

ORIGINAL RESEARCH

Effects of cryolipolysis on lower abdomen fat thickness of healthy women and patient satisfaction: a randomized controlled trial



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trial

Abstract

Objective: To analyze the effects of cryolipolysis on the fat thickness of the lower abdomen of healthy women and patient's satisfaction.

Methods: Design and setting: a randomized controlled trial, with concealed allocation and blinded assessor. **Participants:** 34 healthy women between 18 and 48 years, skinfold in the lower abdomen ≥ 3 cm, BMI between 18.5 and 27 kg/m², low level of physical activity, and no contraindication to cryolipolysis were allocated to intervention group (IG, $n = 17$) or control group (CG, $n = 17$). **Interventions:** The IG received one session of cryolipolysis with -10°C of temperature for 50 min. The CG was not submitted to any kind of intervention. Both groups did the evaluation protocols at baseline, 30, 60 and 90 days after the intervention. **Main outcome measures:** fat thickness was measured by ultrasonography (US), skinfold (SF) and abdominal circumference (AC1 and AC2).

Results: No significant differences between the IG and CG were demonstrated at any evaluation at any time of follow up for the variables US (30 days: 0.05 cm (95%CI: -0.12 ; 0.22), 60 days: 0.05 cm (95%CI: -0.11 ; 0.20) and 90 days: 0.04 cm (95%CI: -0.7 ; 0.25)), SF (30 days: -0.09 cm (95%CI: -0.25 ; 0.08), 60 days: -0.14 cm (95%CI: -0.36 ; 0.09) and 90 days: -0.001 cm (95%CI: -0.237 ; 0.234)), AC1 (30 days: 0.42 cm (95%CI: -1.1 ; 1.9), 60 days: -0.1 cm (95%CI: -1.74 ; 1.54) and 90 days: -0.007 cm (-1.9 ; 1.9)) and AC2 (30 days: 0.183 cm (95%CI: -0.84 ; 1.20), 60 days: -0.13 cm (95%CI: -1.61 ; 1.35) and 90 days: -0.31 cm (95%CI: -1.61 ; 1.00)).

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Conclusions: The current study showed that a single application of the utilized protocol of cryolipolysis does not produce any significant effect on fat thickness of the lower abdomen of healthy women.

Clinical Trial Registration number: NCT03160976 (<https://clinicaltrials.gov/ct2/show/NCT03160976>).

Contribution of the Paper: the study is one of the first studies in the literature with methodological rigor to report an unfavorable result for localized abdominal fat treatment with a single session of cryolipolysis.

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Introduction

Socio-cultural aspects, such as the idealization of skinny and physically perfect bodies, influence female body perception.^{1,2} Diets, exercises and esthetic procedures are alternatives that may help improve the perception of physical appearance.^{3–6} Therefore, a few modalities, have been developed for the purpose of sculpting the body and reducing localized fat more safely and non-invasively, such as cryolipolysis.^{5,7} This technology uses low temperatures^{8,9} to induce a process of apoptosis and inflammation that will eliminate the adipocytes and consequently reduce the adipose layer of the treated region.³ According to Manstein et al.,¹⁰ this technique generates prolonged, localized and controlled cooling which is capable of damaging the fatty tissue without damaging the skin and other adjacent tissues.¹⁰ This selective lesion occurs due to the greater susceptibility of the fat cells to cold exposure.^{11,12}

Research on cryolipolysis has been growing and new evidence is available. The latest systematic review showed that reduction of the adipose layer can approach 30% per treated region.^{3,5} There are a few clinical trials showing that the reduction of the fat layer can reach 17.4%–20.4% after 2 months^{13,14} and 21.5%–25.5% after 6 months of treatment.^{7,14} In addition, an epidemiological study showed that two sessions per area were required to obtain some satisfactory result, with the exception of the abdomen that acquired satisfactory results with only 1 session in 21% of the cases.¹⁵

Although the literature reports the efficacy and safety of cryolipolysis^{4,7,14,16–18} this evidence has some methodological issue, such as nonrandomization and no comparator group, which may result in important biases. Also, there is no consensus in the literature regarding the ideal treatment protocol, like parameters of the device, periodicity and number of sessions required per body region.^{3,5} Another contradictory point concerns the population that presents the best therapeutic response, since the studies do not present a specific range of body mass index.^{13,19,20}

These divergences between studies are a factor of imprecision for clinical decision-making and elaboration of the treatment plan. Thus, the objective of the present study was to evaluate the effects of one single session of cryolipolysis on the subcutaneous adipose layer thickness of the lower abdomen, adverse effects, pain and patient satisfaction of

healthy women through a randomized controlled trial with a blinded assessor.

