 901-912
24. **Friedmann D, Mahoney L, Fabi S et al. (2013):** A pilot prospective comparative trial of high-intensity focused ultrasound versus cryolipolysis for flank subcutaneous adipose tissue and review of the literature. *American J Cosmetic Surg.*, 30: 152-158.
25. **Kotlus B, Mok C (2013):** Evaluation of cryolipolysis for subcutaneous fat reduction. *American J Cosmetic Surg.*, 30: 89-93.
26. **Stevens W, Bachelor E (2015):** Cryolipolysis conformablesurface applicator for nonsurgical fat reduction in lateral thigh. *Aesthet Surg J.*, 35 (1): 66-71
27. **Dierickx C, Mazer J, Sand M et al. (2013):** Safety, tolerance, and patient satisfaction with noninvasive cryolipolysis. *Dermatol Surg.*, 39: 1209-1216.
28. **Garibyan L, Sipprell W, Jalian H et al. (2014):** Three-dimensional volumetric quantification of fat loss following cryolipolysis. *Lasers SurgMed.*, 46 (2): 75-80
29. **Zelickson B, Burns A, Kilmer S (2015):** Cryolipolysis for safe and effective inner thigh fat reduction. *Lasers Surg Med.*, 47 (2): 120-127.

30. **Kim J, Kim D, Ryu H (2014):** Clinical effectiveness of noninvasive selective cryolipolysis. *J Cosmet Laser Ther.*, 16 (5): 209-213.
31. **Boey G, Wasilenchuk J (2013):** Non-invasive fat reduction in the inner thigh using a prototype cryolipolysis applicator. *Lasers Surg Med.*, 45 (S25): 20
32. **Irwin M, Yasui Y, Ulrich C *et al.* (2003):** Effect of exercise on total and intra-abdominal body fat in postmenopausal women: a randomized controlled trial. doi: 10.1001/jama.289.3.323.
33. **Ross R, Janssen I (2001):** Physical activity, total and regional obesity: dose-response considerations. *Med Sci Sports Exerc.*, 33 (6): S521–S527
34. **Despres J, Pouliot M, Moorjani S *et al.* (1991):** Loss of abdominal fat and metabolic response to exercise training in obese women. *Am J Physiol.*, 261: E159–E167.
35. **Klein K, Bachelor E, Becker E *et al.* (2017):** Multiplesame day cryolipolysis treatments for the reduction of subcutaneous fat are safe and do not affect serum lipid levels or liver function tests. *Lasers Surg Med.*, 49 (7): 640–644.