Methods

Study design and ethical aspects

A randomized, controlled trial with outcomes assessor blinding was conducted. The thickness of the subcutaneous adipose layer was considered the primary endpoint. Pain, adverse effects and satisfaction were considered as secondary outcomes. The project was approved by the Ethics Committee of the Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Porto Alegre, RS, Brazil (report number 1.970.012). It was also prospectively registered at Clinical-Trials.gov (NCT03160976 identifier) and written informed consent was obtained from all subjects prior to any procedure.

Settings and participants

All procedures were conducted at the Physical Therapy Laboratory of UFCSPA between May and October 2017. The individual was enrolled by verbal invitation and electronic folders in social media and the recruitment was done in the city of Porto Alegre, mainly among the university's internal community and university students. Inclusion criteria were: women between 18 and 48 years; skinfold in the lower abdomen region ≥ 3 cm; body mass index (BMI) between 18.5 and 27 kg/m²,²¹ low level of physical activity according to the International Physical Activity Questionnaire (IPAQ).²²

Cold intolerance, cryoglobulinemia, cold-induced urticaria, paroxysmal cold hemoglobinuria, Raynaud's disease, current or recent pregnancy, areas of hypoesthesia in the abdomen, cutaneous lesion, skin disease, skin laxity, skin healing problems, sickle cell anemia, chronic infections, cardiovascular or metabolic diseases, use of anti-inflammatory drugs, antidiabetic drugs, immunosuppressants or anticoagulants, umbilical hernia, surgeries in the abdominal region, muscular diastasis and up to 5% weight change throughout the study were considered exclusion criteria. All volunteers were instructed not to change their daily living, eating and physical activity habits

and also were not to be submitted to any other esthetic intervention throughout the study.

Randomization

The randomization was performed using the online software www.random.org. The random sequence of numbers was generated by a researcher external to the study team and concealment of the allocation was assured until the moment of the intervention, stored in opaque envelopes. The volunteers were allocated to the intervention group (IG) or to the control group (CG) by a researcher who did not apply the intervention or evaluated the outcomes. The IG received one application in a single session of cryolipolysis in the lower abdomen within 15 days after the baseline assessment and performed the evaluation protocol. The CG was only evaluated and re-evaluated throughout the follow-up.

Evaluations

All evaluations were performed at baseline, 30, 60 and 90 days after cryolipolysis by the same researcher blinded to the allocation. The volunteers did not perform the assessments in the pre-menstrual or menstrual period. Anthropometric data such as body weight, height and BMI were evaluated during the follow up only for characterization of the sample and for the eligibility criteria, with participants altering their baseline BMI and body weight more than 5% of baseline being excluded from the study.

Evaluations of the adipose layer thickness

Ultrasound equipment (GE Vivid I Ultrasound, General Electric Company, USA) with a high-resolution linear transducer (8L) of 7.5 MHz and depth of 8 cm was used to capture the images of the adipose layer of the lower abdomen. This evaluation was performed with the subject in dorsal decubitus position, with the transducer placed parallel to the longitudinal axis of the body and the points marked for skinfold were used as reference (Fig. 1A). Three images were obtained on each side of the lower abdomen at the end

of the expiration movement. Then the demarcations were transcribed onto an individual map to ensure that follow up images were made at the same points. These 3 images were analyzed with the ImageJ software. To measure the fat layer thickness of each image, five cuts were made from the internal border of the dermis to the superficial aponeurosis of the rectus abdominis muscle²³ (Fig. 1B). These cuts gave a mean value for each image, and these 3 images gave a mean value of the fat layer for each side of the lower abdomen. The average thickness for the entire lower abdomen was then calculated using the following equation: mean value right side + mean value left side divided by 2.

The skinfold measurements were obtained with the volunteers in the orthostatic position at 1 cm below and 3 cm to the right side of the umbilical scar and the plicometer (Cescorf, Mitutoyo, Brazil) was positioned in parallel to the transversal axis of the body.²⁴ Three consecutive measures were performed and the average value was used for each skinfold measurement time.²⁵

Abdominal circumference was measured with a tape measure (RCM, Brazil) positioned parallel to the floor and at two points on the same region of the skinfold and ultrasound images: umbilical scar line (AC1) and 3 cm below (AC2).²⁶

Evaluation of pain, adverse effects and satisfaction

A numerical pain rating scale (NPRS) was used during cryolipolysis session to register the pain level of the GI at the following moments: (M1) first minutes of treatment, (M2) half of treatment, (M3) end of treatment, (M4) during massage.

For the record of the adverse effects, the research team contacted the participants 15 and 30 days after the intervention. The Individual Global Esthetic Improvement Scale (IGAIS) was also used to assess the perception of the results obtained: 0 – no change, 1 – mild improvement, 2 – moderate improvement and 3 – significant improvement with the treatment.⁷

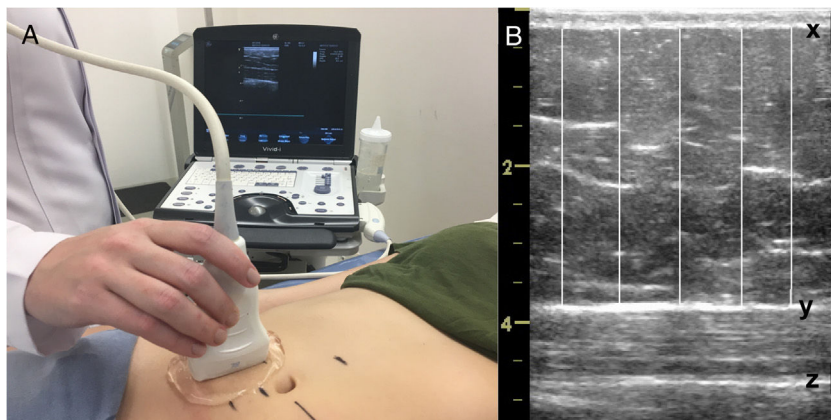


Fig. 1 (A) Ultrasound measurement, (B) image measurement: (x) internal border of the dermis, (y) superficial aponeurosis of the rectus abdominis muscle and (z) inferior aponeurosis of the rectus abdominis muscle.

Intervention protocol

Cryolipolysis was performed with the Crio Top Body Redux equipment (Advice, RO & SU IND E COM, LTDA, Brazil), which is registered with ANVISA under number 80093310027 and pre-calibrated. During the application the room temperature was maintained between 18°C and 25°C and the volunteers were positioned in supine with a 45° elevation of the trunk. The area for placing the antifreeze membrane (Iceprotection. Multigel Industria e Comercio – Brazil. ANVISA 8.03.161-1) and for the application was demarcated based on the individual evaluation map. The cryolipolysis was executed by a single researcher, who was only responsible for the intervention. The treatment protocol used

promoted initial heating of 3 min followed by progressive and continuous cooling. The treatment parameters were adapted from the Kilmer protocol²⁷ and the findings of the review conducted by Derrick et al.³: temperature of –10°C, total time of application of 50 min and moderate vacuum pressure. As soon as the single cooling device was positioned in the target region, suction in the continuous mode was activated and small circular movements were made to better couple the skinfold. At the end of treatment, the membrane was removed and the area was massaged for 5 min with kneading movements to stimulate local blood reperfusion and to normalize the appearance of the skin.⁷ The volunteers were aware that they could stop the procedure at any moment.

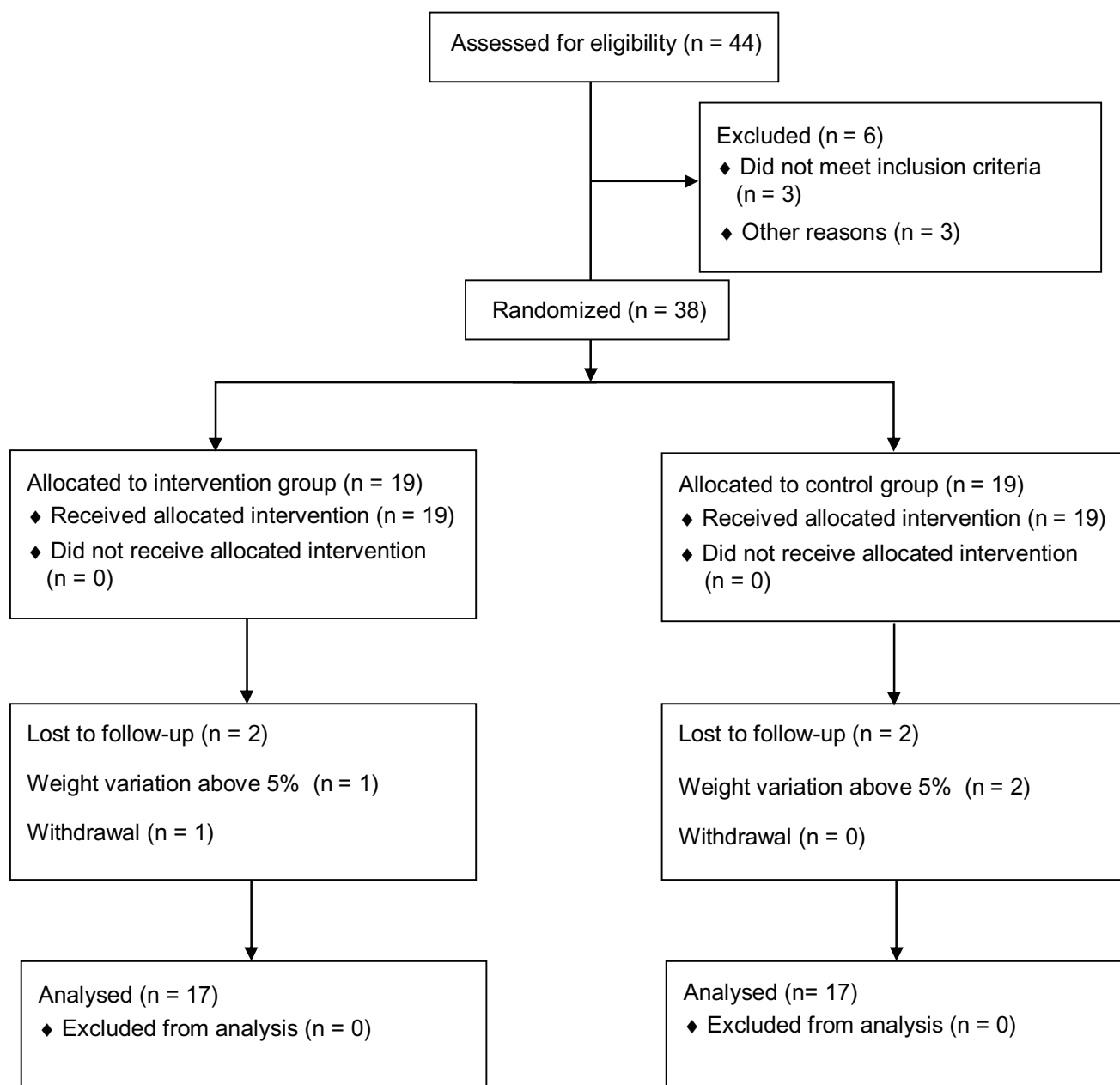


Fig. 2 Flowchart of the study.

Statistical analysis

The sample size was calculated with the GPower software (version 3.1) based on the study of Mahmoud et al.¹³, using skinfold values (IG: 25.14 mm \pm 2.79 and CG: 27.69 mm \pm 2.73) after cryolipolysis intervention. The level of significance was set at 5% and statistical power was set at 80%. Thus, the sample size established was of 14 individuals per group.

The normality of the data was verified with Shapiro–Wilk. Quantitative data were presented through mean, standard deviation and frequencies. The main effects of the cryolipolysis on the studied outcomes were evaluated through Generalized Estimation Equations (GEE) and the post-hoc Bonferroni. An ANCOVA was used to calculate difference between groups and 95% confidence intervals. The analyses were performed by protocol in SPSS 23.0 software (Chicago, USA) and the significance level adopted was 5%.

Results

Forty-four women were evaluated for eligibility criteria, but only 38 were included for randomization and 34 completed the study. Fig. 2 shows the detailed flowchart of participant selection, group allocation and follow up losses. The groups were homogeneous at the beginning of the study as can be seen in Table 1.

No significant differences were demonstrated between the IG and CG at any evaluation time for fat thickness measured by US (30 days: 0.05 cm (95% CI -0.12 , 0.22), 60 days: 0.05 cm (95% CI -0.11 , 0.20) and 90 days: 0.04 cm (95% CI -0.7 , 0.25)), SF (30 days: -0.09 cm (95% CI 0.25 , 0.08), 60 days: -0.14 cm (95% CI -0.36 , 0.09) and 90 days: -0.001 cm (95% CI -0.24 , 0.23)), AC1 (30 days: 0.42 cm (95% CI -1.14 , 1.9), 60 days: -0.1 cm (95% CI -1.74 , 1.54) and 90 days: -0.007 cm (-1.9 , 1.9)) and AC2 (30 days: 0.18 cm (95% CI -0.84 , 1.20), 60 days: -0.13 cm (95% CI: -1.61 , 1.35) and 90 days: -0.31 cm (95% CI: -1.61 , 1.00)). See Table 2.

Table 1 Characteristics of the groups at baseline.

	IG (n = 17)	CG (n = 17)
Age (years)	24.94 \pm 5.04	29.35 \pm 8.77
Weight (kg)	63.05 \pm 6.07	62.14 \pm 6.69
Height (m)	1.62 \pm 0.06	1.63 \pm 0.07
BMI (kg/m ²)	23.93 \pm 1.26	23.43 \pm 1.72
Skinfold (cm)	3.66 \pm 0.46	3.64 \pm 0.50
US (cm)	3.33 \pm 0.40	3.28 \pm 0.59
AC1 (cm)	85.79 \pm 5.94	84.79 \pm 5.81
AC2 (cm)	89.56 \pm 5.10	88.38 \pm 5.03
Use of contraceptive pill % (n)	82.4 (14)	76.5 (13)
Pregnancy history % (n)		
Yes	11.8 (2)	35.3 (6)
No	88.2 (15)	64.7 (11)

Data are expressed in mean \pm SD and frequency. IG, intervention group; CG, control group; n, number of participants; BMI, body mass index; US, ultrasound measurement; AC1, abdominal circumference at umbilical scar; AC2, abdominal circumference 3 cm under the umbilical scar.

The median point on NPRS was 7 (range 3–8) at M1, also 7 (range 5–10) at M4, 3 (range 1–5) at M2 and 2 (range 1–5) at M3. None of the volunteers interrupted the procedure due to pain. The most reported side effects were change in sensitivity, bruises, petechia, edema, pain and itchiness which resolved within the first 30 days after intervention.

The IGAIS, that evaluated the patient's satisfaction, showed that 59% of the participants noticed no change after the protocol, while only 18% and 23% of them reported slight and moderate improvements, respectively. None of the individuals of the IG reported great improvement.

Discussion

We aimed to evaluate the effects of a cryolipolysis protocol on the thickness of the lower abdomen adipose layer of women. No significant changes were noticed between the groups at any follow up time points. The current study is one of the first studies to report an unfavorable result for this localized fat treatment adding to the scientific literature new observations about the application of cryolipolysis on the lower abdomen of healthy women.

Sasaki et al. treated 55 abdomens with a cooling intensity factor (CIF) of 42 (-72.9 mW/cm²) for 60 min followed by massage and found a decrease of 27% (average of 1 cm) of the skinfold between baseline and 6 months after a single application.⁷ With the same treatment protocol, Boey and Wasilenchuk¹⁷ evaluated 9 abdomens with ultrasound and reported a mean reduction of 12.6% \pm 7.2% (0.26 ± 0.19 cm) on the non-massaged side and 21% \pm 8.5% (0.42 ± 2.2 cm) on the massaged side after two months.¹⁷ However, is important to be careful when interpreting these findings due to the absence of a control group.

Even though no favorable results were found for the reduction of the fatty layer, our treatment protocol was based on previous studies that demonstrated the efficacy of cryolipolysis.^{3,27} Moreover, we chose an intervention protocol that resembled the clinical practice, since there is still no consensus in the literature regarding the parameters of the device, periodicity and number of sessions.^{3,5} The CIF values vary between 33 (-64 mW/cm²) and 42 (-72 mW/cm²),³ or go up to -15°C .^{8,9} The minimum application time reported is of 30 min while the maximum time is of 120 min/cycle.³ An in vivo study with subdermal analysis observed that when performing an external exposure to cold with CIF of 42 for 60 min, the adipose tissue can reach temperatures between 7°C and 17°C .⁷ According to Pinto et al.,²⁸ direct exposure of adipose cells (in vitro) at 8°C for 10 or 25 min induces lipid crystallization.²⁸ We applied the cryolipolysis for 50 min and used -10°C external exposure temperature, equivalent to a CIF of 42,²⁹ which fits the parameters noted above.

The adverse effects found are in agreement with those already reported in the literature: erythema, pruritus, edema, altered sensitivity and pain.⁵ The pain was more intense in the first minutes of intervention, but tolerable, considering that no volunteer asked to interrupt the procedure. These findings are similar to the ones reported by Dierickx et al.,³⁰ who reported that 96% of the subjects reported minimal discomfort during the procedure and only

Table 2 Behavior of fat thickness variables during follow up.

	Baseline	30 days	60 days	90 days
<i>Ultrasound (cm)</i>				
IG	3.32 ± 0.39	3.26 ± 0.41	3.29 ± 0.43	3.33 ± 0.44
CG	3.28 ± 0.57	3.16 ± 0.63	3.2 ± 0.62	3.23 ± 0.67
Between-group differences (95% CI)		0.05 (−0.12, 0.22)	0.05 (−0.11, 0.20)	0.04 (−0.7, 0.25)
<i>Skinfold (cm)</i>				
IG	3.66 ± 0.45	3.72 ± 0.47	3.61 ± 0.51	3.55 ± 0.51
CG	3.64 ± 0.49	3.77 ± 0.57	3.71 ± 0.64	3.55 ± 0.61
Between-group differences (95% CI)		−0.09 (0.25, 0.08)	−0.14 (−0.36, 0.09)	−0.001 (−0.24, 0.23)
<i>AC1 (cm)</i>				
IG	85.79 ± 5.76	85.35 ± 6.24	84.44 ± 6.05	84.23 ± 6.28
CG	84.79 ± 5.63	83.91 ± 6.11	83.56 ± 6.00	83.36 ± 6.36
Between-group differences (95% CI)		0.42 (−1.14, 1.9)	−0.1 (−1.74, 1.54)	−0.007 (−1.9, 1.9)
<i>AC2 (cm)</i>				
IG	89.56 ± 4.95	89.06 ± 5.40	88.52 ± 5.65	88.5 ± 5.83
CG	88.38 ± 4.88	87.56 ± 5.93	87.38 ± 5.75	87.31 ± 6.73
Between-group differences (95% CI)		0.18 (−0.84, 1.20)	−0.13 (−1.61, 1.35)	−0.31 (−1.61, 1.00)

Data are mean ± SD. IG, intervention group; CG, control group; AC1, abdominal circumference at umbilical scar; AC2, abdominal circumference 3 cm under the umbilical scar.

4% reported severe pain, which also occurred within the first few minutes of treatment and also did not cause discontinuation of treatment.³⁰

The observation of any changes in the fat thickness of the IG at any assessment time reflected on the results of the IGAS. While 59% of the subjects in our intervention group did not notice any change after treatment, the individual in the study by Sasaki et al.⁷ showed a significant improvement of the fat thickness and reported a moderate change in body remodeling after cryolipolysis.⁷

Among the limitations of this study we can mention the absence of a food diary referring to the nutritional habits of volunteers and a better control of the level of physical activity, two topics that would have helped us to better characterize and analyze the sample during the follow up. Although it is difficult to blind the volunteers due to the characteristics of the treatment, maybe a placebo application could have been used so that the bias of the absence of treatment could be minimized. The absence of biochemical analyzes can also be considered a limitation of the study, since these could help in the understanding of our findings.

Despite the limitations, this is the first randomized clinical trial with blinded assessor of the outcomes that evaluated the effect of a single application/session cryolipolysis on the thickness of the adipose layer in healthy women compared to a control group. The design is one of the strengths of this study, since randomized controlled trials are the gold standard to analyze the efficacy of an intervention.³¹ Our study also stands out for including only one gender, one specific range of BMI and for respecting the physiological menstruation period.

Finally, the results of this study should be considered to help clinical decision regarding the use of this therapy in healthy Brazilian women between 18 and 48 years old, with low level of physical activity and BMI

between 18.5 and 27 kg/m², since the literature lacks evidence with high methodological rigor. In addition, there are some studies that have already demonstrated the benefits of cryolipolysis after more than one session,^{32,33} even associated with diet¹³ or with other therapeutic resources such as shock waves.³⁴ However, besides the study design these studies have different populations,¹³ parameters and periodicity^{13,32–34} and outcomes.³⁴ Despite this, the studies mentioned above should be taken into account and new research is encouraged, with methodological rigor, whether cryolipolysis associated with other resources or diet or with more than one session is able to reduce the infra-abdominal fat layer of healthy women.

Conclusion

A single session of the cryolipolysis with the protocol used was not effective for reducing infra-abdominal adipose layer thickness after 30, 60 and 90 days of its application. Also, the majority of the healthy women were not satisfied since the treatment did not show an improvement in fat thickness. Cryolipolysis caused pain and some adverse effects, such as change in sensitivity, bruises, petechia, edema, and itchiness, that were quickly resolved.

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Conflicts of interest

The authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.bjpt.2019.07.005](https://doi.org/10.1016/j.bjpt.2019.07.005).

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